Laparoscopic accuracy in prediction of appendiceal pathology: oncologic and inflammatory aspects

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Abstract

BACKGROUND: In the prelaparoscopy era, macroscopically normal appendices were routinely resected. The aim of this study was to evaluate the accuracy of laparoscopy.

METHODS: A review of 1,899 patients who underwent appendectomy with multivariate analysis was conducted.

RESULTS: Laparoscopic and open approaches had similar false-positive rates, false-negative rates, accuracy, and sensitivity. The study population included 17 false-negative cases (11% of all macroscopically normal appendices). Tumors were found in 1.1% of our study population. Female gender (1.9% vs .5%; odds ratio, 4; 95% confidence interval, 1.5 to 11; \(P < .005\)) and appendiceal perforation were independent risk factors for harboring a tumor.

CONCLUSIONS: It is suggested that laparoscopy has diagnostic quality similar to that of the open approach. Until randomized trials evaluate the fate of patients who receive false-negative diagnoses, routine appendectomy is recommended. Special attention should be paid to female patients and to patients with perforations, who have a 4-fold increased risk for harboring a tumor.

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Appendectomy for acute appendicitis is the most common nonelective surgery performed by general surgeons. Reginald Fitz,\(^1\) in 1886, was the first to identify inflammation of the appendix. Laparoscopic evaluation for presumed appendicitis allows a surgeon to explore the entire abdomen and pelvis to exclude disorders that mimic appendicitis. Additionally, in the prelaparoscopy era, surgeons routinely removed even macroscopically normal appendices found during surgery for presumed appendicitis so that the scar would not cause confusion in future diagnoses. Laparoscopy, which leaves no typical scar, obviates this practice. However, this creates a dilemma for surgeons. Leaving a macroscopically normal appendix in situ avoids unnecessary surgery, with its attendant complications, and shortens operating time,\(^2,3\) but it poses a risk for failure to treat appendices that may be microscopically inflamed and missing an occult tumor,\(^4\) reported in approximately 1% of appendectomy specimens.\(^5,6\) Data on indications for resection of macroscopically normal appendices remain sparse, and the extent to which laparoscopy influences the decision to operate or not is still unclear. The aims of the present study were to evaluate the diagnostic accuracy of laparoscopy in terms of appendiceal pathology and to identify potential factors that affect it. A further aim was to address the

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dilemma posed by a macroscopically normal appendix found during laparoscopic surgery for presumed acute appendicitis. This is, to our knowledge, the largest hospital-based series to date addressing these issues.

**Methods**

**Study design and setting**

The study was approved by the local institutional review board. The target population included all patients who underwent appendectomy for presumed acute appendicitis between January 2004 and December 2007 at a tertiary medical center. The patients were identified by a search of the hospital’s administrative databases using procedural codes for appendectomy.

For each patient, clinical, operative, and pathologic data were abstracted from the medical charts and electronic databases of the relevant departments (emergency, surgery, pathology, etc) and outpatient clinics.

**Methods of measurement**

The grading system developed, which we previously reported, was used to define the severity of appendicitis in each patient. The final grade assigned was based on both the operative findings and the specimen pathology report, as follows: G0 = normal appendix, G1 = acute appendicitis, G2 = gangrenous appendicitis, G3 = perforated appendix or phlegmon, and G4 = periappendicular abscess. Table 1 demonstrates this grading system. An incorrect diagnosis was defined as an appendix that macroscopically appeared inflamed (G1 to G4) but for which the microscopic evaluation found no inflammation (G0), or vice versa. The result was considered a false-positive if the diagnosis of inflammation on macroscopic evaluation (G1 to G4) was not corroborated by the pathologic study (G0). Independent risk factor for negative appendectomy are shown in Table 4, demonstrating the role of young age (for patients aged <45 years, risk was increased by 2.3-fold), female gender (1.9-fold increased risk), and pregnancy (2-fold increased risk). The alternative diagnoses in cases of negative appendectomy are shown in Table 5.

**Statistical analysis**

Pearson’s chi-square test was used to analyze the statistical significance of differences in categorical variables between groups, and Student’s t test with a 2-tailed distribution was used for continuous variables. Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) for laparoscopic accuracy variables and negative appendectomy rate were calculated using standard unconditional logistic regression. Variables that were significant on univariate analysis were entered into a multivariate unconditional logistic regression model. SPSS version 17 (SPSS, Inc, Chicago, IL) was used for all analyses.

**Results**

**Demographics**

A total of 1,899 patients who underwent appendectomy for presumed acute appendicitis were included in the study. The demographic data are summarized in Table 2. The mean age was 28 years (range, 2 to 94 years); 1,036 patients (55%) were male, and 863 (45%) were female. The laparoscopic approach was used in 1,043 patients (55%); the remainder (856 [45%]) underwent open surgery. The laparoscopy group was significantly older (mean age, 34 vs 22 years; P < .0001) and had a higher proportion of female patients (65% vs 47%; P < .0001).

**Negative appendectomy**

The distribution of the disease grades was as follows: G0, 295 patients (15.5%); G1, 1,281 patients (67%); G2, 133 patients (7%); G3, 125 patients (7%); and G4, 65 patients (3%). The rates of negative appendectomy by demographic and background factors are shown in Table 3. Independent risk factor for negative appendectomy are shown in Table 4, demonstrating the role of young age (for patients aged <45 years, risk was increased by 2.3-fold), female gender (1.9-fold increased risk), and pregnancy (2-fold increased risk). The alternative diagnoses in cases of negative appendectomy are shown in Table 5. There was no difference in the rate of alternative diagnoses by surgical approach (laparoscopy, 7%; open surgery, 9%.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Explanation</th>
</tr>
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<tbody>
<tr>
<td>G0</td>
<td>Normal appendix</td>
</tr>
<tr>
<td>G1</td>
<td>Acute appendicitis</td>
</tr>
<tr>
<td>G2</td>
<td>Gangrenous appendicitis</td>
</tr>
<tr>
<td>G3</td>
<td>Perforated appendicitis or a phlegmon</td>
</tr>
<tr>
<td>G4</td>
<td>Periappendicular abscess</td>
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</tbody>
</table>

Table 1 Pathology grading system for acute appendicitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>28</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,036 (55%)</td>
</tr>
<tr>
<td>Female</td>
<td>863 (45%)</td>
</tr>
<tr>
<td>Surgical approach</td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>1,043 (55%)</td>
</tr>
<tr>
<td>Open</td>
<td>856 (45%)</td>
</tr>
</tbody>
</table>

Table 2 Demographics
Within the group of women of reproductive age with macroscopically normal (noninflamed) appendices, there was no difference by surgical approach in the percentage of patients for whom no diagnosis was established (laparoscopy, 93%; open surgery, 94%; \( P = \text{NS} \)).

### Inflammatory outcome

Incorrect diagnoses were made in 172 patients (9.1%), with no difference in rate by surgical approach (laparoscopy, 8.7%; open surgery, 9.5%; \( P = \text{NS} \)). Patient gender, pregnancy, and reproductive age (in women) had no effect on the rate of incorrect diagnosis. Patients aged \( \leq 45 \) years had a significantly higher percentage of incorrect diagnoses than patients \( > 45 \) years of age (10% vs 5%; OR, 1.9; 95% CI, 1.1 to 3.2; \( P < .01 \)). The incorrect diagnosis was a false-positive in 155 patients (8.1% of the whole cohort). There was no difference in the false-positive rate by surgical approach (laparoscopy, 7.7%; open surgery, 8.7%; \( P = \text{NS} \)). None of the factors tested affected the false-positive rate except age, with patients \( \geq 45 \) years old having a higher false-positive rate than older patients (8.9% vs 4.9%; OR, 1.8; 95% CI, 1.1 to 3.1; \( P < .05 \)).

### Oncologic outcome

Twenty-two patients (1.1%) were found to have tumors. Their mean age was 34 years, compared with 28 years for the patients without tumors (\( P = \text{NS} \)). Twelve patients underwent laparoscopic surgery, and 9 underwent open surgery (\( P = \text{NS} \)). Table 6 presents the tumor types. In only 1 case was the tumor diagnosed intraoperatively. The patient was a 70-year-old man who had undergone gastrectomy for carcinoma 1 year previously. During the appendectomy, the surgeon described a gangrenous appendix containing a hard tumor. Seventeen of the 21 patients with tumors had macroscopically and microscopically inflamed appendices, 2 had macroscopically and microscopically noninflamed appendices, and 2 had microscopically inflamed and macroscopically noninflamed appendices. The latter 4 patients with macroscopically occult tumors accounted for 1.3% of all patients in the cohort with macroscopically normal appendices. The perforation rate in the patients with tumors was 38%, compared with 10% in the patients without tumors (\( P < .0001 \)). Female patients approaches had a positive predictive value of 91% and sensitivity of 99%. The negative predictive value was 90% for laparoscopy and 88% for open surgery; corresponding specificity values were 51% and 42%.
were more likely to harbor tumors than male patients (1.9% vs .5%; OR, 4; 95% CI, 1.5 to 11; \( P < .005 \)). The patients with perforation had tumors in 4% of the appendectomy specimens, compared with 7% in the patients without perforation (\( P < .0001 \)).

**Appendectomy complications**

Rates of wound infection and intra-abdominal abscess by appendicitis grade were as follows: wound infection: G0, 4%; G1, 2.5%; G2, 3.8%; G3, 16.4%; and G4, 7.7%; intra-abdominal abscesses: G0, 1%; G1, 2.4%; G2, 7.5%; G3, 5.7%; and G4, 10.7%. The laparoscopic approach had a higher rate of intra-abdominal abscess (3.9%) compared with the open approach (2.2%), but the difference was not statistically significant (\( P = .055 \)). On the other hand, the laparoscopic approach had a significantly lower wound infection rate than the open approach (1.5% and 7%, respectively, \( P < .0001 \)). Other important complications were small bowel obstruction (\( n = 9 \) [5%]) and inadvertent enterotomy (\( n = 1 \) [0.05%]). Three patients (15%) required reoperation for leakage from the cecum to .15).10 Our finding of a similar negative appendectomy rate remained controversial. A recent meta-analysis9 found no significant difference between the surgical approaches. Laparoscopy had a higher specificity than open approach, perhaps because it afforded surgeons greater ability to preserve pristine tissues during dissection.

Another important measure of laparoscopic diagnostic accuracy is the false-negative rate, which is associated with the negative predictive value. In our study, false-negative diagnoses were made in 17 patients, 11% of the patients with macroscopically normal appendices. There was no association of false-negative diagnosis with surgical approach. The negative predictive value was 90% for laparoscopy and 88% for open surgery. These results compare favorably with those of other studies, which reported rates of 41%18 to 97%19 for the laparoscopic approach and 51.3%20 to 74%21 for the open approach. Phillips et al22 documented a 29% false-negative rate, Roberts et al23 a 7% rate, and Al-Ghanniem et al24 a 3.3% rate; Pedersen et al10 had no false-negatives. It may be argued that microscopic changes are of no clinical significance. In all our false-negative cases, the microscopic findings consisted of early inflammatory changes (G1), and the fate of these appendices, had they not been removed, is impossible to predict. Fitz,1 still in the preappendectomy era, noted that one third of autopsy cases had evidence of prior appendiceal inflammation, suggesting that appendicitis often resolves spontaneously. Recent data support this notion. Teh et al25 and van Dalen et al17 left appendices in situ after laparoscopy for acute abdominal pain, with no subsequent events of appendicitis during follow-up. Moreover, it has recently been shown that antibiotic treatment may be a safe first-line therapy in unselected patients with acute appendicitis.26–28 Nevertheless, leaving macroscopically normal appendices intact raises concerns given their rather high proportion of microscopic inflammation, as found here. Thus, from the perspective of the false-negative rate, it may be unsafe not to resect a macroscopically normal appendix. Randomized controlled studies are needed to determine the fate of macroscopically negative and microscopically positive appendices left in situ.

A previous study reported that neoplasms of the appendix were found in only 1% of appendectomy specimens; more than half were carcinoid tumors.29 These rates are consistent with the present findings. We identified 2 independent risk factors for appendiceal tumor: female sex and appendiceal perforation, each of which increased the risk 4-fold. Sandor and Modlin20 reported a 1.7-fold higher carcinoid incidence in women than in men. The majority of patients with tumor presented with macroscopically normal appendices. Thus, from an oncologic point of view, resecting all macroscopically normal appendices seems to be unjustified, as 98.7% will not have an occult tumor. Indeed, a 1% chance of tumor is considered too low for

**Comments**

The popularity of laparoscopy for presumed acute appendicitis continues to grow.8 Studies have shown that laparoscopic appendectomy has several advantages over open surgery, including fewer wound infections, shorter duration of surgery, reduced pain, shorter hospital stay, and quicker return to normal activity.9 However, its merits in terms of diagnostic accuracy have not been elucidated, and the effect of laparoscopy on the negative appendectomy rate remains controversial. A recent meta-analysis9 found that laparoscopy led to a variable reduction in the rate of negative appendectomies. Although the overall result was nearly significant (relative risk, .37; 95% CI, .13 to 1.01), a single trial10 accounted for most of this effect. These authors10 treated macroscopically normal appendices found during open resection with resection, whereas those found during laparoscopy were left in situ. This protocol led to a significantly lower negative appendectomy rate in the laparoscopy group (1% vs 23%; relative risk, .05; 95% CI, .01 to .15).10 Our finding of a similar negative appendectomy rate for the 2 approaches is in line with most of the other studies in the meta-analysis9,11–16 and probably reflects a general reluctance of surgeons to leave a noninflamed appendix in situ during laparoscopy. Accordingly, our rate of alternative diagnoses was also similar for the 2 approaches (laparoscopy, 7%; open surgery, 9%), as described by others as well.9,11,16 Van Dalen et al17 reported a lower negative appendectomy rate in women of reproductive age after the laparoscopic approach (\( n = 63 \)). However, their study protocol created a bias in the rate calculation because surgeons who operated on the open group were obligated to perform appendectomy even on macroscopically normal appendices, whereas surgeons in the laparoscopy group were not. Our study, conducted in a larger sample (539 women of reproductive age, 125 with negative appendectomies) found no such difference between the surgical approaches. Laparoscopy had a higher specificity than open approach, perhaps because it afforded surgeons greater ability to preserve pristine tissues during dissection.
resection in any organ. Moreover, as we have previously reported, the clinical significance of these occult tumors is uncertain. Thus, in cases of a macroscopically normal appendices, it seems prudent to perform a complete workup, which might include imaging (ultrasound, computed tomography, or magnetic resonance imaging), colonoscopy, and regular patient follow-up before proceeding to appendectomy.

This study was limited by its retrospective, observational design, which precluded the randomization of patients to surgery by different groups. Therefore, we were able to determine associations but not causality. In addition, we did not include patients with unresected macroscopically normal appendices, and the sample was drawn from a tertiary teaching hospital, so generalization of the results might be limited. At the same time, this study presents the largest hospital-based series addressing the issue of laparoscopic diagnostic accuracy with regard to appendiceal pathology. In addition, all data were collected from objective sources (eg, pathologic and operative reports).

Conclusions

This is the largest hospital-based study to evaluate the diagnostic accuracy of laparoscopy in presumed acute appendicitis. Although methodologic limitations ruled out definitive recommendations, our results suggest that laparoscopy has similar diagnostic capabilities to the open approach. Oncologically, it seems excessive to resect all macroscopically normal appendices, because only 1.3% will harbor occult tumors, whose clinical significance is unclear. Nevertheless, 11% of all macroscopically normal appendices will be finally diagnosed as appendicitis. Thus, randomized trials are needed to evaluate the fate of false-negative cases. Until then, we recommend routine appendectomy during laparoscopy for presumed acute appendicitis. Special attention should be paid to female patients and patients with perforation, who have a 4-fold risk for tumor.

References