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Original Contribution

Derivation of a clinical guideline for the assessment of nonspecific abdominal pain: the Guideline for Abdominal Pain in the ED Setting (GAPEDS) Phase 1 Study

Robert T. Gerhardt MD, MPH, FACEP, Brian K. Nelson MD, MS, Sean Keenan MD, Leah Kernan RN, MSN, Andrew MacKersie MD, Michael S. Lane MD

Department of Emergency Medicine, Brooke Army Medical Center/San Antonio Uniformed Services Health Education Consortium, Fort Sam Houston, TX 78234, USA

Department of Radiology, Brooke Army Medical Center/San Antonio Uniformed Services Health Education Consortium, Fort Sam Houston, TX 78234, USA

Department of Emergency Medicine, Texas Tech University Health Sciences Center, El Paso, TX 79905, USA

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Abstract

Objective: The purpose of this study was to identify a clinical guideline for the evaluation of nonspecific abdominal pain (NSAP) using history, physical examination, laboratory analysis, acute abdominal series (AAS) radiographs, and nonenhanced helical computed tomography (NHCT) clinical predictor variables (CPVs).

Setting: The setting of this study was at an urban emergency department (ED) with 70,000 yearly visits.

Methods: This is an institutional review board–approved, prospective, observational study. The primary outcome variable was urgent intervention (UI), defined as a diagnosis requiring surgical or medical treatment to prevent death or major morbidity. Subjects underwent prompted history, physical, laboratory studies, AAS, and NHCT and were followed up to 6 months for ultimate diagnosis and outcome. CPVs were subjected to classification and regression tree analysis.

Results: One hundred sixty-five subjects were analyzed. Thirteen percent of subjects required UI within 24 hours of presentation; an additional 34% underwent elective interventions that mitigated morbidity or mortality. Four guideline models were generated. Model 1 consisted of history and physical, with a sensitivity of 25%, a specificity of 92%, a positive likelihood ratio of 3.17, and a negative likelihood ratio of 0.81. Model 2 consisted of model 1 with laboratory, with a sensitivity of 39%, a specificity of 88%, a positive likelihood ratio of 3.25, and a negative likelihood ratio of 0.69. Model 3 consisted of model 2 with AAS, with a sensitivity of 56%, a specificity of 81%, a positive likelihood ratio of 2.94, and a negative likelihood ratio of 0.54. Model 4 comprised all inputs, including NHCT, with a...
sensitivity of 92%, a specificity of 90%, a positive likelihood ratio of 9.2, and a negative likelihood ratio of 0.089. NHCT was the single most accurate CPV for UI.

**Conclusions:** No clinical guideline was identified exclusive of NHCT that possessed adequate sensitivity for exclusion of UI. NHCT is a rational choice for decision support in the evaluation of NSAP and is likely the single most useful diagnostic adjunct available to augment the clinical evaluation.

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1. **Introduction**

Abdominal pain is a common cause of presentation to emergency department (EDs) and other short-term care facilities [1]. The presentation of acute abdomen or surgical abdomen generally presents little diagnostic difficulty. Nonspecific abdominal pain (NSAP), however, without signs of perforation, infarct, or hemodynamic instability, presents a greater diagnostic and therapeutic challenge. Perhaps, 40% or more of such patients will be discharged without a formal diagnosis, up to 35% will be admitted, and as many as 56% will be misdiagnosed [2-4]. The significant risk for increased morbidity and associated health-care costs resulting from delayed diagnosis or misdiagnosis in what presents initially as NSAP warrants a renewed search for a rational and more accurate approach to its evaluation. Although attempts have been made toward developing consensus guidelines and diagnostic algorithms, no prospective evidence-based clinical guideline for the exclusion of NSAP requiring urgent intervention (UI) has been developed or validated to date [4-6].

Although standing as the bedrock of medical practice, the physical examination often is both insensitive and nonspecific in the diagnosis of NSAP, particularly in elderly populations [7]. Likewise, diagnostic adjuncts such as laboratory studies and plain abdominal radiographs have played fundamental yet controversial roles in the assessment of NSAP. When combined with a plain chest radiograph, the upright and supine plain abdominal radiographs compose the acute abdominal series (AAS) in many institutions. This series is ordered frequently for the evaluation of abdominal pain; however, its low sensitivity and specificity limit utility [8,9]. Recently, nonenhanced helical computed tomography (NHCT) of the abdomen and pelvis has been proposed as a particularly useful adjunct in the initial assessment of both patients with appendicitis and patients with NSAP; however, issues of cost, overdiagnosis, and availability of qualified interpreters remain to be addressed [10]. Despite these questions, a common ED practice pattern of obtaining enhanced or nonenhanced computed tomographic (CT) imaging in patients presenting with NSAP appears to be emerging.

1.1. **Objective**

The purpose of this study was to determine whether it was possible to derive a sensitive, facile, and reproducible clinical guideline for the evaluation of NSAP using history, physical examination, commonly available laboratory studies, AAS, and NHCT as potential inputs.

2. **Materials and methods**

This study was approved by the Human Subjects Committee of the Institutional Review Board of Brooke Army Medical Center/San Antonio Uniformed Services Health Education Consortium and by the Clinical Investigation Regulatory Organization of the US Army Medical Command.

2.1. **Theoretical model**

This study centered on ED patients presenting with NSAP and the determination of whether they would ultimately require UI.

For the purposes of this study, we defined NSAP as encompassing abdominal or pelvic pain of 7 days’ duration or less, not accompanied by signs of peritonitis, hemodynamic instability, or other obvious clinical presentation requiring UI, and which did not consist primarily of a urogenital complaint. UI served as our primary outcome variable of interest and was defined to encompass the need for surgical, endoscopic, or other nonoperative therapeutic treatment of an intra-abdominal or pelvic condition, which if left untreated would result in death or severe morbidity.

We developed a series of specific diagnoses that were considered to meet the definition of UI with the assistance

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Diagnoses constituting criteria for UI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal aortic aneurysm</td>
<td>Liver abscess</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Mesenteric ischemia/ ischemic colitis</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Neoplasm, newly diagnosed</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>Ovarian cyst, ruptured with hemorrhage</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>Pancreatitis, with or without cholelithiasis</td>
</tr>
<tr>
<td>Cholelithiasis, with or without ascending cholangitis</td>
<td>Perforated viscus</td>
</tr>
<tr>
<td>Diverticulitis, with or without perforation</td>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>Renal arterial or venous thrombosis</td>
</tr>
<tr>
<td>Hepatitis, acute fulminant</td>
<td>Sigmoid volvulus</td>
</tr>
<tr>
<td>Ileus</td>
<td>Spontaneous bacterial peritonitis</td>
</tr>
<tr>
<td>Tubo-ovarian abscess</td>
<td></td>
</tr>
</tbody>
</table>

Tubo-ovarian abscess
of a consensus panel of 4 board-certified emergency physicians and 1 board-certified general surgeon who were not otherwise associated with the study. UI diagnoses are displayed in Table 1. Admission solely for observation with subsequent discharge was not coded as a UI episode. The criterion standard for a subject requiring UI (UI+) consisted of a postoperative or clinical diagnosis meeting the criteria in Table 1. The criterion standard for a subject not requiring UI (UI−) consisted of a lack of any UI diagnosis appearing in respective subjects’ medical records at the conclusion of a 6-month follow-up period after initial ED discharge.

2.2. Study design

The design was a prospective, observational, nonconsecutive format, which reflected the existing resources available at our facility.

2.3. Setting and population

We used a convenient sample of patients presenting to the ED of an urban teaching hospital and level 1 trauma center with an annual census in excess of 70,000. Subjects were enrolled by both resident and faculty attending emergency physicians on a 24-hour daily basis. Criteria for inclusion were male and female patients who were military health-care beneficiaries older than 18 years and who presented for initial evaluation of nontraumatic abdominal pain with duration from onset of less than 7 days. Subjects were excluded from the study if acute abdomen was suspected based upon the combined presence of pain, diffuse tenderness, abdominal rigidity, and rebound tenderness; if they manifested signs of shock; if they deteriorated during the ED course; if pregnant; for the primary presenting complaint of vaginal or penile bleeding or discharge; for the primary complaint of dysuria or hematuria; if the data set was incomplete; if they declined to participate; or if they withdrew voluntarily before the completion of the study.

2.4. Measurements

To facilitate both a uniform clinical evaluation and prospective data retrieval, we used a standardized data collection instrument developed specifically for this study. Upon enrollment, each subject received standard emergency treatment as needed. During each ED encounter in which a subject was enrolled, prompted history and physical examination were performed by the enrolling physician. A standard battery of laboratory studies was obtained, which included complete blood count; serum electrolytes, urea nitrogen, creatinine, glucose, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total and direct bilirubin, amylase, and lipase; venous blood gas; urinalysis; and qualitative β human chorionic gonadotropin for premenopausal women. AAS and NHCT were also obtained for each subject. The AAS included upright chest radiograph and upright and supine abdominal radiographs. The NHCT was performed on either a 4-detector helical CT scanner using 5-mm collimation (pitch, 0.875; 120 kV peak; 300 mA · s; Marconi MX8000, Cleveland, Ohio) or on a single-detector helical CT (pitch, 1.6; 120 kV peak; 240 mA · s) (Picker PQ 6000, Transamerican Medical Imaging, Lindon, UT) using 5-mm collimation. Axial images were obtained from the lung bases to the pubic symphysis without intravenous, oral, or rectal contrast. If clinically warranted, additional studies and interventions were performed at the discretion of the attending emergency physician or consultant.

After completion of the clinical evaluation and diagnostic studies, the enrolling emergency physician consulted other specialists and arranged disposition for each subject as considered clinically appropriate. Admitted subjects were
followed through the course of their hospitalization via their electronic inpatient medical records. Subjects who were discharged from the ED were followed for a period of up to 6 months or until a definitive diagnosis for their NSAP was obtained. Postdischarge follow-up was performed by a combination of telephone communication and review of outpatient and subsequent inpatient (when applicable) computerized clinical information databases (clinic appointments, subsequent inpatient records, laboratory and radiology study results, and pathology reports), and survival data, as determined via continued enrollment in the Defense Enrollment Eligibility Reporting System. Using the combination of ED clinical data, admission records, follow-up data, and our consensus definition of UI, we coded each subject retrospectively as a UI+ or a UI−.

Official interpretations by attending radiologists at our institution were used for AAS and NHCT diagnoses. We used these radiological diagnoses to code the AAS and NHCT readings for each subject. If an AAS or NHCT radiological diagnosis met one of the study criteria for UI (see Table 1), then the respective AAS or NHCT was coded as “test-positive.” If the respective radiological diagnosis did not meet UI criteria, then it was coded as “test-negative.”

2.5. Data analysis

Clinical predictor variables (CPVs) were abstracted from the clinical data collection form, laboratory and radiology reports, and pathology inpatient and outpatient records. A listing of the CPVs that we extracted and analyzed is depicted in Table 2. Decision modeling was accomplished using classification and regression tree (CART) modeling, specifying UI as the target variable. The modeling technique chosen was quick, unbiased, and efficient statistical tree (AnswerTree 3.0; SPSS Inc, Chicago, IL). Four models were generated. Model 1 used history and physical CPVs only. Model 2 used history, physical, and laboratory CPVs. Model

<table>
<thead>
<tr>
<th>Table 3</th>
<th>GAPEDS phase 1: subject demographics and selected clinical data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UI+ (n = 57)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>56 (52-61)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>44</td>
</tr>
<tr>
<td>Maximum temperature (°F)</td>
<td>99.4 (99.1-99.7)</td>
</tr>
<tr>
<td>Patient reported (%)</td>
<td>Nausea 80</td>
</tr>
<tr>
<td>Vomiting</td>
<td>43</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>15</td>
</tr>
<tr>
<td>Anorexia</td>
<td>67</td>
</tr>
<tr>
<td>Flatus</td>
<td>72</td>
</tr>
<tr>
<td>Diffuse pain</td>
<td>54</td>
</tr>
<tr>
<td>Rebound</td>
<td>18</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td>12.3 (10.9-13.7)</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>107 (87-127)</td>
</tr>
<tr>
<td>Venous base excess</td>
<td>0.7 (0-0.14)</td>
</tr>
<tr>
<td>Serum glucose</td>
<td>125 (112-138)</td>
</tr>
<tr>
<td>AAS predicted UI (%)</td>
<td>37</td>
</tr>
<tr>
<td>CT predicted UI (%)</td>
<td>94</td>
</tr>
<tr>
<td>Admitted (%)</td>
<td>95</td>
</tr>
</tbody>
</table>

95% confidence intervals are depicted in parentheses, where appropriate.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Subject diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>n</td>
</tr>
<tr>
<td>Admitted</td>
<td>21</td>
</tr>
<tr>
<td>Appendicitisa</td>
<td>14</td>
</tr>
<tr>
<td>Partial colectomy (bowel obstruction)</td>
<td>3</td>
</tr>
<tr>
<td>Incarcerated hernia</td>
<td>2</td>
</tr>
<tr>
<td>Partial colectomy (diverticulitis)</td>
<td>1</td>
</tr>
<tr>
<td>Tubo-ovarian abscess</td>
<td>1</td>
</tr>
<tr>
<td>Nonoperative</td>
<td>46</td>
</tr>
<tr>
<td>NSAP</td>
<td>11</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>8</td>
</tr>
<tr>
<td>Newly diagnosed neoplasm</td>
<td>6</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>4</td>
</tr>
<tr>
<td>Pancreatitis with cholelithiasis (ERCP)</td>
<td>3</td>
</tr>
<tr>
<td>Ileus</td>
<td>2</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2</td>
</tr>
<tr>
<td>Biliary dyskinesia</td>
<td>1</td>
</tr>
<tr>
<td>Colitis</td>
<td>1</td>
</tr>
<tr>
<td>Crohn disease with pancreatitis</td>
<td>1</td>
</tr>
<tr>
<td>Diverticulosis, symptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Pyleonephritis</td>
<td>1</td>
</tr>
<tr>
<td>Hiatal hernia, symptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Rectus sheath hematoma (percutaneous drainage)</td>
<td>1</td>
</tr>
<tr>
<td>Ovarian cyst, ruptured</td>
<td>1</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>1</td>
</tr>
<tr>
<td>Urolithiasis, symptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
</tr>
</tbody>
</table>

Discharged from ED

| Diagnosis | n |
| NSAP | 49 |
| Urolithiasis | 12 |
| Biliary tract dysfunctionb | 8 |
| Diverticulitis | 6 |
| Neoplasm as etiology for pain | 6 |
| Newly diagnosed | 5 |
| Known disease | 5 |
| Ovarian cyst, symptomatic | 6 |
| Diverticulosis, symptomatic | 3 |
| Anatomic ureter obstruction | 1 |
| Constipation vs mild ileus | 1 |
| Epiploic appendagitis | 1 |
| Ileus, mild | 1 |
| Inguinal hernia | 1 |
| Pancreatitis, chronic | 1 |
| Pyleonephritis | 1 |
| Ulcerative colitis | 1 |
| Total | 98 |

ERCP indicates endoscopic retrograde cholangiopancreatography.

a Thirteen with confirmed acute appendicitis and one chronic with periappendiceal diverticulitis.

b Symptomatic cholelithiasis or biliary dyskinesia.

c Discharged to same-day surgery clinic.
3 used history, physical, laboratory, and the AAS CPVs. Model 4 used all of the CPVs, including NHCT. The performance of each model was estimated by calculating sensitivity, specificity, likelihood ratios, and the percentage of cases misclassified.

CART modeling, a form of binary recursive partition analysis, attempts to identify characteristics that may be generalized within the data set. At times, however, the algorithm chooses variables and cut points based on characteristics unique to the data set. Such a model is said to be “overspecified.” An analogy in clinical decision-making would be the clinician using a small unrepresentative experience to make a decision. We attempted to protect against overspecification by performing a cross-validation procedure using 10 sub-

Fig. 1  CART models. A, Model 1: history and physical examination CPVs. B, Model 2: history, physical examination, and laboratory CPVs. C, Model 3: CPVs including history, physical examination, laboratory studies, and AAS. D, Model 4: all CPVs including NHCT. After subjecting all CPVs to CART analysis, the only variable selected was “NHCT results predicts/does not predict UI.”
groups of the data and generating an estimate of the mean percentage of cases misclassified, and by setting penalties for false-positives and false-negatives in proportion to the ratio of UI+’s to UI−’s to equalize the cost of either type of error.

Our desired subject sample size for this initial study was based upon the recommendation of Stiell and Wells [11] for a minimum of 10 positive cases for each potential CPV subjected to binary recursive partitioning analysis. Given prior reports of admission rates for NSAP approximating 40%, using admission as a surrogate for positive diagnosis, and presuming that a facile clinical guideline would possess 7 or less decision points, we arrived at a target sample size of 175 subjects for this initial study.

3. Results

This study was conducted between April 24, 2001, and December 31, 2002. During this period, a total of 2520 patients presented to our ED with complaints that included some form of abdominal pain. From the available hospital census database, we were unable to determine the exact proportion of these patients who would have strictly met our criteria for NSAP, but based upon a historical report [3], we estimated that roughly 1008 (40%) of these would be consistent with NSAP. During the 118 days in which we actually enrolled subjects, we estimate that a total of 195 were potentially available. Of this estimated potential pool, we enrolled a total of 184 subjects (94% of available total). Of these, 19 were excluded: 6 had incomplete clinical data; 4 had no NHCT (3 had no CT, 1 underwent contrast-enhanced helical CT [EHCT]); 3 voluntarily withdrew; 2 had incomplete consent forms; 1 was withdrawn by the enrolling attending physician because of an ED diagnosis of non-ST-segment myocardial infarction; 1 was excluded because of pain with a duration of more than 7 days; 1 was younger than 18 years; and 1 subject presented with isolated vaginal bleeding. No subjects deteriorated during the course of their respective ED evaluations. After exclusion criteria were applied, 165 subjects (89.7%) remained for analysis.

Pertinent subject demographic and clinical data from the study population are displayed in Table 3.

A total of 67 subjects (41%) were admitted from the ED. Twenty-one underwent operative interventions within the first 24 hours of admission; 46 were admitted and received nonoperative invasive procedures or medical management or were observed and released. Their respective diagnoses are displayed in Table 4.

A total of 98 subjects (59%) were discharged directly from the ED: 49 with a final diagnosis of NSAP and the remainder with specific diagnoses not requiring admission. Their respective diagnoses are also displayed in Table 4. One subject who was diagnosed with incarcerated inguinal hernia was discharged to our same-day surgery clinic at the request of the surgical consultant; operative repair was performed later that day. One other subject with an ED discharge diagnosis of symptomatic diverticulosis returned to the ED 5 months later with abdominal pain and jaundice, which was diagnosed at that time via EHCT as a pancreatic mass. Subsequently, a biopsy confirmed pancreatic cancer. During the follow-up period, none of the remaining patients returned to the ED or other clinics within our system for treatment of conditions comprising UI diagnoses.

Diagrams of the clinical prediction guideline models generated by CART analysis are depicted in Fig. 1. Measures of the diagnostic accuracy of the 4 models are depicted in Table 5. CART modeling found a single predictor for UI in model 1: temperature of more than 99.9°F (Fig. 1A). In model 2, temperature was retained (although it increased to 100.2°F) by the program and lipase of more than 300 was added (Fig. 1B). In model 3, the previous predictors were retained (although temperature cutoff returned to 99.9°F and lipase cutoff was reduced to 222) and AAS prediction of need for UI was added (Fig. 1C). In model 4, only the NHCT prediction of need for UI was retained (Fig 1D). All 4 models had similar specificity but not sensitivity. Risk (error rate) varied with model 4 being significantly better than models 1, 2, or 3 in both clinical and statistical sense.

### Table 5  GAPEDS phase 1: accuracy of CART models for prediction of NSAP requiring UI

<table>
<thead>
<tr>
<th>Model</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR−</th>
<th>Risk (95% CI)</th>
<th>Cross-validated risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: History and physical</td>
<td>0.25</td>
<td>0.92</td>
<td>0.65</td>
<td>0.69</td>
<td>3.17</td>
<td>0.81</td>
<td>0.32 (0.25-0.39)</td>
<td>0.32 (0.25-0.39)</td>
</tr>
<tr>
<td>2: History, physical, and laboratory analysis</td>
<td>0.39</td>
<td>0.88</td>
<td>0.64</td>
<td>0.72</td>
<td>3.25</td>
<td>0.69</td>
<td>0.30 (0.23-0.37)</td>
<td>0.35 (0.28-0.42)</td>
</tr>
<tr>
<td>3: history, physical, laboratory analysis, and AAS</td>
<td>0.56</td>
<td>0.81</td>
<td>0.62</td>
<td>0.77</td>
<td>2.94</td>
<td>0.54</td>
<td>0.28 (0.21-0.35)</td>
<td>0.36 (0.29-0.43)</td>
</tr>
<tr>
<td>4: history, physical, laboratory analysis, AAS, and NHCT</td>
<td>0.92</td>
<td>0.90</td>
<td>0.83</td>
<td>0.95</td>
<td>9.2</td>
<td>0.09</td>
<td>0.10 (0.06-0.14)</td>
<td>0.10 (0.06-0.14)</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR−, negative likelihood ratio; CI, confidence interval.
Of the 165 subjects in the study population, 14 (8.4%) received an EHCT scan subsequent to the initial NHCT. Of these, EHCT altered the diagnosis in only 1 instance: an 80-year-old man with diffuse abdominal pain who was admitted for observation. After failing to improve after several hours, an EHCT was obtained, which demonstrated celiac and superior mesenteric arterial plaques and mild bowel edema, consistent with mesenteric ischemia.

Despite a relatively small sample size, we have demonstrated that 13% of subjects presenting initially with NSAP in this study required and underwent surgical intervention for UI within 24 hours of ED arrival. An additional 34% subsequently underwent an elective surgical procedure, other invasive procedure, or medical treatment resulting from diagnosis made during the ED encounter, which may have mitigated subsequent morbidity as a result of early intervention. Although it is possible that clinical judgment alone or combined with ED observation might have provided an appropriate outcome, these subjects received diagnoses facilitated primarily by NHCT, followed by definitive care or discharge without complication. Given the character of our study design, it is unknown what percentage of these patients might have had preventable morbidity or mortality had NHCT not been obtained as a part of their ED evaluation; however, our sample’s admission and NSAP diagnosis rates approximate larger historical reports in the ED setting [2,3].

What may differ from the common experience is that none of our subjects diagnosed with NSAP and released from the ED returned for UI. We suggest that this salutary finding relates to both earlier diagnosis of emerging pathology in patients who would otherwise eventually require UI and the ability to definitively exclude UI from those patients for whom no specific diagnosis could be reached. Both scenarios were facilitated by NHCT.

In this study, NHCT was the single best predictor of need for UI, and inversely, of no need for UI. We caution, however, against the sole reliance upon NHCT for diagnosis, particularly for patients in whom the history and physical examination are clearly indicative of a pathological process requiring UI. Such patients would benefit first from urgent specialty consultation, followed by directed imaging studies if requested by the consultant. For patients with benign presentations, corroborating historical information, and physical signs and symptoms that resolve with ED intervention, disposition without NHCT may be appropriate. For those patients with equivocal findings, NHCT will likely make its greatest contribution by benefit first from urgent specialty consultation, followed by definitive care if requested by the consultant. We propose that this potential use of NHCT might signal a paradigm shift in the initial evaluation of NSAP from one driven by myriad specific diagnoses to a model designed simply to exclude the need for UI.

NHCT is widely available, quickly performed, and possesses none of the risks associated with contrast material. Although EHCT can be very helpful for evaluating multiple intra-abdominal diseases such as bowel ischemia, pancreatitis, and aneurysms, recent studies suggest that NHCT may be an acceptable imaging option in the clinical evaluation of acute appendicitis, diverticulitis, and urolithiasis [13-16]. NHCT also outperforms AAS for the diagnosis or exclusion of hemoperitoneum and possesses utility in the diagnosis of pancreatitis, pyelonephritis, cholelithiasis, and diverticulitis via the ability to observe perivisceral fat stranding as an
indicator of inflammation [17,18]. The estimated radiation dosage by NHCT in this study was 1.2 to 1.7 rem [19]. We estimate the effective whole-body radiation dosage of AAS in this study to be 0.244 rem [20]. A 1995 report by the Health Physics Society recommended that assessments of radiogenic health risks be limited to dosage estimates approaching and more than 10 rem [21]. Because it provides greater applicable information than AAS with only a moderately elevated radiation risk, we suggest that NHCT may be the more appropriate initial imaging modality for the evaluation of NSAP in nongravid adults.

5. Limitations

This study possesses several limitations. Being a nonconsecutive study conducted at a single center, it is subject to potential selection and observer bias. Data collection was performed by various attending and resident emergency physicians using a standardized form. Although instruction was provided regarding the use of the form and definitions applying to CPVs, no assessments were performed to determine interrater reliability or to qualify the data collection methods beyond standard attending observation. Thus, it is plausible that interobserver bias may have contributed to the poor performance of CPVs alone as a diagnostic tool.

Our design excluded children, pregnant women, and those presenting with primary urogenital complaints, limiting its broad applicability.

We did not specifically assess a priori clinical judgment regarding UI before obtaining laboratory and imaging studies; thus, we were unable to quantify the impact on diagnostic accuracy of adding these studies to the bedside clinical data. As part of the study design, we made the conscious decision not to query clinicians a priori with regard to whether the subject required UI. This decision was made in part because we sought to exclude subjects possessing high clinical indices of suspicion for UI (because they did not meet our definition of NSAP). Secondly, we intended to streamline the data collection process as much as possible. In retrospect, our decision not to assess a priori clinical judgment was erroneous.

Although consensus-based, our definition of UI has not been formally established or validated. In addition, we chose to use the official radiologists’ interpretations from the medical record as the criterion standard for whether NHCT predicted UI, rather than applying the interpretation of a single reviewer or panel of experts. It is unknown to what extent these conditions may have influenced the accuracy of our calculations of diagnostic accuracy.

The determination of sample size in CART-based studies remains controversial. Our method of sample size calculation was admittedly underpowered, although it met appropriate standards by some published interpretations and our findings are consistent with the emerging clinical practice of obtaining NHCT in the evaluation of NSAP. A more precise method, although logistically infeasible in the setting contemporary to the conduct of this study, would have been to incorporate the number of diagnoses requiring UI (22 in all). Had this method been used, we would have sought the inclusion of roughly 550 or more subjects rather than the 165 subjects we analyzed. Thus, it is possible that our relatively small sample size failed to detect other combinations of CPVs that might have led to a guideline exclusive of some laboratory or imaging studies. Despite this, we observed a trend toward only modest improvement in sensitivity at the cost of specificity as the clinical guideline models increased in sophistication. This observation leads us to conclude that despite our small sample size, we believe it is unlikely that a satisfactory clinical guideline will emerge exclusive of NHCT or some more sophisticated method of imaging, such as magnetic resonance imaging. Although the existing logistic and fiscal support of this study limited our ability to enroll subjects and collect data, we anticipate that subsequent and better-supported prospective studies, including a priori clinical judgment, may validate our current models and aid in developing a guideline for when to apply NHCT as a diagnostic tool in patients with NSAP.

6. Conclusions

Despite their initial presentation of NSAP, approximately 13% of our subject sample required UI within 24 hours of ED presentation, and an additional 34% of subjects underwent elective interventions that likely mitigated morbidity and mortality, approximating proportions reported in larger retrospective studies [2,3]. In this sample, NHCT was the single most accurate CPV for UI. All clinical guideline models showed similar specificities, but sensitivities for the models without NHCT were unacceptable. NHCT provided more diagnostic information than all other CPVs combined. We conclude that during the ED evaluation of abdominal pain without a clear clinical diagnosis but where vascular etiologies are unlikely, NHCT is the rational choice for initial radiologic imaging and should be seriously considered before ED discharge.

Acknowledgments

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professionals for their assistance and dedication to excellent patient care.

References

Original Contribution

Low plasma vasopressin/norepinephrine ratio predicts septic shock

I-Yin Lin MD\textsuperscript{a}, Hon-Ping Ma MD\textsuperscript{a}, Aming Chor-Ming Lin MD\textsuperscript{a}, Chee-Fah Chong MD\textsuperscript{a}, Chiu-Mei Lin MD\textsuperscript{a}, Tzong-Luen Wang MD, PhD\textsuperscript{a,b,*}

\textsuperscript{a}Department of Emergency Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei 111, Taiwan

\textsuperscript{b}Department of Surgery, Medical College, Taipei Medical University, Taipei 110, Taiwan

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Abstract To evaluate if low plasma vasopressin and high norepinephrine concentrations predict grave prognosis of sepsis, a prospective sample of consecutive patients visiting the emergency department of a university teaching hospital who met the American College of Chest Physicians criteria of sepsis or severe sepsis was enrolled. Besides septic workup, we measured serum vasopressin and norepinephrine concentrations to correlate the impending outcome. One hundred eighty-two patients aged 27 to 99 years met the inclusive criteria and were classified as those with septic shock (n = 72), severe sepsis (n = 56), and those with sepsis only (n = 54) according to the outcome within 6 hours. Thirty healthy subjects were included as control. The plasma vasopressin level at baseline was significantly lower for those who finally developed septic shock (septic shock group, 3.6 ± 2.5 pg/mL; 95% confidence interval [CI], 3.0-4.2 pg/mL; severe sepsis group, 21.8 ± 4.1 pg/mL, 95% CI, 20.7-22.9 pg/mL; sepsis group, 10.6 ± 6.5 pg/mL, 95% CI, 8.8-12.4 pg/mL, \(P < .001\)), whereas the norepinephrine level was highest for the same group (septic shock group, 3650 ± 980 pg/mL, 95% CI, 3420-3880 pg/mL; severe sepsis group, 3600 ± 1000 pg/mL, 95% CI, 3330-3870 pg/mL; sepsis group, 1720 ± 320 pg/mL, 95% CI, 1630-1810 pg/mL). The vasopressin/norepinephrine ratio was significantly lower for the patients with final diagnosis of septic shock (\(P < .001\)). The mean interval between the time of samples drawn and the time of the most severe occurring sequelae was 2.4 ± 0.8 hours. Receiver operating characteristic analysis revealed that the vasopressin/norepinephrine ratio \(1 \times 10^{-3}\) had a sensitivity of 97% (95% CI, 90%-99%) and a specificity of 85% (95% CI, 78%-91%) for detecting impending septic shock. Low serum vasopressin/norepinephrine ratio can predict impending septic shock.

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1. Introduction

Sepsis is a systemic response to an infection with complicated pathogenesis. The incidence of sepsis is increasing because of the increasing use of invasive procedures. The greatest challenges for an emergency
physician are not only prompt and correct diagnosis, but also early detection of septic complications. The mortality remains quite high for septic shock [1] despite the advances in innovations of antibiotics and supportive managements. Early and effective treatment is, therefore, critical for improving the patient’s outcome. However, the clinical manifestations or laboratory findings that can reliably predict the impending complications of sepsis are still lacking.

Current treatment of septic shock includes early administration of antibiotics, adequate fluid resuscitation, vasopressor, and some empiric therapy such as activated protein C. Since the effects of dopamine on clinical outcome has been questioned [2], norepinephrine has been suggested as the first choice of vasoactive agent in septic shock because of the lower hospital mortality and reliable blood pressure control [3,4]. However, septic shock is usually a catecholamine-resistant vasodilatory shock [5]. Vasopressin deficiency has been demonstrated to be one of the most important factors. Low-dose (0.04 U/min or 4 U/h) arginine vasopressin (AVP) infusion has been advocated for treating catecholamine-resistant vasodilatory shock [6-9]. Vasopressin is an endogenous hormone produced in the hypothalamus and secreted upon osmotic and hemodynamic stimuli. The reanimation of this non-adrenergic vasopressor reminded us what the relationship was between AVP and sepsis. A prospective group study showed plasma vasopressin levels increased at the initial phase of septic shock and declined afterward [10]. Other data from 19 patients in the late phase of septic shock presented the low plasma vasopressin levels and increased sensitivity to exogenous vasopressin [11]. However, these studies still did not demonstrate whether plasma vasopressin concentration itself could be a predicting factor for impending septic shock.

The purpose of this study was to evaluate if low plasma vasopressin and high norepinephrine levels could predict the occurrence of impending septic shock.

2. Materials and methods

2.1. Study design

This is a prospective observational study that sought to find the linkage between plasma vasopressin and norepinephrine concentrations and incoming septic shock. This study protocol was approved by our institutional research committee, and the informed consent was received from each patient.

2.2. Study setting and population

This study was performed at a university teaching hospital emergency department (ED) with an annual census of more than 80,000 patient visits. Adult patients visiting the ED from January 2000 to August 2001 were enrolled if they met the criteria of sepsis. They were categorized into 3 groups such as sepsis, severe sepsis, and septic shock according to their 6-hour outcome (ie, the most severe condition caused by sepsis within the following 6 hours after vasopressin measurement). We excluded patients younger than 18 years, with cardiogenic shock or hemorrhagic shock, pregnant, who received AVP treatment, or who are supported by vasopressor treatment. Patients with initial presentation of septic shock were also excluded because the objective of this study was to predict the probability of occurrence of septic shock in those with less severe condition at presentation.

We followed the criteria from the American College of Chest Physicians/Society of Critical Care Medicine consensus conference in 1992 [12,13]. In summary, systemic inflammatory response syndrome (SIRS) is manifested by 2 or more of the following conditions: (1) temperature higher than 38°C or lower than 36°C; (2) heart rate higher than 90 beats per minute; (3) respiratory rate higher than 20 breaths per minute or PaCO₂ lower than 32 mm Hg; and (4) white blood cell count higher than 12,000/mm³ or lower than 4000/mm³ or bands higher than 10%. Sepsis is defined as SIRS caused by infection. Severe sepsis is defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension, and septic shock is sepsis with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities. In this study, hypotension is defined as mean artery pressure less than 70 mm Hg despite adequate volume resuscitation. Clinical diagnosis obtained at baseline and follow-up was blinded to the results of the vasopressin and norepinephrine measurements.

2.3. Study protocol

We checked the indexes from the 3 groups of patients after informed consent was obtained. The indexes included white blood cell and platelet count; hemoglobin, glucose, blood urine nitrogen, creatinine, aspartate serine transaminase, and C-reactive protein (CRP) levels; and adequate cultures. In addition, we also measured plasma vasopressin and norepinephrine concentrations at initial presentation. Blood samples (5 mL) were drawn from antecubital veins for measurement of plasma vasopressin. The samples were immediately transferred to chilled polyethylene tubes containing 12.5 IU of heparin per milliliter of blood. The tubes were immediately centrifuged at 4°C for 10 minutes at 2000 g, and the plasma was thereafter stored at −80°C for later analysis. Vasopressin was extracted from plasma by means of Sep-Pak cartridges (Millipore, Milford, MA) and measured by radioimmunoassay [14]. Synthetic vasopressin (Ferring, San Diego, CA) served as reference preparation. The detectable lower limit of AVP was 0.1 to 0.3 pg per tube. The within-assay coefficient of variation at the middle-sensitivity range of the standard curve was 7.8%. The between-assay coefficient of variation at the same range was 12%. Plasma vasopressin was determined twice on each
sample. For this assay, the reference range (95%) for healthy control subjects was 1.5 to 3.8 pg/mL.

Another 5 mL of venous blood was drawn for measurement of plasma norepinephrine. The samples were collected in chilled EDTA tubes containing 2 mg of sodium metabisulfite to prevent oxidation of the catecholamines. Plasma was immediately separated in a refrigerated centrifuge and stored at −80°C until analysis. To 1 mL of rethawed plasma, 1.5 mL of 0.4 mmol/L perchloric acid containing 0.5 mmol/L EDTA and 0.5 mmol/L sodium metabisulfite were added to precipitate proteins. After centrifugation at 2000 g for 10 minutes, the supernatants were further extracted by use of the alumina absorption method. Plasma concentrations of epinephrine and norepinephrine were determined by reversed-phase, high-performance liquid chromatography using a LiChrospher 100 RP18 5-μm column (Merck, Darmstadt, Germany), and electrochemical detection was performed according to a method described previously [15].

The patients were closely monitored by the initial physicians, and all of clinical information was recorded hourly within 6 hours after vasopressin and norepinephrine were measured. The 6-hour outcome was determined by the observer and another independent physician.

2.4. Data analysis

The study sample size is determined by the proportion based on the null and an alternative with acceptable type 1 (α = .05) and type 2 (β = .03) errors. All data presented in this study are expressed as mean ± SD. Significance of differences within groups were calculated using repeated analysis of variance (ANOVA) and Student-Newman-Keuls test for post hoc testing. A P value of less than .05 was considered statistically significant. Receiver operating characteristic (ROC) curve of vasopressin was constructed. The statistics were examined by using a statistical software package (SPSS 8.0; SPSS Inc, Chicago, Ill). The ROC curve was drawn by using another software (MedCalc Software; MedCalc, Mariakerke, Belgium).

3. Results

3.1. Clinical characteristics

There were 182 patients aged 27 to 99 years who met the inclusive criteria during a 24-month period (from January 2001 to December 2002). Three categories were classified as those with septic shock (n = 72), those with severe sepsis

![Fig. 1](image-url) The study flow chart demonstrating the initial diagnosis and outcome of the study population.
and sepsis groups \((P < .01)\). On the other hand, there was no significant difference in norepinephrine level between septic shock and severe sepsis groups \((P \neq \text{not significant [NS]})\), whereas both groups had significantly higher norepinephrine levels than sepsis group \((P < .01\) for individual comparisons). In addition, plasma vasopressin and norepinephrine concentrations in healthy control were \(2.6 \pm 0.8\) pg/mL \((95\% \text{ CI, 2.3}-2.9\) pg/mL\) and \(800 \pm 200\) pg/mL \((95\% \text{ CI, 730}-880\) pg/mL\), respectively. There was no significance in vasopressin levels between septic shock group and control subjects \((P = \text{NS})\), although there was significant difference in norepinephrine levels between these 2 groups \((P < .01)\).

### Table 1 Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>Septic shock ((n = 72))</th>
<th>Severe sepsis ((n = 56))</th>
<th>Sepsis ((n = 54))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>70.4 (\pm) 15.2</td>
<td>66.5 (\pm) 16.1</td>
<td>63.2 (\pm) 21.0</td>
</tr>
<tr>
<td>Male</td>
<td>39</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>Malignancy</td>
<td>9</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Chronic renal</td>
<td>12</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Insufficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract</td>
<td>30</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>Respiratory tract</td>
<td>18</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Liver or other</td>
<td>10</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>organ abscess</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue</td>
<td>6</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Values are mean \(\pm\) SD. \(P = \text{NS}\) for each category among 3 groups.

### Table 2 Laboratory findings in patients with sepsis

<table>
<thead>
<tr>
<th></th>
<th>Mean value</th>
<th>95% CI</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasopressin (pg/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>3.6 (\pm) 2.5</td>
<td>3.0-4.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>21.8 (\pm) 4.1</td>
<td>20.1-23.5</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>10.6 (\pm) 6.5</td>
<td>9.5-11.7</td>
<td></td>
</tr>
<tr>
<td>Norepinephrine (pg/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>3650 (\pm) 980</td>
<td>3400-3920</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>3600 (\pm) 1000</td>
<td>3350-3830</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>1720 (\pm) 320</td>
<td>1610-1800</td>
<td></td>
</tr>
<tr>
<td>WBC (per mm(^3))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>12300 (\pm) 7400</td>
<td>10600-14000</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>16500 (\pm) 23900</td>
<td>9800-23200</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>14200 (\pm) 18600</td>
<td>8900-19500</td>
<td></td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>10.9 (\pm) 2.5</td>
<td>10.4-11.4</td>
<td>NS</td>
</tr>
<tr>
<td>Sepsis</td>
<td>10.2 (\pm) 3.0</td>
<td>9.0-11.1</td>
<td></td>
</tr>
<tr>
<td>Platelet ((10^3/mm(^3)))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>174 (\pm) 113</td>
<td>145-208</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>184 (\pm) 102</td>
<td>149-219</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>176 (\pm) 90</td>
<td>148-204</td>
<td></td>
</tr>
<tr>
<td>AST (U/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>151 (\pm) 381</td>
<td>47-255</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>133 (\pm) 216</td>
<td>68-198</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>106 (\pm) 164</td>
<td>54-158</td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>239 (\pm) 420</td>
<td>139-339</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>175 (\pm) 86</td>
<td>151-199</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>172 (\pm) 106</td>
<td>142-202</td>
<td></td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>44 (\pm) 29</td>
<td>37-51</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>42 (\pm) 32</td>
<td>33-51</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>37 (\pm) 31</td>
<td>29-46</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>6.8 (\pm) 22.7</td>
<td>1.3-12.3</td>
<td>NS</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>3.0 (\pm) 2.6</td>
<td>2.2-3.3</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>3.1 (\pm) 3.2</td>
<td>1.2-3.6</td>
<td></td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>3.7 (\pm) 3.2</td>
<td>2.9-4.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean \(\pm\) SD. AST indicates aspartate transaminase; BUN, blood urine nitrogen; Hb, hemoglobin; WBC, white blood cell.
Because the evolutional changes of vasopressin were different from those of norepinephrine, we decided to calculate the vasopressin/norepinephrine ratio for each patient and control subject. The vasopressin/norepinephrine ratio was significantly low for the patients with final diagnosis of septic shock ($0.9 \pm 0.6 \times 10^{-3}$ for septic shock group, $[6.2 \pm 2.6] \times 10^{-3}$ for severe sepsis group, $[6.0 \pm 2.1] \times 10^{-3}$ for sepsis group, and $[3.2 \pm 1.8] \times 10^{-3}$ for healthy controls, $P < .001$ by ANOVA; Fig. 1). Individual comparisons also revealed that the ratio was definitely lower in septic shock group than in severe sepsis group ($P < .001$), in sepsis group ($P < .001$), and in healthy controls ($P < .01$).

As depicted in Fig. 2, ROC analysis revealed that the vasopressin/norepinephrine ratio $1.0 \times 10^{-3}$ (area under curve 0.938; 95% CI, 0.892-0.976) had a sensitivity of 97% (95% CI, 90%-99%), a specificity of 85% (95% CI, 78%-91%), a positive predictive value of 81% (95% CI, 73%-88%), and a negative predictive value of 98% (95% CI, 91%-100%) for predicting septic shock. The positive likelihood ratio was 6.7 (95% CI, 4.2-10.5) and the negative likelihood ratio almost 0 (95% CI, 0.0-0.1). The diagnostic odds ratio was 205.6 (95% CI, 45.8-923.6).

4. Discussion

This study demonstrates that plasma vasopressin level increases progressively in patients with sepsis and severe sepsis and decreases dramatically in patients who eventually develop septic shock within 6 hours. Meanwhile, the plasma norepinephrine concentration keeps elevated and reached a plateau at the severe sepsis stage. The low plasma vasopressin/norepinephrine ratio thus provides good prediction for impending septic shock, whereas plasma vasopressin concentration alone is low either in those developing septic shock or in healthy controls. To our knowledge, this is the first report to find such a ratio that actually may be predictive of impending septic shock.

Endogenous vasopressin release is mediated by plasma osmolality and blood volume or pressure [16]. Our data demonstrate that the vasopressin level rises even before the drop in blood pressure, and it is not released to cope with shock status. This result is comparable with the animal study that proved endotoxin directly stimulates vasopressin secretion independent of plasma osmolarity or blood pressure [17]. Many proinflammatory cytokines such as interleukin and tumor necrosis factor also enhance

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**Fig. 2** Receiver operating curve of the vasopressin/norepinephrine ratio in predicting septic shock (sensitivity 98%, specificity 85%, positive predictive value 81%, and negative predictive value 98% when the ratio is taken at $1 \times 10^{-3}$ with area under curve 0.938). The table below the graph demonstrates the number of patients classified by vasopressin/norepinephrine ratio and the presence or absence of septic shock. V/N indicates plasma vasopressin/norepinephrine ratio.
vasopressin production [18,19] in the pathways, independent of blood osmolarity or volume.

It has been reported that there is a surge of vasopressin secretion in severe sepsis and subsequent decline (or vasopressin deficiency status) in septic shock. Landry et al [11] has discussed about this deficiency of vasopressin in septic shock that was because of increased metabolism or decreased production. Tarek et al [10] also cited that inappropriately low plasma levels of vasopressin are related to a depletion of the storage in the neurohypophysis. Consequently, vasopressin might be stimulated by proinflammatory cytokines in the early stage of sepsis, whereupon it became deficient to react in septic shock because of the depletion of storage. These observations may suggest that use of physiological doses of corticosteroids in severe sepsis and septic shock may reserve vasopressin release and subsequently improve survival [20].

Sepsis means SIRS caused by infection, and septic shock is sepsis with persistent hypotension and inadequate perfusion despite adequate fluid resuscitation. Although the severity of these critical conditions decides the strategy of treatment including choice of antibiotics, timing of inotropic agents, and indications of surgical intervention, there are still many indecisive points about the treatment. Thus, the scoring system of sepsis was advocated since decades ago [12,13]. The American College of Chest Physicians/Society of Critical Care Medicine defined the criteria of sepsis, severe sepsis, and septic shock according to the mortality risk stratification since 1992 [13]. In spite of the above clinical classification, some mediators such as endotoxin and cytokines were proven to be associated with progress of the disease [21-24]. Among these mediators, plasma procalcitonin [25-28], interleukin 6 [22], interleukin 10 [29], and protein C [30-32] are considered as the markers of septic syndrome. However, it remains unclear whether these mediators can provide accurate prediction for the final outcome of sepsis. For example, numerous studies have shown that acquired protein C deficiency is prevalent in most patients with sepsis and is associated with increased morbidity and mortality in patients with severe sepsis and septic shock [30,31]. In addition, protein C deficiency occurs in the presence of a wide range of pathogens, and develops early in the disease process [31]. However, there is still no model for predicting the likelihood of septic shock by protein C levels. Macias and Nelson [32] demonstrated that severe protein C deficiency predicts early death in severe sepsis. Although refractory shock contributes to a significant portion of mortality in their study, respiratory failure and other organ dysfunction are also important factors [32]. The pathological mechanisms in which protein C deficiency is related to high mortality in sepsis cannot be attributed solely to septic shock. Our model may be the first one to use plasma mediators (ie, vasopressin/norepinephrine ratio) to predict the possibility of septic shock accurately.

Our data also revealed that traditional laboratory tests such as hematologic, biochemical measurements, and CRP are not good indicators to predict the outcome of patients with sepsis. The findings are comparable with most of the previous related studies [33,34]. These traditional measures can only help us make the diagnosis of sepsis, whereas the plasma vasopressin/norepinephrine ratio can tell us the possibility of septic shock.

4.1. Limitations

There are 2 major limitations in our study. First, the sample size may be still limited. A large-scale prospective study may be indicated to confirm our observations. Second, the measurements of plasma vasopressin or norepinephrine are not available at each laboratory of the ED. They are time-consuming and technique-dependent, and thus may limit their use at the ED. This limitation, in combination with limited sample size, prevents us from exploring if the plasma vasopressin/norepinephrine ratio can improve the prognosis because of early detection and treatment.

4.2. Conclusion

Low serum vasopressin/norepinephrine ratio that is composed of low plasma vasopressin level and high norepinephrine level can accurately predict impending shock in septic patients.

References


Original Contribution

Diagnostic accuracy and reproducibility in the interpretation of Ottawa ankle and foot rules by specialized emergency nurses

Robert-Jan Derksen MD\textsuperscript{a,}\textsuperscript{*}, Fred C. Bakker MD, PhD\textsuperscript{a}, Pieter C. Geervliet\textsuperscript{a}, Elly S.M. de Lange–de Klerk MD, PhD\textsuperscript{b}, Emil A. Heilbron MD, PhD\textsuperscript{c}, Bart Veenings MD\textsuperscript{a}, Peter Patka MD, PhD\textsuperscript{a}, Henk J.Th.M. Haarman MD, PhD\textsuperscript{a}

\textsuperscript{a}Department of Surgery/Traumatology, VU University Medical Centre, 1007 MB Amsterdam, The Netherlands
\textsuperscript{b}Department of Clinical Epidemiology and Biostatistics, VU University Medical Centre, 1007 MB Amsterdam, The Netherlands
\textsuperscript{c}Department of Radiology, VU University Medical Centre, 1007 MB Amsterdam, The Netherlands

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Abstract

Objectives: The ED is often confronted with long waiting periods. Because of the progressive shortage in general practitioners, further growth is expected in the number of patients visiting the ED without consulting a general practitioner first. These patients mainly present with minor injuries suitable for a standardized diagnostic protocol. The question was raised whether these injuries can be treated by trained ED nurses (specialized emergency nurses [SENs]). The aim of this study was to evaluate the diagnostic accuracy and reproducibility of SENs in assessing ankle sprains by applying the Ottawa Ankle Rules (OAR) and Ottawa Foot Rules (OFR).

Methods: In a prospective study, all ankle sprains presented in the ED from April to July 2004 were assessed by both a SEN and a junior doctor (house officer [HO]) randomized for first observer. Before the study, SENs were trained in applying OAR and OFR. In all patients, radiography was performed (gold standard). The diagnostic accuracy for the application of OAR and OFR was calculated for both groups and was compared using $z$ statistics. Furthermore, from the paired results, reproducibility was calculated using $\kappa$ statistics.

Results: In total, 106 injuries were assessed in pairs, of which 14 were ultimately found to concern acute fractures (prevalence, 13%). The sensitivity for the SEN group was 0.93 (95% confidence interval [CI], 0.64-1.00) compared with 0.93 (95% CI, 0.64-1.00) for the HO group (no significance [ns]). The specificity of the nurses was 0.49 (95% CI, 0.38-0.60) compared with 0.39 (95% CI, 0.29-0.50) for the doctors (ns). The positive predictive value for the SEN group was 0.22 (95% CI, 0.13-0.35) compared with 0.19 (95% CI, 0.11-0.31) for the HO group (ns). The negative predictive value for the nurses was 0.98 (95% CI, 0.87-1.00) compared with 0.97 (95% CI, 0.84-1.00) for the doctors (ns). The interobserver agreement for the OAR and OFR subsets was $\kappa = 0.38$ for the lateral malleolus; $\kappa = 0.30$.

\textsuperscript{*} Corresponding author. Tel.: +31 20 4443602; fax: +31 20 4440274.
E-mail address: rj.derksen@vumc.nl (R.-J. Derksen).

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medial malleolus; \( \kappa = 0.50 \), navicular; \( \kappa = 0.45 \), metatarsal V base; and \( \kappa = 0.43 \), weight-bearing. The overall interobserver agreement for the OAR was \( \kappa = 0.41 \) and \( \kappa = 0.77 \) for the OFR.

**Conclusion:** Specialized emergency nurses are able to assess ankle and foot injuries in an accurate manner with regard to the detection of acute fractures after a short, inexpensive course.

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### 1. Introduction

Emergency departments are confronted with progressive crowding during rush hours. Because of the growing shortage of general practitioners, many patients tend to bypass the general practitioners office and come to the ED without referral [1,2]. Moreover, increased patient demands on (emergency) health care provision also add to the ED workload. Most of the presentations concern minor injuries, such as ankle sprains, which when crowded, have to wait for a long time to be assessed and treated by the attending doctor. The waiting period is often prolonged because of the triage system, which puts more severe injuries first.

Several solutions have been proposed and introduced, of which the physician assistants (PAs) and emergency nurse practitioners (ENPs) are the best-known examples [3-7]. These methods have been proven successful in several investigative settings [8-11]. However, there are disadvantages to the deployment of these midlevel practitioners. Firstly, the educational period is approximately 2 years, in which the nurses are less available for clinical work. After graduation, the midlevel practitioners are only deployed to perform diagnostic and logistic tasks, necessitating the need for an extra regular emergency nurse to perform the nursing tasks. Furthermore, the costs for education and salaries are high in comparison with regular emergency nurses [12].

In this context, the need to investigate the possibility of deploying regular emergency nurses to assess and treat certain injuries after specific training and according to a standardized protocol was established. The injury chosen to test this concept on is the ankle sprain because it is a common, well-defined injury for which the Ottawa Ankle Rules (OAR) and Ottawa Foot Rules (OFR) were developed to indicate whether a foot and/or ankle x-ray is needed [13,14]. Since their introduction in 1992, these rules have been studied and validated extensively [15-18]. However, little is known about the diagnostic accuracy and reproducibility of emergency nurses in interpreting the OAR and OFR [19-21]. Only a few studies have been conducted in which the accuracy and interobserver agreement of these interpretations were subject of research, mostly dealing with midlevel practitioners [22-24]. Therefore, the aim of this study is to assess the diagnostic accuracy and reproducibility of emergency nurses compared with junior doctors (house officers [HOs]) working in the ED in interpreting the OAR and OFR.

### 2. Methods

#### 2.1. Study design

A prospective study was performed from April to June 2004, in which all consecutive ankle sprains of patients aged 18 to 65 years were included. The study was conducted in an urban university teaching ED with an annual patient census of 35,000. Each injury was assessed by both a trained emergency nurse (specialized emergency nurse [SEN]) and an HO by means of the OAR and OFR (Fig. 1). Randomization for first observer took place to prevent a hypothetical influence of the first assessment on the second to affect one observer group more than the other. The data of OAR and OFR assessment were written down on separate medical history forms, without the observers being informed of each other’s scoring results (blinded). The examination findings were scored positive or negative for each subset of the OAR and OFR.

![Fig. 1](image)  
A and B are locations to apply pressure when applying the OAR. C and D are the locations in the midfoot to be tested when applying the OFR. To complete both the OAR and OFR, the ability to bear weight should be tested.
Furthermore, after assessment by both observers, radiographs of each subject were taken to acquire a gold standard. Finally, treatment was initiated by the HO on the basis of his/her own findings and the accompanying x-ray (Fig. 2).

Power analysis was aimed to enable detection of a 15% difference in sensitivity between the observer groups using a power of 80% (2-sided, \( \alpha = .05 \)).

2.2. Observer groups

The emergency nurses were trained before the start of the study in the anatomy and biomechanics (trauma mechanisms) of the ankle and foot, and they were taught how to treat the specific injuries. This was done in a 1-day course provided by a surgeon and a radiologist. All 32 certified emergency nurses were approached to voluntarily participate in the study, of which 16 were recruited. The average age for the recruited group was 36 years (varying from 26 to 56 years). The average clinical experience in the ED for the recruited nurses was 5 years (varying from 6 months to 12 years). Furthermore, all HOs, 9 in total, participated in the study. To preserve a representative control group, the HOs did not attend the course and assessed the injury according to the way they were once taught to do it. The officers’ average age was 28 years (varying from 26 to 30 years), and their average clinical experience (in an ED) was 1 year (varying from 6 months to 1.5 years).

2.3. Study subjects

The inclusion criteria applied were (1) patients having sustained a sprained ankle, (2) patients aged 18 to 65 years, and (3) patients presenting their injury within 48 hours after onset. The exclusion criteria consisted of the following. (1) The injured limb should not have been fractured before in a way that made operative treatment necessary. (2) Patients, who were in any way mentally or physically challenged, making assessment more difficult, were excluded. (3) And, ankle sprains as part of a more severe (poly)trauma were also excluded from the study.

2.4. Outcome parameters and statistical analysis

For both groups, diagnostic accuracy parameters for the indication of an x-ray were calculated, being the sensitivity, specificity, positive predictive value, and negative predictive value (Metatest 0.6, New England Medical Center, Boston, MA). To test if a significant difference was found between the groups with regard to the mentioned accuracy parameters, \( z \) statistics were applied.

For each of the OAR and OFR subsets and the overall Ottawa rules, \( \kappa \) statistics were applied to all included subjects to render interobserver agreement values (SPSS 9.0, Chicago, IL). To isolate the assessment for an ankle and/or foot injury, data were separated into a group presenting with foot pain (\( n = 18 \)), a group presenting with ankle pain (\( n = 70 \)), and a group presenting with both (\( n = 18 \)). After doing so, \( \kappa \) statistics were applied to render interobserver agreement for both the overall OAR and the overall OFR. Finally, the radiograph indication rate was compared between groups using McNemar statistics for paired results (2-sided, \( \alpha = .05 \)).

3. Results

In total, 108 patients were assessed by 2 observers as described before. Of these 108, 2 were excluded afterwards because they were found to exceed the upper age limit. In both excluded patients, clinical investigation results of both observers were in accordance with each other and the gold standard. In total, 106 injuries were included in the study, of which 14 were ultimately judged by the radiologist to concern acute fractures (prevalence, 13%). Of these fractures, 5 were located in the foot and 9 in the ankle. Furthermore, from
2 patients, the nurse observer did not record scoring for the navicular area, thus rendering 2 fewer interobserver pairs with regard to the navicular area and the overall OFR. All 14 fractures were detected by means of the OAR and OFR by both observer groups, except for an avulsion chip of the medial malleolus (deltoid) ligament in the control group and an avulsion chip of the talus (anterior talofibular ligament) in the nurses group. In total, the SEN group found an indication for x-ray in 60 (57%) of 106 injuries by applying the OAR and OFR. In the HO group, the indication for radiography was found in 69 (65%) of 106 injuries. This difference was not found to be statistically significant ($P = .10$).

### 3.1. Diagnostic accuracy

The sensitivity of the SEN group for detecting fractures by means of the OAR and OFR as described was 0.93 (95% confidence interval [CI], 0.64-1.00) compared with 0.93 (95% CI, 0.64-1.00) for the HO group, without a significant difference being found ($P = 1.00$). The specificity of SEN was 0.49 (95% CI, 0.38-0.60) compared with 0.39 (95% CI, 0.29-0.50) for the HO group, revealing no statistically significant difference between the groups ($P = .20$). As for the positive predictive value, the SENs displayed 0.22 (95% CI, 0.13-0.35) compared with 0.19 (95% CI, 0.11-0.31) for the doctors, without a significant difference between the groups ($P = .69$). Finally, the negative predictive value for the SEN group was 0.98 (95% CI, 0.87-1.00) as opposed to 0.97 (95% CI, 0.84-1.00) for the doctors. Again, no significant difference between the observer groups was found ($P = .68$).

### 3.2. Reproducibility

The interobserver agreement for each subset of the OAR and OFR and the overall results were as follows: $\kappa = 0.38$ for the lateral malleolus; $\kappa = 0.30$, medial malleolus; $\kappa = 0.50$, navicular; $\kappa = 0.45$, metatarsal V base; and $\kappa = 0.43$, ability to bear weight. The combined interobserver agreement within the patient group presenting with foot pain (OAR) was $\kappa = 0.77$ and for the group presenting with ankle pain (OAR) was $\kappa = 0.41$ (Table 1).

### Table 1 Interobserver agreement results displayed as $\kappa$ values for the overall OAR and OFR and the subsets

<table>
<thead>
<tr>
<th>Location</th>
<th>$\kappa$</th>
<th>SE</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall OAR</td>
<td>0.41</td>
<td>0.100</td>
<td>Moderate</td>
</tr>
<tr>
<td>Overall OFR</td>
<td>0.77</td>
<td>0.156</td>
<td>Substantial</td>
</tr>
<tr>
<td>OAR and OFR subset results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral malleolus</td>
<td>0.38</td>
<td>0.084</td>
<td>Fair</td>
</tr>
<tr>
<td>Medial malleolus</td>
<td>0.30</td>
<td>0.132</td>
<td>Fair</td>
</tr>
<tr>
<td>Metatarsal V</td>
<td>0.45</td>
<td>0.146</td>
<td>Moderate</td>
</tr>
<tr>
<td>Navicular</td>
<td>0.50</td>
<td>0.133</td>
<td>Moderate</td>
</tr>
<tr>
<td>Weight-bearing</td>
<td>0.43</td>
<td>0.110</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

4. Discussion

The clinical importance of the OAR and OFR has been investigated extensively [14,15,17,18]. It has been proven that the OAR and OFR are of great value in everyday practice, resulting in a reduction of x-rays. Bachmann et al [16] summarized the available literature in an excellent systematic review. The pooled sensitivity found in their study on the OAR and OFR performed by doctors was 0.96 (95% CI, 0.94-0.99), and the specificity was 0.26 (95% CI, 0.19-0.34). Evidence has also been published on the diagnostic accuracy of midlevel practitioners (eg, ENPs and PAs) in interpreting the OAR and OFR [22,23,25]. However, little is known about the ability of regular emergency nurses to interpret the OAR and OFR (after training) [21]. In our study, trained regular emergency nurses displayed a sensitivity of 0.93 (95% CI, 0.64-1.00) and a specificity of 0.49 (95% CI, 0.38-0.60). Fiesseler and colleagues [20] were the first to describe the diagnostic accuracy of regular emergency nurses in interpreting the OAR and OFR in an interobserver setting. The accuracy parameters for the nurses found in their study were quite reasonable, with a sensitivity of 0.92 and a specificity of 0.47 (no CIs were mentioned).

As for the interobserver agreement results found in our study, the $\kappa$ value for the overall OFR is classified as being substantial (0.6-0.8), and for the overall OAR, the $\kappa$ value was in the range of moderate agreement (0.4-0.6). The original validation studies for the OAR and OFR revealed agreement in the $\kappa$ value range of 0.60 to 0.80 [13,14,26]. In the study by Fiesseler et al [20], the conclusion was drawn that the ability of emergency nurses to accurately interpret the OAR was limited, regarding the moderate $\kappa$ values found in their series. However, in interpreting the $\kappa$ values, it is important to keep in mind that they represent the agreement between 2 observers, of which neither should be considered the gold standard. Therefore, moderate $\kappa$ values in these studies do not proof the inability of nurses to accurately interpret the OAR and OFR [27]. Also, it is important to keep in mind that primary studies on diagnostic tests are notorious for overestimation of accuracy and interobserver agreement. Furthermore, it should be noted that the OAR and OFR are subjective clinical tests, of which the threshold for radiograph indication is set to be low (specificity) to acquire a high sensitivity for the tests. The reason for these $\kappa$ values not to approach 1.00 can probably be found in the mismatches found in the nondiseased. Therefore, the moderate/substantial $\kappa$ values for the OAR and OFR, respectively, are probably partly caused by the low specificity of the OAR and OFR in general. Although the interobserver agreement is an important property of a diagnostic test, for clinical practice, diagnostic accuracy parameters are most important.

In our study, the diagnostic accuracy of the trained nurses group is excellent compared with that of the HO group and available literature [14-18]. These results are very promising for everyday clinical practice in the ED. The training process of regular emergency nurses to assess and treat ankle sprains
requires little time and is inexpensive compared with the much more elaborate training program of ENPs and PAs. Not much more than a small conference room, audiovisual equipment, a surgeon, and a radiologist are needed for 1 day to provide for the course. Furthermore, in theory, the concept of SEN can also be applied to other well-defined injuries suitable for a clear protocol.

5. Limitations and future questions

Essential in assessing the accuracy of a diagnostic test (OAR and OFR) is to make use of a valid reference test. Therefore, radiography was performed for every injury. Obviously, in daily practice, the assessment of ankle sprains consists in many cases not only of clinical examination but also of radiographic assessment. We have chosen this study setting for this injury as it enables an evaluation of its sole clinical investigation. In this context, the possibility exists that, without the standard radiography and when having to suffer the clinical consequences of their decision, nurses could act somewhat more cautiously. However, both groups were confronted with the same limitation.

Future studies have to determine if SENs are able to accurately interpret ankle sprains in a setting in which the entire process of clinical and radiographic assessment is evaluated.

6. Conclusion

In conclusion, regular emergency nurses are able to accurately interpret the OAR and OFR in the ED after a short, inexpensive course.

References

Original Contribution

Outcomes of emergency treatment in ruptured hepatocellular carcinoma in the ED

Wei-kung Chen MD\textsuperscript{a,}\textdagger, Yu-Tein Chang MD\textsuperscript{a}, Yun-ting Chung MD\textsuperscript{a}, Horng-ren Yang MD\textsuperscript{b}

\textsuperscript{a}Department of Emergency Medicine, China Medical University Hospital, Taichung 404, Taiwan, ROC
\textsuperscript{b}Trauma and Emergency Center, China Medical University Hospital, Taichung 404, Taiwan, ROC

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Abstract The choice of emergency treatment of ruptured hepatocellular carcinoma (HCC) remains controversial. This study analyzed the prognostic factors for ruptured HCC seen in an ED. Patients were retrospectively classified into survival and mortality groups. Fifty-five patients were enrolled into this study, and the hospital mortality rate was 38.2%. There were no associations of clinical presentation, tumor characteristics, and emergency treatment method with patients’ prognoses. Significantly higher mortality rate was noted in patients with poor liver function. The time between admission and emergency chemoembolization was significantly shorter in the mortality group than in the survival group (mean, 255 vs 394 minutes). The 1-month survival rate was 69\% in patients who received conservative treatment and 59\% in patients who underwent emergency chemoembolization. Routine emergency chemoembolization did not improve outcome and was associated with higher mortality and complication rates, especially in patients with poor liver function. Conservative therapy may be a preferable option for patients with ruptured HCC if they have baseline poor liver function.

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1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary hepatic tumor and one of the most common cancers worldwide. The incidence of spontaneous rupture of HCC reported in the literature varies from 5\% to 26\% \cite{1-5}. Most of these patients have been seen in an ED. The clinical presentation of spontaneous rupture of HCC has been variable; therefore, in some cases, there were delays, misdiagnoses, or incidental discovery \cite{6}. Hepatocellular carcinoma rupture may result in hemoperitoneum and development of shock. The hospital mortality rate of ruptured HCC has been high, ranging from 33\% to 67\% \cite{4,5,7,8}.

The emergency treatment of ruptured HCC is controversial. Emergency treatments include surgical resection or hemostasis, transcatheter arterial embolization (TAE) or transcatheter arterial chemoembolization (TACE), or conservative treatment (transfusion and supportive care). Previous studies have suggested emergency hepatic resection for ruptured HCC to control bleeding and facilitate resection of the tumor \cite{1,9-11}. They suggested that hepatic resection for ruptured HCC was safe and had a better long-term survival rate compared with other treatments. In advanced stage HCC, the blood supply is mostly from the hepatic artery. This pathological characteristic of arterial neovascularity provides
the basis for arterial embolization therapy [12]. Embolization therapy is the choice of treatment in patients with ruptured HCC because it is an effective method of controlling the bleeding [13]. Whether arterial obstruction for treatment of ruptured HCC should be combined with chemotherapy remains unclear.

Some authors have proposed TAE as the initial treatment for controlling hemoperitoneum [14-16]. Recently, several studies demonstrated that greater improvements in survival rates were achieved by TACE than by TAE in nonruptured HCC because of the effect of the embolizing agents, which increase hepatic extraction of the chemotherapy [17,18]. Transcatheter arterial embolization with staged hepatectomy was reported as a rational treatment for patients with ruptured HCC [19,20]. In contrast, some authors reported conservative management as an effective approach for control of intraperitoneal hemorrhage in patients with ruptured HCC. If there was no evidence of hemodynamic instability in these patients, initial conservative management proved effective [21].

For EDs, the first priority of treatment is to stabilize the patient. The physician must then decide the best treatment strategy. However, most studies on the treatment of ruptured HCC have been from the view of surgeons and radiologists. The aim of this study was to investigate the association between clinical presentation, treatment method, and prognosis of cases of ruptured HCC seen in the ED.

2. Methods

This study was a retrospective observational case series study. A hospital chart review was performed. Patients diagnosed with spontaneous ruptured HCC, who were treated in the ED of China Medical University Hospital, a 1300-bed hospital in Taichung City, Taiwan, with more than 100,000 ED visits per year, from January 1996 to August 2004, were enrolled into this study. This study was approved by the institutional review board of our hospital. The data recorded included the sex, age, initial vital signs on arrival at the ED, clinical presentations, history, laboratory data, volume of blood transfusion, and computed tomographic (CT) scan interpretation, as well as prognosis at admission and survival at 1 month. All data were collected by accessing the medical records database of our hospital. One-month survival and mortality rates after discharge were determined by a review of ambulatory care chart records. Patients were contacted by telephone if any were lost during follow-up.

The clinical presentation was classified into sudden and nonsudden. Cases were classified as sudden if there was rapid onset of abdominal pain or symptoms of shock, such as syncope and hypotension. Hepatitis B or C diagnosis was based on serology obtained during the current hospitalization or previously. Underlying diseases recorded included diabetes, hypertension, and cardiac or respiratory diseases. The recorded characteristics of the tumor included location, number of nodules, and size in centimeters. The tumor location was classified into right lobe, left lobe, or both. The number of nodules was classified as single or multiple, and tumor size was measured by abdominal CT scan. If there were multiple nodules, the biggest one was measured and recorded.

Ruptured HCC was diagnosed by sonogram or CT. Abdominal sonogram was carried out in patients with abdominal pain, abdominal fullness, or hypotension either with hepatoma history or not. If there was ascites present, abdominal paracentesis was performed. If it showed bloody ascites, abdominal CT was requested, but if the sonogram identified tumor mass in liver parenchyma, abdominal CT was performed without paracentesis.

Transcatheter arterial chemoembolization is used for the routine management of ruptured HCC in this hospital. The time for emergency TACE was calculated from the time of arrival at the ED to the time when TACE was performed. The procedure of TACE was as follows. A line was introduced in the femoral artery, and the location of hepatic mass was identified. After superselective catheterization of the hepatic artery, 4.8 mg Lipiodol (iodized ethyl esters of fatty acids of poppy seed oil) mixed with 20 mg doxorubicin (adriamycin) and 1 mL cefazolin (1 mg in 5 mL distilled water) were injected for chemoembolization. Then, Gelfoam cubes mixed with cefazolin were injected for proximal vascular embolization. After the procedure, patients were required to rest in bed for 24 hours.

The cases in this study were classified into 2 groups, mortality group and survival group. Statistical analysis was performed by conventional $\chi^2$ test or Fisher exact test to compare discrete variables. The independent sample $t$ test was used to compare continuous variables. One-month survival rate analysis was estimated by the Kaplan-Meier survival method and log-rank test. $P$ values of less than .05 were considered statistically significant.

3. Results

There were 57 ruptured HCCs treated in our ED during the study period. Two cases that received TACE at 3 and 4 days after rupture were excluded. The remaining 55 cases were enrolled into the analysis, which included 21 patients in the mortality group and 34 in the survival group. The overall hospital mortality rate was 38.2% (21 patients).

The patients’ demographics, clinical presentation, and treatment choice are shown in Table 1. Using the Child-Pugh criteria, there were 2 (4%) Child-Pugh class A, 41 (75%) Child-Pugh class B, and 12 (21%) Child-Pugh class C patients. The history of liver cirrhosis had a significant effect on mortality (odds ratio, 3.20; 95% confidence interval [CI], 1.03-9.97). The mortality rate in Child-Pugh class C patients (75%) was 7.25 times higher than in Child-Pugh class B patients (95% CI, 1.67-31.53). The characteristics of tumor size, location, or number did not affect the patients’ hospital prognosis.
### Table 1  The demographic data of mortality and survival groups in patients with hepatoma rupture

<table>
<thead>
<tr>
<th></th>
<th>Mortality group (%)</th>
<th>Survival group (%)</th>
<th>P</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>21</td>
<td>34</td>
<td>.826</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (76)</td>
<td>25 (74)</td>
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</tr>
<tr>
<td>Female</td>
<td>5 (24)</td>
<td>9 (26)</td>
<td>0.87 (0.25-3.06)</td>
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<tr>
<td>Presentation</td>
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<tr>
<td>Nonsudden</td>
<td>11 (52)</td>
<td>22 (65)</td>
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<tr>
<td>Sudden</td>
<td>10 (48)</td>
<td>12 (35)</td>
<td>1.67 (0.55-5.05)</td>
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<td>Hypotension (SBP, &lt;90 mm Hg)</td>
<td>11 (52)</td>
<td>11 (32)</td>
<td>.141</td>
<td>2.30 (0.75-7.03)</td>
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<td>Hepatitis B surface antigen (+)</td>
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<td>13 (38)</td>
<td>.088</td>
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<td>Hepatitis C antibody (+)</td>
<td>8 (38)</td>
<td>18 (53)</td>
<td>.284</td>
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<td>History of hepatoma</td>
<td>12 (57)</td>
<td>13 (38)</td>
<td>.171</td>
<td>2.15 (0.71-6.52)</td>
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<td>Underlying diseases</td>
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<td>13 (38)</td>
<td>.992</td>
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<td>History of cirrhosis</td>
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<td>10 (29)</td>
<td>.041</td>
<td>3.20 (1.03-9.97)</td>
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<td>Child-Pugh score</td>
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<td>Class A</td>
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<tr>
<td>Class B</td>
<td>12 (57)</td>
<td>29 (85)</td>
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<tr>
<td>Class C</td>
<td>9 (43)</td>
<td>3 (9)</td>
<td>7.25 (1.67-31.52)</td>
<td></td>
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<tr>
<td>Tumor location</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Right</td>
<td>11 (52)</td>
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<td>Left</td>
<td>3 (14)</td>
<td>4 (12)</td>
<td>1.43 (0.27-7.57)</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>7 (33)</td>
<td>9 (26)</td>
<td>1.04 (0.17-6.23)</td>
<td></td>
</tr>
<tr>
<td>Nodule</td>
<td></td>
<td></td>
<td>.561</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>14 (67)</td>
<td>20 (59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>7 (33)</td>
<td>14 (41)</td>
<td>0.71 (0.23-2.22)</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td>.498</td>
<td></td>
</tr>
<tr>
<td>Conservative</td>
<td>5 (24)</td>
<td>11 (32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency embolization</td>
<td>16 (76)</td>
<td>23 (68)</td>
<td>1.53 (0.45-5.26)</td>
<td></td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure. Plus signs indicate positive.

### Table 2  Comparison of factors in mortality and survival groups in patients with hepatoma rupture

<table>
<thead>
<tr>
<th>Clinical parameters</th>
<th>Mortality group</th>
<th>Survival group</th>
<th>P</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>60.6</td>
<td>62.1</td>
<td>.700</td>
<td></td>
</tr>
<tr>
<td>Initial heart beat (min)</td>
<td>99</td>
<td>90</td>
<td>.088</td>
<td></td>
</tr>
<tr>
<td>Initial SBP (mm Hg)</td>
<td>93</td>
<td>110</td>
<td>.067</td>
<td></td>
</tr>
<tr>
<td>Initial mean pressure (mm Hg)</td>
<td>70</td>
<td>78</td>
<td>.210</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin level on arrival (mg/dL)</td>
<td>9.0</td>
<td>10.6</td>
<td>.045</td>
<td></td>
</tr>
<tr>
<td>Follow-up hemoglobin level (in 24 hours)</td>
<td>9.7</td>
<td>10.5</td>
<td>.066</td>
<td></td>
</tr>
<tr>
<td>Packed RBC transfusion (1 U = 250 mL)</td>
<td>5.5</td>
<td>3.4</td>
<td>.016</td>
<td></td>
</tr>
<tr>
<td>Platelet count ($\times 10^3$)</td>
<td>178</td>
<td>197</td>
<td>.612</td>
<td></td>
</tr>
<tr>
<td>Serum albumin level (g/dL)</td>
<td>2.6</td>
<td>3.0</td>
<td>.025</td>
<td></td>
</tr>
<tr>
<td>Aspartate aminotransferase (IU/L)</td>
<td>181</td>
<td>134</td>
<td>.279</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase (IU/L)</td>
<td>119</td>
<td>88</td>
<td>.296</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/L)</td>
<td>148</td>
<td>102</td>
<td>.038</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin level (mg/dL)</td>
<td>4.5</td>
<td>1.6</td>
<td>&lt;.000</td>
<td></td>
</tr>
<tr>
<td>Ammonia (µg/dL)</td>
<td>124</td>
<td>66</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>Blood glucose (mg/dL)</td>
<td>184</td>
<td>172</td>
<td>.705</td>
<td></td>
</tr>
<tr>
<td>INR (PT/PT control data)</td>
<td>1.78</td>
<td>1.38</td>
<td>.008</td>
<td></td>
</tr>
<tr>
<td>Time for TACE (min)</td>
<td>255</td>
<td>394</td>
<td>.010</td>
<td></td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>7.7</td>
<td>6.3</td>
<td>.187</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (d)</td>
<td>7.4</td>
<td>11.5</td>
<td>.017</td>
<td></td>
</tr>
</tbody>
</table>

RBC indicates red blood cell; INR, international normalized ratio; PT, prothrombin time.
The continuous variables, including age, vital signs, biochemical data, duration between arrival at ED and start of emergency embolization, and hospital days, are shown in Table 2. The age, vital signs on arrival, initial mean blood pressure, and follow-up hemoglobin level at 24 hours were no different between the 2 groups. However, mortality group had higher volume of blood transfusion and lower albumin as well as higher alkaline phosphatase, total bilirubin, ammonia, and international normalized ratio (INR) levels. The mean time for implementing TACE in the mortality group was 255 minutes (range, 94-577 minutes), which was significantly shorter than that in the survival group (mean, 394 minutes; range, 150-1008 minutes). The mean hospital stay after rupture was 7.4 days (range, 1-17 days) in the mortality group, which was significantly shorter than that in survival group (mean, 11.5 days; range, 4-20 days).

The complications in these 2 groups are shown in Table 3. One hundred percent of the patients in the mortality group had complications during hospitalization. Overall, esophageal variceal bleeding was the most frequent (13%) complication. The most frequent complications in mortality group were hypovolemic shock and esophageal variceal bleeding, followed by hepatorenal failure and acute hepatic failure. Fever (12%) was the most frequent complication in the survival group.

The 1-month survival rates after conservative treatment or emergency TACE are shown in Fig. 1.

### Table 3 Complications of patients with ruptured HCC in mortality and survival groups

<table>
<thead>
<tr>
<th>Complications</th>
<th>Mortality group</th>
<th>Survival group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conservative</td>
<td>Emergency TACE</td>
<td>Conservative</td>
</tr>
<tr>
<td>No. of patient</td>
<td>5</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Esophageal varices bleeding</td>
<td>2 (40)</td>
<td>3 (19)</td>
<td>0</td>
</tr>
<tr>
<td>Peptic ulcer bleeding</td>
<td>1 (20)</td>
<td>2 (13)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Fever</td>
<td>0</td>
<td>1 (6)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Hypovolemic shock</td>
<td>0</td>
<td>5 (31)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatorenal failure</td>
<td>0</td>
<td>4 (25)</td>
<td>0</td>
</tr>
<tr>
<td>Acute hepatic failure</td>
<td>1 (20)</td>
<td>3 (19)</td>
<td>0</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>2 (40)</td>
<td>2 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>0</td>
<td>2 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>2 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>0</td>
<td>1 (6)</td>
<td>0</td>
</tr>
</tbody>
</table>

Values are presented as n (%) unless otherwise noted.

The continuous variables, including age, vital signs, biochemical data, duration between arrival at ED and start of emergency embolization, and hospital days, are shown in Table 2. The age, vital signs on arrival, initial mean blood pressure, and follow-up hemoglobin level at 24 hours were no different between the 2 groups. However, mortality group had higher volume of blood transfusion and lower albumin as well as higher alkaline phosphatase, total bilirubin, ammonia, and international normalized ratio (INR) levels. The mean time for implementing TACE in the mortality group was 255 minutes (range, 94-577 minutes), which was significantly shorter than that in the survival group (mean, 394 minutes; range, 150-1008 minutes). The mean hospital stay after rupture was 7.4 days (range, 1-17 days) in the mortality group, which was significantly shorter than that in survival group (mean, 11.5 days; range, 4-20 days).

The complications in these 2 groups are shown in Table 3. One hundred percent of the patients in the mortality group had complications during hospitalization. Overall, esophageal variceal bleeding was the most frequent (13%) complication. The most frequent complications in mortality group were hypovolemic shock and esophageal variceal bleeding, followed by hepatorenal failure and acute hepatic failure. Fever (12%) was the most frequent complication in the survival group.

The 1-month survival rates after conservative treatment or emergency TACE are shown in Fig. 1.

### 4. Discussion

In the present study, the clinical presentation of HCC rupture, which included symptoms of abdominal pain, syncope, hypotension, or abdominal fullness, varied widely. Forty percent of patients presented with sudden onset of symptoms. This finding was similar to prior studies, which reported sudden abdominal pain as the main presentation of ruptured HCC [4,16,21,22]. However, the different clinical presentation did not affect the hospital outcome. The varied clinical presentation of ruptured HCC may be explained by the different mechanisms involved in the development of this life-threatening condition. A possible cause of ruptured HCC is rapid tumor growth, resulting in tumor necrosis or erosion of vessels [2,5]. Very severe symptoms may have been caused by tumor invasion of the artery leading to active bleeding, whereas less acute symptoms may have been due to tumor necrosis or vein erosion.

Shock was reported as an important factor affecting patients’ prognosis [4]. In this study, the initial presentation with or without hypotension did not affect the hospital prognosis. However, patients in the mortality group had lower initial hemoglobin level and higher volume of blood transfusion, which suggests the possibility of more active bleeding from the tumor in this group. Because of the wide variation of presentations, bedside abdominal sonogram, combined with paracentesis if ascites was present, was recommended to be performed in the ED in patients with previous liver
disease presenting with abdominal pain, fullness, or signs of internal bleeding.

Our results revealed that hospital mortality was significantly related to the patients’ liver function, such as level of serum albumin, total bilirubin, ammonia, and INR. This finding was consistent with those of previous reports [4,21]. The patients in the mortality group required a higher number of blood units transfused, possibly because of more severe coagulopathy. Invasive procedures such as emergency laparotomy applied in these patients may be harmful. The results of the present study confirm that patients with a poor liver function had a poor prognosis irrespective of treatment modality.

In this study, the most frequent complication in patients with ruptured HCC was esophageal variceal bleeding (13%). This occurred more frequently in patients who received emergency TACE than in those who received conservative treatment. In cirrhosis and hepatic malignancies, disorders of the coagulation pathway are frequent causes of portal vein thrombosis, resulting in esophageal varices. Arterial embolization may change the esophageal variceal pressure, resulting in bleeding after the procedure [23]. The incidence of gastrointestinal bleeding after TAE in patients with ruptured HCC was 21%, which was higher than the incidence of 5.5% reported by Lin et al [24], who investigated patients with HCC without rupture. This may have been due to the poorer liver function in patients with ruptured HCC than in those with nonruptured HCC.

The major cause of death after emergency TACE was hypovolemic shock. Of the 5 patients in the mortality group, 2 who had hypovolemic shock had received repeated embolization because of uncontrollable bleeding. Rerupture postembolization is another possible cause of rebleeding and subsequent need to redo the procedure. A rerupture rate of 35% after emergency embolization was reported by Ohtomo et al [25]. Acute hepatic failure was another life-threatening complication in patients with ruptured HCC who underwent emergency embolization. Hemorrhage causes hypoxia of the liver leading to liver failure. Repeated embolization was associated with a high risk for hepatic failure. An incidence of 2.1% was reported for acute hepatic failure after TAE [26]. In addition, hepatic failure after TAE is relatively common in patients with pre-existing poor liver function [27]. Although TAE provided effective hemostasis, the risk for hepatic failure in patients who received embolization was especially high [8,14,19,28]. Physicians considering emergency embolization should take the volume of reserve normal liver function into account. In this study, all the patients received TACE rather than TAE. A comparison of outcomes of TACE and TAE performed in patients with ruptured HCC has not been previously reported in literature. Theoretically, the results of arterial obstruction for controlling bleeding by embolization or chemoembolization should be similar. However, in clinical practice, TACE has been shown to be more effective in the treatment of HCC in nonrupture patients [29]. Whether there are differences in side effects between TAE and TACE requires further study.

None of our patients with ruptured HCC underwent emergency resection because most patients had more advanced tumor invasion and poor liver function. In addition, the tumor nodule was multiple in 38%, tumor size larger than 10 cm in 17%, and Child-Pugh class C was noted in 22% of patients. These patients were not thought to be good candidates for emergency hepatectomy. Undergoing difficult emergency resection results in increased blood loss or blood transfusion [21,22]. Perioperative blood transfusion has been related to shorter disease-free survival because of the immunosuppressive effect of transfusion [30]. Emergency liver resection has rarely been advocated

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of reported cases</th>
<th>No. of survival cases in different emergency treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Operation</td>
<td>Embolization</td>
</tr>
<tr>
<td>Ong and Taw [32]</td>
<td>42</td>
<td>47 (16/34)</td>
</tr>
<tr>
<td>Chearanai et al [3]</td>
<td>63</td>
<td>36 (13/36)</td>
</tr>
<tr>
<td>Hirai et al [28]</td>
<td>47</td>
<td>0</td>
</tr>
<tr>
<td>Hsieh et al [16]</td>
<td>17</td>
<td>71 (12/17)</td>
</tr>
<tr>
<td>Chen et al [10]</td>
<td>27</td>
<td>74 (20/27)</td>
</tr>
<tr>
<td>Lai et al [33]</td>
<td>60</td>
<td>29 (16/56)</td>
</tr>
<tr>
<td>Dewar et al [7]</td>
<td>41</td>
<td>34 (11/32)</td>
</tr>
<tr>
<td>Miyamoto et al [19]</td>
<td>172</td>
<td>54 (38/71)</td>
</tr>
<tr>
<td>Okazaki et al [34]</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>Xu and Yan [35]</td>
<td>87</td>
<td>39 (7/18)</td>
</tr>
<tr>
<td>Chen et al [5]</td>
<td>23</td>
<td>96 (22/23)</td>
</tr>
<tr>
<td>Ngan et al [14]</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>Yoshida et al [8]</td>
<td>18</td>
<td>100 (3/3)</td>
</tr>
<tr>
<td>Marini et al [21]</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>835</td>
<td>50 (169/335)</td>
</tr>
</tbody>
</table>

Values are presented as % (n) unless otherwise noted. Hyphens indicate insufficient information.
based on the reported high mortality rate and the poor long-term survival [15,31].

A review of emergency treatments for ruptured HCC reported in literature was conducted using PubMed. The database was searched for studies from 1970 to 2004 using "ruptured hepatocellular carcinoma" and "spontaneous rupture of hepatocellular carcinoma" as keywords. Studies involving 10 or more patients that clearly mentioned emergency treatment and survival rate were included in the review. Methods of treatment, patient numbers, and survival rates in the relevant studies were recorded (Table 4). There were 835 ruptured HCC reported in 15 studies from 1972 to 2004. Emergency operation, including resection, plication, packing, or hepatic artery ligation, was performed in 335 patients. Embolization or conservative treatment was applied in 216 and 222 patients, respectively. The 1-month survival rate was 50% in patients who underwent emergency operation, 62% in those who received emergency embolization, and 29% in patients who received conservative treatment. In this study, the 1-month survival rate in the conservative treatment group was higher than in the emergency TACE group (69% vs 59%). However, our review of literature revealed that 1-month survival rate in patients who received conservative treatment (29%) was lower than that in those who received emergency embolization (62%). The difference may be because conservative treatment was carried out in patients with contraindication for operation or who had previously received embolization. These patients’ conditions were poor, which resulted in a high mortality rate when they subsequently received conservative treatment. Bleeding from ruptured HCC was not always to exsanguination, so the symptoms may not have been so severe and the clinical course may have been indistinguishable from that of non-ruptured HCC. In this study, the time between admission and receiving emergency chemoembolization in the survival group was longer than that in the mortality group, indicating that embolization was not the main factor that determined prognosis. Mortality was not dependent on the immediate treatment. If the vital signs could be stabilized after resuscitation or transfusion, then conservative treatment at the ED was an option because there tended to be fewer complications.

There were several limitations in this study. First, this was a retrospective study and this may have affected the quality of the data. Second, the case number was relatively small, which limits the extent to which firm conclusions can be drawn. Finally, the duration of follow-up was relatively short, so it was not possible to determine the long-term outcomes of these different emergency treatments.

A prospective randomized control study is difficult to perform in ruptured HCC. In the present retrospective study, conservative treatment was a successful choice for ruptured HCC in some patients. Emergency TACE was performed in ruptured HCC with exsanguination. Routine emergency TACE may not be indicated because of the high incidence of complications, especially in patients with poor liver function.

References


Original Contribution

Pediatric health screening and referral in the ED

Leslie S. Zun MD, MBA\textsuperscript{a,b,*}, LaVonne Downey PhD\textsuperscript{c}

\textsuperscript{a}Department of Emergency Medicine, Rosalind Franklin University of Medicine and Science, Chicago Medical School, IL 60069, USA
\textsuperscript{b}Department of Emergency Medicine, Mount Sinai Hospital, IL 60608, USA
\textsuperscript{c}Roosevelt University, Chicago, IL 60605, USA

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Abstract

Introduction: Many studies have demonstrated the importance of performing preventive care in the ED. The primary objective of this study was to identify unmet health needs in the ED of the pediatric patient population. The secondary objective was to determine if the patient’s parent or guardian would accept health referrals and bring the child to follow up with a doctor.

Methods: Age- and sex-specific algorithms concerning preventive care were developed from the US Department of Public Health Clinicians’ Book of Preventative Health. A convenience sample of patients and their families who presented to the ED were asked to participate in the study. The exclusion criteria consisted of patients who were institutionalized, unstable, and had parents who were unable to communicate or declined to participate. After 1 week, the parents were followed up by telephone to find out if they had made an appointment with a doctor as recommended. One month after the ED visit, the health care’s computer system was queried to confirm that the appointment had been completed. Data were analyzed using SPSS (version 10.0; SPSS, Chicago, Ill), and tests of significance used were the Pearson $\chi^2$, frequency test, and crosstabs. This study was institutional review board–approved as exempt.

Results: Two hundred three pediatric patients were enrolled. Most of the patients had a primary care physician (87.1%, 176/203) and insurance (85.6%, 172/203). Only 25 (12.3%) of 203 needed any referrals, with an acceptance rate of 72.0% (18/25) and completion rate of 40% (10/25). The most frequent unmet need was for urine, lead, and anemia screening (19.4%, all 20/103). Few patients needed immunizations (1.0%, 2/203), alcohol screening (2.0%, 2/100), or blood pressure testing (3.0%, 3/100). Analysis of the correlation between getting 1 or more referrals and race was found to have a significant relationship ($\chi^2 = 19.69$, $df = 6$, $P = .003$) but not with sex, age group, insurance, or primary care physician ($P > .05$).

Conclusion: In this study, 12.3% of the patients were found to have unmet health care needs. Insurance status had no bearing on the need for referrals. Assessment in the pediatric population for unmet health care needs was found to be a low-yielding, labor-intensive process.

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1. Introduction

According to Healthy People 2010, section 14.24a, an important goal is to increase the proportion of young children who receive vaccines [1]. Immunization rates vary from state to state, from urban localities vs rural ones, and by ethnic groups. Various authors have found that the immunization rate of children is significantly less than the mandated 100%. In 1998, 73% of children received all vaccines recommended for universal administration [2]. National statistics for immunizations among children aged 19 to 35 months vary in urban areas from 63% to 87% [3]. McConnochie and Roghmann [4] found that the 27% of the youths whom they evaluated were missing 1 or more immunizations at age 4.4 years. They also found that ED records accounted for 18% of missed immunization opportunities.

Numerous authors have proposed preventive screening, testing, and treatment in the ED. The Society of Academic Emergency Medicine’s Public Health and Education Task Force generated a list of targeted ED interventions aimed at patients in the general and high-risk groups: screening, counseling, immunization, chemoprophylaxis, health promotion material, social services, and ED surveillance [5]. The Society of Academic Emergency Medicine’s Public Health and Education Task Force on Preventative Services found from evidence-based review that alcohol screening and intervention, HIV screening, identification of hypertension, pneumococcal vaccination, smoking cessation, and social services needs assessment and referral were useful [6]. Williams and others [7] found that, although emergency physicians feel responsible for promoting the health of their patients, few routinely screen and counsel patients on prevention and many were not confident of their ability to help their patients with respect to preventive care. Controversy exists as to the role of the ED in pediatric immunizations. Szilagyi and others [8] found that 30% of the surveyed pediatricians and family physicians recommended that immunizations be administered in the ED.

In response to the controversy, we postulated that identification and referral would be preferred to immunization and treatment in the ED. The primary purpose of this study was to determine if pediatric patients have unmet health care needs, as determined by the administration of a health screening and referral tool. The secondary purpose was to determine if the child would follow up with the clinic or doctor referrals.

2. Methods

The guidelines of the US Public Health Service were followed for age- and sex-specific screening and referral needs to develop algorithms for patient referrals [9]. The algorithms were age- and sex-based and questioned the patients’ parent or guardian about key examinations or immunizations. Patients were assigned to 1 of 3 groups based on age and sex: 0- to 10-year-old males/females, 11- to 18-year-old males, and 11- to 18-year-old females. Age and sex were the basis for whether to inquire about blood pressure, vision and hearing screening, immunizations, anemia, lead screening, sexually transmitted disease exposure, alcohol and substance use, tuberculosis, and cigarette smoking (Appendix A). The CAGE assessment tool for alcohol and drug use was used as the means to determine substance abuse problems [10,11]. The patients were referred to 1 of 3 resources: to their private physician, to a multispecialty group practice for unassigned patients with insurance coverage, or to a family medicine clinic for unassigned patients without coverage. The patient or patient’s care provider (ie, parent or guardian) was used as a source material with respect to the reporting of health care compliance.

A convenience sample of patients was approached, primarily during daytime, Monday through Friday, to determine their willingness to being interviewed for a health screening and referral program. The study was conducted in a level 1 pediatric and adult trauma center with a total of 45000 annual ED visits with approximately 25% pediatric patients. The ED is located in an inner city, African American and Hispanic neighborhood, with 40% of the patients on public assistance, 40% of the patients without any insurance, and 10% with commercial or managed care coverage. The inclusion criteria were all stable pediatric patients not in need of immediate intervention. The exclusion criteria eliminated institutionalized or unstable patients and those parents or guardians who were unable to communicate or refused to participate.

Research fellows administered the survey tool to the parents or guardians who agreed to participate in the health-screening program. Patients and their guardians were told that involvement in this program was voluntary and at any time they could stop or withdraw from the study. Participants were told “Welcome to the Emergency Department. This survey is a health screening and referral interview. It will take about 10 to 15 minutes to complete. You will be asked questions about your physical health and the healthcare that you receive. After you have answered all of the questions, you will get your results and referral recommendations. If you agree, we will assist you in obtaining referrals and a copy of this survey will be given to you. Involvement in this program is voluntary and at any time you can stop or withdraw from the study.” The research fellow completed the patient data collection sheet and selected the correct algorithm for the patients’ sex and age group. If the patient had a doctor, they get referred back to their doctor with the referral sheet. If the patient had any sort of insurance (including public aid), they will get a referral to a system clinic, and if they did have any insurance coverage, the patient will be referred to a federally qualified health care clinic. The patient is given a copy of the results, with the referrals listed for each medical problem. The patient is
called after 1 week to determine whether the patient has made an appointment. One month later, the health care system computer was queried to determine if the patient followed up with a health care provider in the health care system. The health care system computer provides visit history for patients seen in the hospital, outpatient clinics, and 50 primary care clinics associated with the health care system, including those that are federally qualified.

The data were inputted into an SPSS file (SPSS, version 10.0; Chicago, Ill) based on the number of items that screened positive, the primary care provider, demographic data, need for services, agreement to the assessment and referral, types and number of referrals, acceptance of referrals, and appointments made with physicians. A convenience sample was obtained to have a sample of at least 50 patients in each age/sex group. The data were analyzed to determine if there were any correlations between age, sex, insurance coverage, health care needs and referrals, number and acceptance of referrals, and actual follow-up. Age and sex groups were lumped in the analysis because of the small number of patients with unmet health care needs. Pearson $\chi^2$ analysis was used because of the categorical nature of most variables. The study was institutional review board–approved as exempt because it is for an “improvement in the current provision of medical care.”

### 3. Results

A total of 210 patients in the ED were approached for the study. The parents or guardians of 7 patients refused to enroll in the study, 3 stated they were not interested, and 4 refused to sign Health Insurance portability and accountability consent form. The demographic profile of the patients surveyed consisted of the following: half were males; 89 (46.1%) of 203, African American; 101 (51.8%) of 203, Hispanic; and 2 (1.0%) of 203, white (Table 1). Most of the patients had a primary care physician (87.1%, 176/203) and insurance (85.6%, 176/203). Only 25 (12.3%) of 203 needed any referrals, with an acceptance rate of 72.5% (18/25) and completion rate of 40.0% (10/25) (Table 2). The most frequent unmet need was for urine, lead, and anemia screening (19.4%, all 20/103) (Table 3). Few patients needed immunizations (1.0%, 2/203), alcohol screening (2.0%, 2/100), or blood pressure testing (3.0%, 3/100).

Because of the categorical and dichotomous nature of most variables, a Pearson $\chi^2$ test was used. Analysis of the correlation between getting 1 or more referrals and race revealed a significant relationship ($\chi^2 = 19.69, df = 6, P = .003$) but not with sex, age group, insurance status, or

### Table 1  Demographic results

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 203)</th>
<th>Aged 0-10 y (n = 103)</th>
<th>Aged 11-17 y (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>101 (50.0)</td>
<td>51 (49.5)</td>
<td>50 (50.0)</td>
</tr>
<tr>
<td>Female</td>
<td>101 (50.0)</td>
<td>52 (50.5)</td>
<td>50 (50.0)</td>
</tr>
<tr>
<td>Missing data</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>89 (46.1)</td>
<td>37 (35.9)</td>
<td>52 (52.0)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>101 (51.8)</td>
<td>61 (59.2)</td>
<td>40 (40.0)</td>
</tr>
<tr>
<td>White</td>
<td>2 (1.0)</td>
<td>1 (9.7)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.0)</td>
<td>2 (1.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>9 (4.5)</td>
<td>2 (1.9)</td>
<td>7 (7.0)</td>
</tr>
<tr>
<td><strong>PCP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>176 (87.1)</td>
<td>95 (92.2)</td>
<td>81 (81.0)</td>
</tr>
<tr>
<td>No</td>
<td>27 (12.9)</td>
<td>8 (7.8)</td>
<td>19 (19.0)</td>
</tr>
<tr>
<td><strong>Insurance status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>172 (85.6)</td>
<td>96 (93.2)</td>
<td>76 (76.0)</td>
</tr>
<tr>
<td>No</td>
<td>23 (10.9)</td>
<td>7 (6.8)</td>
<td>16 (16.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>7 (3.5)</td>
<td>8 (8.0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as n (%). AA indicates African American; PCP, primary care physician.

### Table 2  Referrals

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 203)</th>
<th>Aged 0-10 y (n = 103)</th>
<th>Aged 11-17 y (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of referrals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>87.6 (178/203)</td>
<td>87.4 (90/103)</td>
<td>88.0 (88/100)</td>
</tr>
<tr>
<td>1-3</td>
<td>11.9 (24/203)</td>
<td>11.7 (12/103)</td>
<td>12.0 (12/100)</td>
</tr>
<tr>
<td>4-8</td>
<td>0.5 (1/203)</td>
<td>9.7 (1/103)</td>
<td>0.0 (0/100)</td>
</tr>
<tr>
<td><strong>Accepted referral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>72.0 (18/25)</td>
<td>92.3 (12/13)</td>
<td>55.5 (6/11)</td>
</tr>
<tr>
<td>No</td>
<td>20.0 (5/25)</td>
<td>0.0 (0/13)</td>
<td>45.5 (5/11)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8.0 (2/25)</td>
<td>7.7 (1/13)</td>
<td>0.0 (0/11)</td>
</tr>
<tr>
<td><strong>Made appointment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40.0 (10/25)</td>
<td>61.5 (8/13)</td>
<td>16.7 (2/12)</td>
</tr>
<tr>
<td>No</td>
<td>44.0 (11/25)</td>
<td>30.8 (4/13)</td>
<td>58.3 (7/12)</td>
</tr>
<tr>
<td>Uncertain</td>
<td>16.0 (4/25)</td>
<td>7.7 (1/13)</td>
<td>25.0 (3/12)</td>
</tr>
<tr>
<td><strong>Confirmed appointment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed</td>
<td>40.0 (10/25)</td>
<td>53.9 (7/13)</td>
<td>25.0 (3/12)</td>
</tr>
<tr>
<td>No follow-up</td>
<td>48.0 (12/25)</td>
<td>23.1 (3/13)</td>
<td>75.0 (9/12)</td>
</tr>
<tr>
<td>Unable to find</td>
<td>8.0 (2/25)</td>
<td></td>
<td>0.0 (0/12)</td>
</tr>
</tbody>
</table>

Values are expressed as % (n).

### Table 3  Rank order of positive screenings

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 203)</th>
<th>Aged 0-10 y (n = 103)</th>
<th>Aged 11-17 y (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urine screening</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead</td>
<td>19.4 (20/103)</td>
<td>19.4 (20/103)</td>
<td></td>
</tr>
<tr>
<td>Anemia testing</td>
<td>19.4 (20/103)</td>
<td>19.4 (20/103)</td>
<td></td>
</tr>
<tr>
<td>Hearing testing</td>
<td>14.6 (15/103)</td>
<td>14.6 (15/103)</td>
<td></td>
</tr>
<tr>
<td>Vision testing</td>
<td>14.6 (15/103)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papanicolaou smear</td>
<td>10.0 (2/20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexually transmitted disease</td>
<td>10.0 (3/29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes</td>
<td>10.0 (10/100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug Abuse</td>
<td>4.0 (4/100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>3.0 (3/100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3.0 (6/203)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.0 (2/100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunizations (aggregated)</td>
<td>1.0 (2/203)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as % (n).
primary care physician ($P > .05$) (Table 4). Acceptance of the referral was correlated with insurance status ($\chi = 10.606$, $df = 4$, $P = .031$) and not with sex, age group, race, or primary care physician ($P > .05$). None of the variables were correlated with actual follow-up ($P > .05$).

### 4. Discussion

Contrary to the findings of several other studies, this study demonstrated that only a relatively small population of ED pediatric patients has unmet health care needs. We cannot explain why this study had a low rate of needed immunizations when other authors found that the unimmunized rate was 27% [4]. The study found relative need for urine, anemia, and lead screening (19.4%). Therefore, screening of ED pediatric patients overall in this study had a low yield.

The study was performed by research fellows rather than ED staff because of their limited time in a busy level 1 trauma center. We found that continuation of the screening and referral process, either by the ED staff or research personnel, would be labor-intensive and costly. There may be value in determining the health care needs of a population using less costly means. A recent study at the University of Chicago demonstrated that ED patients are willing and interested in participating in a self-assessment and health education study while waiting to be seen in the ED. The major goal of this program was to demonstrate that patients would be willing to be educated on health risk topics [12]. Another study used a computer-directed assessment of patients’ medical needs before surgery [13]. Kempner [14] used a self-administered questionnaire for psychosocial screening in the pediatric age population. Lutner et al [15] found that patients would use a small handheld device to answer health-related questions. It is uncertain whether the conversion of the staff-administered health screening and referral program to a self-directed computer program would be used and would alleviate the cost involved in administering the program. Gregor and others [16] used an interactive computer program in the ED in an attempt to prevent alcohol misuse among adolescents.

The study was based on the recommendations promulgated by the US Department of Public Health’s Task Force on Preventive Care [9]. However, there is some dispute as to the proper preventive recommendations for children. Elstel [17] performed an analysis of 5 organizations and found that all groups recommended immunizations and screening for health issues such as hypertension, obesity, and tobacco use. We did not survey for birth-related testing for hemoglobinopathy, phenylalanine level, thyroxine resin uptake, thyroid-stimulating hormone, or interventions for high-risk populations. The study did not address the need for counseling for injury prevention, sexual behavior, diet and exercise, substance use, or dental care. We did not screen for HIV/AIDS and violence exposure or victimization because they were not among the recommendations of the US Department of Public Health, despite the epidemic levels of those diseases in the community studied. Although the National Depressive and Manic-Depressive Association recommend age-appropriate screening and diagnosis of children and adolescents with these disorders, they were not addressed in this study [18]. It would be valuable to develop screening tools and determine the best means to assess for these conditions that are prevalent in the community served by the sample ED population.

The health care assessments were based on the US Department of Public Health recommendations [9]. Not all the recommendations were sufficiently straightforward; several required some interpretation. Standard questions to perform the health care assessment were not found in the recommendation and were developed for the survey. The survey tool used in this study was not validated. The assessment for alcohol and substance abuse was not provided in the recommendations; therefore, the CAGE assessment was used.

There are many other limitations to this study. The convenience sample of the patients in the inner city may not properly represent the general population in the United States. The study was performed primarily during the weekdays, limiting its generalization to the rest of the week. The study was limited by the number of respondents in each group for analysis purposes. Parents and guardians who did not respond or refused to enroll in the study also limited the value of the results. The study was dependent upon the parents or guardians to provide the source information concerning immunizations and other health care issues.

However, Goldstein and others [19] found that there were a large number of inaccurate assessments of children immunization status in the ED. In a study with a similar conceptual framework, Vaughan and others [20] screened

<table>
<thead>
<tr>
<th>Referral, yes or no, and Acceptance of referrals and Followed up and</th>
<th>$z$</th>
<th>$df$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>4.115</td>
<td>4</td>
<td>.391</td>
</tr>
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<td>Race</td>
<td>19.69</td>
<td>6</td>
<td>.003</td>
</tr>
<tr>
<td>Age group</td>
<td>19.839</td>
<td>18</td>
<td>.342</td>
</tr>
<tr>
<td>Insurance</td>
<td>7.966</td>
<td>6</td>
<td>.241</td>
</tr>
<tr>
<td>PCP</td>
<td>5.175</td>
<td>3</td>
<td>.159</td>
</tr>
<tr>
<td>PCP</td>
<td>2.831</td>
<td>2</td>
<td>.243</td>
</tr>
<tr>
<td>PCP</td>
<td>5.175</td>
<td>3</td>
<td>.159</td>
</tr>
<tr>
<td>Acceptance of referrals and Followed up and</td>
<td>PCP</td>
<td>15.412</td>
<td>8</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Race</td>
<td>19.442</td>
<td>4</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Age group</td>
<td>17.341</td>
<td>12</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Insurance</td>
<td>10.606</td>
<td>4</td>
</tr>
<tr>
<td>Followed up and</td>
<td>PCP</td>
<td>2.831</td>
<td>2</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Sex</td>
<td>2.114</td>
<td>3</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Race</td>
<td>15.412</td>
<td>8</td>
</tr>
<tr>
<td>Followed up and</td>
<td>Age group</td>
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<td>24</td>
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<tr>
<td>Followed up and</td>
<td>Insurance</td>
<td>12.925</td>
<td>8</td>
</tr>
<tr>
<td>Followed up and</td>
<td>PCP</td>
<td>15.412</td>
<td>8</td>
</tr>
</tbody>
</table>
youth in schools and referred the youth to a clinic for follow-up. The tool that they developed had a moderate amount of false positives through single-item identification. Referrals were made to services in the health care system, but the quality of the services provided was not determined. The study did determine if the appointment was made but did not determine if the appointment was completed and whether the required test or immunization was actually performed. The study used an unvalidated set of questions to assess the patients’ unmet health care needs.

5. Conclusion

Few patients in this study proved to have had unmet health care needs. This study demonstrated that screening pediatric patients in the ED for unmet health care needs is resource-intensive and has a low yield, providing an unfavorable cost benefit ratio. The study was based on the interpretation of US Public Health Service criteria for age-based health care needs.

Acknowledgments

We thank Olga Borisovsky for her assistance with patient enrollment.

Appendix A. Screening performed by age and sex

<table>
<thead>
<tr>
<th></th>
<th>Aged 0-10 y, male/female</th>
<th>Aged 11-17 y, male</th>
<th>Aged 11-17 y, female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Vision testing</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hearing testing</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia testing</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sexually transmitted disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Drug abuse</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>DPT</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Polio</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HiB</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DPT indicates diphtheria-pertussis-tetanus; MMR, measles, mumps, and rubella; HiB, Haemophilus influenzae type B; X, used in screening test.

References

Original Contribution

Lumbar puncture needle length determination

Keith K. Abe MD, MSa, Loren G. Yamamoto MD, MPH, MBAa,b,*, Erick M. Itoman MDa,b, Terri A.F. Nakasone RNb, Stacy K. Kanayama MDb

a Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, HI 96826, USA
b Emergency Department, Kapiolani Medical Center For Women And Children, Honolulu, HI 96826, USA

Received 18 February 2005; accepted 5 March 2005

Abstract

Introduction: Appropriate lumbar puncture (LP) needle length selection may be more difficult for less experienced practitioners or for patients who are of unusually large or small body habitus. The purpose of this study is to determine if there is a relationship between body height and weight, and the percutaneous depth to the spinal canal, which can more reliably assist in selecting an LP needle length.

Methods: This is a retrospective cohort study of patients who received an abdominal computed tomographic scan (for any reason) from July 1999 to December 2000. Lumbar puncture depth was measured on the computed tomographic scan and was used to derive a formula.

Results: The final data pool consisted of 175 patients, aged 25 days to 80 years, with height of 48 to 181.5 cm, weight of 3.0 to 127.3 kg, and body mass index of 11.7 to 49.7 kg/m². Using this data set, the formula for predicting the required LP depth is (weight in kilograms, height in centimeters):

\[
\text{LP depth (cm)} = 1 + \frac{17}{\text{weight/height}}
\]

Using linear regression comparing the skin to mid–spinal canal depth measurements with the calculated LP depths, \(R^2\) was 0.81 (\(P < .001\)). This formula selected a needle that was too short in 6% (less than that of 4 other previously published LP needle length selection methods) and a needle that was too long in 31%.

Conclusion: Compared with other formulas, this formula might be a more reliable predictor for estimating the required LP needle length, but this must be validated by further studies. It should be noted that none of the formulas were perfect.

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1. Introduction

Lumbar puncture (LP) is a common procedure performed in the diagnostic evaluation of patients at risk for meningitis, encephalitis, subarachnoid hemorrhage, and other neurologic conditions. Lumbar puncture is also performed therapeutically in some instances. Standard LP needles come in 1.5, 2.5, 3.5 and 5.0 inch lengths (3.8, 6.4, 8.9, and 12.7 cm, respectively). Selection of LP needle length is typically based on experience; however, an unusually obese or cachectic patient may pose more of a challenge. Appropriate LP needle selection may be more difficult for less experienced practitioners or
for patients who are of unusually large or small body habitus.

For example, which LP needle length would be most appropriate for a 15-year-old, 110-kg, 168-cm man who presents to the ED with short-onset fever, headache, and nuchal rigidity?

In searching for published recommendations on LP needle length selection, 4 references were identified [1-4]. Bonadio et al [1] described 158 children aged 1 to 18 years. They derived a formula based on body surface area (BSA):

\[
\text{Depth of LP (cm)} = 0.77 \text{ cm} + 2.56 \times \text{BSA (m}^2\text{)}.
\]

Craig et al [2] described 107 children aged 0 to 16 years. They derived a formula based on height alone:

\[
\text{LP depth (cm)} = \text{height (cm)} \times 0.03.
\]

Hasan [3] described 586 children (age range not specified). He derived a formula based on weight alone:

\[
\text{Epidural depth (cm)} = 0.8 + 0.05 \times \text{weight (kg)}.
\]

Henretig and King [4] published a textbook recommendation as an empirical estimate of LP needle length provided as a function of age. For premature infants and term newborns to 2-year-old children, 1.5-in needles are recommended. For children aged 3 to 12 years, 2.5-in needles are recommended. For those older than 12 years, 3.5-in needles are recommended. A footnote that “larger needles may be required depending on patient habitus” was included.

The purpose of this study is to determine if there is a relationship between body height and weight and the percutaneous depth to the spinal canal, which can more reliably assist in selecting an LP needle length.

2. Methods

This is a retrospective cohort study of patients who received an abdominal computed tomographic (CT) scan (for any reason) from July 1999 to December 2000. The CT scans were reviewed, and at the level of the iliac crest, the following distances were measured as noted in Fig. 1:

(1) skin overlying the spine to the posterior margin of the spinal canal (depth to posterior canal) and (2) posterior to anterior margin of the spinal canal (depth of spinal canal).

Age, sex, height, and weight were recorded from the CT and medical records. Those who did not have a height and weight documented on their chart within 3 days of the CT were excluded.

Lumbar puncture depth was defined as the distance from the skin at the midline of the back to the center of the spinal canal (ie, the depth to the posterior canal + half the depth of the spinal canal). Relationships to patient height and weight (eg, height/weight, height/weight^2, [height/weight]^2, [height/weight]^3), as well as established parameters noted previously (BSA, height, weight, and age), were studied by regression analysis. The best predictive formula for measured LP depths was thus derived.

The predictive formulas from the studies mentioned previously were then compared with the formula derived in this study. Patient body parameters were used to estimate a predicted needle length, and this was compared with the distance measured on CT. The predicted needle length was considered “too short” if the needle would be unable to reach the spinal canal based on CT measurements. The predicted needle length was considered “too long” if a shorter needle, which would have reached the spinal canal, could have been used. The results for each of the different predictive formulas were compared.

3. Results

The final data pool consisted of 175 patients aged 25 days to 80 years (median, 16 years; mean, 20.0 ± 15.2 years). Height ranged from 48 to 181.5 cm (median, 153.5 cm; mean, 143.8 ± 28.4 cm). Weight ranged from 3.0 to
mass index (BMI) ranged from 11.7 to 49.7 kg/m² (median, 127.3 kg (median, 52.7 kg; mean, 51.3 kg). Body mass index (BMI) ranged from 11.7 to 49.7 kg/m² (median, 127.3 kg (median, 52.7 kg; mean, 51.3 kg).

Using this data set, the formula for predicting the required LP depth is (weight in kilograms, height in centimeters)

\[
\text{LP depth (cm)} = 1 + 17 \times \frac{\text{weight}}{\text{height}}.
\]

This will be referred to as the Abe (pronounced ah-beh) formula during this report to distinguish this from the formula described by other study authors. To obtain the depth in inches (since LP needle lengths come in inch length values), this value should be divided by 2.54 cm/in. Using linear regression comparing the skin to mid–spinal canal depth measurements with the calculated LP depths, \( R^2 \) was 0.81 (\( P < .001 \)) (Fig. 2). Table 1 compares the \( R^2 \) values of the different LP needle length determination methods, published from their original data sets, and the newly calculated \( R^2 \) values using this current data set. The formulas of Bonadio et al [1] and Hasan [3] have high \( R^2 \) values as well.

When the other LP needle length determination methods were compared with the Abe formula using the height, weight, and LP depth measurements from the current data set, the frequency of selecting needles that are too short or too long was determined and tabulated in Table 2. The other LP needle length determination methods had high frequencies of selecting LP needle lengths that were too short. The Abe formula had the lowest number of needles that were too short. However, 31% of the time, the Abe formula selected a needle that was too long.

The age distribution for the 2 other studies for which the age distribution is provided [1,2] (see Table 3) consisted mostly of infants (65% [1] in one study and 71% [2] in the other study). The other 2 studies did not provide an age distribution of their patient study group. Our study had a much broader age representation. Table 4 stratifies needle selection miss rates (too short or too long) by age groups. This shows that the Abe formula still has the lowest rates of avoiding needles that are too short in all age groups.

### Table 1 Comparison of \( R^2 \) values published from their original data sets

<table>
<thead>
<tr>
<th>Study</th>
<th>( R^2 )</th>
<th>( P )</th>
<th>Calculated ( R^2 ) using current data set (( P &lt; .001 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abe et al (wt/ht)</td>
<td>0.81</td>
<td>&lt;.001</td>
<td>0.81</td>
</tr>
<tr>
<td>Bonadio et al [1] (BSA)</td>
<td>0.93</td>
<td>N/A</td>
<td>0.74</td>
</tr>
<tr>
<td>Craig et al [2] (ht)</td>
<td>0.8</td>
<td>&lt;.01</td>
<td>0.79</td>
</tr>
<tr>
<td>Hasan [3] (wt)</td>
<td>0.8</td>
<td>&lt;.01</td>
<td>0.79</td>
</tr>
<tr>
<td>Henretig and King [4]</td>
<td>N/A</td>
<td>N/A</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Linear regression compares the calculated needle depth with the measured (on CT scan) needle depth from the skin to the center of the spinal canal. wt indicates weight; ht, height; N/A, not available.

### Table 2 Frequency of selecting LP needles that are too short or too long using LP depth data from this data set

<table>
<thead>
<tr>
<th>Study</th>
<th>Too short</th>
<th>Too long</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abe et al [1]</td>
<td>1 (1)</td>
<td>97 (55)</td>
</tr>
<tr>
<td>Bonadio et al [1] (BSA)</td>
<td>54 (31)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Craig et al [2]</td>
<td>3 (15)</td>
<td>19 (55)</td>
</tr>
<tr>
<td>Hasan [3]</td>
<td>53 (30)</td>
<td>87 (50)</td>
</tr>
<tr>
<td>Henretig and King [4]</td>
<td>75 (71)</td>
<td>7 (4)</td>
</tr>
</tbody>
</table>

Using the posterior margin of spinal canal (end of the length barely reaches the dural sac)

- Too short: 1 (1)
- Too long: 97 (55)

Using midpoint of spinal canal (end of the length ends up in the middle of the dural sac)

- Too short: 54 (31)
- Too long: 87 (50)

### Table 3 Age distribution of LP needle length determination study groups

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-1</td>
</tr>
<tr>
<td>Abe et al</td>
<td>175</td>
</tr>
<tr>
<td>Bonadio et al [1]</td>
<td>158</td>
</tr>
<tr>
<td>Craig et al [2]</td>
<td>107</td>
</tr>
<tr>
<td>Hasan [3]</td>
<td>586</td>
</tr>
<tr>
<td>Henretig and King [4]</td>
<td>No age distribution given (empirical)</td>
</tr>
</tbody>
</table>

* These numbers are estimates. In the study, no age distribution was given, but the age distribution can be estimated based on the average age for height on standard growth charts.

### Table 4 Frequency of selecting LP needles that are too short or too long using LP depth data (using the midpoint of the spinal canal) stratified by age groups

<table>
<thead>
<tr>
<th>Study</th>
<th>0-24 mo (n = 11)</th>
<th>2-5 y (n = 18)</th>
<th>6-12 y (n = 41)</th>
<th>13-18 y (n = 33)</th>
<th>≥19 y (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too short</td>
<td>0 (1)</td>
<td>0 (6)</td>
<td>1 (2)</td>
<td>2 (6)</td>
<td>8 (11)</td>
</tr>
<tr>
<td>Too long</td>
<td>6 (33)</td>
<td>6 (33)</td>
<td>6 (33)</td>
<td>15 (45)</td>
<td>18 (25)</td>
</tr>
</tbody>
</table>

Values are presented as n (%).
4. Discussion

The selection of an appropriate LP needle length for a patient is often based upon a physician’s previous experience. Such a valuable judgment tool, however, is lacking in physicians who have not done many LPs. Also, this experience is probably not applicable to patients of unusual body habitus. Accurate selection of LP needles is important to optimize patient care. Selecting a needle that is too short subjects the patient to unnecessary trauma with an excessive number of attempts and duration of the procedure. Selecting a needle that is too long increases the technical difficulty of the procedure because inserting short needles is easier than inserting long needles.

The Abe formula in this study appears to be more reliable for selecting needle lengths in comparison with previously published formulas. Because our data set is that used to derive this Abe formula, it is expected that the “best” formula would be derived to fit our set of data (the derivation data set). Thus, it cannot be assumed that our Abe formula is the best until it is validated by a separate data set (a validation data set).

A study that does not include many older children and adults will not be able to derive an accurate formula for the older children and adults. In general, for infants and children younger than 2 years, needle selection is more standardized because there is less body size variability (compared with teens and adults), resulting in less variability in the LP depth. Our Abe formula is based on a broader age distribution of patients (pediatric and adults, with infants comprising <5% of the study group). Formulas that are derived from a cohort lacking obese study subjects will probably be less accurate for obese patients. Our Abe formula is based on a broad BMI study group. Body mass index distribution among the other 4 studies was not disclosed in the other 4 publications, but it is likely that the 2 studies dominated by infants [1,2] are not very likely to have a wide range of BMI values.

Using our study data, the Abe formula had the lowest number of needles that were too short, yet the Abe formula selected a needle that was too long 31% of the time. In examining the rates of selecting a needle that is too short, vs too long, there is a trade-off with no needle selection method being close to perfect in avoiding both too short and too long needles. However, it would be preferable to choose a needle that is too long rather than a needle that is too short. The other formulas frequently selected needles that were too short. In theory, this could be corrected by adding a constant (eg, 1 cm) to the formulas. This would reduce the formula’s rate of selecting a needle that is too short while increasing the formula’s rate of selecting a needle that is too long. Because the $R^2$ values for the Abe formula and the formulas of Bonadio et al [1] and Hasan [3] were roughly similar, it is likely that once this correction is made to the formulas of Bonadio et al [1] and Hasan [3], their frequencies of selecting a needle that is too short would decline and they would probably be similar to the Abe formula. Because the formulas of Bonadio et al [1] and Hasan [3] were derived with predominantly small children, their constant might have been too small.

This study includes some limitations. (1) Heights and weights may not routinely be obtained in an ED (although they are not difficult to obtain). (2) And, the compatibility of CT measurements with the actual LP procedure may be questioned. One concern is that there is a difference in angulation of approach to the spinal column for an actual LP procedure in contrast to the perpendicular distance measured on CT. This small angulation or parallax error is likely negligible because the ratio of the 2 distances approaches 1.0 when the parallax error angle is small. Another concern for a CT measurement is that the soft tissue distance to the spinal canal for a patient in a flexed position might be less than that for a patient lying supine for a CT. Although flexing the spine will widen the spaces between spinous processes, it is unlikely that flexion will substantially decrease or increase the thickness of the soft tissues and, hence, the distance from the skin to the spinal column. The supine position of the patient in a CT scanner could similarly affect the distance from the skin to the spinal canal.

Another observation in the study was that, despite a considerable range of patient ages (1 month–80 years) and sizes, there was relatively little variation in anterior-posterior spinal canal dimensions. The range of the spinal canal depth (distance from the anterior to the posterior aspect of the spinal canal) measured on CT was 1.0 to 2.6 cm with a mean of 1.6 ± 0.28 cm.
Our study did not include patients with musculoskeletal deformities, which can severely affect the ratio of weight to height more so than obesity alone. For example, patients with severe spinal deformities were not included in this study. This formula should not be extrapolated to such patients.

Considerations for future study include a validation data set of CT scans of varying body sizes to determine the accuracy of the Abe formula. Currently, clinicians select an LP needle length using current clinical standards. Based on the data set of CT scan measurements in this study, these 4 published clinical standards [1-4] are likely to have a moderate degree of inaccuracy. Although not yet validated, application of the current Abe formula might be helpful, especially in obese patients, but the true utility of the Abe formula cannot be determined until further validation studies are completed.

In the clinical scenario described in the Introduction for a 110-kg, 166-cm man, an intern selected a 3.5-in needle. However, the Abe formula predicts a distance of 12.3 cm (4.8 in). Thus, a 5-in needle was used instead.

In conclusion, the depth to the spinal canal had a better correlation with patient weight-height ratio than with the individual variables of age, BSA, height, or weight that were used in other published studies. The Abe formula, LP depth = 1 + 17 \times \frac{\text{weight/height}}{C^2}$, might be a more reliable predictor for estimating the required LP needle length, but this must be validated by further studies. This formula resulted in significantly fewer estimates that were too short or too long for entry into the spinal canal of study subjects in comparison with other published formulas. This formula might be more useful for less experienced practitioners in selecting LP needles and/or when selecting an LP needle length for obese patients. It should be noted that none of the formulas were perfect. Selecting a needle that is too short occurs more frequently with obese patients. It is prudent to select a longer needle for an obese patient if the formula calculates a depth that is barely within the range of the needle at hand.

References

Acoustic reflectometry esophageal profiles minimally affected by massive gas ventilation

David T. Raphael MD, PhD, Peter Crookes MD, PhD, Dimiter Arnaudov MD, Maxim Benbassat MD

Department of Anesthesiology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA
Department of Surgery, The Esophagus Center, University of Southern California, Los Angeles, CA 90033, USA

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Abstract Acoustic reflectometry can be used to distinguish between breathing tube placement in an esophagus vs the trachea via characteristic area-distance profiles for both cavities. In the cardiopulmonary resuscitation setting, capnography may be useless because the patient has little or no pulmonary circulation. With the breathing tube in the esophagus, can massive ventilation with a manual resuscitation bag, as might occur in the cardiopulmonary resuscitation setting, markedly alter the form of the obtained esophageal reflectometry profile? Nine hounds were induced, endotracheally intubated, mechanically ventilated, and anesthetized. Area-distance profiles were obtained with a 2-microphone acoustic reflectometer customized to measure areas up to 50 cm. Acoustic reflectometer profiles were obtained in intubated esophagi as follows: (1) baseline nonventilated state, (2) after aggressive 2-handed manual ventilation with high inspiratory pressures, rapid respiratory rates, and large tidal volumes for periods of 0.5, 1, and 1.5 minutes, upon detachment of the resuscitation bag, and (3) after esophagogastric decompression. We hypothesized that massive gas ventilation has no effect on the esophageal peak areas (null hypothesis), and used a paired $t$ test for statistical significance ($P < .05$). For times of 0.5, 1.0, and 1.5 minutes, the ventilation volumes (mean ± SD) were 25 ± 7, 49 ± 8, and 70 ± 18 L. Massive gas ventilation caused minimal broadening and slight distal spread of the basal “hump.” The mean peak area change was 0.18 ± 0.35 cm². For a paired $t$ test ($n = 9, df = 8$), the corresponding $t$ value was 1.54, with a $P$ value of .16, which was incompatible with the null hypothesis. The experimental observations indicate a minimal effect of massive gas ventilation on the acoustic reflectometry esophageal profile. Hence, operator recognition of the altered canine acoustic reflectometer profile as that of an esophageal cavity is maintained, indicating that acoustic reflectometry may be useful in correctly identifying the site of breathing tube placement in out-of-hospital cardiac arrest situations despite massive esophageal ventilation.

1. Introduction

Acoustic reflectometry [1,2] is a technique for the analysis of reflected sound waves within a hollow tube to estimate the inner cross-sectional area at any given distance into the tube. In the context of anesthesia, this capability can...
be used to distinguish between signals arising from the trachea and the esophagus because the characteristic area-distance profiles are quite different for these 2 structures. For a human endotracheal tube (ETT) airway cavity, the profile shows constant cross-sectional area throughout the length of the ETT, followed by a rapid rise in the area past the carina (see Fig. 1A) [3]. For a human esophageal intubation, the profile shows constant cross-sectional area throughout the length of the ETT, followed by a sudden decrease in the cross-sectional area (see Fig. 1B). This occurs because the nonrigid human esophagus is soft and collapses around the distal end of the ETT, thereby preventing further transmission of the acoustic impulse down the cavity.

In a study of human cavity recognition with 2-microphone acoustic reflectometry in the operating room setting [4], 198 of 200 tracheal intubations were correctly identified (99% success rate), as were all 14 esophageal intubations (100% success rate).

Acoustic reflectometry does not rely on detection of carbon dioxide to distinguish between an esophageal and an endotracheal intubation. This is vital in the cardiopulmonary arrest setting, when capnography may be useless because the patient has little or no pulmonary circulation and, therefore, may not produce a detectable amount of exhaled carbon dioxide [5].

The esophageal detector device (EDD) consists of a syringe or suction bulb that, after intubation, attaches to an ETT adapter. Studies have demonstrated the high reliability of the EDD in adult patients undergoing anesthesia in the operating room setting [6-8]. In out-of-hospital patients with cardiac arrest, however, with vomitus or blood in the airways, the EDD failed to confirm ETT placement in more than 25% of patients [9]. Other reported drawbacks include a slow inflation of the suction bulb, lasting as long as 30 seconds [10], and inability to use the device in children younger than 1 year owing to a failure rate of 25%, even with a small modified syringe [11]. In response to the application of suction, the lower airway in infants and children collapses easily. Hence, the Pediatric Advanced Life Support manual states that there is insufficient data to recommend routine use of an EDD in infants and non-adolescent children [12]. By comparison, the acoustic reflectometer (AR) does not produce any suction effect and does not cause tracheal collapse in children.

In a cadaver study [13], Toomey syringe aspiration was shown to be inaccurate in detecting esophageal intubation after gastric insufflation with 10 breaths with an Ambu bag through an esophageally placed ETT. The Toomey syringe uses an aspiration threshold of 20 mL, with minimal resistance as an indication of tracheal tube placement. Subsequent to gastric insufflation, the mean volume of air aspirated from esophageally placed ETTs was 35.4 mL (above the syringe threshold) vs 13.7 mL without insufflation. Furthermore, operators determined position in only 58% (15/26) of cadavers after insufflation vs 100% (26/26) of cadavers not undergoing gastric insufflation [13].

Given the previous difficulties with EDDs, it is appropriate to explore the possible use of an AR in a simulated cardiopulmonary resuscitation setting involving massive gas insufflation. The reflectometer, through its area-distance profiles, allows a “quick look” into the cavity and may be helpful in this regard.

During human endoscopic procedures, it is commonly observed that modest gas insufflation by the endoscopist expands the esophagus to a diameter corresponding to that of the endoscope itself. One theoretical concern is whether, with a breathing tube in the esophagus, aggressive massive ventilation with a manual reservoir bag might markedly alter the shape of the reflectometry profile such that it would not be readily recognizable as that of an esophageal intubation. Endoscopy per se can provide a qualitative impression of this evident esophageal distensibility, but it cannot provide any quantifiable measure as to how a reflectometry measurement might be affected. Because it would not be permissible to conduct a massive gas insufflation study in humans, we performed a series of
experiments in dogs with an AR to measure the extent of esophageal distension.

Humans usually have a collapsed esophagus. However, dogs generally exhibit passive distension of the esophagus in their basal state, as confirmed by radiographs of anesthetized dogs, which show a passively dilated esophagus with regurgitated stomach gas [14]. It should be noted that the carnivore esophagus of the dog is able to markedly distend its diameter to accommodate large chunks of meat and bone fragments.

A canine model was chosen because the dog esophagus has been well studied and its similarities to the human esophagus are well known. In particular, the lower esophageal sphincter (LES) can undergo transient LES relaxations (TLESRs) in the face of gastric distension [15].

2. Materials and methods

We hypothesized that massive gas ventilation has no effect on the esophageal peak areas (null hypothesis). We studied the difference in the peak esophageal area before and after massive ventilation using a paired t test for statistical significance ($P < .05$). With approval of the University of Southern California Animal Care and Use Committee and with veterinary supervision, 9 mixed hound dogs (mean weight, 25 kg; range, 18-31 kg) about to be euthanized were prepared for general anesthesia. Animals had nothing by mouth for a 10-hour period before the study. An 18-g intravenous catheter was placed in the cephalic vein, followed by sedation with 5 mg of acepromazine. Induction agents were subcutaneous atropine (0.04 mg/kg), intravenous sodium Pentothal (5-10 mg/kg), and pancuronium (0.1 mg/kg). Endotracheal intubation was performed with Sheridan ETTs with 8 to 9 mm inner diameter (ID). Conventional monitors (electrocardiogram, pulse oximetry, and blood pressure) were used. Animals were mechanically ventilated with a Narkomed 2A Drager (North American Drager, Telford, Pa) anesthesia machine, with tidal volumes of 10 mL/kg and rates of 10 breaths per minute, with the use of 100% oxygen and 1.5% to 2% isoflurane.

Acoustic reflectometry profiles were obtained with the use of a Hood Labs (Pembroke, Mass) Eccovision 2-microphone AR (see Fig. 2). The reflectometer wavetube is 30 cm in length and was customized to measure areas up to a maximal axial distance of 50 cm from the distal end of the wavetube. The ID of the wavetube is 1.27 cm (area, 1.2668 cm$^2$). The reflectometer pulses are of 2 milliseconds’ duration and are characterized by a spectral range of 200 to 5000 Hz (low-pass filter). An ensemble of pulses is repeated at the rate of 5/s (0.2 seconds). The sampling rate is 40 kHz, and the step length (the incremental distance between successive axial distance points) is 0.4288 cm. The area-distance profile appears on the screen within 0.2 seconds of manual triggering of a sample acquisition. The reflectometer profile is a plot of area vs distance. The vertical coordinate, indicated in square centimeters, corresponds to the total cross-sectional area of the cavity at a given axial length into it. The horizontal coordinate in the profile corresponds to axial distance, in centimeters, with the origin taken to be the end of the reflectometer wavetube.

For comparative purposes, we obtained initial esophageal and tracheal profiles in a single dog. The canine AR esophageal profile was done with a 9-mm-ID ETT introduced through the mouth. Because of the long mouth and neck, we chose to obtain a sample tracheal intubation profile with a 6.5-mm-ID Univent tube (Fuji Systems Corp, Tokyo, Japan) placed through a suprasternal tracheostomy site. To obtain the corresponding AR endobronchial profile, the same Univent ETT was used with endoscopic visualization to position and inflate the endobronchial cuff within the left bronchus. The 3 profiles from this single dog are superimposed in Fig. 3.

In all dogs, the protocol was as follows.

1. A breathing tube with 8 to 9 mm ID was placed in the esophagus, and the cuff was inflated.
2. A baseline AR esophageal profile was done.
3. Esophageal ventilation was provided via an adult Capno-Flow pulmonary resuscitation bag (Tyco Healthcare, Pleasanton, Calif), which was connected to an auxiliary 100% oxygen source flowing at 15 L/min. No pop-off valve was present. Aggressive 2-handed manual ventilation, with high inspiratory peak pressures (>30 cm water), was performed at rates of 40 to 50 breaths per minute, with volumes of approximately 600 to 1000 mL per breath, for stopwatch-timed periods of 0.5, 1, and 1.5 minutes.
4. Total delivered inspiratory flow was measured with a Fraser Harlake RM 121 spirometer (Orchard Park, NY) placed between the ETT and the manual resuscitation bag. At the end of each aggressive manual ventilation period, the reservoir bag was detached, the AR device was quickly attached to the esophageal breathing tube, and an AR profile was generated.
5. The ETT was removed from the esophagus.
6. An orogastric tube was passed into the stomach. The esophagogastric cavity was decompressed with an orogastric tube attached to a vacuum suction system (Vacumax; Medical Industries of America, Adel, Iowa).
7. After suctioning, the ETT was reinserted to the same depth in the esophagus, and an AR profile was obtained to assess the effect of suctioning.

Fig. 4 For dog A, the effects of aggressive manual bag ventilation of the esophagus are shown via area-distance profiles. The baseline unventilated esophagus is shown at the top. First-row ventilation shows 15 L in 0.5 minute; second row, 30 L in 1 minute; and third row, 39 L in 1.5 minute. The column on the left shows the effect of ventilation. The column on the right shows the effect of suctioning after the ventilation. In the second row, after a 30-L ventilation, the use of suctioning collapsed the esophagus. After a 39-L ventilation, suctioning flattened the esophageal profile.
3. Results

For dog A, the effects of aggressive ventilation of the esophagus with a manual resuscitation bag are shown via A to D profiles in Fig. 4. The baseline profile, without ventilation, is shown at the top. The column on the left shows the effect of ventilation. The column on the right shows the effect of suctioning after the ventilation. First-row ventilation shows 15 L in 0.5 minute; second row, 30 L in 1 minute; and third row, 39 L in 1.5 minutes. In the second row, after a 30-L ventilation effort, the use of suctioning collapsed the dog esophagus and resulted in an essentially flat line AR trace distal to the ETT, and after a 39-L effort, suctioning flattened the profile by eliminating the peak area “hump”. This hump represents the dilation of the canine esophagus in response to the incoming food bolus equivalent, namely, the tip of the ETT.

In Fig. 5, for each of the 9 dogs, the esophageal baseline profiles without ventilation (green trace) are compared with the profiles corresponding to the 1.5 minutes of maximal ventilation (red trace). In all baseline esophageal profiles up to a range of 50 cm, the profile area exhibited a hump immediately distal to the ETT, followed by a lowered valued plateau. In this study, upon disconnection of the manual ventilation bag from the ETT, there was never any whooshing sound, suggestive of a pent-up pressure. However, the abdomen was noted to be markedly distended and tympanitic but was readily decompressible with orogastric tube suctioning.

In 8 of the 9 dogs, according to AR profiles, the esophagus was not empty and collapsed but appeared to contain some air even in the basal and unventilated state (passive distension). Only 1 dog had a collapsed esophagus before initiation of ventilation. With ventilation times of 0.5, 1.0, and 1.5 minutes, the corresponding ventilation volumes (mean ± SD) were 25 ± 7, 49 ± 8, and 70 ± 18 L. Massive gas ventilation caused minimal broadening and slight distal spread of the basal hump, which was

![Fig. 5](image-url)
minimally increased in amplitude in 6 of the cases, unaltered in 2, and decreased in 2 cases. The mean peak area of the basal hump was 1.23 ± 0.60 cm² (range, 0-1.9 cm²). The mean peak area of the postventilation hump peak area was 1.41 ± 0.46 cm². (range, 0.6-2.3 cm²). Hence, the mean peak area change in the hump in response to massive gas ventilation was 0.18 ± 0.35 cm². For a paired t test (n = 9, df = 8), the corresponding t value was 1.54, with a P value of .16, which was incompatible with the null hypothesis.

Therefore, there was a minimal alteration in the esophageal peak area induced by massive intraluminal esophageal ventilation. The largest peak area change (postventilation area – basal area) of 0.6 cm² was seen in the single dog with an initially collapsed esophagus.

4. Discussion

The passive distension of the canine esophagus has been previously mentioned. As some animal studies indicate [16,17], general anesthesia in the dog abolishes TLESRs. This may be in part responsible for the prevention of regurgitant backflow and the nonrelease of stomach gas. The previous study indicates that upon disconnection of the manual ventilation bag from the ETT and the immediate attachment of the reflectometer within seconds, there is minimal distension of the esophagus as measured by acoustic reflectometry. We explain these observations as follows. The pressures exerted by resuscitation bag ventilation open the esophageal sphincter and create, for the duration of the ventilation, a temporary common esopha-gogastric cavity. The introduced gas is retained within the stomach, and part of it is transmitted downstream. Upon disconnection of the bag, the esophagus is opened to ambient air, and any residual esophageal distension pressure promptly disappears because the indwelling tube is stenting open the upper esophageal sphincter. The canine esophagus recoils back toward its basal state of passive distension, and this process can be expedited with the use of a suction device to the point of esophageal collapse. A less likely explanation is that reactive peristaltic waves can also be initiated by sudden stretching of the esophageal wall, and the presence of a contraction may account for the few paradoxical cases where the postventilation peak area was slightly less than the basal measurement; this is unlikely because deep anesthesia more or less abolishes peristalsis. An alternative explanation for this seeming anomaly is that dynamic fluctuations in the reflectometer area determination may have resulted in an outlying measurement.

Massive gas ventilation only minimally altered the canine esophageal area-distance profile as determined by acoustic reflectometry. The identification of a canine esophageal intubation was readily evident by observing (1) the presence of a hump of limited width, which corresponds to the local dilation of the esophagus in response to the presence of the distal ETT, (2) the much smaller cross-sectional plateau area in the esophageal segment beyond the hump, and (3) the elimination of the esophageal distension and the production of esophageal collapse, with the introduction of a suction catheter into the cavity.

In contrast to the air-containing canine esophagus, humans in the resting state generally have a collapsed esophagus, which only opens to accommodate swallowed or regurgitated material. In humans, unlike in dogs, the reported effect of inhalational agents is to lower the barrier pressure exerted by the LES [18], and in the cardiac arrest setting it is lost altogether.

Assuming that the elastic properties of the human esophagus are similar to those of the dog, it may not be unreasonable to assume that the maximal human change in the peak area (postventilation area – basal area) would be comparable to that observed in this dog study, that is, about 0.6 cm² (as in the single dog [B], which exhibited an initially collapsed esophagus distal to the ETT). This change is slightly larger than the area of an adult ETT (0.4 cm²), but it does not result in area values that approach the tracheobronchial area values noted in a single canine examination (>10 cm²) nor in the original pilot human study (>10 cm²) [3]. Consequently, despite some theoretical physiological differences between the human and canine esophagus, it is likely that in the cardiopulmonary resuscitation setting there is an area threshold above which it is possible to be certain that the tube is not in the esophagus. In the present canine study, a value of 3 cm² would totally separate the measurements made within the trachea from even the most massively distended esophagus. Because humans do not have a hump in their basal AR esophageal profile, a similar smaller-valued cutoff would allow a quantitative area distinction between tracheal and esophageal placement.

Massive gas ventilation in an esophageally intubated, out-of-hospital patients with cardiac arrest will cause severe gastric distension. Gas release from the stomach into the esophagus will occur intermittently or continuously, either from persisting TLESRs or from total loss of LES tone. The increased amount of esophageal gas aspirated with a Toomey suction syringe will exceed the syringe aspiration threshold, and the intubator will falsely conclude that a tracheal intubation has occurred when, in fact, the tube is in the esophagus. This false-positive problem is a potential failing of all EDD suction-based devices in this type of scenario.

As this limited study of massive esophageal gas ventilation indicates, upon disconnection of the resuscitation bag, the release of stomach gas into the esophagus neither results in a significant distension pressure that can significantly alter the diameter of the esophageal wall, nor does it alter the recognizability of the AR profile as that of an esophageal intubation.
5. Conclusions

Massive gas ventilation only minimally altered the canine esophageal area-distance profile as determined by acoustic reflectometry, such that operator recognition of the AR profile as that of an esophageal cavity is maintained. We therefore suggest that a miniaturized portable AR may have the potential to aid the clinician to discriminate within seconds between an esophageal and a true endotracheal intubation in the emergency out-of-hospital cardiac arrest setting during massive gas ventilation. The method necessarily must be studied further in humans, but the experimental data from this canine pilot study are encouraging.

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References

Brief Report

An assessment of a tracheal tube introducer as an endotracheal tube placement confirmation device

Aaron E. Bair MD\textsuperscript{a,\*}, Erik G. Laurin MD\textsuperscript{a}, Brandi J. Schmitt MS\textsuperscript{b}

\textsuperscript{a}Department of Emergency Medicine, University of California, Davis School of Medicine, Sacramento, CA 95817, USA
\textsuperscript{b}Department of Cell Biology and Human Anatomy, University of California, Davis School of Medicine, Sacramento, CA 95817, USA

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Abstract

Introduction: Early detection of an inadvertent esophageal intubation can be particularly challenging in cases when the current standard of care, carbon dioxide detection, is unreliable. We sought to determine the sensitivity and specificity of an inexpensive and portable device, the gum elastic bougie (Eschmann Tracheal Tube Introducer, SIMS Portex, Inc, Keene, NH), as an endotracheal tube placement confirmation device.

Methods: We conducted a prospective blinded trial in 20 human cadavers. Each cadaver was randomized to a mixed series of 5 esophageal and 5 tracheal intubations. Each intubation was assessed with the bougie twice, once by a novice to the technique, and once by an assessor who was constant through the trial. Assessors used the bougie to “feel” for “clicks” of the tracheal rings and to appreciate “hang up” of the bougie as it was advanced into the smaller airways. Absence of these findings was presumed to indicate an esophageal intubation. Actual placement was confirmed by bronchoscopy. Each assessor made an independent determination of tube location. Descriptive statistics were used to summarize the data.

Results: Overall, 93% (95% confidence interval [CI], 86%-97%) of tracheal placements were correctly identified. The constant assessor was able to correctly identify 98% (95% CI, 90%-100%). Tracheal rings were detected in 92% of tracheal placements. Ring clicks were 95% specific for tracheal intubation. Hang up was reported in 100% of tracheal placements with a specificity of 84%. Overall, 95% (95% CI, 88%-98%) of esophageal intubations were detected. The constant assessor detected 100% of esophageal intubations.

Conclusion: In the cadaver model used in this study, the gum elastic bougie (Eschmann Tracheal Tube Introducer) shows promise as an endotracheal tube confirmation device.

1. Introduction

Endotracheal tube placement verification is a fundamental component of emergency airway management. An unrecognized nontracheal intubation can have devastating consequences. End-tidal carbon dioxide detectors and
various aspirator devices are used commonly for endotracheal tube confirmation. Although there are multiple techniques and devices that are commonly used for endotracheal tube confirmation, none of these are perfectly reliable. For example, there are circumstances when carbon dioxide detection is unreliable (ie, low perfusion states). In addition, aspiration techniques have been shown to be unreliable in the setting of obesity, foreign material within the airway, and with prior insufflation of the stomach [1-4]. Hence, there are commonly encountered circumstances when these techniques of endotracheal tube confirmation may not be dependable. In these potentially difficult cases, there is a need for an additional technique of endotracheal tube confirmation.

The gum elastic bougie (Eschmann Tracheal Tube Introducer, SIMS Portex, Inc, Keene, NH) was originally developed as an endotracheal tube introducer, not as a dilator, as the term bougie might imply. The usual technique for use during intubation relies on the successful placement of the bougie into the trachea followed by passage of an endotracheal tube over the bougie. As the bougie is introduced into the trachea, the angled tip slides along the tracheal rings and transmits a palpable series of “clicks.” Furthermore, if the bougie is successfully placed into the airway, it will hit resistance and “hang up” as the tip advances into the smaller airways of the bronchial tree. This determination takes only seconds to perform. When used as an adjunct for endotracheal tube placement, appreciable clicks and hang up are useful clues when laryngoscopy is limited by anatomy or obscured by foreign material (ie, emesis, blood) [5]. Over the past 40 years since its development, the bougie has become a favored difficult airway adjunct in Britain and is commonly referenced in the anesthesia literature [5-9]. In addition, it has recently been reported as a useful adjunct in the emergency department [10,11].

In addition to the already described use for difficult intubation, the bougie may also be useful for distinguishing endotracheal from esophageal tube placements. Our primary objective in this study was to assess the sensitivity and specificity of the gum elastic bougie (Eschmann Tracheal Tube Introducer) as an endotracheal tube placement confirmation device. In addition, we sought to determine if limited experience with the device and the technique would markedly reduce its utility. We hypothesized that the gum elastic bougie could be used with good sensitivity and specificity, even among novice users, to determine location of tube placement.

2. Methods

2.1. Study design

This was a prospective, blinded, randomized comparative study of bougie sensitivity and specificity as an endotracheal tube placement confirmation device.

2.2. Participants

2.2.1. Novice assessors

For purposes of this study, we sought a population of providers who were unfamiliar with use of the bougie. Flight nurses from the university-associated air medical transport service were recruited to participate in this study. The flight nurses, although skilled in airway management, had no prior training in the study technique. The goal was to have each nurse participate only once to limit the influence of experience. Each nurse was given a brief (approximately 5 minutes) descriptive overview of the use of the bougie for endotracheal tube confirmation. This overview consisted of a verbal description immediately before the actual demonstration of a single endotracheal tube placement. For training purposes, a single endotracheal tube placement was used to demonstrate the tactile concepts of clicks and hang up.

2.2.2. Experienced assessor

For purposes of this study, we sought an individual who would be available for assessment of each of the specimens during the study period. This person was trained and practiced in the bougie technique before the initiation of the study. Our intention was that the technical performance of this individual would be analogous to that of the experienced and skilled provider. The individual selected was a regular employee of the laboratory and not trained as a medical provider. In contrast to the novice assessors, this assessor had no prior airway management training before the trial. This individual assessed every specimen enrolled in this trial.

2.3. Interventions and measurements

2.3.1. Specimens

Access to 20 nonfixed, nonfrozen human cadavers was obtained through the Donated Body Program at the affiliated medical school. Over a period of approximately 4 months, as the cadaver specimens became available, the study team was assembled to perform the requisite intervention and data gathering. The Human Subjects Institutional Review Board granted approval for this study.

2.3.2. Bougie confirmation technique

The bougie product used consistently in this trial was the Eschmann Tracheal Tube Introducer, a flexible intubating stylet measuring 60 cm by 5 mm. An 8.0-mm Hi-Lo cuffed endotracheal tube (Mallinkrodt, Tyco Healthcare, Mansfield, MA) was placed in either the trachea or the esophagus according to randomization. To maximize the number of tracheal rings accessible to the bougie, the endotracheal tubes were placed in the trachea with the balloon cuff just past the vocal cords. The esophageal tubes were placed under direct visualization at a corresponding depth. After intubation, placement was confirmed with bronchoscopy. The participants, who were blinded to placement, were instructed to orient the direction of the bougie tip anteriorly and insert it into the tube. Tube lengths and bougie lengths were then
aligned and the lubricated bougie was then passed out of the tip of the tube in an effort to feel clicks (Fig. 1). Subsequently, the bougie was advanced and the presence or absence of terminal resistance (ie, hang up) was noted. As the study was designed as a preliminary analysis of the technique and generally only takes a matter of seconds to perform, no time limit was imposed on the participants.

2.3.3. Study protocol

All cadaver specimens were randomized to a mixed series of 5 esophageal and 5 tracheal intubations. The order of either esophageal or tracheal intubation and the proportion of each were determined in advance by a computer-generated randomization scheme. The study participants were blinded to tube placement and to each other’s questionnaire responses. The 2 different participants then assessed each intubation independently. The participants were then asked to respond in writing to questions on a structured data-gathering form. The participants responded “yes” or “no” to whether clicks and hang up were appreciable. Ultimately, they had to decide whether the tube had been placed in the trachea or esophagus.

2.3.4. Data analysis

Descriptive statistics were used to analyze the data. We performed all statistical analyses using Stata 7.0 for Windows (Stata Corp, College Station, Tex). Data were summarized as percentage frequency occurrence for categorical variables. When appropriate, 95% confidence intervals (CIs) were calculated. Our sample size was limited by cadaver availability over a finite period and, as such, an a priori sample size calculation was not performed.

3. Results

Twenty human cadavers were used to perform 200 assessments in this trial. Of these, 102 were randomized to a tracheal placement. Thirteen (65%) of the cadavers used in this study were male. None of the cadavers in this trial had evidence of prior tracheal or laryngeal surgery.

Table 1 describes the proportion of endotracheal and esophageal intubations, as well as the relative performance of the novice assessors and the experienced assessor. Of note, the experienced assessor was able to detect 100% (95% CI, 93%-100%) of the esophageal intubations in this trial. As a group, the novice assessors identified 90% (95% CI, 78%-97%) of the esophageal intubations. Overall, 95% of esophageal intubations were identified.

Among tracheal intubations, 93% (95% CI, 86%-97%) were correctly identified overall. The experienced assessor tended to be more accurate and was able to correctly identify 98% (95% CI, 90%-100%) of the tracheal placements. In contrast, the novice assessors identified 88% (95% CI, 76%-96%) of the tracheal placements. Tracheal rings were detected in 92% of tracheal placements overall (Table 2). Ring clicks were 95% specific for tracheal intubation. Hang up was detected in 100% of tracheal placements with a specificity of 84%.

4. Discussion

In this study, we evaluated the use of the gum elastic bougie or Eschmann Tracheal Tube Introducer as an endotracheal tube confirmation device. The device itself consists of a 60-cm, resin-coated rod with a woven Dacron polyester core. The tip is a 2-cm segment that is angled approximately 30°. The leading tip of the device is designed to improve ease of insertion into a partially
visualized glottis by allowing a variable angle of approach into the trachea [12]. In addition, the angled tip has the potential to provide rapid feedback to the intubator regarding the location of the tip. This tactile feedback could be useful for intubation, as well as endotracheal placement confirmation.

The importance of accurate endotracheal tube placement confirmation is well known, as an unrecognized esophageal intubation can be life-threatening. Although multiple devices currently exist for esophageal intubation detection, they each have limitations [1,3,13-15]. Likewise, clinical indicators such as “direct visualization” of the glottis during intubation attempts and “breath sound” assessment after tube placement are known to lack adequate sensitivity for detecting inadvertent esophageal intubation [16-18]. Thus, additional objective information is advised to confirm tube placement. For example, end-tidal carbon dioxide is commonly used in addition to other clinical indicators to confirm placement. However, end-tidal carbon dioxide detection is limited in low perfusion states such as cardiac arrest [19]. Likewise, the use of bulb or syringe aspiration techniques is limited by matter in the airway or morbid obesity [3]. In contrast, the use of the bougie method for tube placement determination would theoretically not have those same limitations because it relies only on the presence or absence of palpable clicks and “hang up” of the bougie within the airway. The use of a bougie is independent of expired carbon dioxide and could possibly perform well in situations that would otherwise limit bulb techniques such as obesity and the presence of airway secretions.

We have found no literature that addresses the use of the bougie as an endotracheal tube confirmation device for use in the manner that we have described here. There has been, however, a report in the literature to suggest that the bougie is reliable at detecting tracheal placement in the setting of difficult airway management [5]. To our knowledge, however, there has been no trial assessing this technique to differentiate endotracheal from esophageal intubations. In our study using cadavers, we found that the bougie technique was 95% sensitive and 93% specific for correctly identifying tracheal intubations. In addition, our data show that even minimal training in this technique results in high success rates.

5. Limitations

This study has multiple limitations. There are inherent limitations in a study involving cadaver specimens. In particular, we found that because of the stiffening of the tissues, there was a significant amount of resistance to the bougie in the esophagus of some specimens. It appears that among the novice assessors, this was confused as tracheal hang up and this resulted in several esophageal placements being misidentified as tracheal. In retrospect, it might have been better to include both a tracheal and an esophageal placement in the training phase for the novice assessors. In a living subject, with normal tissue distensibility, we predict that the performance of the novice assessors would be improved as they would be less likely to encounter esophageal resistance and to confuse it with tracheal hang up. If this were the case, then the sensitivity and specificity would be improved over what we have reported. In addition, this study did not evaluate the bougie technique in specimens with particulate matter in their airways nor those that were morbidly obese. These are 2 groups in which the syringe aspiration technique has a higher error rate. It remains unclear how the bougie would perform in such conditions. Furthermore, for this study, all endotracheal tubes were placed relatively high in the trachea. In actual clinical practice, main-stem intubations occur. In such cases, the clicks would likely not be felt. However, the hang-up would still be readily apparent. Finally, as this study was designed as a preliminary study to analyze sensitivity and specificity, no time limits were imposed on the participants of this trial. As such, this limits the applicability of our findings to clinical practice. However, it merits noting that during the development phase of this study, the use of the bougie was observed to require only approximately 5 seconds to use.

6. Conclusions

In a cadaver model, we found that the bougie technique could be both sensitive and specific in correctly differentiating tracheal from esophageal intubations. It performed well when used by those with little experience in the technique but better by an individual with more experience. The bougie technique has potential to be a useful diagnostic adjunct for endotracheal tube placement confirmation in selected difficult patients and merits further study.

Acknowledgments

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References


Brief Report

Most lay people can correctly identify indigenous venomous snakes

Stephen W. Corbett MDa,*, Brian Anderson MDa, Brett Nelson MDa, Sean Bush MDa, William K. Hayes PhDb, Mike D. Cardwell BAa

aDepartment of Emergency Medicine, Loma Linda University Medical Center, Loma Linda, CA 92354, USA
bDepartment of Natural Sciences, Loma Linda University, Loma Linda, CA 92354, USA

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Abstract We attempted to determine how accurately members of the public can identify venomous snakes. Six different snakes indigenous to southern California were displayed in cages for 265 people to view at a street fair. These included 4 nonvenomous snakes and 2 venomous snakes. People were asked whether the snake was venomous and the name of the snake, if they knew it. Overall, people recognized whether a snake was venomous or nonvenomous 81% of the time. They were most accurate at identifying rattlesnakes as being venomous (95%) but incorrectly identified nonvenomous snakes as being venomous 25% of the time. Men were more accurate than women, and adults were more accurate than children. Subjects were less well able to identify the exact species of snakes. The results suggest that there may be no need to capture, kill, or bring a snake to the hospital for identification, at least in this geographic area. © 2005 Elsevier Inc. All rights reserved.

1. Introduction

There are several thousand crotaline snake envenomations each year in the United States resulting in 1 to 2 deaths [1-3], although there is some evidence that these numbers may be underreported [4]. Management decisions in cases of suspected snakebites are problematic because the identity of the snake is often not known [1-3], many bites are dry and do not produce envenomation [5], and the treatment can be associated with significant morbidity [6].

To more accurately identify those patients requiring antivenin, some sources have suggested that the captured or killed snake be brought to the ED with the victim [7-11]. The inherent danger in this practice is obviously the risk of additional envenomations (to the victim or others) from the attempts to capture, kill, or transport the snake. To determine the need for this practice in southern California, we tested the lay public’s ability to identify indigenous venomous and nonvenomous snakes.

2. Methods

Specimens of live venomous and nonvenomous snakes were displayed to the public to determine how accurately they could be identified. All snakes were mature specimens and were common to the geographic area. The displayed nonvenomous snakes were gopher snake (Pituophis melanoleucus catenifer), San Bernardino mountain king snake (Lampropeltis zonata parvirubra), California common king snake (Lampropeltis getulus californiae), and California rosy boa (Lichanura trivirgata gracilis). The displayed...
venomous snakes were Mojave rattlesnake (*Crotalus scutulatus scutulatus*) and southern Pacific rattlesnake (*Crotalus viridis helleri*).

A suburban street mall or “farmers market” was chosen as a venue. This market has occurred on a weekly basis for many years and is well known to the surrounding community. A main street is closed to all but pedestrian traffic on market days. Various vendors have booths or tables lining the street. The market is quite popular and is attended by people of different ages and backgrounds.

For the purposes of this experiment, the department of emergency medicine was given space to display snakes. Each specimen was safely secured in a glass aquarium approximately 2 cu ft in size. The aquaria were placed on 3 tables so that subjects could pass between the tables and view each specimen in sequence. The area was well lit and subjects were able to view each snake at a distance of 2 to 3 ft.

Potential subjects were told, “We would like you to look at several live snakes and tell us which ones you think are poisonous and which ones you think are nonpoisonous.” For the purpose of this study, subjects were told that poisonous meant venomous. A data form was numbered from 1 to 6, and the words poisonous and nonpoisonous were printed next to each. Subjects were instructed to circle their choice for each snake based on the corresponding number on the snake container. In addition, they were told to write down the name of the snake, if they knew it. Consecutive subjects were given data forms and allowed to pass through the display area. A herpetologist was on the premises to supervise the displays. No snakes were harmed in this study. Verbal consent was obtained from subjects before their participation. This protocol was approved by the Loma Linda University Medical Center’s Institutional Review Board.

χ² Analysis was used to determine whether the accuracy of venomous snake identification was associated with the subject’s sex or age. Differences with a probability of occurring by chance alone less than 1 in 20 were considered to be significant (*P* < .05). Descriptive statistics were used as needed.

3. Results

A total of 281 subjects were entered into the study. Of these, 265 completed the data forms and were eligible for analysis. Of those that indicated their ages, 72 were children (<18 years) and 169 were adults (≥18 years). Median age was 25 years with a range from 4 to 64 years. Of those that indicated their sex on the form, 104 were female and 110 were male (these data are noted in Table 1).

The percentage of subjects who correctly identified the snakes as being poisonous or nonpoisonous is shown in Table 1 for each of the 6 different types of snake. The public correctly identified whether the snake was venomous 81% of the time. For the nonvenomous snakes, many people inaccurately identified them as being poisonous. This was most apparent with the mountain king snake where more than 40% felt that it was poisonous. Overall, nonvenomous snakes were incorrectly identified as poisonous 25% of the time. Subjects generally identified both rattlesnakes (95%, overall) as being poisonous.

Women correctly identified the snakes as venomous or nonvenomous 79% of the time, whereas men correctly identified the snakes as venomous or nonvenomous 83% of the time (χ² = 4.51, *P* = .0034). Adults were correct 83% of the time and children were correct 75% of the time (χ² = 10.71, *P* = .001). The responses by age and sex for each snake type are also shown in Table 1.

Subjects were less well able to identify the species of the snakes when they were asked to write this on the data sheets. Only 26% (68/265) recognized the gopher snake, and 16% (43/265) recognized the rosy boa. Although many realized that 2 snakes were from the king snake genus (*Lampropeltis*), only 4% and 8% knew the species mountain king and common king snake, respectively. Subjects had a similar problem with respect to identifying the venomous snakes. Many realized that these snakes were rattlesnakes. Very few correctly identified them as Mojave (5% [13/265]) or southern Pacific rattlesnakes (2% [6/265]).

4. Discussion

Antivenin administration is associated with some morbidity. The primary complications of Antivenin (Crotalidae Polyvalent (Wyeth-Ayerst Laboratories, Collegeville, PA) are hypersensitivity reactions. Anaphylaxis and anaphylactoid reactions occur more than 20% of the time [5,12]. Delayed serum sickness approaches 75% in those receiving large doses [13]. A new preparation, Crotalidae Polyvalent

<table>
<thead>
<tr>
<th>Snake identification results</th>
<th>Gopher snake</th>
<th>Mountain king snake</th>
<th>Common king snake</th>
<th>Rosy boa</th>
<th>Mojave rattlesnake</th>
<th>Southern Pacific rattlesnake</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects (n = 265)</td>
<td>82</td>
<td>60</td>
<td>74</td>
<td>83</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Female (n = 104)</td>
<td>79</td>
<td>55</td>
<td>66</td>
<td>82</td>
<td>91</td>
<td>98</td>
</tr>
<tr>
<td>Male (n = 110)</td>
<td>85</td>
<td>63</td>
<td>79</td>
<td>84</td>
<td>93</td>
<td>96</td>
</tr>
<tr>
<td>Children (n = 72)</td>
<td>79</td>
<td>47</td>
<td>65</td>
<td>81</td>
<td>90</td>
<td>92</td>
</tr>
<tr>
<td>Adults (n = 169)</td>
<td>83</td>
<td>64</td>
<td>75</td>
<td>84</td>
<td>93</td>
<td>99</td>
</tr>
</tbody>
</table>
Immune Fab (Ovine [CroFab, Altana, Inc, Melville, NY]), appears to have fewer side effects but is still being evaluated [6].

Perhaps because of the significant morbidities associated with antivenin administration, several authorities have suggested that the snake be captured and transported to the ED for definitive identification. A textbook of emergency medicine [7] recommends, “when feasible, the snake should be identified or brought to the treating facility with the victim.” A textbook of wilderness medicine [8] suggests, “If the snake is killed, it can be transported to the hospital with the patient.” Similar recommendations are offered on Internet Web sites. Patient education instructions at MDConsult [14] recommend, “Bring it with you after you are certain that it is dead.” Other sites provide similar recommendations in their first aid instructions for snakebites [15-18].

It appears that even dead snakes are not safe. One review describes envenomations from recently shot, decapitated, bludgeoned, or otherwise inadequately killed rattlesnakes [19]. Preserved and frozen heads have also caused problems [20,21]. Because many victims of rattlesnake envenomation were bitten while they were injudiciously handling the snake and many of these victims were also intoxicated [5,22], it would seem best to leave the snake at the scene.

Justification for the practice of bringing in snakes for identification seems even less apparent, given our results. The lay public was quite good at identifying these snakes as being venomous or nonvenomous with an overall accuracy rate of 81%. Although they tended to believe that many of the nonvenomous snakes were poisonous (25%), most were able to identify the venomous snakes as being poisonous (95%). Obviously, the conditions here do not recreate the conditions that might be experienced in a wild snake encounter. Opportunities to study the snake might be limited, dangerous, or compromised by stress. In addition, those subjects participating in this experiment might not be representative of those who are most likely to be bitten. Participants in this study might be more interested in snakes than the general population because they took the time to complete the questionnaire. Nevertheless, this situation provides a reasonable facsimile. The San Bernardino mountain king snake bears a superficial resemblance to the coral snake, perhaps explaining why so many people believed that it was venomous. It would be interesting to test accuracy in an area where coral snakes are indigenous.

Subjects were not as proficient at identifying the precise species of the snakes. This may be less important because in most cases, the exact type of venomous snake has little clinical significance, especially in areas where a single antivenin is used. The poor ability of laypersons to distinguish one rattlesnake species from another makes previous reports relying on such identification suspect. It is not known how well the public can identify different venomous snakes in an area such as Australia, where the choice of antivenin is directed by the species of snake [23]. Under such circumstances, precise identification would play a more important clinical role. Envenomations from exotic snakes are becoming a more prevalent problem [1-3], but it is reasonable to assume that most exotic snake owners would be able to identify the snake that bit them.

The decision to treat a snake bite with antivenin is largely based on clinical parameters. Trying to capture, kill, or transport a snake for identification purposes seems of little value and possibly dangerous. The patient’s own report about the snake may have some historical value in this regard, at least in southern California.

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References

Brief Report

**Lymphocytosis without anemia in a patient presenting with anaphylactic shock**

Youichi Yanagawa*, Toshihisa Sakamoto, Yoshiaki Okada

Department of Traumatology and Critical Care Medicine, National Defense Medical College, Saitama 359-8513, Japan

**Abstract** We retrospectively investigated whether anaphylactic shock tends to be associated with lymphocytosis or not. We reviewed the medical charts of patients who had shock between January 1999 and September 2004. The subjects were divided into 4 groups, consisting of anaphylactic, hemorrhagic, cardiogenic, and septic groups. The results of laboratory examinations were analyzed. Regarding cellular differences, the lymphocyte–total leukocyte ratio in the anaphylactic group was significantly greater than that in the other groups. The average number of lymphocytes in the anaphylactic group was also significantly greater than that in both the hemorrhagic and septic groups. In addition, the average value of hemoglobin in the anaphylactic group was significantly greater than that in the other groups. The identification of lymphocytosis without anemia may therefore enable clinicians to accurately differentiate various states of shock in patients presenting with shock at the ED.

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1. Introduction

In EDs, the cause of shock is sometimes difficult to diagnose correctly. We recently treated a female case who presented with shock, ischemic changes on an electrocardiogram, and positive findings for heart-type fatty acid–binding protein and lymphocytosis. A coronary angiogram showed negative findings, and she was thereafter found to have a food allergy after performing an allergen examination.

Anaphylactic shock is an immediate allergic reaction. These reactions consist of hypotension, erythema, or asthma, induced by the release of chemical mediators from mast cells when IgE-coated antigens bind to the surface receptor of mast cells.

Common causes of an increase in the lymphocyte number are virus infection and leukemia. However, an increase in the lymphocyte number associated with an immediate allergic reaction has not yet been reported. We therefore investigated the lymphocyte count in patients demonstrating various types of shock.

2. Methods

We reviewed the medical charts of the patients who had shock at our department between January 1999 and September 2004. They were divided into 4 groups according to the causes, thus consisting of an anaphylactic, hemorrhagic, cardiogenic, and septic group. Shock was defined as follows: a systolic pressure of 90 mm Hg or less, with some clinical manifestations such as pallor, cyanosis, hydrosis, restlessness, and/or a consciousness disturbance. Any patient with cardiopulmonary arrest was excluded from the study. The hemorrhagic group was defined as the patients with shock who had obvious bleeding source, including trauma (n = 105). The cardiogenic group was defined as the patients...
with shock who had a hypokinetic cardiac wall motion and had an obstruction of coronary artery confirmed by angiography (n = 35). The septic group was defined as patients with shock who had an infectious focus and whose pathogenic bacteria were confirmed (n = 18). The anaphylactic group was defined as patients with shock who had an obvious allergen (n = 17: drugs, 7; food, 5; bee sting, 5).

The following variables were analyzed between the anaphylactic group and the other groups: sex, age, systolic blood pressure on arrival, pulse rate on arrival, duration of time from the scene of the accident or incident to arrival, and survival rate at the time of discharge. The normal value of C-reactive protein in our hospital was less than 0.6 mg/dL.

Both of the $\chi^2$ test and Student t test were used for statistical analyses. A $P$ value less than .05 was considered to be significant.

### 3. Results

All subjects were directly transferred to our hospital within 1 hour from first call and without receiving any medication. All blood sampling was done on arrival. Table 1 shows the background of the subjects. The age and the ratio of male patients in the cardiogenic group were greater than those in the anaphylactic group.

Table 2 shows the results of the laboratory findings. Regarding cell differential, the lymphocyte ratio in the anaphylactic group was significantly greater than that in the other groups. The number of lymphocytes in the anaphylactic group was significantly greater than that in both the hemorrhagic and septic groups. The number of lymphocytes in the anaphylactic group was greater than that in the cardiogenic group, but the difference was not significant ($P = 1$). The range of the white blood cell count of all cases, the range of the neutrophil ratio of 16 of 17 cases, and the range of the lymphocyte ratio of 15 of 17 cases in the anaphylactic group overlapped with those in the other groups. The hemoglobin concentration in the anaphylactic group was significantly greater than that in the other groups. Fig. 1 demonstrates a correlation between the lymphocyte ratio and hemoglobin level in each group.

Table 3 shows the survival rate at the time of discharge. The outcome of the anaphylactic group was significantly better than that of the other groups.

### 4. Discussion

The lymphocyte–total leukocyte ratio in the patients with anaphylactic shock was greater than those in the patients...
with the other kinds of shock. A possible cause for such lymphocytosis was the hypersensitivity induced by a previous viral infection, such as Epstein-Barr virus, in which the presence of both lymphocytosis and hypersensitivity has been reported [1]. However, according to reviewing the medical charts, no patients in the anaphylactic group had any history of a recent common cold before admission. In the anaphylactic group, no liver dysfunction was observed, and the C-reactive protein levels were within the normal levels, except for 2 cases (0.7 and 0.8 mg/dL, respectively). Accordingly, there is little possibility that the observed lymphocytosis had been induced by viral infection. Another possible cause of the lymphocytosis might be the occurrence of lymphocyte mobilization from a spleen or marginal pool into the vessels due to shock stress. Some reports have described the occurrence of lymphocytosis to be due to catecholamine release from sympathetic nerves stimulated by invasive stresses, including trauma [2-4]. Characteristically, catecholamine administration induced a quick (<30 minutes) mobilization of the lymphocytes (mainly, natural killer cell), followed by an increase in the number of granulocyte in combination with a decrease in the number of lymphocytes. In this study, however, the lymphocyte–total leukocyte ratio in the anaphylactic shock group was greater than that in the patients with other kinds of shock, although no difference was observed in both the level of hypotensive stress and the duration of sampling blood from the scene of accident or incident. Accordingly, other factors in addition to catecholamine in anaphylactic reaction may contribute to an increase in the number of lymphocytes.

Regarding hemoglobin, it is natural for the hemoglobin concentration to be low in cases with long-term bleeding. Knottenbelt [5] reported that patients with trauma and shock demonstrated significantly lower hemoglobin values in comparison to patients with trauma without shock. He hypothesized that the low hemoglobin levels immediately after trauma were indicative of serious ongoing hemorrhaging. Sepsis was also associated with anemia because of a decrease in erythrocyte production and a dysfunction of erythropoietin receptor [6]. Our results show the hemoglobin value in the cardiogenic group to be lower than that in the anaphylactic group; however, the average age in the cardiogenic group was higher than that in the anaphylactic group. Anemia is more common in the elderly than in young persons because erythropoietin secretion decreases with age [7]. When we corrected the difference in the age between the cardiogenic and anaphylactic group, no statistical difference in the hemoglobin value was observed between the 2 groups.

Because multiple factors contribute to the induction of shock, it is not always easy to diagnose the cause of shock correctly in the emergency ward. We did not encounter any fatal cases of anaphylactic shock in the present study; however, the occurrence of anaphylaxis can be lethal. As a result, the immediate recognition of anaphylaxis is required [8]. In the case of anaphylactic shock, patients sometimes do not recognize exposure to allergens. Carefully measuring the $\beta$-tryptase levels, which is released by mast cells in an anaphylactic reaction, may be useful for making an accurate diagnosis of anaphylaxis [9]; however, the routine application of such an examination is limited. Our results suggest

### Table 3

<table>
<thead>
<tr>
<th>Outcome of each group</th>
<th>Anaphylactic</th>
<th>Hemorrhagic</th>
<th>Cardiogenic</th>
<th>Septic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival ratio (%)</td>
<td>100</td>
<td>84.2**</td>
<td>54.2**</td>
<td>55*</td>
</tr>
</tbody>
</table>

* $P < .01$ vs anaphylactic group.  
** $P < .001$ vs anaphylactic group.
that anaphylaxis should therefore be considered in the differential diagnosis of patients who demonstrate shock with lymphocytosis but without anemia.

5. Conclusion

The identification of lymphocytosis without anemia may therefore enable clinicians to accurately differentiate various states of shock in patients presenting with shock at the ED.

References


Review

Emergency management of agitation in schizophrenia

Catherine A. Marco MD*, Jason Vaughan MD

Department of Emergency Medicine, St Vincent Mercy Medical Center, Toledo, OH 43608-2691, USA

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Abstract Schizophrenia is a common psychiatric condition, affecting approximately 1% of the population. Acute emergent presentations often include hallucinations, delusions, thought, and speech disorders. Agitation is common among emergency patients with schizophrenia. Decisional capacity should be assessed in all patients. Reversible causes of agitation should be ruled out, including infection, metabolic disorders, endocrine disorders, trauma, pain, noncompliance, toxicological disorders, and structural brain abnormalities. Agitation may be managed acutely using a combination of pharmacological agents and nonpharmacological interventions. Effective pharmacological agents include several classes of antipsychotic agents and benzodiazepines. Potential life-threatening complications of pharmacological therapy should be anticipated, which may include neuroleptic malignant syndrome (NMS), prolonged QT syndrome, and respiratory depression. Nonpharmacological interventions may include a quiet environment, physical restraints, and behavioral interventions. Disposition decisions should be made based on the etiology of agitation, effective management, decisional capacity, and presence of suicidal or homicidal intentions. Many patients who have required nonpharmacological or pharmacological management of agitation require inpatient psychiatric treatment, either voluntarily or involuntarily. Psychiatric consultation should be sought for patients with schizophrenia and uncertain disposition determinations, or those requiring other complex management decisions.

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1. Introduction and scope of the problem

Schizophrenia is a common psychiatric condition, affecting approximately 1% of the population. It is a major public health concern worldwide and accounts for many hospitalizations. Psychiatric emergency visits are increasingly common in the United States, comprising approximately 4.3 million ED visits annually, approximately 5.4% of total ED visits [1]. Psychoses, including schizophrenia, make up approximately 21% of those ED visits or 900,000 visits annually. Schizophrenia is disproportionately common among homeless persons, with an incidence of 27%, according to 1 study [2].

2. Clinical features of schizophrenia

Onset of symptoms typically occurs in late adolescence or early adulthood, although onset can be at any age. Younger patients (<45 years) account for the majority of resource use [3]. Early symptoms include eccentric behavior, paranoid behavior, and gradual deterioration in functioning. Classically, patients with schizophrenia have an impaired perception of reality. Acutely, patients may present to the ED with acute psychosis, hallucinations, delusions, disorganized speech or behavior, lack of insight, impaired
verbatim skills, or bizarre behavior. Schizophrenia may exist in 1 of several forms, including paranoid, catatonic, disorganized, and undifferentiated. Other psychiatric disorders related to schizophrenia include schizophreniform disorders, schizoaffective disorders, delusional disorders, and other psychotic disorders.

Chronically, symptoms are ideally managed with a combination of antipsychotic drugs in conjunction with psychiatric counseling, family counseling, supported employment, skills training, and behavioral therapy [4]. The primary categories of traditional antipsychotic agents include the phenothiazines (Thorazine, Mellaril, Stelazine, Prolixin), the thioxanthenes (Navane, Loxitane), the butyrophenones (Haldol, Inapsine), and the dihydridolones (Moban). The newer antitypical antipsychotic agents have demonstrated success in chronic management of schizophrenia, with favorable symptom relief and side effect profiles (agents such as olanzapine [Zyprexa], clozapine [Clozaril], risperidone [Risperdal], ziprasidone [Geodon], and quetiapine [Seroquel]) [5].

There are numerous measures of functioning for the chronic management of schizophrenia, including the Positive and Negative Syndrome Scale, the Brief Psychiatric Rating Scale, the Clinical Global Impression–Schizophrenia scale, the Scale to Assess Unawareness of Mental Disorder, and the Independent Living Skills Survey [6-13]. Unfortunately, most of these outpatient measures are time consuming and impractical in the ED.

Emergent treatment goals for schizophrenic patients in the ED include the initial evaluation and stabilization, protection of staff and patients (using restraints or pharmacological management if necessary), psychiatric evaluation (including assessment of suicidal or homicidal risk), physical examination to rule out any treatable exacerbating conditions, treatment of reversible conditions, management of acute psychosis and agitation, and appropriate disposition [14-17].

### 3. Diagnostic tests for the agitated schizophrenic patient

Diagnostic tests may be an important adjunct to the history and physical examination of the agitated schizophrenic patient. Treatable medical conditions should be ruled out as a potential etiology of psychotic symptoms or exacerbation of underlying psychotic symptoms. Most commonly, agitation results from noncompliance with maintenance therapy or disease progression. However, treatable etiologies of agitation must be ruled out. Factors which may contribute to agitation include metabolic disorders, endocrine disorders, infectious disorders, pain, toxicological etiologies, and structural brain abnormalities (Table 1) [18-21]. Decisions regarding diagnostic tests must be made in the context of the available history and physical examination. For known schizophrenic patients with typical behavioral features, expectant management and serial neurological examination are appropriate. For patients with atypical features, such as delirium, history of trauma, overdose, fever, headache, or other similar findings, additional diagnostic tests should be considered, including computed tomography of the brain, lumbar puncture, serum chemistry panel, complete blood count, endocrine tests, and toxicological screens.

### 4. Measurement of agitation

Many clinicians use clinical judgment to assess the level of agitation. Several studies have identified factors associated with violent or aggressive behavior, including male sex, age (late teens to 20s), substance abuse, history of violence,
hostility during the initial interview, delusions, hallucinations, noncompliance, depression, suicidal tendency, and low intelligence [22-27]. Standardized scales are also available. One example is the 7-point Behavioral Activity Rating Scale [28,29] (Table 2). Other measures of agitation that may be used acutely include the Brief Psychiatric Rating Scale and the Clinical Global Impression of Severity [4-7]. However, for agitated patients, rapid clinical decision making is a priority, and action often must be taken to protect the safety of staff and patients before the feasibility of any standardized test.

5. Nonpharmacological management

Numerous nonpharmacological strategies can be used to treat agitation in schizophrenic patients in the ED; often, the need for pharmacological modalities can be eliminated or reduced by the use of such strategies. Examples of effective nonpharmacological treatments may include placating the patient in a quiet nonthreatening environment, reduction of external noise and other stimuli, behavioral management (ie, granting privileges for appropriate behavior), close observation, calm conversation, and active listening. Consultations from experts in psychiatry, psychology, pastoral care, or social work may be helpful (Fig. 1).

6. Physical restraints

When caring for psychiatric patients, the safety of staff and patients is the primary objective [30,31]. In an unsafe environment, patients cannot be appropriately managed. Resultantly, some patients may need to be physically restrained to assure safety of the environment. Restraints are commonly used for psychiatric patients in emergency departments; 1 study indicated that 8.5% of psychiatric emergency patients are treated with physical restraints [32]. The use of physical restraints should be limited to cases in which the safety of the patient, other patients, or staff is threatened. Some examples might include patients who are violent or suicidal patients who pose an immediate elopement risk. In general, physical restraints should be used in the least restrictive manner possible and for the least amount of time mandated by the clinical situation to achieve the desired goals. According to Joint Commission of Accreditation of Healthcare Organizations requirements, institutions must have restraints policies that stipulate physician orders, nursing documentation, types of restraints, and patient monitoring and assessment, when using physical restraints. According to policy set by the American College of Emergency Physicians, “Restraints should be individualized and afford as much dignity to the patient as the situation allows,” and “Any restraints should be humanely and professionally administered.” In addition, this policy states that protocols should ensure appropriate observation, treatment, assessments, and documentation [33]. Restraints should never be used for competent patients who refuse medical therapy [34].

Physical restraints may include a variety of devices and strategies that limit movement, including limb restraints (such as “4-point” or “5-point” restraints), ambulatory restraints (which may restrain a patient to a chair or bed, but allow limb movement), and seclusion.

Physical restraints may be associated with adverse outcomes. Some adverse outcomes are related to improperly applied restraints, which may result in limb injury, escape from restraints, falls with other resultant injuries, or injury or

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Seven-Point Behavioral Activity Rating scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>Behavior</td>
</tr>
<tr>
<td>1</td>
<td>Difficult of unable to rouse</td>
</tr>
<tr>
<td>2</td>
<td>Asleep, responds normally to verbal or physical contact</td>
</tr>
<tr>
<td>3</td>
<td>Drowsy, appears sedated</td>
</tr>
<tr>
<td>4</td>
<td>Quiet and awake (normal level of activity)</td>
</tr>
<tr>
<td>5</td>
<td>Signs of overt (physical or verbal) activity, calms down with instruction</td>
</tr>
<tr>
<td>6</td>
<td>Extremely or continuously active, not requiring restraint</td>
</tr>
<tr>
<td>7</td>
<td>Violent, requires restraint</td>
</tr>
</tbody>
</table>

Initial assessment
Airway, breathing, circulation, vital signs

Unstable
Airway intervention, intravenous access, circulatory support

Stable
Cooperative with history and physical examination?

Cooperative
History and physical examination. Consider organic causes of agitation, such as trauma, overdose, medical effect, electrolyte imbalance, etc.

Uncooperative
Violence posing danger to self or staff?

Yes

No

Medical/trauma workup as indicated by history and physical examination (See Table 1)

Consider medications to control agitation, psychosocial interventions, psychiatric consultation and/or disposition

Fig. 1 Algorithm for the management of agitation in the schizophrenic patient.
death secondary to asphyxiation [35]. Asphyxiation from the use of restraints is an important adverse outcome to consider and prevent, particularly when using torso restraints [36]. Many patients who have asphyxia are concomitantly intoxicated with alcohol or other substances, which substantially increase risk. The risk of asphyxiation is also increased when patients are restrained in the prone position or when other linens or devices are placed over the head or mouth. Other adverse outcomes are related to improper observation and assessment of patients after the use of restraints, such as dehydration, incontinence, aspiration, or injury from other patients. Some adverse outcomes may be unpredictable and unpreventable, such as rhabdomyolysis, vomiting, increased agitation, thrombosis, or sudden death, which may be related to catecholamine excess [37]. The risk of sudden death while in restraints is small but measurable. One study identified 142 patients who had died in physical restraints over a 10-year period [38], although some authors suggest that this figure is underestimated.

Some authors have suggested strategies to reduce the use of physical restraints, including early patient communications, psychiatric interventions, team approach, involvement of family, and fastidious monitoring of psychiatric patients [39,40].

7. Pharmacological management of acute agitation

Antipsychotic drugs, also known as the neuroleptics or major tranquilizers, have been used for many years to treat acute psychotic reactions (Table 3). This class of medications can be further subdivided into traditional agents (or typical), atypical agents, and other antipsychotics. Historically, the traditional agents have been used as first-line medications for the treatment of the acutely agitated patient, in part because of the availability of parenteral preparations. Since the recent introduction of parenteral forms of both olanzapine and ziprasidone, these medications have been gaining popularity as a first-line treatment option because of their more favorable side effect profile [41-43].

7.1. Traditional (typical) antipsychotics

Traditional agents include the phenothiazines, butyrophenones, dibenzoxazepines and thioxanthenes. Traditionally, the typical antipsychotics have been used for a variety of conditions, including the treatment of agitated or psychotic states, nausea and vomiting, Tourette syndrome, intractable hiccups, and pruritis [44].

The phenothiazines are a drug class that have been available for many years and are considered to be low-potency typical antipsychotic agents. As with all other antipsychotics, the phenothiazines act as antagonists on the dopamine D2 receptors [45]. The agents act by blockade of the D2 receptors in the mesolimbic and mesocortical paths in the brain. The prototypical phenothiazine is chlorpromazine (Thorazine), an agent which has antipsychotic therapeutic effects and has increased efficacy through parenteral administration (up to 4-10 times efficacy), because of unpredictable gastrointestinal absorption. The drug has a large volume of distribution and is rapidly distributed throughout the body. Higher concentrations can be found in the liver, lungs, spleen, and adrenals than in the brain. The phenothiazines are metabolized by the cytochrome p450 system. In addition to blockade at the D2 receptors, the phenothiazines also block the receptors of other neurotransmitters including acetylcholine, serotonin, histamine, and norepinephrine. The blockade of additional receptors, in addition to the nonselective blockade of the D2 receptors, results in adverse effects such as dry mouth, blurred vision, constipation, urinary retention, tachycardia, sedation, hypotension, and dilated pupils.

Other potentially serious side effects of the phenothiazines include motor disturbances caused by the blockade of the dopamine receptors in the extrapyramidal system of the basal ganglia. While taking the medication, the patient may develop parkinsonian symptoms such as rigidity of the limbs, resting tremors, slowed movements, restlessness, and reduction in spontaneous activity [46]. These symptoms occur when 70% to 80% of the dopamine receptors in the caudate nucleus, globus pallidus, and putamen are occupied with the drug.

Tardive dyskinesia is a serious motor disturbance that may be encountered with the use of the phenothiazines and butyrophenones. This is a severely disabling disorder characterized by involuntary hyperkinetic movements of the trunk, tongue, face, and limbs. This disorder generally occurs a few months to years after initiation of treatment and may be irreversible. This disorder is generally caused by an up-regulation of receptors in the abovementioned areas of the brain as a result of chronic receptor blockade.

The butyrophenones are another important class of antipsychotics, including agents such as haloperidol (Haldol) and droperidol (Inapsine). Many authors consider haloperidol to be the typical antipsychotic of choice for treatment of acute agitation [47]. Haloperidol is considered a high-potency antipsychotic. Haloperidol, such as the phenothiazines, acts on the dopamine D2 receptors. Unlike the phenothiazines, haloperidol has a much greater affinity for the receptor and as a result is considered a high-potency antipsychotic. This higher affinity for the dopamine receptors also results in increased incidence of extrapyramidal symptoms and tardive dyskinesia.

Droperidol is another high-potency butyrophenone similar in pharmacological properties to haloperidol. Some studies have demonstrated superiority of droperidol compared with haloperidol in efficacy at 10, 15, and 30 minutes when administered intramuscularly. However, the drug received a “black box” warning from the Food and Drug Administration in 2001 in the United States and Europe because of risk of QTc prolongation and potential risk of
<table>
<thead>
<tr>
<th>Pharmaceutical class</th>
<th>Agent</th>
<th>Trade name</th>
<th>Typical dose (mg)</th>
<th>Primary route</th>
<th>Alternative route</th>
<th>Time of onset</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenothiazine</td>
<td>Chlorpromazine</td>
<td>Thorazine</td>
<td>25-50</td>
<td>IM</td>
<td>PR</td>
<td>30-60 min</td>
<td>NMS, seizures, tardive dyskinesia, agranulocytosis, seizures</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Fluphenazine</td>
<td>Prolixin</td>
<td>1.25</td>
<td>IM</td>
<td></td>
<td>60 min</td>
<td>NMS, agranulocytosis, seizures</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Trifluoperazine</td>
<td>Stelazine</td>
<td>1-2</td>
<td>IM</td>
<td>PO</td>
<td>30-60 min</td>
<td>NMS, agranulocytosis</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Thioridazine</td>
<td>Mellaril</td>
<td>50-100</td>
<td>PO</td>
<td></td>
<td>1-2 h</td>
<td>NMS, agranulocytosis, Torsades, prolonged QT</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Perphenazine</td>
<td>Trilafon</td>
<td>5-10</td>
<td>PO</td>
<td></td>
<td>1-2 h</td>
<td>NMS, agranulocytosis, cardiac arrest, seizures</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>Promethazine</td>
<td>Phenergan</td>
<td>25-50</td>
<td>IV, IM</td>
<td>PO, PR</td>
<td>20 min</td>
<td>NMS, agranulocytosis, seizures, EPS</td>
</tr>
<tr>
<td>Butyrophenone</td>
<td>Haloperidol</td>
<td>Haldol</td>
<td>1-10</td>
<td>IV, IM</td>
<td>PO</td>
<td>20 min</td>
<td>NMS, seizures, EPS, tardive dyskinesia, Prolonged QT</td>
</tr>
<tr>
<td>Butyrophenone</td>
<td>Droperidol</td>
<td>Inapsine</td>
<td>2.5-5</td>
<td>IV, IM</td>
<td></td>
<td>3-10 min</td>
<td>NMS, agranulocytosis, bronchospasm</td>
</tr>
<tr>
<td>Dibenzoazepine</td>
<td>Loxapine</td>
<td>Loxitane</td>
<td>12.5-50</td>
<td>IM</td>
<td>PO</td>
<td>20-30 min</td>
<td>NMS, agranulocytosis, seizures</td>
</tr>
<tr>
<td>Thioxanthenes</td>
<td>Thiothixene</td>
<td>Navane</td>
<td>2-10</td>
<td>PO</td>
<td>PO</td>
<td>60 min</td>
<td>NMS, agranulocytosis, seizures, tardive dyskinesia</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Midazolam</td>
<td>Versed</td>
<td>1-2</td>
<td>IV, IM</td>
<td></td>
<td>0.5-5 min</td>
<td>Respiratory arrest, cardiac arrest</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Lorazepam</td>
<td>Ativan</td>
<td>0.5-2</td>
<td>IV, IM</td>
<td>PO</td>
<td>15-20 min</td>
<td>CV collapse, respiratory depression, blood dyscrasias</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Oxazepam</td>
<td>Serax</td>
<td>10-30</td>
<td>PO</td>
<td></td>
<td>2-3 h</td>
<td>Leukopenia, hepatic dysfunction, drowsiness</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Diazepam</td>
<td>Valium</td>
<td>2-10</td>
<td>IV, IM</td>
<td>PO, PR</td>
<td>15-45 min</td>
<td>CV collapse, respiratory depression, blood dyscrasias, hypotension</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Alprazolam</td>
<td>Xanax</td>
<td>0.25-0.5</td>
<td>PO</td>
<td></td>
<td>45-90 min</td>
<td>Seizures, tachycardia, syncope, suicidal ideation</td>
</tr>
<tr>
<td>Atypical</td>
<td>Clozapine</td>
<td>Clozaril</td>
<td>12.5-25</td>
<td>PO</td>
<td></td>
<td>15 min</td>
<td>NMS, agranulocytosis, seizures, severe hypotension</td>
</tr>
<tr>
<td>Atypical</td>
<td>Risperidone</td>
<td>Risperdal</td>
<td>1-4</td>
<td>PO</td>
<td></td>
<td>Days</td>
<td>NMS, EPS, severe hypotension, severe hyperglycemia</td>
</tr>
<tr>
<td>Atypical</td>
<td>Ziprasidone</td>
<td>Geodon</td>
<td>10</td>
<td>IM</td>
<td>PO</td>
<td>30 min</td>
<td>NMS, prolonged QT, EPS, severe HTN</td>
</tr>
<tr>
<td>Atypical</td>
<td>Quetiapine</td>
<td>Seroquel</td>
<td>25-250</td>
<td>PO</td>
<td></td>
<td>Weeks</td>
<td>NMS, prolonged QT, tardive dyskinesia, severe hypotension</td>
</tr>
<tr>
<td>Atypical</td>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>10</td>
<td>IM</td>
<td>PO</td>
<td>15-45 min</td>
<td>NMS, EPS, severe hypotension, severe hyperglycemia</td>
</tr>
<tr>
<td>Other</td>
<td>Aripiprazole</td>
<td>Abilify</td>
<td>10-15</td>
<td>PO</td>
<td></td>
<td>Days-weeks</td>
<td>NMS, tardive dyskinesia, orthostatic hypotension, syncope</td>
</tr>
</tbody>
</table>

CV indicates cardiovascular; PR, per rectum; EPS, extrapyramidal system; HTN, hypertension.
ventricular dysrhythmias and sudden cardiac death. Many institutions have completely eliminated its use because of this warning. However, many authors consider droperidol to be a safe and effective drug when prescribed in appropriate doses, with appropriate monitoring [48-51].

7.2. Atypical antipsychotic agents

The atypical antipsychotic agents are a newer class of drugs which are gaining popularity in the treatment of the acutely agitated patient because of their more favorable side effect profile. The atypical agents act by blockade of the dopamine D2 receptors as well as by blocking the serotonin 5-HT receptors. The atypical antipsychotics are as effective as the typical antipsychotics and have reduced incidence of extrapyramidal side effects including akathisia, dystonia, and tardive dyskinesia [52].

Of the atypical agents, 2 currently have an intramuscular (IM) form available—olanzapine (Zyprexa) and ziprasidone (Geodon). Both are at least as effective as haloperidol at producing rapid tranquilization in the acutely agitated patient. Peak plasma concentrations of ziprasidone are achieved within 30 to 45 minutes with a half-life of 2.2 to 3.4 hours after an IM injection. Similar results were obtained after IM injection of olanzapine with peak plasma concentration achieved within 15 to 30 minutes. As noted above, ziprasidone may be associated with prolongation of the QT interval, and appropriate precautions should be taken when administering the drug.

7.3. Benzodiazepines

Benzodiazepines are a class of drugs, a subset of sedative-hypnotic agents, which commonly result in anxiety effects, muscle relaxation, somnolence, and seizure control. Because of their relaxation and antianxiolytic effects, they may be appropriately used for the treatment of agitation in psychotic patients. Benzodiazepines act by potentiating the activity of -aminobutyric acid (GABA), 1 of the major inhibitory central nervous system neurotransmitters. As a result of benzodiazepine binding to the GABA receptors, enhanced GABA neurotransmission typically results in muscle relaxation, sedation, anxiolysis, and anticonvulsant effects.

The onset of action of benzodiazepines is dependent on the rate of absorption from the gastrointestinal tract (if administered by mouth). The peak serum concentration of most benzodiazepines occurs within 1 to 3 hours. Benzodiazepines undergo primarily hepatic metabolism, and many benzodiazepines are metabolized to pharmacologically active metabolites, some of which have a longer half-life than the parent compound.

Benzodiazepines may be effectively used as single agents or in combination with other antipsychotic agents, such as haloperidol, droperidol, olanzapine, or other antipsychotic agents [53-58]. Several studies have demonstrated increased efficacy in control of agitation when used in combination with antipsychotic agents, such as haloperidol or droperidol [59]. Rapidly acting agents, such as midazolam (Versed), have the important benefit of faster time to onset [60,61]. The dosage should be titrated to effect, and multiple doses of a single agent may be required [62,63].

When prescribing benzodiazepines, it is essential that the physician consider the half-life and potential adverse effects of the agent used. The half-lives of benzodiazepines vary greatly, from the short half-life of midazolam (2 hours) to the long half-life of agents such as diazepam (Valium) (35 hours). Agents with short half-lives are generally preferred for use in the ED, such as midazolam (Versed), lorazepam (Ativan), oxazepam (Serax), and alprazolam (Xanax). Midazolam has the unique advantage of relatively predictable IM absorption. All benzodiazepines have the potential to cause adverse effects, such as excessive sedation, ataxia, and confusion. Serious adverse effects, such as respiratory depression or hypotension, are extremely rare when benzodiazepines are used as single-agent therapy. The risk of such adverse effects increased when used in combination with other agents, in particular, opioid agents.

8. Life-threatening complications of pharmacological agents

8.1. Neuroleptic malignant syndrome

NMS is a potentially fatal rare complication of several of the antipsychotic agents, including clozapine, risperidone, olanzapine, clopiaptine, clozapine, ziprasidone, and quetiapine [64-67]. Incidence has been reported to vary from 0.02% to 2.44% of patients taking antipsychotic agents and is highest among the typical antipsychotic agents [68]. Symptoms include altered mental status, hyperthermia, muscle rigidity, autonomic instability, and movement disorder. Elevated creatine kinase levels may be seen. Risk factors for NMS include mental retardation, psychomotor agitation, acute catatonia, acute disorganization and confusion, IM administration, and increased or new dosage; elevated environmental temperature was not found to be a risk factor [69,70]. Management of NMS includes supportive care, including airway management, hydration, and cooling. Pharmacological management is controversial and may include administration of anticholinergic agents, benzodiazepines, dantrolene, or bromocriptine [71-74]. Although the mechanism of action of dantrolene is not well elucidated, it is thought that it acts by depression of the intrinsic mechanisms of excitation contraction coupling in skeletal muscle [75].

8.2. Prolonged QT syndrome

Many antipsychotic agents may prolong the QTc interval, including ziprasidone (Geodon), thioridazine (Mellaril), haloperidol (Haldol), chlorpromazine (Thorazine), fluphenazine (Prolixin), and quetiapine (Seroquel) [76,77]. The
reported incidence varies but may be as high as 6.7% of schizophrenic patients on long-term antipsychotic agents [78]. This complication should be considered for all patients receiving these agents; preliminary electrocardiogram and cardiac monitoring may be appropriate for such patients. The risk of prolonged QTc interval is increased in patients with congenital long QT syndrome, female sex, parenteral antipsychotic administration, hypokalemia, and use of sympathomimetics [79-83]. As a result of the QT-interval prolongation, the individual may be predisposed to ventricular dysrhythmias including torsade de pointes and ventricular fibrillation.

8.3. Respiratory depression

The risk of respiratory depression should be considered as a possible complication of pharmacological therapy, and the risk is increased with the use of combination pharmacological therapy. All pharmacological agents should be used in the minimum effective dose and with caution when patients are in physical restraints.

9. Informed consent and informed refusal of care

The issues of informed consent and informed refusal of care pose unique challenges when treating psychiatric patients. As with all patients, any particular preexisting diagnosis or therapy does not preclude the ability of any patient to participate in medical decision making. However, patients with schizophrenia may require greater in-depth analysis of decisional capacity before appropriate informed consent or informed refusal of care.

Informed consent is considered a fundamental principle of medical care, as established by the US legal system in 1957 [84], and upheld since that time [85,86]. The basic principle of informed consent presumes that patients have the moral and legal right to make medical decisions for their own care. Informed consent is considered a fundamental right of patients who possess decisional capacity [87-92].

There are several exceptions to the duty of the treating physician to obtain informed consent from patients. For example, in emergent situations, when immediate treatment is indicated to prevent death or serious harm to a patient lacking decisional capacity, appropriate interventions should be performed, despite difficulties in obtaining informed consent. Other exceptions to this duty to obtain informed consent include patients who waive their right to consent and public health or legal requirements. Schizophrenic patients who lack decisional capacity may fit into 1 of these categories.

Fundamentally, the same standards should be met for informed consent and informed refusal of care. Both informed consent and informed refusal represent a process, not merely a signature. The process should include the following elements: determination of decisional capacity, delivery of information including any risks of refusing treatment, and documentation of the process. For patients who possess appropriate decisional capacity, including psychiatric patients, who pose no imminent threat to self or others, the patient’s wishes regarding medical treatment should be honored.

Assessing decisional capacity is the most important element of the informed consent or refusal process for psychiatric patients [88,93,94]. Decisional capacity is simply a patient’s ability to make an authentic choice. Decisional capacity includes cognitive and affective functions, which are clinically manifest in intellect, memory, judgment, insight, language, attention, emotion, calculation, and expressive and receptive communication skills. Decisional capacity includes the abilities to receive information, process and understand information, deliberate about choices, and form and communicate a choice [95,96]. Particularly for psychiatric patients or other patients for whom capacity may be in question, standardized tests may be valuable in the determination of capacity [97-104]. A standardized test which is easily administered in emergency medicine is the Mini-Mental State Examination (Table 4) [105-107]. Another example of a standardized test is the formulation by the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research [95].

When a schizophrenic patient refuses medical therapy and decisional capacity has been ascertained, several steps may be taken to attempt to improve compliance with therapy. Techniques that may be effective include

<table>
<thead>
<tr>
<th><strong>Table 4</strong> Mini-Mental State Examination</th>
<th>Score</th>
<th>Maximum score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orientation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the (year), (season), (date), (day), (month)?</td>
<td>__ 5</td>
<td></td>
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<tr>
<td>Where are we? (state) (county) (town) (hospital) (floor)</td>
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<tr>
<td><strong>Registration</strong></td>
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<tr>
<td>Name 3 objects and ask patient to repeat</td>
<td>__ 3</td>
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</tr>
<tr>
<td>Attention and calculation</td>
<td></td>
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<tr>
<td>Serial 7’s (1 point for each correct up to 5); option: spell “world” backward</td>
<td>__ 5</td>
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<tr>
<td><strong>Recall</strong></td>
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<tr>
<td>Ask for the 3 objects repeated above</td>
<td>__ 3</td>
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<tr>
<td><strong>Language</strong></td>
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<tr>
<td>Name a pencil and watch (2 points)</td>
<td>__ 9</td>
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<tr>
<td>Repeat “no ifs, ands, or buts” (1 point)</td>
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<tr>
<td>Follow a 3-stage command (3 points)</td>
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<tr>
<td>Read and follow the command, “close your eyes” (1 point)</td>
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<td>Write a sentence (1 point)</td>
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<td>Copy a design (1 point)</td>
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<tr>
<td><strong>Total</strong></td>
<td>__ 30</td>
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</table>
education about medical treatment recommendations; addressing the patient’s values, goals, and concerns; involvement of family or friends (with permission); and consultation with a colleague.

10. Disposition

Disposition decisions should be made based on the current condition of the patient. Many patients who have required nonpharmacological or pharmacological management of agitation require inpatient psychiatric treatment, either voluntarily or involuntarily. Patients who pose a threat to their own safety or that of others should be hospitalized involuntarily. Some patients with agitation due to a reversible treated etiology may be considered for outpatient management. Psychiatric consultation should be sought for patients with schizophrenia and uncertain disposition determinations, or those requiring other complex management decisions.

References

Emergency management of agitation in schizophrenia

Clinical Notes

A modified thumb spica splint for thumb injuries in the ED

Raymond G. Hart MD, MPH\textsuperscript{a,b,*}, Harold E. Kleinert MD\textsuperscript{c}, Kathleen Lyons RN\textsuperscript{d}

\textsuperscript{a}Department of Emergency Medicine, University of Louisville School of Medicine, Louisville, KY 40202, USA
\textsuperscript{b}Hand Injury Prevention and Research, Christine M. Kleinert Institute for Hand and Microsurgery, Inc, Louisville, KY 40202, USA
\textsuperscript{c}Department of Surgery, University of Louisville School of Medicine, Louisville, KY 40202, USA
\textsuperscript{d}Christine M. Kleinert Institute for Hand and Microsurgery, Louisville, KY 40202, USA

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Abstract There are a significant number of hand and upper extremity injuries treated in US emergency departments (EDs) each year. Many of these involve the thumb and wrist. These injuries encompass the range from fractures, strains, and sprains to more specific injuries such as gamekeeper thumb and de Quervain tenosynovitis. These injuries often require diagnosis, splinting, and referral to a hand or orthopedic surgeon. The splint described in this article is presently being used for patients with de Quervain tenosynovitis, but it may have more widespread application in emergency medicine. It is a safe and simple splint that is underused in EDs for splinting thumb injuries.

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1. Introduction

There were 110.2 million emergency department (ED) patient visits in the United States in 2002 [1]. Of those visits, hand and finger injuries were estimated to be 4.8 million [2]. The thumb is estimated to be more than 20% of those injuries or nearly 1 million ED visits per year.

Work-related musculoskeletal disorders of the hand and upper extremity have become more common [3,4]. A reported 588,000 persons complained of prolonged hand discomfort and were given a diagnosis of trigger finger, ganglion cyst, tenosynovitis, epicondylitis, synovitis, de Quervain disease, or tenosynovitis by a medical person [5]. Of these, 28% were thought to be work-related. Each of these injuries must be carefully diagnosed, splinted when necessary, and appropriately referred.

There are a number of varied injuries that may result from trauma to the thumb. A sprain or strain is common and can be painful and debilitating. A thumb fracture will definitely need follow-up evaluation and care. An intra-articular fracture at the first carpometacarpal (CMC) joint, called a Bennett or Rolando fracture, is a particular example. These injuries can lead to pain, weakness, and instability of the thumb. There are also several specific thumb injuries that require splinting and referral. A gamekeeper thumb, which is an injury to the ulnar collateral ligament at the thumb metacarpophalangeal (MCP) joint, requires a splint and referral. De Quervain tenosynovitis, which usually results from overuse, causes a painful thumb and improves with appropriate splinting. In addition, dislocation of any joint of the thumb requires reduction, splinting, and follow-up care. Other injuries to the thumb include nail-bed and fingertip...
injuries, soft tissue injuries, and lacerations. Furthermore, possible flexor or extensor tendon lacerations and neurovascular bundle injuries that may require exploration by a hand surgeon will need splinting from the ED.

There are choices the emergency physician must consider for splinting. A soft dressing may be adequate for some injuries, perhaps with an elastic bandage added for support. There are prefabricated splints that can adequately immobilize a thumb injury. There are also volar or dorsal foam-backed splints that can be fashioned and applied to the thumb. However, when immobilization is needed, the most effective splint for the thumb is the thumb spica splint. The thumb spica provides support to the wrist and thumb. The immobilization will promote healing, protect the injured thumb, and decrease pain.

2. Methods

The splint recommended is presently being used in the hand surgery practice for patients with de Quervain tenosynovitis. Patients seen with the diagnosis may have radiographs and may begin nonsteroidal anti-inflammatory drugs. They will likely also receive a steroid injection and will have a splint placed for 3 to 4 days. It is fashioned specifically to the patient’s thumb, wrist, and forearm. It is inexpensive and lightweight and can be removed without difficulty. It also allows for possible swelling of the digit.

The splint is simple to make and apply. First, obtain about 4 sheets of 4-in plaster. These 4-in strips should be folded longitudinally in half, with an accompanying 12-in-long × 2-in-wide stockinet prepared (Fig. 1). The plaster is then slipped into the stockinet, and the entire splint is dipped in water (Fig. 2). Warm water provides rapid setting of the plaster; thus, cool or only lukewarm water is suggested to allow the physician time to fashion the splint appropriately. A dressing of 4-in Webril can be applied initially as with other plaster splints, but it is not mandatory with this particular splint. The patient’s thumb should be positioned in a comfortable, neutral position. Take the wet splint from the basin of water, and with 2
fingers, strip the excess water; then, apply the splint, supporting the volar surface of the thumb first (Fig. 3). Apply the splint in a cross fashion around the dorsum of the thumb at approximately the MCP joint. The splint will cross the wrist and provide 8 to 10 cm of support proximally, with the wrist in a neutral position (Figs. 4 and 5). After the thumb and wrist have been positioned comfortably, the splint can be adjusted and straightened to provide maximal comfort and no opportunity for sharp or hard edges. An elastic bandage can then be applied to ensure support for the splint, thumb, and wrist (Fig. 6). The splint can be fashioned to accommodate swelling and, if necessary, in such a way that the elastic bandage and splint may be quickly and easily removed if the patient experiences excessive pain or swelling (Fig. 7).

3. Discussion

Hand injuries are common in the ED. Thumb injuries, in particular, can be subtle, and the emergency physician must be aware of potential complicated injuries. These injuries are overlooked at great risk to the patient and can be devastating because the thumb is crucial to the dexterity of the human hand. One of its most important functional aspects is its extensive mobility, and it is the most vital and important digit of the hand.

The CMC joint is the most important joint of the thumb from a functional standpoint [6,7]. The thumb interphalangeal joint and MCP joints both flex and extend. The CMC joint, however, allows palmar abduction and adduction, as well as radial abduction and adduction. The thumb also can move in opposition and reposition. Its movements allow the complexity of human prehension.

Unfortunately, some hand injuries can ultimately lead to disability. Instability, pain, and loss of function at the CMC joint can lead to a lifetime of pain and disability. It is incumbent on the emergency physician to properly diagnose, treat, and refer these injuries; part of the treatment must include the appropriate splint. It is essential to know which of these injuries require referral and the urgency of follow-up with a hand or orthopedic surgeon.

The CMC joint of the thumb is a common site for degenerative arthritis [8-10]. The degeneration of first CMC osteoarthritis generally occurs in the fifth decade of life and affects women more than men. There are tremendous functional demands placed on this highly mobile joint [6]. In addition, it must be stable enough to allow for powerful pinching loads. The CMC joint has a relatively large and loose capsule to accommodate the extensive range of motion, and it is reinforced by at least 5 ligaments. In addition, patients with rheumatoid arthritis have a significantly higher incidence of related hand pathology [11].

De Quervain tenosynovitis is an inflammation of the extensor pollicis brevis and abductor pollicis longus tendons [12]. This also includes the layers of the tendon sheaths. It occurs commonly in women aged between 30 and 50 years. It can occur from a variety of causes including bathing, grinding, polishing, and screwdriver use. It has
recently been described as a postpartum/newborn condition [13,14]. These patients complain of pain and tenderness along the radial aspect of the wrist, with swelling dorsally over the first extensor tendon compartment. It may be possible to palpate the swelling at the anatomic snuffbox near the radial styloid, and any motion of the thumb or the wrist may be painful. These patients benefit greatly from the splint described.

Correct splinting is critical in all cases but particularly with the hand and thumb. A splint must provide support and protection, and the splint material chosen should be inexpensive but secure. It should immobilize the thumb to decrease pain, rest the injured part, and prevent further injury. Splints can be made static for immobilization or dynamic to allow controlled mobility. It is essential that the chosen splint applied does not cause its own complications. The most frequent are itching, pain, stiff joints, and pressure sores.

A splint misapplied to the thumb can lead to a digital neuropathy similar to a Bowler thumb lesion [15,16]. This is a compression neuropathy caused by extra neural mechanical pressure applied to the ulnar digital nerve of the thumb. This nerve is susceptible to injury for 4 reasons: it is immediately beneath the skin, it travels directly over bony structures, it has a fixed position with minimal excursion, and there is no pain associated with the nerve trauma, only resulting numbness.

Poorly chosen and designed splints can lead to these complications. These complications may occur more frequently in prefabricated splints in that they are inflexible, made to standard sizes, and do not allow uniform contact with the tissues [16]. Custom-made splints allow better molding, individual variability, and careful specific tissue contact.

The splint applied must provide joint protection. Joint protection is defined as minimizing or eliminating stress placed on the joint during the performance of activities of daily living [7]. Regardless of design, a static splint applied to the thumb should position the base of the thumb in relative palmar abduction and incorporate slight flexion and medial rotation. Staged splinting has also proven effective for thumb conditions in infants [17].

There are splints specifically designed for the MCP joint of the thumb [18]. The goal stated for these splints is to maintain the thumb in a stable position, minimize compression over the dorsal surface of the MCP joint, and enhance overall function of the hand. These splints stabilize the thumb MCP joint in approximately 15° to 20° of flexion with slight opposition.

Spica (Latin for “ear of wheat”) is defined as “a figure of eight bandage with turns that cross one another regularly like the letter V, usually applied to anatomic areas of quite different dimensions,” such as the thumb [19]. The proposed splint is a modified thumb spica splint. It has a stand-alone unit of removable plaster with only a single cross or turn of the material and is supported with an elastic bandage.

The thumb splint described supports multiple joints and will afford maximal protection to the entire thumb and radial wrist region. This is especially desirable for an acutely injured, painful thumb in an active person. The wrist should be immobilized in about 10° to 20° extension, the CMC joint in relative palmar abduction, the MCP joint in 30° flexion, and the interphalangeal joint in a neutral position.

The splint described is used to treat patients in this hand surgery practice with de Quervain tenosynovitis who require a steroid injection and splinting. It was initially devised and popularized by Dr Bruce Butler. The splint has proven itself over the years to be inexpensive, patient-specific, comfortable but secure, durable, and effective. Many of the thumb injuries seen in the US EDs require splinting. The splint described is an option that may have widespread application for just those injuries.

References


Diagnostics

The San Francisco Syncope Rule vs physician judgment and decision making

James V. Quinn MD, MSa,*,1 Ian G. Stiell MD, MScb, Daniel A. McDermott MDc, Michael A. Kohn MD, MPPd, George A. Wells PhDc

aDivision of Emergency Medicine, Stanford University, Palo Alto, CA 94304, USA
bDivision of Emergency Medicine, University of California, San Francisco, CA 94143, USA
cDepartment of Emergency Medicine, University of Ottawa, Ottawa, Ontario K1Y-4E9, Canada
dDepartment of Epidemiology, University of California, San Francisco, CA 94143, USA
eDepartment of Epidemiology, University of Ottawa, Ottawa, Ontario K1Y-4E9, Canada

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Abstract

Objective: To compare a clinical decision rule (San Francisco Syncope Rule [SFSR]) and physician decision making when predicting serious outcomes in patients with syncope.

Methods: In a prospective cohort study, physicians evaluated patients presenting with syncope and predicted the chance (0%-100%) of the patient developing a predefined serious outcome. They were then observed to determine their decision to admit the patient. All patients were followed up to determine whether they had a serious outcome within 7 days of their emergency department visit. Analyses included sensitivity and specificity to predict serious outcomes for low-risk patients and comparison of areas under the receiver operating characteristic curve for the decision rule, physician judgment, and admission decisions.

Results: During the study period, there were 684 visits for syncope with 79 visits resulting in serious outcomes. The area under the receiver operating characteristic curve was 0.92 (95% confidence interval [CI], 0.88-0.95) for the SFSR compared with physician judgment 0.89 (95% CI, 0.85-0.93) and physician decision making 0.83 (95% CI, 0.81-0.87). Physicians admitted 28% of patients in a low-risk group, with a median length of stay of 1 day (interquartile range, 1-2.5 days). The SFSR had the potential to absolutely decrease admissions by 10% in this low-risk group and still predict all serious outcomes.

Conclusions: Physician judgment is good when predicting which patients with syncope will develop serious outcomes, but contrary to their judgment, physicians still admit a large number of low-risk patients. The SFSR performs better than current physician performance and has great potential to aid physician decision making.

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* Corresponding author. Tel.: +1 650 736 4391; fax: +1 650 723 0121.
E-mail address: quinnj@stanford.edu (J.V. Quinn).
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1. Introduction

Syncope is a transient loss of consciousness with a return to preexisting neurologic function. A common problem, 1 of 4 people will faint during their lifetime, and 1% to 2% of all emergency department (ED) visits and hospital admissions are related to a transient loss of consciousness [1-4].

Patients with syncope create a difficult dilemma for physicians. Most causes are benign, but occasionally, it is a symptom associated with significant morbidity and mortality. Some patients will require emergent hospitalization for workup and treatment of life-threatening or potentially life-threatening causes, others should get outpatient evaluation, whereas some patients need no further evaluation.

It has been suggested that the use of hospitalization for patients with syncope is inefficient and highly variable [5-10]. Many things can cause syncope and the potential diseases that cause it span multiple specialties, making it difficult to develop an optimal disposition for these patients. Accordingly, a survey of physicians revealed that the disposition of patients with syncope was the second most common decision problem for North American physicians [11]. A highly sensitive and specific decision rule that would aid and improve physician decision making could have the potential to significantly reduce health care costs and improve efficiency and patient care.

The San Francisco Syncope Study is a prospective multiphase study. Phase 1 involved derivation of a decision rule using 684 patients to help predict patients at risk for

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Fig. 1  San Francisco Syncope Rule.
acute outcomes. Variables were assessed for their interobserver agreement and univariate association with acute outcomes. The final San Francisco Syncope Rule (SFSR), derived from recursive partitioning of the most important variables, was found to be highly sensitive and specific (Fig. 1) [12]. To justify the time and effort involved in validating and disseminating a decision rule, it is important to know if the rule can improve upon the diagnostic accuracy and reliability of unstructured physician judgment and eventual decision making. We sought to determine whether the SFSR would have performed better than physician decision making during phase 1 of the study.

2. Methods

The multiphase San Francisco Syncope Study was undertaken with reference to previously described guidelines for developing clinical decision rules [13,14]. In particular, outcomes were clearly defined and predictor variables were carefully chosen before the study began. A significant number of patients independently assessed by 2 physicians to measure agreement for subjective variables and appropriate multivariate methods were used to derive the rule [11].

This prospective cohort study was conducted at a large university teaching hospital and included patients presenting with acute syncope or near syncope as a reason for their ED visit. Patient enrollment was achieved by prospectively screening patients with complaints of syncope, loss of consciousness, fall, collapse, seizure, light-headedness, tachycardia, bradycardia, shortness of breath, and chest pain. Patients were excluded if they had altered mental status, alcohol- or illicit drug-related loss of consciousness, a definite seizure, or transient loss of consciousness caused by head trauma. A dedicated research nurse reviewed daily patient logs and ensured enrollment of all possible patients. All attending physicians and house staff were asked to carry their normal assessment and disposition of each patient. After their clinical interaction, each physician completed a standardized data form with assessments of historical and physical findings. In addition to information about potential clinical decision rule variables, physicians were also asked to prospectively estimate the probability (0%-100% at 11 different prediction intervals) that the patient would have a serious outcome within 7 days. This judgment was based only on their clinical assessment and considered the occurrence of 1 of the following outcomes within the next 7 days: death, myocardial infarction, arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, significant hemorrhage, or any condition causing a return ED visit and hospitalization for a related event. When feasible, a second physician was asked to independently fill out a study form to assess physician agreement. A study nurse completed follow-up on all patients to determine whether they had a serious outcome. The Committee on Human Research at the University of California, San Francisco, approved the study protocol without the need for written informed consent. Patients followed up by direct contact had the opportunity to give verbal consent during the telephone interview.

Using data at the various prediction intervals, receiver operating characteristic (ROC) curves were constructed for judgment alone eventual admission decision and the SFSR. Areas under the ROC curves with 95% confidence intervals (CIs) were analyzed. An arbitrary low-risk threshold of a 2% or less chance of a serious outcome was used to help determine the potential value of the SFSR for helping with admission decisions in a low-risk group of patients.

3. Results

This phase of the San Francisco Syncope Study took place from June 30, 2000, to February 28, 2002. There were 684 visits analyzed and their characteristics are summarized in Table 1. Fifty-five percent of all patients were admitted, 59% were female and the average age was 62 years. All patients had some form of follow-up. Ninety-six percent of patients had direct confirmation of their outcome with less than 4% requiring indirect follow-up through checks to local hospital and the death registry. Seventy-nine (11.5%) patients developed serious outcomes by day 7 with 49 of these occurring after their ED visit.

The respective areas under the ROC curves for predicting short-term serious outcomes were physician judgment 0.89 (95% CI, 0.85-0.93), physician decision to admit
0.83 (95% CI, 0.81-0.87), and the SFSR 0.92 (95% CI, 0.89-0.95) (Fig. 2).

Physicians classified 54% of patients in the cohort as having a less than 2% chance of serious outcome by day 7, and we categorized these patients as low risk (Table 2). Among this low-risk group, there were no deaths, 1.4% had serious outcomes, and 28% were admitted. Admitted patients stayed a median of 1 day (interquartile range, 1-2.5 days). Physician judgment had a sensitivity of 94% (95% CI, 86%-98%) for predicting patients at low risk with a specificity of 52% (95% CI, 51%-53%). For comparison purposes, the SFSR had good overall sensitivity of 96% (95% CI, 92%-100%) and specificity of 62% (95% CI, 58%-66%) (Table 3), and if used to guide admission decisions in this low-risk group, the SFSR would have predicted all serious outcomes and that only 18% of patients needed admission in this group, providing a potential absolute decrease of 10% in those patients admitted without missing a serious outcome.

### 4. Discussion

Overall physician judgment is good for discriminating those patients with syncope at risk for serious outcomes. However, unstructured physician judgment is problematic. It still misclassifies a small number of important outcomes, and more importantly, because it is unstructured and variable among physicians, physicians do not trust their judgment and thus decide to admit many low-risk patients. This study has shown that the SFSR performs better than overall physician decision making and there appears to be an important opportunity, especially among low-risk patients, to allow more efficient medical decisions.

The problems associated with unstructured physician judgment, combined with the potential for rare adverse consequences, lead to the inefficient use of admissions for patients with syncope. Overall physicians admitted 55% of patients in this derivation set, including 28% whom the physicians felt were at low risk. Physicians even admitted 9% of patients in the study whom they felt had zero chance of having a serious outcome. In the derivation set, the SFSR suggests that admission rates could potentially be lowered to less than 45% overall, and in the low-risk group defined in this study, we also found that admissions could have been potentially decreased by 10% [12]. This improvement in efficiency could reduce health care costs and improve patient care.

Instead of focusing on all patients, we focused this analysis on this low-risk group for several reasons. These patients represented a large percentage of the cohort, and because physicians still admitted a large number of these low-risk patients, we felt that it presented the best opportunity for the rule to influence decision making and change behavior. We felt that physicians would consider discharge of low-risk patients when the decision rule predicted them at low risk than discharging patients whom they felt were moderate or high risk although the rule predicted the patient to be low risk. We thus feel that this group represents a tremendous opportunity to improve the efficiency of admissions for patients with syncope who present to the ED.

It is possible that some of the admissions in the low-risk group were not for syncope, but for another medical or social condition requiring admission. It should be noted that the rule was designed to risk stratify patients and
predict patients at risk for serious outcome by day 7 as a proxy for those requiring emergent medical admission. Our rationale being that if a serious outcome happened 7 days after an initial ED visit, it would be hard to justify that an emergent admission 7 days earlier was the only way to diagnose and treat that patient. Some may argue that an acute admission could be warranted for diagnosing a serious condition that could present as a serious outcome in 14 days, 1 month, or even a year; that rationale assumes that only important diagnosis can be made as an inpatient and that outpatient follow-up is inefficient or unavailable. Although this may be a reason for admitting some patients, our study like others showed that majority of low-risk patients stay only 1 day in the hospital and have very little if any testing [6]. Thus, it is unlikely that the large numbers of admissions in this low-risk group could be solely attributed to poor follow-up on discharge and thus need to admit to provide workup of these patients.

Finally, by including patients who by definition already had their serious outcome on presentation, the ROC curve for physician judgment is likely an overstatement of the performance of physician judgment. However, we felt that it was only fair to include all outcomes for physician judgment when we were using all outcomes to demonstrate the performance of the rule. Most important is that regardless of the cases included in our analysis, the decision rule always had a greater area under the ROC curve. Although the significance of the differences in the areas of the ROC curves is debatable, the rule appears to perform better, and because it adds structure and reliability to unaided judgment, we feel that it has the potential to be a valuable aid in physician decision making.

5. Conclusions

The limitations of physician judgment have resulted in the variable and inefficient use of admissions for patients presenting with syncope. In the first phase of this study, we have developed a highly sensitive and specific rule and demonstrated its value compared with physician judgment alone for identifying patients at acute risk for serious outcomes and guiding admission decisions. The SFSR is currently under prospective validation. We believe that a reliable decision rule will guide and lead to more efficient medical decision making.

References

The usefulness of urine fluorescence for suspected antifreeze ingestion in children

Tania Parsa MD\textsuperscript{a,1}, Sandra J. Cunningham MD\textsuperscript{a,b,*}, Stephen P. Wall MD\textsuperscript{b}, Steven C. Almo PhD\textsuperscript{c}, Ellen F. Crain MD, PhD\textsuperscript{a,b}

\textsuperscript{a}Department of Pediatrics (Jacobi Medical Center), Albert Einstein College of Medicine, Bronx, NY 10461, USA
\textsuperscript{b}Department of Emergency Medicine (Jacobi Medical Center), Albert Einstein College of Medicine, Bronx, NY 10461, USA
\textsuperscript{c}Department of Biochemistry, Albert Einstein College of Medicine, Bronx, NY 10461, USA

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Abstract

Purpose: To evaluate urine fluorescence as a diagnostic tool.

Procedures: Using a Wood lamp, 60 physicians, assigned to group 1 or 2, independently rated 150 urine specimens from nonpoisoned children as fluorescent or nonfluorescent. Interobserver and intraobserver agreements were assessed. Physician ratings were compared with fluorometry results. The prevalence of urine fluorescence was determined by fluorometry.

Main Findings: Group 1 reported fluorescence in 80.7% (95% CI 73.4%-86.6%) of urine specimens; group 2 reported fluorescence in 69.3% (95% CI 61.3%-76.5%). Interrater agreement was poor (72.5%, $\kappa = 0.25$, 95% CI 0.13-0.37); intrarater agreement was good (physician group 1: 97.9%, $\kappa = 0.93$, 95% CI 0.77-1.00; physician group 2: 93.3%, $\kappa = 0.85$, 95% CI 0.69-1.00). The prevalence of urine fluorescence was 100% (95% CI 98.1%-100%).

Conclusion: Our data suggest that determination of urine fluorescence using a Wood lamp is a poor screening tool for suspected antifreeze ingestion in children.

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1. Introduction

Ethylene glycol, a component of a variety of automotive products including deicers and antifreeze, is a colorless, odorless, viscous liquid with the potential for severe multisystem toxicity when ingested. In 2003, the American Association of Poison Control Centers reported 5816 exposures; 676 of these were in children younger than 6 years, and 869 occurred in children aged 6 to 19 years [1]. A toxic dose of ethylene glycol is estimated to be 0.5 mL/kg or more, and the minimum lethal dose of ethylene glycol is 1.4 mL/kg [2].

Sodium fluorescein is added to some brands of antifreeze to help mechanics identify potential engine coolant leaks; a 30-mL volume of 100% antifreeze contains 0.6 mg of sodium fluorescein [3]. Sodium fluorescein is freely soluble...
in water and has intense yellowish green fluorescence visually detectable to a lower limit of 20 ng/mL when exposed to ultraviolet light [4]. The fluorescence disappears when the solution is acidic (pH < 4.5) but reappears when the solution is made neutral or alkaline [4].

Because metabolic derangements may be absent initially after ethylene glycol ingestion, and serum levels are not readily available, many toxicologists recommend that the urine of patients with suspected antifreeze ingestion be examined with a Wood lamp for the presence of fluorescence [5]. Fluorescence is the emission of light by certain substances when excited by ultraviolet energy. A Wood lamp is a source of long-wavelength ultraviolet light that runs from 320 to 380 nm with a peak intensity at 365 nm. A Wood lamp excites sodium fluorescein to produce visible fluorescence in the urine. However, the Hazardous Substances Data Bank of the National Library of Medicine lists 148 additional substances that contribute to urine fluorescence including food products such as riboflavin and niacin, medications such as amoxicillin and carbamazepine, and endogenous compounds such as reduced nicotinamide adenine dinucleotide phosphate and porphyrins [6]. The ubiquity of compounds causing urine fluorescence in a nonpoisoned population calls into question the use of the Wood lamp as a modality for diagnosing antifreeze ingestion. The objectives of this study were to determine the prevalence of urine fluorescence in a population of nonpoisoned children and to determine the ability of physicians to detect urine fluorescence using a Wood lamp.

2. Methods

We collected 150 urine specimens from a convenience sample of children aged 1 to 17 years presenting to a pediatric ED in an urban public hospital for reasons unrelated to poisoning. A convenience sample of physicians assessed urine fluorescence by direct observation under a Wood lamp. Children were eligible if they could provide a voided urine specimen, or if any urine remained from a specimen collected for diagnostic purposes. Exclusion criteria were dehydration, a condition requiring emergency management, and/or a condition associated with family stress.

After obtaining verbal consent, the investigator recorded the child’s age and sex and the parent’s report of the child’s exposure to sodium fluorescein or to any medication, dietary supplement, or substance known to cause urine fluorescence within the prior 48 hours. No identifying information was collected. The questionnaire was paired with the urine specimen, and both were labeled with the same number. The pH of each urine specimen was determined, and two 5-mL aliquots from each of 5 specimens were transferred to borosilicate glass tubes (specimens 1-10).

Three additional urine specimens (specimens 11-13) were prepared following standard chemical laboratory procedures. Specimen 11 contained 20 ng/mL of sodium fluorescein, the minimal concentration considered perceptible to the human eye [4]. Urine specimen 12 contained 1.2 ng/mL of sodium fluorescein, and urine specimen 13 contained 3.6 ng/mL of sodium fluorescein, the amounts of sodium fluorescein that were estimated to be present 2 hours after ingestion of a minimally toxic dose of ethylene glycol (0.5 mL/kg) in a 10- and 50-kg child, respectively [2,7]. To estimate these concentrations, we used urinary excretion rates after oral ingestion of sodium fluorescein in an adult population determined by Barry and Behrendt [7].

To assess physicians’ ability to detect urine fluorescence using a Wood lamp, 60 physicians were recruited in pairs, each pair consisting of physician 1 and physician 2. The 13 urine specimens were presented sequentially to physician 1 and then to physician 2 in each pair after random reassortment of the specimens. In a darkened room, physicians independently classified urine as fluorescent or nonfluorescent by direct observation under a Wood lamp (Ultraviolet Examination Light, model no. 31602, Burton Medical Products Corp, Chatsworth, Calif). Each physician was recruited only once. Participating physicians were not provided with any specialized training in the use of the Wood lamp before study initiation nor with any information regarding the study purpose or design. Both the physicians and the investigator were blinded to specimen order and identity.

Each of the 13 urine specimens was individually transferred to a cuvette and placed in a fluorometer (Photomultiplier Detection Systems, model no. 814, Photon Technology International Inc, Monmouth Junction, NJ), which was used as the gold standard for determination of urine fluorescence. At 25°C and with a slit width of 2 nm, specimens were excited at a wavelength of 350 nm to simulate the use of the Wood lamp by physicians in the pediatric ED. Specimens were also excited at the signature wavelength of sodium fluorescein, 490 nm, to check for the presence of sodium fluorescein (Fig. 1).

The intensity of the emission of 20 ng/mL of sodium fluorescein in lactated Ringer solution in the yellow-green wavelength range of 500 to 600 nm was 3900 arbitrary units. We defined urine as positive for fluorescence if, when excited at 350 nm, the urine produced an emission wave in the range of 500 to 600 nm greater than or equal to 3900 (Fig. 2). Lactated Ringer solution was used as the diluent because it is free of native fluorescence. The presence of urine fluorescence was determined by fluorometry with the technician blinded to the physician results. The fluorometer was calibrated before each use by the technician.

To investigate whether the physician’s ability to evaluate urine fluorescence is related to the concentration of sodium fluorescein and the intensity of the resultant emission, we added sodium fluorescein to lactated Ringer solution to produce samples with the following concentrations: 10, 20, 39, 78, 156, 312, 624, and 1248 ng/mL. One randomly selected urine specimen from our convenience sample of
nonpoisoned children was split into 8 aliquots of 5 mL. Using standard biochemical techniques, we added sodium fluorescein to each aliquot to produce the above 8 concentrations. The 8 resultant urine samples and the lactated Ringer samples were placed in the fluorometer and excited at 350 and 490 nm. The intensities were visually compared with the intensity of the original urine specimen.

The outcome measures were interobserver and intraobserver agreements of the physicians’ evaluation of urine fluorescence using the Wood lamp and the prevalence of urine fluorescence in nonpoisoned children using the fluorometer. Interobserver and intraobserver agreements were determined using simple agreement and the $\kappa$ statistic with 95% confidence intervals (CIs). Exact binomial 95% CIs were used to assess proportions for the categorical variables. Medians and 95% CIs for the medians generated with bias-corrected empirical bootstrapping were used to assess the continuous variables [8,9]. To determine the physician’s ability to detect urine fluorescence using a Wood lamp, we used the fluorometer as the standard and calculated the proportion of physicians detecting true fluorescent urine with 95% CIs. To determine the prevalence of urine fluorescence in nonpoisoned children, we calculated the proportion of urine specimens that met our study definition of fluorescence when excited at the Wood lamp wavelength of 350 nm with 95% CIs. We also calculated the median emission intensity of urine from nonpoisoned children within the range of 500 to 600 nm with 95% CIs. We then compared the median emission intensity to the emission intensity produced by 20 ng/mL of sodium fluorescein in lactated Ringer solution when excited at the Wood lamp wavelength of 350 nm. Alpha was set at .05 with a power of .80 for all statistical tests. Assuming a sensitivity for the Wood lamp examination of 90% for detecting urine fluorescence and to determine this sensitivity to within 5%, we needed to collect at least 134 fluorescent urine specimens to achieve statistical rigor.

The institutional review board of the Albert Einstein College of Medicine and the Jacobi Medical Center approved the study and determined that written informed consent was not required.

### 3. Results

Urine specimens were collected from 150 nonpoisoned children. The mean age was 9.86 years (±4.56 years), and 53.3% were boys. Within 24 hours before presentation, 43% of children had ingested a multivitamin, vitamin-fortified cereal, or a medication known to cause urine fluorescence. The pH of all urine specimens was 7 to 7.5. Physician reports of urine fluorescence by group are noted in Table 1. Physicians had poor interrater agreement (simple agreement 72.5%, $\kappa = 0.25$, 95% CI 0.13-0.37) and good intrarater agreement (physician group 1: simple agreement 97.9%, $\kappa = 0.93$, 95% CI 0.77-1.00; physician group 2: simple agreement 93.3%, $\kappa = 0.85$, 95% CI 0.69-1.00). There was no association between physician determination of fluorescence using the Wood lamp and ingestion by children in our sample of a substance that causes urine fluorescence ($P = .35$ for physician group 1 and $P = .11$ for physician group 2).

All urine specimens from nonpoisoned children excited at 350 nm in the fluorometer met our study definition of fluorescence for antifreeze.

#### Table 1

<table>
<thead>
<tr>
<th>Specimen</th>
<th>+1.2 ng/mL (n = 30)</th>
<th>+3.6 ng/mL (n = 30)</th>
<th>+20 ng/mL (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpoisoned children (n = 150)</td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Physician group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1  81 (73-87)</td>
<td>83 (65-94)</td>
<td>83 (65-94)</td>
<td>87 (69-96)</td>
</tr>
<tr>
<td>2  69 (61-77)</td>
<td>77 (58-90)</td>
<td>63 (44-80)</td>
<td>76 (58-90)</td>
</tr>
</tbody>
</table>
fluorescence. The median emission wave intensity was 48,450 units (95% CI 43,650-54,900). The prevalence of urine fluorescence was 100% (95% CI 98%-100%).

There were no observable differences between the emission wave intensity in the range of 500 to 600 nm of a randomly selected urine sample from a nonpoisoned child and the same urine sample with increasing concentrations of sodium fluorescein until a concentration of 312 ng/mL was reached (Fig. 3).

Fig. 4 represents a Wood lamp evaluation of the 8 different concentrations of sodium fluorescein added to lactated Ringer solution and to a randomly selected urine specimen from a nonpoisoned child, and 8 randomly selected urine specimens from our convenience sample of nonpoisoned children.

4. Discussion

Our data suggest that the determination of urine fluorescence using a Wood lamp is a poor screening tool for suspected antifreeze ingestion in children. All the urine specimens in our sample of nonpoisoned children were fluorescent, using a fluorometer as the gold standard, whereas physician rating of fluorescence using the Wood lamp was variable. Despite good intrarater agreement, physicians had poor interrater agreement.

There are few studies in the literature evaluating the usefulness of the Wood lamp as a diagnostic tool. In 1990,
Winter et al [3] determined that examination of urine under a Wood lamp was a useful adjunctive diagnostic test for suspected ethylene glycol ingestion. In 2001, Casavant et al [10] found that most urine specimens from their sample of nonpoisoned children were fluorescent and that there was interrater variability. Wallace et al [11] reported that Wood lamp determination of urine fluorescence was of limited diagnostic utility. There were some limitations to each of these studies. In the study by Winter et al [3], healthy adult volunteers ingested 0.6 mg of sodium fluorescein, and urine was evaluated with a Wood lamp at 2-hour intervals postingestion. At 2 hours postingestion, the urine concentration of sodium fluorescein was 31.9 ± 4.9 ng/mL, approximately one tenth of the concentration of sodium fluorescein at which there was an observable difference in emission wave intensity in our study. In addition, investigators used a grouped specimen presentation format. This format may provide visual clues that improve examiners’ ability to distinguish between sodium fluorescein-containing and sodium fluorescein-free specimens (Fig. 4). Moreover, grouped specimen presentation does not mimic clinical practice. Casavant et al [10] collected urine specimens from 30 children hospitalized for reasons unrelated to poisoning and from 16 healthy controls. Physicians identified the specimens as fluorescent or not fluorescent by Wood lamp examination. The majority of urine specimens were rated as fluorescent; however, there was poor agreement between physician ratings. In addition, the presence of fluorescence was not confirmed by fluorometry. The specimens in the study by Casavant et al were collected in glass and plastic containers, which can have high native fluorescence. However, the authors reported that there was no background fluorescence in the containers in their control arm. Wallace et al [11] reported physician rating of fluorescence in urine specimens obtained before and at 1 to 2 hours after ingestion of 0.6 mg of sodium fluorescein by healthy adult volunteers. Specimens were presented sequentially and in grouped format. The presence of sodium fluorescein in urine specimens was not confirmed by fluorometry.

To address some of these limitations, we used borosilicate glass tubes, free of native fluorescence. Moreover, we chose a sequential format presentation for the urine specimens, which more closely represents clinical use of the test. We used fluorometry as the gold-standard measure of fluorescence to evaluate the accuracy of physician rating of fluorescence using a Wood lamp and to confirm the presence or absence of sodium fluorescein in each of the urine specimens from our sample. We found that 100% of the urine specimens in our sample were fluorescent in the yellow-green color range of 500 to 600 nm as determined by the fluorometer. We found no association between fluorescence and the child’s exposure within the prior 48 hours to medications, vitamins, or other substances known to be associated with urine fluorescence. There are some limitations to our study. We did not train physicians to detect urine fluorescence. However, our data suggest that training would have little impact on the physician’s ability to detect urine fluorescence with a Wood lamp because all urine, with and without sodium fluorescein, was fluorescent as determined by the fluorometer. Furthermore, only at a urine concentration of 312 ng/mL of sodium fluorescein was there an observable difference in emission intensity. Extrapolating from our sample of children to achieve this concentration of sodium fluorescein in the urine 2 hours postingestion, a 50-kg individual would have to ingest 4 L of antifreeze containing fluorescein. However, if adult urine does not have baseline fluorescence, it might be possible to detect a change from none to any fluorescence rather than a gradation of fluorescence. Because there are no data on the pharmacokinetic parameters of sodium fluorescein excretion in children, we used data from an adult population studied by Barry and Behrendt to estimate the amount of sodium fluorescein excreted 2 hours postingestion of a minimally toxic dose by a 10- and a 50-kg child.

The samples in our study did not include urine from children who had ingested antifreeze or sodium fluorescein. Although actual ingestions may have affected our results in unanticipated ways, our data suggest that the amount of sodium fluorescein present in a minimally toxic dose of ethylene glycol is unlikely to be differentiated from background urine fluorescence by Wood lamp evaluation or fluorometry. Moreover, we did not look at intrarater agreement among physicians for the urine specimens containing sodium fluorescein. Although we made an effort to investigate whether children had ingested a substance within the past 48 hours known to cause urinary fluorescence, we did not screen for all possible substances, and we relied on parental recall.

Finally, our study population consisted only of children younger than 18 years, and we do not know whether our results can be extrapolated to adults. Although adults would be more likely to ingest a substantially larger volume of ethylene glycol, a typical adult ingestion is unlikely to approach 4 L, the amount necessary to produce an observable difference in emission intensity 2 hours postingestion. However, the possible absence of baseline urine fluorescence in adults may facilitate identification of fluorescence at lower concentrations of sodium fluorescein.

5. Conclusions

In our study, the prevalence of urine fluorescence among children presenting to the pediatric ED for reasons unrelated to poisoning was 100%, as determined by fluorometry. Physicians had good intraobserver but poor interobserver agreement in determining urine fluorescence with a Wood lamp. Physicians were unable to differentiate background fluorescence in the urine from nonpoisoned children from the fluorescence of urine containing sodium fluorescein. We conclude that the determination of urine fluorescence with a
Wood lamp is a poor screening tool for suspected antifreeze glycol ingestion in children.

Acknowledgments

The authors thank Polly Bijur, PhD, Anthony J. Ciorciari, MD, Benjamin M. Schaefer, MD, and Hugh Booth, RPh, for their assistance with study design; Wendy Zencheck, BS, for technical assistance; and Adhi N. Sharma, MD, for encouraging investigation of this topic.

References

Diagnostics

The electrocardiogram in right ventricular myocardial infarction

Steven Moye MDa, Mark F. Carneya, Christopher Holstege MDa, Amal Mattu MDb, William J. Brady MDa,*

aDepartment of Emergency Medicine, University of Virginia, PO Box 800699, Charlottesville, VA 22908, USA
bDepartment of Emergency Medicine, University of Maryland, Baltimore, MD 21201, USA

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Abstract Right ventricular (RV) myocardial infarction most often occurs in the setting of inferior wall myocardial infarction. Right ventricular infarction complicates approximately 25% (range, 20%-60%) of inferior acute myocardial infarction; it is uncommon to quite rare in anterior and lateral wall acute myocardial infarction. With infarction of the RV, the RV will fail. As such, left ventricular filling pressures are entirely dependent upon the patient's preload; with significant reductions in the preload, hypotension likely results (this hypotension may be worsened by nitroglycerin and morphine). The clinical presentation, in the setting of an ST-elevation myocardial infarction (STEMI) of the inferior wall, involves hypotension, jugular venous distension, and the following electrocardiographic findings: ST-segment elevation of greatest magnitude in lead III (compared with leads II and aVF), ST-segment elevation in lead V1, and/or ST-segment elevation in right chest leads (RV1 through RV6). Therapy, in addition to appropriate management for STEMI, relies largely on enhancing the preload with intravenous fluid and judicious use of vasodilator medications. Patients with inferior wall STEMI with RV infarction have a markedly worse prognosis (both acute cardiovascular complications and death) compared with patients with isolated inferior wall STEMI. © 2005 Published by Elsevier Inc.

1. Introduction

Right ventricular (RV) infarction occurs in the setting of approximately 25% of inferior wall acute myocardial infarctions (AMIs) with a range of 20% to 60%. Right ventricular involvement usually occurs because of the occlusion of the right coronary artery (RCA) proximal to the RV branch, with associated acute inferior wall infarction; less commonly, RV infarction results from occlusion of a dominant circumflex artery in the setting of acute lateral wall myocardial infarction (MI). In the setting of inferior AMI, the clinical findings of hypotension and raised jugular venous pressure are highly suggestive of RV infarction. It has also been suggested that nitrate-induced hypotension is suggestive of RV infarction. It is important to diagnose RV infarction because the associated hypotension will likely respond to intravenous (IV) fluid administration, whereas diuretic agents, morphine, and nitrates may further compound the situation. Patients with inferior wall AMI with coexistent RV infarction have larger-sized infarcts and more
often experience inhospital complications and higher cardiac mortality rates.

The standard 12-lead electrocardiogram (ECG) does not define the RV well. The 12-lead ECG will reveal the typical ST-segment elevation in the inferior leads as well as ST-segment elevation in the right precordial leads, especially lead V1. In contrast to the anteroseptal AMI with increasing ST-segment elevation as one moves from the right to mid precordial leads, RV AMI will demonstrate a decreasing magnitude of ST-segment elevation in the V1 through V4 distribution. Several different additional lead applications may be used to define RV injury, including a complete reversal of the standard left-sided precordial leads (resulting in RV1 through RV6) or the simplified approach using only RV4. In either case, the degree of ST-segment elevation in the right-sided leads may be of a small magnitude because of the relatively smaller RV muscle mass.

In this report, we review the clinical presentation of RVMI, stressing the clinical and ECG diagnosis (Tables 1 and 2). Furthermore, treatment and prognostic implications, again stemming from the ECG, are reviewed.

2. Case presentations

2.1. Case 1

A 54-year-old woman with a history of diabetes mellitus presented to the emergency department (ED) with chest pain of 4 hours’ duration that was associated with vomiting and diaphoresis. The examination was significant only for pronounced diaphoresis; the vital signs were normal. The 12-lead ECG (Fig. 1A) demonstrated ST-segment elevation in leads II, III, and aVF, consistent with an AMI of the inferior wall. In addition, ST segment depression was noted in leads V1 through V3 with prominent R waves in leads V1 and V2, findings consistent with a posterior wall infarction. The posterior wall involvement was confirmed by additional ECG leads V8 and V9 (Fig. 1B).

The patient received aspirin, sublingual nitroglycerin, and oxygen. The pain worsened with development of hypotension with a blood pressure of 70/40 mm Hg. An IV fluid bolus of 250 mL restored a normal blood pressure (110/75 mm Hg). Further analysis of the ECG in Fig. 2 revealed ST-segment elevation in lead RV4, suggestive of an RV infarction.

The patient received thrombolytic therapy with resolution of both his pain and the ECG findings. Serum troponin values were elevated, consistent with AMI. The patient was ultimately taken to the cardiac catheterization laboratory where a 90% occlusion of the RCA was successfully stented. The patient was discharged from the hospital with the diagnosis of inferoposterior AMI with RV infarction.

2.2. Case 2

A 62-year-old man with a history of hypertension presented to the ED with substernal chest pain. The pain had appeared approximately 2 hours before arrival in the ED and was associated with diaphoresis and nausea. Examination revealed a diaphoretic man in moderate distress with clear lung fields; vital signs were significant for a blood pressure of 67/45 mm Hg. A 12-lead ECG (Fig. 2A) revealed normal sinus rhythm with ST-segment elevation in the inferior leads as well as lead V1. While an IV fluid bolus was administered, the patient received an aspirin. Blood pressure increased to 95/65 mm Hg. Additional right-sided thoracic ECG leads (Fig. 2B) demonstrated ST-segment elevation. The ED diagnosis was inferior wall AMI complicated by RV infarction.

The patient was urgently transferred to the cardiac catheterization laboratory where a proximal RCA thrombus was noted and successfully opened and stented. The patient had an uneventful recovery from the MI that was confirmed by elevated serum troponin values and inferior wall hypokinesis on the echocardiogram.

3. Discussion

Myocardial infarction usually refers to the sudden insufficiency of a coronary artery because of thrombi, emboli, or arterial spasm—or all 3 events—that causes myocardial dysfunction followed by a segment of necrosis of the left ventricle (LV). Descriptors such as anterior, posterior, lateral, or inferior describe the portion of the LV that undergoes necrosis. Right ventricular infarction describes damage to the myocardium of the RV. Isolated RV infarctions are rare. The 12-lead ECG directly images the LV, whereas the RV is minimally evaluated with the standard ECG (Fig. 3).

Most RV damage is associated with LV inferior, inferoposterior, or lateral MI. Approximately 30% of patients with inferior wall AMI will have RV involvement

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Table 1  Clinical features associated with RV MI

<table>
<thead>
<tr>
<th>Clinical features associated with RV MI</th>
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</thead>
<tbody>
<tr>
<td>Systemic hypotension (&lt;90 mm Hg)</td>
</tr>
<tr>
<td>Hemodynamic sensitivity to vasodilators</td>
</tr>
<tr>
<td>Jugular venous distension</td>
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<tr>
<td>Hepatomegaly</td>
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</tbody>
</table>

Table 2  Electrocardiographic features of RV MI

<table>
<thead>
<tr>
<th>ECG features suggestive of RV MI</th>
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<tbody>
<tr>
<td>Inferior wall ST-elevation AMI</td>
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<tr>
<td>Greatest magnitude ST-segment elevation in lead III in inferior wall STEMI</td>
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<tr>
<td>ST-segment elevation in lead V1</td>
</tr>
<tr>
<td>ST-segment elevation in right-sided thoracic leads (isolated RV4 vs entire RV1 through RV6)</td>
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</table>

STEMI indicates ST-elevation myocardial infarction.
The electrocardiogram in right ventricular myocardial infarction

Fig. 1  A, Twelve-lead ECG with ST-segment elevation in the inferior leads. Note that the most significant degree of ST-segment elevation is in lead III. These findings are consistent with an inferior wall AMI with RV infarction. Also, ST-segment depression with prominent T waves is seen in V₁ through V₃, consistent with posterior wall AMI. B, Three additional ECG leads, RV₄ (RV) and V₈ and V₉ (posterior wall), confirm the findings on the 12-lead ECG: ST-segment elevation in leads V₈ and V₉ confirm posterior wall AMI; similar ST-segment elevation in lead RV₄ supports RV infarction.

Fig. 2  A, Twelve-lead ECG with ST-segment elevation in leads II, III, and aVF, consistent with inferior wall AMI. Note that the degree of ST-segment elevation is of greatest magnitude in lead III, consistent with an RV infarction. B, Right-sided ECG leads demonstrating ST-segment elevation in leads RV₂ through RV₆.
Cohn et al [2] were the first to describe the hemodynamic syndrome associated with RV infarction as hypotension, elevated venous pressures, and shock without evidence of congestive heart failure. Probably only one third to one half of patients with RV infarction will have hemodynamically significant findings [3].

Most RV infarcts involve occlusion of the RCA in that it supplies most of the RV myocardium. The RCA proximal segment perfuses the sinoatrial (SA) node plus the right atrial free wall. The RCA middle segment perfuses the lateral and inferior RV free wall. The posterior LV, inferior septum, inferior LV free wall, and the atrioventricular (AV) node are supplied by the distal RCA segment. Approximately 10% of patients have an RV that is perfused by the circumflex artery. Because the distal RCA segment perfuses the inferior LV, most RV infarctions will involve the inferior LV as well. Proximal occlusions of the RCA that cause RV free wall injury frequently compromise the SA node, right atrium, and the AV node.

Right ventricle infarction identifies a syndrome of RV dysfunction and may not always be associated with an infarction [4]. Most RV infarctions diagnosed by the ECG do not progress to necrosis and scar formation [5-8]. The RV myocardium probably recovers more readily than similarly injured LV tissue. This phenomenon may be due to the collateral perfusion from the left coronary artery and from greater penetration from the ventricular blood by the thebesian veins. Also, the RV myocardium contracts against a lower pressure and probably has a lower work demand than that of the LV [4].

The syndrome of hypotension, jugular venous distension, shock, and an absence of congestive heart failure in the setting of RV myocardial infarct described by Cohn et al [2] in conjunction with an inferior wall MI should make RV infarction suspect. A greater than expected drop in blood pressure after the administration of nitrates, morphine, or other vasodilating agents should also raise suspicion for RV infarction.

Because the RCA also supplies the SA node and the AV node, bradycardia, supraventricular dysrhythmias, and AV conduction blocks may be seen. The RV portion of the interventricular septum, if damaged in the event, may contribute significantly to conduction abnormalities. Zehender et al [9] found that RV infarction occurring in association with LV MI had a significant reduction in morbidity and mortality if fibrinolysis was applied. Identification of RV infarction is therefore clinically important and highly useful in treatment considerations for MI [9].

The standard 12-lead ECG does not image the RV to any significant extent (Fig. 3). Electrocardiographic findings for RV infarction include ST-segment elevation in the inferior distribution as well as in the right precordial chest leads (Figs. 1A, 2A, 4-7), particularly lead V1 (perhaps the only lead on the standard ECG that reflects changes occurring in the RV) (Figs. 2A, 4, and 6). Note that lead V1 images a portion of the RV; right-sided leads directly image the RV (Fig. 3). At times, coexisting acute posterior wall AMI may...
obscure the ST-segment elevation resulting from RV infarction in lead V1 as seen in the patient with the acute inferoposterior MI with RV involvement (Figs. 1A and 7A).

In the setting of inferior wall AMI, if the degree of ST-segment elevation is disproportionally greater in lead III relative to the other inferior leads, RV infarction is also suggested (Figs. 1A, 2, 6, and 7). If ST elevation in lead III is greater than lead II, the clinician should consider RV infarction. This disproportionate ST-segment elevation results from the imaging axis, or lead orientation, of the inferior leads. Lead III most directly images the RV (Fig. 3).

Recordings from leads placed on the right side of the chest are much more sensitive and specific in detecting the changes of RV infarction (Fig. 3). The right-sided precordial electrodes are placed across the right side of the chest in a mirror image of the standard left-sided leads and are labeled V1R through V6R (Figs. 2, 5, and 7); RV1 through RV6 is another commonly used nomenclature for this lead distribution. The clinician may use either the entire right-sided leads V1R through V6R or the single lead V4R. Lead V4R (right fifth intercostal space midclavicular line) is the most useful lead for detecting
ST-segment elevation associated with RV infarction (Figs. 1B, 4, and 5) and may be used solely in the evaluation of the possible RV infarction [10]. ST-segment elevation in lead V4R greater than 1.0 mm has been shown to be a reliable marker of RV infarction [10]. Saw et al [11] found that ST-segment elevation in lead V4R was more specific than the disproportionate lead III ST-segment elevation (56% vs 78%, respectively); these authors, however, preferred the disproportionate lead III ST-segment elevation because of its potential presence on all 12-lead ECGs. Robalino et al [12] found that ST-segment elevation in lead V4R greater than 1 mm has 87% specificity and 100% sensitivity when occlusion of the RCA is proximal to the first ventricular branch.

Right-sided precordial leads are mirror images of the normal precordial leads. Lead V4R has shown similar rates of RV infarction when compared with an entire complement of right chest leads [10]. ST-segment elevation from RV infarction has a lesser amplitude than that seen in LV infarction, resulting from a smaller myocardial mass of the RV. ST elevation of 1.0 mm or greater in V4R is considered significant.

Regardless of the ECG lead applied, the ST-segment elevation that occurs in association with RV infarction is frequently quite subtle, reflecting the relatively small muscle mass of the RV; at other times, the ST-segment elevation is quite prominent, similar in appearance to the ST-segment changes seen in the standard 12 leads.

In addition to ST-segment elevation in the inferior leads, RV AMI is suggested by sinus bradycardia and AV node block. Proximal RCA occlusion endangers not only the RV ventricular branches but also the AV nodal artery.
Recognition of RV infarction is important for clinical treatment of AMI. Because RV infarction is often associated with inferior wall infarction, a larger portion of myocardium is endangered. This relatively large infarction increases the urgency of reperfusion by thrombolytic agents, angioplasty, or coronary artery bypass graft. Impairment of RV function may lead to a deleterious drop in LV preload and, subsequently, a drop in cardiac output. This preload reduction may result in hypotension or shock. Whereas LV dysfunction may result in congestive heart failure requiring diuretics and fluid removal, RV dysfunction may require aggressive IV fluid therapy. If aggressive fluid therapy does not satisfactorily improve hypotension, the use of an inotrope such as dobutamine may be indicated. Atropine may be used for bradycardia and pacing for AV block.

4. Conclusion

Identification of RV infarction is important for the clinician. It has immediate clinical implications and serves as a predictor for morbidity and mortality. Simple ECG methods can be used to predict the presence of an RV infarct. The clinician should be suspicious of an RV infarct anytime an inferior wall infarction is present. Management of an RV infarction includes volume loading, reperfusion, rate control, and inotropic support. Right ventricular infarctions can be detected with simple ECG tests; the clinician can then alter therapy accordingly.

References

Closed reduction of prosthetic hip dislocation by emergency physicians

Carl A. Germann MD\textsuperscript{a}, Daniel A. Geyer\textsuperscript{b}, Andrew D. Perron MD\textsuperscript{a},*  

\textsuperscript{a}Department of Emergency Medicine, Maine Medical Center, Portland, ME 04102-3175, USA  
\textsuperscript{b}Maine Medical Center Research Institute, Scarborough, ME 04074, USA  

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Abstract  
Objective: The purpose of this study was to determine the frequency of successful closed reduction (CR) of dislocated prosthetic hips performed by emergency physicians (EPs) as well as the incidence of acute complications.  
Methods: The study design was an explicit chart review set at an academic ED with an annual census of 55,000. The study was performed on March 1, 1999 to February 28, 2004. Patients were identified using coded ED diagnoses, and data were obtained by a trained abstractor.  
Results: One hundred twelve dislocations in 66 patients had attempted CR in the ED. Eighty-one had CR attempted solely by an EP with 91% success. Twenty-eight of the remaining 31 (90%) had successful CR performed by either an orthopedic surgeon or both an EP and an orthopedic surgeon. Overall, 10 patients (9%) failed ED CR. No postreduction complications were identified in any patient.  
Conclusions: EPs can safely and successfully perform CR on patients with dislocated total hip arthroplasties.

1. Introduction

Hip dislocation is a common complication that occurs in 1% to 10% of patients after total hip arthroplasty (THA) and up to 26.6% of patients after revision THA\textsuperscript{[1,2]}. Patients having this injury frequently present to the ED for evaluation. As the first health care provider to have contact with this patient population, emergency physicians (EPs) have an opportunity to expedite the care of these individuals. However, although EPs are skilled at making the diagnosis of these injuries, their treatment has traditionally been performed primarily by or in conjunction with an orthopedic surgeon. This is despite the fact that closed reduction (CR) is regarded as the first treatment of choice and may be easily performed with the assistance of procedural sedation in the ED.

ED physician-performed prosthetic hip reduction can be beneficial for the patient, ED, and the hospital. Performing prompt CR may allow for less duration of pain and decreased total time spent in the ED. Immediate reduction...
2. Materials and methods

2.1. Study design

This was a retrospective explicit chart review with a standardized data collection form completed by a single investigator (C.A.G.), who was trained to abstract data before the start of the study. All variables were specifically defined before the start of data collection. Specific items reviewed included EP notes, orthopedic surgeon notes, radiology reports, nursing notes, and OR records. When data were conflicting, ambiguous, or missing, they were recorded as unknown. A portion (20%) of the charts were independently reviewed by a second investigator (D.K.G.) to ensure consistency. During the data collection portion of the study, periodic meetings were held with the reviewer to ensure compliance with intended data abstraction. This project was reviewed by our internal review board and by the Human Investigation Committee and considered exempt because of its retrospective nature.

2.2. Study setting and population

The setting for this study was an academic ED with an annual ED census of 55,000 patients. The ED is staffed by emergency medicine residents (post-graduate year [PGY] 1-3) and attending level physicians 24 hours a day. The study dates were from March 1, 1999, to February 28, 2004, covering a 5-year period.

2.3. Subject identification

Patients were identified using ED admission and discharge diagnosis codes. All patients identified as having a prosthetic hip dislocation were included in the study cohort. Patients were allowed to be enrolled more than once for recurrent ED visits.

2.4. Outcome variables

Data were collected from the paper chart, online dictated records, and radiology reports and were entered into a standardized data collection form. Demographic data and outcome variables examined included patient demographics: age, sex, date of presentation; dislocation characteristics: type (anterior or posterior), side of dislocation (right or left), and mechanism of dislocation; medical history: history of prior dislocation; process characteristics: site of reduction (ED or OR), total time in ED, time in ED for reduction, number of reduction attempts, use of procedural sedation, and provider for ED attempts; and complication characteristics: presence of any orthopedic complication. An orthopedic complication was prospectively defined as any reported osseous, hardware, neurological, or vascular injury identified during the same hospital visit.

2.5. Data analysis

Data were entered into Microsoft Excel (Redmond, Wash), and descriptive statistics were calculated.

3. Results

Initially, 138 charts were identified as having a "dislocated lower extremity" by diagnostic coding and thereby met criteria for potential inclusion in the study. Of these 138 identified charts, 116 were found on chart review to have a prosthetic hip dislocation and were included in the data set. The remaining 22 were found to have either a hip fracture without dislocation or a lower extremity dislocation that did not involve the hip. The 116 dislocation encounters involved 66 patients. Twenty percent (24) of these charts underwent a double chart review by a second reviewer. There were no discrepancies identified in the data that underwent this duplicate abstraction.

The mean age of patients was 65 years, with a range from 33 to 91 years old. Forty-eight (41%) patients were men, and 68 (59%) were women. Eighty-seven dislocations (75%) were posterior, and 18 (16%) were anterior. Five patients (4%) had a type of dislocation recorded as superior, whereas 4 (3%) were recorded as superolateral. Two patients (2%) did not have the type of dislocation recorded (NR) and could not be determined from the available medical records. In 25 (22%) cases, the individual may also lead to a decreased rate of morbidity and any potential neurovascular complications associated with dislocation. Likewise, by performing immediate reduction and expediting ED throughput, ED staff and resources can be used more efficiently. This can also serve to unburden the operating room (OR) staff and resources by preventing unneeded OR reductions under general anesthesia or procedural sedation.

There is a paucity of emergency medicine literature to date on this subject with no studies looking at the success rate and postreduction complication associated with treatment of this condition. Previously published series of hip dislocation have come from orthopedic literature and have largely focused on demographics and operative theory. The purpose of this study was to establish the characteristics of hip dislocation in the ED and specifically to determine the rate of successful reduction in the ED, as well as the rate of acute complications seen with prosthetic hip dislocation and reduction in a general ED population. In addition, this retrospective study sought to compare the total time spent in the ED for those patients undergoing CR in the ED vs those performed in the OR.

Of note, the assessment of data regarding procedural sedation was not a goal of this study. The risks and complications associated with deep sedation are considered a separate entity to those occurring secondary to prosthetic hip dislocation and reduction.
had no prior dislocation, whereas 86 (74%) had prior dislocation. In 5 patients (4%), it could not be determined if there had been a prior dislocation. The time between THR and dislocation ranged from 6 days to 25+ years with a mean of 7.6 years. In 5 cases, these data could not be identified from the record. One patient had an associated fracture identified on a prereduction radiograph, which was recorded as a “bony fragment lateral to the superior acetabulum.” A prereduction and postreduction neurovascular examination was recorded in all patients. The mechanism of dislocation was categorized as “bent over” (42.2%), “fall” (20.7%), “twist” (16.4%), “other” (8.6%), “standing/sitting” (7.8%), and NR (4.3%).

Four of the 116 patients were taken directly to the OR for CR without any attempts in the ED. There is no documentation in any of these cases as to why reduction was not attempted in the ED. Of the remaining 112, 102 (91%) had successful reductions performed in the ED. All of the patients undergoing an ED reduction attempt received procedural sedation. Eighty-one patients had hip reduction attempted by an EP (attending or resident) with a 91% success rate. Twenty-eight (90%) of the remaining 31 patients had successful reduction performed by either an orthopedic surgeon (attending) or by both an EP and an orthopedic surgeon while in the ED (Fig. 1). In all cases, postreduction x-rays were performed to confirm the adequacy of reduction. All of the failed ED reductions (10) went to the OR for successful CR. Twenty-two (22%) of the 102 patients with a successful ED reduction did not have the number of attempts recorded. Of the remaining 80 patients (78%), the number of ED attempts ranged from 1 to 4 with a mean of 1.3 attempts. Seventy-three (91%) of the 80 patients required only 1 attempt. No orthopedic complication was recorded in any patient prereduction or postreduction.

Total time spent in the ED ranged from 1 hour and 25 minutes to 13 hours and 40 minutes with a mean of 4 hours and 25 minutes. Of the 112 patients who had reduction attempted in the ED, the mean time spent in the ED was 4 hours and 21 minutes. Of the 4 patients who had no attempts at reduction in the ED, the total time spent in the ED averaged 6 hours and 3 minutes. The actual procedure time (as determined from conscious sedation flow sheets) for successful ED reduction ranged from 1 to 41 minutes with a mean of 10 minutes. Fourteen patients had no procedure times recorded. All 4 of the patients who had reduction performed in the OR were discharged from the hospital after the procedure. One hundred of the 112 patients who had reduction attempted in the ED were discharged after the procedure.

4. Discussion

Dislocations of prosthetic hip joints are not uncommon in an ED practice. Due to the violent force frequently causing dislocation, complications can accompany these injuries. The potential acute complications associated with prosthetic hip dislocation are fracture, hardware damage, and neurological and vascular injury. The vast majority of data on prosthetic hip dislocations come from the orthopedic literature. A review of the emergency medicine literature on prosthetic hip dislocation demonstrates a relative paucity of data regarding acute complications and success rates of reduction. To date, no large emergency medicine series has
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quantified the success of EP reduction or type and rate of acute complications associated with this common condition in a general ED population.

After THA, instability in the form of dislocation is second in frequency to loosening as a major complication of this procedure [3]. The prevalence of dislocation after THA has been reported to range from less than 1% to greater than 15% [1,4-8]. The wide variation is probably caused by multiple factors including differing study cohorts, surgical techniques, type of prosthesis, as well as inconsistent clinical follow-up. Most studies, however, report a prevalence of 2% to 5% for primary THA [6,9-14]. The prevalence of dislocation after revision THA is greater, with a rate of up to 26.6% after multiple procedures [15].

Fifty-five to 95% of all dislocations occur within the first 3 months after THA [10,16,17]. One study found that 68% of dislocations had occurred by 1 month postoperatively, with more than half of the patients in the study experiencing a dislocation before discharge from the hospital [12]. Dislocations that occur in the first 3 months postoperatively are generally caused by relaxed soft tissues and immature scar formation [18,19]. Dislocations between 4 months and 5 years are usually caused by component malposition or dysfunction of abductor mechanism [18,19]. Instability that arises more than 5 years postoperatively is usually caused by acetabular wear [18]. Over time, stretching of the pseudo capsule caused by extremes of motion may lessen soft tissue constraints and allow for dislocation [20]. If dislocation occurs, approximately 60% of patients will have only 1 dislocation [3,21]. Our study found that 74% of our study patients had at least 1 prior dislocation, and in a number of patients, there was a history of multiple dislocations.

Dislocations after THA can occur in a posterior or anterior direction. Posterior dislocation is clearly the most common instability mode and accounts for 75% to 90% of the dislocation reported [5]. This is consistent with our finding of 75% of dislocations as posterior. Posterior dislocation is usually secondary to a combination of excessive flexion, adduction, and internal rotation. This may occur when the patient sits on a low chair or is rising from the sitting position or when bending over. “Bending over” comprised the most frequent mechanism in this cohort involving 42.2% of patients. An anterior dislocation occurs during excessive extension, adduction, and external rotation. An example of this mechanism would be turning while walking. The mechanism and direction of dislocation will often depend upon the surgical approach used for the original hip arthroplasty as well [5].

Fractures of the femur, acetabulum, or pubic ramus can occur after a THA and during dislocation. These complications are relatively rare with previous studies reporting femoral fracture rates of 0% to 2.3% after THA [22-26]. One larger study of 3000 THA procedures noted a 0.1% fracture rate [22]. Most postoperative femoral fractures occur near the tip of the stem or proximal to it [27]. However, femoral neck, intertrochanteric, and acetabular fractures are more commonly found with traumatic nonprosthetic dislocation and associated with significant traumatic force. Fractures of the acetabulum involving prosthetic hips are also rare and primarily associated with older prosthetic devices with clinical studies reporting no fractures with newer components [28-32]. During traumatic dislocation of a nonprosthetic hip, the fibrous capsule may rupture inferiorly and posteriorly allowing the head to pass over the posterior margin of the acetabulum which may cause the femoral head carry with it a segment of acetabular bone. In our cohort, 1 patient was found to have a prereduction “bony fragment” which is likely an osteophyte. Osteophyte development, loose cement, or prosthetic fragments may come apart during dislocation and cause joint impingement or failure of CR [33]. No fractures were identified as resulting from CR in the ED.

The neurovascular examination after a hip dislocation should focus on the sciatic nerve and femoral vessels. Sciatic nerve palsy is more likely to occur in conditions such as traumatic dislocation of a nonprosthetic hip or during the THA procedure itself. Sciatic palsies may be present in approximately 10% of patients who experience traumatic hip dislocation. During dislocation, the nerve may tear or be compressed by a subsequent hematoma or a dislocated femoral head or prosthesis. The sciatic neuropathy may produce paralysis of the peroneal muscles. The femoral artery is the most likely vessel to be injured, particularly after an anterior dislocation. Of course, because of the prosthetic femoral head, the patient is not at risk for developing avascular necrosis. Nonetheless, arterial injury may occur, and comparative examination of arterial flow should be considered including ankle-brachial index and blood pressure measurements. At a minimum, prereduction and postreduction peripheral pulses should be assessed and documented. Our study demonstrated no neurovascular injuries either prereduction or postreduction. This may demonstrate an inadequacy of a comprehensive physical examination or simply a lack of neurovascular compromise in this cohort. Nonetheless, all of these patients had documented physical examinations both prereduction and postreduction.

Multiple factors have been identified that put patients with THA at an increased risk for dislocation. Elderly patients tend to have a higher dislocation rate, presumably from a decreased musculature around the hip and an increased incidence of falls [34]. Female sex has also been recognized as a contributing factor with a female/male ratio of 2.1 to 3.1 [3,10,20,35,36]. An increased incidence of dislocations has also been demonstrated in patients with cerebral dysfunction, psychosis, and alcoholism [35].

The dislocation rate has been found to double with revision surgery when compared with primary surgery which would make previous surgery perhaps the most significant risk factor for dislocation [3]. Surgical factors that have a role in maintaining hip stability include the surgeon’s level of experience, surgical approach, orientation
of the prosthetic components, design of the implant, and restoration of soft tissue tension of the hip [35]. Not surprisingly, the frequency of dislocation after THA has been found to correlate inversely with the individual surgeon’s experience in performing hip placement [37]. Another important risk factor is that of patient noncompliance with range-of-motion restrictions in the early postoperative period [16]. This compliance is essential for capsular healing [16,38].

CR has been reported to be possible in 95% of 331 dislocations in the series of Woo and Morrey [3] and 64% to 100% of cases in smaller studies [33,39-41]. Another large cohort demonstrated successful CR in more than 90% of patients [12]. Our study found a success rate of 91% for EPs compared with a 90% success rate for reduction in conjunction with or by an orthopedic surgeon alone. Although the method of relocation was not part of this study, at our institution, reduction is largely attempted by using longitudinal traction, knee flexion, and gentle internal and external rotation. If procedural sedation is performed, an additional physician would be required to manage the potential complications of deep sedation.

The prevalence of redislocation after conservative treatment is highly variable, with 2 large studies showing an incidence if approximately 33% [3,9]. The prevalence of recurrent dislocation necessitating operative treatment has been reported to range from 13% to 42% [4,42]. Several authors have found that reoperation for recurrent dislocation has led to a 40% to 90.5% success rate in curing the instability [16,43-45].

Timing of surgical correction of THA after dislocation is debatable. In general, treatment for the dislocation must be surgical for patients with recurrent dislocations [46]. Surgical treatment has been recommended after a second dislocation, and this continues to be a good rule for dislocation management [21,33,42,46]. Revision surgery most commonly takes the form of component revision with revision of the acetabulum occurring in approximately three quarters of cases [3,19,33,47,48].

There are a number of limitations to our study. Perhaps the most significant limitation is the retrospective nature of our study. Performance of a neurovascular examination is crucial both before and after any reduction attempt, as it is the documentation of any such examination. Given the retrospective nature of this study, we cannot account for the quality or consistency of the prereduction and postreduction neurovascular examinations. It is also possible that a deficit could have been missed on examination or improperly documented. Finally, complications from hip dislocation can present in a delayed fashion. This is particularly true of vascular injuries, but also can be the case in neurological injuries. These delayed complications would not be accounted for if they occurred after discharge as there was no systematic follow-up. These factors limit our ability to provide a true incidence of orthopedic complications.

5. Conclusion

It is important for EPs to be comfortable with the diagnosis and CR of a hip dislocation. It is equally important for EPs to be familiar with the type and frequency of acute complications that can accompany these dislocations. In our retrospective series, we found no such complications. Our study demonstrates that ED physicians can successfully reduce prosthetic hip dislocations and, by doing so, perhaps decrease the patient’s time of discomfort, promote faster ED throughput, and save hospital resources that can then be devoted to improving other aspects of patient care.

References

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Spermatic cord injury associated with blunt trauma

Akira Takasu MD*, Kentarou Morita MD, Naoyuki Kaneko MD, Toshihisa Sakamoto MD, Yoshiaki Okada MD

Department of Traumatology and Critical Care Medicine, National Defense Medical College, Saitama 359-8513, Japan

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Spermatic cord injury due to blunt trauma is an entity rarely encountered in clinical practice, and it may be mainly characterized by the onset of severe pain, swelling, or hematoma in the groin area. We present a case of a fresh spermatic cord injury caused by blunt trauma, which was correctly diagnosed after a surgical exploration.

A 53-year-old healthy man had a strong blow from a handlebar on the right groin region in a motorcycle accident. He was transferred to our hospital from a rural hospital 3 hours after the accident because a hematoma was suddenly expanding in the right groin. On presentation, a 12 cm diameter painful subcutaneous hematoma of the right groin extending into the right hemiscrotum was found (Fig. 1). There was no medical history of blood dyscrasias, anticoagulant therapy, inguinal hernia, or urinary symptoms. His vital signs were normal. Contrast-enhanced computed tomographic (CT) images showed a large subcutaneous hematoma with contrast medium extravasation at the groin level and the edematous spermatic cord at the pudendal level (Fig. 2). There was no evidence of either any external iliac or femoral artery injuries. The preoperative diagnosis was a large subcutaneous hematoma bleeding from disrupted subcutaneous vessels.

He was taken to the operating room for the removal of the hematoma and hemostasis 5 hours after the accident. Under satisfactory spiral anesthesia, an 8-cm diagonal incision was made over the hematoma of the right groin. A large subcutaneous hematoma as well as the contused spermatic cord was found. The cord was severely damaged at a level approximately 4 cm distal from the internal inguinal ring, and it was bleeding modestly from the internal or external cremasteric vessels. A large hematoma was contained along the distal length of spermatic cord. The vas deferens was intact. A rupture of external oblique aponeurosis and transverse fascia was found after removing the 300-g subcutaneous hematoma. A search for these layers resulted in the discovery of preperitoneal fat without any active bleeding. Based on these findings, a right orchiectomy was performed, and then, the floor of the inguinal canal was repaired by joining the edge of the internal muscle and aponeurosis of the transverse oblique muscle to the Poupart ligament. The external oblique aponeurosis was

* Corresponding author. Tel.: +81 429 95 1888; fax: +81 429 96 5221. E-mail address: atakasu@me.ndmc.ac.jp (A. Takasu).

Fig. 1 A large subcutaneous hematoma measuring 12 cm in diameter in the right groin.
also closed. The patient subsequently recovered without any sequelae and was discharged 10 days after the operation.

Blunt spermatic cord injury is extremely rare. To our knowledge, only 3 cases of such injuries have been reported so far in the English literature since 1960 [1-3]. Rabkin and Amar [1] described a case of a traumatic false aneurysm of the spermatic artery of 4 weeks’ duration in a 19-year-old man after a motor scooter accident. Gordon et al [2] reported a 22-year-old man demonstrating a ruptured varicocele with a sudden increase in the intra-abdominal pressure, with transmission to the varicocele by a blunt abdominal trauma. Kumar et al [3] reported a case of spermatic cord injury with an organized hematoma occurring in a 30-year-old man 2 months later after he had been kicked in the groin. All of them were diagnosed intraoperatively. We believe that our case is the first report describing a fresh spermatic cord injury due to a direct blunt trauma to the groin.

Our preoperative diagnosis of subcutaneous hematoma from a bleeding of subcutaneous vessels such as superficial epigastric or external pudendal artery was incorrect. An operative inspection revealed the injured spermatic cord with bleeding from the spermatic vessels. Based on this operative finding, we reviewed the preoperative CT and found a capsule around the contrast medium extravasation, which was considered to indicate spermatic fascia (Fig. 2A). A careful CT analysis might provide more definitive information regarding spermatic cord injury.

We performed an orchiectomy because the inhibition of the blood flow due to the spermatic cord injury seemed to induce a high incidence of ischemic orchitis. The age of the patient also led us to choose this approach. Some controversy still remains regarding the performance of an orchiectomy for the treatment of spermatic cord injury. It is likewise unknown how often and when necrotic orchitis occurs after spermatic cord injury. Testicular atrophy, a sequela of ischemic orchitis, is a well-known complication of primary inguinal hernioplasty due to spermatic cord injury from the trauma of surgical dissection [4,5]. Only a 15-min interruption of the testicular blood supply was reported to lead to irreversible ischemic damage of the testis 2 months after insult in a rat model [6]. These findings therefore seem to support our rationale for performing an orchiectomy. However, successful testicular salvage was reported in all 3 previously reported cases [1-3]. We agree that more aggressive testicular salvage is indicated instead of an orchiectomy in young male subjects [7].

In summary, we described a rare case of spermatic cord injury due to blunt groin trauma with an enlarged subcutaneous hematoma. This injury should always be considered in a patient with inguinal and scrotal swelling or hematoma occurring after traumatic accidents. To date, such injuries have always been diagnosed intraoperatively. Future experiences should help to make an accurate preoperative diagnosis using, for example, either CT scans or ultrasonography.

References

Case Report

Pulmonary tumor embolism—diagnosis in the ED

Chun-Lin Chi MDa, Kao-Lang Liu MDb, Ang Yuan MDa, Wan-Ching Lien MDa, Wen-Jone Chen MD, PhDa, Hsiu-Po Wang MDa,*

aDepartment of Emergency Medicine, National Taiwan University Hospital, Taipei 100, Taiwan
bDepartment of Radiology, National Taiwan University Hospital, Taipei 100, Taiwan

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The 34-year-old man presented to our ED with shortness of breath and abdominal distension. He had been diagnosed with hepatocellular carcinoma (HCC) for 4 months. On arrival, the blood pressure was 126/71 mm Hg, the pulse rate was 104 beats per minute, and the oxygen saturation was 87%. Physical examination revealed a man in prominent respiratory distress. The sclera was icteric, and the conjunctiva was pink. No murmur was detected by cardiac auscultation, and the breathing sound decreased over right lung field. The abdomen was distended with shifting dullness. Arterial blood gas (\( F_{\text{io}_2} = 32\% \)) revealed the following: pH 7.4; \( P_{\text{CO}_2} \), 32.2 mm Hg; \( P_{\text{O}_2} \), 183.6 mm Hg; \( \text{HCO}_3^- \), 19.4 mEq/L.

Elevation of the right hemidiaphragm and prominent right pulmonary trunk was noted in chest radiography. The electrocardiogram showed Q wave and inverted T wave over lead III. Abdominal ultrasonography revealed thrombus in inferior vena cava (IVC). Echocardiogram showed dilatation of right atrium and right ventricle with pulmonary hypertension, which is suggestive of pulmonary embolism. Thrombus in superior vena cava and IVC were also noted.

For a definite diagnosis of pulmonary embolism, the patient underwent spiral (helical) computed tomographic (CT) scan of chest immediately. Chest CT demonstrated multiple filling defects of the pulmonary arteries to the right lower lobe, left lingular segment of left upper lobe, and left lower lobe (Fig. 1). There are also filling defects in the hepatic IVC (Fig. 2). Ventilation-perfusion scan performed during admission was consistent with the diagnosis of pulmonary embolism. Marked improvement of symptom was noted after treatment with low-molecular-weight heparin. Follow-up CT scan 1 month later demonstrated partial resolution in right lower lobe.

Fig. 1 Contrast-enhanced chest CT scan in oblique coronal reformation shows emboli (arrow) over right inferior pulmonary artery.

* Corresponding author.
Hepatocellular carcinoma is the fourth most common cancer in the world [1]. In Taiwan, it has surpassed lung cancer as the leading cause of cancer death since 2002. In an ED setting, common complaints among patients with HCC include poor appetite, abdominal distension, abdominal pain, and dyspnea. Furthermore, dyspnea is of high prevalence (65.8%) in the terminal patients with HCC and decompensated liver cirrhosis (Child-Pugh class C) [2], and the symptom often results from hepatic hydrothorax, elevation of diaphragm due to massive ascites, or pulmonary metastasis. Thus, the differential diagnosis of dyspnea in patients with HCC is of great importance, and further management should be undertaken immediately to avoid severe subsequent complications.

Pulmonary tumor embolism can range from asymptomatic microemboli detected only at autopsy to massive emboli complicated by cardiovascular collapse and death [3]. Pulmonary tumor embolism has been frequently associated with cancers of breast, lung, prostate, stomach, and liver [4]. In as many as 68% of patients, tumor embolization is not clinically relevant or remains asymptomatic and is incidentally discovered at autopsy [4]. In one series, pulmonary tumor embolism occurred in about 50% of 79 patients with HCC [5]. An analysis of medicolegal autopsies showed that 0.9% of the 329 cancer deaths were attributed to pulmonary tumor embolism [6]. Besides, pulmonary tumor embolism is usually not diagnosed until postmortem examination. Goldhaber et al [7] reported that a correct antemortem diagnosis could only be accomplished in 1 of 17 cases of autopsy-proven cases [8]. Abdominal ultrasonography is a noninvasive procedure commonly arranged for patients with HCC to evaluate the status of hepatic tumor. Identification of IVC thrombus by ultrasonography is crucial to dyspneic patients with HCC because the sentinel sign would alert caregivers to arrange further surveys for suspected pulmonary tumor embolism.

Among diagnostic modalities for pulmonary embolism, CT scan has 2 major advantages: the thrombus can be directly visualized and alternative diagnosis can be established on lung parenchymal images that are not evident on chest radiography. Compared with conventional CT, the sensitivity of multirow detector spiral CT for acute pulmonary embolism increased from about 70% to more than 90% [9,10]. Treatment of pulmonary tumor embolism is conservative, although embolectomy and cardiopulmonary bypass had been applied in patients with renal cell carcinoma and clear cell sarcoma [11,12]. Chemotherapy was successful in 1 case of embolism because of trophoblastic malignancy, which is chemoresponsive [13]. The use of anticoagulant or steroid remains controversial.

In summary, we report a case of a patient with HCC presenting with dyspnea resulting from pulmonary tumor embolism. In contrast to other autopsy-proven cases, we accomplished this diagnosis antemortem. The possibility of pulmonary tumor embolism should be considered in patients with cancer presenting with acute dyspnea and rapid deterioration. Identification of IVC thrombus by abdominal ultrasonography plays an important role in early recognition of this catastrophic disease. Chest spiral CT scan should be considered as the main imaging test for suspected acute pulmonary embolism because of its high sensitivity and high specificity. Emergency physicians must consider pulmonary tumor embolism in their differential diagnoses of acute dyspnea in patients with HCC.

References

Case Report

Emergency plasmapheresis for unstable angina in a patient with hyperviscosity syndrome

Shmouel Ovadia MD*, Lyudmila Lysyy MD, Sharon Floru MD

Department of Internal Medicine “C,” E. Wolfson Medical Center, Haolhamim 4 Holon, Israel

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1. Single case report

The subject is a 66-year-old man who underwent a left nephrectomy in 1976 because of renal cell carcinoma. He is post–myocardial infarction, presently with stable ischemic heart disease, hypertension, and anemia from vitamin B12 deficiency. Two weeks before admission, the subject reported weakness, lack of appetite, and weight loss. A few days later, swelling of the testicles with no fever appeared. On admission, physical examination revealed bilateral epididymal sensitivity. Electrocardiogram revealed normal sinus rhythm with first degree atrioventricular block. Examination by a urologist produced a diagnosis of acute bilateral epididymitis.

In the course of hospitalization, he was treated with cefuroxime and ciprofloxacin, with gradual improvement in his condition. Notable in the course of his hospitalization were polyclonal hypergammaglobulinemia and a relative serum viscosity of more than 4.0 (normal, 1.4-1.8). On urine testing, all of the serum proteins and partial monoclonal bands were observed. Because of the results, the following were performed: bone x-rays, which were normal, and bone marrow biopsy, in which were found lymphoid infiltrates, mostly formed of small cells. On immunohistochemical coloring, a polyclonal increase of plasma cells was found, colored to both κ and λ and to different immunoglobulins. The cells were positively colored for CD20. On consultation with the hematologic unit, lymphoproliferative disease was ruled out.

A week after the bone marrow biopsy, the patient began to report swelling and pain in the area of the right parotid gland. On examination by an ear, nose, and throat physician and ultrasound of the affected gland, acute infection of the right parotid gland was diagnosed. Ultrasound revealed a homogeneous structure of the gland, with a number of lymph nodes in and around the gland. At this point, with the possible diagnosis of Sjögren syndrome, Schirmer test was performed, which was found to be regular, with no dryness. Biopsy of the small salivary glands of the lower lip revealed periductal and perivesicular infiltration of lymphocytes, a histologic picture typical of Sjögren syndrome.

To support the diagnosis, additional antibody tests were performed: anti-Ro (SS-A) was 398.30 U/mL and anti-La (SS-B) was 238.2 U/mL, which is considered highly positive (see Fig. 1).

The diagnosis of Sjögren syndrome was therefore made on the basis of a clinical picture, which included hemolytic anemia (positive Coombs test), involvement of exocrine glands (parotid and epididymal), a positive biopsy with involvement of the salivary glands, dryness of the mouth (xerostomia), and a sensation of dryness of the eyes in spite a negative Schirmer test. Furthermore, antibody tests were positive and supported the diagnosis of Sjögren syndrome.

During hospitalization, the patient experienced severe chest pain, with anterior ST-segment changes on electrocardiogram, which did not respond to standard treatment. The decision was made to administer 3 sessions of plasmapheresis, which resulted in symptom-free angina. Although it is
not standard protocol to treat patients with Sjögren syndrome with plasmapheresis, this was done because of the patient’s deterioration due to his unstable angina as a result of his hyperviscosity syndrome. At 2-year follow-up, after continuing treatment with Imuran and cyclophosphamide, the patient is still free of any ischemic or anginal symptoms.

2. Discussion

Hyperviscosity is an impairment in blood flow due to increased blood viscosity that can derive from an increase in the plasma proteins and red blood cells. Hyperviscosity can appear in diseases such as Waldenström macroglobulinemia, multiple myeloma, and autoimmune diseases [1]. Hyperviscosity can result in visual abnormalities, neurologic damage, coagulopathies, and thrombosis. Sjögren syndrome can be expressed as hypergammaglobulinemia. The irregular rheologic characteristics of the serum result from the molecular structure of the monoclonal paraproteins, which can accumulate because of the formation of polymers. In these models, IgG behaves as an antigen and antibody and can undergo polymerization to a dimer and more complex models and molecules. Generally, medium chains are the cause of formation of these complexes.

To date, few cases of rheumatologic diseases with hyperviscosity, and even fewer cases of Sjögren syndrome with hyperviscosity, have been reported [2-4]. In only 1 case could we find a report on treatment with plasmapheresis. The treatment of rheumatoid diseases with plasmapheresis is generally very limited and Sjögren syndrome is not considered an indication for the use of this therapy. Our attempt at treatment of the patient under discussion was successful, with no complications. As far as we know, this is the first case of Sjögren syndrome with unstable angina that was treated successfully with plasmapheresis. Follow-up over the course of 2 years has not indicated a need to repeat the treatment. We therefore believe that the use of plasmapheresis should be considered in the treatment of Sjögren syndrome with hyperviscosity and ischemic heart disease.

References

Case Report

Bilateral angle-closure glaucoma after combined consumption of “ecstasy” and marijuana

Peter Trittibach MD, FEBO, Beatrice E. Frueh MD, David Goldblum MD*

Department of Ophthalmology, University of Bern, CH-3010 Bern, Switzerland

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3,4-Methylenedioxymethamphetamine (MDMA, ‘Ecstasy’) is a widely abused, psychoactive recreational drug, which increases the release of monoamine neurotransmitters and inhibits the reuptake of serotonin.

We report a 29-year-old Caucasian woman who was repatriated from her holiday in North Africa to our ophthalmic emergency unit with a two-week history of severe recurrent headaches, malaise and blurred vision. On examination, best-corrected visual acuity was 20/400 in the right eye and 20/40 in the left eye. Intraocular pressures (IOP) were 38 mmHg, and 40 mmHg, respectively. Slit lamp examination showed bilateral conjunctival hyperemia, shallow anterior chambers and corneal edema. Gonioscopy revealed bilateral circular closed angles. The pupils were mid-dilated and non-reactive to light. ‘Glaukomflecken’ (opacities of the anterior lens epithelium due to raised IOP) were noted in the anterior lens. Optic nerve heads of both eyes demonstrated a slight enlarged cup. After topical application of pilocarpine 2%, timolol 0.5%, brimonidine 0.2% and intravenous acetazolamide, IOP returned to normal values and symptoms quickly improved. Bilateral laser iridotomy was also initially performed. The patient received later a trabeculectomy with mitomycin on the left eye. After laser iridotomy failure on the right side, a surgical iridectomy was performed.

4 months after her first visit, visual acuity was 20/25 in the right eye, and 20/32 in the left eye due to lens opacities. IOP was 8 mm Hg (right eye) and 9 mm Hg (left eye) without medications. Initial visual fields showed typical glaucomatous defects with a subsequent partial improvement.

Two years before the actual presentation, a diagnosis of migraine ophthalmique had been established by a neurologist and had been treated episodically with ergotamine with little success. An ophthalmic evaluation at that time revealed no abnormalities except for an anatomically narrow anterior chamber angle in both eyes. Later on the patient realized, that the attacks of ‘migraine’ with headache and transient blurred vision always started after the consumption of MDMA as had her last attacks in North Africa. These episodes disappeared spontaneously after a few hours. In North Africa, the patient consumed for the first time MDMA and marijuana together. After cessation of ecstasy consumption no further acute glaucomatous episodes or ‘migraine attacks’ were observed up to one year after her last control.

Several drugs are known to precipitate angle-closure glaucoma by narrowing the angle of the anterior chamber, by pupillary dilation and/or forward movement of the iris/lens diaphragm (pupillary block glaucoma), and by swelling of the ciliary body/epithelium, lens or vitreous body [1]. MDMA is well known for its cerebral, cardiovascular and hepatic toxicity [2,3]. Cases of bilateral sixth nerve palsy, retinal hemorrhages and central serous chorioretinopathy after MDMA consumption have been described before [4–6]. As a synthetic amphetamine derivate it increases the release of monoamine neurotransmitters (serotonin, noradrenaline and dopamine) and inhibits the reuptake of serotonin from the synaptic gap. It therefore influences pupillary diameter inducing mydriasis and depressing...
pupillary reaction to light [7,8]. In our patient, the ‘migraine’ attacks were probably always due to intermittent acute angle closures, resulting from the mydriasis induced through the combined serotonergic and adrenergic action of MDMA in her predisposed eyes with narrow anterior chamber angles. THC (tetrahydrocannabinol), a cannabinoid contained in marijuana, can itself produce a mydriasis [9,10]. Therefore the bilateral angle-closure glaucoma in North Africa was perhaps triggered by a combined mydriatic effect of MDMA and THC.

In conclusion, physicians should be alerted that the combined consumption of MDMA (and marijuana) may deteriorate vision including the possibility that it could induce migraine-like headache due to acute angle-closures in predisposed patients.

References

Correspondence

Tracheal bronchus mimicking bronchial intubation endoscopically: report of a case with airway burn

To the Editor,

Malfunction of an endotracheal tube must be corrected promptly. On the other hand, especially in cases of airway burn, unnecessary correction of the endotracheal tube must be avoided to prevent endotracheal mechanical stimulation, and repeated intubation may be difficult because of progressive airway edema. Therefore, emergency physicians must evaluate the position of the endotracheal tube correctly expeditiously. We present a case of airway burn with congenital tracheal bronchus mimicking bronchial intubation endoscopically. Radiological findings led us to the correct diagnosis.

A 76-year-old man was transferred to our hospital for treatment of superficial burn and airway burn. Endotracheal intubation was performed, and the correct position of the endotracheal tube confirmed by portable chest film (Fig. 1). The chest film did not reveal the details of the tracheal structure clearly, mainly because the portable radiograph does not ensure high-quality pictures like those with stationary equipment, and tracheal bronchus was not noticed. Tracheal endoscopy via an endotracheal tube for estimation of airway damage revealed the finding of trifurcation without normal carinal bifurcation (Fig. 2). We were worried about accidental bronchial intubation after the radiography, but a repeat chest film did not reveal any tube malposition. We therefore suspected congenital tracheal bronchus, and we treated the patient without removing or correcting the endotracheal tube. Computed tomography for evaluation of lung damage clearly revealed the tracheal bronchus (Fig. 3).

Fig. 1 A portable chest film revealed the correct position of the tip of the endotracheal tube (arrow). The finding of tracheal bronchus is unclear.

Fig. 2 Endoscopy revealed congenital tracheal bronchus (arrow) mimicking trifurcation of the bronchus. The right main bronchus (R) and the left main bronchus (L).

Fig. 3 Coronal reconstruction of the computed tomographic results revealed tracheal bronchus (arrow).
The patient subsequently made a full recovery from the airway burn and was transferred to the department of plastic surgery for continued treatment of the superficial burn.

Tracheal bronchus, which is an aberrant or accessory bronchus, is not rare: the incidence of tracheal bronchus is approximately 2% [1-3]. Almost all cases of tracheal bronchus arise from the right wall of the trachea, and malfunction of the endotracheal tube in association with tracheal bronchus is rare because almost all cases of tracheal bronchi are branched within 2 cm of the carina [1-3]. Tracheal bronchus detected during emergency endoscopy has received little attention in the emergency medicine literature. Emergency physicians must be aware, however, that apparent discrepancies between the radiological estimation and endoscopic findings can occur because the tracheal bronchus may not be noticed with a portable radiograph.

Naoya Yama MD
Kazumitsu Koito MD, PhD
Masato Hareyama MD, PhD
Department of Radiology
School of Medicine
Sapporo Medical University
Sapporo 060-8543, Japan
E-mail address: nyama@sapmed.ac.jp

Satoshi Nara MD
Hiroyuki Okamoto MD
Yoshihiko Kurimoto MD, PhD
Eichi Narimatsu MD, PhD
Department of Traumatology and Critical Care Medicine
School of Medicine
Sapporo Medical University
Sapporo 060-8543, Japan

Yasufumi Asai MD, PhD
Hiroyuki Okamoto MD
Satoshi Nara MD
Naoya Yama MD
Kazumitsu Koito MD, PhD
Masato Hareyama MD, PhD


References


Hypermethemoglobinemia in a substance abuser

To the Editor,

In September 2004, a 44-year-old male substance abuser was admitted in the emergency department after having been found unconscious on the street. On admission, he was deeply cyanotic with normal level of consciousness (Glasgow score of 15), free from cardiovascular troubles (blood pressure, 130-80 mm Hg; heart rate, 73 beats per minute). The patient denied have used toxics although he had a known history of substance abuse and chronic obstructive pulmonary disease. Arterial blood color was chocolate-brown and blood gases analysis showed a moderate respiratory alkalosis with a decrease in arterial oxygen pressure despite a 6 L/min oxygen mask therapy (pH, 7.46; PCO2, 35 mm Hg; PO2, 54 mm Hg; HCO3, 24 mmol/L; SaO2, 84.7%). In addition, the biochemistry laboratory blood gas analyzer co-oximetry module (ABL 725, Radiometer, Copenhagen, Denmark) measured a methemoglobinemia (MetHb) at 38.7%.

When cyanosis is unresponsive to adequate oxygen therapy with fairly normal blood gases, one has to bear in mind dyshemoglobinemia. Because congenital abnormalities in hemoglobin (Hb) structure and inherited deficiencies in enzymes responsible for MetHb reduction are uncommon, nitrite intoxications should be considered especially in substance abuse subjects. Aliphatic nitrites [1] (butyl, amyl, isobutyl), so-called “poppers,” are clear liquids usually coming in small glass bottles and sold on the internet or in adult bookstores in France. Legislation varies between countries but poppers are available worldwide with mail-order vendors. Inhalation of nitrite poppers vapors causes muscles around blood vessels to relax, making the heart speed up and leading to a rush sensation and euphoric effects. Aside from the spectrum of acute effects expected by the user, abuse of poppers may lead to intoxication characterized by unconsciousness and anoxia. This observation of hyperMetHb is connected to the general oxidizing property of the nitrites that transform Fe2+ of the Hb heme in Fe3+ and prevent binding oxygen leading to cyanosis [2]. HyperMetHb is a life-threatening situation (death may occur when MetHb > 70%) that requires fast diagnosis and antidotal treatment with methylene blue that quickly reduces MetHb to Hb.

Intoxication of poppers was suspected in this patient because of the high level of MetHb. On re-questioning, the patient acknowledged to have inhaled a whole bottle of poppers in the hour before. Immediately after diagnosis, in the intensive care unit, the treatment with intravenous methylene blue (2 mg/kg) was conducted, which rapidly improved the patient’s clinical course and dropped the MetHb level below 1.1% within 1 hour. The day after, blood gases on room air were measured and showed a lowered PO2 (68 mm Hg) because of his previous lung state but with a normal MetHb.

Poppers usage is not uncommon. The French ESCAPAD (Enquête Santé et Consommation au cours de l’Appel de Préparation à la Défense) study recently showed that 5.2% of the 16668 subjects aged 17 to 19 years already experienced poppers [3]. Interestingly, a depressive 28-year-old male substance abuser was admitted to the emergency department 2 weeks after the previous subject after having been found drowsy and vomiting on the street. He was deeply cyanotic and MetHb level was found at 61.1%. The patient was
questioned and finally acknowledged to have inhaled and ingested poppers. He was then treated in the intensive care unit for intravenous injection of methylene blue, which rapidly improved his condition.

Our observations show that inhalation of poppers may be excessive in substance abuse subjects who may not use them moderately. Systematic measurement of MetHb with co-oximetry was the key to diagnosis because none of these subjects acknowledged spontaneously the use of poppers. This emphasizes the usefulness of MetHb measurement in cyanotic patients unresponsive to oxygen therapy to administer the methylene blue antidotal treatment.

Bénédicte Bénétteau-Burnat PhD
Pascal Pernet PhD
Michel Vaubourdolle PhD
Service de Biochimie A
Hôpital St-Antoine, AP-HP
75571, Paris Cedex 12, France
E-mail address: benedicte.beneteau-burnat@sat.ap-hop-paris.fr

Patrick Pelloux MD
Laurent Casenove MD
Service d’Accueil des Urgences
Hôpital St-Antoine, AP-HP
75571, Paris Cedex 12, France

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References

Nasal ulcers in the ED: from Wegener’s granulomatosis

To the Editor,

Generalized symptoms such as fever, cough, and malaise are common emergency department (ED) complaints. It would be easy for a physician to become complacent about common symptoms. However, bizarre and exotic diseases occur. Therefore, the astute physician keeps a broad differential in mind when evaluating and treating patients.

An 18-year-old Hispanic man presents to our ED with a 1-week history of fever, chills, night sweats, nonproductive cough, and malaise. He began feeling ill 1 month ago with anorexia and fatigue. He denies shortness of breath, chest pain, rash, arthralgias, or hemoptysis. He was recently seen by his ears, nose, and throat physician and presumptively diagnosed with mononucleosis. His medical history is significant for a spontaneous pneumothorax 1 year ago and recurrent sinusitis. He has no allergies and takes no medication. The patient denies smoking, drinking, and illicit drug use. He denies recent travel, exposure to tuberculosis, or sexually transmitted diseases.

On physical examination, the patient is in no acute distress and saturating well on room air, with temperature of 101.0° C; heart rate, 92 beats per min; respirations, 18/min; and blood pressure, 116/63 mm Hg; head, eyes, ears, nose, and throat, bilateral nasal septal ulcers and tenderness and erythema on pharynx and soft palate; cardiac, regular rate and rhythm; lungs, clear bilaterally, with decreased breath sounds left upper lobe; abdomen, soft, nontender, positive bowel sounds; neuro, no focal deficits; and skin, warm, dry, and no rash.

Laboratory tests revealed white blood cell count of 13.5 (1000/mL), negative results for influenza and monospot, no acid-fast bacillus in sputum, unremarkable urinalysis, and erythrocyte sedimentation rate of 110 mm/hr. Chest radiography demonstrated right hilar enlargement, left upper lobe opacities, and a right cavitating lesion (Fig. 1). Empiric antibiotics were started. The ED evaluation concluded with a computed tomographic (CT) scan of the chest and consultations to pulmonology and infectious disease. Computed tomographic scan was preliminarily read as multiple cavitating lesions with infiltration bilaterally (Fig. 2).

The patient was admitted in contact isolation, and antifungal therapy was added. The working differential included infectious etiologies (tuberculosis, histoplasmosis, blastomycosis, human immunodeficiency virus, and nocardia) and noninfectious causes (Wegener’s granulomatosis, sarcoidosis, and Goodpasture’s disease). On day 1 of hospitalization, bronchoscopy revealed erythematous bronchiolar walls, with no acid-fast bacilli or fungi observed. A maxillofacial CT scan demonstrated left maxillary mucoperiosteal ulcers in the ED: from Wegener’s granulomatosis

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Fig. 1 Chest radiograph showing pulmonary destructive lesions.
osteoal thickening with ossified densities (Fig. 3). On day 2, the antineutrophil cytoplasmic antibodies (c-ANCA) result returned positive. He was diagnosed with Wegener’s granulomatosis and started on 1 g of methylprednisolone intravenously for 3 days and 25 mg of methotrexate a week. He was discharged home on hospital day 5 with 60 mg of prednisone daily and weekly methotrexate injections.

Wegener’s granulomatosis affects 1 in every 30,000 to 50,000 people. There are only 500 new cases diagnosed annually in the United States. The disease occurs at any age, but peaks in the fourth to fifth decade of life, with 85% of patients older than 19 years. It affects males and females equally. Ninety-seven percent of patients are white, 2% black, and 1% are of other ethnicities. It is a systemic vasculitis of the medium and small arteries and venules in the upper and lower respiratory tracts and kidneys. Essentially, all patients with Wegener’s granulomatosis present with upper airway or pulmonary pathology, but one third are asymptomatic [1,2].

The most common presenting symptoms include persistent rhinorrhea, purulent or bloody nasal discharge, oral and nasal ulcers, myalgias, and sinus pain [2]. Nonspecific complaints of fever, night sweats, anorexia, weight loss, and malaise occur. Other frequent complaints include cough, dyspnea, hemoptysis, and pleuritic pain. Pulmonary symptoms without upper respiratory tract involvement are unusual. Common laboratory abnormalities include leukocytosis, thrombocytosis, and marked elevation of the erythrocyte sedimentation rate. Nodules, cavitary lesions, and infiltrates commonly occur on chest radiography.

The diagnosis of Wegener’s granulomatosis is suggested from clinical and laboratory findings and from the presence of circulating ANCA directed against proteinase 3 (c-ANCA) [3,4]. The presence of 2 or more of the following 4 criteria is suggestive of Wegener’s granulomatosis: nasal or oral ulcers with purulent or bloody discharge, infiltrates with cavitations on chest radiography, microscopic hematuria, and granulomatous inflammation on arterial biopsy [4].

Initial treatment consists of cyclophosphamide and steroid therapy. Once remission occurs over a period of months to years, less toxic agents such as methotrexate are used. In the past, approximately 80% of patients with untreated Wegener’s granulomatosis died within a year of disease onset, and 90% died within 2 years. Today, the prognosis has been dramatically improved. With appropriate treatment, patients survive for much longer periods and lead relatively normal lives. Approximately 50% of patients with Wegener’s granulomatosis have disease relapse within 2 years of stopping medication [5]. Therefore, it is extremely important for patients to have regular follow-up.

In conclusion, Wegener’s granulomatosis is a vasculitis that primarily affects small- and medium-sized arteries in the upper airway, lungs, and kidneys. A positive c-ANCA is suggestive of Wegener’s granulomatosis and confirmed by biopsy. Without treatment, Wegener’s granulomatosis is rapidly progressive with 80% fatality at 1 year, making this differential diagnosis important for emergency physicians.

Randy Johnson MD, MS
Megan Crisham MD
Department of Emergency Medicine
Emergency Medicine Residency Program
Resurrection Medical Center
Chicago, IL 60631, USA

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Correspondence

References


Resident physician predictions of survival from cardiopulmonary resuscitation

To the Editor,

Cardiopulmonary resuscitation (CPR) is highlighted frequently on television, portraying unrealistically high success rates. Multiple surveys have also revealed unrealistically high expectations of success. Jones et al [1] found expectations to be as high as 75% among the American public and attributed this to the use of television as a source of information. Roberts et al [2], in a study of attending physicians and nurses, found predictions of 24% and 30% survival for adult CPRs, respectively. Overall survival rates to hospital discharge, however, average less than 16% both for out-of-hospital and inhospital arrests [3-9].

Our goal was to examine expectations of success of CPR among residents because we found no studies of prediction rates for residents. We also sought to determine differences between emergency medicine (EM) and non-EM residents’ expectations, hypothesizing that EM physicians were more familiar with CPR and therefore have more realistic expectations. Overly optimistic expectations for success rates of CPR have important adverse implications because lofty optimism may be conveyed to family members while also leading to prolonged futile resuscitations.

We administered a structured survey to residents at scheduled educational conferences at several suburban and urban teaching hospitals. The survey distribution was prefaced by an expectation of prompt return, and the surveys were briefly reviewed for completeness before acceptance by the monitor.

The survey included demographics of the residents, percentage of estimates of patient survival to hospital discharge after CPR, and estimates of surviving patients’ likelihood to return to previous level of neurologic function after a CPR event for 2 groups: older and younger than 55 years.

We used SPSS (version 7.5 for Windows, SPSS, Chicago, IL) using 2-tailed Student t tests, with α set at .05. A priori power calculations revealed that we needed 120 surveys in each group to have an 80% power to detect a difference of 10%. The institutional review board approved the study.

Of the 266 surveys, there were 146 EM and 120 non-EM residents. The number of non-EM responding residents included 51 family practice, 24 internal medicine, 22 pediatrics, and 23 from other residencies. We estimated a complete survey return of greater than 95%.

There were differences in resident level of training between EM and non-EM groups: 2.5 ± 0.1 years for EM and 1.9 ± 0.1 years for non-EM. The mean age was 31 years for both groups. Emergency medicine residents were more likely to have completed courses in advanced cardiac life support (99% vs 82%), pediatric advanced life support (64% vs 36%), and APLS (19% vs 7%). More EM residents took part in a CPR save in the past 2 years: 88% for EM vs 66% for non-EM residents.

The EM residents’ predictions were consistent with reported success rates, whereas non-EM residents responses for all CPR success categories were statistically significantly higher (see Table 1).

There has been widespread use of CPR since its formal introduction to the medical community in the early 1960s. With nearly 600,000 sudden cardiac deaths occurring annually in the United States, successful resuscitation does take place but is not the norm. Previous studies have shown expectations of success to be unrealistically high.

Our study shows that EM residents have statistically lower perceptions of CPR and more realistic perceptions of CPR success rates than non-EM residents. The differences in expectations between the EM and non-EM groups were greater than 10% in all categories. Emergency medicine residents’ more accurate perception of CPR and its outcome may be due to their greater familiarity with CPR. These differences, however, may be attributed in part to the greater number of resuscitation courses taken by EM residents and the greater number of years spent in residency in our sample: 2.5 years for EM vs 1.9 years for non-EM residents.

We surveyed residents mainly in the metropolitan New York City area. We did not have enough residents in each of the other residencies to allow further subset analyses, and by chance, our samples were not equivalent for average years in training. One may attempt to ascribe these differences in expectations between EM and non-EM residents to differences in survival rates in the areas in which they practice. It has been shown, however, that CPR survival rates among hospitalized patients and patients in the prehospital setting are similar [10-17].

Ultimately, unrealistically high expectations place burdens on CPR providers to prolong their attempts despite futility. This may have a cost for providers of prehospital care who rush to the hospital, risking accidents en route. Furthermore,

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1 Previously post-graduate year-3; currently Emergency Medical Services Fellowship Director and assistant professor of Emergency Medicine, University of Maryland School of Medicine, Baltimore.
futile prolonged attempts to resuscitate take resources away from other patients. We recommend that a portion of all resuscitation courses deal with actual resuscitation rates and the downside of prolonged futile resuscitations.

Donald Alves MD
Department of Emergency Medicine
University of Maryland School of Medicine
Baltimore, MD 21201, USA
Department of Emergency Medicine
Morristown Memorial Hospital
Morristown, NJ 07960-6136, USA
E-mail address: hvngchstpn@aol.com

John Allegra MD, PhD
Paul Allegra BA
Michele Wallace BSc
Department of Emergency Medicine
Morristown Memorial Hospital
Morristown, NJ 07960-6136, USA


References


Table 1

<table>
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<tr>
<th>Predictions of residents</th>
<th>&lt;55 y</th>
<th>&gt;55 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>EM</td>
<td>Non-EM</td>
<td>P</td>
</tr>
<tr>
<td>Survival to hospital discharge (%)</td>
<td>16 ± 1</td>
<td>35 ± 2</td>
</tr>
<tr>
<td>Survivors functionally intact (%)</td>
<td>14 ± 2</td>
<td>34 ± 3</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
ANNOUNCEMENT

2006 CERTIFYING EXAMINATION IN PEDIATRIC EMERGENCY MEDICINE

Examination Date: November 16, 2006.
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Acknowledgments
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