Surgical Site Infections: Classification, Risk factors, Pathogenesis and Preventive Management

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Abstract

Surgical site infections are one of the most common nosocomial infections besides pneumonia, urinary tract infections, and blood-stream infections. Wound classification is an important predictor of the risk of postoperative SSIs. Surgical site infections (SSIs) are defined as infections occurring up to 30 days after surgery (or up to one year after surgery in patients receiving implants) and affecting either the incision or deep tissue at the operation site. These infections have a tremendous impact on morbidity and mortality as SSIs doubled the patient’s risk of death after surgery. Staphylococcus aureus, coagulase-negative staphylococci, Enterococcus spp. and Escherichia coli are the most common causative pathogens. Much of the morbidity and mortality caused by SSI is preventable.

Key words: Surgical, Infection, Urinary tract, Morbidity, Mortality.

1. INTRODUCTION

Surgical site infections (SSIs) are the most common post-operative complications even in hospitals with most modern facilities and standard protocols of preoperative preparation and antibiotic prophylaxis.1 About 3-5% of patients who undergo elective surgery, develop SSIs. These are the third commonest nosocomial infections and account for approximately 10-40% of all health care associated (HAI) infections. In 2002, US centre of disease control have estimated...
that about 27 million operations are performed each year in United States which result in approximately 300000 SSIs every year and cause approximately 8000 patient deaths. These infections have a tremendous impact on morbidity and mortality as SSIs doubled the patient’s risk of death after surgery. Extra bed occupancy is an important factor responsible for increasing financial cost associated with these infections because of additional postoperative hospital stay of about 7-10 days which result in extra expenditure of about 3000-29000 US dollars per SSI depending on surgical procedure and pathogen.2,3

1.1 Definition and classification of SSI

In 1992, CDC revised its definition of ‘wound infection’, by creating the definition, ‘surgical site infection’, to prevent the confusion between the infection of a surgical incision and the infection of a traumatic wound.4 Surgical site infections (SSIs) are defined as infections of skin or underlying soft tissues at the surgical site, occurring within 30 days following National Healthcare Safety Network (NHSN) operative procedure in which an incision was closed primarily. An NHSN operative procedure is a procedure that is performed on a patient who is an NHSN inpatient (A patient whose date of admission to the healthcare facility and the date of discharge are different calendar days) or an NHSN outpatient (A patient whose date of admission to the healthcare facility and date of discharge are the same calendar day); and takes place during an operation (defined as a single trip to the operating room (OR) where a surgeon makes at least one incision through the skin or mucous membrane, including laparoscopic approach, and closes the incision primarily before the patient leaves the OR. A complete list of qualifying procedures can be found at http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf. Primary closure is defined as closure of all tissue levels during the original surgery, regardless of the presence of wires, wicks, drains, or other devices or objects extruding through the incision. However, regardless of whether anything is extruding from the incision, if the skin edges are not fully reapproximated for the entire length of the incision (e.g., are loosely closed with gaps between suture/staple points), the incision is not considered primarily closed and therefore the procedure would not be considered an operation. In such cases, any subsequent infection would not be considered an SSI, although it may be an HAI if it meets criteria for another specific infection site (e.g., skin or soft tissue infection). CDC classifies SSIs in three categories: superficial incisional, deep incisional and organ/space SSI.5

Fig 1: Schematic representation of the anatomical classification of surgical site infections

1.2 Superficial incisional SSI

Infection occurs within 30 days after any NHSN operative procedure, and involves only skin and subcutaneous tissue of the incision and patient has at least one of the following:
1) purulent draining from the superficial incision.
2) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision (incisional drainage).
3) at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat, and superficial incision is deliberately
opened by surgeon, and is culture positive or not
cultured.
4) Diagnosis of superficial incisional SSI by the
surgeon or attending physician.

Do not report the following conditions as SSI
1. Stitch abscess (minimal inflammation and discharge
confined to the points of suture penetration).
2. Infection of an episiotomy or newborn circumcision
site.
3. Infected burn wound and localized stab wound
infection (considered as skin or soft tissue infection
depending on its depth).
4. Incisional SSI that extends into the fascial and
muscle layers (see deep incisional SSI).

Note: Specific criteria are used for identifying infected
episiotomy and circumcision sites and burn wounds.
Episiotomy and circumcision are excluded from
definition of SSIs because these are not NNIS
operative procedures.

There are two specific types of superficial incisional
SSIs:
1. Superficial Incisional Primary (SIP) –a superficial
incisional SSI that is identified in the primary incision
in a patient that has had an operation with one or more
incisions (e.g., C-section incision or chest incision for
CBGB).
2. Superficial Incisional Secondary (SIS)–a superficial
incisional SSI that is identified in the secondary
incision in a patient that has had an operation with
more than one incision (e.g., donor site incision for
CBGB).

1.3 Deep incisional SSI
Infection occurs within 30 or 90 days after the NHSN
operative procedure and involves deep soft tissues
(fascial and muscle layers) of the incision and patient
has at least one of the following:
1) Purulent drainage from the deep incision but not
from the organ/space component of the surgical site.
2) A deep incision spontaneously dehisces or is
deliberately opened by a surgeon and is culture positive
or not cultured and when the patient has at least one of
the following signs or symptoms: fever (>38°C),
localized pain, or tenderness, unless site is culture-
negative.
3) An abscess or other evidence of infection involving
the deep incision is found on direct examination,
during reoperation, or by histopathologic or radiologic
examination.
4) Diagnosis of a deep incisional SSI by a surgeon or
attending physician.

Notes:
1. Report infection that involves both superficial and
depth incision sites as deep incisional SSI.
2. Classify infection that involves superficial
incisional, deep incisional, and organ/space sites as
deep incisional SSI. This is considered a complication
of the incision.

There are two specific types of deep incisional SSIs:
1. Deep Incisional Primary (DIP) – a deep incisional
SSI that is identified in a primary incision in a patient
that has had an operation with one or more incisions
(e.g., C-section incision or chest incision for CBGB).
2. Deep Incisional Secondary (DIS) – a deep incisional
SSI that is identified in the secondary incision in a
patient that has had an operation with more than one
incision (e.g., donor site incision for CBGB).

1.4 Organ/Space SSI
Infection occurs within 30 or 90 days after the NHSN
operation and infection involves any part of the
anatomy (organs or spaces), other than the skin
incision, fascia or muscle layers that is opened or
manipulated during an operation and at least one of
the following:
1. Purulent drainage from a drain that is placed into the
organ/space.
2. Organisms isolated from an aseptically obtained culture or fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

**1.5 Wound classification and risk of acquiring SSI**

Operative wound classification was developed by US National Research Council group in 1964. Four wound classes with an increasing risk of SSIs were described: clean, clean-contaminated, contaminated and dirty wounds.6

*Clean wounds*- when no inflammation is encountered and the respiratory, gastrointestinal, genital and urinary tract is not entered. Elective, not emergency, primarily closed, no break in technique. Elective inguinal hernia repair is an example of a clean operative procedure. SSI rate is usually less than 2% in clean operated wounds.

*Clean-contaminated wounds*- when the operative procedure enters into a colonized viscus or cavity of the body, but under elective and controlled circumstances with minimal spillage. Urgent or emergency case that is otherwise clean, minor technique break. Elective intestinal resection like appendicectomy, pulmonary resection, gynaecologic procedures, and head-neck cancer operations that involve the oropharynx are examples of clean-contaminated procedures. SSI rate is 3% to 11% in clean-contaminated wounds.

*Contaminated wounds*- operations with major breaks in sterile technique (e.g. open cardiac massage) or gross spillage from the gastrointestinal tract, entry into biliary or genitourinary tract in the presence of infected bile or urine and incisions in which acute, non purulent inflammation is encountered are included in this category. Infection rate is greater than 10% even with preventive antibiotics.

*Dirty wounds*- Surgical procedures performed when active infection is already present are considered dirty wounds. Abdominal exploration for acute bacterial peritonitis and intra-abdominal abscess are examples of this class of surgical site. SSI rate can exceed 20% in dirty wounds.7-10

CDC developed the National Nosocomial Infection Surveillance (NNIS) Risk Index system, for comparison of infection rates between institutions and analysis of SSI rates within a given institute over time.11 The risk index has a range from 0 to 3 points. A point is added to the patient's risk index for each of the following 3 variable.12

1 point: the patient has an operation that is classified as either contaminated or dirty.

1 point: the patient has an American Society of Anesthesiologists (ASA) preoperative assessment score of III, IV, or V.

**1.6 Physical Status Classification (ASA Score) for Surgical Patients**13

- I : patient in normal health
- II : patient with mild systemic disease resulting in no functional limitations
- III : patient with severe systemic disease that limits activity, but is not incapacitating
- IV : patient with severe systemic disease that is a constant threat to life
- V : moribund patient not likely to survive 24 hours

1 point: the duration of the operation exceeds the T time. The T time is the 75th percentile of the procedure duration, rounded to the nearest hour, and is calculated for each category of surgical procedure.14

**2. PATIENT RELATED RISK FACTORS FOR SSI**
Certain conditions which diminish the efficacy of the immune response and delays wound healing such as:

- Diabetes,
- Malnutrition,
- Smoking,
- Obesity,
- Alcoholism,
- Extremes of age,
- Steroid therapy,
- Chemotherapy, radiotherapy,
- Peripheral vascular disease, skin disease at operation site, pre-existing infection, chronic inflammatory conditions increase the risk of acquiring SSI.

### Table 1: The T point for common surgical procedures

<table>
<thead>
<tr>
<th>Operation</th>
<th>T point (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery bypass graft</td>
<td>5</td>
</tr>
<tr>
<td>Bile duct, liver or pancreatic surgery</td>
<td>4</td>
</tr>
<tr>
<td>Craniotomy</td>
<td>4</td>
</tr>
<tr>
<td>Head and neck surgery</td>
<td>4</td>
</tr>
<tr>
<td>Colonic surgery</td>
<td>3</td>
</tr>
<tr>
<td>Joint prosthesis surgery</td>
<td>3</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>3</td>
</tr>
<tr>
<td>Abdominal or vaginal hystectomy</td>
<td>2</td>
</tr>
<tr>
<td>Ventricular shunt</td>
<td>2</td>
</tr>
<tr>
<td>Herniorrhaphy</td>
<td>2</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>1</td>
</tr>
<tr>
<td>Limb amputation</td>
<td>1</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>1</td>
</tr>
</tbody>
</table>

Cigarette smoking causes constriction of peripheral blood vessels, leading to tissue hypovolemia and hypoxia, therefore interfere with primary wound healing.\(^{15-17}\) Studies have shown that obesity is strongly associated with increased risk of SSI. Adipose tissue (obesity defined as BMI ≥ 30 kg/m\(^2\)) is poorly vascularised and the consequent effect on oxygenation of the tissues and functioning of the immune response is thought to increase the risk of SSI.\(^{18,19,20}\)

Diabetes mellitus is a major predictor of post-surgical mortality and morbidity because of the pre-existing complications of chronic hyperglycaemia, which include vascular atherosclerotic disease and peripheral as well as autonomic neuropathies.\(^{21}\) Patients facing surgery should have fasting serum glucose (FSG) as well as Hemoglobin A1c (HbA1c) drawn to evaluate the presence of pre-existing diabetes. If either or both of these tests indicate uncontrolled and/or pre-existing diabetes (FSG > 110 mg/dL or HbA1c ≥ 7%), then the patient should be set on a predetermined regimen shown to be effective in controlling serum glucose if implemented and followed.\(^{22,23}\) Any remote infections should be identified and treated prior to operation as these are linked to increase SSI rates three to five fold.\(^8\)

Studies have shown that obesity is strongly associated with increased risk of SSI. Adipose tissue (obesity defined as BMI ≥ 30 kg/m\(^2\)) is poorly vascularised and the consequent effect on oxygenation of the tissues and functioning of the immune response is thought to increase the risk of SSI.\(^{18,19,20}\)

Serum albumin level (normal range 3.4-5.4g/dl) is most commonly used to assess nutritional status, patients who are malnourished have less competent immune response and are at increased risk for acquiring infections. Depending on the surgical urgency, delay of surgery until the patient’s nutritional status improves may be indicated. Preoperative and postoperative fasting should be kept at a minimum for these patients, as even short-term deprivation may exacerbate risks.\(^{24,25}\)

### 3. PATHOGENESIS OF SSIS

In most patients, infection does not develop at operative site because innate host defenses are quite efficient in the elimination of contaminants at the surgical site.\(^{26}\) Pathogens that cause SSI are acquired either endogenously from the patient’s own flora present on skin or from opened viscus or exogenously from contact with operative room personnel or the environment. However, the period of greatest risk remains the time between opening and closing the operating site.\(^{27}\) Prolonged operations that increase the length of time increases the risk of exogenous contamination.\(^{28}\) In clean surgeries which do not open the abdomen or genital tract such as cardiothoracic surgeries, neurosurgeries, orthopaedic, ophthalmic and breast surgeries, Staphylococcus aureus (MRSA) is the predominant pathogen causing SSI and associated with
poor outcome. The emergence of methicillin-resistant strains of *S. aureus* (MRSA) have increased the morbidity and mortality from wound infections. Other gram positive organisms such as coagulase negative staphylococci, enterococci and *Streptococcus* species, are involved less frequently.\textsuperscript{29-32} Surgeries which enter into hollow visera like appendicectomy, colorectal, gastroduodenal, biliary tract and urologic operations, exposes surrounding tissues to gram negative bacilli such as *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Proteus* species, gram positive organism like *Enterococcus*, and anaerobes.\textsuperscript{33-35} In surgeries of the head and neck region, anaerobes such as *Peptostreptococcus*, *Propionibacterium*, *Prevotella*, *Veillonella*, *Bacteroides*, and *Clostridium* species, are mainly responsible for SSIs because these organisms are present normally in oropharyngeal region as commensal and therefore gain access to surgical site easily.\textsuperscript{36} SSIs can be monomicrobial or polymicrobial. Polymicrobial infections usually occur at surgeries of oropharyngeal, axilla, perineum and GIT region because of mixed aerobic and anaerobic organisms. Yeast of *Candida* species can also be a part of polymicrobial SSI.\textsuperscript{37} Development of SSI depends on interplay of four factors:

### 3.1 Inoculum of bacteria

- Procedures involving the sites which are heavily colonized with bacteria such as bowel (10\textsuperscript{3}-10\textsuperscript{6} bacteria/ml of distal small bowel contents, 10\textsuperscript{5}-10\textsuperscript{6} bacteria/ml in right colon, 10\textsuperscript{10}-10\textsuperscript{12} bacteria/gm of stool in rectosigmoid colon), female genital tract (10\textsuperscript{6}-10\textsuperscript{7} bacteria/ml) are at higher risk of developing SSI as large inoculums of bacteria lodge into wound during the course of operation.\textsuperscript{37,39}

### 3.2 Virulence of bacteria

The more virulent the bacterial contaminant, the greater the probability of infection. *Staphylococcus aureus*, *Clostridium perfringens*, *Streptococcus pyogenes* require only a small inoculum to cause severe necrotizing infection at the surgical site. *Bacteroides fragilis* and other *Bacteroides* species are ordinarily organisms of minimal virulence as solitary pathogens, but when combined with other oxygen-consuming organisms, they will result in microbial synergism and cause very significant infection following operations of the colon or female genital tract.

### 3.3 Microenvironment around surgical site

Presence of necrotic tissue, dead space, foreign bodies at the surgical site increases the probability of infection.

### 3.4 Innate and acquired host defences

When a surgical incision is made through skin and subcutaneous tissues, human inflammatory response in activated.\textsuperscript{40} Acute surgical wounds normally proceed through an orderly and timely reparative process resulting in sustained restoration of anatomic and functional integrity. If an acute wound fails to heal within six weeks, it can become a chronic wound. Early inflammation (the first 24 hours) begins with haemostasis through vasoconstriction, thrombin formation by activation of complement proteins and platelet aggregation. Platelets release cytokines and many growth factors such as platelet derived growth factor (PDGF), transforming growth factor (TGF-β), fibroblast growth factor (FGF), keratinocyte growth factor (KGF), epidermal growth factor (EGF) and insulin like growth factor (IGF-1). These factors causes chemotaxis of neutrophils, fibroblasts and monocytes towards the site of wound, stimulates proliferation and migration of epithelial cells like keratinocytes, stimulates angiogenesis and promotes extracellular matrix synthesis.
PMNs are also a major source of cytokines early during inflammation, especially TNF-α, also release proteases such as collagenases. Following functional activation neutrophils scavenge necrotic debris, foreign material, and bacteria. PMNs do not survive longer than 24 hours. If wound contamination persists or secondary infection occurs, continuous activation of the complement system and other pathways provides a steady supply of chemotactic factors, resulting in a sustained influx of PMNs into the wound. Sterile incisions will heal normally without the presence of PMNs. By about 24 hours after creation of the surgical wound, monocytes enter the surgical site. When microbial contamination has been minimal and the early arriving neutrophils have been able to adequately control the bacteria that are present, then monocytes produce local chemical signals to regulate the wound-healing process. However, if microbial contamination and proliferation overwhelm the initial neutrophil infiltration, the monocyte assumes the role of a proinflammatory cell with the release of potent cytokines. Tumor necrosis factor (TNF)-alpha is produced by the monocytes and serves numerous functions; notably, it becomes a potent paracrine signal to upregulate vigorous neutrophil activity within the wound. TNF-alpha-stimulated neutrophils consume microbes, and lysosomal vacuoles may release reactive oxygen intermediates and acid hydrolases into the extracellular space from its lysosomal vacuoles, with further tissue injury and further activation of the initiator signals. Interleukin (IL)-1, IL-6, and other proinflammatory signals are released by the activated monocyte and serve as endocrine signals responsible for fever, stimulation of acute phase reactants, and other responses. Serotonin is released from mast cells which causes vasodilation and increased vascular permeability. During late inflammation (24-72hrs), Vasodilation is followed by increased permeability of the microvasculature, followed by stasis, which leads to accumulation of leucocytes along the vascular endothelium which then migrate through the vascular wall into the interstitial tissue. The combination of intense vasodilation and increased vascular permeability leads to clinical findings of inflammation, rubor (redness), tumor (swelling), calor (heat), and dolor (pain). The function of this phase of wound healing is to ensure that the wound bed is free of bacteria and other contaminants and to create the optimum environment for the production of granulation tissue and for epithelialisation. Over the next few days to weeks, regeneration takes place and characterised by an increase in fibroblast and endothelial cell mitogenic activity, with epithelial cell migration and synthesis of collagen. Maturation is the final phase of wound healing which can take up to two years to complete. In this phase, granulation tissue gradually matures into scar tissue, which over time pale, shrinks and thins.

4. PREVENTIVE MANAGEMENT OF SSI

4.1 Preoperative phase
Preoperatively, attention should be paid to improve the patient’s health by ensuring optimum glycaemic control in diabetics, stopping smoking, improving nutritional state and correcting anaemia. All patients should take bath with soap on night prior to or the day of operation.

4.2 Hair removal- The CDC recommends that hair not be removed unless it will interfere with the operation,
and if hair is to be removed it is done immediately before the operation with electric clippers rather than shaving. Shaving by razor results in microscopic cuts and abrasions, thus cause disruption of the skin’s barrier defense against microorganism colonization and increase the risk of post-operative SSI.\(^{41-44}\)

### 4.3 Antibiotic prophylaxis

Preoperative antibiotic prophylaxis should be given to patients undergoing clean surgery involving the placement of a prosthesis or implant, clean-contaminated surgery and contaminated surgery.\(^{45,46}\) Administer the initial dose of prophylactic antimicrobial agent by the intravenous route timed such that a bactericidal concentration of the drug is present in the serum and tissues at the time of incision. Maintain therapeutic levels of the drug in serum and tissues throughout the operation. Continue antimicrobial therapy until, at most, a few hours after the incision is closed in the operating room and should be discontinued within 24 hours of the end of surgery.\(^{47,48}\) If there is significant unexpected contamination encountered during an operation or existing infection then prophylaxis should be converted into a treatment regime. Do not use nasal decontamination with topical antimicrobial agents such as mupirocin and chlorhexidine aimed at eliminating *S. aureus* routinely to reduce the risk of SSIs.\(^{49-52}\)

### 4.4 Patient theatre wear

Specific theatre wear should be given to patients that allow easy access to the operative site as well as other areas for placement of intravenous cannulas, catheters and epidurals, etc. The operating team should remove hand jewellery, artificial nails and nail polish before operation.\(^{53}\)

### 4.5 Intraoperative phase

**Patient skin preparation in the operating room:** Skin antiseptics are used to reduce the number of resident microflora on the skin around the incision. Prepare the skin at the surgical site immediately before incision using an antiseptic. Chlorhexidine or providone-iodine are most suitable. Iodine-based antiseptics are effective against a wide range of gram-positive and gram-negative organisms including MRSA, as well as tubercle bacillus, fungi, and viruses. The fungal coverage of chlorhexidine is reduced when compared with iodophore and alcohol based solutions. Alcohol is rapidly bactericidal, but once evaporated, has no persistent antimicrobial effect. For this reason, alcohol is often combined with either iodine or chlorhexidine in surgical preparations.

Optimal oxygenation and good hydration should be maintained during surgery. Give patients sufficient oxygen during surgery and in the recovery period to ensure that a haemoglobin saturation of more than 95% is maintained.

**Perioperative blood glucose control:** Elevated blood glucose levels cause the release of pro-inflammatory cytokines that depress the immune system, thus increasing susceptibility to SSI.\(^{54}\) Improved glycemic control during the first 48 hours after surgery has been shown to reduce SSIs in cardiovascular surgery and surgical ICU patients.\(^{55}\) In addition, hyperglycemia (>200 mg/dL) has been associated with increased SSI risk in the immediate postoperative period.\(^{56}\)

**Hand decontamination:** The operating team should wash their hands prior to the first operation on the list using an aqueous antiseptic surgical solution, with a single-use brush or pick for the nails, and ensure that hands and nails are visibly clean.\(^{57,58}\) Before subsequent operations, hands should be washed using either an alcoholic hand rub or an antiseptic surgical solution. If hands are soiled then they should be washed again with an antiseptic surgical solution.\(^{59-61}\)

**Wound closure and wound dressings:** Wound dressing material should ensure that the wound remains moist, free from devitalised tissue, toxic chemicals or particles released from the dressing material.
4.6 Postoperative phase

Changing dressings and wound cleansing: Regular cleansing of the wound and surrounding area is necessary for the removal of excess wound exudates, foreign bodies and wound crusts.

5. TREATMENT

Minor infections may respond to drainage of pus after removal of sutures and topical antisepsis. In clinically serious infections, microbiological cultures should be sought and antibiotic therapy is given according to results of drug sensitivity testing. Unnecessary antibiotic therapy carries the risk of development of drug resistance and adverse drug reactions.62

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