BLOOD GLUCOSE CONTROL AND SURGICAL SITE INFECTIONS IN CANCER PATIENTS: A LITERATURE REVIEW

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Abstract

Background: Surgical site infections (SSI) are the most common acquired infection during hospitalization and a major cause of morbidity, mortality, increased health care costs and delays in treatments for cancer patients.

Objective: The objective of this literature review was to gain a better understanding of the relationship between uncontrolled blood glucose and the odds of developing a SSI among cancer patients.

Interventions/Methods: A database search (which engaged PubMed, Medline, Cumulative Index to Nursing and Allied Health Literature and The Cochrane Database of Systematic Reviews) was completed using the key words: 'surgical site infection' or 'surgical wound infection' OR 'SSI' AND cancer or neoplasms OR oncology OR tumor OR malignancy AND diabetes OR hyperglycemia AND risk factors. Twenty-seven studies met the inclusion criteria to be included in this review.

Results: The odds ratio for history of diabetes or hyperglycemia and SSI following cancer surgery varied across studies. This is likely explained in part by the fact that some types of surgery are more invasive than others, are more lengthy, and involve areas of the body that are more prone to infection. The study with the highest rate of SSI (62.1%) was among patients with oral cancer and the study with the lowest rate of SSI (3.1%) was among patients with spinal cancer.

Conclusion: The literature review results suggested an association between SSI and patients with a history of diabetes mellitus or hyperglycemia.

Key Words:
Diabetes, cancer, literature review, surgical site infections, surgery, glucose

Introduction

Surgical site infection (SSI) following surgery can be devastating for patients, families and the entire health care team. In patients who experience surgery as a treatment for cancer, especially those who also have issues with diabetes or hyperglycemia, SSI can result in substantial morbidity and increased health care costs from longer hospital stays and consequent poor clinical outcomes. This is particularly important for cancer patients, as SSI can cause delays in chemotherapy and other treatments (Al-Naimi et al., 2015).

While SSI is known to be associated with uncontrolled blood glucose levels following surgery among cancer patients (Ambiru et al., 2007), and is the most common acquired infection during hospitalization (Badia et al., 2017), very little evidence had been available looking at the collective literature on risk of SSIs for cancer, as it related to the patients' blood glucose levels.

Observational studies suggest that postoperative hyperglycemia increases the rates of SSI and likely worsens patient's outcomes (Jeon et al., 2012; Jenks et al., 2014; Kalalla, et al., 2015). Several risk factors for the development of SSI have been reported, such as age, poor nutritional status, diabetes mellitus, smoking, and altered immune response (Atkinson et al., 2017). Ma et al., (2019) reported that elevated blood glucose was an independent factor influencing the occurrence of SSI. Another study reported a greater risk of SSI among patients with advanced breast cancer who had higher blood glucose levels during or immediately after surgery (Vilar-Compte et al., 2008). Therefore, proper management of blood glucose, regardless of whether patients have diabetes mellitus or not, is effective in decreasing the rates of SSI in cancer patients undergoing surgery, which in turn will likely decrease the length of hospital stay and health care costs (Ma et al. 2019).

Background

SSI and Patients with Diabetes, Cancer, and Surgeries

As early as the 1950s, researchers reported that people with uncontrolled diabetes were more likely to become infected during surgery compared to those without diabetes (Bortz & Burraughs, 1954). Today, there is considerable evidence to support the notion that patients with diabetes are more prone to infections than patients without diabetes. However, questions remain about the practical implications of reducing infections in patients with hyperglycemia before and during surgery (Pozzilli, et al., 2016). SSI may have negative outcomes for patients, nurses, and health care organizations. One study reported a significant decrease in patients' quality of life in relation to SSI occurrence, (Anderson et al., 2010), while another study reported that the relative health care cost for patients with SSIs were 1.43 times greater compared to patients without SSIs (Schweizer, 2014). Lastly, when comparing length of hospital stay among patients with or without an SSI, results reported a decrease in length of hospital stay from 14.2 (SD 10.9) to 8.1 (SD 2.4) days among patients without SSIs (Ozdemir, 2016).

Chronic hyperglycemia is associated with poor surgical outcomes and is a risk factor for SSI (Underwood et al., 2013). Patients with chronic hyperglycemia may also face longer hospital stays, repeat surgeries, pain, and an increased risk of death (Harrop et al., 2012). Although SSIs are a worldwide health concern, patients in the Gulf region may be at greater risk partly due to the high incidence of diabetes and certain types of cancers in this area (Hague et al., 2019). One study in Saudi Arabia found that 20 out of 228 patients (i.e., 8.7%) experienced SSIs after a variety of surgeries (Al-Naami, 2009).

Patients undergoing cancer surgeries have higher rates of SSI than non-cancer patients undergoing surgery partly due to a weakened immune system. Cancer can upset the body's ability to manufacture immune cells if there is organ involvement (Cancer Research UK, 2016). Furthermore, cancer treatments (e. g. radiotherapy) may indirectly reduce the body's ability to defend against disease (Iversen, 2013).

Some cancer surgeries pose a greater risk of developing an SSI. For example, one study reported that patients with malignant musculoskeletal tumors developed SSIs in 12.2% of cases (Satoshi et al., 2014), while another study reported that patients with oral cancer developed SSIs 40.6% of the time (Karakida, et al., 2010). In contrast, the incidence of SS1 among patients undergoing orthopedic surgery (0.83%) or surgery for spinal canal stenosis (0.28%) was low.

Although chemotherapy and radiation are the most useful and common treatments for cancer, surgery remains the primary treatment for solid tumors and provides the highest opportunity for cure (Bird et al., 2021). High success rates can be realized when the cancer is in its early stage and the surgery is combined with radiotherapy and chemotherapy. Other treatment options that may be necessary during this time include such options as the creation of an ostomy in order to improve patients' quality of life (Bird et al., 2021).

The aim of this literature review is to explore the relationship between the risk of SSI and uncontrolled blood glucose levels in adult patients with cancer. The primary research question was "Is there a relationship between SSI and uncontrolled blood glucose before, during and after surgery in adult patients with cancer?" A better understanding of this relationship is important because this knowledge can be used to inform clinical practice and health policy.

Methods

This review was guided by the work of Long (2002) because this method is clinically focused and provides a framework that allowed the research question (described above) to be answered. This method includes major sections such as the study's general properties, settings, sample, ethics, group comparability, outcome measurements, as well as a section on analysis of policy and practice implications.

Literature Search Strategy

A database search of PubMed, Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Cochrane was completed in 2016. Keywords used were 'surgical site infection' OR 'surgical wound infection' OR 'SSI' AND cancer or neoplasms OR oncology OR tumor OR malignancy AND diabetes OR hyperglycemia AND risk factors. Table 1 below illustrates the inclusion/ exclusion criteria for this review.

This initial search generated 532 citations (CINHAL (27 articles), Medline (128), PubMed (157) and the Cochrane database (220). After reading the title and abstract 501 articles were excluded because they were not relevant to the topic. Thirty-one studies met the inclusion criteria. and a further three were discarded as they did not contain relevant information, yielding 31 articles. Review of the reference section of the retained articles resulted in the addition of six articles (n=31). The first and second author reviewed these articles and met to reach consensus as to what articles to include or to exclude. Next, four more articles were discarded. Hence, 27 articles were included in this review. Figure 1 (below) illustrates the search strategy and outcome.

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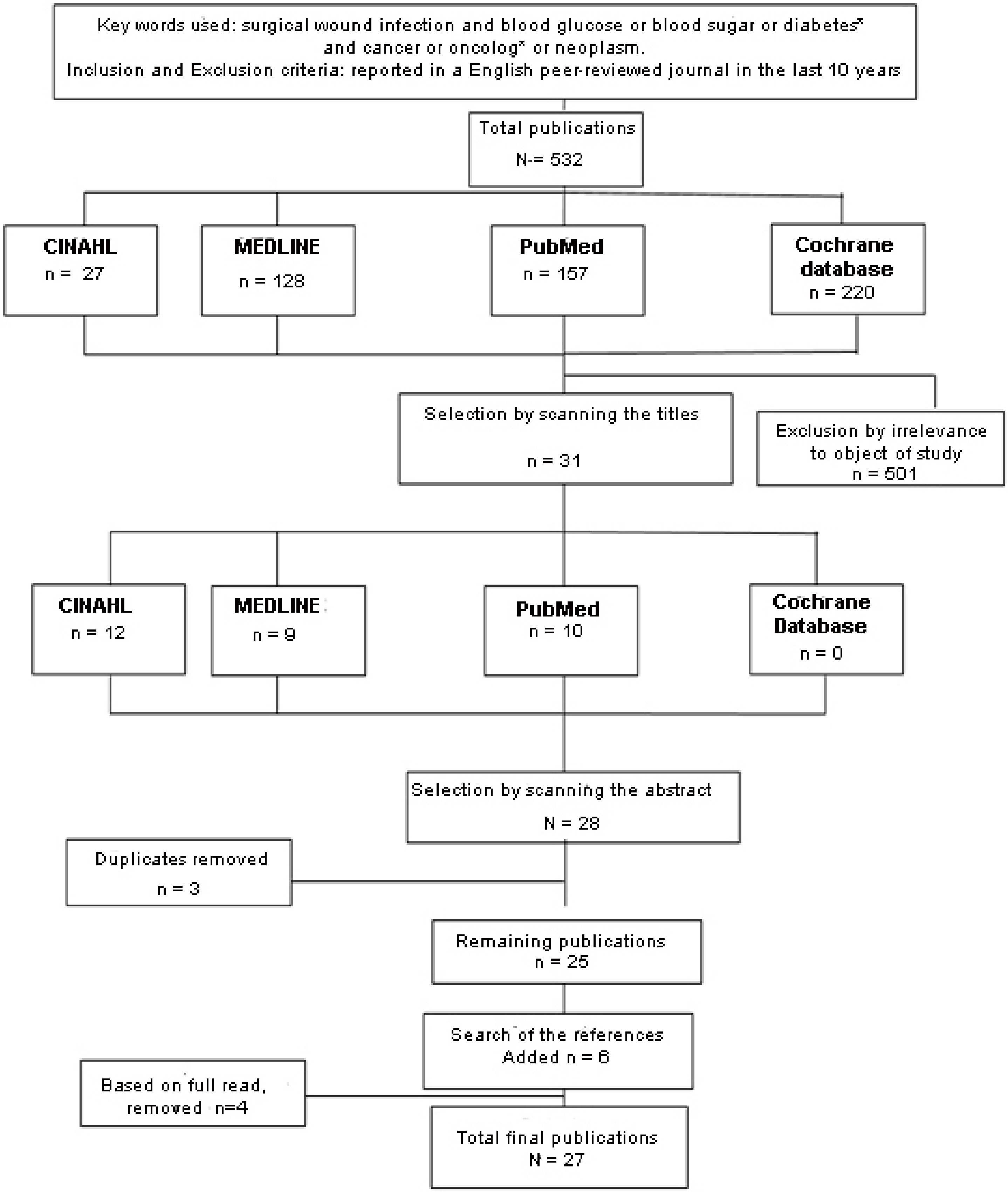
Table 1: Inclusion and exclusion criteria

Inclusion	Exclusion
Adult patients (18 years and older) with cancer who underwent surgery for cancer	Not an adult patient with cancer who did not undergo surgery
Adult patients with or without diabetes	Not an adult patient with or without diabetes
Article published in English or Arabic from 2006 to 2016	Article not published in English or Arabic between 2006-2016
Article is original research	Not original research (secondary source such as literature review)
Article focused on the rate of SSI among cancer patients	Article did not focus on rate of SSI among cancer patients

Figure 1: Search Strategy and Outcome



Assessment of the Methodological Quality of the Articles

The Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal Tool (Dearholt & Dang, 2012) was used to assess the methodological quality of the 27 articles. This appraisal tool ranks the evidence level and quality according to the methodology of the study and the completeness of the report of that study. Methodologies are ranked from 1 to 6, based on the strength of evidence, and quality is ranked from A to C based on the overall rating of the quality appraisal. A is high quality, B is good quality and C is low quality (or the study has major flaws). Most of the studies were assessed to be level III for level of evidence with the exception of the experimental studies and all, but one study was ranked as A or B for quality. The study that ranked a "C" was excluded from this review.

Data Extraction and Data Analyses

Based on the work of Long (2002), data extraction tables were developed. These tables included the following data: citation, year, country; purpose statement, number of participants, type of cancer; guideline or criteria used to measure SSI; and results (overall rate of SSI and OR). The data in these tables were critically analyzed and presented in the results section below.

Results

Characteristics of the Studies

Twenty-one studies were retrospective and chart reviews were the most common method for data collection. The remaining six studies could be classified as prospective designs and included the following types of studies (i.e., cohort (n=2), nested case control (n=1), cross sectional (n =1), RCT (n=1) and case control (n=1).

The studies included a range of different types of cancer such as gynecological, hepatic biliary-pancreatic, breast, head and neck, oral/oropharyngeal, spinal, colon rectal, brain, and esophageal cancer. Two studies focused on the relationship between high blood glucose levels and SSI (Vilar-Compte et al., 2008; Jackson et al., 2012), while the other studies focused on diabetes as a possible risk factor for SSI.

Most of the studies were from Asian countries (i.e., Japan, South Korea, China, Singapore, Taiwan, and India). Fewer studies were from the USA and Latin America and none of the studies were conducted in Middle Eastern countries. There was a total of 66,043 participants across all 27 studies and the sample size ranged from 53 to 9,638. Studies included patients undergoing surgery for hepatic-biliary-pancreatic (n=1) gynecologic (n=4), breast (n=4), head and neck (n=4), oral (n=3), spinal (n=2), colorectal (n=5), brain (n=4).

Studies used different definitions to confirm the presence of SSI (e. g. Centers for Disease Control and prevention (CDC), and the National Nosocomial Infections Surveillance System (NNIS). The most common guideline used was CDC. Some studies measured SSI daily for at least 30 days after surgery and one study measured the outcome every two weeks for one year.

Results: Literature Review

Due to the variety of cancers measured and surgeries assessed, there was a range of different results related to the outcome of interest (i.e., SSI). Some types of cancer surgery are more invasive than others and some areas of the body are more prone to infection. The study with the highest prevalence of SSI (i.e., 62%) was a study of 111 patients with oral cancer in Croatia (Belusic-Gobic et al., 2006) and the study with the lowest SSI rate (3.1%) was among patients with spinal cancer in Japan (Demura et al., 2009).

One of the measures that is commonly used to examine at the relationship between a variable and its outcome is odds ratio (OR) (Szumilas, 2010). All ORs that were not reported in the article were calculated by the researchers based on the data provided in the literature. Table 2 presents the ORs (next page).

Discussion

Most of the studies showed a relationship between SSI and uncontrolled glucose levels among diabetic and non-diabetic adult patients undergoing surgery. Overall, patients who have diabetes or hyperglycemia are more likely to have SSIs than those who do not have diabetes or high glucose levels. Notably, one study found that the presence of diabetes worked as a protective mechanism toward SSI (Jackson et al., 2012). This is surprising given that patients with cancer carry a greater risk for a SSI, even in the absence of diabetes or high blood glucose. Most hospital protocols aim to maintain a blood glucose levels less than 200 d/L in patients, regardless of the reason for admission (Shi et al., 2017). It is still unclear whether this is the correct cut point to aim for, to achieve the most positive outcomes. Therefore, it is important to test the blood glucose of patients and respond in order to keep them within a reasonable range as directed by the diabetes specialist.

It would be reasonable to question whether monitoring and controlling blood glucose levels might have deleterious effects on patients and patient care. For example, it could be hypothesized that lowering the blood glucose levels before surgery may cause negative outcomes. However, in those studies that measured blood glucose in order to control blood sugar levels during surgery, none of the patients suffered from hypoglycemia. Rather, patients on insulin drips whose blood glucose was continuously measured to maintain glucose levels at less than 150 d/L or 200 d/L. experienced less hypoglycemia.

Table 2: Odds Ratios of having an SSI among cancer patients with uncontrolled blood glucose levels undergoing surgery

Study	OR (C1) (95%) (p value)	Study	OR (C1) (95%) (p value)
Al-Naimi et al. (2015) USA	0.5 (0.28-0.9) p=0.001	Liu et al. (2007) Taiwan	2.51(0.92-10.44) p=0.002
Ambiru et al. (2008) Japan	6.6 (3.5-12.5) p<0.001	Lotfi et al. (2007) Brazil	p=0.129
Angrita et al. (2011) Colombia	10.9 (4.5-26.3) p<0.0001	Ma et al. (2016) China	6.07(3.95-8.5) p<.0001
Bakkum-Gamez et al. (2011) USA	2.2 (1.1-4.5) p=0.03	Mahdi et al. (2014) USA	p=0.001
Barreto et al. (2015) India	0.22 (0.07-0.63) p=0.01	Nakamoura et al. (2006) Japan	2.45(1.02-5.8) p=0.252
Belusic-Gobic et al. (2006) Croatia	p=0.13	Nakamoura et al. (2008) Japan	p=0.03
Bianchini et al. (2016) Italy	1.04 (0.41-2.60) p=0.930	Ogihara et al. (2008) Japan	p=0.38
Chaichana et al. (2015) USA	6.09 (1.38-9.354) p=0.02	Okabayashi et al. (2009) Japan	9.6(1.14-80.5) ***p=0.030
Chapman et al. (2015) USA	1.8 (0.85-3.85) p=0.032	Park et al. (2015) Korea	2.15(1.108-4.19) p=0.02
Davis et al. (2013) USA	0.0036 (1.10-1.59) p<0.0001	Serra-Aracil et al. (2011) Spain	9.43(1.04-85.9) p=0.047
Demura et al. (2009) Japan	17.1(3.64-43.6) p=0.011	Tuomi et al. (2015) USA	3.1(1.1-8.4) p<0.0001
Edwards et al. (2014) USA	1.24 (0.49-3.14)	Vilar-Comte et al. (2008) Mexico	2.9(1.2-6.8) p=0.04
Jackson et al. (2012) USA	1.44 (1.1-1.87)* 1.21 (0.97-1.52)**		
Lee et al. (2011) South Korea	33 (11-98) p<0.0001 p=0.0001		
Li et al. (2013) China	3.9 (0.92-10.44) p=0.077		
Vilar-Comte et al. (2008) Mexico	2.9 (1.2-6.8) p=0.004		

Legend: * = OR for Mild hyperglycemia:**= OR for moderate hyperglycemia, *** = unadjusted OR, OR= odds ratio, CI= confidence interval, Another important question is whether or not the statistical significance found in many of the studies was also clinically significant. For example, continuous blood glucose monitoring and control may be expensive and time-consuming. None of the studies in this review looked at cost-effectiveness or time commitment that nurses spend doing these activities. However, it would be reasonable to assume that an overall time saving for hospital staff is likely when SSI are prevented.

According to Franciosi et al. (2001), although continuous blood glucose monitoring is very useful in metabolic control, frequent blood glucose monitoring for diabetic patients could increase patients' stress, worries and lead to depressive mood. Therefore, nurses and physicians should be aware of this possible stress and if present they should intervene with tailored strategies. Many risk factors for SSI were identified in this review. Overall, most studies indicated a significant association between SSI and diabetic patients with cancer or those with uncontrolled blood glucose with cancer. However, there were some differences among studies related to contributing factors and SSI. In some studies, SSI was rare. For instance, a study that included patients with spinal cancer showed a SSI rate of only 3.1% (Demura et al., 2009), while another study among patients with brain cancer found a SSI rate of 5% (Chaichana, 2015). In some cases, variation in the rate of SSI among patients with similar types of cancer was found. For example, one study reported a 19.1% rate of SSI among women with breast cancer (Angarita et al., 2011), while another study reported a much lower rate (i.e., 7.3%) among breast cancer patients (Edwards et al., 2014). Other contributing factors include patient adherence to treatment, patient's nutrition status, stage of disease, length of stay in the hospital, hygiene, and health care practices and skills.

Okabayashi et al. (2009) described the amount of insulin required by patients undergoing hepatic resection. This RCT assessed the use of continuous glucose monitoring and an artificial pancreas (i.e., continuous insulin drip). The group that had a continuous insulin drip required on average 175 units plus another 93 units of insulin during the first 18 hours post-surgery while the group receiving usual care (sliding scale) used less than 24 units in total, for the first 18 hours after surgery. Patients whose blood glucose was monitored and treated through a sliding-scale had a significantly higher infection rate and, also received significantly lower amounts of insulin during the perioperative and postoperative period compared to the group that were on a continuous insulin drip.

Conclusion

Most of the studies in this review showed a relationship between uncontrolled blood glucose and SSI rates among cancer patients undergoing surgery. There were higher odds of having SSI in patients who were diagnosed with diabetes compared to those without the disease. Results of studies that measured blood glucose regardless of diabetic status found a higher incidence of SSI in patients with hyperglycemia. Therefore, close monitoring should be done for those patients with a history of diabetes or hyperglycemia during pre, intra, and postoperative periods. More research continues to be carried out, contributing to the evidence on the relationship between SSI and blood glucose control in patients with cancer (Belluse et al., 2020). Integrating monitoring and control as a part of the operative experience is likely to reduce costs and improve outcomes for surgical cancer patients.

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