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Surgical Site Infections: Predisposing factors and Prevention

Murtaza Mustafa,HM,Iftikhar,S.Hamed,EM.IIIzam,AM.Sharifa,T.Win
[1,2,3,6,]*Faculty of Medicine and Health Sciences, UniversitySabah,Malaysia,Kota Kinabalu, Sabah, Malaysia.*
[4] *Clinic Family Planning Association,KotaKinabalu,Sabah,Malaysia.*
[5] *Quality Unit,Hospital Queen Elizabeth,Kota Kinabalu,Sabah,Malaysia.*

Abstract:*Despite medical advancements Surgical site infections (SSIs) remain important clinical problem worldwide and heavy financial burden on healthcare. Wound infection occurs after surgery depends on patient related factors, procedure related factor, microbial factor, and perioperative antimicrobial prophylaxis. Operative wound are classified as clean wound, clean contaminated, contaminated, and dirty infected wound. Frequently isolated pathogens include Staphylococcus aureus,coagulase negative Staphylococcus,MRSA,CA-MRSA(community acquired methicillin resistant Staphylococcus aureus),multidrug resistant pathogens and anaerobic bacilli. Use of known prophylaxis measure is the best practice. Supplement oxygen may be useful. Intensive glucose control can lead to reduction in deep wound infection in diabetic patients. Prophylactic antibiotic must ensure that tissue concentrations remain well above the MIC values. CDC recommendations on prophylactic antibiotic dosing are beneficial. Noble perception that all SSIs are preventable is unrealistic andincorrect, given the presence of many risk factors.*

Keywords: *Surgical site infections. Risk factors, Prevention, Antibiotic prophylaxis,*

I. Introduction

Surgical site infections (SSIs) are defined as infections occurring up to 30 days after surgery, and affecting either the incision or deep tissue at the operation site[1].SSIs are common nosocomial infections worldwide. National Center for Health Statistics and National Healthcare Safety Network(NHISN) suggests that between 25,000 and one million SSIs complicate the approximately 26.6 million inpatient surgical procedures performed annually in the Unites States[2,3].The impact of SSIs in the United States alone has been estimated to be 3.7 million excess hospital days and 1.6 billion in excess costs[4].Whether the a wound infection occurs after surgery depends on a complex interaction between (a) patient related factors(e.g,. host immunity, nutritional status, the presence or absence of diabetes)(b)procedure related factors(e.g. Implantation of foreign bodies, degree of trauma to host tissues);(c) microbial factors(tissue adherence and invasion);and(d)perioperative antimicrobial prophylaxis[5].Classification of the operative wound include clean wound(class1),clean contaminated wound(class 11),contaminated wound(class 111),and dirty infected wound(class iv)[6].The patient's endogenous skin flora, with gram positive organisms in general, and staphylococcal species, in particular, are the predominant cause of incisional infections of clean surgical procedures[7].Over the past decade with the emergence of various multidrug- resistant pathogens particularly CA-MRSA(community acquired methicillin resistant *Staphylococcus aureus*) are noted in doubling in prevalence of MRSA SSIs from 2000 to 2005[8].Wolcott and colleagues conclude that the high prevalence of anaerobic bacilli and the overwhelming predominance of two previously uncharacterized*Bacteroides*suggest that such bacteria may be a leading contributor to such infections(SSIs)[9].Preoperative prophylactic antibiotics should be utilized according to the classification of the surgical wound. Prophylactic antibiotics are unnecessary in clean laparoscopic procedures, such as antireflux surgery, adrenalectomy, and splenectomy [10].Prevention of SSIs include, utilizing known infection prophylaxis measures is best surgical practice and much more preferable than dealing with the morbidity of surgical-site infection[11].Preoperative interventions that may reduce SSIs include preoperative antiseptic showering and clipping rather than shaving hair at the operative site[11].Paper reviews the current literature and predisposing factors and prevention of SSIs.

II. Predisposing factors

Patients with increased predisposing (risk)factors. The hospital Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention (CDC) published guidelines for the prevention of surgical-site infections in 1999.Both patient and operation characteristics were examined to determine risk factors (predisposing factors) and prevention measures pertinent to SSI.The patient characteristics found to possibly increase the risk of SSI including diabetes, nicotine use, steroid use malnutrition, prolonged preoperative hospital stay, preoperative nares colonization with *Staphylococcus aureus*,and perioperative transfusion. In addition, older age, obesity, remote body site infection, and systematic immunocompromised may increase risk of SSI[6,1,12].

Diabetes mellitus has often been noted as a risk factor for SSI,acute fluctuation in glucose control may also be important. In a prospective study of 1000 cardiothoracic surgery patients, hyperglycemia (serum glucose >200 mg/dL.) in the 48 hours post procedure were associated with 102% increase in the risk for wound infection [13].Risk also increased incrementally with further elevations in glucose, however, the degree of long-term glucose(as measured by glycosylated hemoglobin levels at time of surgery) did not impact infection risk. As a result of this and similar studies, intensive glucose control during the perioperative period among cardiac surgical patients is now considered a basic SSI prevention practice [14].

Advance age in adults has been noted as a risk factor for SSI;however questions often arise as to whether age serves simply as a marker for underlying illness or whether immunosenescence associated with advance leads to an increased link of infection. In contrast a recent study of greater than 72,000 surgical patients found that, after adjustment for hospital type, procedure type, and duration, wound class, and American Society Anesthesiologists (ASA) score, the risk of SSI decreased with advance age(decrease of 1.1%/ year as patient age increased[15].

Surgical procedure factors.Surgical procedure itself can lead to increased risk factor for SSI.Breaks in the sterile technique during the procedure, failure or incomplete preparation of the skin with antiseptic cleansers, improper ventilation of the operating suite, and use of flash (i.e., emergent/immediate) sterilization of surgical instruments[16],can all contribute the development of of SSI.The rate of contamination of sterile instrument trays correlat4s with the duration such trays are left exposed and uncovered [17].Increased traffic in the operating room(0R)may lead to increased bacterial shedding and airborne contamination. At study of nearly 3000 surgical procedures noted a fourfold increase in SSI frequency between surgical cases with 0 to 8 people entering the 0R during the case and those more than 17 people in the room [18].While this finding was not significant in multivariate analysis, it seems prudent that 0R traffic be minimized as a part of good surgical practice. The method of hair removal is important, as shaving with a razor (vs. use of clippers or no hair removal at all) leaves small micro abrasions around the operating site that may harbor bacteria. Finally, failure to administer prophylactic antibiotics) correct dose, correct timing prior to incision) is a major factor in in the development of SSI[5]..

Patient risk factor evaluation.Manyrisk factors for infection are unrelated; hence a patient with one risk factor is also likely to have others. Methods to ascertain an individual's overall risk for the development of an SSI have been devised to account for the multiple factors involved in the pathogenesis of wound infections. Developed and tested on more than 58,000 patients during the Centers for Disease Control and Prevention Study on the Efficacy of Nosocomial Infection Control(SENIC),one each index takes into account the traditional(evaluation)assessment of the level of wound contamination together with three patient-and procedure related risk factors[19].Undergoing an operation involving the abdomen, having a procedure lasting longer than two hours, and the presence of three or more discharge diagnosis(as a surrogate for identifying the complicating patient) were all independent risk factors for a wound infection. Their inclusions with the traditional wound classification system predicted the risk of wound infection twice as well as the wound classification system [5].

This model has been modified further, resulting in the National Nosocomial Infection Surveillance system(NNIS)risk index which includes the three following variables:(1) a patient with an ASA postoperative assessment score of 3,4,or 5;(2) an operation classified as contaminated or dirty-infected; and(3)an operation lasting longer than T hours where T refers to the 75th percentile duration for the specific procedure[20,21].Use of laparoscopic has been found to reduce the rates of SSIs in selected surgical populations(all patients undergoing laparoscopic cholecystectomy and colonic surgery regardless of risk and those with no risk factors for infection[NNIS) score of 0 undergoing laparoscopic appendectomy or gastric surgery)Laparoscopic use has therefore been added to the NNIS index for these patients subgroups[3].Risk assessment using such indices has allowed detailed stratified descriptions of procedure-specific SSI rates to be generated over the past decade[3].Even with the improvement in risk assessment afforded by these indices, critics have noted that for some procedures, such as cesarean section and various neuro-surgical procedures, the NNIS index may not adequately stratify risk. Therefore, further modification of risk assessment tools for SSI will need to occur in order to accurately stratify postsurgical infection risk, particularly in the new era of public reporting and inter-facility comparison of infection rate [22].

III.Prevention

Utilizing known infection prophylaxis measures is best surgical practice and much more preferable than dealing with the morbidity of surgical site infection. The majority of the published literature reports on the use of prophylactic antibiotics in open surgery. Nevertheless, prevention of surgical site infection in laparoscopic procedures is very similar to that of open surgery. In addition to prophylactic antibiotic administration, a variety of interventions specifically address prevention of surgical site-infection in laparoscopy [11].

The admirable goal, increasingly noted perception that all SSIs are preventable is unrealistic and incorrect, given the presence of many risk factors.(e.g. patient risk factors, and surgical procedures).that are largely unalterable(such as patient comorbid diseases and obesity).That said, the goal should be to eliminated all potential preventable infections through the use of evidenced –based processes. Many interventions have been put into practice over the past century to reduce the risk of SSI. These interventions can be grouped into two major categories. The first line of defense involves measures that reduce bacterial inoculation into the wound site. These include familiar rituals such as the application of antiseptics to the skin of patient, the washing and gloving of surgeon's hands, the use of sterile drapers, strict adherence to sterile techniques, airflow control, and use of sterile gowns, caps, and masks by operating room personnel[5].

Efforts to reduce patient colonization with staphylococci may also be of benefit. A randomized, placebo-controlled trial found that mupirocin applied to the nares of patients undergoing elective cardiothoracic, neurosurgical, oncology, gynecologic and general procedures beginning on the day prior to surgery and continued for up to 5 consecutive days resulting in S.aureus nosocomial infections from 7.7% to 4 % in those with preoperative carriage of *S.aureus*.However,the rates of nosocomial and specifically ,SSIs in all patients, regardless of *S.aureus* carriage status, were not reduced with mupirocin[23].Preoperative showering with a solution containing chlorhexidine suppresses bacterial colonization of the skin ,however a meta-analysis of six trials encompassing more than 10,000 patients did not find a significant impact of chlorhexidine showering on SSI rates[24].Such findings may be due to the removal of chlorhexidine during or soon after showering, which may minimize chlorhexidine's beneficial quality of prolonged bacterial killing[5].For preoperative hair removal methods that do not cause abrasions, such as clippers or depilatories,are preferred[25].This recommendation is supported by a large randomized trial of1,013 patients in which SSI occurred in 3.2 % of patients following hair removal with clippers the morning of surgery versus 10.% in those who underwent day-of-surgery shaving with a razor[26].Although some recommendations advocate no preoperative hair removal[6]Heath Dorion and colleagues content that preoperative interventions that reduce SSI include preoperative antiseptic showering and clipping rather than shaving hair at the operative site [11].There is minimal evidence to support an increased risk of wound infection with hair removal by clippers or depilatories on the morning of surgery as compared with no hair removal[25].Drains and intravascular devices should be removed as quickly as possible to avoid the risk of direct andhematogenous seeding of the operating site[5].

The second major class of prevention measures is directed toward improving host containment and elimination of bacteria that have circumvented the front line of defense and have been inoculated into the wound. Most authorities have emphasized that the single most important factor in preventing wound infection is surgical technique. Gentle handling of wound tissues, avoidance of dead space, devitalized tissues, and hematomas, and careful approximation of tissue planes are believed to be critical in maintaining an infection-free incision. Goodsurgical technique along with minimizing hypothermia and use of vasoconstrictive medications help to improve tissue perfusion and oxygenation, thereby improving the delivery and function of neutrophils [5].

In colorectal surgery, active measures to maintain normothermia during surgery have been associated with a reduction in SSI compared to patients allowed to experience routine mild perioperative hypothermia[27].The role of hypoxia prevention, however is somewhat unclear in colorectal patients, administration of supplemental oxygen(fraction of inspired oxygen[$F10_2$]80%) resulted in significantly lower SSI rates(5.2 % vs 11.2 % in those receiving 30% $F1\ 0_2$),[28].A secondrandomized, double blind-trial of patients undergoing major intra-abdominal surgical procedures randomized to receive either 80% or 35 % $F1\ 0_2$ intraoperatively, however, found the incidence of infection was significantly higher in those patients who received the higher oxygen concentration(25.0% in those 80 % $F10_2$ group vs 11.3 % in the 35 % $F1\ 0_2$ group)[29].A third study in colorectal surgical patients, noted reduction of in SSI risk with 80% $F10_2$(11.4% vs 24.4 % in the group receiving 30 % $F10_2$[30].Pooling the data from these three studies results in relative reduction in SSI of 24 % when 80 % $F10_2$ is used. Although this does not reach significant statistical significance, these data when coupled with pathophysiologic rationale for preventing hypoxia of the wound bed, suggest that use of supplemental oxygen may be beneficial [31].

Intensive glucose control via continuous insulin infusion (CII) targeted to maintain glucose levels, less than 200mgmdL during the perioperative period(lasting through the second post-operative day) has been shown to reduce SSI in cardiac surgery patients, when compared in a study of more than2,400 diabetic patients, intensive glucose control with CII led to a reduction in the incidence of deep wound infection in diabetic cardiac surgery patients from 2.0% to 0.8 %(P=0.1)Although only studied in cardiac surgical patients, the pathophysiologic effects of hyperglycemia on wound healing and immune function should not differ for other patients. Thus, it the author's opinion [5] that the benefit of strict glucose control to prevent SSIs should translate to other surgical procedures. Avoiding malnourishment also may reduce the risk of postoperative infection [32-34].Conversely, investigations of mechanisms to directly the host immune system (administration of granulocyte-macrophage colony stimulating factor, exclusive use of autologous blood transfusions or administration of histamine type 2[H2] receptor antagonist) are either too preliminary or no inconclusive to provide for clinical practice[35-37].

Antibiotic prophylaxis.Preoperative prophylactic antibiotics should be utilized according to the classification of the surgical wound. Prophylactic antibiotics are unnecessary in clean laparoscopic procedures, such as antirefluxsurgery,adrenalectomy,and splenectomy.Interestingly, evidence is not sufficient to determine whether the use of antibiotics for laparoscopic procedures utilizing mesh prostheses reduces the incidence of mesh infection [38]..

The in vivo interaction between inoculated bacteria and prophylactically administered antibiotic is one of the most important determinations of the fate of the wound. For example, without antibiotic prophylaxis the reported risk of developing a *S.aureus* SSI after cardiac surgery is 21 % to 44 % an incidence that approximates the frequency of skin/nares colonization with *S.aureus*.[39].Every effort should be made to ensure that adequate antibiotic levels are maintained above the minimum inhibitory concentration(MIC) of the pathogens concern throughout the surgical procedure.IN cardiothoracic procedures in particular, the use of cardiopulmonary bypass can dramatically reduce serum vancomycin levels as a result of alterations in drug clearance and volume of distribution, potentially placing the wound at increased risk for infection[40].In contrast, cephalosporin levels tend to fall at a slower rate during bypass periods. Understanding the pharmacokinetics of the various antimicrobials used in perioperative prophylaxis is therefore vital to ensure adequate antibiotic levels at surgical wound site during the entire procedure. The efficacy of perioperative prophylaxis in preventing SSI after many surgical procedures is unquestioned. Not only have the benefits of early administration been duplicated by numerous investigators using different animal models, different pathogens, and different antibiotics, literally hundreds of clinical trials have verified the efficacy of perioperative antibiotics [.5].

CDC recommendations on prophylactic antibioticdosing.CDC recommends that antibiotic prophylaxis be used for all clean-contaminated procedures and certain clean procedures (i.e., those in which intravascular prosthetic material or a prosthetic joint will inserted and those in which an incisional or organ/space SSI would pose catastrophic risk[6].Dirty or contaminated procedures usually do not require antimicrobial prophylaxis because patients undergoing these procedures are already on targeted antimicrobial therapy for established infections; however if the treatment regimen does not adequately cover all pathogens of concern, consideration should be given to providing additional prophylaxis (i.e.,in a procedure with a high incidence of MRSA SSI, additional prophylaxis with vancomycin may be warranted if treatment regimen does not include coverage against MRSA)[41].

The keys in selecting and appropriate prophylactic antibiotic regimen include consideration of patient's allergies and antimicrobial costs, knowledge of the ecology of local nosocomial wound pathogens, consideration of antibiotic penetration into the specific surgical site tissue, and assurance of appropriate antibiotic dosing and delivery. Based on prospective studies of antibiotic prophylaxis, prophylactic regimens have been recommended for awide variety of surgical procedures [42, 43], and many acceptable combinations of antibiotic prophylaxis have been used. Thecephalosporin's have traditionally been the drugs of choice for the vast majority of operative procedures [6].It should not be presumed that cephalosporin's will remain prophylactic agents of choice. Various classes of antibiotics have been shown to differ appreciably in activity against bacteria in the stationary phase of growth, post antibiotic effect, diffusibility into devitalized tissues or fibrin clots, resistance to enzymatic degradation, activity within abscesses, and penetration of and activity within neutrophils that may have ingested but be unable to wound bacteria. Each of these variables may affect the efficacy of an agent used for prophylaxis, and it is likely that preferred prophylactic regimens will change over time in response to an improved understanding of the pathophysiology of infection and to antimicrobial resistance among wound pathogens [5].

In particular, the emergence of CA-MRSA as a cause of SSI has clouded the issue of appropriate antimicrobial prophylaxis [44].Current recommendation suggest consideration of using vancomycin as empiric therapy for the treatment and prophylaxis of presumptive staphylococcal infection when the local rates of MRSA are high however, the exact threshold at which vancomycin use should occur has not been clearly defined. Routine administration of vancomycin for surgical prophylaxis has been a controversial proposal. A randomized trial of 855 cardiac surgical patients comparing routine use of vancomycin versus cefazolin for prophylaxis noted that, while the rate of MRSA SSI was higher in the cefazolin group, those received vancomycin had higher rate of methicillin –sensitive *S.aureus*SSI.Thus, there was there was no significant difference in overall SSI rates between the two groups[45].An interrupted time series analysis of more than 6,000 cardiac surgery patients,however, found that no coronary artery bypass graft (CABG) patients, follow a switch from cefazolin to vancomycin, the monthly SSI rates decreased by 2.1 per 100 procedures, particularly due to a decrease in SSI due to vancomycin-sensitive pathogens(i.e.,MRSA)[46].

Timing and duration of antibiotic prophylaxis.Except in elective colonic surgical procedures in which oral antibiotics must be administered several hours before the procedure, the initial dose of systematic antibiotics must be administered in a timely fashion so that antibiotic levels in the tissue at time of the incision are adequate. Administration too early before or after the time of incision will result in suboptimal tissue levels, and potentially increased risk of postoperative wound infection. Guidelines and studies vary somewhat on the exact timing ranging from 2 hours to no more than 30 minutes before incision. The SCIP quality improvement project defines appropriately timed antibiotic prophylaxis as delivery of antibiotic within 1 hour prior to incision with the exception that vancomycin and fluoroquinolones should be given within 2 hours prior to incision because of the need for longer fusion time. This definition has become widely used as a metric that indicates delivery of standard, high-quality surgical care [14].*As critical as providing an appropriate timed initial dose of antibiotic is ensuring that tissue concentrations remains well above the MIC values of common pathogens during entire procedure. To achieve this goal, antibiotics should also be re-administered during long surgical* procedure [47].

Prophylaxis duration.In the early years of surgical prophylaxis, prolonged courses (7-10 days) of antibiotics seemed routine [48].Over time, the benefit of prolonged courses of antimicrobials has been appropriately questioned, particularly due to the pathophysiologic changes at the area of incision(i.e. coagulation ,necrosis, induced hemostasis via cautery of blood vessels) that likely limit the ability of antibiotics to reach the wound bed during the early postoperative period[48].A commonly espoused rationale for prolonging the duration of surgical prophylaxis following incision closure includes a desire to “cover” the wound while surgical drains remain in place or to ”protect” against infection of central venous catheters (CVCs).However, a study in the United Kingdom found that prolonged prophylaxis until the patient’s CVC were removed(vs 3 doses of cefuroxime preoperatively) did not lead to a reduction in CVC colonization, a surrogate for CVC infections[49,].Antibiotic impregnated cement placed directly into the operative wound(as local antimicrobial brachy- therapy) is increasingly being used as a method of antibiotic prophylaxis and treatment, particularly in procedures involving replacement of infected prosthetic joints. The aminoglycosides and vancomycin are the compounds most commonly used for brachytherapy; oxacillin and cefazolin have been comparable elution characteristics but are less frequently used because of concerns regarding beta-lactam allergy [50].

Adverse effects of antibiotic prophylaxis include allergic reactions ranging in severity from minor skin rashes to anaphylaxis. *Clostridium difficile*-associated diarrhea (CDAD) has been associated with several prophylactic agents, and in one study the rate of CDAD was 14.9 % cases per 1000 in surgical patients, who received antibiotic prophylaxis as their sole antibiotic exposure.Another notable side effect is profound hypotension and flushing associated with vancomycin prophylaxis (the red man’s syndrome), usually associated with rapid infusions of the antibiotics [51,52].

IV.Conclusion

Surgical site infections (SSIs),are postoperative infections affecting surgical sites. SSI depends on patient related factor, procedure related, microbial factors, and perioperative antimicrobial prophylaxis. Prevention of SSIs includes use of known infection prophylaxis measures and the best surgical practice.

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