Relationship between Age and the Risk of Surgical Site Infection: A Contemporary Reexamination of a Classic Risk Factor

Thomas R. Talbot and William Schaffner
Departments of Medicine and Preventive Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

(See the article by Kaye et al., on pages 1056–62.)

Due in large part to many landmark innovations in the care of the surgical patient, such as the use of anesthesia [1] and the development of the principles of antibiotic prophylaxis [2, 3], the number of surgical procedures performed annually has climbed steadily, with >24 million surgical procedures performed in 2001 in the United States alone [4]. Unfortunately, as surgical volume has increased and with the development of novel surgical procedures, the number of persons at risk of morbidity from surgical site infections (SSIs) has also increased. According to the most-recent estimates, 500,000 SSIs occur annually in the United States, leading to an estimated 3.7 million excess hospital days and >$1.6 billion in excess costs [5, 6]. A patient who develops an SSI while hospitalized has an ∼60% greater risk of being admitted to the intensive care unit, is ≥5 times more likely to be readmitted to the hospital within 30 days after discharge, and incurs an attributable extra hospital stay of 6.5 days, leading to a direct cost of an additional $3000/infection [7].

Attempts to reduce such morbidity have appropriately focused on the identification of specific risk factors for SSI. Such factors may be specific to single surgical types, such as the use of internal mammary arteries for coronary arterial bypass grafting [8, 9], but many are applicable to most surgical procedures. In general, these risk factors can be categorized into 2 groups: characteristics of the surgical patient and characteristics of the procedure itself (figure 1) [10, 11]. Some risk factors—in particular, patient characteristics such as altered immune responses and obesity—are inherent at the time of surgery and are not amenable to any practical modification to reduce the conferred risk of SSI. However, others are modifiable in the short period preceding the surgical incision, thus leading to a reduction in risk of SSI for the individual surgical patient.

An added dimension in the prevention of SSIs is the rapid development of novel technological tools intended to help shorten operative duration, reduce the degree of tissue damage, and diminish the rate of SSI. Minimally invasive procedures using endoscopic techniques have increased in use [12–15], with reductions in rates of SSI noted with laparoscopic procedures [16]. The advent of robotic surgery has promised to minimize the degree of tissue damage by increasing the precision of surgical incisions [17–19]. Finally, the growing use of antimicrobial and antiseptic-impregnated operative materials—such as sutures, mesh, and bandages—is hoped to provide long-term instillation of prophylactic antibiotics into the surgical field to reduce SSIs [20–23].

The need to deftly and thoroughly examine the impact of these promising novel technologies on infectious outcomes seems readily apparent. New technology can be costly and difficult to implement, and the demonstration of improvement in all patient outcomes and, in particular, SSIs with any new procedure is imperative. What is less obvious but could be equally important, however, is the need for contemporary examination of classic risk factors for SSI. For instance, numerous studies have identified an increased risk of SSI in persons with diabetes mellitus [10, 24–31]. The increased risk of infection due to diabetes has long been attributed to physiologic alterations precipitated by inadequate long-term glucose control [32–34]. Thus, although the presence of diabetes could be used to stratify a patient’s preoperative risk of SSI, conclusions about the degree to which such risk could be reduced in the perioperative period, especially after years of poor glycemic control, seemed pessimistic.
But, as the classic relationship between diabetes and SSI was reexamined, an interesting trend appeared. The risk of SSI in persons with diabetes was also significantly related to perioperative hyperglycemia [26, 30, 35–37]. Equally striking was that this association also held for persons with impaired perioperative glycemic control but without previously diagnosed diabetes [30]. These novel examinations of a classic risk factor for SSI have led to the use of continuous insulin infusion in surgical patients and a subsequent reduction not only in SSI but also in overall mortality [38–40]. Thus, an established risk factor for SSI that was an “unmodifiable” patient comorbidity became a modifiable target for intervention in contemporary surgical practice.

The latest example of a new examination of an “old” risk factor for SSI, with some revealing results, can be found in an impressive study investigating the relationship between age and risk of SSI in the current issue of the *Journal of Infectious Diseases*, conducted by Kaye et al. [41]. As summarized nicely in table 2 of their article [41], increasing age in adults has often been identified as a risk factor for SSI. However, controversy exists as to whether age serves simply as a marker for underlying illness or whether immunologic senescence associated with increased age leads to an increased risk of infection. Others have actually noted, albeit generally in single-site investigations with a relatively small sample size, that the risk of SSI decreases as patient age increases [42, 43].

In the largest study of age and SSI to date, Kaye et al. used prospective surveillance data collected from selected adult surgical procedures performed in a network of 1 tertiary care institution and 10 community-based hospitals. SSIs were identified prospectively by use of standardized Centers for Disease Control and Prevention criteria, and various clinical data—such as patient age, type of surgical procedure, American Society of Anesthesiologists (ASA) score, operative duration, and wound class—were collected at the time of surgery. To thoroughly assess the relationship between age and risk of SSI, patient age was examined as a dichotomous as well as a continuous variable.

In a derivation cohort of $>72,000$ patients and 873 SSIs (rate of SSI, 1.2%), patient age $\geq 65$ years was significantly associated with an increased risk of SSI compared with patient age $<65$ years. However, a more detailed analysis adjusted for hospital type, procedure type and duration, wound class, and ASA score, with age as a continuous variable, found that the rate of SSI peaked at age 65 years, with a subsequent decrease of 1.1%/year as patient age increased. These findings were confirmed in a validation cohort of similar size with a similar rate of SSI, in which the risk of

### Patient Characteristics
- Extremes of age
- Diabetes
- Perioperative hyperglycemia
- Concurrent tobacco use
- Infection at another site at time of surgery
- Obesity
- Malnutrition
- Low preoperative serum albumin level
- Concurrent corticosteroid use
- Prolonged preoperative hospital stay
- Prior irradiation to surgical field
- Impaired immune response
- Colonization with *Staphylococcus aureus*

### Procedural Characteristics
- Lack of preoperative antiseptic showering
- Shaving of site the night before procedure
- Use of razor for hair removal
- Improper preoperative skin preparation
- Improper antimicrobial prophylaxis (type, dose, timing of delivery)
- Failure to timely redose antibiotics in prolonged procedures
- Inadequate operating room ventilation (lack of laminar airflow)
- Increased operating room traffic
- Break in aseptic technique
- Perioperative hypothermia or hypoxia
- Surgical technique (hemostasis, tissue trauma)
- Perioperative blood transfusion

**Figure 1.** Selected patient and procedural characteristics associated with increased risk of surgical site infection [10, 11].
SSI peaked at age 65 years, followed by a 1.3% decrease in incidence of SSI per year >65 years.

Before one infers from this well-designed study that increased age actually protects against development of SSIs, some limitations of the study must be acknowledged [41]. Differences in the surveillance methods existed at the individual study sites. The types of procedures differed by institution (only cardiothoracic, neurosurgical, and orthopedic procedures were examined at the tertiary hospital, whereas all types of surgical procedures were examined at the other 10 sites), by type of SSI included (superficial SSIs were assessed only at the community-based institutions, not at the tertiary center), and by the year of implementation of surveillance, which ranged from 1991 at one hospital, to 1994 at the tertiary hospital, to 1999 at the remaining 9 hospitals. In addition, nearly three-quarters of the procedures were performed at the community hospitals, which could indicate a patient population with a lesser severity of disease and, thus, a potentially lower inherent risk of SSI. Nonetheless, the association between increasing age and decreasing risk of SSI remained after adjustment for type of procedure and hospital. Furthermore, although the ASA score serves as a basic surrogate for the presence and severity of underlying illnesses in the study population, full details on comorbid patient conditions known to increase risk of SSI—such as perioperative glucose control and tobacco use—were not included in the analysis, as acknowledged by the authors.

Despite these limitations, the study by Kaye et al. [41] has many strengths. Primarily, the sheer volume of patients and procedures studied affords substantial power to their findings, since >144,000 patients were included for analysis. This large sample size allowed for the study team not only to derive the relationship between age and risk of SSI but also to validate their findings in a similarly large sample of patients. The examination of age not only as a categorical variable but also as a continuous variable greatly enhanced their study. The use of different surgical types and multiple institutions reflects the generalizability of their results. In addition, the data were collected prospectively by use of standardized definitions of SSIs.

Many derivative questions remain: Were older patients, and especially older patients with underlying comorbid illnesses, less likely to be referred for surgery or more likely to be medically managed for their illnesses than younger patients (referral bias)? Do such trends in patient referral and selection differ on the basis of the specific surgical procedure of interest? Were clinicians more aggressive in the care of younger patients, thus performing more-extensive surgical procedures that could result in increased operative tissue damage or infer a greater risk of SSI, compared with more-conservative procedures performed in elderly patients? Is there a difference in the detection of SSIs between younger and older patients? Was there, as Kaye et al. note, a “hardy survivor” effect, in that the persons who lived to older age had a genetic “leg-up” on those who did not live to ages >65 years? For example, did these persons have intrinsic differences in their immune systems that allowed them to fight various insults more successfully than their colleagues? If increasing age is truly associated with decreased risk of SSI, is there a biologically plausible physiologic explanation for such findings? Future investigations into such issues will help to further refine the relationship between age and risk of SSI.

Finally, the thorough and thoughtful re-examination of the classic risk factor for SSI, age, by Kaye et al. also emphasizes the continued need for independent funding of investigations into the epidemiology and prevention of nosocomial infections. Traditionally, large-scale examinations of nosocomial infections, hospital epidemiological projects, and infection-control interventions have not been attractive to extramural funding sources. There is now a need for sophisticated investigations using large population-based data systems and detailed analyses to augment the time-honored standard of identification of risk factors through case-control investigations, programs that will obviously require an increase in dedicated resources. However, with the growing public and private interest in identifying measures to reduce the rates of nosocomial infections, especially SSIs [44, 45], the importance of designing and funding careful examinations of both the classic and novel aspects of surgical procedures and patients, to reduce SSI morbidity, cannot be overemphasized.

References

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