The Role of Postoperative Factors in Surgical Site Infections: Time to Take Notice

Farrin A. Manian
Department of Medicine, Harvard Medical School, Massachusetts General Hospital, Boston

Surgical site infections (SSIs) continue to occur, in many instances despite high compliance with best practice measures primarily revolving around pre- and intraoperative periods. Postoperative factors have traditionally been considered to play a relatively minor role in the causation of SSIs. An increasing body of evidence, however, suggests that many SSIs occur as a result of pathogens gaining access to surgical wounds either hematogenously, through drains, or through slowly healing wounds due to systemic anticoagulation or other factors, particularly in the setting of high compliance with standard perioperative antibiotic prophylaxis. Evidence also supports frequent acquisition of methicillin-resistant Staphylococcus aureus (MRSA) during the postoperative period. These findings, coupled with lack of clear efficacy of various pre- and intraoperative interventions such as MRSA decolonization and use of vancomycin for prophylaxis against this organism, should force us to consider the important role that postoperative factors may play in the causation of SSIs in the current era.

Keywords. postoperative; surgery; wound infection.
results in reducing the risk of SSIs [4]. So what else can we do to reduce the risk of SSIs when our compliance with the current best practice measures is already high?

In my view, when facing the current challenge of preventing SSIs, it may be helpful to remind ourselves that even >50 years since the discovery of the importance of proper timing of antibiotic prophylaxis in the prevention of experimental surgical wound infections [9], their pathophysiology remains far from being fully elucidated [10]. As such, all potential factors, including less traditional ones, deserve renewed consideration. There are several reasons why we should give serious considerations to the potential role of many postoperative factors in our current quest to prevent SSIs (Table 1).

First, there is increasing epidemiologic and experimental evidence that pathogens may access fresh surgical sites postoperatively through the hematogenous route [2, 22, 23], drains [17–20], slowly healing wounds, or continuously oozing incisions with or without hematoma [11–16]. In a study involving cardiac procedures where 97% of case subjects were reported to have received standard antimicrobial prophylaxis preoperatively, patients with central venous catheter–related bacteremia occurring following surgery were significantly more likely to develop subsequent SSIs due to the same organism [22]. In the same study, the authors estimated that 5%–15% of SSIs might be prevented by eliminating catheter-related infections [22]. In a recent prospective cohort study of mediastinitis and endocarditis following cardiac surgery where 100% of patients received standard antibiotic prophylaxis 30 minutes before incision, only postoperative factors such as respiratory insufficiency, microorganisms in blood cultures, and ICU stay were independent risk factors for the development of SSIs; none of the preoperative or intraoperative factors studied were independent predictors of SSIs [23].

In a proof-of-concept study involving disinfection of drains in breast surgery patients who received standard antibiotic prophylaxis within 30 minutes prior to skin incision, 2 of 9 (22%) patients with high colony-forming unit counts of drain fluid at 1 week developed subsequent SSI, compared with 4 of 91 (4%) patients with less heavily colonized fluid or no growth ($P = .08$) [17]. In another breast surgery study where all patients received cefazolin within 30 minutes before surgery, bacterial colonization of the drain was independently associated with higher incidence of SSIs, with a median of 6 days between the detection of colonization and the date of SSI diagnosis [20]. In a retrospective case-control study involving spinal fusion surgery, of >40 patient- and surgery-related risk factors studied (including the timing of prophylactic antibiotics and surgery duration), only the duration of drains (mean odds ratio, 1.6 per day drain was present), body mass index, and male sex were independently associated with SSIs [19]. In the same study, >90% of procedures received appropriately timed standard antibiotic prophylaxis [19]. The results of these 3 studies suggest that retrograde migration of organisms may be an important mechanism underlying some SSIs, similar to that commonly invoked in central venous catheter–related infections [26].

In addition to central venous catheter infections and presence of drains, several studies have implicated anticoagulation therapy (routinely recommended for patients at moderate or high risk of thromboembolic event) during the postoperative period as a cause of persistent oozing of the incision, slow wound healing, and subsequent SSIs [11, 14–16]. When reported, >90% of SSIs in these studies received standard antibiotic prophylaxis [14, 15]. In a recent meta-analysis involving 6 orthopedic surgery articles, skin closure by use of staples (often used for quicker closure of the incision in the operating room) was significantly more likely to be associated with SSIs compared with the use of sutures [12]; "routine antibiotics" were reported to have been administered in 4 studies. Although the conclusions of this work were limited by significant heterogeneity among analyzed studies, potentially poor stapling technique with its attendant inaccurate coaptation of the dermal margins, poor wound healing, and subsequent increase in SSI risk [12] was postulated as a possible explanation. In another study involving a 20-year surveillance program of hip and knee joint replacement at a single institution where 97% of cases received cefazolin prophylaxis, of 9 preoperative, 5 intraoperative, and 5 postoperative factors studied, only hematoma formation and days of postoperative drainage were significant predictors of SSI [13].

Another reason to consider postoperative factors in the causation of SSI is based on the evidence from studies involving methicillin-resistant Staphylococcus aureus (MRSA) and gram-negative bacilli as causative pathogens, particularly when

<table>
<thead>
<tr>
<th>Postoperative Factor</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound-related</td>
<td></td>
</tr>
<tr>
<td>Continued oozing</td>
<td>[11–16]</td>
</tr>
<tr>
<td>Drains</td>
<td>[17–20]</td>
</tr>
<tr>
<td>Hematoma</td>
<td>[13]</td>
</tr>
<tr>
<td>Staples</td>
<td>[12]</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>[11, 14, 16]</td>
</tr>
<tr>
<td>Contiguous focus</td>
<td>[21]</td>
</tr>
<tr>
<td>Patient-related</td>
<td></td>
</tr>
<tr>
<td>Bloodstream infection</td>
<td>[2, 22, 23]</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>[23]</td>
</tr>
<tr>
<td>Antibiotic prophylaxis &gt; 2h following surgery</td>
<td>[24]</td>
</tr>
<tr>
<td>Healthcare setting–related</td>
<td></td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>[23]</td>
</tr>
<tr>
<td>Hospital ward</td>
<td>[25]</td>
</tr>
<tr>
<td>Long-term-care facility/rehabilitation center</td>
<td>[24]</td>
</tr>
</tbody>
</table>
prophylactic antibiotics are administered [18, 21, 24, 27–33]. In a retrospective case-control study of MRSA vs non–MRSA SSIs with 95% of patients receiving standard antibiotic prophylaxis within 2 hours prior to incision, none of the usual pre- and intraoperative factors (including failure to use vancomycin as prophylaxis) studied were independently associated with MRSA SSI; only postoperative factors such as transfer to a long-term-care facility, postoperative use of antibiotics for >24 hours, and, to a marginal degree, use of drains for >24 hours following surgery were independently associated with MRSA SSI [24]. The authors posited that MRSA SSI may be caused by factors operational even after the incision is closed. Indeed, in a study of the acquisition of MRSA in vascular patients undergoing arterial surgery [27], 80% of MRSA-positive patients appeared to have acquired this pathogen de novo during the postoperative period, with infectious complications occurring only in those who acquired MRSA during their hospitalization. In a similar study involving S. aureus poststernotomy mediastinitis with all patients receiving vancomycin and cefotaxime during anesthesia induction, none of 8 patients with MRSA SSI had an identical isolate in preoperative nasal cultures, and the same clone of MRSA was present in all cases [28]. In another study involving orthopedic surgery, successful preoperative MRSA decolonization had no impact on the risk of subsequent SSI due to this organism [29]. Although the authors of this study suggested that preoperative decolonization might have been unsuccessful despite negative repeat cultures, postoperative acquisition of MRSA might have provided an equally plausible explanation. Postoperative acquisition of MRSA may also explain reports of unproven efficacy of MRSA screening and decolonization and unclear impact of anti-MRSA perioperative antibiotics in preventing SSIs due to this organism [18, 24, 28–33].

Besides MRSA, SSIs caused by gram-negative bacilli (GNB) may also be associated with postoperative factors. In a study of cardiac surgery patients uniformly receiving vancomycin prophylaxis, chest wound infection caused by GNB was independently associated with postoperative thoracentesis [21]. Because pleural effusions were often related to postoperative pneumonia, measures to reduce such complications were suggested by the authors as a means of reducing SSIs. The potential role of postoperative factors in causing GNB infections is further supported by Anwar et al [25], who found an increase in urogenital organisms (eg, Pseudomonas aeruginosa) causing SSIs among head and neck surgical patients when the urology and head and neck surgical wards were combined for fiscal reasons. Although unproven, it is possible that postoperative exposure of fresh head and neck wounds to common urinary pathogens from nearby patients might have played a role. This situation is not dissimilar to the increasing trend toward early posthospital transfer of freshly operated patients to long-term-care or rehabilitation facilities [34], where high endemic rates of colonization with multidrug-resistant pathogens is commonly observed among facility residents [35].

Third, although factors contributing to SSIs are often divided into 3 seemingly exclusive categories (pre-, intra-, and postoperative factors), the potential interplay among these factors should not be ignored. For example, although poor preoperative functional status may increase the risk of SSIs [5], its impact may also potentially be felt during the postoperative period through its association with slower wound healing, use of drains, and transfer to another healthcare facility for recuperation following surgery [18]. Even preoperative colonization of pathogens such as S. aureus does not necessarily exclude the possibility of postoperative mode of infection due to their persistent colonization of skin and subsequent infection of the surgical site through drains, bacteremia, or poorly healing wounds. Of interest, a recent study of SSIs involving 6263 coronary artery bypass graft and arthroplasty procedures reported by the National Healthcare Safety Network hospitals in the United States found that methicillin-sensitive S. aureus (MSSA) was the most commonly identified pathogen despite widespread use of standard antimicrobial prophylaxis with activity against this organism [36], prompting concerns about the adequacy of the current methods for SSI prevention [10]. MSSA contamination of the surgical site during the postoperative period may offer an explanation for these findings.

The need to reexamine the efficacy of a previously entrenched approach in tackling HAIs is not new to this field. For example, for decades heavy reliance on hand hygiene to curb hospital-associated infections overshadowed many other potential sources of infection in hospitalized patients, including the environment. In fact, for years it was widely held that hospital surfaces contributed "negligibly to nosocomial infections occurring endemically in hospitalized patients" [37]. In recent years, however, it has become increasingly clear that persistently contaminated hospital room surfaces may also play an important role in the transmission of many nosocomial pathogens such as Clostridium difficile and vancomycin-resistant enterococci [38]. Under such circumstances, even >90% compliance with hand hygiene and isolation practices may not be sufficient to stop transmission of these pathogens to hospitalized patients [39]. Similarly, without adequately addressing postoperative factors, SSIs may continue irrespective of high compliance rates with pre- and intraoperative preventive measures. Of interest, a recent study of the impact of adherence to the current surgical care improvement project measures estimated that even if adherence were increased to 100%, it would result in a <25% decrease in the SSI rates [40]. If this estimate is confirmed, it would suggest that there are still significant opportunities to reduce SSI rates by exploring novel means that may lie outside of our traditional toolkit of preventive measures.

Serious consideration of postoperative factors in the causation of SSIs may have several notable implications. First, it
may lead to their more frequent inclusions—and better clarification of their role—in future epidemiologic studies. Second, recognizing the importance of postoperative factors in SSIs may also help in the proper interpretation of the results of existing works. Specifically, studies reporting apparent breakthrough SSIs despite implementation of standard antibiotic prophylaxis may be less likely to reflexively recommend an alternative and/or broader-spectrum prophylactic antibiotic regimen [21, 29, 36]—with its attendant risk of promoting antimicrobial resistance—without first considering other alternative explanations for their findings. Last, acknowledgement of postoperative factors as potential contributors to the risk of SSIs should make us rethink the merits of automatically attributing these complications to specific surgeon or surgery-related practices prior to closure of the incision alone.

Clearly, we need better understanding of the pathophysiology of SSIs through conduction of high-quality experimental as well as randomized controlled studies. In the meantime, the weight of the current evidence suggests that surgeons and healthcare facilities with high rates of compliance with the current best practice measures should not automatically accept SSIs as an “inevitable” complication of the procedure. The period of vulnerability to wound infection does not appear to end with surgical closure of the wound. Consequently, for every patient with an SSI we may need to routinely inquire about systemic processes as well as the “how,” “where,” and “who” of wound care during the postoperative period. Undoubtedly, this approach will require closer scrutiny of the care rendered not only during the postoperative period in the hospital but following patient discharge as well, particularly in nursing facilities or rehabilitation centers. Furthermore, implementation of preventive strategies during the postoperative period may be more challenging than those carried out during the more defined and controlled pre- and intraoperative periods. However, given the current era of “zero tolerance” for HAIs and substantial morbidity and cost associated with many SSIs, these efforts will likely be worthwhile and potentially lifesaving.

Albert Einstein famously defined insanity as doing the same thing over and over again and expecting different results. We should heed his advice when dealing with SSIs. It is time to take notice of postoperative factors.

Notes

Disclaimer. The content is solely the responsibility of the author and does not necessarily represent the official views of Harvard Catalyst, Harvard University, its affiliate academic healthcare centers, or its corporate contributors.

Potential conflicts of interest. Author certifies no potential conflicts of interest.


