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Original Article

Attributable Costs of Surgical Site Infection and Endometritis after Low Transverse Cesarean Delivery

Margaret A. Olsen, PhD, MPH; Anne M. Butler, MS; Denise M. Willers, MD; Gilad A. Gross, MD; Barton H. Hamilton, PhD; Victoria J. Fraser, MD

Background. Accurate data on costs attributable to hospital-acquired infections are needed to determine their economic impact and the cost-benefit of potential preventive strategies.

Objective. To determine the attributable costs of surgical site infection (SSI) and endometritis (EMM) after cesarean section by means of 2 different methods.

Design. Retrospective cohort.

Setting. Barnes-Jewish Hospital, a 1,250-bed academic tertiary care hospital.

Patients. There were 1,605 women who underwent low transverse cesarean section from July 1999 through June 2001.

Methods. Attributable costs of SSI and EMM were determined by generalized least squares (GLS) and propensity score matched-pairs by means of administrative claims data to define underlying comorbidities and procedures. For the matched-pairs analyses, uninfected control patients were matched to patients with SSI or with EMM on the basis of their propensity to develop infection, and the median difference in costs was calculated.

Results. The attributable total hospital cost of SSI calculated by GLS was $3,529 and by propensity score matched-pairs was $2,852. The attributable total hospital cost of EMM calculated by GLS was $3,956 and by propensity score matched-pairs was $3,842. The majority of excess costs were associated with room and board and pharmacy costs.

Conclusions. The costs of SSI and EMM were lower than SSI costs reported after more extensive operations. The attributable costs of EMM calculated by the 2 methods were very similar, whereas the costs of SSI calculated by propensity score matched-pairs were lower than the costs calculated by GLS. The difference in costs determined by the 2 methods needs to be considered by investigators who are performing cost analyses of hospital-acquired infections.

Surgical site infections (SSIs) are associated with substantial morbidity, longer hospital length of stay, and hospital readmissions. Most estimates for the costs of SSI come from older studies that used simple statistical methods or no statistical comparisons, with only crude estimates for the attributable costs of infection. Attributable costs can vary depending on the type of statistical method used, as shown by Hollenbeak et al for the costs of SSI after coronary artery bypass surgery.

In many studies, attributable costs were calculated for SSI that occurred after a variety of different operations, rather than calculated for SSI after individual surgical procedures. Not all SSIs are alike, however. SSIs after operations involving major organ spaces, such as cardiac or orthopedic surgery, may very well have higher attributable costs than do SSIs after less extensive operations. In addition, costs of SSI likely vary according to the depth of the infection. Attributable costs of SSIs have been reported to be highest for organ-space infection, compared with attributable costs of deep incisional or superficial incisional SSIs.

Accurate estimates of the attributable costs of SSI are needed, from the hospital perspective, to weigh the cost-benefit of infection prevention strategies and to determine the impact of the Deficit Reduction Act and the ruling by the Centers for Medicare and Medicaid Services. This ruling, which went into effect in October 2008, denies upgrade to the higher diagnosis-related group for secondary diagnoses considered to be “preventable hospital-acquired conditions,” including some SSIs.

Most studies that examined hospital costs associated with
SSIs have determined total hospital costs attributable to infection. More recently, an argument has been made to focus on direct costs (primarily consumables), because they are most subject to savings by implementation of effective infection control interventions. On the other hand, fixed costs, such as costs for most nursing staff, electricity, and maintenance, are not subject to immediate savings through prevention of infection. Therefore, calculation of the attributable direct costs of SSI may be necessary to inform cost-benefit analyses of infection control interventions.
We used administrative claims data from a retrospective cohort of women who underwent low transverse cesarean section at our academic tertiary care hospital and 2 different statistical methods to determine the attributable total and direct costs for SSI and endometritis (EMM).

**Methods**

This study was conducted at Barnes-Jewish Hospital, a 1,250-bed tertiary care hospital affiliated with Washington University School of Medicine in Saint Louis, Missouri. All patients who underwent low transverse cesarean section surgery, defined by an *International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM)* procedure code for low transverse cesarean section (74.1), from July 1, 1999, through June 30, 2001, were eligible for the study. For inclusion, patients were required to have an operative note that indicated use of a low transverse uterine incision. Potential SSI and EMM case patients were identified using *ICD-9-CM* discharge diagnosis codes consistent with incisional infection (998.50, 998.51, 998.59, 674.32, or 674.34) or EMM (670.02 or 670.04) during the original surgical admission or at readmission (inpatient, outpatient surgery, or emergency room) to the hospital within 60 days of surgery and/or excess antibiotics utilization after surgery, as described previously. Excess antibiotic utilization was defined as 2 or more days of antibiotics beginning with postoperative day 2, or any antibiotics at readmission to the hospital within 60 days of surgery. Hospital medical records were reviewed for all patients who met the *ICD-9-CM* or antibiotics criteria, and signs and symptoms of infection were recorded. EMM was defined as fever beginning more than 24 hours or continuing at least 24 hours after delivery plus fundal tenderness. SSIs were verified by chart review in accordance with the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance system definitions. During the period of this study, routine prophylactic antibiotics (cefazolin or cefotetan) were given at cord clamp.

Demographic information, microbiology and laboratory results, and *ICD-9-CM* diagnosis and procedure codes were collected for the original surgical admission by means of the Barnes-Jewish Hospital Medical Informatics database. *ICD-9-CM* diagnosis codes used to identify underlying comorbidities were also collected for the 12 months preceding the date of surgery. Comorbidity and procedure variables were created from claims data with the Healthcare Cost and Utilization Project Clinical Classifications Software.

Hospital cost data were obtained from the Barnes-Jewish Hospital cost accounting database (Trendstar; McKesson) for the surgical admission and any inpatient, outpatient surgery, and emergency readmission to the hospital within 30 days after surgery, excluding the costs and hospital days before the day of the cesarean section. Costs were calculated for each department (eg, room and board or pharmacy) by multiplying the department’s actual cost components by the charges for each patient charge code recorded during hospitalizations, divided by total departmental costs. Departmental costs were summed to calculate total hospital costs for each patient. All costs were inflation adjusted to 2008 US dollars by means of the medical care component of the Consumer Price Index.

Patient characteristics were compared by the Student *t* test, *χ*² test, or Fisher exact test, as appropriate. Crude costs were compared by the Mann-Whitney *U* test. Generalized least squares (GLS) models were fit to estimate the costs associated with SSI and EMM (the primary independent variables), while taking into account the variation of other factors significantly associated with costs. Frequency analyses were performed on the claims data to identify diagnoses and procedures that might be important predictors of cost. Variables that applied to fewer than 10 patients were excluded. Linearity assessments were performed for continuous variables. The natural log of total costs was used as the dependent variable to normalize the highly skewed distribution, and an estimator (“feasible GLS estimator”) was used to weight the observations to account for heteroskedasticity. The multivariate GLS model was determined by evaluating all biologically plausible variables, with use of *P* ≤ .05 for entry and *P* > .20 for exclusion.
TABLE 3. Results of the Generalized Least Squares Model for Determining Attributable Costs of Surgical Site Infection (SSI) and Endometritis (EMM) After Low Transverse Cesarean Section ($n = 1,597$)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proportion of patients</th>
<th>Estimated $\beta$ coefficient</th>
<th>SE</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable of interest</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSI</td>
<td>0.05</td>
<td>0.36</td>
<td>0.03</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>EMM</td>
<td>0.08</td>
<td>0.39</td>
<td>0.03</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Demographic characteristic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age $&lt;$18 years</td>
<td>0.05</td>
<td>0.06</td>
<td>0.03</td>
<td>.088</td>
</tr>
<tr>
<td>Age $&gt;$35 years</td>
<td>0.13</td>
<td>0.04</td>
<td>0.02</td>
<td>.106</td>
</tr>
<tr>
<td>Absence of private insurance$^a$</td>
<td>0.60</td>
<td>0.02</td>
<td>0.02</td>
<td>.192</td>
</tr>
<tr>
<td><strong>Procedure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labor induction</td>
<td>0.19</td>
<td>0.04</td>
<td>0.02</td>
<td>.040</td>
</tr>
<tr>
<td>Ovarian procedure</td>
<td>0.01</td>
<td>0.26</td>
<td>0.08</td>
<td>.002</td>
</tr>
<tr>
<td>Central venous catheter$^b$</td>
<td>0.01</td>
<td>0.51</td>
<td>0.07</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Medical condition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antepartum hemorrhage</td>
<td>0.03</td>
<td>0.09</td>
<td>0.04</td>
<td>.032</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>0.04</td>
<td>0.10</td>
<td>0.04</td>
<td>.008</td>
</tr>
<tr>
<td>Coagulation and hemorrhagic disorders</td>
<td>0.02</td>
<td>0.08</td>
<td>0.06</td>
<td>.135</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0.11</td>
<td>0.15</td>
<td>0.02</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>0.02</td>
<td>0.12</td>
<td>0.06</td>
<td>.049</td>
</tr>
<tr>
<td>Gonorrhea or syphilis</td>
<td>0.01</td>
<td>0.13</td>
<td>0.07</td>
<td>.060</td>
</tr>
<tr>
<td>Urinary tract or kidney infection$^c$</td>
<td>0.03</td>
<td>0.11</td>
<td>0.04</td>
<td>.009</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.01</td>
<td>0.37</td>
<td>0.07</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pulmonary collapse or insufficiencies$^d$</td>
<td>0.02</td>
<td>0.16</td>
<td>0.06</td>
<td>.010</td>
</tr>
<tr>
<td>Maternal cardiac conditions</td>
<td>0.03</td>
<td>0.13</td>
<td>0.04</td>
<td>.002</td>
</tr>
<tr>
<td>Diabetes mellitus or gestational diabetes</td>
<td>0.11</td>
<td>0.05</td>
<td>0.02</td>
<td>.022</td>
</tr>
<tr>
<td>Pre-eclampsia (mild)</td>
<td>0.08</td>
<td>0.10</td>
<td>0.03</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pre-eclampsia (severe)</td>
<td>0.09</td>
<td>0.23</td>
<td>0.03</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>0.01</td>
<td>0.62</td>
<td>0.08</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multiple gestation</td>
<td>0.06</td>
<td>0.10</td>
<td>0.03</td>
<td>.001</td>
</tr>
<tr>
<td>Obstetric laceration and/or trauma</td>
<td>0.02</td>
<td>0.20</td>
<td>0.06</td>
<td>.001</td>
</tr>
<tr>
<td>Severe complication of delivery</td>
<td>0.02</td>
<td>0.53</td>
<td>0.06</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>0.43</td>
<td>0.02</td>
<td>0.02</td>
<td>.149</td>
</tr>
<tr>
<td>Intrauterine fetal death</td>
<td>0.01</td>
<td>0.19</td>
<td>0.09</td>
<td>.040</td>
</tr>
</tbody>
</table>

NOTE. Adjusted $R^2 = 0.24$ for the model after accounting for natural log transformation of costs. SE, standard error.

$^a$ Presence of public aid, Medicare, Medicaid, or no health insurance.

$^b$ Inserted before the onset of SSI and/or EMM in case patients.

$^c$ Diagnosed on or after the day of cesarean section.

$^d$ Atelectasis, pulmonary edema, acute respiratory distress syndrome, or respiratory failure.

Conclusion. All independent variables were checked for collinearity. Models were checked for functional form misspecification by means of the Ramsey regression specification error test and for heteroskedasticity by means of the Breusch-Pagan test. Because the GLS model used the natural logarithm of costs as the dependent variable, an intermediate regression was performed to predict costs in US dollars. Each coefficient obtained in the GLS model represented the mean difference in the natural logarithm of costs between individuals with and without that variable, assuming all other predictors of costs remained constant. To calculate the attributable costs of SSI and EMM, the regression equation was solved separately for (1) patients with SSI, (2) patients with EMM, and (3) patients without infection, and was back transformed by exponentiating the result. The attributable costs of SSI and EMM were calculated by subtracting the difference in calculated costs between women with SSI or EMM and women without infection.

The second method for determining attributable costs of SSI and EMM was a propensity score matched-pairs analysis. A logistic regression model was created to predict the probability of developing SSI. The model was adjusted for all variables suspected to affect the risk of developing SSI, as defined by $P < .20$ in univariate analysis or biologic plausibility. SSI case patients and control patients were matched 1:1 on the basis of their propensity to develop SSI by means of the nearest-neighbor method within calipers of 0.10 standard deviations.SSI case patients without a suitable control...
TABLE 4. Attributable Total Costs of Surgical Site Infection and Endometritis After Low Transverse Cesarean Section Calculated by 2 Different Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Surgical site infection</th>
<th>Endometritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS</td>
<td>$3,529 ($3,105–$4,011)</td>
<td>$3,956 ($3,481–$4,496)</td>
</tr>
<tr>
<td>Matched-pairs</td>
<td>$2,852 ($2,006–$4,378)</td>
<td>$3,842 ($3,254–$5,111)</td>
</tr>
</tbody>
</table>

**Note.** CI, confidence interval; GLS, generalized least squares.

* Estimates adjusted for covariates in Table 3.

**Costs are the medians and 95% CIs based on the binomial distribution.**

The medians were used for the matched-pairs analyses because the cost differences were not normally distributed.

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patient were excluded from the analysis. Comparisons were performed between unmatched and matched SSI case patients by means of the χ² or Fisher exact test, with correction for multiple testing (α/number of tests). These methods were repeated to create propensity score matched-pairs for EMM case patients and control patients. Attributable costs were calculated as the median of the differences in cost between matched-pairs. The median difference in cost was compared with the Wilcoxon signed-rank test, with 95% confidence intervals [CIs] calculated in Stata.

Statistical analyses were performed using SPSS, version 14.0 (SPSS), and Stata, version 9.2 (StataCorp). Approval for this study was obtained from the Washington University Human Research Protection Office.

**Results.**

Of 1,605 patients who underwent low transverse cesarean section during the study period, complete cost data was available for 1,597 patients (99.5%). Cost data was missing for 1 patient with both SSI and EMM, 2 patients with EMM, and 5 patients without infection. Characteristics of the low transverse cesarean section cohort with complete cost data are shown in Table 1. Eighty patients (5.0%) developed SSI and 121 (7.6%) developed EMM, including 19 patients (1.2%) with both SSI and EMM. SSI case patients had significantly higher body mass index and were significantly more likely to have ICD-9-CM diagnosis codes for chorioamnionitis, mild pre-eclampsia, fetal distress, pulmonary collapse or insufficiencies, atelectasis, pulmonary edema, acute respiratory distress syndrome, or respiratory failure, gestational infection, or sepsis and to have ICD-9-CM procedure codes for an ovarian operation, laparotomy, or tracheostomy and/or mechanical ventilation. Compared with patients without infection, women with EMM were younger, more likely to be African American, and less likely to have private medical insurance. Patients with EMM were significantly more likely to have ICD-9-CM diagnosis codes for chorioamnionitis, sepsis, mild pre-eclampsia, fetal distress, premature rupture of membranes, or failed labor and to have ICD-9-CM procedure codes in the surgical admission for amniointusion, labor induction, and laparotomy. EMM occurred significantly less often in patients who had undergone a previous cesarean section or who had tubal ligation at the time of the cesarean section. The median length of surgical stay, beginning with the day of cesarean section, was significantly longer for women with SSI (4.5 days) or EMM (5.4 days), compared with the corresponding stay for uninfected control patients (4.0 days; P < .001 for both).

Table 2 presents crude hospital costs for SSI and EMM case patients and uninfected patients. Patients with SSI or EMM had significantly higher unadjusted costs for the surgical admission plus any readmission within 30 days of surgery, compared with such costs for uninfected patients (P < .001 for both). Room and board, pharmacy, and laboratory departmental costs were also significantly higher for SSI and EMM case patients, compared with such costs for uninfected patients (P < .001 for all). The crude increases in length of hospital stay (beginning with the date of surgery and including length of stay during hospital readmissions that began within 30 days after surgery) were 2.2 days for SSI and 1.8 days for EMM (P < .001 for both, Mann-Whitney U test).

Both SSI and EMM were independent predictors of hospital costs (P < .001) in the GLS model (Table 3). Procedures associated with significantly increased costs included labor induction, ovarian procedures, and placement of a central venous catheter. Other medical conditions that strongly affected costs included severe complications of delivery, pneumonia, pulmonary collapse or insufficiencies, intratracheal fetal death, chorioamnionitis, maternal cardiac conditions, and obstetric laceration and/or trauma. There was an increasing dose-response relationship between costs and mild pre-eclampsia, severe pre-eclampsia, and eclampsia, as indicated by the progressively larger values for the β coefficients.

The attributable costs of SSI and EMM estimated by GLS are presented in Table 4. After adjustment for the variables listed in Table 3, the attributable total costs estimated by GLS were $3,529 for SSI and $3,956 for EMM. In a separate analysis, the estimated attributable direct cost was $2,054 (95% CI, $1,797–$2,347) for SSI and $2,726 (95% CI, $2,386–$3,116) for EMM.

In the propensity score matched-pairs analyses, 68 of the 80 SSI case patients were matched with control patients and 110 of the 121 EMM case patients were matched with control patients. Twelve SSI case patients and 11 EMM case patients were excluded because a nearest-neighbor control was not available. All covariates were balanced between matched SSI case patients and control patients and matched EMM case patients and control patients after controlling for multiple comparisons. Unmatched SSI case patients had significantly higher median total costs, compared with those for matched SSI case patients ($16,088 vs $9,973; P = .008). Costs were not significantly different for unmatched versus matched EMM case patients ($10,262 vs $11,346; P = .540).

The median difference in total costs between the matched SSI case and control pairs was $2,852, and the median dif-
ference in direct costs was $1,675 ($P < .001, Wilcoxon signed-rank test). The median difference in total costs between the matched EMM case and control pairs was $3,842, and the median difference in direct costs was $2,357 ($P < .001, Wilcoxon signed-rank test). The median difference in the hospital length of stay (beginning with the date of surgery through the date of discharge, plus inpatient readmissions that began within 30 days after surgery) for the matched pairs was 2.0 days for SSI and 1.8 days for EMM ($P < .001 for both, Wilcoxon signed-rank test).

**Discussion**

We used 2 different statistical methods to calculate attributable total and direct costs associated with SSI and EMM. We found that the attributable costs of EMM calculated by GLS and propensity score matched-pairs were virtually the same (approximately $3,900), whereas the attributable costs of SSI calculated by GLS ($3,529) were higher than the costs calculated by the matched-pairs method ($2,852).

GLS modeling is commonly used for econometric analyses but relies on the careful specification of the model and inclusion of factors associated with both hospital costs and infection to reduce bias of the estimates. The advantage of the propensity score matched-pairs method is that costs are compared for individuals with similar likelihood of developing infection, and the difference in costs should therefore represent the true incremental costs of diagnosing and treating the infection. The disadvantage of this method is the loss of infected case patients due to the inability to find suitable matched control patients with equivalent likelihood of developing infection. The unmatched case patients tend to be individuals with very high probability of infection, because not as many uninfected patients have high probabilities of infection. Thus, the attributable costs calculated with this method exclude the sicker patients with more underlying comorbidities, and the calculated costs tend to be lower than the costs calculated by GLS. This was true for the attributable costs of SSI; in contrast, the attributable costs of EMM calculated with the 2 methods were remarkably similar.

The attributable total costs of SSI after cesarean section calculated in this study (approximately $3,500) were lower than costs of SSI reported in most previous studies following other operations (range, approximately $3,400–$17,700). It is not surprising that the total costs we calculated for cesarean section SSIs are on the low end of the scale of reported SSI costs, because the SSIs were primarily superficial incisional infections treated with antibiotic therapy and/or local wound care. To our knowledge, there is only one other report of the crude costs of SSI after cesarean section. Mugford et al. found that SSI added £716 (1986–1987 British pounds), which translates to $2,435 in US 2008 dollars, consistent with our findings.

Our calculation of $3,956 in attributable total costs due to EMM was higher than the costs estimated in previous studies.

To our knowledge, there are only 2 published reports of costs associated with EMM; one reported in 1980 calculated costs of $850 in a matched-pairs analysis (approximately $3,085 in US 2008 dollars), and the other more recent study estimated costs of $815 in 2001 US dollars ($688 for treatment of EMM plus $126 for fever evaluation, approximately $1,087 in US 2008 dollars) due to EMM after elective cesarean section based on decision tree analysis. It is unclear from this analysis, however, whether costs associated with excess length of stay were included in the attributable costs.

In the study by Mugford et al., 76% of the excess costs due to SSI resulted from staffing due to longer length of hospital stay in patients with infection. In our study, room and board costs were also the biggest driver of increased crude costs for women with SSI, whereas pharmacy costs made the largest contribution to increased costs for women with EMM. Excess room and board costs were responsible for 48% of the increased crude costs in patients with SSI and 29% of the increased crude costs in women with EMM, compared with the crude costs of uninfected women. Pharmacy costs made up 32% of the increased crude costs for women with SSI and 47% of the increased crude costs for women with EMM, compared with the crude costs of women without infection. Thus, although the attributable costs of the 2 infections were very similar, the cost centers driving the increase for the 2 infections were different. In contrast to the 12% higher attributable total costs of EMM, compared with those of SSI ($3,956 vs $3,529), the attributable direct cost of EMM estimated with GLS was 33% higher than the direct cost of SSI ($2,726 vs $2,054 direct cost for SSI). This is consistent with the finding that pharmacy costs (74% of which were direct costs) contributed more to the total crude costs of EMM. In contrast, room and board costs made up a higher percentage of the total crude costs of SSI, and a much smaller proportion of the room and board costs were in the direct cost category (40% direct costs).

The limitations of this study are the focus on hospital costs of infection, rather than total costs from a societal perspective, including costs of additional clinic visits, outpatient antibiotic therapy, home health visits, and so forth. We excluded SSIs that were diagnosed and treated solely in the outpatient setting, because those infections would not be associated with increased hospital costs. We expect that the exclusion of outpatient infections has minimal impact on the costs of EMM, because patients with EMM are almost always hospitalized for intravenous antibiotic therapy.

In summary, we used 2 different methods to calculate hospital costs attributable to SSI and EMM after low transverse cesarean section. The costs of EMM calculated by the 2 methods were very similar, whereas the cost of SSI calculated by GLS was higher than the cost calculated using propensity score matched pairs. Investigators can use these results to determine the most appropriate method for calculation of attributable costs on the basis of the goal of their cost analyses. The results of this study can be used to determine the cost-
benefit of routine prophylactic antibiotic administration and other infection control interventions to prevent postoperative infection after cesarean section.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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