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Original Article

Surgical site infection incidence and risk factors in thoracic surgical procedures: A 12-year prospective cohort study

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Abstract
Introduction: Surgical site infections (SSI) continue to be a major problem for thoracic surgery patients. We aimed to determine incidence rate (IR) and risk factors for SSI in patients with thoracic surgical procedures.
Methodology: During 12 years of hospital surveillance of patients with thoracic surgical procedures, we prospectively identified SSI. Patients with SSI were compared with patients without SSI.
Results: We operated 3,370 patients and 205 (6.1%) developed SSI postoperatively. We detected 190 SSI among open thoracic surgical procedures (IR 7.1%) and 15 SSI after video-assisted thoracic surgery (IR 2.1%). Five independent risk factors for SSI were identified: wound contamination ($p = 0.013$; relative risk (RR) 2.496; 95%, confidence interval (CI): 1.208-5.156), American Society of Anesthesiologist (ASA) score ($p = 0.012$; RR: 1.795; 95% CI: 1.136-2.834), duration of drainage ($p < 0.001$; RR: 1.117; 95% CI: 1.085-1.150), age ($p = 0.036$; RR: 1.018; 95% CI: 1.001-1.035) and duration of operation ($p < 0.001$; RR:1.005; 95% CI:1.002-1.008).
Conclusion: The results are valuable in documenting risk factors for SSI in patients undergoing thoracic surgery. The knowledge and prevention of controllable risk factors is necessary in order to reduce the incidence of SSI.

Key words: surgical site infection; thoracic surgical procedures; risk factor.

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Introduction
Despite the recent advances in operating surgical techniques, better understanding of the pathogenesis of infections and widespread use of modern antiseptic agents and prophylactic antibiotics, surgical site infections (SSI) continue to be a major problem for patients undergoing thoracic surgery [1-3] SSI are associated with increased morbidity, in-hospital mortality, prolonged hospitalization, and increased costs [4]. Surveillance of SSI provides useful data in identifying risk factors that contribute to the development and outcome of SSI [5]. Risk factors for SSI can be divided into host and perioperative factors, which can be further divided into preoperative, intraoperative, and postoperative factors. Some of them are controllable, and some are non-controllable. Preoperative identification of risk factors and patient risk stratification are critical to effectively assess individualized risks, postoperative expectations, and consider the possibility of reducing SSI and other healthcare associated infections (HAI).

In the present study, we aimed to determine the incidence and risk factors of SSI in patients with thoracic surgical procedures hospitalized in a tertiary hospital in Belgrade (Serbia).

Methodology
Setting

The Military Medical Academy (MMA), Belgrade, Serbia, a teaching hospital of the University of Defense, is a 1200-bed tertiary healthcare center divided in 27 departments according to medical specialty. The Clinic for Thoracic Surgery is a 24-bed department of MMA. The Department of Infection Control performs continuous surveillance of HAI, including SSI, on patients of MMA. Hospital surveillance was performed only on those patients who were hospitalized longer than 48 hours.

Study population

Through regular hospital surveillance of surgical patients with thoracic surgical procedures, we prospectively identified SSI during the study period, from 1st January 2006 to 31st December 2017. Patients were visited on daily basis, for data-collection purposes, by the infection control nurse and a thoracic surgeon. An infectious disease specialist was included in diagnosis and treatment of all SSI and other HAI. Reviewing the clinical chart information on patient characteristics, risk factors related to health care were collected. We gathered data on the following variables: patients characteristics existing before surgical procedures - gender, the presence of underlying diabetes mellitus, age, tobacco use, body mass index (BMI), American Society of Anesthesiologist (ASA) score, preoperative infection, outcome of treatment (survived/deceased), factors related to healthcare including the length of hospital stay (LHS), intensive care unit (ICU) admission, length of stay in ICU, preoperative length of stay, the presence of central vascular catheter (CVC), preoperative showering and characteristics dependent on surgical procedure – wound microbiology of contamination of surgical site, duration of operation, surgical method (open thoracic surgical procedures or video-assisted thoracic surgery - VATS), conversion, drainage, duration of drainage and National Healthcare Safety Network (NHSN) risk. Only the first episode of SSIs was included for patients who had more than one SSI during the study period. The incidence rate (IR) of SSI was based on SSI detected during hospital stay combined with SSI identified on readmission following the initial operation. Post-discharge surveillance was not performed.

All patients underwent perioperative prophylaxis consisting of intravenous administration of 1.5 g cefuroxime within 60 min before the surgical incision and repeat doses every 8 hours for 48 hours. Patients with documented –β lactam allergy received clindamycin.

All patients had got the same immediate preoperative treatment according to approved skin preparation protocols and use of disinfection solutions.

In the cohort study, the group of surgical patients with SSI was compared with the group of patients without SSI.

Definition

According to surgical method operative procedures were divided in open thoracotomy procedures (thoracic drainage, wedge resection, lobectomy, bilobectomy, mediastinal tumor, chest wall tumor, exploratory thoracotomy) and VATS (VATS pleural procedure, VATS lung biopsy, VATS wedge resection, VATS lobectomy, VATS mediastinal) (Table 1). Conversion was defined as unplanned open thoracotomy during VATS.

SSI and hospital acquired pneumonia (HAP) were defined according to the Centers for Disease Control (CDC) and the National Healthcare Safety Network (NHSN) surveillance definitions. According to these definitions SSI include superficial incisional, deep incisional and organ/space infection [6,7]. All patients were assessed before operation by an anesthesiologist for the ASA score [8]. The wound class was assigned after completion of the operative procedure based on actual occurrences as clean, clean/contaminated, contaminated, and dirty/infected [9,10]. Rates of SSI were stratified according NHSN risk index, (previous National Nosocomial Infections Surveillance - NNIS system) [11,12]. The NHSN risk index comprises 3

Table 1. Surgical site infection (SSI) rates, by operative procedures and risk index category n = 3370.

Operative procedure category	Total number of patients with specific procedure (N)	Patients risk index category			Cumulative rate of SSI (%)
		0 Rate of SSI (%)	1 Rate of SSI (%)	2, 3 Rate of SSI (%)	
Thoracic drainage	72	3/34 (8.8)	4/23 (17.4)	4/15(26.7)	11 (15.3)
Wedge resection	658	4 /465 (0.9)	6/153 (3.9)	5/40 (12.5)	15 (2.3)
Lobectomy	944	14/232(6.0)	32 (6.4)	27 (12.7)	73 (7.7)
Bilobectomy	57	0/16 (0)	3/27 (11.1)	11/30 (36.7)	14 (24.5)
Pneumonectomy	288	0/16 (0)	22/184(12.0)	18/88 (20.4)	40 (13.9)
Extirpation of mediastinal tumour	159	0/65 (0)	2/71 (2.8)	3/23 (13.0)	5 (3.1)
Resection of chest wall tumour	168	2/84 (2.4)	5/47 (10.6)	10/37 (27.0)	17 (10.1)
Exploratory thoracotomy	206	0/9 (0)	3/179 (1.7)	2/18 (11.1)	5 (2.4)
Decortication	118	1/ 23 (4.3)	4/47 (8.5)	5/48 (10.4)	10 (8.5)
VATS/Pleural procedure	154	2/91 (2.2)	2/60 (3.3)	0/3 (0)	4 (2.7)
VATS/Lung biopsy	204	1/157 (0.6)	3/46 (6.5)	0/1 (0)	4 (2.0)
VATS/ Wedge resection	161	3/135 (2.2)	1/25 (4.0)	1/1 (100)	5 (3.1)
VATS/Lobectomy	30	0/3	1/15 (6.7)	1/12 (8.3)	2 (6.7)
VATS/Mediastinum	151	0/124 (0)	0/24 (0)	0/3 (0)	0

dichotomous variables: ASA score (> 2), wound classification (contaminated or dirty), and procedure duration in minutes (> 75th percentile or > 180 minutes for thoracic surgery). Each risk factor (dichotomous variable) represents 1 point; thus, the NHSN SSI risk index ranges from 0 to 3.

Microbiological testing

The microbiological testing was performed at MMA's Institute of Medical Microbiology.

Statistical analysis

IR was defined as the number of SSI and HAP per 100 patients.

Data analyses were performed with SPSS, version 18.0 (SPSS, Inc., Chicago, IL). Results were expressed as the mean (±) SD or as proportion of the total number of patients. The χ^2 test or Fischer exact test were used for categorical variables and relative risk (RR), and the corresponding 95% confidence intervals (CI) were calculated. For parametric continuous variables, mean values were compared using Student *t* test. For nonparametric, continuous variables, the Mann-Whitney *U* test was used. Risk factors independently associated with HAP were identified by the stepwise logistic regression analysis of variables selected by univariate analysis, with a limit for entering and removing variables at 0.05.

Table 2. Risk factors for the development of surgical site infection (SSI).

Patients characteristic	Patients with SSI (n = 205) (%)	Patients without SSI (n = 3165) (%)	Crude RR	ULRA p	MLRA RR (95%CI)	MLRA p
Male, n (%)	160 (78.0)	2067 (65.3)	1.889	< 0.001		
Diabetes mellitus, n (%)	20 (9.8)	255 (8.1)		0.390		
Age, years ± SD	60.23 ± 10.37	56. 33 ± 14.04	1.024	< 0.001	1.018 (1.001-1.035)	0.036
Tobacco use, n (%)	78 (38.0)	954 (30.1)	1.423	0.018		
Body mass index ± SD	24. 94 ± 4.28	25.56 ± 4.05	0.963	0.034		
ASA score > 2, n (%)	165 (80.5)	1578 (49.8)	4.154	< 0.001	1.795 (1.136-2.834)	0.012
Preoperative infection, n (%)	9 (4.4)	40 (1.3)	3.587	0.001		
Postoperative infection, n (%)	47 (22.9)	173 (5.5)	5.145	< 0.001		
In-hospital mortality, n (%)	39 (19.0)	51 (1.6)	14.345	< 0.001		
Procedures during hospitalization						
ICU hospitalization, n (%)	91 (44.4)	666 (21.0)	2.995	< 0.001		
Length of ICU stay, (days) ± SD	2.56 ± 7.94	0.38 ± 2.10	1.135	< 0.001		
Preoperative length of stay, (days) ± SD	4.51 ± 5.033	3.97 ± 5.522		0.171		
Central vascular catheter, n (%)	89 (43.4)	736 (23.3)	2.532	< 0.001		
Preoperative showering, n (%)	203 (99.0%)	3138 (99.1%)		0.854		
Characteristics depends of surgery procedure						
Wound microbiology contamination, n (%)				< .001	2.496 (1.208-5.156)	0.013
Clean	11 (5.4)	401 (12.7)	0			
Clean/contaminated	165 (80.5)	2594 (82.0)	2.319			
Dirty/infected	29 (14.1)	170 (5.4)	6.219			
Duration of operation, (minutes) ± SD	152.29 ±72.098	110.60 ± 57.018		< .001	1.005 (1.002-1.008)	< 0.001
Surgical method - VATS, n (%)	15 (7.3)	685 (21.6)	3.499	< .001		
Conversion, n (%)	5 (2.4)	66 (2.1)		0.733		
Drainage, n (%)	199 (97.1)	2959 (93.5)	2.309	0.047		
Duration of drainage (days) ± SD	15.11 ± 17.92	3.68 ± 3.49	1.234	< 0.001	1.117 (1.085-1.150)	< 0.001
NHSN risk index				< 0.001		
0	31 (15.1)	1407 (44.5)	0			
1	87 (42.4)	1314 (41.5)	3.005			
2 and 3	87 (42.5)	444 (14.0)	8.893			

SSI: surgical site infection; RR: relative risk, ULRA: univariate linear regression analysis; MLRA: multivariate linear regression analysis; SD: standard deviation; ASA score - American Society of Anesthesiologists' physical status classification, ICU: intensive care unit; VATS: video-assisted thoracoscopic surgery; NHSN: National Healthcare Safety Network; p: probability.

Informed, written consent was obtained from all participants. The Research Ethics Board of the MMA approved the research protocol.

Results

From January 1, 2006 to December 31, 2017, a total of 3,370 different thoracic surgical procedures were evaluated (Table 1). The mean age of patients was 56.56 years (range 14 to 89, median 59.00 years). There were 2227 (66.2%) men and 1143 (33.9%) women. The median LHS was 11.00 (mean + SE = 14.41 + 13.10) days, ranging from 3 to 195 days.

Open thoracotomy procedures were more common than VATS (2670 vs 700, respectively). A total of 205 (6.1%) patients were complicated by SSI, of which 190 SSI cases were detected among open thoracic surgical procedures (IR: 7.1%) and 15 SSI cases after VATS (IR: 2.1%). There were 16 (7.8%) superficial, 56 (27.3%) deep incisional, and 133 (64.9%) organ-spaces or body cavity infections (pleural empyema without bronchial dehiscence). All decortications were performed due to chronic empyema, and were not followed by higher rate of SSI (8.5%). The majority of SSI, 125 (61.0%) were found during the course of hospitalization. All SSI detected after the patient`s discharge, 80 (39.0%), required readmission to hospital. During hospitalization, postoperative HAI, different than SSI, was detected in 220 patients (6.5%). Among them, 143 (4.2%) had HAP. A total of 128 cases were detected among open thoracic surgical procedures (IR: 4.8%) and 15 HAPs after 700 VATS thoracic surgical procedures (IR: 2.1%). Also, we detected other 77 HAI (11 bloodstream infections, 18 urinary tract infections, and 48 diarrhea, among them 11 *Clostridium difficile* infections).

Using the NHSN risk index, there were: 1438 (42.7 %) surgical procedures with risk 0 and the IR of 2.2%; 1401 (41.6%) with risk 1 and the IR of 6.2%; 507 (15.0%) with risk 2 and the IR 15.2%; and 24 (0.7%) with risk 3 and the IR 41.7%. Table 1 shows the number of procedures and IR of SSI by the NHSN risk index.

The characteristics of the patients and SSI related risk factors according to univariate analysis are shown in Table 2**.** Univariate analysis showed that the occurrence of SSI was significantly associated with the following variables: gender, age, tobacco use, BMI, ASA score, preoperative infection, ICU admission, length of stay in ICU, usage of CVC, duration of operation, surgical method, chest tube pleural drainage, duration of drainage (keeping the drain in place), contaminated and dirty/infected wound, and NHSN risk index. Diabetes mellitus, preoperative showering, and conversion were not found to be associated with SSI. Multivariate logistic regression analysis identified five independent risk factors associated with SSI occurring in these patients: wound microbiology contamination, ASA score, duration of drainage, age and duration of operation (Table 2).

Microbiological etiology

Microorganisms were isolated in 124 (61.5%) out of 205 recorded SSI. Among these, 27 (21.8%) SSI were polimicrobial. *Pseudomonas aeruginosa* was the most frequently isolated microorganism, causing 48 (38.7%) of laboratory confirmed SSI, followed by bacteria from the *Enterobacteriaceae* group which were isolated in 34 (27.4%) of laboratory confirmed SSI. *Staphylococcus aureus* was the third most frequent causative agent of SSI causing 24 (19.3%) of the laboratory confirmed SSI out of which 70.8% (17/24) were methicillin resistant. Apart from these, other identified species were: *Acinetobacter* spp. in 18.5% of laboratory confirmed SSI, *Enterococcus* spp. in 9.7%, *Stenotrophomonas maltophilia* in 4,8%, coagulase-negative staphylococci in 2.4%, *Streptococcus* spp. and *Corynebacterium* spp. (each causing 1.6% of laboratory confirmed SSI), and *Moraxella* spp. and *Haemophilus* spp. (each causing 0.8% of laboratory confirmed SSI).

Discussion

Incidence rate of SSI and HAP

SSI in patients with thoracic surgical procedures causes significant morbidity and mortality and prolongs hospital stays [1-5]. In this study we analyzed SSI in a large cohort of patients with thoracic surgical procedures. During the 12-year study period, 205 or 6.1% of surgical patients were diagnosed with SSI in the postoperative period. The overall IR of SSI was higher than the IR reported in the studies of Ceken *et al*. [3] and Dubiel *et al*. [5].

Tsiouris *et al*. showed that thoracic surgery patients, classified as functionally dependent preoperatively, were at high risk for major morbidity and mortality [4]. In that group of patients (812 patients were analyzed separately) overall IR of SSI was 2.2%, and after open thoracotomy IR was 3.5% [4]. In our study, IR of SSI was 7.1% after open thoracotomy, and 2.1% after VATS. These differences could be related to different types of operative procedures conducted, characteristics of hospital populations studied, and quality of healthcare.

In our study, the IR of SSI was highest in the group of patients undergoing bilobectomy (24.5%). The lobectomy was the most common operative procedure performed in our patients, accounting for 944 (28.0%) of the studied operative procedures with SSI IR of 7.7%. During open lobectomy, Imperatori et al. reported IR of SSI of 17.0%, IR of wound infection of 3.9% and IR of empyema of 3.2% in period 2006-2015 [1]. These differences could be explained by the fact that the authors from Italy were calculating IR of lobectomy and bilobectomy together/combined, and in our study, we were calculating IR of lobectomy and bilobectomy separately. Also, there are some differences in the methods used for surveillance of HAI.

Similarly, to authors from Poland [5], we did not register any SSI after VATS for mediastinal procedures.

A previous study confirmed the inefficiency of one or two doses of cefazolin, 2g, at the induction of anesthesia, followed by cefazolin 1g every 4 hours, if the operation lasted more than 4 hours, in preventing postoperative pneumonia after major lung resection [13]. These authors reported 24.4% of postoperative pneumonia in 312 consecutive cases of major pulmonary resection [13]. On the other hand, prospective study of infection risk factors in 988 lung resection showed an overall rate of postoperative pneumonia of 10.4% with short time course of antibiotic [2]. Rovera *et al*. reviewed 346 consecutive VATS procedures (139 patients undergoing lung wedge resection and 207 undergoing intrathoracic biopsy– pleural or mediastinal), with reported similar IR of HAP in both groups (2.8% and 3.4%, respectively) [14]. The present study showed that 143 (4.2%) patients had HAP in the postoperative period. Among open thoracic surgical procedures, IR of HAP was 4.8%; and among VATS, it was 2.1%. The reason for the relatively small IR of HAP could be our practice of giving prolonged perioperative prophylaxis with cefuroxime (48h after operative procedure), but this needs further confirmation.

Risk factors for SSI

Previous studies have identified different, independent risk factors for SSI, also including patients' characteristics**,** procedures during hospitalization and characteristics depends of thoracic surgery procedure [1-5]. In the present study multivariate logistic regression analysis identified five independent risk factors associated with SSI: wound microbiology contamination, ASA score, duration of pleural drainage**,** age, and duration of operation.

In their evaluation of 6376 patients, who underwent thoracic surgical procedures and identified in the National Surgical Quality Improvement Program (NSQIP) during period of 2005-2009, Tsiouris *et al*. showed that wound classification (dirty), dependent functional status preoperatively, and emergency procedures were independent risk factors for morbidity and mortality. Also, they concluded that performance of open thoracotomy surgery predicted morbidity, but not mortality (4). In our study, patients with dirty/infected wound had 2.5 greater risk to acquire SSI than patients with clean wounds (RR: 2.496; 95% CI: 1.208-5.156), and in–hospital mortality rate was significantly higher in patient with SSI than in patients without SSI (19.0% *vs* 1.6%; $p < 0.001$).

Diabetes mellitus, ASA score ≥ 3, preoperative white blood cell count and the number of blood products used preoperatively were found to be independent risk factors for SSI in the study of Ceken *et al.* [3]. In our patients, ASA score ≥ 3 almost doubled the risk of SSI ($p = 0.012$; RR: 1.795; 95% CI: 1.136-2.834), but the presence of diabetes mellitus was not statistically significantly different among patients with and without SSI (9.8% vs 8.1%, p: 0.390).

Previous studies showed that duration of surgery was independent risk factors for SSI (1,12). Our findings support that longer duration of operation increased the risk for SSI (RR: 1.795; 95% CI: 1.136-2.834).

Duration of drainage

An adequate chest drainage system aims to drain fluid and air and restore the negative pleural pressure facilitating lung expansion. Duration of chest tube drainage was found to be an independent risk factor for SSI in our study, but has not been mentioned in the relevant studies addressing SSI. Prolonged pleural drainage is one of the modifiable risk factors which obliges to meticulously control air leaks. Shortage of modern seal products in developing countries opens another sort of problems.

Age was independently associated with SSI in our patients ($p = 0.036$; RR: 1.018; 95% CI: 1.001-1.035). The same was reported by Imperatori *et al.* (2), but there are studies which did not show the association of age and the incidence of SSI [3,5].

Dubiel *et al*. reported that mean LHS for patients with SSI was 22.6 days (from 15 to 74 days), and for patients without SSI was 10.6 days [5]. Ceken *et al*. showed that mean LHS was significantly higher in patients with SSI, than in patients in the control group (33.16±17.68 vs.12.38±7.52) [3]. The current study obtained very similar results. The LHS in patients with SSI was 41.24 ± 26.69, and in patients without SSI it was 12.67 ± 9.34 ($p < 0.001$; RR: 1.078; 95% CI: 1.064-

1.092). LHS was independently associated with SSI and has got a great influence on the final hospital costs.

Microbiological etiology

Several studies have shown that the causative pathogen of SSI may vary with geographical location, among various procedures, from hospital to hospital or even in different wards of the same hospital [15-19]. In recent years, there has been a growing frequency of Gram-negative organisms as a cause of serious HAI [20]. Incorrectly prescribed antibiotics contribute to the spread of antimicrobial resistance. The problem gets more complicated in developing countries due to overcrowded hospitals, inappropriate use of antimicrobials and poor infection control practices. Ceken *et al*. reported that 9% of SSI after thoracic surgery were polimicrobial and that *S. aureus* was the most common isolated cause of SSI (25%) followed by *coagulase-negative staphylococci* (18%), *Enterobacteriaceae* (17%), *Acinetobacter baumannii* (13%) and *Pseudomonas aeruginosa* (8%) [3]. *S. aureus* was also the most common isolated cause of SSI in study of Macrina *et al.* [21]. On the contrary, Dubiel *et al*. showed that in 16% of SSI more than one bacteria species was isolated and that Gram-negative bacilli – *Enterobacteriaceae* and anaerobic bacteria were isolated most often (19% for each group), followed by coagulase-negative *staphylococci* (16%), *Enterococcus* spp. (16%), *Streptococcus pneumoniae* (6%), *Moraxella catarrhalis* (3%), and *Staphylococcus aureus* (3%) [5].

The present study showed that 21.8% of laboratory confirmed SSI were polimicrobial and *Pseudomonas aeruginosa* was the most frequently isolated microorganism (38.7% of laboratory confirmed SSIs), followed by bacteria from the *Enterbacteriaceae* group with 27.4% (34/124) of laboratory confirmed SSIs. *S. aureus* was the third most frequent causative agent for SSIs with 19.3% (24/124) of laboratory confirmed SSIs out of which 70.8% (17/24) were methicillin resistant (*MRSA*).

Limitations and strengths of study

The first limitation is that this is a single center study. Another limitation is the possibility of confounding variables that were not examined in our study. Although confounding variables were chosen after an exhaustive search of the literature, the potential for oversight and exclusion does exist. We tried to find all of the data in order to gain an understanding of the risk factors; we did not include some parameters, namely the presence of chronic obstructive pulmonary diseases, data about chemo/radio therapy, pulmonary function tests, and arterial blood gases (although they were a compulsory part of the preoperative preparation of the patients). Analysis of these factors could have enhanced the relevance of our results. We have not analyzed separately the influence of chest trauma on appearance of SSI because this issue deserves a special paper.

The strengths of this study are its prospective cohort design and a large study sample, consisting of more than 3000 patients, who were treated during the 12 years period. Furthermore, the additional strength of the study is the fact that the research staff at MMA has significant experience in conducting research studies of similar kind, which ensured the highest integrity, reliability, and validity of the data that was collected for the purposes of this study.

Conclusion

SSI in thoracic surgery are very frequent and serious complications which prolong hospital stay, influence the cost of hospital treatment, and have direct impact on higher rate of morbidity and mortality. In order to reduce or minimize the consequences of SSI we must know the most important and responsible risk factors and pay the greatest attention to dealing with them. We must be focused on the risk factors that could be controlled with our proper approach and knowledge of any conditions and causalities of infection.

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