Background. Several initiatives aim to reduce postoperative infection across a variety of surgical patients as a means to improve overall quality of care and reduce variation across centers. However, the association of infection rates with hospital-level outcomes and resource utilization has not been well described. We evaluated this association across a multicenter cohort undergoing congenital heart surgery.

Methods. The Society of Thoracic Surgeons Congenital Heart Surgery Database was linked to resource utilization data from the Pediatric Health Information Systems Database for hospitals participating in both (2006 to 2010). Hospital-level infection rates (sepsis, wound infection, mediastinitis, endocarditis, pneumonia) adjusted for patient risk factors and case mix were calculated using Bayesian methodology, and association with hospital mortality rates, postoperative length of stay (LOS), and total costs evaluated.

Results. The cohort included 32,856 patients (28 centers); 3.7% had a postoperative infection. Across hospitals, the adjusted infection rate varied from 0.9% to 9.8%. Hospitals with the highest infection rates had longer (LOS) (13.2 vs 11.7 days, \( p < 0.001 \)) and increased hospital costs ($71,100 vs $65,100, \( p < 0.001 \)), but similar mortality rates (odds ratio 0.99, 95% confidence interval 0.80 to 1.21, \( p = 0.9 \)). The proportion of variation in costs and LOS explained by infection was 15% and 6%, respectively.

Conclusions. Infection after congenital heart surgery contributes to prolonged LOS and increased costs on a hospital level. However, given that infection rates alone explained relatively little of the variation in these outcomes across hospitals, further study is needed to identify additional factors that may be targeted in initiatives to reduce variation and improve outcomes across centers.


Previous studies have demonstrated that outcomes and hospital costs after congenital heart surgery are variable across centers [1–3]. However, the mechanisms underlying this variation are unclear. Several recent federal initiatives have aimed to reduce the occurrence of postoperative complications and morbidities, including postoperative infection, in patients undergoing a variety of surgical procedures as a means to improve overall quality of care and reduce resource utilization [4, 5].

In the congenital heart surgery population, it has been shown that patients with postoperative infection have higher morbidity and mortality. In the largest series, analysis of 30,078 operations in the Society of Thoracic Surgeons Congenital Heart Surgery (STS-CHS) Database from 2002 to 2006 showed that those with postoperative infection had higher in-hospital mortality and longer length of stay (LOS) when compared with those who did not have infection [6]. However, although postoperative infection is known to contribute to adverse outcomes on a patient level, the association of hospital-level infection rates with hospital performance, measured by outcomes such as survival or resource utilization, has not been well described. Thus, the extent to which differences in hospital infection rates may contribute to variability in outcomes such as mortality, LOS, and costs across hospitals performing congenital heart surgery is unclear [1–3].

This study utilizes linked clinical data from the STS-CHS Database and resource utilization data from Pediatric Health Information Systems (PHIS) Database to describe hospital infection rates across a large multicenter cohort undergoing congenital heart surgery, and association with hospital-level outcome measures including mortality, LOS, and costs.
Material and Methods

Data Source
De-identified data from the STS-CHS and PHIS databases were linked at the individual patient level using the method of “indirect identifiers” as previously described and verified [7–9]. The STS-CHS Database is the largest existing pediatric heart surgery registry, and collects data on all children undergoing heart surgery at greater than 100 participating North American centers. The PHIS Database is a large administrative database that collects information from the hospital bill from 41 US children’s hospitals. Linking these datasets enables us to capitalize upon the strengths of both datasets, including the detailed information captured in the STS-CHS Database for case ascertainment, risk adjustment, and capture of postoperative complications (including infection), and the resource utilization information collected in the PHIS Database [7]. This study was not considered human subjects research by the Duke Institutional Review Board in accordance with the Common Rule (45 CFR 46.102(f)).

Study Population
Hospitals participating in both the STS-CHS and PHIS Databases from 2006 to 2010 were eligible for inclusion (n = 33 hospitals). From these hospitals, children (0 to 18 years) undergoing any cardiovascular operation (with or without cardiopulmonary bypass) classified in the Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery (STAT) risk stratification system were included (n = 44,198 patients) [10]. For the purposes of this analysis, those undergoing heart transplant (n = 676 patients) and those with preoperative sepsis or endocarditis (n = 429 patients) were excluded. Hospitals with greater than 15% missing data on key study variables (n = 5 hospitals) were excluded. This exclusion was applied, in part, in order to exclude hospitals who did not code complications, including infection, consistently. Finally, from the remaining hospitals, patients with missing LOS or postoperative complications data (n = 148 patients) were excluded.

Data Collection: STS-CHS Database
Data collected from the STS-CHS Database included patient demographics, preoperative risk factors, and noncardiac or genetic abnormalities (of note, this included the presence of DiGeorge syndrome/22q11 deletion), history of previous cardiothoracic surgery, primary procedure of the index (first) operation of the admission, use of delayed sternal closure, postoperative complications (including postoperative infection) and LOS, and in-hospital mortality [11]. Postoperative infection included sepsis, wound infection, mediastinitis, endocarditis, or pneumonia, as collected and defined in the STS-CHS Database [11].

Data Collection: PHIS Database
Resource utilization information collected from the PHIS Database included payer type, medication utilization (perioperative corticosteroids), and total hospital charges. Costs were estimated from charges using hospital- and department-specific cost or charge ratios, adjusted for regional differences using the Centers for Medicare and Medicaid Services price and wage index, and indexed to 2006 dollars.

Analysis
Preoperative, operative, and postoperative variables were described using standard summary statistics in the overall cohort, and in those with and without postoperative infection.

On a patient-level, the association of postoperative infection with outcome was first examined. This was done in order to examine the validity of our dataset before proceeding with any of the hospital-level analyses. Based on multiple previous studies, we expected to find that on a patient level, infection was associated with adverse outcomes [6, 12–15]. In the present analysis, the association of postoperative infection with outcome was evaluated using multivariable regression adjusting for age, weight, sex, prematurity, preoperative length of stay, any noncardiac or genetic abnormality, any STS-CHS preoperative risk factor, previous cardiothoracic surgery, payer type, STAT mortality category (category 1 = operations with lowest mortality risk, category 5 = operations with highest mortality risk), perioperative corticosteroids, use of delayed sternal closure, postoperative mechanical circulatory support, and year of surgery [10]. Logistic regression was used for the in-hospital mortality endpoint and negative binomial regression with log link for the continuous endpoints (postoperative LOS and total hospital costs). These models included hospital indicator variables to account for center effects. For the purposes of this analysis, LOS and hospital costs were evaluated in hospital survivors. In order to examine the potential impact of hospitals at the extremes of complication coding on our results, a sensitivity analysis was performed. In this analysis, approximately 20% (n = 6) of the hospitals at the extremes of rates of postoperative infection were excluded, and the analysis repeated to evaluate the sensitivity the results regarding the association of infection and outcome to inclusion or exclusion of these hospitals.

Next, in order to examine infection at the hospital level, Bayesian hierarchic models were used to calculate adjusted infection rates for each hospital. The models were adjusted for patient characteristics and case mix (as described above) in order to account for any differences across hospitals. This methodology also accounts for increased variability in outcomes from centers with smaller sample size and shrinks estimates from smaller centers toward the population average to provide more stable estimates [16]. Hospitals were categorized based on adjusted infection rate (top 25%, middle 50%, and bottom 25%). Outcomes (in-hospital mortality, LOS, and total hospital costs) across hospital infection groups were examined using logistic or negative binomial regression as described above, with the addition of group indicators. Adjusted outcomes for hospital
infection groups were calculated by averaging the predicted rates of patients from these hospitals assuming they all had the given group’s estimated effect. Because those who die early may not be at risk of developing infection (and thus hospitals with more early deaths may appear to have lower infection rates), for this portion of the analysis we excluded those who died within 7 days of surgery. Finally, we estimated the amount of between-center variation in outcome explained by hospital infection rates by fitting another set of Bayesian hierarchic models with hospital infection rates in addition to patient risk factors. The estimated variances of the center level intercept of these models were compared with those from models without infection rate. The percentage reduction in estimated variance was used to quantify the amount of between-center variation explained by hospital infection rates. All analyses were performed using SAS version 9.2 (SAS Institute Inc, Cary, NC), R version 2.15 (R Foundation for Statistical Computing, Vienna, Austria), and WinBUGS version 1.4.3 (the BUGS project, Cambridge, UK). A p value less than 0.05 was considered statistically significant.

Results

Study Population

The study cohort included 32,856 patients from 28 centers. Patient characteristics overall and in those with and without infection are displayed in Table 1. The unadjusted rate of postoperative infection in the overall study population was 3.7%, and was highest in the following subgroups of patients: any noncardiac or genetic abnormality (5.3%), STAT categories 4-5 (7.5%), neonates (8.4%), and those with delayed sternal closure (11.5%). The types of infection are displayed in Table 2. Sepsis and wound infection were the most common.

Association of Infection With Patient-Level Outcomes

Unadjusted outcomes in the overall study cohort included the following: an in-hospital mortality rate of 3.1%; median postoperative LOS of 6 days, interquartile range 4 to 11 days (mean LOS 11.8 ± 19.3 days); and median total hospital costs of $37,819, interquartile range $25,384 to $68,337 (mean hospital costs $65,257 ± $93,524). On a patient level, infection was associated with significantly increased in-hospital mortality, prolonged postoperative LOS, and increased total hospital costs [Table 3]. Similar results were observed when hospitals at the extremes of infection rates were excluded (as described in detail in Materials and Methods).

Table 1. Study Population Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n = 32,856)</th>
<th>Without Infection (n = 31,631)</th>
<th>With Infection (n = 1,225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, days</td>
<td>207 (52-1,249)</td>
<td>216 (61-1,295)</td>
<td>31 (7-192)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>6.6 (3.9-14.2)</td>
<td>6.8 (4.0-14.5)</td>
<td>3.8 (3.1-6.1)</td>
</tr>
<tr>
<td>Gender, male</td>
<td>18,182 (55.3%)</td>
<td>17,519 (55.4%)</td>
<td>663 (54.1%)</td>
</tr>
<tr>
<td>Any non-CV/genetic abnormality</td>
<td>9,234 (28.1%)</td>
<td>8,741 (27.6%)</td>
<td>493 (40.2%)</td>
</tr>
<tr>
<td>Any STS preop risk factor</td>
<td>7,621 (23.2%)</td>
<td>7,049 (22.3%)</td>
<td>572 (46.7%)</td>
</tr>
<tr>
<td>Previous CT surgery</td>
<td>9,888 (30.1%)</td>
<td>9,570 (30.3%)</td>
<td>318 (26.0%)</td>
</tr>
<tr>
<td>Preop LOS, days</td>
<td>0 (0-3)</td>
<td>0 (0-3)</td>
<td>3 (0-8)</td>
</tr>
<tr>
<td>Payer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>13,780 (41.9%)</td>
<td>13,190 (41.7%)</td>
<td>590 (48.2%)</td>
</tr>
<tr>
<td>Private</td>
<td>12,436 (37.9%)</td>
<td>12,032 (38.0%)</td>
<td>404 (32.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>6,013 (18.2%)</td>
<td>5,806 (18.3%)</td>
<td>207 (16.9%)</td>
</tr>
<tr>
<td>STAT category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>23,897 (72.7%)</td>
<td>23,342 (73.8%)</td>
<td>555 (45.3%)</td>
</tr>
<tr>
<td>4-5</td>
<td>8,959 (27.3%)</td>
<td>8,289 (26.2%)</td>
<td>670 (54.7%)</td>
</tr>
<tr>
<td>CPB (vs non-CPB) operation</td>
<td>26,801 (81.6%)</td>
<td>25,801 (81.6%)</td>
<td>1,000 (81.6%)</td>
</tr>
<tr>
<td>Perioperative corticosteroids</td>
<td>17,543 (53.4%)</td>
<td>16,764 (53.0%)</td>
<td>779 (63.6%)</td>
</tr>
<tr>
<td>Delayed sternal closure</td>
<td>2,949 (9.0%)</td>
<td>2,611 (8.3%)</td>
<td>338 (27.6%)</td>
</tr>
<tr>
<td>Postop mechanical circulatory support</td>
<td>594 (1.8%)</td>
<td>488 (1.5%)</td>
<td>106 (8.7%)</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) or frequency (percent).

CPB = cardiopulmonary bypass; CT = cardiothoracic; CV = cardiovascular; LOS = length of stay; STS = Society of Thoracic Surgeons; STAT = Society of Thoracic Surgeons-European Association of Cardiothoracic Surgery.

Table 2. Type of Postoperative Infection

<table>
<thead>
<tr>
<th>Infection</th>
<th>Overall Cohort (n = 32,856)</th>
<th>Those With Infection (n = 1,225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>628 (1.9%)</td>
<td>628 (51.3%)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>430 (1.3%)</td>
<td>430 (35.1%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>142 (0.4%)</td>
<td>142 (11.6%)</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>108 (0.3%)</td>
<td>108 (8.8%)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>33 (0.1%)</td>
<td>33 (2.7%)</td>
</tr>
</tbody>
</table>

* Values sum to greater than 100% due to some patients having greater than 1 type of infection.
Table 3. Association of Infection With Patient-Level Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>Adjusted Estimate Without Infection</th>
<th>Adjusted Estimate With Infection</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>6.1 (5.1–7.3)</td>
<td>2.8 (2.2–3.6)</td>
<td>2.8%</td>
<td>6.0%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

For dichotomous variables (mortality), unadjusted and adjusted odds ratios and 95% confidence intervals are presented. For continuous variables, the ratio of length of stay or hospital costs in those with and without infection, and 95% confidence interval, is presented. The p value presented refers to the adjusted data.

CI = confidence interval; LOS = length of stay.

Association of Infection With Hospital-Level Outcome Measures

Across hospitals, the unadjusted infection rate ranged from 0.9% to 9.5%. The infection rate adjusted for patient characteristics and case mix varied from 0.9% to 9.8% (Fig 1). When hospitals were ranked according to adjusted infection rates (Fig 2A-C), those with the highest rates had significantly longer LOS and higher hospital costs, but similar mortality rates, as displayed in Table 4. The proportion of variation in total hospital costs and LOS explained by differences in postoperative infection was 15% and 6%, respectively.

Comment

In this multi-institutional analysis, we found that postoperative infection rates after congenital heart surgery varied widely across hospitals. Hospitals with higher infection rates had significantly longer LOS and increased costs. However, the magnitude of these differences was relatively small, with infection rates alone explaining only 15% of the total variation in costs and 6% of the total variation in LOS across hospitals.

This study supports the results of previous analyses which have shown that postoperative infection after congenital heart surgery is associated with increased morbidity and mortality on a patient level [6, 12–15]. However, prior studies did not examine the relationship between infection and hospital-level outcome measures. Our group and others have shown that many of these measures, including mortality, LOS, and hospital costs vary across institutions performing congenital heart surgery [1–3]. It was not known whether differences in infection rates contribute to the variation in these measures across centers [4, 5].

In the present analysis we found that differences in hospital infection rates alone were not associated with differences in hospital mortality rates. Given the wide variety of operative and perioperative factors that may influence survival, this finding is not surprising. Recent studies in the adult literature have demonstrated similar findings, in that metrics reflecting certain intermediate aspects of perioperative care and quality that may have some association with outcome on a patient level do not necessarily correlate well with differences in survival or other outcomes when measured on a hospital level [17, 18]. It has been hypothesized that this may be due to the relatively rarity of these intermediate events or their weak association with the outcome of interest [17, 18]. Our results are also consistent with previous analyses in the congenital heart surgery population, as well as in those undergoing other surgical procedures, which have shown that postoperative complication rates in general do not appear to explain differences in performance across hospitals (as measured by mortality rate) [19, 20]. Rather, it is the rate of death in patients who develop a complication (the “failure to rescue rate”) that appears to be more important [19, 20]. There are ongoing studies in the congenital heart surgery population further investigating this concept.

In contrast to our findings regarding mortality, we found that hospitals with higher infection rates did have significantly longer LOS and higher hospital costs. Previous studies have suggested that LOS is one of the primary drivers of hospital costs; thus it follows that factors which influence LOS will also have an impact on costs [3]. While our data support that reducing postoperative infection
may be 1 potential mechanism to reduce resource utilization, it is also important to note that we found that the proportion of total variation in hospital costs and LOS explained by differences in postoperative infection was relatively small (15% and 6%, respectively). Therefore, there are likely other factors that may play a more important role and require further study.

Finally, this study highlights the advantages of linking administrative and clinical datasets together. While administrative datasets contain valuable resource utilization information, it has been shown that their accuracy regarding case ascertainment, risk adjustment, and outcomes assessment can be limited in comparison with clinical registry data [21, 22]. Combining these datasets together optimizes the strengths and minimizes the weaknesses of each, and allows analyses not possible with either dataset alone. Specifically, in this study we were able to utilize the information regarding postoperative infection collected in the STS-CHS Database, and relate this to resource utilization data collected in the PHIS Database.

**Limitations**

The limitations of this study are primarily related to the nature of the datasets utilized in this analysis. While there...
are standard definitions for each of the postoperative complications collected in the STS Database, it may be possible that there is variation in how these are coded across hospitals. However, our findings of a significant association of infection with morbidity and mortality on a patient level similar to that demonstrated by previous studies, and consistent findings when centers at the extremes of the distribution of coding of infection were excluded, support the validity of the data. In this study, we were limited to evaluating infections captured in the STS Database. For example, the database currently does not collect information on urinary tract infections. We were also unable to evaluate infection occurring after hospital discharge, as the datasets utilized primarily collect in-hospital data. Future evaluation of readmission data from these datasets could allow analysis of later infection requiring rehospitalization. Our study was limited to the hospitals submitting data to both the STS and PHIS databases, and it is possible the extent of variation in infection or other variables may be greater on a national level. Finally, a complete understanding of mechanisms underlying variation in outcome and resource utilization across centers will require future analyses of factors in addition to postoperative infection.

Conclusions
This study suggests that initiatives aimed at reducing infection after congenital heart surgery may play a role in reducing variation in LOS and costs across centers. However, given that infection rates alone explained relatively little of the total variation in these outcomes across hospitals, further study is needed to identify other factors in addition to postoperative infection which may be targeted in quality improvement initiatives.

The following authors have received support: National Heart, Lung, and Blood Institute (1K08HL103631, principal investigator (PI): Pasquali; 1RC1HL099941, co-PIs: J Jacobs, Li); Dr Shah, National Institute of Allergy and Infectious Diseases (K01AI73729) and Robert Wood Johnson Foundation Physician Faculty Scholar program.

References

DISCUSSION

DR JAMES JAGGERS (Aurora, CO): Just a couple of points of clarification. When you talk about infection, are you talking about all sources of infection, sepsis, catheter related bloodstream infections, wound infections?

DR PASQUALI: The infections that we included in this study were those that I mentioned in the Methods [Materials and Methods], which included all of those captured in the STS [Society of Thoracic Surgeons] database. So it did include sepsis,
mediastinitis, wound infection, endocarditis, pneumonia. The most prevalent type of infection in our series and was sepsis, by far, similar to other reports.

DR JAGGERS: So in order to be captured, say that it’s an infection, does it have to be included in both of the data sets?

DR PASQUALI: We used the STS side for the capture of clinical information, including complications data. The presentation that is coming up by the group from CHOP [Children’s Hospital of Philadelphia] will talk a lot more about the advantages of using a clinical data source or clinical registry as opposed to administrative data for the capture of infection data, so I won’t comment much more on that. But we used the clinical side of the data to capture infection information. And for the purpose of this study, the PHIS [Pediatric Health Information System] data was used primarily to look at resource utilization or the cost data.

DR JAGGERS: And before Karl talks, just one question about that. My understanding was the PHIS database did not include costs, but does include charges. You used the mathematical formula to derive cost?

DR PASQUALI: Correct. PHIS, like many other administrative data sources, captures charge information, and then using that information you can estimate costs. The advantage of using their data set is that they have a uniform way of capturing charge information across all of their hospitals, so it is consistent, rather than pulling that information from each individual hospital’s cost accounting system. We are also able to take that information and adjust for hospital and department-specific cost-charge ratios and adjust for regional differences using the CMS [Centers for Medicare & Medicaid Services] price/wage index. So it gives us a pretty uniform look across hospitals when trying to compare this type of information.

DR KARL F. WELKE (Seattle, WA): Sara, a very nice study and very well presented. I wanted to build on something that Jim mentioned; that is the difference in types of infections. All infections are not created equal. For example, mediastinitis is potentially a much bigger problem than a urinary tract infection. One thing that happens with infections is clustering within hospitals. A hospital may have an outbreak of a certain type of infection or infections by a certain pathogen. Such grouping of infections within hospitals could drive cost and variation. Did you consider this possibility?

DR PASQUALI: We did, and this gets back to the validity of the data, and we did several different things to investigate that. The first is that, as I mentioned, we excluded hospitals who didn’t consistently code complication data across the board, because we felt we didn’t have reliable information to classify whether you had an infection or not. Most of the data I presented was hospital level data, but we also looked at patient level data in the beginning to confirm the validity of the data set. Many previous studies have shown that on a patient level infection is associated with poor outcome. So the first thing we did was to use the data in the STS database to confirm those findings, because we thought if we couldn’t demonstrate that, then we would have concern about using these data in the first place to look at infection, and we did find a similar association.

And then the third thing we did, to get more to your question, is that we looked at whether our results were consistent if we excluded certain hospitals, so those at the extremes of the end of coding of certain complications, and we found consistent associations and consistent results when we did that.

DR PHILIP SMITH (Akron, OH): Sara, transparency often has a way of offering opportunities for improvement. Do you have any plan to reveal what centers are part of this study?

DR PASQUALI: In terms of the STS policy on that, anyone that submits data to the database knows who they are, but the rest of the centers and data in your feedback reports are blinded. The data in any analyses done with the STS Database are also blinded. In terms of quality improvement, though, which gets to your question, many of the quality collaboratives in the adult cardiac world have shown that there is benefit to knowing who is performing in which manner so that you can learn from the best performing hospitals, and that has certainly been the case in the Michigan quality collaboratives and others throughout the country. There is a new quality collaborative starting in our field called PC-4 (Pediatric Cardiac Critical Care Consortium), which is focusing specifically on cardiac patients who require ICU [intensive care unit] care, both surgical and medical, and one of the foundations of their collaborative is that all the data is collected and presented in an unblinded fashion, in order to serve as a foundation for their quality improvement efforts. So, in terms of quality improvement, I think it can be very important to know the identity of centers so that you can learn from those who tend to do the best job.

DR MICHAEL MITCHELL (Milwaukee, WI): In preparation for our next talk, in your analysis, did you find that there was a significant difference in reporting rates for infections between the two databases, because my impression is that hospitals tend to massively over-report and we tend to under-report?

DR PASQUALI: We did not specifically look at that in this analysis, but the next study that is going to be presented looked at that exact question, so they will have a lot more to say about that. We used the clinical data from the STS to identify those with infection for our study.