

Correlation Between Postoperative Hyperglycemia and the Occurrence of Surgical Site Infections After Surgery for Gastroenterological Malignancy: A Retrospective Analysis

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Research Article

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Abstract

Background: Surgical site infection (SSI) is one of the most important complications after surgery for gastroenterological malignancy in that it leads to prolonged postoperative hospital stay and increased inpatient cost. Especially in case for malignancy, SSI sometimes delays the initiation of postoperative treatments including adjuvant chemotherapy and that can negatively affect prognosis.

Methods: Patients with gastroenterological malignancy who underwent surgery in our institution were retrospectively reviewed and categorized according to the occurrence of incisional SSI; SSI group and no SSI group. The clinicopathological characteristics between two groups were compared, i.e. age, sex, body mass index, location of malignancy, results of postoperative blood examination, operation time, and amount of blood loss. Then, the same analysis was performed in the subpopulation that included colorectal cancer patients.

Results: The 528 patients enrolled in the present study consisted of 330 males and 198 females of mean age 68 ± 11 years at the time of their operation. The numbers of patients with diseases of the esophagus, stomach, small intestine, colon and rectum, liver, gallbladder, and pancreas were 25, 150, 7, 255, 51, 5, and 35, respectively. Open surgery was performed in 303 patients and laparoscopic surgery in 225. Incisional SSI occurred in 46 patients (8.7%). Univariate analysis showed that postoperative hyperglycemia (serum glucose level ≥ 139 mg/dL within 24 h of operation) was the sole significant risk factor for incisional SSI ($p=0.026$). Multivariate analysis showed that postoperative hyperglycemia was an independent risk factor for incisional SSI (odds ratio 1.89, 95% confidence interval 1.009–3.614). In a subgroup analysis of patients who underwent colorectal surgery, the SSI occurred in 27 patients (10.5%). It also showed that postoperative hyperglycemia was a significant risk factor for incisional SSI ($p=0.033$), in addition to open surgery ($p=0.024$).

Conclusions: Postoperative hyperglycemia was the independent risk factor for incisional SSI after surgery for gastroenterological malignancy. Prevention of postoperative hyperglycemia is important in achieving a decrease in the rate of incisional SSI.

Background

Surgical site infections (SSIs) are reported to be one of the largest contributors to overall inpatient cost [1–5]. Furthermore, especially for patients with gastroenterological malignancy, SSI sometimes leads to delayed initiation of postoperative treatments. Determining the risk factors for SSI could potentially improve intraoperative and postoperative wound management in patients at risk. Many papers have reported different preoperative, intraoperative, and postoperative risk factors for SSI in abdominal surgery [6–8], such as perioperative transfusion, cirrhosis, or anastomosis of the bowel. On the other hand, numerous studies have reported diabetic patients to be subject to postoperative infectious diseases including SSI [9–11]. Martin et al. analyzed the association between diabetes and the risk of SSI in their

large systematic review and meta-analysis and reported the overall effect size for the association between diabetes and SSI as odds ratio (OR) 1.53 [9].

In diabetic patients, meticulous perioperative management of the serum glucose level can reduce the chance of SSI. We considered that the postoperative hyperglycemia, rather than diabetes mellitus itself, could be associated with SSI occurrence, while not only known diabetic patients but also unknown or non-diabetic patients could be at risk of postoperative hyperglycemia in some circumstances. In fact, Ata et al. revealed that a high serum glucose level was the only significant predictor of SSI for colorectal surgery patients [12].

The guidelines of the Centers for Disease Control and Prevention (CDC) divide SSI into three types: incisional, deep, and organ/space infections [13]. We considered that the risk factors and preventive measures for each of the three types differ. In the present study, we focused on incisional SSI and its risk factors in patients who underwent gastroenterological surgery for malignant diseases.

Methods

Patients

Patients with gastroenterological malignancy who underwent operations in our hospital were reviewed. Gastroenterological malignancy included malignant diseases (cancer, neuroendocrine tumor, and gastrointestinal stromal tumor as preoperative diagnosis) of the esophagus, stomach, small intestine, colon and rectum, liver, gallbladder, biliary duct, and pancreas. Based on the concept that SSI occurrence was associated with the operative procedure rather than the location of the disease itself, patients with disease of the distal biliary duct and papilla of Vater who received pancreatic resection were classified into "pancreas." We then divided the study patients into two groups, the SSI group and the no-SSI group, and compared clinical characteristics between them. Furthermore, we conducted the same comparison for the subgroup of patients with colorectal malignancy.

Patients with diabetes mellitus were defined as those who received pharmacological treatment for diabetes before the operation or those with a higher hemoglobin A1c level than normal. "Current smoker" was defined as an individual who smoked within 1 month before surgery.

Diagnosis

The patients with incisional SSI based on the definition of the guidelines of the CDC were included in the SSI group [14]. The wound was examined by a doctor and a nurse at least once a day until discharge of the patient from hospital. After discharge, the wound was examined by an outpatient doctor until 30 days after surgery. The diagnosis of SSI was made after discussions with surgeons, nurses, and members of the SSI surveillance team.

Statistical analysis

Continuous variables are presented as the mean \pm standard deviation, and categorical variables as number and percentage. The χ^2 and Mann–Whitney U tests were used to compare the two groups. Variables with associations with SSI in the univariate analyses (variables with p value \leq 0.1) were included in the multivariate logistic regression model. The effect of the associations was expressed as the odds ratio (OR) and 95% confidence interval (CI). All statistical analyses were conducted by one of the physicians participating in the study (T.Y.) using JMP, version 10 (SAS Institute, Cary, NC, USA). All reported p values are two-sided. A p value of less than 0.05 was considered to indicate statistical significance.

Postoperative serum glucose level was determined as the level within 24 h of the operation. The cutoff value of the continuous variables was determined using the receiver-operating characteristic curve.

Results

A total of 528 patients were enrolled in the present study, after we excluded 17 patients whose data of postoperative blood examination within 24 h of operation were unavailable. Table 1 shows the clinical characteristics of all patients, consisting of 330 males and 198 females of mean age 68 ± 11 years at the time of surgery. The numbers of patients with cancer of the esophagus, stomach, small intestine, colon and rectum, liver, gallbladder, and pancreas were 25, 150, 7, 255, 51, 5, and 35, respectively. Open surgery was performed for 303 patients and laparoscopic surgery for 225. Mean operation time was 327 minutes and the mean intraoperative blood loss was 348 mL. Intraoperative blood transfusion was performed for 52 patients.

Table 1
Clinical characteristics of all patients

Variables	Mean±SD or n(%)
Age (years)	68±11
Male	330 (62.5)
BMI (kg/m ²)	22.6±3.7
Diabetes mellitus	87 (16.5)
Current smoker	51 (9.7)
Alb (mg/dl)	4.1±0.5
Postoperative serum glucose	143±41
ASA classification	
I	48 (9.1)
II	401 (75.9)
III	78 (14.8)
IV	1 (0.2)
Organ	
Esophagus	25 (4.7)
Stomach	150 (28.4)
Intestine	7 (1.3)
Colon and Rectum	255 (48.3)
Liver	51 (9.7)
Gall bladder	5 (9.5)
Pancreas	35 (6.6)
Operative procedure	
Open	303 (57.4)
Laparoscopic	225 (42.6)
Length of operation (minutes)	327±161
Blood loss (g)	348±490

Data presented as mean ± standard deviation or n (%); BMI, body mass index; ASA, American Society of Anesthesiologists

Variables	Mean±SD or n(%)
Intraoperative blood transfusion	52 (9.8)
Data presented as mean ± standard deviation or n (%); BMI, body mass index; ASA, American Society of Anesthesiologists	

Patient selection is shown in Fig. 1. Incisional SSI occurred in 46 patients (8.7%). Table 2 shows the comparison between the SSI and no-SSI groups. Univariate analysis showed that postoperative hyperglycemia (serum glucose level ≥ 139 mg/dl within 24 h of operation) was the sole significant risk factor for incisional SSI ($p=0.026$). As shown in Table 3, multivariate analysis showed that postoperative hyperglycemia was an independent risk factor for SSI (OR 1.89, 95% CI 1.009–3.614, $p=0.047$). Diabetes mellitus itself was not associated with the occurrence of incisional SSI, nor with other factors (age, sex, body mass index, smoking, operative procure, etc.).

Table 2
Comparison of clinical characteristics between SSI and no-SSI groups.

Variables	SSI group	No-SSI group	p value
	n=46	n=482	
Age (years)	68±11	68±11	0.945
Male	34 (74)	296 (61)	0.094
BMI ≥25 kg/m ²	13 (28)	110 (23)	0.362
Diabetes mellitus	9 (20)	78 (16)	0.555
Current smoker	5 (10)	46 (10)	0.771
Alb (mg/dl)	4.0±0.6	4.1±0.5	0.296
Postoperative hyperglycemia	28 (61)	221 (46)	0.026*
ASA classification ≥ III	9 (20)	70 (15)	0.360
Organ			0.100
Esophagus	1 (2)	24 (5)	
Stomach	6 (13)	144 (30)	
Intestine	0	7 (1)	
Colon and Rectum	27 (59)	228 (47)	
Liver	5 (11)	46 (10)	
Gall bladder	1 (2)	4 (1)	
Pancreas	6 (13)	29 (6)	
Emergency surgery	2 (4)	8 (2)	0.201
Operative procedure			0.080
Open	32 (70)	271 (59)	
Laparoscopic	14 (30)	211 (44)	
Length of operation (minutes)	352±199	325±157	0.824
Blood loss (g)	389 [0-1730]	295 [0-1039]	0.143
Intraoperative blood transfusion	6 (13)	46 (10)	0.447
*p < 0.05			
Data presented as mean ± standard deviation or n (%); BMI, body mass index; ASA, American Society of Anesthesiologists			

Table 3
Multivariate logistic regression analysis of the risk factors of incisional SSI

Variables	Odds ratio	95% confidence interval	p value
Male	1.77	0.913-3.669	0.092
Open surgery	1.50	0.778-3.008	0.231
Glucose \geq 139	1.89	1.009-3.614	0.047*
*p < 0.05			

In a subgroup analysis of patients who underwent colorectal surgery, the SSI occurred in 27 patients (10.5%). Table 4 shows the comparison of the SSI and no-SSI patients. Univariate analysis revealed the same result of postoperative hyperglycemia as a significant risk factor for incisional SSI (p=0.033), in addition to open surgery (p=0.024).

Table 4
Comparison of clinical characteristics between SSI and no-SSI groups among patients who underwent colorectal surgery (n=255)

Variables	SSI group	No-SSI group	p value
	n=27	n=228	
Age (years)	67±12	68±11	0.446
Male/Female	17	126	0.356
BMI ≥25 kg/m ²	7	50	0.563
Diabetes mellitus	6	26	0.109
Current smoker	2	15	0.870
Alb (mg/dl)	4.0±0.7	4.1±0.5	0.937
Postoperative hyperglycemia	15	79	0.033*
ASA classification ≥ III	3	39	0.427
Emergency surgery	2	7	0.248
Operative procedure			0.024*
Open	13	62	
Laparoscopic	14	166	
Length of operation (minutes)	266±141	318±152	0.392
Blood loss (g)	50 [0-1100]	148 [0-4177]	0.300
Intraoperative blood transfusion	2	6	0.178
*p < 0.05			
Data presented as mean ± standard deviation or n (%); BMI, body mass index; ASA, American Society of Anesthesiologists			

Discussion

Several reports have analyzed risk factors for SSI after different surgical approaches for patients with different diseases. In orthopedic surgery, many reports regarding risk factors for SSI have been published because of its need for a specifically clean procedure [15–18]. On the other hand, in gastroenterology there has been extensive analysis of risk factors and prevention of SSI in colorectal surgery because of its high rate of SSI occurrence. However, thus far no reports have focused on the risk factors for SSI in all forms of gastroenterological surgery to treat malignancy.

We found that postoperative hyperglycemia was the sole independent risk factor for incisional SSI, with no other clinical and perioperative factors influencing the occurrence of SSI. Although there is ample evidence showing that perioperative hyperglycemia has been associated with postoperative infective complications, these studies analyzed all infectious disease including SSI, pneumonia, and urinary tract infections [19–21]. Previous reports that focused on the association between postoperative hyperglycemia and the SSI rate highlighted specific surgical procedures, such as colorectal surgery, cardiothoracic surgery, and sleeve gastrectomy [10, 11, 22]. On the other hand, Ata et al. analyzed a total of 2,090 general and vascular surgery patients in whom only the postoperative serum glucose level was associated with SSI [12]. Although this result was consistent with our present findings, the study included a diverse array of surgeries for many diseases, clean or dirty, benign or malignant, as well as gastroenterological or cardiovascular. Our study selected patients with the common circumstance of gastroenterological malignancy, and we considered that this inclusion criterion was reasonable for the improvement of postoperative wound management, which is performed by doctors and nurses in the same department.

In the present study, patients with colorectal malignancy were exclusively analyzed as a subgroup in addition to the analysis of all patients with gastroenterological malignancy. Although the subgroup result was slightly different of that of all study patients, open surgery was also the principal risk factor for incisional SSI. One could theorize that especially in open colorectal surgery, the longer incision on the skin will be more prone to intraoperative contamination by fecal ascites in comparison with laparoscopic surgery. Although several previous studies have analyzed patients who underwent elective colorectal surgery, they have not focused on the postoperative serum blood glucose level, preferring to evaluate the presence or absence of diabetes [23–25]. Thus, the results of our subgroup analysis should be of further value for the prevention of SSI after colorectal surgery.

Unfortunately, in our retrospective study the data on intraoperative body temperature were not available and we were unable to conduct a detailed analysis of the correlation between this factor and SSI occurrence. The guidelines for safe surgery published by the World Health Organization describe that “maintenance of normothermia during surgery” reduces the rate of SSI [26]. Reports have proved the association between intraoperative hypothermia and the incidence of SSI [27, 28]. Tsuchida et al. reported that severe hypothermia (<35.0°C) and late-nadir hypothermia (<36°C more than 2 h after anesthesia induction) were significant risk factors for SSI in prolonged gastroenterological surgery [27]. On the other hand, contrasting results were also reported in some studies [29, 30], and the appropriate intraoperative body temperature remains a controversial aspect. Further study of the impact of intraoperative hypothermia on SSI is therefore warranted.

One of the measures to reduce SSIs is to build the preventive SSI care bundle (i.e., the use of systematic approaches). Many reports have indicated the effectiveness of bundles, especially for colorectal surgery [31, 32]. Some bundles include strict glycemic control [33–35]. Recently in our hospital we have adopted the statute that all severely diabetic patients should be admitted more than 1 week before the operation and should receive specific management of blood glucose level by diabetic physicians to reduce potential

perioperative complications caused by hyperglycemia. The results reported herein are important in that they indicate the importance of postoperative management of blood glucose levels, not only for severely diabetic patients but for all patients with gastroenterological malignancy.

Our study has several limitations. First, the study was conducted at a single center and was based on a small number of patients. A large-scale multicenter study is needed to confirm our findings. Second, operative and postoperative management involving the types of sutures or dressings and antibiotics used perioperatively were dependent on different clinicians, resulting in an inconsistent quality of care. Finally, other factors not included in our analysis may influence eventual outcomes.

Conclusions

Postoperative hyperglycemia was the independent risk factor for incisional SSI after surgery for gastroenterological malignancy. Prevention of postoperative hyperglycemia is therefore important in achieving a decrease in the rate of incisional SSI.

Abbreviations

SSI; surgical site infections

Declarations

Ethics approval and consent to participate: All study participants provided informed consent, and the study design was approved by the ethics review board of Kitano Hospital (reference no. 2201013). The study was performed in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and/or analysed during the current study are not publicly available because individual privacy could be compromised but are available from the corresponding author as a hyperlink to the deposited file on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: TY designed the study. TY and MY acquired the data, TY analyzed and interpreted the data, drafted and revised the manuscript. SU and HT helped to revise the manuscript. All authors read and approved the final version of manuscript.

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Figures

Fig. 1

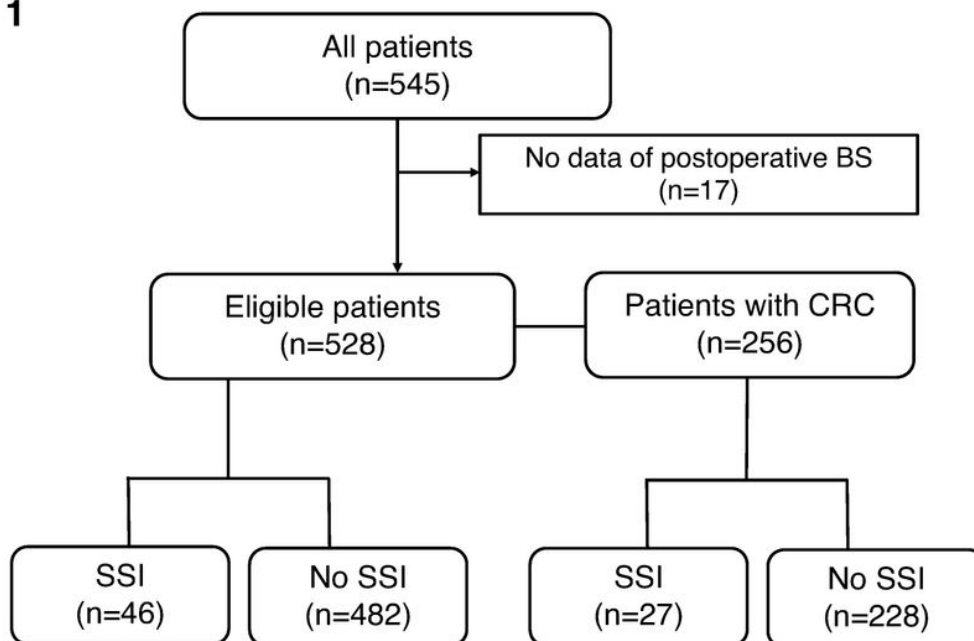


Figure 1

Patient selection