The Effect of Increasing Age on the Risk for Surgical Site Infection

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1st Reader: W.E.

2nd Reader: K.Y.
ABSTRACT

Introduction: The National Nosocomial Infection Surveillance System (NNIS) risk adjustment system is used to predict risk of SSI. The objective of this study was to determine the relationship between age and SSI, and to determine whether the addition of age improves the predictive value of the current NNIS risk index.

Methods: This was a retrospective cohort study of 144,485 patients who underwent surgery between February 1, 1991 and July 31, 2002 at one of 11 hospitals: Duke University Medical Center and 10 community hospitals in the Duke Infection Control Outreach Network (DICON). Our cohort was randomly divided into two groups: a derivation cohort and a validation cohort. Logistic regression was used to control for the effect of NNIS variables (wound class, American Society of Anesthesiologists (ASA) score and duration of procedure). The function of age that best predicts SSI in the derivation cohort was obtained by restricted cubic splines and these results were confirmed in the validation cohort.

Results: There were 1684 SSIs in the cohort (SSI rate=1.2%). The mean age of the cohort was 52.4 years (range 17-108). The most common procedures were orthopedic (41.8%), obstetric/gynecologic (10.7%) and cardiothoracic (10.0%). In the derivation cohort, there were 72,139 procedures and 873 SSI (SSI rate=1.2%). After adjusting for NNIS variables, hospital and type of procedure, there was a significant linear relationship between age and SSI \((p=0.006)\). SSI risk increased by 1% per year between ages 17-65 \((p=0.002)\). Interestingly, after age 65, SSI risk decreased by 1% for each additional year \((p=0.008, \text{relative to the pre-65 effect})\). In the validation cohort, there were 72,334 procedures and 811 infections (SSI rate=1.1%). The relationship between age and SSI was the similar to the relationship in the derivation cohort.

Conclusions: Age independently predicted SSI and added significant predictive power to the NNIS risk index after adjustment for NNIS risk variables. SSI risk increased in a linear fashion until age 65. After age 65, SSI risk decreased in a similar fashion for each additional year of age. The decrease in SSI risk after age 65 should be further investigated.
Introduction

Surgical sites infections (SSI) are the most common type of nosocomial infection in surgical patients and are the third most frequently reported nosocomial infection in the United States, accounting for 14 to 16% of all nosocomial infections.\textsuperscript{1,2} According to a report by the National Nosocomial Infections Surveillance (NNIS) system, of 738,398 operations performed during January 1992 through June 1998, 19,267 (2.6%) subsequent SSIs were reported.\textsuperscript{3} SSIs are an important cause of increased hospital stay and morbidity and mortality for surgical patients.\textsuperscript{2,4-7} Patients who develop an SSI are more likely to die, be admitted to an intensive care unit and require readmission to the hospital compared to surgical patients who do not develop SSI.\textsuperscript{4,7}

The current system used to adjust the incidence and risk of SSI is the NNIS risk index developed by the Centers for Disease Control and Prevention (CDC). This system incorporates three well-established predictors of SSI, including the American Society of Anesthesiologists (ASA) score, wound class, and duration of procedure; this system has been consistently validated since its inception.\textsuperscript{8-12}

In the NNIS risk index, wound class and operative duration are surgical variables and measure risk associated with operative environment and techniques. The ASA score is the only measure of SSI risk associated with the patient and their underlying co-morbid illnesses. The ASA score is based on an assessment of general health status by the anesthesiologist in the pre-operative setting. Age is one of several variables that is indirectly incorporated into the ASA score. Although the ASA score is a proven predictor for SSI, length of hospital stay, and risk for death, it suffers from subjectivity and poor inter-rater reliability and is often unavailable.\textsuperscript{13-16}
It has long been assumed that the risk of SSI increases with increasing age (as is the case with other infections) due to various age related factors, such as decreased immune function and increased prevalence of co-morbid illnesses. However, previous research has produced conflicting results regarding the relationship between age and SSI. Some studies have shown an increased risk of SSI with increased age, others have found no significant relationship between the two variables. Other studies have indicated a possible protective effect of increased age on the development of SSI, but these studies were underpowered and did not provide conclusive results.

The aim of the current study was to determine the most effective method to utilize age as a predictor of SSI and to externally validate this finding. We hypothesized that age would be an independent predictor for SSI and would supplement the NNIS risk index for risk adjustment of SSI.
Methods

Study design, case definition and study setting

This retrospective cohort study included patients undergoing surgical procedures at 11 study hospitals between February 1, 1991 and July 31, 2002. Patients less than 17 years of age were excluded. All surgical site infections (SSI) were prospectively identified by trained infection control practitioners using standard CDC criteria.23 Procedures that were performed on patients with pre-existing infections at the operative site were excluded.

Duke University Medical Center (DUMC) is a 750 bed tertiary care hospital located in Durham, North Carolina. Prospective surveillance for all cardiothoracic, neurosurgical and orthopedic procedures has been conducted since 1994. This study included DUMC operative data from 1994-2002. Duke Infection Control Outreach Network (DICON) includes 17 hospitals located in the Southeastern United States. Ten of these hospitals provide prospectively collected surgical data to the DICON Operative Database. This study utilized data from the DICON Operative Database, including data from 1999-2002 for 9 hospitals; and data from 1991-2002 for 1 hospital. SSI surveillance was conducted using the same definitions and methods at all study hospitals.

Data Collection

Variables collected included hospital, medical record number, age, type of surgical procedure, wound class, ASA score and duration of procedure. For patients who developed an SSI, additional data collected included date of culture, anatomic source of culture, type of organism recovered and whether the organism was methicillin

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resistant (for Staphylococcus aureus only). All data was prospectively collected at the time of surgery or the time of SSI diagnosis.

**Statistical Analysis**

P values were calculated with Fisher's exact test for dichotomous variables, the chi-square test for ordinal variables, and student's t-test or Wilcoxon rank-sum test for continuous variables. Risk ratios (RR) and 95% Confidence Intervals (CI) were calculated for dichotomous variables. Multivariable analysis was performed using logistic regression. Dummy variables were created to account for missing variables. All p values were 2-sided.

The cohort was randomly divided into two sub-cohorts: a derivation and a validation cohort. In bivariate analysis, age was evaluated as a dichotomous, ordinal and continuous variable in the derivation cohort. After controlling for other variables with logistic regression, restricted cubic spline analysis was used to explore the relationship between age and SSI. After an optimal age predictor was derived in the derivation cohort, the adjusted relationship between the age variable and SSI was tested in the validation cohort. Validation of the age variable was performed by comparing 1) \( \beta \) coefficients and p values from the derivation and validation cohort models, and 2) graphic displays obtained from the restricted cubic spline analysis for age and SSI.
Results

144,485 patients were enrolled in the study and 1,684 developed an SSI (SSI rate 1.2%). Table 1 shows the percentage of cases by procedure type and the SSI rate for each procedure type. The most frequent procedure categories were orthopedic (41.8% of all procedures), obstetric/gynecologic (10.7%) and cardiothoracic (10.0%). The procedure categories with the highest rates of SSI were other gastrointestinal (3.1%), cardiothoracic (2.3%) and vascular (1.7%).

Table 2 shows the distribution of the cohort and SSI rates at the different study hospitals. The majority of patients underwent surgery in a community hospital (73.9%) as opposed to the tertiary care hospital (26.1%). Overall, the SSI rate for the tertiary care institution (1.4%) was higher than the rate for the network of community hospitals (1.1%) (p<0.001).

78.6% of SSI had a pathogenic organism identified by culture. Among this group of “culture-positive” SSI, Staphylococcus aureus was the most common isolate (N=661, 39.3%). Of this group, 301 were methicillin resistant (45.5% of all S. aureus isolates).

Table 3 shows the descriptive and perioperative characteristics of the cohort and the corresponding associations between these variables and risk for SSI. Significant predictors of SSI included operative duration greater than the 75th percentile CDC cut-point (Relative Risk [RR] 2.2, 95% Confidence Interval [CI] 2.0, 2.4) (p<0.001), ASA score ≥3 (RR 2.9, 95% CI 2.6,3.2) (p<0.001) and wound class score>2 (RR 2.3, 95% CI 2.0,2.7) (p<0.001).

Figure 1 shows the breakdown of the cohort by decade. 27,479 patients were age 45-54 years at the time of surgery (19.0%); this age group represented the most
common decade for study subjects. Only 210 patients were greater than 95 years of age (0.2%); this age group was the least common age category for study subjects. The mean age for patients with an SSI (57.1, standard deviation [SD] 16.9 years) was significantly greater than the mean age for those without an SSI (52.3, SD 17.8 years) (p<0.001). Age≥65 years was a significant predictor of SSI (RR 1.6, 95% CI 1.5, 1.8).

Figure 2 shows the SSI rate stratified by age decade. Between ages 17 and 65, the SSI rate increased for each decade of increasing age: the rate peaked in the decade 65-74 years of age (SSI rate=1.73%). Interestingly, after age 74, the SSI rate decreased with each decade of increasing age. There were no SSI among patients ≥95 years of age.

The cohort was randomly divided in half, into 2 smaller cohorts: a derivation cohort and a validation cohort. In the derivation cohort there were a total of 72,143 patients, and 873 developed an SSI (SSI rate 1.2%); and in the validation cohort, there were 72,334 patients, and 811 developed an SSI (SSI rate of 1.1%). The characteristics of the derivation cohort, validation cohort and combined cohorts were similar. In the derivation cohort, the mean age in the group with SSI (57.3, SD 16.8 years) was higher than the mean age of the group without SSI (52.2, SD 17.8 years) (p<0.001). SSI was more common in patients greater than 65 years of age (1.7%) than in patients less than 65 years of age (1.0%) (RR of 1.6, 95% CI 1.4, 1.9, p<0.001).

After adjusting for NNIS risk variables (ASA score, wound class and operative duration), type of operative procedure and hospital, the relationship between age and SSI was studied using restricted cubic spline methodology (Figure 3). There was a significant relationship between age and SSI (p=0.006). SSI risk increased by 1% per year.
between the ages of 17-65 (95% CI 0.4,1.8, p=0.002). Interestingly, SSI risk decreased by 1% for each additional year after age 65 (p=0.008, relative to pre-65 years of age effect).

In the validation cohort, the relationship between age and SSI was similar to the relationship in the derivation cohort. The mean age in the group with SSI (57.1, SD17.0 years) was significantly higher than the mean age of the group without SSI (52.4, SD 17.8 years) (p<0.001). The relationship between the derived age variable (i.e. the variable obtained from the derivation cohort) and SSI, is shown in Figure 4; this relationship is adjusted for NNIS risk variables, type of procedure and hospital. The relationship between the derived age variable and SSI remained significant (p<0.04).

For ages 17-65, SSI risk increased by 1% per year (95% CI 0.1, 1.5). After age 65, SSI risk decreased by 1% per year (p=0.02)

To further study the relationship between age and SSI after age 65, it was hypothesized that ASA score might be a confounder of the relationship between age and SSI. To evaluate this, ASA score was removed from the adjusted model in the derivation cohort. With ASA score removed from the model, the relationship between age and SSI before age 65 was unchanged; however, after age 65, the risk for SSI remained relatively stable, and did not decrease significantly with increasing age (Figure 5).
Conclusions

In this study, age was a strong predictor of SSI and added significant predictive power to the NNIS risk index. After adjusting for the NNIS risk factors, procedure type and hospital, SSI risk increased in a linear fashion until age 65. Interestingly, after age 65, there was a linear decrease in SSI risk for each additional year of age.

Our finding of an increase in SSI risk with increasing age up to age 65 corroborates earlier findings that increasing age does increase the risk of SSI, and probably relates to increased susceptibility to infection in general among aging persons.\textsuperscript{7,17,19-21} The decrease in SSI risk after age 65 was a particularly interesting, unexpected finding. Although some investigators have noted that increasing age might be protective for SSI diagnosed exclusively in the outpatient setting or at a single VA institution, others have not identified an association between increasing age and SSI risk.\textsuperscript{2,18,22} No studies to our knowledge, have definitively identified a protective effect of increasing age after age 65 in a large, multi-center cohort including multiple different types of surgical procedures. One possible explanation for this relationship is that the surgical population above age 65 is relatively healthy: surgeons are probably more particular regarding selection of elderly patients for surgery than they are for younger patients. Alternatively, the decrease in risk after age 65 may be due to a “hardy survivor” effect, where those who survive to older ages may be inherently healthier than some middle-aged persons, resulting in a type of natural selection bias. In fact, as a result of surgical selection bias and the hardy survivor effect, the population of surgical patients over the age of 65 might actually be healthier than the population of patients younger than 65, resulting in lower SSI rates in the older patient group.
We also hypothesized that the decrease in adjusted SSI risk after age 65 was due in part to confounding by ASA score. This was confirmed: when ASA was removed from the derivation model, there was no longer a clinically significant decrease in SSI after age 65 (Figure 5). To explain these associations, we hypothesized the following: elderly patients are more frequently assigned inappropriately high ASA scores than younger patients, regardless of underlying co-morbidity, and thus, have inappropriately inflated ASA scores. Thus, increasing age is associated with increasing ASA score. Because the ASA score is also associated with SSI, ASA score confounds the relationship between age and SSI.

When added to the standard NNIS risk index, age provided statistically significant additional predictive power for SSI. These results indicate that age may be valuable as an addition to the NNIS risk index. Age has several favorable characteristics that would facilitate its use in risk adjustment: it is an objective measure, is readily available and is routinely collected at the time of surgery.

There were several limitations to this study. The number of indicators for co-morbid illnesses other than ASA score was limited. In addition, the study was confined to one geographic locale which may limit its generalizability to other regions. Some SSI might have been missed, and been inappropriately classified as “not infected”. This would have probably led to an underestimate of the relationship between age and SSI, and would not have falsely inflated this association.

The study had some important strengths. All data was collected prospectively by trained Infection Control personnel. The study size was extremely large, allowing for the division of the cohort into two cohorts: 1 cohort was used for exploration of the
relationship between age and SSI; and 1 cohort was used to externally validate this relationship. Several hospitals (both community and tertiary care) and a variety of operative procedures were included in the study, making the results generalizable.

This study was the first adequately powered investigation of the relationship between age and SSI. Age may be a useful adjunct to the current NNIS risk index. Further investigation of the relationship between age and SSI is needed, particularly among patients older than 65. However, the results from this study indicate that patients over the age of 65 do not have an increased risk for SSI. Among elderly patients, risk for SSI should not be used as a deterrent for surgery.
Table 1. Percentage of Cases and Surgical Site Infection (SSI) Rates by Procedure Type

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>Cases (n=144,485)</th>
<th>% of Total Cases</th>
<th>SSI (n=1,684)</th>
<th>SSI Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedics</td>
<td>60441</td>
<td>41.8%</td>
<td>549</td>
<td>0.9%</td>
</tr>
<tr>
<td>Obstetric/Gynecologic</td>
<td>15484</td>
<td>10.7%</td>
<td>121</td>
<td>0.8%</td>
</tr>
<tr>
<td>Cardiothoracic</td>
<td>14386</td>
<td>10.0%</td>
<td>332</td>
<td>2.3%</td>
</tr>
<tr>
<td>Other GI</td>
<td>10051</td>
<td>7.0%</td>
<td>309</td>
<td>3.1%</td>
</tr>
<tr>
<td>Biliary</td>
<td>7966</td>
<td>5.5%</td>
<td>37</td>
<td>0.5%</td>
</tr>
<tr>
<td>Skin</td>
<td>7932</td>
<td>5.5%</td>
<td>29</td>
<td>0.4%</td>
</tr>
<tr>
<td>Neurosurgery/Head &amp; Neck</td>
<td>7856</td>
<td>5.4%</td>
<td>59</td>
<td>0.8%</td>
</tr>
<tr>
<td>General</td>
<td>7648</td>
<td>5.3%</td>
<td>78</td>
<td>1.0%</td>
</tr>
<tr>
<td>Vascular</td>
<td>7292</td>
<td>5.1%</td>
<td>121</td>
<td>1.7%</td>
</tr>
<tr>
<td>Renal/Genitourinary</td>
<td>2855</td>
<td>2.0%</td>
<td>16</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
Table 2. Operative Procedures (cases) and Surgical Site Infection (SSI) Rates at Study Hospitals

<table>
<thead>
<tr>
<th>Institution</th>
<th>Cases (n=144,485)</th>
<th>% of Total Cases</th>
<th>SSI (n=1,684)</th>
<th>SSI Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Hospital 1</td>
<td>9508</td>
<td>6.6%</td>
<td>114</td>
<td>1.2%</td>
</tr>
<tr>
<td>Community Hospital 2</td>
<td>60114</td>
<td>41.6%</td>
<td>681</td>
<td>1.1%</td>
</tr>
<tr>
<td>Community Hospital 3</td>
<td>1667</td>
<td>1.2%</td>
<td>39</td>
<td>2.3%</td>
</tr>
<tr>
<td>Community Hospital 4</td>
<td>4858</td>
<td>3.4%</td>
<td>33</td>
<td>0.7%</td>
</tr>
<tr>
<td>Community Hospital 5</td>
<td>3921</td>
<td>2.7%</td>
<td>22</td>
<td>0.6%</td>
</tr>
<tr>
<td>Community Hospital 6</td>
<td>11352</td>
<td>7.9%</td>
<td>130</td>
<td>1.2%</td>
</tr>
<tr>
<td>Community Hospital 7</td>
<td>2623</td>
<td>1.8%</td>
<td>19</td>
<td>0.7%</td>
</tr>
<tr>
<td>Community Hospital 8</td>
<td>4688</td>
<td>3.2%</td>
<td>8</td>
<td>0.2%</td>
</tr>
<tr>
<td>Community Hospital 9</td>
<td>7199</td>
<td>5.0%</td>
<td>96</td>
<td>1.3%</td>
</tr>
<tr>
<td>Community Hospital 10</td>
<td>859</td>
<td>0.6%</td>
<td>7</td>
<td>0.8%</td>
</tr>
<tr>
<td><strong>Total for Community Hospitals</strong></td>
<td><strong>106789</strong></td>
<td><strong>74.0%</strong></td>
<td><strong>1149</strong></td>
<td><strong>1.1%</strong></td>
</tr>
<tr>
<td>University Hospital</td>
<td>37696</td>
<td>26.0%</td>
<td>535</td>
<td>1.4%</td>
</tr>
<tr>
<td><strong>Total for Cohort</strong></td>
<td><strong>144485</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1684</strong></td>
<td><strong>1.2%</strong></td>
</tr>
</tbody>
</table>
Table 3. Descriptive and Perioperative Variables and Corresponding Associations with Surgical Site Infection (SSI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Surgical Site Infection (SSI) (n=1,684)</th>
<th>No SSI (n=142,801)</th>
<th>p value</th>
<th>RR, {95% CI}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ± standard deviation (SD)</td>
<td>57.1 ± 16.9</td>
<td>52.3 ± 17.8</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Age &gt;=65 (%)</td>
<td>666 (39.6%)</td>
<td>40865 (28.6%)</td>
<td>&lt;0.001</td>
<td>1.6 {1.5, 1.8}</td>
</tr>
<tr>
<td>Operative Duration (OR) duration, median, Interquartile range (IQR)</td>
<td>155 (88, 259)</td>
<td>92 (50, 165)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>OR duration &gt; 75%ile cutpoint (%)</td>
<td>734 (43.6%)</td>
<td>37305 (26.1%)</td>
<td>&lt;0.001</td>
<td>2.2 {2.0, 2.4}</td>
</tr>
<tr>
<td>ASA score &gt;= 3 (%)</td>
<td>984 (58.4%)</td>
<td>46859 (32.8%)</td>
<td>&lt;0.001</td>
<td>3.0 {2.6, 3.2}</td>
</tr>
<tr>
<td>Wound class &gt;2 (%)</td>
<td>183 (10.9%)</td>
<td>7105 (5.0%)</td>
<td>&lt;0.001</td>
<td>2.3 {2.0, 2.7}</td>
</tr>
<tr>
<td>National Nosocomial Infections Surveillance (NNIS) Risk Index score, median, (IQR)</td>
<td>1 (1,2)</td>
<td>1 (1,2)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1. Distribution of Entire Cohort by Decade
Figure 2. SSI Rate by Decade for Entire Cohort

Decade, years

SSI/100 cases
Figure 3. Adjusted Relationship Between Age and SSI in Derivation Cohort
Figure 4. Adjusted Relationship Between Age and SSI in Validation Cohort

Adjusted Relationship Between Age and SSI in Validation Cohort
Figure 5. Adjusted Relationship Between Age and SSI in Derivation Cohort Without ASA Score in the Model
References


