Risk factors predisposing to deep sternal wound infection

Czynniki ryzyka predysponujące do wystąpienia głębokiego zakażenia rany mostka

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Abstract

Introduction: Despite advances in surgical procedures, there is an increasing trend of infectious complications with substantial morbidity, prolonged length of hospitalization (LOS), readmissions and growing financial expenses. The knowledge of predisposing risk factors with regard to causative pathogens may decrease the incidence of infections.

Materials and methods: The aim of our study was to determine risk factors for deep sternal wound infections (DSWI), and their stratification according to microbiological cultures in 4484 patients undergoing cardiac surgery at the Department of Cardiac Surgery, Kosice, Slovakia during 2007-2010.

Results: We observed 97 (2.2%) DSWI. Incidence of DSWI increased from 0.9% to 3.1%. G+, G– and polymicrobial flora were recovered in 47.1%, 32.2% and 20.7% of patients, respectively. Significant risk factors were: obesity (BMI > 30), LOS before surgery > 2 days, LOS at ICU > 3 days, extracorporeal circulation (ECC) > 120 minutes, discharge to another medical facility, reperfusion syndrome, early surgical re-exploration, dialysis, diabetes mellitus and new-onset atrial fibrillation. We have identified the patient risk profile for DSWI caused by specific pathogens. Risk factors for G+ DSWI were BMI < 30 ($p = 0.048$) and peripheral atherosclerotic arterial disease ($p < 0.05$). The risk of G– infection was observed in women, patients older than 65 years ($p = 0.01$), after emergent operations ($p < 0.05$), postoperative re-exploration ($p = 0.02$) and mechanical ventilation > 48 hours ($p < 0.05$). Polymicrobial DSWI were in patients with ECC of > 120 minutes, longer (> 6 days) postoperative stay ($p = 0.01$) and in patients readmitted from another hospital ($p = 0.047$).

Conclusion: Our study suggests that considering the patient risk profile in patients with DSWI can improve optimization of empirical antimicrobial therapy.

Streszczenie

Wstęp: Pomimo postępów w zakresie zabiegów chirurgicznych zauważa się zwiększenie częstości występowania powikłań infekcyjnych wiążących się ze znaczną zapadalnością, długotrwałą hospitalizacją, ponownym przyjęciem do szpitala i narastającymi kosztami leczenia. Znajomość czynników ryzyka predysponujących do wystąpienia głębokiego zakażenia rany mostka oraz jego patogenów może wpłynąć na zmniejszenie częstości zakażeń.

Materiał i metody: Celem badania było określenie czynników ryzyka występowania głębokiego zakażenia rany mostka oraz ich stratyfikacja według hodowli mikrobiologicznej u 4484 pacjentów poddanych zabiegom kardiochirurgicznym na Oddziale Kardiochirurgii w Koszycach na Słowacji w latach 2007–2010.

Wyniki: Zaobserwowano 97 (2,2%) przypadków głębokiego zakażenia rany mostka. Zapadalność na głębokie zakażenia rany mostka wzrosła z 0,9% do 3,1%. G+, G– oraz florę wielobakteryjną stwierdzono odpowiednio u 47,1%, 32,2% i 20,7% pacjentów. Do znamiennych czynników ryzyka należały: otyłość (BMI > 30), hospitalizacja przed zabiegiem > 2 dni, hospitalizacja na OIOM-ie > 3 dni, ECC > 120 min, wypisanie do innej placówki medycznej, zespół reperfuzyjny, wczesna ponowna eksploracja chirurgiczna, dializa, cukrzyca oraz nowo rozpoznane migotanie przedsionków. Określono profil ryzyka głębokiego zakażenia rany mostka spowodowanego specyficznymi patogenami. Czynniki ryzyka dla głębokiego zakażenia rany mostka wywołanego G+ stanowiły: BMI < 30 ($p = 0,048$) oraz choroba miażdżycowa tętnic obwodowych ($p < 0,05$). Ryzyko zakażenia G– obserwowano u kobiet powyżej 65. roku życia ($p = 0,01$), po zabiegach w trybie nagłym ($p < 0,05$), ponownej eksploracji pooperacyjnej ($p = 0,02$) oraz wentylacji mechanicznej > 48 godz. ($p < 0,05$). Wielobakteryjne głębokie zakażenie

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rany mostka wystąpiło u pacjentów z ECC > 120 min, dłuższej (> 6 dni) hospitalizacji pooperacyjnej (p = 0,01) oraz u pacjentów przyjętych z innego szpitala (p = 0,047).

Wnioski: Nasze badanie sugeruje, iż określenie profilu ryzyka u pacjentów z głębokim zakażeniem rany mostka może zoptymalizować empiryczne leczenie przeciwbakteryjne.

Słowa kluczowe: głębokie zakażenie rany mostka, zabiegi kardiochirurgiczne, czynniki ryzyka.

Introduction

Incidence of surgical site infections as a complication of major cardiac surgery is estimated to be around 2.6%, and these infections account for almost 38% of all nosocomial infections in surgical patients [1].

Cardiothoracic surgery interventions are a form of "clean" surgery, with the risk of infectious complications up to 5%. Despite technical advances in surgical procedures, there is an increasing trend towards more frequent infectious complications with substantial morbidity, prolonged length of hospitalization, readmissions and growing financial expenses due to resistant bacteria.

The aim of our study was to define risk factors that may contribute to the development of deep sternal wound infection (DSWI) caused by Gram-positive (G+), Gram-negative (G-) or polymicrobial flora. Such knowledge of the patient risk profile associated with specific pathogens can improve the appropriateness of empirical antibiotic regimens in patients admitted to cardiosurgery departments with DSWI.

Material and methods

We have done a retrospective observational cohort study of 97 patients readmitted to the Department of Cardiac Surgery in Kosice, Slovak Republic during the years 2007-2010, for DSWI after cardiac surgery (CABG and/or valve replacement). Inclusion criteria were readmission for DSWI requiring surgical re-exploration and intravenous antibiotic therapy.

We have analyzed specified history data, demographic data (age, sex, comorbidities), possible risk factors (preoperative, perioperative and postoperative risk factors), causative pathogens and antimicrobial therapy, in all patients. DSWI was defined as deep soft tissue-muscle involvement, with dehiscence, secernation, and frequently accompanied by sternal instability and fistulation.

Statistical analysis: descriptive methods for nominal variable frequencies – basic cohort analysis – were used. For continuous variables, numerical descriptors including arithmetic mean and standard deviation were used. Most continuous variables were then categorized by literature data. Differences between nominal variables were analyzed with the χ^2 test including Cochran and Mantel-Haenszel methods for odds ratio calculation (OR). Differences between two categories in specified continuous variables were analysed by t-test. Differences among several categories of continuous variables were evaluated by ANOVA analysis and post-hoc Tamhane test. For all applied statistical tests, a p value of < 0.05 was considered as significant.

Results

There were 4484 cardiothoracic operations performed during the 4-year period. Overall, we have observed 97 (2.2%) DSWI. The incidence of DSWI during the 4-year period increased from 0.9% to 3.1%. The number of women and men in our cohort was 61 and 36, respectively (p < 0.001). Average age was 67.1 ±9.6 years for women and 61.3 ±7.8 years for men.

According to the type of surgery, there were 16 (14.4%), 81 (83.5%) and 9 (9%) patients with isolated valve replacement, coronary artery bypass grafting and combined procedures (CABG and valve replacement), respectively.

Early wound infection (readmission in 30 days), intermediate type infection (hospitalization in 90 days) and late infection (hospitalization after 90 days) were observed in 64, 26 and 7 patients, respectively. There were no deaths directly related to DSWI.

Causative pathogens

From 97 patients, there were 87 with positive microbiology cultures. In 10 patients we have not recovered any pathogen, mostly due to prolonged prior antibiotic therapy. G+ pathogens were recovered in 47.1% of patients, G– pathogens in 32.2% of patients, and 20.7% of patients had polymicrobial flora.

The spectrum of all causative pathogens is depicted in Figures 1, 2 and 3.

Risk factors

To obtain the odds ratio, determining the tendency towards development of DSWI, we included possible preoperative risk factors: age, body mass index (BMI), the length of stay (LOS) before surgery, chronic obstructive pulmonary disease (COPD), diabetes mellitus, systolic function of left ventricle (ejection fraction – EF), perioperative risk factors: the length of extracorporeal circulation, type of procedure (CABG or valve replacement), and postoperative risk factors: early re-exploration for bleeding, perioperative myocardial infarction, reperfusion syndrome, new onset paroxysmal atrial fibrillation and type of discharge (outpatient or transfer to another department) (Fig. 4).

The odds ratio (OR) in obese patients with BMI over 30 and DSWI, compared with patients without DSWI, was 1.87 (95% CI 1.06-3.3), p = 0.032. The group of diabetics was at a statistically significant risk of development of DSWI, with OR 2.63 (95% CI 1.47-4.69), p = 0.001. LOS of more

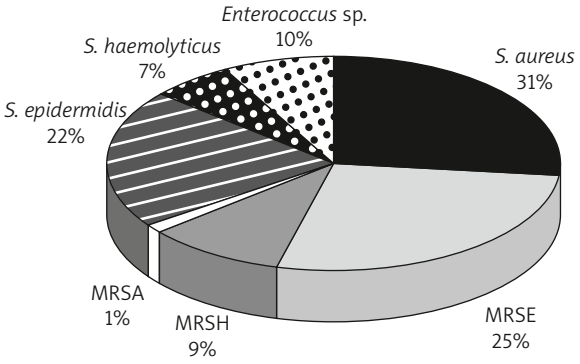

Fig. 1. Frequency of G+ pathogens

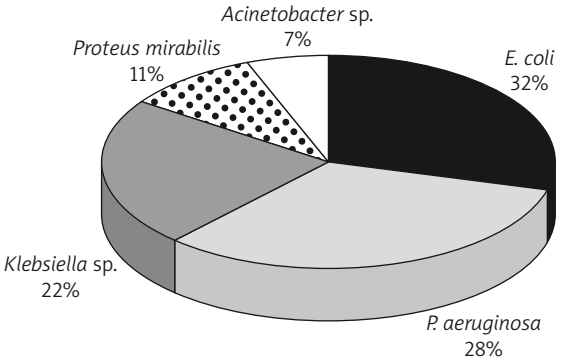

Fig. 2. Frequency of G– pathogens

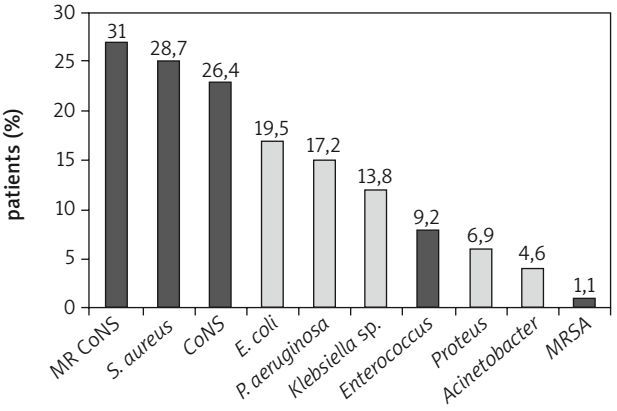

Fig. 3. Frequency of all causative pathogens

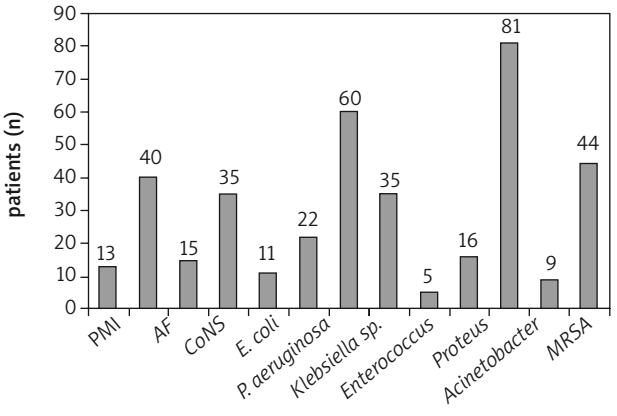

Fig. 4. Preoperative, perioperative and postoperative risk factors

than 2 days before cardiothoracic surgery was a statistically significant risk factor, with OR 4.57 (95% CI 2.49-8.33), $p = 0.001$. The duration of ECC is a significant perioperative risk factor. Duration of more than 120 minutes in our study had an OR of 4.35 (95% CI 1.38-13.7), $p = 0.012$. Considering postoperative risk factors, LOS in the ICU of more than 3 days is statistically significant for DSWI, with OR 2.31 (95% CI 1.3-4.12), $p = 0.004$. We have found a high odds ratio for DSWI in patients who had early surgical re-exploration due to postoperative bleeding, OR 5.52 (95% CI 2.48-12.35), $p = 0.001$. Another postoperative risk factor with statistical significance is the reperfusion syndrome characterized by neurocognitive impairment restlessness, with OR 8.7 (95% CI 1.93-38.46), $p = 0.005$.

Acute postoperative renal failure with oliguria and retention of nitrogen metabolites requiring dialysis is a strong predictor for DSWI, with OR of 6.06 (95%CI 1.31-28.57), $p = 0.021$. New onset atrial fibrillation, mostly on the second or third postoperative day, has an OR of 2.7 (95% CI 1.41-5.1), $p = 0.002$. The final risk factor for DSWI is type of discharge from hospital, meaning that discharging the patient to another hospital for ongoing care is more risky than discharging the patient to an outpatient setting, with OR of 4.54 (95% CI 2.3-8.96), $p < 0.001$.

We have identified the patient risk profile for DSWI with G+, G– pathogen or polymicrobial flora (Tab. I).

The risk of having DSWI caused by **G+ bacterial pathogens** increases with longer preoperative LOS in other hospitals (> 8.4 days) while on antibiotic therapy and with venous, arterial or urinary catheters. There was a tendency towards developing DSWI in men, patients younger than 65 years and patients on dialysis. Risk factors with statistical significance were BMI equal to or less than 30 ($p = 0.048$) and peripheral atherosclerotic arterial disease ($p < 0.05$).

On the other hand, the risk of having DSWI caused by **G– bacterial pathogens** was observed in women and patients who were > 65 years old ($p = 0.01$). Because of the trend towards G– bacterial infection in patients with short preoperative LOS, we made a subanalysis, and found that DSWI after emergent interventions had higher incidence of G– pathogens, with statistical significance ($p < 0.05$). These patients had an operation in acute myocardial infarction, which resulted in the need of intra-aortic balloon counterpulsation (IABC). Moreover, 80% of IABC devices were used in this group of patients. Also, postoperative surgical re-exploration for bleeding with administration of more than 2 blood transfusions is a significant risk factor for DSWI with G- flora ($p = 0.02$). Prolonged mechanical ventilation of > 48 hours plays an important role as well ($p < 0.05$).

Polymicrobial DSWI were significantly more frequent in patients with the duration of ECC of > 120 minutes, longer

(> 6 days) postoperative hospital stay at the cardiothoracic ward (p = 0.01) and in patients readmitted from another hospital after initial discharge (p = 0.047). A trend towards polymicrobial DSWI was noted in patients with BMI over 30.

Discussion

Statistically significant risk factors for DSWI identified in our study are summarized in Table II.

According to our study, already overweight with BMI > 30 is a significant risk factor for DSWI. As observed in our patients, BMI > 40 is associated with polymicrobial infections, and the literature states that such BMI leads to the development of DSWI in 2.6% of surgical patients [2]. The explanation for this lies in inadequate serum and tissue concentrations of administered antibiotics, technical difficulties during tissue suture and inadequate blood perfusion of fatty tissues. All this is a result of increased autonomic tonus, increased neurohumoral activation and increased oxidative stress in obese patients [3-5]. Other factors that preclude successful wound healing are impaired mobility and chest instability due to enormous tension in sternal wires, mostly in patients with neurocognitive impairment caused by reperfusion syndrome, as observed in our patients.

Diabetic patients are at greater risk for postoperative complications as compared with non-diabetic surgery patients. Hyperglycaemia-induced extracellular hyperosmolarity leads to lymphocyte degradation and immune system alteration with production of free radicals. Shortage of insulin leads to a decrease in 2,3 biphosphoglycerate in red blood cells, which in turn reduces the affinity of haemoglobin to oxygen. Therefore, strict euglycaemia is strongly suggested during peri- and postoperative periods. Levels of glucose greater than 8.3 mmol/l significantly increase the risk of postoperative infections by almost 30% [6].

Furnary et al. stated that targeting levels of glucose below 6 mmol/l, in diabetics, reduces risk of DSWI by 66% [7]. In addition, Steriovsky et al. published in 2010 a study in which they found that in patients with complete skeletonisation of both internal thoracic arteries (not a simple collection of pedicle with surrounding tissue), diabetes was not a significant predictor for impaired wound healing, while hyperlipoproteinaemia was [8].

Another important risk factor for acquiring DSWI in our study is atrial fibrillation. Uncoordinated heart movements contribute to decreased stroke volume that is translated into tissue hypoperfusion and possible internal thoracic artery embolisation [9].

We have found that procedures with ECC time > 120 minutes are associated with development of DSWI. Wound margins dry out, the number of bacteria increases, and low temperature followed by vasoconstriction leads to inadequate tissue perfusion. Only a small amount of bacterial colonies is needed for DSWI in cases where there is a presence of necrotic tissue, haematoma and foreign materials [10].

Tab. I. Risk profile with regard to microbiological cultures

		p
risk profile G+	BMI < 30	0.05
	peripheral atherosclerotic disease	0.05
	dialysis	NS (marked trend)
	age < 65 years	NS (marked trend)
risk profile G–	age > 65 years	0.01
	emergent surgery	< 0.05
	re-exploration	0.02
	mechanical ventilation > 48 hours	< 0.05
risk profile polymicrobial	ECC > 120 min	0.01
	LOS > 6 days	0.01
	readmission from medical facility	< 0.05
	BMI > 30	NS (marked trend)

BMI – body mass index, LOS – length of stay, ECC – extracorporeal circulation.

Tab. II. Statistical significance and OR of selected risk factors

Risk factor	Patients with DSWI vs patients without DSWI	p
age < 65 years	OR is 0.78 (95% CI 0.44-1.37)	0.388
women	OR is 0.96 (95% CI 0.53-1.72)	0.882
obesity (BMI > 30)	OR is 1.87 (95% CI 1.06-3.30)	**0.032**
LOS before surgery (> 2 days)	OR is 4.57 (95% CI 2.49-8.33)	**< 0.001**
LOS at anesthesiology dpt. (> 3 days)	OR is 2.31 (95% CI 1.30-4.12)	**0.004**
ECC (> 120 min)	OR is 4.35 (95% CI 1.38-13.7)	**0.012**
lower EF (< 40%)	OR is 1.72 (95% CI 0.68-4.36)	0.252
discharge to outpatient setting vs another medical facility	OR is 4.54 (95% CI 2.30-8.96)	**< 0.001**
CABG	OR is 1.00 (95% CI 0.47-2.14)	1.000
valve replacement	OR is 1.00 (95% CI 0.52-1.91)	1.000
perioperative myocardial infarction	OR is 1.00 (95% CI 0.44-2.28)	1.000
reperfusion syndrome	OR is 8.7 (95% CI 1.93-38.46)	**0.005**
re-exploration	OR is 5.52 (95% CI 2.48-12.35)	**< 0.001**
dialysis	OR is 6.06 (95% CI 1.31-28.57)	**0.021**
diabetes mellitus	OR is 2.63 (95% CI 1.47-4.69)	**0.001**
COPD	OR is 0.58 (95% CI 0.28-1.20)	0.142
new onset atrial fibrillation	OR is 2.7 (95% CI 1.43-5.1)	**0.002**

BMI – body mass index, LOS – length of stay, ECC – extracorporeal circulation, EF – ejection fraction, CABG – coronary artery bypass graft, COPD – chronic obstructive pulmonary disease.

According to our observation, postoperative surgical re-exploration is another significant risk factor for DSWI. The use of more than 2 blood products in patients with bleeding and the need for surgical re-exploration may have contributed to such observation. Pathophysiology of this phenomenon can be explained by transfusion-related immunomodulation (TRIM): a) deactivation of immune sys-

tem by active leukocytes, b) immunomodulation initiated by soluble biological substances released from leukocytes during product storage c) immunomodulation initiated by soluble human leukocyte antigen peptides [11]. Therefore, we assume that cautious use of blood products may decrease the incidence of DSWI.

Operations performed after prolonged preoperative hospital stay at other departments carry a significant risk of colonization with nosocomial pathogens, and subsequent perioperative incisional or haematological wound inoculation. Such patients are at increased risk for G+ wound infection, with a tendency for frequent methicillin-resistant *Staphylococcus aureus* (MRSA) acquisition. This applies mostly to obese and dialysis patients. Literature data show that infection with MRSA increases postoperative 90-day mortality almost 3-fold, and hospital financial expenses are doubled [12, 13]. At our department, this seems not to be a problem, which might be explained by mostly community admitted patients and elective operations. The mechanism of MRSA pathogenicity lies in the Panton-Valentine leukocidin (PVL) gene, which is responsible for formation of biofilm with an affinity for artificial surfaces and the ability to destroy leukocytes and perpetuate tissue necrosis. The presence of PVL is significantly more frequent in MRSA (87%) as compared to methicillin-sensitive *Staphylococcus aureus* (MSSA) (24%) (p = 0.001) [14].

Coagulase-negative staphylococci (CoNS) are also associated with wound and catheter related infections. Longstanding insertion of peripheral intravascular, urinary catheters and intracardial electrodes can therefore promote haematological wound inoculation. Recent guidelines state that the maximum recommended insertion period must be less than 96 hours. Our observation that younger patients with normal BMI (BMI < 30) are at significantly increased risk for G+ infection is extraordinary, but is also described by Itani et al. [15].

Factors associated with G– wound infections are emergent operations with inadequate short-term ATB prophylaxis, suboptimal operational field preparation – rough shaving (skin microtrauma), tissue hypoperfusion as a consequence of already ongoing myocardial infarction with low cardiac output and low perfusion pressure. As we have proved, emergent procedures have a higher incidence of perioperative myocardial infarctions or patients already have ongoing myocardial infarction, with the necessity of subsequent IABC implantation for low cardiac output. All this is followed by prolonged intubation and ventilation. We have observed that mechanical ventilation of > 48 hours was a significant risk factor. The most common G– pathogens associated with prolonged ventilation are *P. aeruginosa* and *Acinetobacter* sp. [16]. Our finding of more frequent G– infections in patients with re-exploration (p = 0.02) has profound implications for antimicrobial strategies in these high-risk patients.

Polymicrobial infections are encountered in older patients, patients with longer LOS, patients with comorbidities and also patients readmitted after previous discharge to another medical facility [15]. We have established that ECC of > 120 minutes is a major perioperative risk factor for polymicrobial infections, which has not been mentioned in the literature. Coincidence with peripheral vascular diseases, ischaemic or venous ulcers increases the risk, as well [17]. Moreover, morbid obesity, smoking and ethylism are also associated with the risk of polymicrobial DSWI [18].

Conclusion

Our study suggests that considering the patient risk profile for infections divided by Gram staining in patients presenting with DSWI can improve optimization of empirical antimicrobial therapy, which can then be translated into reduced bacterial resistance, shorter LOS and decreased financial expenses. We assume that the knowledge of issues related to DSWI is multidisciplinary and may help many physicians with different expertise and from other departments in subsequent postoperative management of cardiosurgery patients.

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