Surgical site infection following elective mesh repair of inguinal hernia: an analysis of risk factors

Yeye Zhuo
The First Affiliated Hospital of Shantou University Medical College
Xinxin Li
The First Affiliated Hospital of Shantou University Medical College
Juntian Chen
The First Affiliated Hospital of Shantou University Medical College
Qian Zhang
The First Affiliated Hospital of Shantou University Medical College
De Cai (570894243@qq.com)
The First Affiliated Hospital of Shantou University Medical College https://orcid.org/0000-0002-4625-0940

Research article

Keywords: Surgical site infection, Risk factors, Elective mesh repair of inguinal hernia, Neutrophil-lymphocyte ratio

Posted Date: January 15th, 2020

DOI: https://doi.org/10.21203/rs.2.20847/v1

Abstract

Background: Surgical site infection (SSI) is a complication of mesh repair of inguinal hernia (IH) with an increase in length of stay and costs. We investigated both controllable and non-controllable risk factors for SSI following elective mesh repair of IH.

Methods: A retrospective analysis was conducted of 1177 adult patients who underwent elective mesh repair of IH (not receiving antibiotic prophylaxis) from January 2010 to September 2019. Demographics, surgical variables and laboratory data were extracted from the electronic medical records. Receiver operating characteristic (ROC) analysis was performed to determine the optimal threshold of continuous variables. Independent risk factors for SSI were identified by univariate and multivariate analyses.

Results: In total, 647 open and 530 laparoscopic IH repairs were included. The overall SSI rate within 30 days after surgery was 3.2% (39/1342 hernias) in the absence of antibiotic prophylaxis. Both the preoperative neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were negatively correlated with the postoperative period of SSI ($r = -0.368$, $P = 0.021$; $r = -0.334$, $P = 0.038$, respectively). On multivariate analyses, body mass index (BMI) > 24.6 kg/m 2 (odds ratio [OR], 1.152; 95% confidence interval [CI], 1.041-1.275), current smoker (OR, 4.226; 95% CI, 1.222-14.611), preoperative NLR > 1.97 (OR, 3.670; 95% CI, 1.675-8.041), and open approach (OR, 4.866; 95% CI, 1.877-12.618) were significantly related to postoperative SSI.

Conclusion: The controllable risk factors (elevated BMI, current smoker) found out here may help to identify patients at high-risk of SSI, allowing targeted preventive measures. Preoperative NLR > 1.97 is a previous unrecorded predictor for SSI following elective mesh repair of IH. Further study is needed to ascertain the magnitude of their effect.

Introduction

Inguinal hernia (IH) repair is one of the most common general procedures performed worldwide, with more than 20 million operations performed annually [1]. The repair contains reinforcing the posterior wall of the inguinal canal, usually using a polypropylene mesh; either via an open anterior approach or posteriorly from within the abdomen with laparoscopy. Over 75% of repairs were accomplished with the implantation of mesh in the developed countries [2].

Although hernia recurrence have been greatly reduced with the use of mesh compared to that of non-mesh repair [3], bacterial biofilm clinging to mesh has the potential to lead to the development of surgical site infections (SSI) [4]. One meta-analysis published in 2007 [5], encompassing 6 randomized clinical trials (RCTs) reported a 2.89% SSI rate following mesh repair of IH (open and laparoscopy) in the absence of antibiotic prophylaxis. A 2.59% SSI rate was found in the latest Cochrane meta-analysis published in 2018 [3], including 20 RCTs, essentially flat to the past decade.

SSI often results in an increase in hospitalization time, associated increase in expenses, and a decrease in quality of life [6]. The identified risk factors for SSI range widely and remain controversial. These include controllable factors such as obesity, long operative time, nonsterilized instruments, days of drainage and urinary catheter [7, 8]. Non-controllable risk factors available in the literature comprise diabetes, age > 65 years, steroid use and concurrent ipsilateral hydrocele repair [9–11]. Lots of techniques for the prevention of SSI have been recommended [12], including preoperative factors (showering with soap, antimicrobial prophylaxis), intra-operative factors(skin preparation with an alcohol-based antiseptic, normothermia), and postoperative factors (shortening duration of drainage use, right nursing intervention).

We reviewed SSIs occurring after mesh repair of IH in our institution, making an attempt to add more evidence in regard to the presence of existing risk factors and also to identify any underlying novel risk factors, with a focus on the postoperative SSI in patients not receiving antibiotic prophylaxis.

Methods

Patients and study design

This retrospective observational study was conducted in the Department of Gastrointestinal Surgery, the First Affiliated Hospital of Shantou University Medical College. We identified all elective mesh repair of IH performed between January 2010 and September 2019 from the electronic medical records, and a total of 1974 mesh repairs (in 1774 adult patients) were recorded. There was one chief surgeon attending in every operation as required. Regularly the skin was shaved with a razor the day before surgery and prepared using ioprep. Lichtenstein repair was applied for open approach while trans-abdominal preperitoneal repair (TAPP) and totally extraperitoneal repair (TEP) were used for laparoscopic approach. Both operative procedures were performed under standard techniques as published previously. Patients were routinely required to return for a postoperative clinical examination 30 days after discharge. Details of hospitalization, subsequent visit and any additional hospital visits within 30 days after surgery were obtained through electronic patient records and available paper document.

Notably, patients who received antibiotic prophylaxis were excluded from this study. Patients with lacking data on the postoperative assessment and/or who underwent another concomitant surgery were also excluded. The institutional review board of the First Affiliated Hospital of Shantou University Medical College approved this study.

Data collection

Particulars of postoperative SSIs within 1 month were collected. Moreover, we included 36 variables with the aim to explore the risk factors related to SSI. Demographic factors (at the time of surgery) included age, body mass index (BMI), smoking status, drinking condition and gender. Accompanied diseases including diabetes mellitus, hypertention, pulmonary disease (chronic obstructive pulmonary disease, asthma and chronic bronchitis) and malignant tumor were retrieved from medical charts. Chronic drug therapy that may have an effect on the development of SSI including current glucocorticoid use (oral and inhaled) and statin use [13] were gathered. The following operative data were abstracted: American Society of Anesthesiologists (ASA) score, hernia type (direct, indirect, and combined), hernia characteristics (left, right, and bilateral), duration of IH presentation (reflected in number of years), prior history of IH repairs, lengths of preoperative hospital stay, surgical technique (open and laparoscopy), operative time (from the start of incision to completion of skin closure), intraoperative blood loss and surgical drains. Pre-operative blood examination (within 24 hours prior to the surgical operations) covered white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), monocyte (MON), eosnophils (EOS), basophil granulocyte (BASO), red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean red blood cell hemoglobin (MCH), platelet (PLT) and serum albumin (ALB). Serum neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were calculated as the absolute neutrophil or platelet count divided by the absolute lymphocyte, respectively. We did not considered about type of anesthesia as an additional risk factor for SSI.

SSI was diagnosed by the surgeons adapted from guidelines by the U.S. Centers for Disease Control and Prevention (CDC) [14]. Superficial SSI was defined as an infection that arose within 30 days postoperatively and involved only skin or subcutaneous tissue. Deep SSI was defined as an infection arose within 1 year postoperatively and involved the fascial and muscle layers.

Statistical analyses

We compared the demography, previous history of medicine, surgical factors and related laboratory values between the patients with SSI and the other patients who were not suffered from SSI. All continuous variables were evaluated as binary categories, allowing the calculation of relative risk. Receiver operating characteristics (ROC) curves were used to determine a cutoff for each continuous variable (i.e., age, BMI, duration of IH presentation, preoperativestay and laboratory results). The optimal cut-off value including the sensitivity and specificity of related variables was calculated by Youden’s index. On the condition that no definite cut-offs could be found in their ROC curves, certain continuous variables’ own average values were chosen as their cut-offs, and some blood results were evaluated categorically according to reference ranges used in our hospital laboratory. Categorical data were assessed by 2-sided Pearson’s chi-square test or Fisher’s exact test. The Pearson correlation coefficient was evaluated to assess correlations between variables. Variables with a P value < 0.05 in the univariate analysis were then entered into a forward stepwise multivariate analysis. We assess the goodness of fit of the model by the Hosmer-Lemeshow test. A P value of less than 0.05 was set as statistically significant. Statistical analysises were performed using SPSS 23.0 (IBM Corp., Armonk, NY).

Results

Patient characteristics

In total, 1177 patients were enrolled in the final analysis based on the inclusion and exclusion criteria (561 with antibiotic prophylaxis, 36 with missing data). There were 165 bilateral hernia operations performed among the eligible patients, thus, the total number of hernias was 1342. Demographic data and surgery-related information are shown in Table 1.

Table 1
Patient demographics and surgery-related information

	n = 1177
Age (year)	59.4 ± 16.0 [18–94]
Gender	
male	1124 (95.5)
female	53 (4.5)
BMI	22.6 ± 3.1 [11.6–33.2]
ASA score	
□	137 (11.6)
□	975 (82.8)
□	62 (5.3)
□	3 (0.3)
Type of hernia	
Direct	173 (14.7)
Indirect	962 (81.7)
Combined	42 (3.6)
Hernia characteristics	
Left	412 (35.0)
Right	600 (51.0)
Bilateral	165 (14.0)
Operation technique	
Open	647 (54.9)
TAPP	182 (15.5)
TEP	348 (29.6)
Initial operation	1148 (97.5)

Continuous dataare presented as the mean ± standard deviation (SD) [Range].

Categorical data are presented as the number with the percentage in parenthesis.

BMI: body mass index; ASA: American Society of Anesthesiologists; TAPP: trans-abdominal preperitoneal repair, TEP: totally extraperitoneal repair

Feature of SSI

There were 39 SSIs developing among the 1177 patients within 30 days after mesh repair of IH according to electronic medical records, revealing a 3.2% (39/1342) overall SSI rate in the absence of antibiotic prophylaxis. All of the recorded infections were superficial SSIs. SSIs were observed within a mean interval of 4.6 (4.0) days postoperatively (range, 1–18 days) during the original admission, with most (82.1%, 32/39) found within the first post-operative week. The causative agent was isolated in the secretions from surgical site in 21 infected patients. The most common microorganism isolated was staphylococcus aureus (11). The other microorganism included staphylococcus epidermidis (4), pseudomonas aeruginosa (4), enterococcus faecalis (2) and methicillin-resistant staphylococcus epidermidis (1). All these patients were resolved by intravenous antibiotic treatment and/or wound drainage (12.8%, 5/39), without removal of the mesh. On the other hand, both the preoperative NLR and PLR level were negatively related to the postoperative period of SSI ($r = -0.368$, $P = 0.021$; $r = -0.334$, $P = 0.038$, respectively) (Figs. 1 and 2).

Risk factors for SSI

Among the 36 variables which may predispose patients to postoperative SSIs, 7 continuous variables' optimal cut-offs were identified by ROC curve analysis and Youden's index (Fig. 3). Table 2 summarized their corresponding optimal cut-off values, area under the ROC curves (AUCs) and 95% confidence interval (CI) for these continuous variables.

Table 2

Optimal cut-off value of continuous variables identified by the ROC analysis

Variables	Cut-off value	Area under the ROC curve (AUC)	95% CI	P	Sensitivity	Specificity
BMI (kg/m^2)	24.6	0.604	0.516–0.691	0.027	43.6%	75.9%
NEU (10^9/L)	3.39	0.601	0.521–0.682	0.031	87.2%	34.3%
LYM (10^9/L)	1.86	0.655	0.571–0.738	0.001	58.0%	71.8%
BASO(10^9/L)	0.025	0.600	0.507–0.693	0.033	73.4%	43.6%
ALB (g/L)	37.8	0.707	0.626–0.787	0.000	75.0%	61.5%
NLR	1.97	0.662	0.581–0.743	0.001	74.4%	51.8%
PLR	168.02	0.614	0.522–0.707	0.015	35.9%	85.0%

ROC: receiver operating characteristic curve; BMI: body mass index; NEU: neutrophil; LYM: lymphocyte; BASO: basophil; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

The univariate analysis (Table 3) revealed that a total of 12 variables, including BMI > 24.6 kg/m^2 (43.6% vs. 24.2%, P = 0.007), current smoker (25.6% vs. 11.3%, P = 0.009), diabetes mellitus (12.8% vs. 4.6%, P = 0.025), previous history of IH repairs (7.7% vs. 2.3%, P = 0.045), NEU > 3.39 × 10^9/L (84.6% vs. 65.2%, P = 0.016), LYM < 1.86 × 10^9/L (71.8% vs. 42.0%, P = 0.000), BASO < 0.025 × 10^9/L (43.6% vs. 26.6%, P = 0.022), ALB < 37.8 g/L (61.5% vs. 25.2%, P = 0.000), NLR > 1.97 (74.4% vs. 48.2%, P = 0.002), PLR > 168.02 (35.9% vs. 15.0%, P = 0.001), open approach (87.2% vs. 53.9%, P = 0.000) and operative time > 77 min (35.9% vs. 21.0%, P = 0.029), were found to be significantly related to SSI.

Table 3
Univariate analysis of risk factors predicting SSI following mesh repair of inguinal hernia

Variables	**SSI (n = 39, 3.2%*)**	**No SSI (n = 1138, 96.8%*)**	**OR**	**95%CI**	**p**
Demographic factors, yes					
Age ≥ 65 years	18 (46.2)	509 (44.7)	1.059	0.558–2.009	0.860
Gender (male)	39 (100)	1085(92.2)	1.856	0.250-13.779	0.545
BMI > 24.6 kg/m^2	17(43.6)	275(24.2)	2.425	1.269–4.633	0.007
Current smoker	10(25.6)	129(11.3)	2.697	1.285–5.663	0.009
Alcoholism	3(7.7)	35(3.1)	2.626	0.772–8.939	0.122
Comorbidity, yes					
Diabetes mellitus	5(12.8)	52(4.6)	3.071	1.154–8.176	0.025
Hypertension	7(17.9)	192(16.9)	1.078	0.469–2.478	0.860
Pulmonary disease	2(5.1)	54(4.7)	1.085	0.255–4.621	0.912
Malignancy	3(7.7)	41(3.6)	2.230	0.659–7.540	0.197
Chronic drug treatment, yes					
Current steroid use	2(5.1)	53(4.7)	1.107	0.260–4.714	0.891
Current statin use	1(2.6)	52(4.6)	0.550	0.074–4.081	0.558

Data are presented as the number with the percentage in parenthesis.

*There were 39 infected cases among 1342 hernias which were surgically treated (1012 unilateral hernia and 165 bilateral hernia repairs). SSI: surgical site infection; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; MON:monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

Variables	SSI (n = 39, 3.2%*)	No SSI (n = 1138, 96.8%*)	OR	95%CI	p
Procedure-related factors, yes					
ASA score ([illegible]-[illegible])	3(7.7)	62(5.5)	1.446	0.433–4.827	0.549
Type of hernia			0.610	0.263–1.419	0.251
Direct	5(12.8)	168(14.8)			
Indirect	34(87.2)	928(81.5)			
Combined	0	42(3.7)			
Hernia characteristics			0.844	0.519–1.372	0.493
Left	15(38.5)	397(34.9)			
Right	20(51.3)	580(51.0)			
Bilateral	4(10.3)	161(14.1)			
Duration of inguinal hernia presentation > 3.5 year	10(25.6)	270(23.7)	1.109	0.533–2.304	0.782
Previous history of inguinal hernia repairs	3 (7.7)	26 (2.3)	0.281	0.081–0.970	0.045
Preoperative stay > 3 days	6 (15.4)	176 (15.5)	0.994	0.410–2.407	0.989
Pre-operative blood results					
WBC (reference 3.5–9.5 × 10^9/L)			0.548	0.247–1.216	0.139
< 3.5	0	5 (0.4)			
> 9.5	8 (20.5)	136 (12.0)			

Data are presented as the number with the percentage in parenthesis.

*There were 39 infected cases among 1342 hernias which were surgically treated (1012 unilateral hernia and 165 bilateral hernia repairs). SSI: surgical site infection; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphoc-

yte; MON:monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

Variables	SSI (n = 39, 3.2%*)	No SSI (n = 1138, 96.8%*)	OR	95%CI	p
NEU (> 3.39×10^9/L)	33 (84.6)	742 (65.2)	2.935	1.220–7.065	0.016
LYM (< 1.86×10^9/L)	28 (71.8)	478 (42.0)	3.515	1.733–7.129	0.000
MON (reference 0.1–0.6 × 10^9/L)			0.546	0.288–1.038	0.065
< 0.1	1 (2.6)	7 (0.6)			
> 0.6	17 (43.6)	356 (31.3)			
EOS (reference 0.02–0.52 × 10^9/L)			1.299	0.452–3.736	0.627
< 0.02	1 (2.6)	24 (2.1)			
> 0.52	3 (7.7)	68 (6.0)			
BASO (< 0.025×10^9/L)	17 (43.6)	303 (26.6)	2.129	1.116–4.064	0.022
RBC (reference 4.3–5.8 × 10^{12}/L)			0.907	0.454–1.812	0.783
< 4.3	11 (28.2)	292 (25.7)			
> 5.8	1 (2.6)	35 (3.1)			
HGB (reference 130–175 g/L)			0.773	0.380–1.573	0.477
< 130	11 (28.2)	258 (22.7)			
> 175	0	7 (0.6)			
HCT (reference 0.40–0.50)			1.307	0.644–2.653	0.459

Data are presented as the number with the percentage in parenthesis.

*There were 39 infected cases among 1342 hernias which were surgically treated (1012 unilateral hernia and 165 bilateral hernia repairs). SSI: surgical site infection; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphoc-

yte; MON:monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

Variables	SSI (n = 39, 3.2%*)	No SSI (n = 1138, 96.8%*)	OR	95%CI	p
< 0.40	11 (28.2)	366 (32.2)			
> 0.50	0	20 (1.8)			
MCV (reference 82–100 fl)			1.051	0.367–3.007	0.927
< 82	2 (5.1)	97 (8.5)			
> 100	2 (5.1)	25 (2.2)			
MCH (reference 27–34 pg)			0.861	0.300-2.472	0.782
< 27	2 (5.1)	88 (7.7)			
> 34	2 (5.1)	14 (1.2)			
PLT (reference 125–350 × 10^9/L)			0.904	0.212–3.850	0.891
< 125	1 (2.6)	24 (2.1)			
> 350	1 (2.6)	29 (2.5)			
ALB(< 37.8 g/L)	24 (61.5)	287 (25.2)	4.744	2.455–9.168	0.000
NLR > 1.97	29 (74.4)	548 (48.2)	3.122	1.508–6.467	0.002
PLR > 168.02	14 (35.9)	171 (15.0)	3.167	1.614–6.214	0.001
Intraoperative factors, yes					
Surgical technique			5.824	2.261–14.998	0.000
Laparoscopic	5 (12.8)	525 (46.1)			

Data are presented as the number with the percentage in parenthesis.

*There were 39 infected cases among 1342 hernias which were surgically treated (1012 unilateral hernia and 165 bilateral hernia repairs). SSI: surgical site infection; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; MON:monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

Variables	SSI (n = 39, 3.2%*)	No SSI (n = 1138, 96.8%*)	OR	95%CI	p
open	34 (87.2)	613 (53.9)			
Duration of surgery > 77 min	14 (35.9)	239 (21.0)	2.106	1.078–4.115	0.029
Intraoperative blood loss > 8 ml	16 (41.0)	485 (42.6)	0.937	0.490–1.792	0.843
Use of postsurgical drains	7 (17.9)	271 (23.8)	0.700	0.305–1.604	0.399
Data are presented as the number with the percentage in parenthesis.					
*There were 39 infected cases among 1342 hernias which were surgically treated (1012 unilateral hernia and 165 bilateral hernia repairs). SSI: surgical site infection; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphoc-					
yte; MON:monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio					

In the multivariable analysis, we excluded 2 variables that were deemed “redundant” (NEU and LYM), with the purpose of avoiding multi collinearity. BASO < 0.025×10^9/L, ALB < 37.8 g/L, PLR > 168.02 and operative time > 77 min were not in the model equation by the forward stepwise procedure, and the ultimate statistical results identified as the independent risk factors for SSIs: BMI > 24.6 kg/m^2 (odds ratio [OR], 1.152;95% CI, 1.041–1.275), current smoker (OR, 4.226; 95% CI,1.222–14.611), NLR > 1.97 (OR, 3.670; 95% CI,1.675–8.041), and open approach (OR, 4.866; 95% CI,1.877–12.618) (Fig. 4). The analysis displayed a well Hosmer-Lemeshow test value indicative of goodness of fit (χ^2 = 9.096, P = 0.334).

Discussion

IH repair is traditionally regarded as a clean wound operation. However, the reported rate of SSI following IH repair varies widely in the literature, with most indicated higher than the defined value for a clean operation (an infectious rate < 2%) [8]. Identification of risk factors for SSI would be helpful to reduce infection rate by modification of those factors amenable to intervention. A few studies have reported that up to 60% of SSIs could be prevented by adopting strategies that include some evidence-based measures [15]. On the other hand, antibiotic prophylaxis is a usually accepted and recommended method for the prevention of SSI owing to its good activity and adequate concentration against potential pathogenic bacterium, but it also comprises risks of allergic side effects, bacterial resistance and increased costs [16]. The discussion on risk factors in our study may help to identify some unmodifiable factors used to select the best candidates for antibiotic prophylaxis. We excluded the patients receiving antibiotic prophylaxis in order to ensure the homogeneity of the data. Since the use of prosthetic material has become the rule nowadays, we focused our study only on mesh repair.

Controllable factors

Elevated BMI is associated with poor wound healing and increased incidence of SSIs, which has been reported by numerous other authors [17–19], possibly because of its relationship with other comorbidities, longer operation times, greater bleeding, and decrease in peri-operative subcutaneous tissue oxygenation [20].The larger impact of elevated BMI for superficial SSI than that for deep SSI could be explained mainly by the potential for dead spaces which may harbor fluid collections and infection during wound closure [21]. This may be similar cause leading to our own findings (all SSIs observed here were superficial). Although weight loss should be included in the list of optimization measures ahead of elective surgical intervention according to the available evidence, there has been no consistent appropriate range of BMI in the literature. In a large case series with 57,951 initial open IH repair based on the USA personal use file database, an BMI $\geq$ 35 kg/m^2 was found to be an independent risk factor for SSI [22]. However, H. Yang et al. came to a conclusion that patients with a BMI > 25 kg/m^2 had an increased risk for mesh infection following IH repair than those with a normal BMI from their 10-year experience in one Chinese center [23]. A BMI > 25 kg/m^2 was also observed to be significantly associated with SSI in a Sweden's study carried out in 2010 [11]. The different cut-off values for BMI may be explained by the differences in study population and study year. WHO has recommended lower BMI cutoffs for the definition of obesity and clinical preventive measures among Asians, in view of Asians being at higher risk of BMI related comorbidities at lower BMI cutoffs compared to international standards [24]. Coinciding with the study of H. Yang et al., we recommended that BMI should be kept within the range of 18.5–24.6 kg/m^2 so as to decrease SSIs rate. Further exhaustive studies with a larger sample size are needed to develop a predictive model effectively to confirm the warning value of BMI.

Patients in our study who were current smokers had a 4.2-fold increased risk of superficial SSIs. The effect of patient smoking on SSI was previously discussed in the literature [18, 25, 26]. Smoking is known to increase tissue hypoxia via vascular vasospasm and a global increase in systemic inflammation [27]. Hypoxia promotes the colonization of bacteria and breaks oxidative bacterial killing mechanisms thus making the tissue vulnerable to infection [28]. Additionally, the temporary detrimental vasoactive effect on peripheral tissue blood flow induced by smoking may lead to infection developing in tissues characterized by a marginal blood supply [29] such as superficial SSIs which were found in our study. Antioxidant supplement such as vitamin C or/and vitamin E may attenuate the injury of smoking on inflammatory cells and endothelial function. Moreover, abstinence from smoking with the duration of at least 4 weeks preoperatively may decrease SSIs through the amelioration of inflammatory cell function and host defense, which has been revealed in several RCTs [30, 31]. It was not clear how smoking cessation affected SSI in our study because we lacked accurate data of each patient's quit-smoking status. However, the recorded smoking cessation (range, 1-10yearspreoperatively) information of 116 patients were all found in no-SSI group.

Non-controllable risk factors

Interestingly, our study found that a higher NLR may be related to a raised risk of SSI. To our knowledge, higher NLR as a risk factor has not been identified associated with mesh repairs of IH previously. The development of SSIs has been believed to be related to the impairment of the immune system through systemic inflammation [32]. Colonized bacteria may begin to replicate and adhere to the surgical wounds if the host’s immune response is not sufficient to overcome the bacteria’s effect. NLR is one of the commonly used and convenient inflammatory markers that reflect this immune response [33], and it has been applied for the prediction of SSI in patients after several surgical operations such as colorectal[34], total knee arthroplasty [35], lumbar spinal[36], and head and neck cancer[37]. Yombi JC et al. found that NLR was a superior biomarker than C-reaction protein (CRP) to be included in the follow-up of early infectious complications after total knee arthroplasty, because it had a faster normalization than CRP [35]. Similarly, in the report of Deniz Bolat et al [38], NLR was noted as a potential laboratory value for predicting early penile prosthesis implant infection. The relationship between early SSI development (within 30 days postoperatively) and higher NLR that revealed in our study is corroborative of those reported in previous papers. Moreover, we observed a negative correlation between the preoperative NLR level and the postoperative period of SSI, further confirming higher NLR as a risk factor for SSI. A converse conclusion came from the literature - a lower preoperative NLR level tended to have a higher incidence of postoperative failure of incision healing - based on the following pathomechanism: neutrophils played an important role on bactericidal action and the purification of necrotized tissues upon injury; the exhaustion and insufficiency of neutrophils may lead to the appearance of excessive abnormal fibrin of granulation tissue in the wound and the inhibition of granulation tissue’s formation [39, 40].

Our findings revealed that using a cut point of > 1.97, preoperative NLR level predicted postoperative SSI with a high sensitivity (74.4%) and specificity (51.8%). This cut-off was within the reported normal reference intervals for NLR (0.88-4.0) [36]. The similar normal threshold of preoperative NLR level in predicting postoperative SSI was also found in the study of Josse JM et al ($\geq$ 2.3) [34] and Son HJ et al ($\geq$ 2.9) [37]. A lower threshold may help to find out the surgical patients with intermediate risk of postsurgical SSI, who could not be usually identified early. The NLR may be an useful tool in the befitting preoperative treatment planning, conjuncting with standard perioperative risk assessment, with the aim to alleviate the occurrence or severity of a prospective adverse event.

Platelets are rich in proinflammatory agents and are possible to release highly active microparticles. PLR has been accepted as indicator revealing shifts in PLT and LYM counts due to acute inflammatory. Increasing evidence has suggested that PLR can afford valuable information to clinicians when encountering some infection related diseases, such as chronic obstructive pulmonary disease, rheumatic diseases and diabetic foot infection [41–43]. NLR negatively correlated with the postoperative period of SSI in our study, but it was not an independent risk factor for SSI by multivariate analyses, possibly due to the relative small number of infections identified here.

The open technique was also associated with increased SSI following mesh repairs of IH. Laparoscopic approach seems to be preferable in terms of risk for both superficial SSI and mesh infection [44]. The analysis of registry data in Germany showed a 0.1% superficial SSI rate and a 0.06% deep infection incidence in laparoscopic IH repair [45]. On the contrary, they recommende-

d antibiotic prophylaxis to be administered for open IH repair for its watchful SSI rate. The overall SSI rate was found to be significantly lower for laparoscopic than for the open approach (0.08% vs. 0.94%, P = 0.016), in a retrospective study including 1760 Chinese patients [46]. Our results were consistent with those from the aforementioned studies. The SSI rate here was 5.3% (34/647) and 0.9% (5/530) for open and laparoscopic approach, respectively. The lower SSI rate in laparoscopic approach may be explained by the short incision, the way for mesh introduced to the preperitoneal space (through the port) and the site where the mesh placed (not near the incision) [19]. However, the laparoscopic operation is not suitable for all the patients as it is preformed under general anesthesia and requires a higher surgical cost. It is, therefore, recommended a comprehensive assessment of the necessity of antibiotic prophylaxis by the surgeons prior to open surgery.

The present study was limited by several factors. A limitation is the retrospective property of the study. However, a retrospective approach allowed a large study population. We lacked data of several potential risk factors related to SSI due to our observational study design, such as intraoperative body temperature and the dosage of smoking. Additionally, although we focused on mesh repairs, the limited follow-up time resulted in no mesh infections identified in our study.

Conclusions

Our study afforded additional evidence for some risk factors following elective mesh repairs of IH, whereas some are rare but important. In agreement with previous published studies, our analysis suggested that BMI > 24.6 kg/m^2 and current smoker were potentially controllable risk factors which significantly increased the risk of SSI, while open technique was a non-controllable risk factor. In contrast to the published data, age, diabetes, operative time and use of drainage were not significant in our study, possibly due to confusion with other variables. The role of preoperative NLR is a novel finding and warrants further exploration – it appeared to be an objective, cheap and convenience biomarker for the early prediction of SSI following elective mesh repairs of IH.

Abbreviations

IH: inguinal hernia; SSI: surgical site infection; RCTs: randomized clinical trials; TAPP: trans-abdominal preperitoneal repair, TEP: totally extraperitoneal repair; BMI: body mass index; ASA: American Society of Anesthesiologists; WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; MON: monocyte; EOS: eosnophils; BASO: basophil granulocyte; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean red blood cell hemoglobin; PLT: platelet; ALB: serum albumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; CDC: Centers for Disease Control and

Prevention; ROC: receiver operating characteristics; AUCs: area under the ROC curves; CI: 95% confidence interval; CRP: C-reaction protein.

Declarations

Acknowledgements

Not applicable

Consent to publication

Not applicable

Authors’ contributions

Study conception and design: YYZ and DC; Acquisition of data: XXL, JTC and QZ; Analysis and interpretation of data: YYZ and XXL; Drafting of manuscript: YYZ; Critical revision: DC

Funding

This work was supported by the Medical Research Fund of Guangdong Province in China (grant number A2018447) and Science and technology plan medical and health category project of Shantou (grant number 18040494011014). The fundings were mainly used for the data collection in this study, and the study designation, analysis, interpretation of data and writing were also almost carried out without the supporting of the funding.

Availability of data and materials

The data sets generated and/or analysed during the current study are not publicly available due to the data is confidential patient data but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The institutional review board of the First Affiliated Hospital of Shantou University Medical College approved this study. The informed consent was waived because of the anonymous collection of patients’ information.

Competing interests

The authors declare that they have no competing interests.

References

1. Gutlic N, Gutlic A, Petersson U, et al. Randomized clinical trial comparing total extraperitoneal with Lichtenstein inguinal hernia repair (TEPLICH trial). Br J Surg. 2019;106 (7): 845-855.
2. Kouhia S, Vironen J, Hakala T, et al. Open Mesh Repair for Inguinal Hernia is Safer than Laparoscopic Repair or Open Non-mesh Repair: A Nationwide Registry Study of Complications. WORLD J SURG. 2015;39 (8): 1878-1884, 1885-1886.
3. Lockhart K, Dunn D, Teo S, et al. Mesh versus non-mesh for inguinal and femoral hernia repair. Cochrane Database Syst Rev. 2018;9: D11517.
4. Arciola CR, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. NAT REV MICROBIOL. 2018;16 (7): 397-409.
5. Sanabria A, Dominguez LC, Valdivieso E, et al. Prophylactic antibiotics for mesh inguinal hernioplasty: a meta-analysis. ANN SURG. 2007; 245 (3): 392-396.
6. Boonchan T, Wilasrusmee C, McEvoy M, et al. Network meta-analysis of antibiotic prophylaxis for prevention of surgical-site infection after groin hernia surgery. Br J Surg. 2017;104 (2): e106-e117.
7. LSJ SF. Antibiotic prophylaxis for hernia repair. Cochrane Database Syst Rev. 2012;15 (2): D3769.
8. Bittner R, Arregui ME, Bisgaard T, et al. Guidelines for laparoscopic (TAPP) and endoscopic (TEP) treatment of inguinal hernia [International Endohernia Society (IEHS)]. SURG ENDOSC. 2011;25 (9): 2773-2843.
9. Kuwayama DP, Augustin J. Concurrent hydrocelectomy during inguinal herniorrhaphy is a risk factor for complications and reoperation: data from rural Haiti. HERNIA. 2017; 21(5): 759-765.
10. Lundstrom KJ, Sandblom G, Smedberg S, et al. Risk factors for complications in groin hernia surgery: a national register study. ANN SURG. 2012;255 (4): 784-788.
11. Rosemar A, Angeras U, Rosengren A, Nordin P. Effect of body mass index on groin hernia surgery. ANN SURG. 2010;252 (2): 397-401.
12. Berrios-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA SURG. 2017;152 (8): 784-791.
13. Hauer-Jensen M, Fort C, Mehta JL, et al. Influence of statins on postoperative wound complications after inguinal or ventral herniorrhaphy. HERNIA. 2006;10 (1): 48-52.
14. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory

Committee. AM J INFECT CONTROL. 1999;27 (2): 97-132, 133-134, 96.

15. Anderson DJ, Podgorny K, Berrios-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014;35 Suppl 2:S66-S88.
16. International guidelines for groin hernia management. HERNIA. 2018;22 (1):1-165.
17. Pessaux P, Lermite E, Blezel E, et al. Predictive risk score for infection after inguinal hernia repair. AM J SURG. 2006;192 (2):165-171.
18. Mavros MN ASAV. Risk factorsfor mesh-related infections after hernia repair surgery:a meta-analysis of cohort studies. WORLD J SURG. 2011; 35: 2389-2398.
19. Yang H, Liu Y, Chen J, et al. The Management of Mesh Infection After Laparoscopic Inguinal Hernia Repair. Surg Laparosc Endosc Percutan Tech. 2019; 29 (1): 40-42.
20. Meijs AP, Koek M, Vos MC, et al. The effect of body mass index on the risk of surgical site infection. Infect Control Hosp Epidemiol. 2019;40 (9): 991-996.
21. Huttunen R, Karppelin M, Syrjanen J. Obesity and nosocomial infections. J HOSP INFECT. 2013; 85 (1): 8-16.
22. Sereysky J, Parsikia A, Stone ME, et al. Predictive factors for the development of surgical site infection in adults undergoing initial open inguinal hernia repair. HERNIA. 2019
23. Yang H, Xiong Y, Chen J, et al. Study of mesh infection management following inguinal hernioplasty with an analysis of risk factors: a 10-year experience. HERNIA. 2019
24. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. LANCET. 2004; 363 (9403): 157-163
25. LeBlanc KA, Whitaker JM, et al. Laparoscopic incisional and ventral hernioplasty: lessons learned from 200 patients. HERNIA. 2003; 7 (3): 118-124.
26. Zhuo Y, Zhang Q, Tang D, et al. The effectiveness of i.v. cefuroxime prophylaxis of surgical site infection after elective inguinal hernia repair with mesh: A retrospective observational study. EUR J CLIN PHARMACOL. 2016; 72 (9) :1033-1039.
27. Frohlich M, Sund M, Lowel H, et al. Independent association of various smoking characteristics with markers of systemic inflammation in men. Results from a representative sample of the general population (MONICA Augsburg Survey 1994/95). EUR HEART J. 2003; 24 (14): 1365-1372.
28. Sorensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. ANN SURG . 2012; 255 (6): 1069-1079.
29. Yuksel EP, Yuksel S, Soylu K, et al. Microvascular abnormalities in asymptomatic chronic smokers: A videocapillaroscopic study. MICROVASC RES. 2019;124:51-53.
30. Moller AM, Villebro N, Pedersen T, et al. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. LANCET. 2002; 359 (9301): 114-117.
31. Kelley KE, Fajardo AD, Strange NM, et al. Impact of a Novel Preoperative Patient-centered Surgical Wellness Program. ANN SURG. 2018; 268 (4): 650-656.

32. Sartelli M, Guirao X, Hardcastle TC, et al. 2018 WSES/SIS-E consensus conference: recommendations for the management of skin and soft-tissue infections. WORLD J EMERG SURG. 2018;13:58.
33. de Almeida JR, Yao C, Ziai H, et al. Postoperative wound infections, neutrophil-to-lymphocyte ratio, and cancer recurrence in patients with oral cavity cancer undergoing surgical resection. ORAL ONCOL. 2019;97:23-30.
34. Josse JM, Cleghorn MC, Ramji KM, et al. The neutrophil-to-lymphocyte ratio predicts major perioperative complications in patients undergoing colorectal surgery. COLORECTAL DIS. 2016; 18 (7): O236-O242.
35. Yombi JC, Schwab PE, Thienpont E. Neutrophil-to-lymphocyte ratio (NLR) distribution shows a better kinetic pattern than C-reactive protein distribution for the follow-up of early inflammation after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2016; 24 (10): 3287-3292.
36. Shen CJ, Miao T, Wang ZF, et al. Predictive value of post-operative neutrophil/lymphocyte count ratio for surgical site infection in patients following posterior lumbar spinal surgery. INT IMMUNOPHARMACOL. 2019;74:105705.
37. Son HJ, Roh JL, Choi SH, et al. Nutritional and hematologic markers as predictors of risk of surgical site infection in patients with head and neck cancer undergoing major oncologic surgery. Head Neck. 2018; 40 (3): 596-604.
38. Bolat D, Topcu YK, Aydogdu O, et al. Neutrophil to Lymphocyte Ratio as a predictor of early penile prosthesis implant infection. INT UROL NEPHROL. 2017; 49 (6): 947-953.
39. Brinkmann V, Reichard U, Goosmann C, et al. Neutrophil extracellular traps kill bacteria. SCIENCE. 2004; 303 (5663): 1532-1535.
40. Kaitu'U-Lino TJ, Morison NB, Salamonsen LA. Neutrophil depletion retards endometrial repair in a mouse model. CELL TISSUE RES. 2007; 328 (1): 197-206.
41. Yao C, Liu X, Tang Z. Prognostic role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio for hospital mortality in patients with AECOPD. Int J Chron Obstruct Pulmon Dis. 2017;12:2285-2290.
42. Gasparyan AY, Ayvazyan L, Mukanova U, et al. The Platelet-to-Lymphocyte Ratio as an Inflammatory Marker in Rheumatic Diseases. ANN LAB MED. 2019;39 (4): 345-357.
43. Demirdal T, Sen P. The significance of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and lymphocyte-monocyte ratio in predicting peripheral arterial disease, peripheral neuropathy, osteomyelitis and amputation in diabetic foot infection. Diabetes Res Clin Pract. 2018;144:118-125.
44. Dreuning K, Maat S, Twisk J, et al. Laparoscopic versus open pediatric inguinal hernia repair: state-of-the-art comparison and future perspectives from a meta-analysis. SURG ENDOSC. 2019; 33 (10): 3177-3191.
45. Kockerling F, Bittner R, Jacob D, et al. Do we need antibiotic prophylaxis in endoscopic inguinal hernia repair? Results of the Herniamed Registry. SURG ENDOSC. 2015; 29 (12): 3741-3749.
46. Li J, Wang X, Feng X, et al. Comparison of open and laparoscopic preperitoneal repair of groin hernia. SURG ENDOSC. 2013; 27 (12): 4702-4710.

Figures

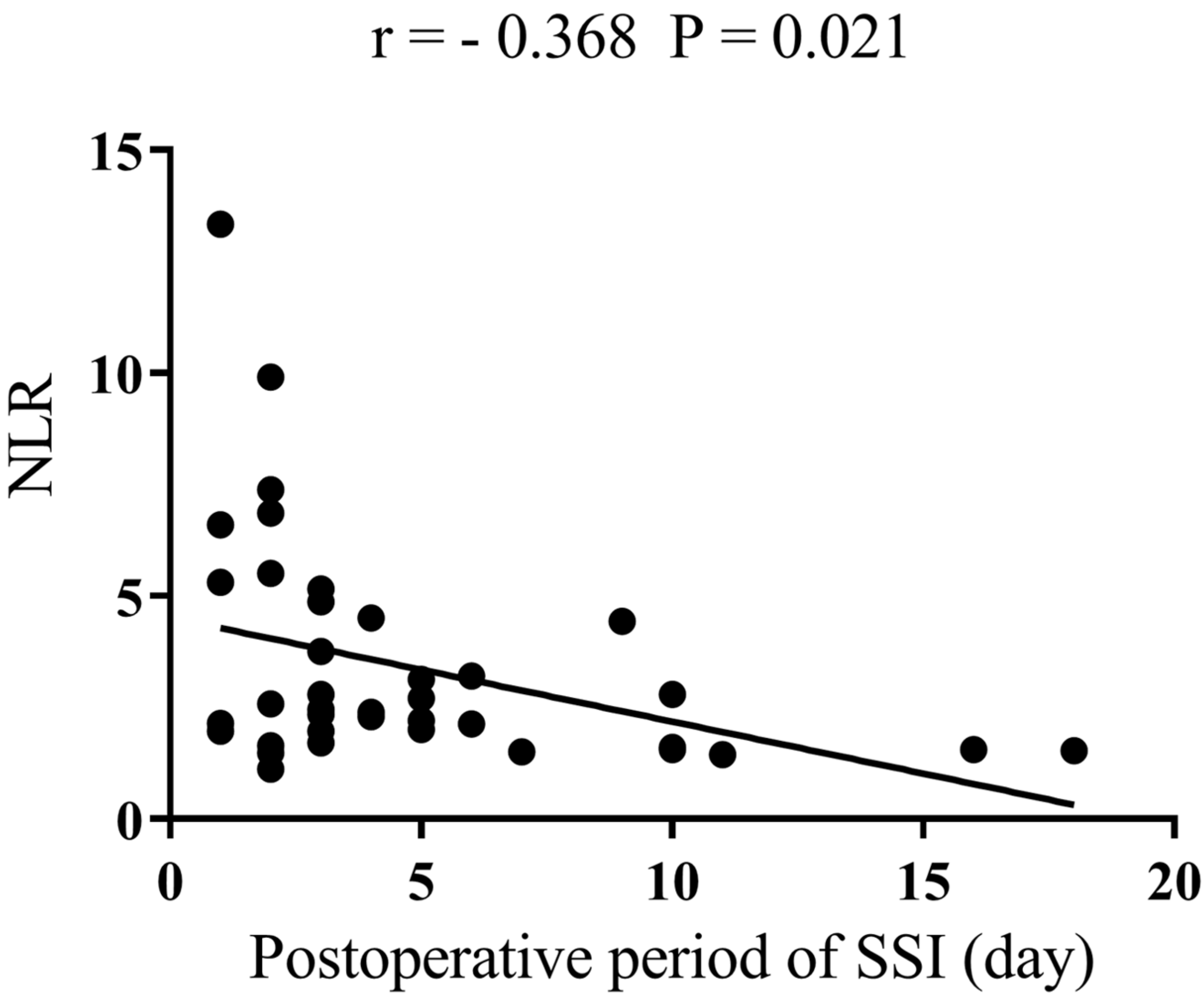

Figure 1

Relationship between preoperative neutrophil-lymphocyte ratio (NLR) and postoperative period of surgical site infection. The preoperative NLR is significantly negatively correlated with the postoperative period of surgical site infection (SSI; r = -0.368, P = 0.021).

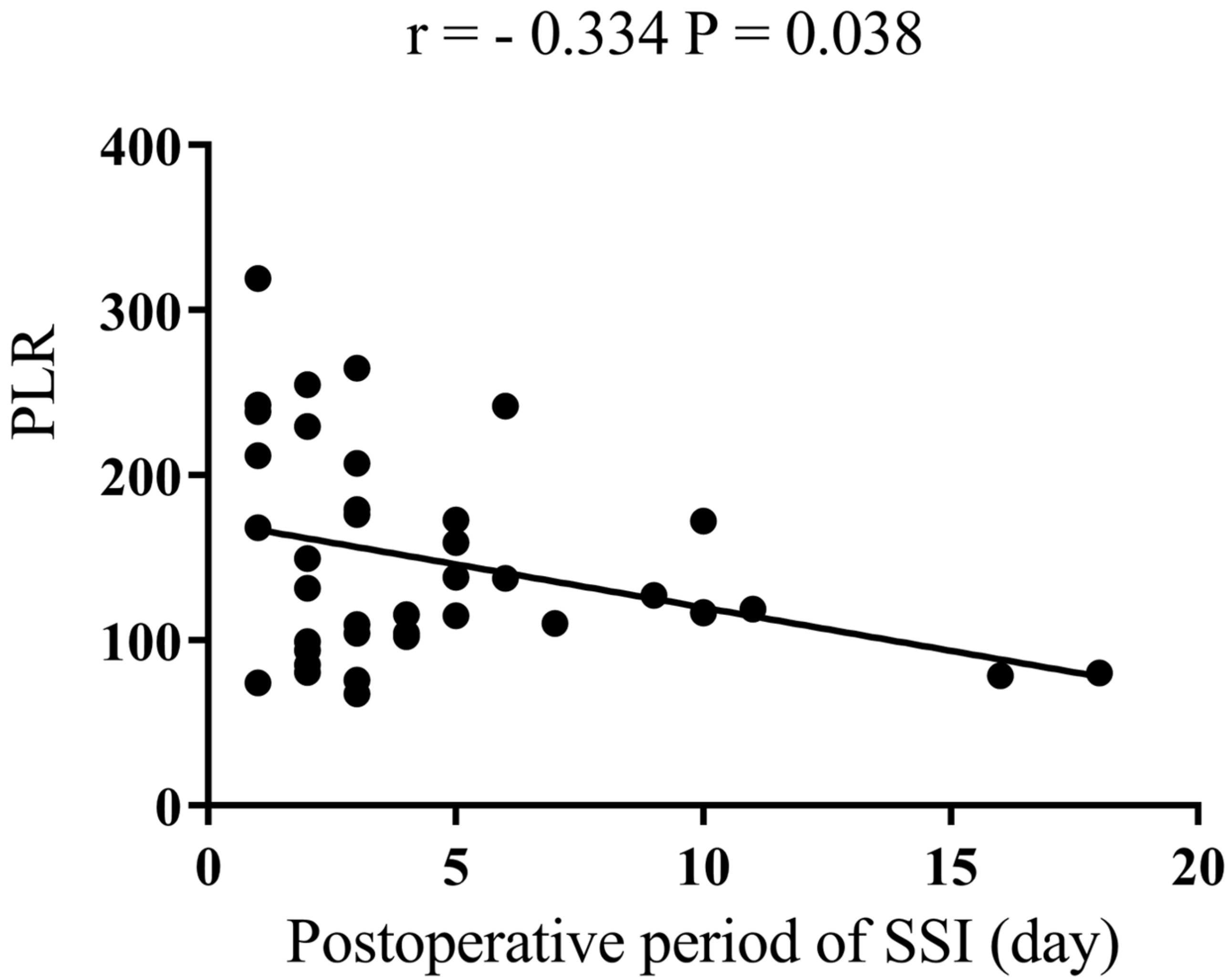

Figure 2

Relationship between preoperative platelet-lymphocyte ratio (PLR) and postoperative period of surgical site infection. The preoperative PLR is significantly negatively correlated with the postoperative period of surgical site infection (SSI; r = -0.334, P = 0.038,).

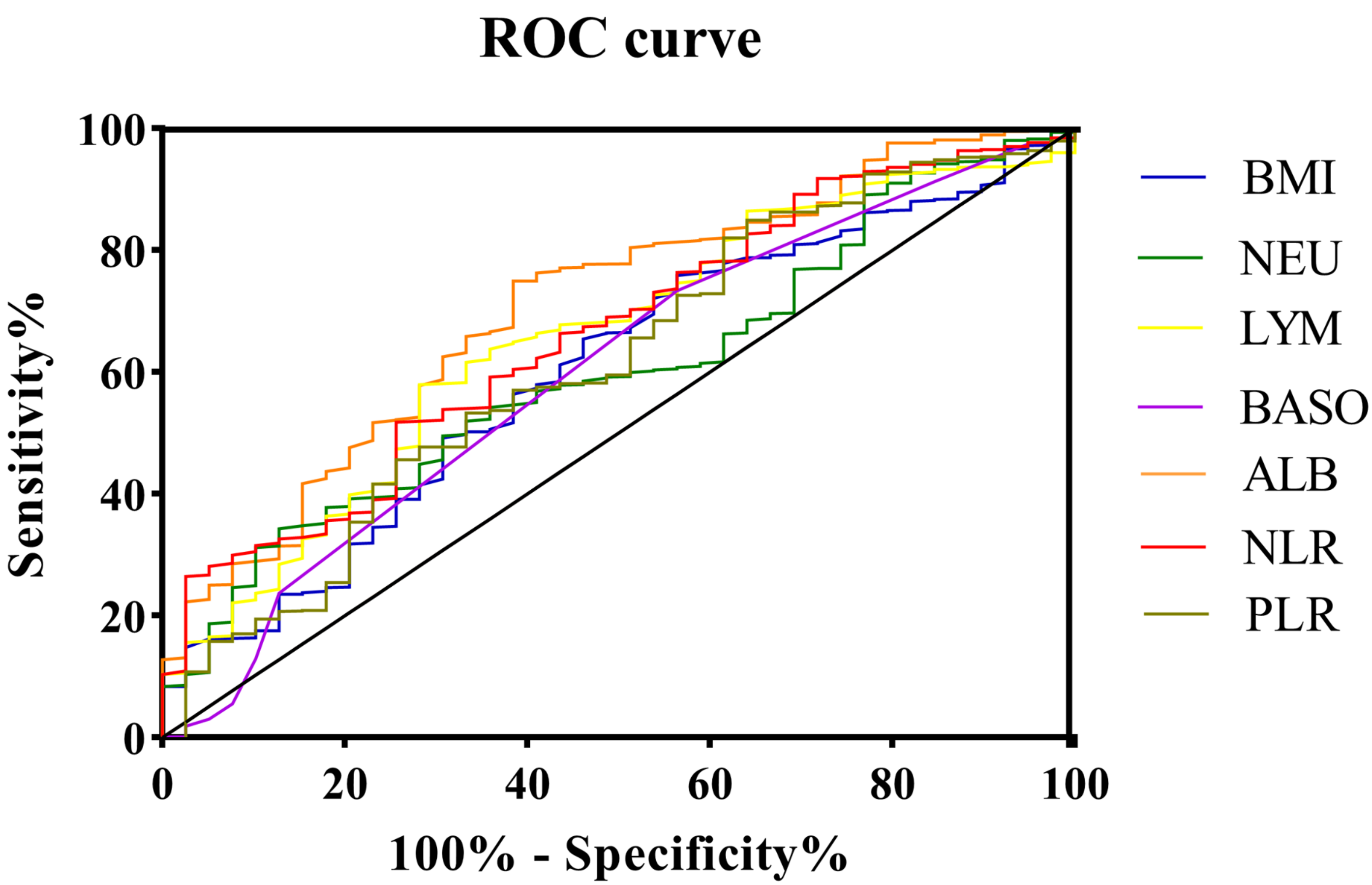

Figure 3

The optimal cut-off values of continuous variables detected by receiver-operating characteristic (ROC) analysis. A total of 7 continuous variables' optimal cut-offs were identified by ROC curve analysis. BMI: body mass index; NEU: neutrophil; LYM: lymphocyte; BASO: basophil; ALB: serumalbumin; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio

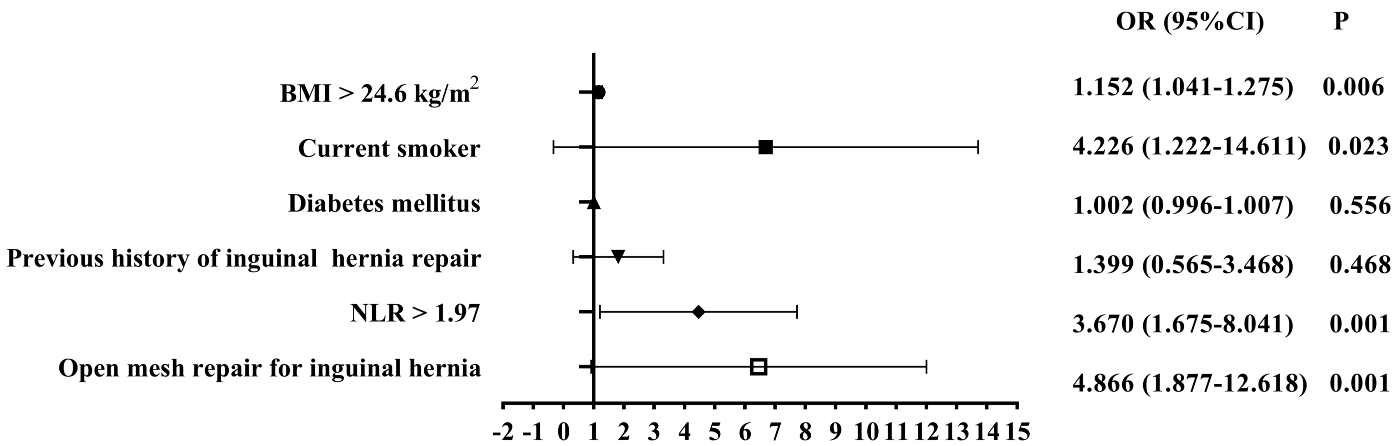

Figure 4

Odds ratios for risk factors of developing surgical site infections by forward stepwise multivariable logistic regression analysis. Four variables (with a $P < 0.05$ in the univariate analysis) containing BASO < 0.025×109/L, ALB < 37.8g/L, PLR >168.02 and duration of surgery > 77 min were not in the model equation. SSI: surgical site infection; BMI: body mass index; NLR: neutrophil-lymphocyte ratio