MAJOR ARTICLE

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

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Background. An increasing number of older persons undergo surgery, but the relationship between increasing age and risk of surgical site infection (SSI) has not been established. The objective of the present study was to determine the relationship between increasing age and risk of SSI.

Methods. The present cohort study included patients who underwent surgery between February 1991 and July 2002. Patients >17 years of age were divided randomly into derivation and validation cohorts. The study was conducted at 11 hospitals. SSIs were prospectively identified by use of Centers for Disease Control and Prevention criteria.

Results. The study included 144,485 consecutive surgical patients and 1684 SSIs (rate of SSI, 1.2%). There were 72,139 procedures and 873 SSIs in the derivation cohort. Adjusted analyses revealed a significant relationship between age and risk of SSI ($P = .006$). Risk of SSI increased by 1.1%/year between ages 17 and 65 years ($P = .002$). At age ⩾65 years, risk of SSI decreased by 1.2% for each additional year ($P = .008$). There were 72,334 procedures and 811 SSIs in the validation cohort. The relationship between age and risk of SSI was similar in the validation cohort.

Conclusions. Increasing age independently predicted an increased risk of SSI until age 65 years. At ages ⩾65 years, increasing age independently predicted a decreased risk of SSI.

Surgical site infections (SSIs) occur in >325,000 patients each year in the United States and cost more than $1 billion/year [1, 2]. SSIs are an important cause of increased hospital stay, and they directly affect the morbidity and risk of mortality of surgical patients, particularly older patients [3–7]. In a recent study by McGarry et. al., older patients with *Staphylococcus aureus* SSIs had a 3-fold increase in mortality, longer postoperative hospital stays, and higher hospital charges than did younger patients with *S. aureus* SSIs [8].

Different groups of investigators have reported contradictory results concerning the relationship between increasing age and risk of SSI. For example, several investigators concluded that increasing age was associated with a greater risk of all types of postoperative infections; in some of these studies, increasing age was associated with an increased risk of development of SSI [9–13]. However, the factors responsible for the above findings remain controversial. Some investigators have speculated that factors indirectly related to age—such as an increased prevalence of comorbid conditions, an increased severity of acute illness, and a decreased host response to bacterial invasion—in older patients are the real reasons older patients appear to have an increased risk of SSI [14–16]. To make matters even more confusing, some investigators have concluded that increasing age was not an independent risk factor for SSI [4, 9, 11, 14, 17–19]. Indeed, in some of these studies, advanced age was associated with a decreased risk of SSI, particularly for SSIs diagnosed after discharge from

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the hospital [9, 11, 13]. Because many of the preceding studies involved small numbers of patients with SSIs and thus lacked sufficient statistical power, we believe that the relationship between age and risk of SSI is unresolved and that this question warrants further study using a large cohort.

A better understanding of the relationship between age and risk of SSI could be useful in several ways. First, internists and surgeons who consider patients for surgery might more appropriately incorporate age into a risk-benefit algorithm pertaining to operative risk. Second, by better identifying patients at risk of SSI, public health and hospital epidemiologists and health-care economists can more effectively allocate resources and focus strategies for prevention of SSIs. Third, a better understanding of the relationship between age and risk of SSI could be used to further improve risk indices for SSI.

The specific objective of the present study was to determine the relationship between age and risk of SSI. We hypothesized that increasing age would be an independent predictor of SSI and used a large database of prospectively collected surgical data from 11 different hospitals to test this hypothesis.

PATIENTS AND METHODS

Patients. The present cohort study included patients undergoing surgical procedures at 11 study hospitals between 1 February 1991 and 31 July 2002. Procedures involving patients <17 years of age and procedures that were performed on patients with preexisting infections at the operative site were excluded. Informed consent was waived by the institutional review board of participating hospitals, and no human experimentation was performed.

Hospitals and setting. 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. The present study included DUMC operative data collected from 1994 to 2002. The Duke Infection Control Outreach Network (DICON) includes 25 hospitals located primarily in the southeastern United States. Data concerning surgical procedures and subsequent SSIs were collected prospectively from 9 of these hospitals (with a total of 1821 beds) from 1999 to 2002 and from 1 hospital (217 beds) from 1991 to 2002.

Case definition. All SSIs were prospectively identified by trained infection-control practitioners (ICPs) using standard Centers for Disease Control and Prevention criteria [20]. Surveillance was conducted by use of the same definitions and methods at all study hospitals, except for 1 difference: surveillance was conducted only on infections classified as "deep" or "organ space" at DUMC; superficial infections were also included in SSI surveillance at DICON-affiliated hospitals. Of the total SSIs included in the DUMC and DICON SSI databases, ~5% are superficial and all others are deep or organ space. ICPs used culture results from the clinical microbiology laboratory, readmission flags, and surgeon surveys to identify patients with potential SSIs. All patients with potential SSIs were analyzed on a case-by-case basis to determine whether they met the criteria for an SSI.

Six hundred four (35.9%) of the SSI cases identified during the study period by ICPs were reevaluated by a study nurse. In instances in which the SSI status was uncertain after initial review, the study nurse discussed the case with a single investigator (K.S.K.), who made a final decision as to whether the case was an SSI. After the above review process, the false-positive rate for the diagnosis of SSIs was 3%. SSIs as originally identified by ICPs were included in the analysis.

Databases and variables. The present study used the operative databases previously established by DUMC and DICON personnel. Variables in these preexisting databases included hospital, patient identifying numbers, age, type of surgical procedure, wound class, American Society of Anesthesiologists (ASA) score, and operative duration [21, 22]. For patients who developed an SSI, additional data were collected, including date of onset, anatomic source of cultures, and pathogen and susceptibility test results. All of these data were collected prospectively, at the time of surgery or at the time of diagnosis of individual SSIs.

Statistical analysis. Analyses were conducted to (1) develop a model relating age to risk of SSI and (2) confirm this relationship in a second sample. The cohort was randomly divided into 2 subcohorts: a derivation cohort and a validation cohort. Only 1 random selection of the derivation and validation cohorts was performed. Bivariable analysis was conducted by use of the goodness-of-fit χ^2 test for discrete variables and the Wilcoxon rank sum test for ordinal and continuous variables. All reported P values are 2-sided. Multivariable analysis was performed by use of logistic regression, by use of ASA score, operative duration, wound class, hospital, and type of procedure as control variables. Odds ratios (ORs) and 95% confidence intervals (CIs) are shown for all predictors.

Other than missing ASA scores or wound class category (for 6% of patients), there were no missing data. For the patients for whom data were missing, the mean for continuous variables or the mode for discrete values was imputed for the missing variable, and dummy variables were computed and added to the model, to account for missing data and to assess bias due to the missing values [23].

To model the impact of age on risk of SSI, age was initially evaluated as a dichotomous, ordinal, and continuous variable in the derivation cohort, with controlling for other variables by logistic regression. To model the functional form of the relationship between age and risk of SSI, restricted cubic splines [24] were used to explore the relationship. The use of restricted cubic splines is a nonlinear data exploratory measure that allows for the investigation of the relationship between 2 variables without specifying the relationship. After an optimal age predictor was derived in the derivation cohort, this functional form was used to assess the adjusted relationship between the age variable and SSI in the validation cohort. Validation of the age variable was performed by comparing (1) ß coefficients and *P* values for the age variable from the derivation and validation cohort models and (2) graphic displays of the predicted age and risk of SSI in the derivation and validation cohorts.

RESULTS

During the study period, a total of 144,485 patients underwent surgical procedures at the 11 hospitals. The most common surgical procedures were orthopedic (41.8%), gastrointestinal (12.5%), obstetric/gynecologic (10.7%), cardiothoracic (10.0%), skin and integumentary systemic (5.5%), neurosurgical (5.3%), general (5.3%), other (5.3%), vascular (5.1%), and genitourinary (2.0%). The majority of patients underwent surgery in a community hospital (73.9%). The age range of the study population is shown in figure 1.

Of the 144,485 surgical patients, 1684 developed an SSI (rate of SSI, 1.2%). The procedures with the highest rates of SSI were gastrointestinal (3.1%), cardiothoracic (2.3%), and vascular (1.7%). The SSI rate at DUMC was significantly higher than the overall rate at the community hospitals (1.4% vs. 1.1%; *P* < .001). Approximately 39% of SSIs were diagnosed during the original hospitalization, ~49% were diagnosed on readmission to the hospital, and ~12% were diagnosed in the outpatient setting. A pathogenic organism was identified by culture in 78% of patients with an SSI. *S. aureus* (*n* = 661) was the most commonly identified pathogen. Of the 661 *S. aureus* infections, 301 (45.5%) were due to methicillin-resistant *S. aureus* isolates.

As expected, operative duration was significantly longer in patients with SSI than in those without SSI (table 1). The percentage of patients with an operative duration greater than the National Nosocomial Infections Surveillance (NNIS) 75th percentile cutoff, an ASA score ≥3, and wound class >2 was significantly higher among patients with SSI (table 1).

The mean age of patients with an SSI (57.1 years [SD, 16.9 years]) was significantly greater than the mean age of patients without an SSI (52.3 years [SD, 17.8 years]) (*P* < .001). Age ≥65 years was a significant predictor of SSI (OR, 1.6 [95% CI, 1.5–1.8]) (table 1). Between the ages of 17 and 65 years, the rate of SSI increased for each decade of increasing age and peaked at age 65–74 years (rate of SSI, 1.7%). Beginning at age 74 years, the risk of SSI decreased for each subsequent decade. There were no SSIs among patients ≥95 years of age (*n* = 210) (figure 1).

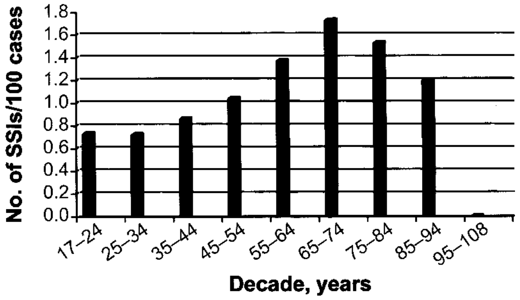

Figure 1. Rate of surgical site infection (SSI), by decade of age for the entire cohort. The no. of operative procedures in each age category are as follows: 17–24 years, *n* = 8244; 25–34 years, *n* = 18,246; 35–44 years, *n* = 26,061; 45–54 years, *n* = 27,479; 55–64 years, *n* = 22,920; 65–74 years, *n* = 23,126; 75–84 years, *n* = 14,685; 85–94 years, *n* = 3501; and ≥95 years, *n* = 210. The peak rate of SSI occurred in patients 65–74 years of age. The lowest rate of SSI (0%) occurred in patients ≥95 of age.

The characteristics of age and perioperative variables of the derivation cohort, validation cohort, and combined cohorts were similar. The derivation cohort consisted of 72,143 patients; 873 developed an SSI (rate of SSI, 1.2%). SSIs were more common in patients ≥65 years of age than in younger patients (1.7% vs. 1.0%, respectively; OR, 1.6 [95% CI, 1.4–1.9]). After adjusting for NNIS risk variables (ASA score, wound class, and operative duration), type of operative procedure, and type of hospital (university vs. community), the relationship between age and risk of SSI was assessed by use of restricted cubic spline methodology. This analysis demonstrated an inverted V relationship between age and risk of SSI, with a peak rate of SSI occurring at age 65 years (figure 2). Subsequently, 2 linear splines (measures that ascertain a change in slope after a specified point) were used to model the relationship between age and risk of SSI. The relationship between increasing age and risk of SSI remained statistically significant (*P* = .006). Between the ages of 17 and 65 years, the risk of SSI increased by 1.1%/year (95% CI, 0.4%–1.8%; *P* = .002). However, at ages ≥65 years, risk of SSI decreased by 1.2% for each additional year of age (*P* = .008, relative to effect at <65 years of age), effectively indicating a decreased SSI rate at ages ≥65 years.

The validation cohort consisted of a total of 72,342 patients, 811 of whom developed an SSI (rate of SSI, 1.1%). The relationship between the derived age variable and risk of SSI was analyzed, adjusting for NNIS risk variables, type of operative procedure, and hospital (university vs. community). The relationship between the derived age variable and risk of SSI was also statistically significant in the validation cohort (*P* = .04). Between the ages of 17 and 65 years, risk of SSI increased by 0.8%/year (95% CI, 0.1%–1.5%; *P* = .02). Similar to the derivation cohort, risk of SSI decreased by 1.3%/year at ages ≥65 years (*P* = .02, relative to the effect at age <65 years). The effect of age on risk of SSI was similar for the university hospital and the community hospitals.

Table 1. Age and perioperative variables in patients with and without surgical site infection (SSI).

Variable	SSI (n = 1684)	No SSI (n = 142,801)	P	OR (95% CI)
Age, mean ± SD, years	57.1 ± 16.9	52.3 ± 17.8	<.001[a]	
Age ⩾65 years, no. (%)	666 (39.6)	40,865 (28.6)	<.001[b]	1.6 (1.5–1.8)
Median operative duration, IQR, min	155 (88, 259)	92 (50, 165)	<.001[a]	
Operative duration greater than NNIS 75th percentile cutoff, no. (%)	734 (43.6)	37,305 (26.1)	<.001[b]	2.2 (2.0–2.4)
ASA score ⩾3, no. (%)	984 (58.4)	46,859 (32.8)	<.001[b]	3.0 (2.6–3.2)
Wound class >2, no. (%)	183 (10.9)	7105 (5.0)	<.001[b]	2.3 (2.0– 2.7)

NOTE. ASA, American Society of Anesthesiologists; CI, confidence interval; IQR, interquartile range; NNIS, National Nosocomial Infections Surveillance; OR, odds ratio.

[a] Wilcoxon rank sum test.

[b] Goodness-of-fit χ^2 test.

DISCUSSION

In the present study, age was a strong predictor of SSI, but the relationship between age and risk of SSI was complex. After adjusting for the NNIS risk variables, procedure type, and type of hospital, risk of SSI increased in a linear fashion until age 65 years. Previous studies that have examined the relationship between age and risk of SSI have provided conflicting results, but these studies were hampered by 5 problems. First, most studies involved small sample sizes (table 2) [4, 9, 11, 14, 17]. Second, several studies were performed at a single institution [4, 9, 11, 12, 17, 19]. Third, most of these prior studies examined risk of SSI after a single category of surgery [10, 17, 19]. Fourth, the largest, multicenter study used surgical data from the 1970s [13]. Finally, several of the prior studies reported rates of SSI 3–15 times higher than those in the present study (table 2) [9, 11, 12, 14, 17].

Despite the differences in methodology and study designs, a few prior studies reported an increased risk of SSI with increasing age [10, 12, 13]. For example, in one retrospective cohort study involving 9016 surgical patients from a community hospital and 1136 SSIs, increasing age was associated with an increased probability of an SSI (OR by decade, 1.22) [12]. In another study, which examined a stratified random sample of 71,200 surgical patients from 338 hospitals throughout the United States and 2478 SSIs, the risk of SSI increased with age until age 75 years [13]. Potential explanations for this finding include increasing immune dysfunction and accumulation of comorbid conditions with increasing age [25, 26].

We were surprised to find that, after age 65 years, risk of SSI decreased in a linear fashion for each additional year of age, in both study cohorts. These findings are concordant with the findings of other studies that concluded that older age was not an independent risk factor for SSI (table 2) [4, 14, 17, 19], but none of the investigators responsible for these studies documented a decreased risk of SSI with increasing age, which we observed. However, a few other investigators have reported an association between a decreased risk of SSI and increasing age. In the nationwide nosocomial infection study by Haley et al. noted above, the percentage of patients with SSIs decreased after age 75 years [13]. In addition, 2 groups of investigators noted a decreased risk of SSI with increasing decade of age in patients with SSIs diagnosed after discharge from the hospital [9, 11]. We are aware of no other study that definitively identified a protective effect of increasing age after age 65 years.

We were not able to determine why patients ⩾65 years of age had a decreased risk of SSI. It is possible that, in contrast to younger patients, older patients who are at increased risk of postoperative complications (e.g., frail elderly patients with multiple comorbid conditions) less frequently undergo surgery than do their healthy peers, because clinicians and/or patients

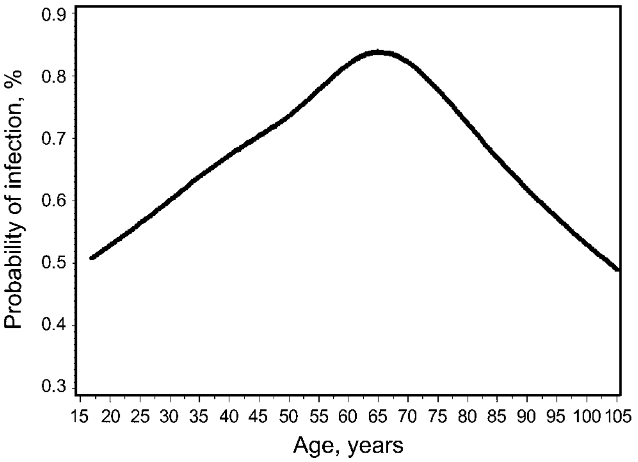

Figure 2. Adjusted relationship between age and surgical site infection (SSI) in the derivation cohort (this relationship was adjusted for the effects of operative duration, wound class, American Society of Anesthesiologists score, hospital, and type of operative procedure). The relationship between age and risk of SSI in the derivation cohort is depicted by use of cubic spline analysis. Subsequently, 2 linear splines (measures that ascertain a change in slope after a specified point) were used to model the relationship between age and risk of SSI. The relationship between increasing age and risk of SSI remained statistically significant (P = .006).

Table 2. Published literature pertaining to the relationship between age and risk of surgical site infection (SSI).

Authors, year of publication [reference]	Study design	Study period	No. of hospitals	Type of surgical procedure	No. of study patients (no. of SSIs)	Analyses	Results
Haley et al., 1981 [13]	Prospective cohort	1975–1976	338	Multiple	71,200 (2478)	Univariate	Increase in the proportion of infected patients with age, until 75 years of age, then a decrease noted
Byrne et al., 1994 [9]	Prospective randomized controlled trial	Unclear	1	Multiple	3466 (582)	Univariate	Risk of SSI diagnosed in the inpatient setting increased with age; risk of SSI diagnosed in the outpatient setting decreased with age
Borger et al., 1998 [19]	Retrospective cohort	1990–1995	1	Cardiac	12,267 (92)	Multivariate	Age did not predict SSI
de Boer et al., 1999 [10]	Prospective cohort (2 studies combined)	1992–1993	8, 26	Orthopedic	4872 (55); 6437 (142)	Multivariate	Risk of SSI increased with age category and peaked between 75 and 99 years of age
Scott et al., 2001 [12]	Retrospective cohort	1995–1997	1	Multiple	9016 (1133)	Multivariate	Risk of SSI detected 2–7 days after surgery increased by decade of age (OR, 1.22)
Delgado-Rodriguez et al., 2001 [11]	Prospective cohort	1995–1997	1	General surgery	1506 (123 before discharge; 103 after discharge)	Multivariate	Risk of SSI diagnosed before discharge increased with decade of age (OR, 1.3); risk of SSI diagnosed after discharge decreased with decade of age (OR, 0.9)
Malone et al., 2002 [4]	Prospective cohort	1995–2000	1	Noncardiac	5031 (162)	Multivariate	Age did not predict SSI
Olsen et al., 2002 [17]	Retrospective cohort	1996–1999	1	Coronary artery bypass graft	1980 (83)	Multivariate	Age ⩾65 years did not predict SSI
Pessaux et al., 2003 [14]	Prospective randomized controlled trials (3 trials combined)	1982–1986; 1987–1989; 1994–1996	Many, but number unclear	Multiple	4718 (191)	Multivariate	Age did not predict SSI

NOTE. OR, odds ratio.

judge their risk of adverse clinical outcomes to be too high. In addition, the decreased risk for the very old patients (i.e., ⩾80 years of age) may be due to a "hardy survivor" effect. In other words, persons who survive to much older ages may have a genetic make-up that enables them to better withstand threats to health than some middle-aged persons [27, 28]. Together, these preceding 2 phenomena may have resulted in the selection of a relatively healthy group of older patients at decreased risk of SSI, compared with younger, sicker patients. A third potential explanation for our finding of decreased risk of SSI in patients ⩾65 years of age is that SSIs were detected less frequently in older patients than in younger patients because the clinical manifestations of infection, such as fever, were atypical or were not present [25]. A fourth potential explanation for our finding is that older patients underwent operative procedures with low risk of SSI, whereas younger patients might have undergone more complicated surgeries with greater associated risk of SSI. However, the distribution of types of operative procedures was similar for patients <65 years of age and for patients ⩾65 years of age (data not shown).

When age was studied as a dichotomous variable, age ⩾65 years was associated with increased risk of SSI; but, when age was analyzed as a continuous variable, the risk of SSI decreased after age 65 years. The difference in effect between the 2 age variables and risk of SSI is due to the relatively high frequency of SSIs among patients 65–70 years of age in our cohort. When age was analyzed as a dichotomous variable, this high-risk group was analyzed together with all other patients >70 years of age, thereby masking the effect of decreasing risk of SSI after age 65. Studies that analyze age only as a dichotomous variable might not identify important characteristics associated with this variable.

Age added statistically significant predictive power to the NNIS risk index for the prediction of SSI. Age is a variable that is readily available, objective, and routinely collected by NNIS hospitals. In the future, age might be used to supplement the NNIS risk index.

We recognized several potential weaknesses of the present study. First "residual confounding" may have been a problem, because we were not able to control for selected risk factors known or suspected to be positively associated with risk of SSI, such as male sex and length of hospital stay. In addition, we could not completely control for comorbid conditions such as diabetes mellitus, obesity, and malnutrition. However, we used the standard variables for risk of SSI, including ASA score, a well-validated predictor of postoperative mortality and SSI [22] that takes into account illnesses such as diabetes mellitus, obesity, and malnutrition [29–31]. Second, we recognize that some SSIs may have occurred in the outpatient setting and, therefore, escaped detection. However, because surveillance methods at the study hospitals include flagging patients for readmission to the hospital and surgeon surveys, the likelihood of missing SSIs diagnosed after discharge was minimized. Moreover, even if some outpatients with SSIs were misclassified as "uninfected," this misclassification bias should have been random. Even if present, the net result of this bias would not have falsely inflated the relationship between age and risk of SSI but rather would have led to an underestimate of this association.

Our study had several important strengths. All data were collected prospectively by use of standardized criteria by trained ICPs. The sample size and number of SSIs was large, allowing for the division of the cohort into 2 subcohorts; 1 cohort for exploration of the relationship between age and risk of SSI and 1 for validation of this relationship. We were able to statistically control for the effects of NNIS risk variables, for type of procedure, and for hospital. Several hospitals (both community and tertiary care) and a variety of operative procedures were included in the study, improving the generalizability of the results.

Further investigation of the relationship between age and risk of SSI is needed, particularly among patients ⩾65 years of age and for specific procedures. Future studies could focus on some of the possible explanations for the results we observed. For example, do elderly patients undergoing surgery have fewer comorbid conditions or better functional status than patients with surgical conditions who are treated conservatively? Is there a bias toward deferring surgery for elderly patients? Also, further studies are needed to look at the associated risk of anesthesia, cardiovascular complications, and overall mortality of surgery in elderly patients—specifically to see whether the risk for these complications similarly drops or stabilizes at a specific threshold age. Despite the unresolved questions discussed above, we believe that our data suggest that patients ⩾65 years of age do not have an increased risk of SSI.

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