Development of Risk-Index Tool to Predict Surgical Site Infections

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Table of Contents

English Abstract

Surgical site infections (SSI) are one of the most common complications following surgery. SSIs can incur many consequences for the patient including extended hospital stay, increased hospital costs, increased risk of entering the ICU as well as increased risk of morbidity and mortality. There are three types of SSIs: superficial incisional SSIs, the most common yet the least severe, deep incisional SSIs and organ/space SSIs, the most life-threatening. Due to the high emergence of resistant bacteria, treatment with common antibiotics is ineffective in the majority of patients with an SSI. Therefore, more attention must be paid preoperatively and intraoperatively to prevent SSIs rather than to treat these infections. The data of the literature have identified risk factors that predispose surgical patients to SSIs, however validated risk-index tools have not been developed to quantify the risk of SSI. The data for this study was obtained from the NSQIP (National Surgical Quality Improvement Program) database established at the JGH and included patients undergoing surgery at this institution between November 2009 and December 2011. The database was selected because it is prospective, non-biased and comprehensive. Bivariate analyses and stepwise multivariate logistic regression were used to identify the following five risk factors that were independently and significantly associated with the risk of an

SSI: male gender, inpatient status, hypertension, corticosteroid use and partial or total dependence for everyday activities prior to surgery. Logistic regression models with an ROC curve analysis were used to develop a risk scoring tool for SSI and limits for incremental risk categories. Patients with a score below 43.17 were at low-risk, those with a score between 43.17 and 63.40 were at moderate-risk and those with a score above 63.40 were at high-risk for SSI development. Compared to low-risk patients, moderate-risk patients had a relative risk of 3.963 ($p<0.001$, 95% CI=2.58-6.08) of developing an SSI and high-risk patients had a relative risk of 6.48 ($p<0.001$, 95% CI=4.16-10.10) of acquiring an SSI. Overall, approximately 3% of low-risk patients, 10% of moderate-risk patients and 16% of high-risk patients of the NSQIP database developed any type of SSI. In this study, a simple risk tool for quantifying SSI risk created at the JGH was developed. The tool has external validity for the JGH population. Validation in other populations will be required in future studies.

French Abstract

Les infections du site opératoire (ISO) constituent une des plus fréquentes complications à la suite d'une chirurgie. Les ISOs ont plusieurs conséquences chez le patient incluant un séjour prolongé à l'hôpital, des coûts d'hôpitaux plus élevés, un risque plus accru de requérir des soins intensifs ainsi qu'un risque de morbidité et de mortalité plus élevé. Il existe trois types d'ISOs : ISO incisionelle superficielle, le plus commun néanmoins le moins sérieux, ISO incisionelle profonde et ISO d'organe et/ou d'espace, le plus dangereux des trois. À cause de l'émergence accrue des bactéries résistantes aux antibiotiques, les traitements de certaines ISOs sont inefficaces chez la majorité des patients avec une ISO. En conséquence, plus d'attention doit être fournie avant et pendant la chirurgie afin de prévenir à tout prix les ISOs au lieu de se concentrer sur les traitements de cettes infections. Les données pris de la littérature scientifique ont identifié des facteurs de risque qui prédisposent les patients chirurgicaux pour le développement des ISOs. Cependant, aucun modèle de risque valide n'a été produit afin de quantifier le risque de développer un ISO. Les données pour cette étude ont été obtenues grâce à la base de données NSQIP (National Surgical Quality Improvement Program) établie à l'Hôpital Général Juif et incluent les patients qui ont subi une chirurgie à cet hôpital entre novembre 2009 et décembre

2011. Nous avons choisi d'utiliser la base de données NSQIP puisqu'elle est prospective, impartiale et compréhensive. Des analyses bivariées et des régressions logistiques multivariées ont été employées afin d'identifier les cinq facteurs de risque suivants qui sont indépendamment et significativement associés avec le risque d'un ISO : le sexe male, l'hospitalisation du patient, l'hypertension, l'usage de corticostéroïdes et la dépendance (partielle ou totale) pour des activités quotidiennes avant la chirurgie. Des modèles de régression logistique avec une analyse de courbe ROC ont été utilisés pour développer un outil de pointage de risque pour ISO et délimite les catégories en incréments de risque. Les patients avec un score inférieur de 43.17 sont considérés des patients à risque minime de développer un ISO, ceux avec un score entre 43.17 et 63.40 ont un risque modéré d'acquérir un ISO et ceux avec un score de 63.40 ou plus haut ont un risque élevé pour le développement d'un ISO. Comparé à des patients qui ont un risque minime, les patients avec risque modéré ont un risque relatif de 3.96 fois ($p<0.001$, 95% CI=2.58-6.08) de développer un ISO et les patients à risqué élevé ont un risque relatif de 6.48 ($p<0.001$, 95% CI=4.16-10.10) d'acquérir un ISO. Dans cette étude, un outil de risque simple afin de quantifier le risque d'ISO à l'hôpital Général Juif a été développé. L'outil possède la validité externe pour la population de cet hôpital. La validation pour les autres populations sera requise dans des études futures.

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I. Introduction

Surgical site infections (SSI) are one of the most common complications following surgery. The CDC (Center for Disease Control and Prevention) estimates that 25% of the annual 1.8 million health-care associated infections are SSIs. (Mangram, Horan, Pearson, Silver, & Jarvis, 1999) This high incidence of SSIs is due to the increasing number of surgeries. (Setiawan, 2011) The NNIS states that 38% of nosocomial infections among surgical patients are SSIs and, among all hospitalized patients, SSIs occupy between 4% and 16% of all nosocomial infections. (Spear, 2008) In Canada, two million surgeries are performed per year and 50,000 SSIs occur, accounting for approximately 14 to 16% of all hospital-acquired infections. However, 40 to 60% of all SSIs are considered preventable. (McElroy) Therefore, there is a need to implement effective prevention interventions. Reported rates of SSI are most likely underestimates since a majority of the SSIs occur after discharge and, as a result, are never included in federal and provincial records. In 2009, the study conducted by McIntyre et al. showed that 50% of all SSIs were diagnosed after discharge. (McIntyre, Warner, Nester, & Nathens, 2009)

SSIs have long-term effects for the patient and for society. These surgical complications increase hospital costs, the length of the hospital stay and morbidity, disability and mortality rates. (Setiawan, 2011) (Mangram, Horan,

Pearson, Silver, & Jarvis, 1999) Globally, 77% of all surgical patient deaths are related to infections (Mangram, Horan, Pearson, Silver, & Jarvis, 1999) and, compared to non-infected patients, SSI patients are twice as likely to die, are 60% more likely to stay in the Intensive Care Unit (ICU) and are five times more likely to be readmitted to hospital after discharge.

If a patient develops an SSI, he/she will also require additional treatment and therefore this complication will extend the hospital stay by an average of 16.8 days. The patient's hospital costs will also rise. These expenses can reach over $35,000 if the causing bacteria are MRSA (methicillin-resistant *Staphylococcus aureus*) which do not respond to antibiotics. (Kirkland, Briggs, Trivette, Wilkinson, & Sexton, 1999) Any surgical complication, including SSIs, will cause an added burden on the patient that may affect his/her overall health post-surgically. (Barie, Nichols, & Wilson, 2006)

All surgical patients are at risk of developing an SSI since natural flora bacteria such as *Staphylococcus aureus* can cause opportunistic infections particularly if they are immunocompromised. (Tietjen, Bossemeyer, & McIntosh, 2003) Furthermore, SSIs can occur following any type of surgery. Also, due to the increase of resistant bacteria in the community which incurs added difficulty of treating infections, more effort must be devoted to prevent SSIs as opposed to discovering new treatments. (Setiawan, 2011) (Tietjen, Bossemeyer, & McIntosh, 2003)

There are known risk factors that can predispose a patient to develop an SSI. Some of these elements are dependent on the surgical staff and the hospital while others are patient-dependent related to his/her lifestyle presurgically. (Spear, 2008)

Objectives: Identification of patients at increased risk for an SSI can lead to focused interventions for these populations. This more devoted and focused approach to prevention should be easier to implement compared to general policies. The aim of the current study will be to develop a user-friendly quantitative tool for identifying patients at high risk for an SSI.

Rationale: To date there is no quantitative tool for measuring the risk of an SSI. Identifying patients at high risk for an SSI can increase the effectiveness of preventive intervention with controlling costs.

II. Review of the Literature

Definition and characteristics of SSIs. According to the Centers for Disease Control and Prevention (CDC), a surgical site infection is defined as a nosocomial infection occurring on the surgical site within 30 days of an operation and up to one year following an implant surgery. (Mangram, Horan, Pearson, Silver, & Jarvis, 1999) SSIs can be classified into three categories: superficial incisional SSI, deep incisional SSI and organ/space SSI. Information characterizing these infections is shown in Table I.

Causes of SSIs. The cause of an SSI is the entry of a pathogenic microorganism in the body in the area of the surgical incision. Most often, the causing bacteria originate from the patient's endogenous flora present on the skin, mucous membranes or hollow viscera. Many factors determine whether an infection will occur or not, such as the bacterial inoculum, its virulence and the effect of the microenvironment. A larger incision will permit a high amount of potentially pathogenic bacteria to enter the organism and cause an opportunistic infection.

Table I: Classification and criteria of diagnosis of surgical site infections
(Mangram, Horan, Pearson, Silver, & Jarvis, 1999)(Setiawan, 2011)(Horan, Gaynes, Martone, Jarvis, & Emori, 1992)

Type of SSI	Characteristics of the infection
Superficial incisional	Infection involves only the skin or subcutaneous tissue. Also presents with one or more of the following characteristics:
	- Purulent drainage from superficial incision (with or without laboratory confirmation).
	- Isolated organisms from a culture of fluid or tissue from the superficial incision obtained aseptically.
	- At least one of the symptoms of infection: pain or tenderness, localized swelling, redness, or heat *and* superficial incision has been opened by the surgeon intentionally.
	- The diagnosis of a superficial incisional SSI may be made by a surgeon or attending physician.
Deep incisional	Infection involves deep soft tissues (such as the fascial and muscle layers) of the incision. Also presents with one or more of the following characteristics:
	- Purulent drainage from deep incision of the surgical site (not from the organ/space).
	- Deep incision spontaneously dehisces or is intentionally opened by the surgeon when the patient has at minimum one of the following signs or symptoms: fever (>38^{o}C), localized pain, or tenderness.
	- The diagnosis of a deep incisional SSI may be made by a surgeon or attending physician.
Organ/space	Involves any part of the anatomy (such as organs or spaces), other than the incision, which has been opened or manipulated during surgery. Must also present with at least one of the following criteria:
	- Purulent drainage from a drain placed through a stab wound into the organ/space.
	- Organisms have been isolated aseptically from a culture of fluid or tissue which is in the organ/space.
	- An abscess or other evidence of a present infection involving the organ/space of the surgical site is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
	- The diagnosis of an organ/space SSI may be made by a surgeon or attending physician.

This is why laparoscopic surgeries are associated with a decreased amount of SSIs. For instance, Boni et al. observed that 1.1% and 4% of patients undergoing cholecystectomies laparoscopically and with open surgery, respectively, had a surgical site infection. Moreover, bacteria virulence also affects the development of the infection. Highly virulent bacteria can produce toxins or other factors that increase their chance of invading a tissue and causing infection. (Boni, et al., 2006) Finally, the resistance of the patient is correlated with the risk of infection. An immunocompromised patient is more likely to develop an SSI than an immunocompetent patient. (Spear, 2008) (Boni, et al., 2006) One can calculate the overall risk of acquiring an SSI using the effect of the three factors mentioned above using the following formula: Risk of SSI = (Dose of bacterial contamination) X (virulence) / (Resistance of patient) (Boni, et al., 2006)

The pathogens that cause post-surgical wound infections are most often Gram-positive cocci (notably *Staphylococci*) but this varies according to the type of bacteria present near the area. Groin/perineal infections are typically caused by Gram-negative bacteria. Moreover, SSIs following gastrointestinal surgery are most likely caused by one of the bacteria in the intrinsic bowel flora, for example Gram-negative bacilli (such as *Escherichia coli*) and other Gram-positive microbes. Overall, the most common microorganism that causes SSIs is *Staphylococcus aureus*. These cause approximately 20% of all SSIs, followed by coagulase-negative *Staphylococci* (14%) and *Enterococci* (12%). (Mangram, Horan, Pearson, Silver, & Jarvis, 1999)

Risk factors of SSIs. The risk of acquiring an SSI is strongly correlated with the type of surgery. The classification of surgeries can be found on Table II.

Table II: Classification of surgeries according to operative wound (Setiawan, 2011) (Mangram, Horan, Pearson, Silver, & Jarvis, 1999)

Type of operation	Characteristics	Incidence of SSIs
Class I Clean	Involves "uninfected operative wound in which the respiratory, gastrointestinal and genitourinary tracts were not entered; including incisional surgery due to blunt trauma". (Setiawan, 2011)	<2%
Class II Clean-Contaminated	Enters the respiratory, gastrointestinal and/or urinary tracts however no unusual contamination has occurred.	5-15%
Class III Contaminated	Procedure on an open wound with major breaks in sterile technique.	15-30%
Class IV Dirty/Infected	Surgery on an old wound with dead tissue or involved existing infection or perforated bowel. The pathogens that cause SSI were present at the site before the operation.	>30%

Clearly, the level of contamination influences the risk of acquiring an SSI. A patient undergoing a dirty surgery is much more likely to develop an SSI than a patient undergoing a clean surgery not only because of the type and quantity of bacteria present, but also because of the length of the surgery and the surgeon's technique. (Setiawan, 2011) (Mangram, Horan, Pearson, Silver, & Jarvis, 1999) It is however important to consider other factors in the risk of developing an SSI.

Research on risk factors for SSIs typically focuses on individual variables. Studies done by Miki et al., Korinek et al., Jeong et al., Tang et al. and Askarian et al.

show that male sex is an independent risk factor for SSI. (Miki, Inoue, Mohri, Kobayashi, & Kusunoki, 2006) (Korinek, et al., 2005) (Jeong, et al., 2012) (Tang, et al., 2001) (Askarian, Yadollahi, & Assadian, 2012)

Obesity could increase a patient's risk of surgical site infection. (Harrop, Styliaras, Cher Ooi, Radcliff, Vaccaro, & Wu, 2012) (Lynch, Ranney, Shijie, Lee, Samala, & Englesbe, 2009) Since the patient has a larger skin surface, and therefore more bacteria on the skin, the risk of bacteria entering the organism during surgery is larger. Also, the surgeon must make a larger and deeper incision in order to reach the organ of interest. This increases the number of pathogenic microorganisms entering the body and hence the risk of SSI rises. In fact, the risk of superficial incisional SSI is increased "because of the amount of dead space created during surgical wound closure and associated local fat necrosis". (Harrop, Styliaras, Cher Ooi, Radcliff, Vaccaro, & Wu, 2012) A study conducted by Giles et al. including patients who underwent lower extremity bypass demonstrated that obesity independently predicts postoperative SSI. (Giles, Hamdan, Pomposelli, Wyers, Siracuse, & Schermerhorn, 2010)

Another important risk factor for the development of SSI is diabetes. More than 9 million Canadians have been diagnosed with diabetes or prediabetes. (Canadian-Diabetes-Association, 2012) Diabetes is a risk factor for many other illnesses and complications, such as heart failure, kidney disease, bone and joint disorders, ocular complications and nerve disease. (MedlinePlus, 2012) (Morricone, et al.,

1999) (McCormack & Leith, 1998) The glucose level in the blood also diminishes immune function and thus increases the risk of developing an SSI. The study conducted by Ferrazzi et al. showed that, of the patients who underwent CABG surgery (coronary artery bypass graft), 35% to 50% of patients with complications (including SSI) had diabetes. (Ferrazzi, Allen, Crupi, Reyes, Parenzan, & Maisonnet, 1986) It is important that surgical patients have their glucose levels monitored prior to surgery by testing for fasting serum glucose (FSG) and Hemoglobin A1c (HbA1c), which will evaluate the presence or absence of diabetes. If the tests are positive and the surgery is elective, the procedure should be postponed while the patient's diet is altered to follow a predetermined regimen that has been shown to control serum glucose levels. (Dronge, Perkal, Kancir, Concato, Aslan, & Rosenthal, 2006) (Hoogwerf, 2006) In fact, the majority of surgical patients experience perioperative hyperglycemia, even if they are not insulin resistant or diabetic. Some believe that this predisposes the patient to an SSI even if not diabetic; however this is not a consensus among scientists. (Helblad, Nilsson, Engstrom, Berglund, & Janzon, 2002) (Parsons, et al., 2002)

Some have shown that preoperative hyperglycemia is a risk factor for postoperative mortality and morbidity, including SSI. Capes et al. conducted a meta-analysis which showed that non-diabetic patients with glucose ranging from 6.1 to 9.0 mmol/L had an increased risk (RR = 3.9) of morbidity or mortality. They also stated that non-diabetic patients with higher levels of glucose (above 8.0 mmol/L) had an increased risk of cardiovascular complications such as

congestive heart failure or cardiogenic shock. (Capes, Hunt, Malmberg, & Gerstein, 2000)

Proper nutrition can prevent any sort of surgical complications, including nosocomial infections. (Ulicny & Hiratzka, 1991) (Sungurtekin, Sungurtekin, Balci, Zencir, & Erdem, 2004) (Nozoe, Kimura, Ishida, Saeki, Korenaga, & Sugimachi, 2002) Conversely, malnutrition can predispose a patient to develop an SSI postsurgically. For instance, a prospective, randomized, double-blind trial by Snyderman et al. that studied oncologic surgical patients determined that perioperative adequate nutrition diminished the patient's risk of postoperative infection considerably compared to patients not provided with the nutritional supplemented formula. In fact, 25% of the Impact groups (who received supplemental nutrition) developed a postoperative infection compared to 41% of the "Standard" groups who acquired a nosocomial infection. Of these hospital-acquired infections, 18% were SSIs, 44% involved the lungs, 15% involved the gastrointestinal tract, 8% involved the genitourinary tract and 15% occurred in other sites. (Snyderman, et al., 1999)

Malnutrition can also be linked to a high weight loss (more than 10% of the patient's body mass) six months or less before surgery. Malone et al. found a significant association between the amount of weight loss and SSI risk. In their study, 12.3% of patients who lost more than 10% of their body weight had an SSI as opposed to 7.1% of patients who maintained their body weight. (Malone, Genuit, Tracy, Gannon, & Napolitano, 2002)

There has been much evidence that tobacco use has many negative health effects. One of these is that smoking can predispose a surgical patient to a postoperative infection. In the study by Jacob et al., mice exposed to a water-soluble condensate of tobacco smoke (WSC) were incapable of responding to an antigen due to the immunosuppression of T lymphocytes in their spleens. The T cells were also unable to interact with B cells and macrophages to appropriately destroy the antigen. This effect was not observed in the mice not exposed to WSC; therefore one can conclude that smoking is a risk factor for any type of infection, including SSI. (Jacob, Stelzer, & Wallace, 1980) Tobacco has many components that decrease many immune cells' function. (Sopori, 2002) (Stämpfli & Anderson, 2009) For instance, nicotine skews the effector macrophage function towards the T_H-2 type immune response, hydrocarbons affect gene regulation mediated by loop-helix-loop proteins and adaptively upregulates metabolic and bio-transforming enzymes, not to mention the multiple effects of the oxidants and reactive nitrogen moieties in the tobacco. (Stämpfli & Anderson, 2009) As a result, it is not surprising that, in a study by Delgado-Rodriguez et al., past smokers had an increased risk of SSI (adjusted OR = 1.46, CI 95% = 1.02-2.09). This however was not observed with current smokers. Furthermore, a long history of smoking (≥51 pack-years) increases the patient's risk of staying in the intensive care unit (adjusted OR = 2.86, CI 95% = 1.21-6.77) and of dying in the hospital (adjusted OR = 2.56, CI 95% = 1.10-5.97). (Delgado-Rodriguez, et al., 2003) Smoking has other consequences that affect SSI development and healing. For

example, one of the effects of smoking is decreased circulation of oxygen in the bloodstream. This has many consequences during and following surgery. Oxygen stimulates the immune system to kill antigens and promotes wound healing. Consequently, the wound of a patient who smokes will heal slower than a non-smoking patient. (Haridas & Malangoni, 2008)

Alcohol abuse has been identified as an independent risk factor for SSIs. Tonnesen et al. found elevated rates of morbidity following colorectal surgeries in patients who consumed 60 gm or more of alcohol daily. Thirty percent of the complications consisted of SSIs. (Tonnesen, et al., 1992) (Rantala, Lehtonen, & Njinikoski, 1997) However, the exact mechanism of the interaction between alcohol and the immune system is currently unknown. (Rantala, Lehtonen, & Njinikoski, 1997) (Tonnesen, et al., 1992) It is however known that alcohol affects many physiological systems such as the hemostatic, cardiovascular, central nervous system and the immune systems. (Tonnesen, et al., 1992)

Functional status prior to surgery is an important risk factor for postoperative surgical site infection caused by Methicillin-Resistant *Staphylococcus aureus* (MRSA). As will be discussed later, it is difficult to treat an infection caused by resistant bacteria, such as MRSA, with common antibiotics. Anderson et al. compared patients infected by MRSA to two groups: to patients infected with MSSA (Methicillin-Sensitive *Staphylococcus aureus*) and to uninfected patients.

The need for assistance with 3 or more daily activities increases the patient's risk of developing an SSI. In fact, the OR for SSI of the dependent patients compared with uninfected patients was 3.97. The OR for SSI of the dependent patients compared to patients infected with MSSA was 3.88. We can therefore state that functional status can increase the risk of mortality and of hospital stay since infections caused by resistant bacteria are more difficult to treat. Anderson et al. further state that poor functional status is an important risk factor for SSI regardless of the patient's age. (Anderson, et al., 2008) It has yet to be shown if functional status preoperatively is an independent risk factor for SSI caused by bacteria other than MRSA. Further studies are required to make this type of association.

Patients with chronic obstructive pulmonary disease (COPD) also have an increased risk of SSI due to the lower amount of oxygen circulating in the patient's body. Oxygen stimulates the immune system to kill pathogenic microorganisms. Furthermore, tissue oxygenation accelerates wound healing. One could therefore assume that a patient with COPD has an increased risk of postoperative SSI and, also, the wound of this type of patient will heal at a slower pace than patients with a healthy respiratory system. (Haridas & Malangoni, 2008)

Hypertension is another risk factor for SSIs. Many researchers have found that patients with elevated blood pressure have an increased risk of developing an SSI.

Cardoso Del Monte et al. demonstrated that female hypertensive patients who underwent a cesarean section had an RR of 2.47 (95% CI, 1.21-5.04) of developing an SSI compared to patients with healthy blood pressure who underwent the same procedure. (Cardoso Del Monte & Pinto Neto, 2010) Also, the meta-analysis by Xue et al. shows that hypertensive patients undergoing breast surgery have an increased risk of 1.69 (RR) of acquiring an SSI as opposed to non-hypertensive patients. (Xue, Qian, Yang, & Wang, 2012)

A patient with a pre-exisiting auto-immune illness who has been prescribed corticosteroids will have a weakened immune system since these drugs target immune cells to diminish auto-immune symptoms such as inflammation. Therefore, a patient who undergoes surgery who presents with a weakened immune system has an increased risk of developing any sort of postoperative infection, including SSI. Lee et al. confirm the fact that steroid use is one of the risk factors predisposing surgical patients undergoing midline laparotomies to SSIs. (Lee, et al., 2011)

Disseminated cancer is also a risk factor in the development of an SSI postsurgically since it affects the regulation of at least two organs and therefore modifies the body's homeostasis. This could affect the patient's ability to combat infection. In fact, SSI consists of the most frequent comorbidity following

colorectal oncologic surgeries. (Biondo, Kresisler, Fraccalvieri, Basany, Codina-Cazador, & Ortiz, 2012)

Chemotherapy and radiotherapy are two processes that can affect many cells of the organism, including white blood cells, and therefore the ability to kill pathogens. However, the processes in which the two procedures affect the immune system differ. In the case of chemotherapy, for the treatment to be effective, the drugs must interact with the immune system. Therefore, a patient undergoing chemotherapy will have an increased risk of infection since the immune system is already attempting to destroy the cancerous cells. (McDonnell, Nowak, & Lake, 2011) Radiotherapy, on the other hand, damages cancerous cells as well as human cells. The latter cells can repair themselves as opposed to neoplastic cells which do not possess the ability to do so. Nonetheless, many cells of the immune system are vastly affected by radiotherapy and these effects could persist for a long period of time. Following external beam radiotherapy (RT), Standish et al. observed that women with stage I-III breast cancer presented with lymphopenia, low functional activity of natural killer (NK) lymphocytes, decreased monocyte phagocytosis and decreased production of the anti-inflammatory cytokine TNF-alpha. Lymphocyte count did not increase in the duration of the six-week follow-up period. However, the patients did not experience neutropenia, anemia or interferon-gamma production. These results demonstrate the large effect of radiotherapy on the immune system and on the diminishment of its ability to combat infection (Standish, et al., 2008)

Finally, many researchers use the ASA score to predict SSI risk since it categorizes patients according to their general health. An ASA of 1 indicates that a patient is healthy as opposed to an ASA of 5 which states that the patient is moribund and is not expected to survive regardless if he/she has a surgery. However, Peersman et al. concluded that this "is not a good predictor of infection" unless it is cross-checked with present co-morbidities, for example current infections. (Peersman, Laskin, Davis, Peterseon, & Richart, 2008)

Most of these risk factors are in the patient's control and can be modified. For instance, obesity, diabetes, nutrition, tobacco use, functional status, COPD, cardiac failure and hypertension are elements that can be regulated by the patient. On the other hand, some risk factors, such as admission status of the patient (inpatient/outpatient), the anesthesia technique and the level of the resident are controlled by the surgical staff. Some factors cannot be controlled by the patient or by the surgical staff, such as gender, auto-immune illness, state of the case (emergent/elective), sepsis, the patient's transfer origin, the wound classification, surgical subspecialty of the operation and the ASA class. It is however important for the surgical staff to closely monitor all co-morbidities and every aspect of the case to adequately prepare for surgery and for possible postsurgical complications such as SSI.

If a risk factor is modifiable by the patient or by the surgical staff, every precaution should be taken to prevent surgical complications. For instance, the

patient should consume a healthy diet regularly in his/her daily life prior to surgery to prevent obesity, type 2 diabetes mellitus, malnutrition, cardiac failure and hypertension. Regular exercise will also maintain the patient's health and will keep him/her physically functional prior to surgery. The individual should also avoid tobacco and not abuse alcohol. Moreover, the surgical staff should monitor the patient's nutrition before surgery. Finally, if the patient has cancer and must undergo chemotherapy or radiotherapy, it is preferable for these to occur after the surgery to maximize the immune system's ability to fight infection. If the risk factors are not monitored by the patient and by the surgical staff, the patient has an increased risk of postsurgical consequences, such as surgical site infection. This complication could contribute to the many added costs, length of stay in the hospital, possibility of entering the ICU and risk of mortality. (Setiawan, 2011) (Mangram, Horan, Pearson, Silver, & Jarvis, 1999)

Bacterial resistance and treatments of SSIs. Treatments for SSIs differ depending on the specific case. Most cases are treated by debridement of the wound and/or by administering intravenous antibiotics, depending on the severity of the case. (Pull ter Gunne, Mohamed, Skolasky, van Laarhoven, & Cohen, 2010) (Mulholland & Doherty, 2011)

Nonetheless, treatment is difficult if the infection is caused by resistant bacteria such as MRSA or VRE (vancomycin-resistant *Enterococci*). Many beta-lactam-based antibiotics, such as cephalosporins and penicillins, have proven to be

ineffective to treat infections caused by resistant strains of bacteria, the most common and known in the scientific community being MRSA, a *Staphylococcus aureus*. Many bacteria have acquired resistance in nature by genetically exchanging genes located on plasmids known as cassettes, such as *mec* for *S. aureus* strains. (Barie, Nichols, & Wilson, 2006) (van Duijn, Dautzenberg, & Oostdijk, 2011) Many healthy individuals possess these strains without even having knowledge of it, since these bacteria are generally on the flora of human beings yet do not cause infection. However, in the case of individuals with an altered immune system, such as surgical patients, if these bacteria move to another part of the organism than where they usually reside in, for example during surgery, they can cause opportunistic infections.

The problem with resistant bacteria escalated in the mid-1980s when antibiotics were initially overused. This caused the gradual emergence of resistant strains of bacteria. For instance, in 1987, close to 20% of the *S. aureus* strains were MRSA and this rate climbed to 59% in 2004. (Barie, Nichols, & Wilson, 2006) (Lowy, 1998) (NNIS, 2004) This rise of bacterial resistance is not showing any signs of stabilizing or declining. (Barie, Nichols, & Wilson, 2006) (Rao, 1998) Moreover, treatment of an infection caused by resistant bacteria is very difficult since the microorganisms have developed mechanisms to prevent the antibiotics' activity or to not be perceived by the drug by modifying bacterial properties. Also, an infection caused by resistant bacteria will extend the patient's hospital stay and increase his/her hospital costs, not to mention the patient's added emotional and

physical burden. These reasons are why the surgical staff must always focus on prevention of SSI rather than treating an infection after it arises.

*Current SSI prophylactic guidelines at the Jewish General Hospital. A*t the JGH in Montreal, guidelines have been created in order to prevent SSIs. The surgical department implemented an SSI prevention program in 2008, which includes six main guidelines: proper administration of prophylactic antibiotics, timing and location of hair removal prior to surgery, preoperative warming of the patient, adequate skin preparation, maintenance of perioperative glucose and adequate nutritional support. Firstly, prophylactic antibiotics must be administered within one hour of surgery and the infusion must be completed before the initial incision is made. It is also important to properly choose the antibiotic according the most probable bacteria entering the body during surgery. In order to accomplish this task, a guide is present in every Operating Room (OR) in the JGH to choose the appropriate drug for each surgical procedure. It is also essential to keep in mind to administer additional doses every four hours in the cases of long operations. Secondly, appropriate hair removal is important to prevent SSIs. If possible, no hair removal is the best option in this regard, however in many cases it is required to clear the skin (where the incision will be made) of any hair. If necessary, clipping the hair is the recommended guideline and should be done as close to the beginning of surgery as possible. Thirdly, hypothermia of the patient must be avoided at all costs due to the many effects of temperature on the immune system, as mentioned earlier. The patient should be warmed with forced-air as well as

with a blanket intraoperatively. The ambient temperature in the OR should also be monitored. Other precautions to be taken are that the patient should wear hats and booties perioperatively and receive warm liquid lavages. In the case of abdominal surgeries, the patient should receive warmed IV fluids. Furthermore, an adequate antiseptic skin preparation of chlorexhidine should be administered twice before surgery (one preoperative shower the night preceding surgery and one the morning of the surgery). Moreover, the patient's glucose levels must be maintained perioperatively and be tested the day prior to surgery and the day of the operation. All these precautions as well as adequate nutritional support are current guidelines at the JGH in the surgical department and they will decrease all patients' risk of developing a surgical site infection. (Morin et al., April 2012) However, the same prophylactic measures are provided for every surgical patient even though many high-risk patients may require additional care or other low-risk patients do not necessitate certain measures such as prophylactic antibiotic administration. The risk-index tool created in this M.Sc. project will provide the knowledge to determine which patients are considered low-risk, moderate-risk and high-risk which will subsequently allow appropriate prophylactic SSI management.

SSI facts of common surgeries in accordance with NICE guidelines. The National Institute of Clinical Excellence (NICE) has drafted a document which includes all studies concerning SSIs and the adequate precautions for many types of surgeries. (Collier, et al., 2008) This document includes guidelines for the most common

cardiac surgery, the coronary artery bypass graft (CABG) (Benetis, 2005) (Crestanello, et al., 2012) (Hekmat, et al.,2005), as well as the most common general surgery, the hernia repair (hernioplasty) (Rutkow & Robbins, 1993) (Bringman, et al., 2003). The most common orthopedic and spinal surgeries are knee arthroscopy and lumbar discectomy, respectively. (Lubowitz & Appleby, 2011) (Rose, 2008) (Babcock, Matava, & Fraser, 2002) (Parker, et al., 2010) (Nandoe Tewarie, Bartels, & Peul, 2007) (DeBerard, LaCaille, Spielmans, Colledge, & Parlin, 2009) Unfortunately, no information entailing SSI prevention is provided concerning these two types of surgeries.

The NICE guidelines have detailed several methods to diminish SSIs following CABG surgery. For instance, one study proved that antibiotic prophylaxis was effective in reducing SSI rates. In fact, patients who were administered prophylactic antibiotic had an OR of 0.08 compared to patients who received a placebo preoperatively (95% CI 0.03-0.27). However, a variety of other studies examining the effectiveness of disposable or reusable gowns, antiseptic skin preparation and closing of the skin (staples or sutures) showed no statistical difference between the tested methods. (Collier, et al., 2008)

Additional information was provided concerning SSI prevention for hernia repairs (hernioplasties). For example, antibiotic prophylaxis was also shown to be effective in preventing surgical site infections compared to administration of a placebo preoperatively (OR 0.48, 95% CI 0.27-0.85). Moreover, there was no statistical difference while studying the effectiveness of disposable or reusable drapes and gowns in the prevention of SSIs for elective surgeries (of which the

majority of surgeries were hernia repairs and uncomplicated cholecystectomies). (Collier, et al., 2008)

As a result of these conclusions, NICE has composed a set of guidelines concerning SSI prevention separated into preoperative, intraoperative and postoperative phases. In the preoperative phase, it is advised that patients bathe the night before or the morning of the surgery. Furthermore, if necessary to remove the hair of the surgical site, NICE suggests utilizing electric clippers with a single-use disposable head on the day of the surgery. Antibiotic prophylaxis is recommended prior to clean-contaminated and contaminated surgery. If the clean surgery involves the placement of a prosthesis or an implant, it is also recommended to give prophylactic antibiotics and, in the case of dirty or infected surgeries, it is advised to administer additional antibiotic treatment. The staff should also be dressed appropriately in specific non-sterile theatre wear. (Collier, et al., 2008)

Intraoperatively, NICE recommends the operating team to wear sterile gowns and wash their nails and hands using an antiseptic surgical solution (as well as prior to any subsequent operations). The patient's skin should be prepared with an antiseptic preparation, such as povidone-iodine or chlorhexidine, immediately before the first incision. In addition, patient homeostasis should be closely monitored throughout the procedure. For instance, patient temperature should be maintained and should not become hypothermic. Optimal oxygenation during and

following surgery (haemoglobin saturation above 95%) and adequate perfusion are essential.

Following surgery, the main guideline is the adequate dressing and cleansing of the wound. An aseptic non-touch technique is appropriate for changing or removing dressings and sterile saline is utilized to cleanse the wound for up to 48 hours following surgery (after use regular tap water if the wound has been opened). If an SSI is suspected, antibiotic treatment should be given. Once again, it is important to choose the proper antibiotic which targets the most likely pathogen. It is important to recall resistance patterns during the selection of the drug.

III. Methods

Data Acquisition. Data was obtained from electronic medical records from the NSQIP (National Surgical Quality Improvement Program) database in the Jewish General Hospital. This information concerning SSI risk factors was acquired in May 2012.

The NSQIP database was created in 2009 and includes all patients who underwent surgery at the Jewish General Hospital. The database constitutes a valid, prospective, non-biased and comprehensive source of records. By utilizing this database, selection bias is eliminated. However, one inconvenient of NSQIP is the generalization of patients.

Thirty-seven potential risk factors were evaluated to assess their association with an SSI. All risk factors included in the database were included in the project in order to make as many conclusions as possible concerning which risk factors could predispose a patient to an SSI. Table III describes the classification of the risk factors. The outcomes evaluated were as follows: any type of SSI, postoperative superficial incisional SSI, postoperative deep incisional SSI, postoperative organ/space SSI.

Patient Population. Inclusion criteria consisted of all surgical cases in the NSQIP database from November 2009 to December 2011. In total, data concerning 2907 patients was acquired. Surgical cases were categorized according to the type of procedure performed. The patients who underwent operations with no incision and those whose hospital stay did not exceed 24 hours were excluded from the study population.

Table III: Criteria and their variables included in statistical analyses

Criteria	Variables
Gender	Male; Female
Patient status	Inpatient; Outpatient
Emergent surgery status	Elective; Emergent
Transfer origin	Not transferred, admitted directly from home; Transfer from other or inpatient
Anesthesia technique	General; Spinal, local, epidural, regional or MAC
Surgical subspecialty	Vascular; General
BMI	Normal (BMI 18.5 to 25); Under/overweight (below 18.5 or above 25)
Diabetes	Non-diabetic; Diabetic (type I or II)
Smoker	No; Yes
Alcohol abuse	No; Yes
Dyspnea	No; Yes (upon moderate exertion or at rest)
Functional status prior to surgery	Independent; Partially or totally dependent
Ventilator usage	No; Yes
COPD	No; Yes
Pneumonia[1]	No; Yes
Congestive heart failure[2]	No; Yes
Myocardial infarction[3]	No; Yes
History of angina[2]	No; Yes
Hypertension[4]	No; Yes
PVD[5]	No; Yes

Gangrene[6]	No; Yes
Renal failure[7]	No; Yes
Dialysis[8]	No; Yes
Disseminated cancer	No; Yes
Open wound[9]	No; Yes
Steroid use[10]	No; Yes
Weight loss >10%[11]	No; Yes
Bleeding disorders	No; Yes
Preoperative transfusion[12]	No; Yes
Chemotherapy[13]	No; Yes
Radiotherapy[13]	No; Yes
Sepsis[14]	No; Yes (SIRS, sepsis or septic shock)
Highest level of resident	5 to 8 years of residency; 0 to 4 years of residency
Wound classification	Class I or II (clean or clean-contaminated); Class III or IV (contaminated or dirty/infected)
ASA class	ASA 1 or 2 (no disturb or mild disturb); ASA 3 or 4 (severe disturb or life threat)
Other procedures[15]	No; Yes
Concurrent procedures[16]	No; Yes

1 Patient must be on current antibiotic treatment at the time he/she is brought to the OR; must meet specific radiologic and symptomatic criteria.
2 Within 30 days prior to surgery.
3 Within 6 months prior to surgery.
4 Patient has persistent elevation of systolic blood pressure >140 mmHg **or** a diastolic pressure >90mmHg **or** requires an antihypertensive treatment at the time the patient is being considered as a candidate for surgery.
5 A history of any type of angioplasty or revascularization procedure for atherosclerotic PVD or a patient who has had any type of amputation procedure for PVD.
6 Rest pain or gangrene. Includes patients with ischemic ulceration and/or tissue loss related to peripheral vascular disease. Does not include Fournier's gangrene.
7 Elevated levels of BUN and creatinine (the latter above 3 mg/dl).
8 Currently requiring or on dialysis.
9 With or without infection. The wound must communicate to the air by direct exposure.
10 Patient has required the regular administration of oral or parenteral corticosteroid medications in the 30 days prior to surgery for a chronic medical condition.
11 Within 6 months prior to surgery. Patients who have intentionally lost weight are excluded.
12 Preoperative blood loss necessitating any transfusion (minimum of 1 unit) of whole blood/packed red cells transfused during the 72 hours prior to surgery.
13 Within 90 days prior to surgery.
14 Within 48 hours prior to surgery. Includes any case of SIRS, sepsis or septic shock.
15 An additional operative procedure performed by the same surgical team under the same anesthetic which has a CPT code different from that of the Principal Operative Procedure.
16 An additional operative procedure performed by a different surgical team under the same anesthetic which has a CPT code different from that of the Principal Operative Procedure.

Data adjustments. All data adjustments are shown in Table IV. It is important to mention that all criteria were transformed into numerical value where 1 was the risk factor and 0 was not in order to follow with statistical analyses.

Table IV: Criteria in original classifications and following adjustments

Criteria	Original classification	Altered classification
Transfer origin	1. Not transferred, admitted directly from home 2. Acute care hospital (inpatient) 3. Nursing home/ chronic care facility/ intermediate care unit 4. Transfer from other 5. Transfer from outside Emergency Department	0. Not transferred, admitted directly from home 1. Transfer from other or inpatient
Anesthesia technique	1. General 2. Epidural 3. Spinal 4. Regional 5. Local 6. Monitored anesthesia care (MAC) 7. Other 8. None	0. Spinal, local, epidural, regional or MAC 1. General
BMI	In numerical values	0. Normal (BMI between 18.5 and 25) 1. Under/overweight (below 18.5 or above 25)
Diabetes	1. Non-diabetic 2. Diabetic requiring therapy with a non-insulin anti-diabetic agent 3. Diabetic requiring insulin therapy	0. Non-diabetic 1. Diabetic (type I or II)
Dyspnea	1. No dyspnea 2. Dyspnea upon moderate exertion 3. Dyspnea at rest	0. No dyspnea 1. Dyspnea (upon moderate exertion or at rest)
Functional status prior to surgery	1. Independent 2. Partially dependent 3. Totally dependent	0. Independent 1. Partially or totally dependent
Sepsis	1. No sepsis	0. No sepsis

	2. SIRS 3. Sepsis 4. Septic shock	1. Sepsis (including SIRS and septic shock)
Highest level of resident	In numerical values (each year is equivalent to 1)	0. 5 to 8 years of residency 1. 0 to 4 years of residency
Wound classification	1. Class I clean 2. Class II clean-contaminated 3. Class III contaminated 4. Class IV dirty/infected	0. Class I or II (clean or clean-contaminated) 1. Class III or IV (contaminated or dirty/infected)
ASA class	1. ASA 1 (no disturb) 2. ASA 2 (mild disturb) 3. ASA 3 (severe disturb) 4. ASA 4 (life threat) Note: No patients had an ASA of 5.	0. ASA 1 or 2 1. ASA 3 or 4
Other procedures	In numerical values (for example, if two procedures were performed: the value of 2 was noted)	0. No other procedures 1. Yes, two or more procedures

Statistical Analyses. All statistical analyses were performed using the Statistical Packages for Social Sciences v16.0 (SPSS). In order to determine all potential significant risk factors that predispose a patient for developing an SSI (in general), a superficial incisional SSI, a deep incisional SSI and an organ/space SSI, bivariate binary logistic regression analyses and Chi Square tests were performed. All results with p-values under 0.05 were considered significant. Those factors with a significant association for SSI risk with bivariate analysis were entered in a multivariate logistic regression model.

The variables that remained significantly associated with the risk of an SSI in the multivariate logistic regression analysis were used to develop the SSI risk score. The weight of each variable was a function of the logistic regression parameter

estimate. More specifically the weight was the proportion of the variable parameter estimate to the score of the parameter estimates over all variables. Therefore the total score will have a range between 0 and 100.

Each patient was assigned an SSI score based on the presence or absence of each risk factor. To establish the cutoff values defining low, moderate and high-risk patients, ROC curve analyses were used.

The SSI score classification was validated using logistic regression models to assess the relative rate of observed SSIs in moderate and high-risk patients in comparison to the low-risk group.

IV. Results

Patient Characteristics. Two thousand nine-hundred and seven patients were included in the analyses. Fifty and a half percent (1468) of the patients were male and the majority were inpatients (68.2%; 1982 patients). The mean patient age was 61 years old though the age range varied from 18 to 95 years old. In total, 260 different types of surgeries were performed. The most common surgeries were as follows: laparoscopic cholecystectomy (254 surgeries, 8.8%), partial colectomy (244 surgeries, 8.4%), partial mastectomy (167 surgeries, 5.8%), laparoscopic appendectomy (166 surgeries, 5.7%) and open appendectomy (102 surgeries, 3.5%). Tables V, VI and VII describe the patient population.

Table V: Characteristics of age of the NSQIP patient population

	Minimum	Maximum	Mean
Age	18	95	61

Table VI: Characteristics of gender of the NSQIP patient population

	Number of patients	Percentage
Male	1468	50.5
Female	1437	49.5

Table VII: Most frequently performed surgeries of the NSQIP database

Type of surgery	Number of surgeries	Percentage
Partial mastectomy	167	5.8
Partial colectomy	244	8.4
Appendectomy	102	3.5
Laparoscopic appendectomy	166	5.7
Laparoscopic cholecystectomy	254	8.8

Note: All surgeries that constitute more than 3% of total surgeries were included in this table.

Concerning SSI outcome, 5.2% (148) of the patients developed a superficial incisional SSI, 0.3% (9) of the patients acquired a deep incisional SSI and 3.9% (111) of patients developed an organ/space SSI. Overall, Table VIII shows that 9.2% (268) of the 2907 patients developed any type of surgical site infection.

Table VIII: Frequency distribution of SSIs (any type, superficial incisional, deep incisional and organ/space)

Type of SSI	Number of infections	Percentage
Any type of SSI	268	9.2
Superficial incisional SSI	148	5.2
Deep incisional SSI	9	0.3
Organ/space SSI	111	3.9

Table IX describes the distribution of the 37 studied risk factors and Table X describes the SSI incidence for each of the risk factors. The highest difference in the SSI was observed for inpatients compared to outpatients (90.20%), followed by those who obtained general anesthesia (87.90%), who underwent general surgery (85.30%), those treated by a resident with less than 4 years of experience (82.80%), who had an abnormal BMI (64.70%) and who underwent an additional procedure by the same surgical team under the same anesthestic (61.50%).

Table IX: Frequency distribution of the 37 studied risk factors

Risk factor	Count	Percentage
Male	1468	50.5
Inpatient status	1982	68.2
Emergent surgery	1188	40.9
Transfer from other location or inpatient (not admitted from home)	168	5.8
General anesthesia	2416	83.1
General surgery	2326	80
Under/overweight (BMI below 18.5 or above 25)	1133	39
Diabetic	455	15.7
Smoker	443	15.2
Alcohol abuse	34	1.2
Dyspnea (upon moderate exertion or at rest)	176	6.1
Partially or totally dependent	141	4.9
Ventilator usage	29	1
COPD (severe)	90	3.1
Pneumonia	13	0.4
Congestive heart failure	38	1.3
Myocardial infarction	29	1
History of angina	23	0.8
Hypertension	1264	43.5
PVD	185	6.4
Gangrene	138	4.7
Renal failure	11	0.4
Dialysis	42	1.4
Disseminated cancer	132	4.5
Open wound	147	5.1
Steroid use	92	3.2
Weight loss >10%	123	4.2
Bleeding disorder	197	6.8
Preoperative transfusion	11	0.4
Chemotherapy	87	3
Radiotherapy	49	1.7
Sepsis (or SIRS or septic shock)	283	9.7
Resident with less than 4 years of residency	2200	75.7
Wound classification III or IV (contaminated or dirty/infected)	592	20.4
ASA class 3 or 4 (severe disturb or life threat)	1109	38.1
Other procedures	1353	46.5
Concurrent procedures	117	4

Table X: SSI incidence (any type, superficial incisional and organ/space) according to risk factor presence and absence

Risk factor category	Variables	SSI outcome (any type)				Postop Superficial Incisional SSI				Postop Organ Space SSI			
		No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %
Gender	Female	1325	50.20%	112	42.30%	1365	49.50%	72	48.30%	1395	50.10%	42	35.30%
	Male	1315	49.80%	153	57.70%	1391	50.50%	77	51.70%	1391	49.90%	77	64.70%
Patient status	Outpatient	898	34.00%	26	9.80%	905	32.80%	19	12.80%	917	32.90%	7	5.90%
	Inpatient	1743	66.00%	239	90.20%	1852	67.20%	130	87.20%	1870	67.10%	112	94.10%
Surgery Status	Elective	1117	51.40%	114	46.70%	1166	51.00%	65	48.50%	1183	51.30%	48	42.50%
	Emergent	1058	48.60%	130	53.30%	1119	49.00%	69	51.50%	1123	48.70%	65	57.50%
Tobacco Use	No	2242	84.90%	222	83.80%	2346	85.10%	118	79.20%	2357	84.50%	107	89.90%
	Yes	400	15.10%	43	16.20%	412	14.90%	31	20.80%	431	15.50%	12	10.10%
Alcohol Abuse	No	2614	98.90%	259	97.70%	2727	98.90%	146	98.00%	2758	98.90%	115	96.60%
	Yes	28	1.10%	6	2.30%	31	1.10%	3	2.00%	30	1.10%	4	3.40%
Ventilator Usage	No	2614	98.90%	264	99.60%	2729	98.90%	149	100.00%	2760	99.00%	118	99.20%
	Yes	28	1.10%	1	0.40%	29	1.10%	0	0.00%	28	1.00%	1	0.80%
COPD	No	2560	96.90%	257	97.00%	2673	96.90%	144	96.60%	2700	96.80%	117	98.30%
	Yes	82	3.10%	8	3.00%	85	3.10%	5	3.40%	88	3.20%	2	1.70%
Pneumonia	No	2634	99.70%	260	98.10%	2747	99.60%	147	98.70%	2778	99.60%	116	97.50%
	Yes	8	0.30%	5	1.90%	11	0.40%	2	1.30%	10	0.40%	3	2.50%
Congestive Heart Failure	No	2608	98.70%	261	98.50%	2722	98.70%	147	98.70%	2752	98.70%	117	98.30%
	Yes	34	1.30%	4	1.50%	36	1.30%	2	1.30%	36	1.30%	2	1.70%
Myocardial Infarction	No	2614	98.90%	264	99.60%	2729	98.90%	149	100.00%	2760	99.00%	118	99.20%
	Yes	28	1.10%	1	0.40%	29	1.10%	0	0.00%	28	1.00%	1	0.80%
History of Angina	No	2621	99.20%	263	99.20%	2736	99.20%	148	99.30%	2766	99.20%	118	99.20%
	Yes	21	0.80%	2	0.80%	22	0.80%	1	0.70%	22	0.80%	1	0.80%

Risk factor category	Varia-bles	SSI outcome (any type)				Postop Superficial Incisional SSI				Postop Organ Space SSI			
		No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %
Hypertension	No	1506	57.00%	137	51.70%	1565	56.70%	78	52.30%	1581	56.70%	62	52.10%
	Yes	1136	43.00%	128	48.30%	1193	43.30%	71	47.70%	1207	43.30%	57	47.90%
PVD	No	2474	93.60%	248	93.60%	2586	93.80%	136	91.30%	2607	93.50%	115	96.60%
	Yes	168	6.40%	17	6.40%	172	6.20%	13	8.70%	181	6.50%	4	3.40%
Gangrene	No	2517	95.30%	252	95.10%	2629	95.30%	140	94.00%	2654	95.20%	115	96.60%
	Yes	125	4.70%	13	4.90%	129	4.70%	9	6.00%	134	4.80%	4	3.40%
Renal Failure	No	2632	99.60%	264	99.60%	2747	99.60%	149	100.00 %	2778	99.60%	118	99.20%
	Yes	10	0.40%	1	0.40%	11	0.40%	0	0.00%	10	0.40%	1	0.80%
Dialysis	No	2605	98.60%	260	98.10%	2719	98.60%	146	98.00%	2748	98.60%	117	98.30%
	Yes	37	1.40%	5	1.90%	39	1.40%	3	2.00%	40	1.40%	2	1.70%
Disseminated Cancer	No	2531	95.80%	243	91.70%	2636	95.60%	138	92.60%	2666	95.70%	108	90.80%
	Yes	110	4.20%	22	8.30%	121	4.40%	11	7.40%	121	4.30%	11	9.20%
Open Wound	No	2520	95.40%	239	90.20%	2632	95.50%	127	85.20%	2643	94.80%	116	97.50%
	Yes	121	4.60%	26	9.80%	125	4.50%	22	14.80%	144	5.20%	3	2.50%
Steroid Use	No	2563	97.00%	251	94.70%	2673	97.00%	141	94.60%	2700	96.90%	114	95.80%
	Yes	78	3.00%	14	5.30%	84	3.00%	8	5.40%	87	3.10%	5	4.20%
Weight Loss >10%	No	2537	96.10%	246	92.80%	2642	95.80%	141	94.60%	2676	96.00%	107	89.90%
	Yes	104	3.90%	19	7.20%	115	4.20%	8	5.40%	111	4.00%	12	10.10%
Bleeding Disorder	No	2462	93.20%	247	93.20%	2570	93.20%	139	93.30%	2598	93.20%	111	93.30%
	Yes	179	6.80%	18	6.80%	187	6.80%	10	6.70%	189	6.80%	8	6.70%
Preoperative Transfusion	No	2549	99.60%	254	99.60%	2659	99.60%	144	100.00 %	2690	99.60%	113	99.10%
	Yes	10	0.40%	1	0.40%	11	0.40%	0	0.00%	10	0.40%	1	0.90%
Chemotherapy	No	2561	96.90%	259	97.70%	2674	97.00%	146	98.00%	2704	97.00%	116	97.50%
	Yes	81	3.10%	6	2.30%	84	3.00%	3	2.00%	84	3.00%	3	2.50%

Risk factor category	Variables	SSI outcome (any type)				Postop Superficial Incisional SSI				Postop Organ Space SSI			
		No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %
Radio-therapy	No	2598	98.30%	260	98.10%	2712	98.30%	146	98.00%	2741	98.30%	117	98.30%
	Yes	44	1.70%	5	1.90%	46	1.70%	3	2.00%	47	1.70%	2	1.70%
Diabetes	Non-diabetic	2239	84.70%	213	80.40%	2340	84.80%	112	75.20%	2347	84.20%	105	88.20%
	Diabetic	403	15.30%	52	19.60%	418	15.20%	37	24.80%	441	15.80%	14	11.80%
Dyspnea	No dyspnea	2480	93.90%	251	94.70%	2589	93.90%	142	95.30%	2620	94.00%	111	93.30%
	Dyspnea	162	6.10%	14	5.30%	169	6.10%	7	4.70%	168	6.00%	8	6.70%
Functio-nal Status	Independent	2529	95.70%	237	89.40%	2634	95.50%	132	88.60%	2660	95.40%	106	89.10%
	Partially or totally dependent	113	4.30%	28	10.60%	124	4.50%	17	11.40%	128	4.60%	13	10.90%
Highest Level of Resident	5 to 8 years of residency	606	23.40%	45	17.20%	625	23.10%	26	17.80%	632	23.10%	19	16.00%
	0 to 4 years of residency	1983	76.60%	217	82.80%	2080	76.90%	120	82.20%	2100	76.90%	100	84.00%
Wound Classifi-cation	Class I or II	2135	80.90%	178	67.20%	2198	79.80%	115	77.20%	2249	80.70%	64	53.80%
	Class III or IV	505	19.10%	87	32.80%	558	20.20%	34	22.80%	537	19.30%	55	46.20%
ASA Class	ASA 1 or 2	1587	61.90%	129	49.60%	1653	61.70%	63	43.20%	1649	60.90%	67	57.30%
	ASA 3 or 4	978	38.10%	131	50.40%	1026	38.30%	83	56.80%	1059	39.10%	50	42.70%
BMI	Normal BMI	627	38.00%	60	35.30%	656	37.90%	31	35.60%	657	37.80%	30	35.70%
	Under/ overweight	1023	62.00%	110	64.70%	1077	62.10%	56	64.40%	1079	62.20%	54	64.30%

Risk factor category	Variables	SSI outcome (any type)				Postop Superficial Incisional SSI				Postop Organ Space SSI			
		No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %	No #	No %	Yes #	Yes %
Transfer Origin	Not transferred, admitted directly from home	2488	94.20%	251	94.70%	2597	94.20%	142	95.30%	2629	94.30%	110	92.40%
	Transfer from other or inpatient	154	5.80%	14	5.30%	161	5.80%	7	4.70%	159	5.70%	9	7.60%
Sepsis	No sepsis	2110	89.80%	179	80.60%	2187	89.10%	102	87.20%	2210	89.70%	79	73.10%
	SIRS, sepsis or septic shock	240	10.20%	43	19.40%	268	10.90%	15	12.80%	254	10.30%	29	26.90%
Surgical Subspe-cialty	Vascular	542	20.50%	39	14.70%	559	20.30%	22	14.80%	565	20.30%	16	13.40%
	General	2100	79.50%	226	85.30%	2199	79.70%	127	85.20%	2223	79.70%	103	86.60%
Concur-rent Proce-dures	No	2539	96.10%	251	94.70%	2647	96.00%	143	96.00%	2679	96.10%	111	93.30%
	Yes	103	3.90%	14	5.30%	111	4.00%	6	4.00%	109	3.90%	8	6.70%
Other Proce-dures	No	1227	50.30%	89	38.50%	1265	49.80%	51	39.20%	1279	49.80%	37	36.30%
	Yes	1211	49.70%	142	61.50%	1274	50.20%	79	60.80%	1288	50.20%	65	63.70%
Anesthesia Technique	Spinal, local, epidural, regional or MAC	459	17.40%	32	12.10%	469	17.00%	22	14.80%	482	17.30%	9	7.60%
	General	2183	82.60%	233	87.90%	2289	83.00%	127	85.20%	2306	82.70%	110	92.40%

Significant Risk Factors in Chi-Square analyses. The data in Table XI summarizes the odds ratios for all risk factors that had a significant ($p<0.05$) association with any type of SSI according to the bivariate analysis. The highest odds ratio was observed for preoperative pneumonia followed by inpatient status.

Table XI: Significant risk factors predisposing patients to any type of SSI

Risk factor	Odds Ratio	p-value
Male gender	1.376	0.014
Inpatient status	4.736	<0.001
Preoperative pneumonia	6.332	0.004
Disseminated cancer	2.083	0.005
Open wound	2.266	0.001
Preoperative weight loss >10%	1.884	0.023
Partially or totally dependent	2.644	<0.001
Level of resident from 0 to 4 years	1.474	0.021
Class III or IV wound	2.066	<0.001
ASA class of 3 or 4	1.648	<0.001
Preoperative sepsis	2.112	<0.001
General anesthesia	1.531	0.031
General surgery	1.496	0.024
Other procedures	1.617	0.001

Tables XII and XIII summarize the significant risk factors ($p<0.05$) that predispose patients to acquire a superficial incisional and an organ/space SSI, respectively, as well as their odds ratios and p-values. For superficial incisional SSIs, the highest odds ratios were observed for open wound and inpatient status whereas for organ/space SSIs, the highest odds ratios were observed for inpatient status, preoperative pneumonia, Class III or IV wound, alcohol abuse and

preoperative sepsis. Due to the low number of deep incisional SSIs, no risk factors were found to be significant in predisposing patients for this type of infection.

Table XII: Significant risk factors predisposing patients to superficial incisional SSIs

Risk factor	Odds Ratio	p-value
Inpatient status	3.343	<0.001
Open wound	3.647	<0.001
Diabetes	1.849	0.003
Partially or totally dependent	2.736	0.001
ASA class of 3 or 4	2.133	<0.001
Other procedures	1.538	0.019

Table XIII: Significant risk factors predisposing patients to organ/space SSIs

Risk factor	Odds Ratio	p-value
Male gender	1.839	0.002
Inpatient status	7.846	<0.001
Alcohol abuse	3.198	0.048
Preoperative pneumonia	7.184	0.014
Disseminated cancer	2.244	0.021
Preoperative weight loss >10%	2.704	0.004
Partially or totally dependent	2.549	0.007
Class III or IV wound	3.599	<0.001
Preoperative sepsis	3.194	<0.001
General anesthesia	2.555	0.004
Other procedures	1.744	0.008

Overall, inpatient status, dependence for everyday activities (partial or total dependence) and other procedures performed by the same surgical team under the same anesthetic are common significant risk factors for the development of SSIs in general, superficial incisional SSI and organ/space SSI. Moreover, male gender, preoperative pneumonia, disseminated cancer, preoperative weight loss of more than 10% of the patient's body mass, a wound classification of III (contaminated) or IV (dirty/infected), preoperative sepsis, SIRS or septic shock and general anesthesia can predispose patients to an SSI in general or to an organ/space SSI. Furthermore, an open wound and a patient's ASA class of 3 (severe disturb) or 4 (life threat) are common significant risk factors for SSIs in general and superficial incisional SSIs. Nonetheless, diabetes is only significant in the development of a superficial incisional SSI whereas alcohol abuse can predispose a patient to develop an organ/space SSI. Even though the resident's level and the surgical subspecialty (general surgery) of the procedure were not found to predispose a patient for superficial incisional and organ/space SSI, they were found to be significant risk factors for SSIs in general.

Table XIV shows all the p-values obtained from bivariate analyses of the 37 studied risk factors. (All significant risk factors are in bold.)

Table XIV: Significance (p-values) of all risk factors in bivariate analyses

Risk factor	Any type of SSI	Superficial incisional SSI	Deep incisional SSI	Organ/ space SSI
Gender	**0.014**	0.801	0.179	**0.002**
Patient status	**<0.001**	**<0.001**	0.065	**<0.001**
Surgery status	0.177	0.594	0.335	0.068
Transfer origin	0.890	0.718	0.415	0.418
Anesthesia technique	**0.031**	0.574	1.000	**0.004**
Surgical subspecialty	**0.024**	0.114	0.698	0.078
BMI	0.507	0.734	0.717	0.731
Diabetes	0.076	**0.003**	0.155	0.302
Tobacco use	0.654	0.061	1.000	0.119
Alcohol abuse	0.121	0.252	1.000	**0.048**
Dyspnea	0.685	0.597	1.000	0.695
Functional status prior to surgery	**<0.001**	**0.001**	1.000	**0.007**
Ventilator usage	0.512	0.399	1.000	1.000
COPD	1.000	0.807	0.247	0.585
Pneumonia	**0.004**	0.141	1.000	**0.014**
Congestive heart failure	0.774	1.000	1.000	0.668
Myocardial infarction	0.512	0.399	1.000	1.000
History of angina	1.000	1.000	1.000	0.619
Hypertension	0.104	0.309	0.515	0.345
PVD	1.000	0.226	1.000	0.246
Gangrene	0.879	0.427	1.000	0.658
Renal failure	1.000	1.000	1.000	0.369
Dialysis	0.584	0.474	0.123	0.690
Disseminated cancer	**0.005**	0.102	0.060	**0.021**
Open wound	**0.001**	**<0.001**	0.374	0.282
Steroid use	0.062	0.141	0.252	0.425
Weight loss >10%	**0.023**	0.408	1.000	**0.004**
Bleeding disorder	1.000	1.000	0.469	1.000
Preoperative transfusion	1.000	1.000	1.000	0.366
Chemotherapy	0.573	0.625	1.000	1.000
Radiotherapy	0.800	1.000	1.000	1.000
Sepsis	**<0.001**	0.544	0.607	**<0.001**

Highest level of resident	**0.021**	0.156	1.000	0.074
Wound classification	**<0.001**	0.465	0.400	**<0.001**
ASA class	**<0.001**	**<0.001**	0.167	0.440
Other procedures	**0.001**	**0.019**	0.125	**0.008**
Concurrent procedures	0.253	1.000	1.000	0.146

Significant Risk Factors in logistic regression analyses. Table XV summarizes the results of the multivariate logistic regression analysis. These data show that the highest independent association of any SSI was observed for inpatient status.

Table XV: Significant independent risk factors predisposing patients to any type of SSI

Risk factor	Odds Ratio	p-value
Male gender	1.854	0.005
Inpatient status	9.491	<0.001
Hypertension	2.464	<0.001
Steroid use	2.485	0.042
Partially or totally dependent	2.577	0.047

Tables XVI and XVII show the significant independent risk factors for superficial incisional and organ/space SSIs ($p<0.05$). These results show that inpatient status had the highest independent odds ratios for superficial incisional and organ/space SSIs. Moreover, partial or total dependence and weight loss more than 10% of body mass prior to surgery are independent predictors for superficial incisional SSIs and organ/space SSIs, respectively.

Inpatient status and hypertension were found to be significant for all three SSI categories (SSI in general, superficial incisional SSI and organ/space SSI). Furthermore, the male gender is a common risk factor that predisposes patients to SSIs in general and organ/space SSIs whereas steroid use and dependence (partial or total) for everyday activities were found to be significant for SSIs in general and superficial incisional SSIs. Moreover, preoperative weight loss more than 10% of the patient's body mass and a wound classification of 3 or 4 were found to be significant only for organ/space SSIs.

Table XVI: Significant independent risk factors predisposing patients to superficial incisional SSIs

Risk factor	Odds Ratio	p-value
Inpatient status	6.592	0.002
Hypertension	2.098	0.017
Steroid use	2.971	0.049
Partially or totally dependent	3.703	0.031

Table XVII: Significant independent risk factors predisposing patients to organ/space SSIs

Risk factor	Odds Ratio	p-value
Male gender	2.097	0.015
Inpatient status	15.067	0.009
Hypertension	2.597	0.002
Preoperative weight loss >10%	3.057	0.013
Class III or IV wound	2.637	0.006

Table XVIII describes the significance values (p-values) of all risk factors studied obtained from multiple logistic regression analyses. (All independent significant risk factors are in bold.)

Table XVIII: Significance (p-values) of all risk factors in logistic regression

Risk factor	Any type of SSI	Superficial incisional SSI	Deep incisional SSI	Organ/ space SSI
Gender	**0.005**	0.224	0.228	**0.015**
Patient status	**<0.001**	**0.002**	0.988	**0.009**
Surgery status	0.713	0.845	0.798	0.960
Transfer origin	0.990	0.908	0.997	0.563
Anesthesia technique	0.134	0.379	0.673	0.199
Surgical subspecialty	0.777	0.523	0.775	0.583
BMI	0.676	0.324	0.437	0.852
Diabetes	0.694	0.627	0.993	0.819
Tobacco use	0.640	0.414	0.980	0.847
Alcohol abuse	0.806	0.916	0.999	0.285
Dyspnea	0.761	0.729	0.998	0.884
Functional status prior to surgery	**0.047**	**0.031**	0.997	0.292
Ventilator usage	0.999	0.999	0.999	0.999
COPD	0.465	0.586	0.986	0.998
Pneumonia	0.197	0.387	0.999	0.433
Congestive heart failure	0.639	0.998	0.999	0.471
Myocardial infarction	0.999	0.998	1.000	0.998
History of angina	0.999	0.999	1.000	0.999
Hypertension	**<0.001**	**0.017**	0.342	**0.002**
PVD	0.542	0.518	0.996	0.505
Gangrene	0.155	0.180	0.998	0.346
Dialysis	0.538	0.090	0.999	0.998
Disseminated cancer	0.682	0.910	0.996	0.851
Open wound	0.949	0.847	1.000	0.756
Steroid use	**0.042**	**0.049**	0.671	0.725
Weight loss >10%	0.228	0.928	0.994	**0.013**
Bleeding disorder	0.174	0.520	0.999	0.254

Preoperative transfusion	0.999	0.999	0.999	0.999
Chemotherapy	0.169	0.498	0.998	0.218
Radiotherapy	0.521	0.998	0.998	0.103
Sepsis	0.344	0.878	0.418	0.159
Highest level of resident	0.767	0.859	0.908	0.786
Wound classification	0.090	0.616	0.726	**0.006**
ASA class	0.779	0.903	0.989	0.625
Other procedures	0.068	0.085	0.409	0.207
Concurrent procedures	0.515	0.742	0.673	0.384

Since logistic regression calculates adjusted results while bivariate tests present crude results (Antonio, Zanolli, Carniel, & Morcillo, 2009) (Dode & Santos, 2009), it is logical that fewer risk factors were found to be significant with logistic regression than in the bivariate analyses. Three of the five significant risk factors found to be significant in multiple logistic regression were also significant in the bivariate results. These risk factors were: male gender, inpatient status and dependence (partial or total) for everyday activities prior to surgery.

Overall, the risk factors included in the final scoring tool were male gender, inpatient status, hypertension, steroid use and partial or total dependence for everyday activities.

Risk factors included in risk-index tool. Fifty and a half percent (1468) of the patients were male, 68.2% (1982) were inpatients, 43.5% (1264) of the patients were hypertensive, 3.2% (92) of the patients had a condition that required

corticosteroid use and 4.9% (141) of the patients were partially or totally dependent prior to surgery.

Individual patient scores. According to the risk factors' respective odds ratios, a specific weight was calculated and assigned to each significant variable. These, as well as the relative weights and scores, are summarized in Table XIX.

Table XIX: Variables and SSI weights in final SSI logistic regression model

Significant risk factor	Negative (0)	Positive (risk factor) (1)	Odds Ratio (OR)	Relative SSI weight	Variable score value
Gender	Female	Male	1.854	0.0982	10
Patient status	Outpatient	Inpatient	9.491	0.5029	50
Hypertension	No	Yes	2.464	0.1306	13
Steroid use	No	Yes	2.485	0.1317	13
Functional status	Indepen-dent	Partially or totally dependent	2.577	0.1366	14
Total			18.871	1	100

If the patient possesses the risk factor, his/her individual patient score would increase by the value in the last column. Patient status is the most influential risk factor in the model. If an individual was an inpatient, his/her score would increase by fifty points. Hypertension, steroid use and functional status prior to surgery have similar odds ratios and therefore add a similar value to the patient's score if the risk factor is present. Hypertension and steroid use add thirteen points each to

the score whereas a dependent patient (partially or totally) for everyday activities would have a value of fourteen added to his/her score. Nonetheless, male gender is the least influential risk factor included in the model with an addition of ten points to the patient's score. Clearly, the patients who possess all five of the risk factors in the risk-index tool have a score of one hundred and those who possess none of them have a score of zero. Table XX presents the frequency distribution of the scores in the study cohort.

Table XX: Frequency distribution representing individual patient SSI scores

Patient score	Frequency	Percentage
0	324	11.1
10	196	6.7
13	228	7.9
14	1	0.0
23	172	5.9
26	2	0.1
27	1	0.0
36	1	0.0
50	454	15.6
60	558	19.2
63	345	11.9
64	30	1.0
73	451	15.6
74	33	1.1
77	52	1.8
86	18	0.6
87	34	1.1
90	2	0.1
100	5	0.2
Total	2907	99.9%

Note: The three categories that have a frequency of 1 patient have a percentage between 0 and 0.049%, increasing the overall percentage to 100%.

The majority of patients (63.3%) have a score between 50 and 73 suggesting that they possess between one and three risk factors. Five patients who presented at the time of surgery with all five risk factors included in the model have a score of one hundred. Moreover, 324 patients (11.1%) possess none of the five risk factors in the model, therefore presenting with a score of zero.

ROC curve. The sensitivity and specificity of the SSI scoring tool was assessed using an ROC curve (Receiver Operating Characteristic). The sensitivity and specificity of the SSI scoring tool are 75.5% and 49.8%, respectively. The false positive rate is 50.2% and the false negative rate is 24.5% for estimating the development of an SSI in surgical patients in the study cohort.

The ROC curve is presented in Figure 1 and has an area under the curve of 0.660 ($p<0.001$, 95% CI= 0.628-0.692). Three sections can be distinguished on the curve. The first has the highest slope representing an exponential relationship, the second has a moderate slope (linear relationship) and the last has the lowest slope and also presents with a linear relationship. Thusly, two cutoff points were established. The first has a value of 43.17 and presents with a sensitivity of 90.2% and a value of 66.0% for 1-specificity (specificity= 34.0%). The second cutoff value is 63.40 and coincides with a sensitivity of 38.1% and 1-specificity of 20.4% (specificity= 79.6%). These cutoffs were used to define patients at low, moderate and high risk for an SSI.

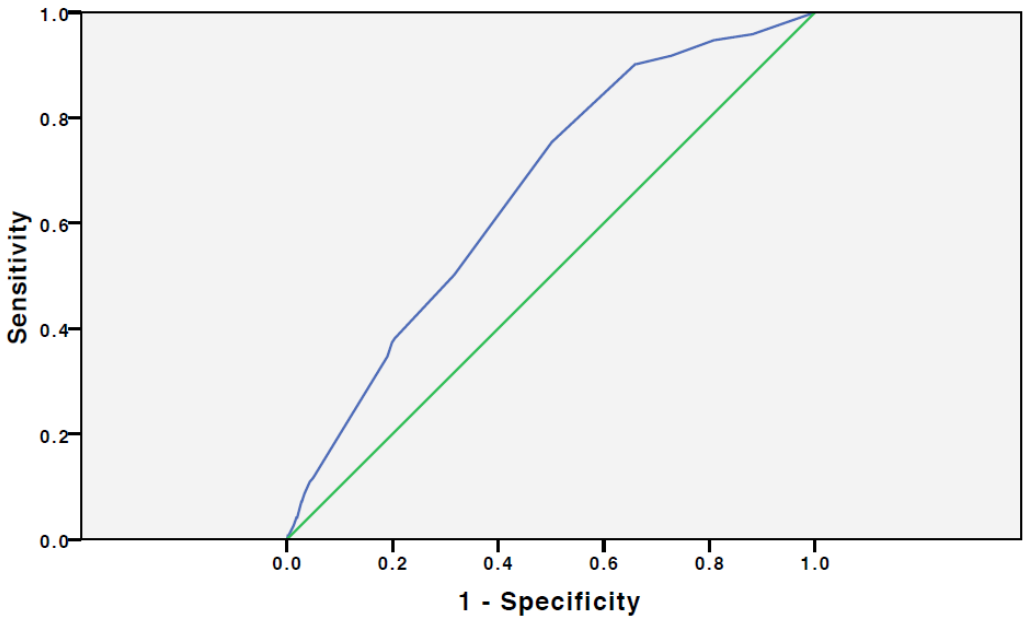

Figure 1: Receiver operating curve analysis for surgical site infection (SSI) risk scoring tool for the NSQIP database at the JGH in Montreal

General SSI outcomes for low-, moderate- and high-risk patients. After establishing the cutoff points, we created three groups according to the risk of developing an SSI. Patients with an individual SSI score below 43.17 have a low risk of developing an SSI, patients with a score between 43.171 and 63.40 have a moderate risk of acquiring this postsurgical infection and patients with a score above 63.401 are high-risk SSI surgical patients. In the NSQIP database, 31.8% (925), 46.2% (1342) and 22.0% (640) of the patients had a low, moderate and high risk of developing any type of SSI, respectively.

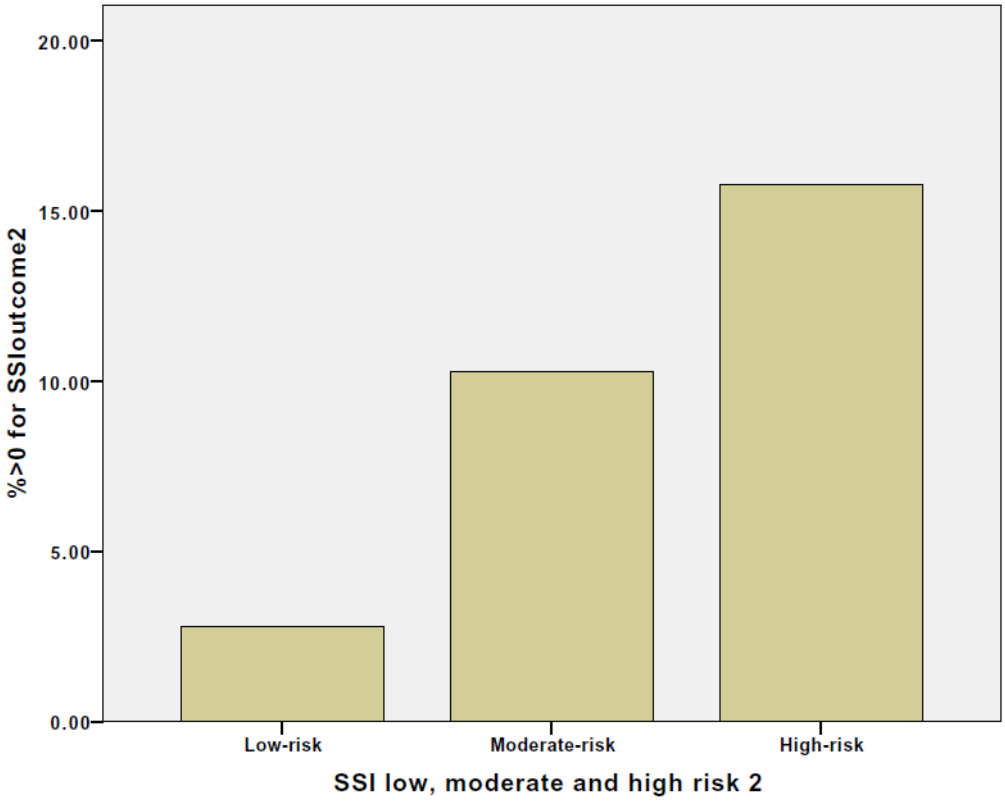

Figure 2: Simple bar chart representing the percentage of SSI outcomes (all types) for low-risk, moderate-risk and high-risk groups

Figure 2 presents the percentages of low-risk, moderate-risk and high-risk patients who develop any type of SSI. Approximately 3% of low-risk patients, 10% of moderate-risk patients and 16% of high-risk patients develop any type of SSI postoperatively.

Binary logistic regression analyses were used to determine each group's odds ratio of developing an SSI. Compared to the low-risk group, the moderate-risk group has an OR of 3.963 ($p<0.001$, 95% CI= 2.584-6.079) and the high-risk group has an OR of 6.479 ($p<0.001$, 95% CI= 4.156-10.101) (Table XXI). The

moderate-risk group has an increased risk of 3.963 compared to the low-risk group. The high-risk group has an OR of 3.255 ($p<0.001$, 95% CI= 2.407-4.400) when compared to the moderate-risk group (Table XXII).

Table XXI: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk patients in the development of any type of SSI

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	3.963	2.584	6.079
High-risk	6.479	4.156	10.101

Note: All p-values are below 0.001.

Table XXII: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk and moderate-risk patients, respectively, in the development of any type of SSI

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	3.963	2.584	6.079
High-risk	3.255	2.407	4.400

Note: All p-values are below 0.001.

Superficial incisional SSI outcomes for low-, moderate- and high-risk patients.

Figure 3 represents the percentages of patients who acquire a superficial incisional SSI. Approximately 2%, 5.5% and 8.5% of low-risk, moderate-risk and high-risk patients develop a superficial incisional SSI, respectively.

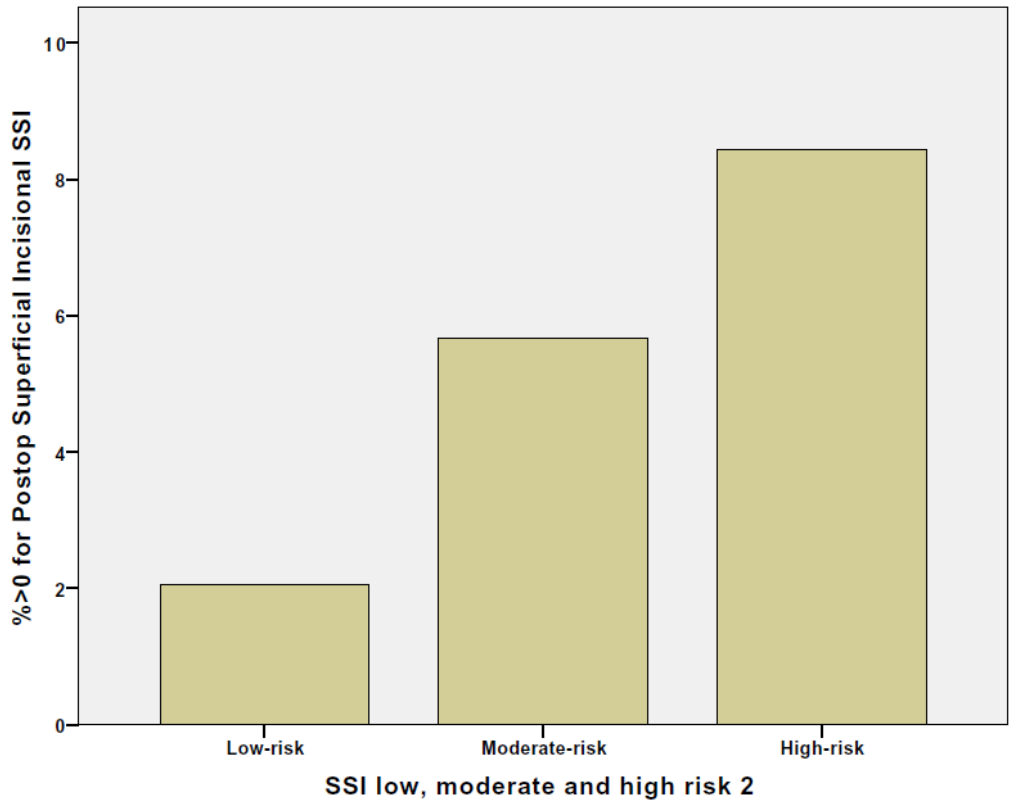

Figure 3: Simple bar chart representing the percentage of superficial incisional SSI outcomes for low-risk, moderate-risk and high-risk groups

Compared to low-risk patients, moderate-risk SSI patients have an OR of 2.863 ($p<0.001$, 95% CI= 1.719-4.767) and high-risk patients have an OR of 4.394 ($p<0.001$, 95% CI= 2.579-7.488) of developing a superficial incisional SSI (Table XXIII).

Compared to low-risk patients, moderate-risk patients have an OR of 2.863 ($p<0.001$, 95% CI= 1.719-4.767) and, compared to moderate-risk patients, high-risk patients have an OR of 2.597 ($p<0.001$, 95% CI= 1.780-3.789) (Table XXIV).

Table XXIII: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk patients in the development of superficial incisional SSIs

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	2.863	1.719	4.767
High-risk	4.394	2.579	7.488

Note: All p-values are below 0.001.

Table XXIV: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk and moderate-risk patients, respectively, in the development of superficial incisional SSIs

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	2.863	1.719	4.767
High-risk	2.597	1.780	3.789

Note: All p-values are below 0.001.

Organ/space SSI outcomes for low-, moderate- and high-risk patients.

Figure 4 shows that less than 1% of low-risk patients develop an organ/space SSI. Furthermore, approximately 4.5% and 8% of moderate-risk and high-risk patients acquire an organ/space SSI, respectively.

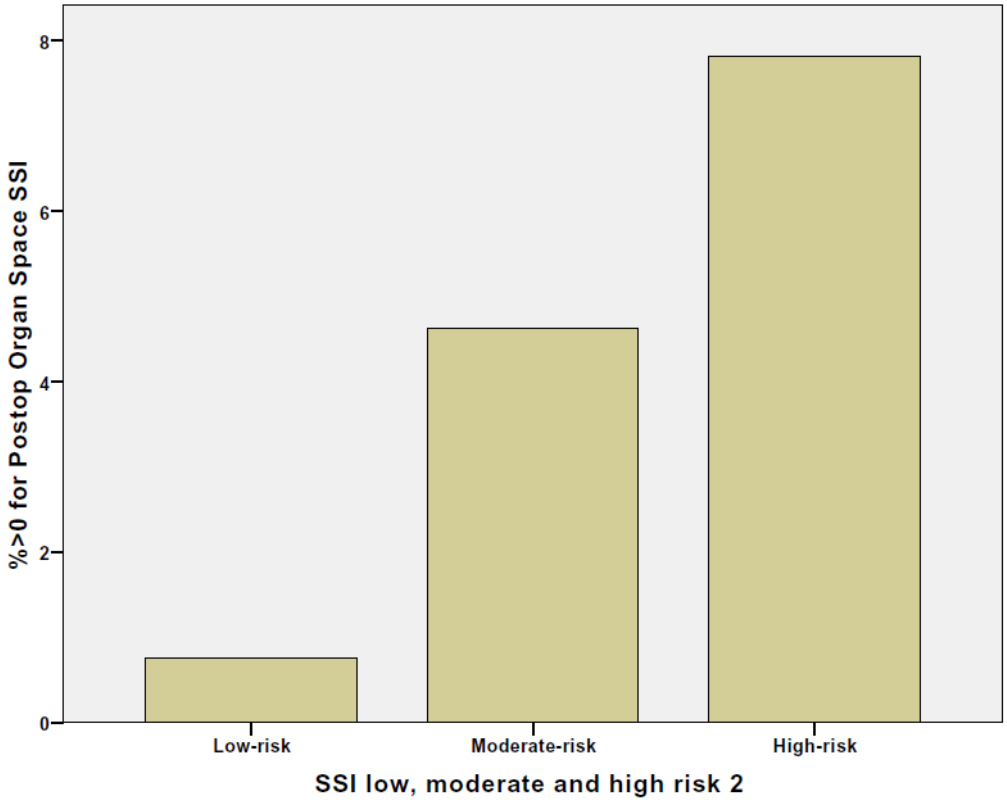

Figure 4: Simple bar chart representing the percentage of organ/space SSI outcomes for low-risk, moderate-risk and high-risk groups

Moderate-risk patients have an OR of 6.352 ($p<0.001$, 95% CI= 2.894-13.942) and high-risk patients have an OR of 11.114 ($p<0.001$, 95% CI= 5.005-24.677) of developing an SSI when compared to low-risk patients (Table XXV).

The results in table XXVI show that, when compared to the low-risk group, moderate-risk patients have an OR of 6.352 ($p<0.001$, 95% CI= 2.894-13.942), and high-risk patients have an OR of 4.410 ($p<0.001$, 95% CI= 2.708-7.181) when compared to moderate-risk patients for developing an SSI.

Table XXV: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk patients in the development of organ/space SSIs

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	6.352	2.894	13.942
High-risk	11.114	5.005	24.677

Note: All p-values are below 0.001.

Table XXVI: Odds Ratios (ORs) and 95% CI of moderate and high-risk patients compared to low-risk and moderate-risk patients, respectively, in the development of organ/space SSIs

	OR	95% CI lower extremity	95% CI higher extremity
Moderate-risk	6.352	2.894	13.942
High-risk	4.410	2.708	7.181

Note: All p-values are below 0.001.

V. Discussion

Surgical site infections are the second most common surgical complication causing significant burden of illness due to increased hospital stay, morbidity, mortality and healthcare costs. (Kirkland, Briggs, Trivette, Wilkinson, & Sexton, 1999) Due to the increasing prevalence of resistant bacteria, it is important to focus on prevention rather than developing new antibiotics that bacteria will eventually become resistant to as well. (Barie, Nichols, & Wilson, 2006) Given limited financial resources, it is also necessary that preventive interventions are applied in a focused and cost-efficient manner. The use of an SSI screening tool will allow the identification of high-risk patients for whom more intensive and aggressive prevention measures should be applied.

In the current study, the following factors were found to have a significant and independent association with the risk of an SSI: male gender, inpatient status, hypertension, preoperative corticosteroid use and partial or total dependence for everyday activities prior to surgery.

These results concur with those reported in the literature. For instance, Miki et al., Korinek et al., Jeong et al., Tang et al. and Askarian et al. have found that male

gender is a significant predictor of SSIs. (Miki, Inoue, Mohri, Kobayashi, & Kusunoki, 2006) (Korinek, et al., 2005) (Jeong, et al., 2012) (Tang, et al., 2001) (Askarian, Yadollahi, & Assadian, 2012) Although no conclusion has been made concerning the reason why males have an increased risk of SSI, it is possible that bacterial skin colonization could be associated to this since differences between males and females have been found concerning skin pH, serum production and skin thickness. (Jeong, et al., 2012)

There is little evidence of a direct association between inpatient status and development of SSI. Hennessey et al. do however state that the duration of inpatient stay is negatively correlated with preoperative albumin levels which is an independent risk factor for SSI. (Hennessey, Burke, Ni-Dhonochu, Shields, Winter, & Mealy, 2010) On the other hand, one can presume that a preoperative stay in the hospital has many effects on the patient. Firstly, it has been shown that preoperative mobility decreases the risk of postoperative complications. (Valkenet, van de Port, Dronkers, de Vries, Lindeman, & Backx, 2011) (Simunovic, Devereaux, & Bhandari, 2011) (Hirsch, 1995) Secondly, a longer preoperative stay can increase the patient's risk of acquiring bacteria circulating in the hospital which are not typically present in his/her flora. This can include resistant bacteria since these types of microorganisms survive in hospital settings by transmitting to individuals with a weakened immune system (for instance surgical patients). (Lipsitch, Bergstrom, & Levin, 2000)

There is evidence in the literature to support that hypertension is an independent risk factor for SSIs although the precise mechanism has not been demonstrated.

Cardoso Del Monte et al. presume that the “chronic alteration in peripheral blood supply as a result of increased vascular resistance” could explain the increased infection rates among hypertensive surgical patients. (Cardoso Del Monte & Pinto Neto, 2010)

Moreover, it is logical that corticosteroid use in the 30 days prior to surgery is a significant risk factor for the development of SSIs since these drugs diminish the patient’s immune function and therefore increases risk of opportunistic infections, including SSI. This hypothesis also concurs with the scientific literature. Lee et al. and Malone et al. found that steroid use is an independent risk factor for SSI development. (Lee, et al., 2011) (Malone, Genuit, Tracy, Gannon, & Napolitano, 2002)

The link between functional status prior to surgery and the risk of SSI has not yet been established and this is a new finding for this analysis. However, this could be related to reduced mobility in patients with lower functional status. Anderson et al. showed that a partially or totally dependent patient prior to surgery has an increased risk of developing an SSI caused by MRSA, but this has not been proven not for any other type of pathogenic microorganism. (Anderson, et al., 2008)

Other risk factors have been shown to be significant in the development of SSIs including obesity, diabetes mellitus, tobacco use, alcohol abuse, COPD, disseminated cancer, chemotherapy, radiotherapy and patient ASA score. However, none of these risk factors were found to be independently associated

with the SSI risk in our analyses. One possible explanation of this is the low number of patients with these risk factors in our database. Another explanation could be that the effect of these factors is captured by the variables that were identified as significant predictors of SSIs in our study. The low number of SSIs could also affect these statistical results. It is important to remember that the low number of nine deep incisional SSIs most probably caused the absence of significant risk factors for this type of infection. Only 5.2% (148 out of 2907 patients) and 3.9% (111 out of 2907 patients) developed a superficial incisional SSI and an organ/space SSI, respectively.

The SSI risk tool is user-friendly and easy to interpret. A presence of a risk factor would add the specific score value to the patient score. One must simply calculate the patient score by adding the values of each of the risk factors present for the patient. The final score varies from 0 to 100 where 0 indicates that the patient does not have any risk factor in the model and where a score of 100 indicates that the patient has all the risk factors included in the model. The final patient score would permit the classification of the patient in one of three groups: low-risk, moderate-risk or high-risk of developing any type of SSI. The decision whether additional or more aggressive prophylactic care (preoperative and intraoperative) is to be administered to the patient should be assessed according to the overall risk-benefit ratio. In general, high-risk patients would receive additional prophylactic SSI care. It is the surgical staff's discretion, according to their expertise, whether additional care is necessary and should be provided to

moderate-risk patients. This decision would have important financial and resource utilization implications since the majority of surgical patients (46.2%) have a moderate risk of developing an SSI.

Table XXVII: Frequency distribution representing the number of risk factors of each patient

Number of risk factors	Frequency	Percent	Cumulative %
0	324	11.1	11.1
1	879	30.2	41.4
2	1108	38.1	79.5
3	537	18.5	98
4	54	1.9	99.8
5	5	0.2	100
Total	2907	100	

The SSI risk tool was developed using the logistic regression parameters standardized to a range from zero to one hundred with higher values indicating greater risk of an SSI. Although 324 patients had an SSI risk tool score of zero (Table XXVII), the overall distribution showed important variance with respect to the score value and the number of combination of risk factors. This is an important observation showing that the risk score can adequately summarize the effects of several risk factors and their combination in homogeneous groups of similar SSI risk. It is interesting to note that although 324 patients (11.1%) did not possess any risk factors in the model, only 31.8% (925) patients had a low risk of

developing an SSI. The majority of the population was moderate-risk patients who possessed more than one risk factor in the model.

As previously mentioned, we produced an ROC curve to determine the cutoff values for low-risk, moderate-risk and high-risk patients in the development of SSIs. The area under the curve of 0.660, though not ideal, still confirms the validity of the model. The sensitivity and specificity of the curve are 75.5% and 49.8%, respectively, signifying that 75.5% of the positives are true positives and 50.2% of the negatives are true negatives. Also, the two cutoff values that were determined are as follows: 43.17 and 63.40. Therefore, a patient with a score below 43.17 is considered a low-risk patient, between 43.17 and 63.399 is considered a moderate-risk patient and above 63.40 is considered a high-risk patient.

The increase from the first to the third category is similar in all three SSI types. Approximately the same percentage of high-risk patients develop superficial incisional and organ/space SSIs even though the odds ratio are quite different. High-risk patients have an OR of 4.394 ($p<0.001$, 95% CI= 2.579-7.488) for superficial incisional SSI development whereas the same category of patients have an OR of 11.114 ($p<0.001$, 95% CI= 5.005-24.677) for organ/space SSI. This can be explained by the higher incidence of superficial incisional SSIs.

Concerning low-risk and moderate-risk patients, higher proportions can be found in the superficial incisional SSI graph compared to the amount of low-risk and moderate-risk patients who develop an organ/space SSI. Two percent of low-risk patients develop a superficial incisional SSI whereas less than 1% of the low-risk patients develop an organ/space SSI. Similarly, nearly 6% patients and approximately 4.5% of moderate-risk patients acquire a superficial incisional SSI and an organ/space SSI, respectively. Even though patients have higher ORs in the development of organ/space SSIs, higher percentages can be found on the superficial incisional SSI graphs since these infections are the most common type of SSI.

The results of the study agree in general with the scientific literature, although some risk factors evaluated in this project were not previously assessed. Some of these risk factors include inpatient status and partial or total dependence for everyday activities prior to surgery. On the other hand, certain risk factors known to independently predict SSIs were not found to be significant in this study, for example, diabetes mellitus, BMI, tobacco use, alcohol abuse, COPD and ASA score. Case-mix and patient profile differences between studies and patient populations may explain this. Even though this project included nearly 3000 patients, a larger population will be required to validate these findings and the SSI scoring tool. The strengths of the study include the following: the NSQIP database analysis is prospective, non-biased and comprehensive. Consequently, selection bias is eliminated. The only disadvantage is the generalization of

patients. Overall, we can state that NSQIP is a valid database which eliminates many types of biases and constitutes a very appropriate choice for this project. This can be observed in the results of this study. For example, since the majority of the significant risk factors in the logistic regression results were present for all three categories (any type of SSI, superficial incisional and organ/space SSI) and simply by observing the relative increase in the incidence of SSIs between specific risk group, we can conclude that our results are internally valid.

VI. Final Conclusion and Summary

Surgical site infections are one of the most common complications following surgery. Due to the increasing emergence of resistant bacteria and since currently available antibiotics are becoming less effective against these microorganisms, more attention should be provided preoperatively and intraoperatively to prevent SSIs rather than focusing on postoperative treatments.

The SSI risk tool developed in this study using the JGH patient population is a valid first version of a tool that, through further research and validation, can be expanded and generalized to other institutions. For instance, the risk factor of inpatient status is a newly presented risk factor in the literature and one of the highest odds ratios in the study (OR= 4.736 lower only to preoperative pneumonia in predisposing patients to an SSI). For the above reasons, inpatient status should be further assessed in a sensitivity analysis to establish if it is a high predisposing risk factor in the development of SSIs.

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