

Contents lists available at ScienceDirect American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/ american-heart-journal-plus-cardiology-research-and-practice

Research Paper

Factors associated with deep sternal wound infection after open-heart surgery in a Danish registry





Lisa Gundestrup^{a,*}, Christoffer Koch Florczak^b, Lars Peter Schødt Riber^a

^a Department of Cardiothoracic and Vascular Surgery, Cardiac section, Odense University Hospital, J.B. Winsløws Vej 4, Penthouse 2 sal, 5000 Odense, Denmark ^b Department of Politics and Society, Aalborg University, Fibigerstræde 1, 28 9220 Aalborg Ø, Denmark

ARTICLE INFO	A B S T R A C T
<i>Keywords</i> : Mediastinitis Deep sternal wound infection Open-heart surgery Risk factors	<i>Objective:</i> To conduct a comprehensive multivariate analysis of variables associated with deep sternal wound infection, after open-heart surgery via median sternotomy. <i>Method:</i> A retrospective cohort of all adult patients, who underwent open-heart surgery at Odense University Hospital between 01-01-2000 and 31-12-2020 was extracted from the West Danish Heart Registry. Data were analyzed using maximum likelihood logistic regression. <i>Results:</i> A total of 15,424 patients underwent open-heart surgery and 244 developed a deep sternal wound infection, equivalent to 1,58 %. After data review 11,182 entries were included in the final analysis, of which 189 developed DSWI, equivalent to 1,69 %. Multivariate analysis found the following variables to be associated with the development of deep sternal wound infection (odds ratios and 95%confidens intervals in parentheses): Known arrhythmia (1.70; 1.16–2.44), Left Ventricular Ejection Fraction (1.66; 1.02–2.58), Body Mass Index 25–30 (1.66; 1.12–2.52), Body Mass Index 30–35 (2.35; 1.50–3.71), Body Mass Index 35–40 (3.61; 2.01–6.33), Body Mass Index 40+ (3.70; 1.03–10.20), Age 60–69 (1.64; 1.04–2.67), Age 70–79 (1.95; 1.23–3.19), Chronic Obstructive Pulmonary Disease (1.77; 1.21–2.54), Reoperation (1.63; 1.06–2.45), Blood transfusion in surgery (1.09; 1.01–1.17), Blood transfusion in intensive care unit (1.03; 1.01–1.06), Known peripheral atherosclerosis (1.82; 1.25–2.61), Current smoking (1.69; 1.20–2.35), Duration of intubation (1.33; 1.12–1.57). <i>Conclusion:</i> Increased risk of deep sternal wound infection after open-heart surgery is a multifactorial problem, while some variables are unchangeable others are not. Focus should be on optimizing the condition of the patient prior to surgery e.g. weight loss and smoking. But also factors surrounding the patient e.g. preventing blood loss and minimizing intubation time.

1. Introduction

Deep sternal wound infections (DSWI) continue to be one of the most dreaded complications after median sternotomy in relation to openheart surgery (OHS). Previously reported with mortality rates ranging between 14 and 30 % and prolonged in hospital stay [1–5]. Though, after the introduction of Vacuum Assisted Closure(VAC) and improved management of patients with DSWI, mortality rates have decreased to around 3–12 % [6,7]. However, the rate of DSWI after OHS have remained relatively unchanged during the last 30 years at 0,2–2,3 % [1,2,5,6,8–14]. This is probably not a sign of lack of improvement of

patients care, but rather due to the fact, that patients referred to surgery have more comorbidities, are older and more complicated than earlier [15].

Several studies have sought to identify risk factors related to the development of DSWI after OHS. Amongst the identified risk factors are Chronic Obstructive Pulmonary Disease(COPD), diabetes, Body mass index (BMI), reoperation for bleeding and procedure type [2,8,10,11,13]. Other factors found to be associated with increased risk of DSWI are prolonged cardio pulmonary bypass (CPB) time, previous heart surgery, hypertension, male gender, mechanical ventilation over 72 h, age, transfusions, NYHA class and peripheral vascular disease

https://doi.org/10.1016/j.ahjo.2023.100307

Received 15 February 2023; Accepted 2 June 2023

Available online 6 June 2023

Abbreviations: DSWI, deep sternal wound infections; OHS, open-heart surgery; VAC, vacuum assisted closure; COPD, chronic obstructive pulmonary disease; BMI, body mass index; CPB, cardiopulmonary bypass; CABG, coronary artery bypass grafting; AVR, aortic valve replacement; WDHR, The West Danish Heart Registry; CI, confidence intervals; ECC, extracorporeal circulation; OR, odds ratio.

^{*} Corresponding author at: Department of Cardiothoracic and Vascular Surgery, Penthouse 2sal Odense University Hospital, J. B. winsløws 4, Odense C, Denmark. *E-mail addresses:* Lisa.gundestrup@rsyd.dk (L. Gundestrup), ckfl@dps.aau.dk (C.K. Florczak), Lars.riber@rsyd.dk (L.P.S. Riber).

^{2666-6022/© 2023} The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

[1,9,12,14]. The aim of this study was to investigate risk factors associated with the development of DSWI in a cohort of patients that have undergone OHS at Odense University Hospital, Denmark (OUH). In previous studies, the number of included patients have often been small resulting in a low number of patients with DSWI, leading to limitations in the statistical analysis. Furthermore, studies have often concentrated on one procedure type, for example coronary artery bypass grafting (CABG) or aortic valve replacement (AVR). In this study we have included a historically large cohort, comprised of all the surgeries performed at our department, and with-in this a reasonably large number of patients with DSWI. This allows us to conduct a more comprehensive multivariate analysis, which prior studies are in lack of.

2. Patients and method

2.1. Study design

This study was performed as a retrospective cohort study with data extracted from The West Danish Heart Registry (WDHR). This registry holds data on every patient that has undergone open-heart surgery in the Region of Western Denmark.

The extracted data include all adult patients (\geq 18 years) who underwent OHS at the Department of Cardiothoracic and Vascular surgery at OUH between 01-01-2000 and 31-12-2020. Surgery types primarily comprised CABG and AVR, but also included procedures such as mitral-and tricuspid-valve surgeries, double- and triple procedures, surgery for aortic dissections, tumor removals and traumatic cardiac injuries amongst others. To be defined as having a DSWI the patients had to have undergone re-sternotomy with verified bacterial growth in cultures from the mediastinum. To make sure all patients with a DSWI was registered correctly, the database was controlled against the ICD-10 codes for DSWI in the electronic patient journal and when discrepancies was detected the electronic journal was reviewed to confirm or deny a DSWI. Variables for the statistical analysis of risk factors were chosen based on previous literature review.

2.2. Statistical analysis

Data were analyzed using maximum likelihood logistic regression and prior to analysis data was reviewed in regards to missing and outlying values. Errors in the database documentation were evaluated and if an obvious correction was not possible, the entry was removed from the dataset. Univariate analysis was performed for each variable before selecting variables for multivariate analysis. Multicollinearity was tested when appropriate and linearity of the numerical variables were tested, and log transformation applied when deemed necessary. Furthermore, data were tested for outliers and a multivariate regression without the outliers was performed to evaluate the effect of the outliers on the statistical outcome.

Data are presented as odds ratios and 95 % confidence intervals (CI). A *p*-value of 0,05 was regarded as significant. The statistical analysis was performed using CRAN R Version 4.0.3.

3. Results

A total of 15,424 adult patients underwent OHS at OUH, between 01-01-2000 and 31–12–2020. DSWI developed postoperatively in 244 patients, equivalent to 1,58 %. To calculate incidence development over time, patients from the total cohort were subdivided into 4 groups, with 5 year intervals according to surgery date, 319 patient where excluded due to missing data. Calculations showed a significant increase in the incidence of DSWI over time for the groups 2010–2014 (p = 0,005) and 2015–2020 (p = 0,012) see Table 1. After exclusion of missing values and unreliable entries, a total of 11,182 entries were included in the final analysis, of which 189 developed DSWI, equivalent to 1,69 %.

The patient characteristics and the results of the univariate analysis

Table 1

incidence (of	DSWI	in	the	total	cohort.	

Year interval	No DSWI (<i>n</i> = 14,861)	DSWI (<i>n</i> = 244)	Incidents	p-Value
2000-2004	3580	42	1.12~%	
2005-2009	2955	40	1.34 %	0.51987
2010-2014	3876	78	1.97 %	0.00513
2015-2020	4450	84	1.85 %	0.01245

can be found in Table 2. A total of 17 variables from the univariate analysis showed association with the development of DSWI. The variables from the univariate analysis can be divided into three categories:

Baseline factors; Treatment for high cholesterol (p = 0.0064), treatment for high blood pressure (p = 0.0196), diabetes (p = 2.4E-05), COPD (p = 1.85E-06), smoking (p = 0.002), LVEF<30 % (p = 5.75E-05), Known arrhythmia (p = 5.68E-5), BMI(25-30: p = 0.03, 30–35:p = 0.0003, 35–40: p = 3.04E-07, >40: p = 0.01), Gender (p = 0.61), Age(60–69: p = 0.02, 70–79: p = 0.001. >80: p = 0.79), known peripheral atherosclerosis (p = 3.2E-09), Active endocarditis (p = 0.72), and previous OHS (p = 0.0001).

Intraoperative factors; Blood transfusion during surgery (p = 3.32E-09), CABG (p = 0.01), AVR (p = 0.50) and ECC time (p = 1,11E-07).

And postoperative factors; Reoperation (p = 6.23E-8), Blood transfusion in intensive care unit (p = 1.67E-12) and Duration of intubation (p = 6.9E-15).

From the univariate analysis, variables with *p*-values <0.05 were chosen for the multivariate analysis. Results of the analysis can be seen in Table 3. In the multivariate analysis 11 variables showed association with the development of DSWI; Known arrhythmia (OR = 1.70; CI:1.68–2.44), Left Ventricular Ejection Fraction (OR = 1.66; CI:1.02-2.58), Body Mass Index 25-30 (OR = 1.66; CI:1.12-2.52), Body Mass Index 30-35 (OR = 2.35; CI:1.50-3.71), Body Mass Index 35-40 (OR = 3.61; CI:2.01-6.33), Body Mass Index 40+ (OR = 3.70; CI:1.03–10.20), Age 60–69 (OR = 1.64; CI:1.04–2.67), Age 70–79 (OR = 1.95; CI:1.23-3.19), Chronic Obstructive Pulmonary Disease (OR = 1.77; CI:1.21-2.54), Reoperation (OR = 1.63; CI:1.06-2.45), Blood transfusion in surgery (OR = 1.09; CI:1.01–1.17), Blood transfusion in intensive care unit (OR = 1.03; CI:1.01-1.06), Known peripheral atherosclerosis (OR = 1.82; CI:1.25–2.61), Current smoking (OR = 1.69; CI:1.20-2.35) and Duration of intubation (OR = 1.33; CI:1.12-1.57). Variables that no longer showed association consists of; treatment for high cholesterol (OR = 1.26; CI:0.85–1.81), treatment for high blood pressure (OR = 1.02; CI:0.74–1.43), diabetes (OR = 1.40; CI:0.95–1.97), age 80+ years (OR = 1.42; CI:0.58-3.12), ECC time (OR = 0.88; CI:0.63-1.35), CABG (OR = 1.29; CI:0.90-1.88), and previous openheart surgery (OR = 1.29; CI:0.85–1.92).

A test for outliers revealed 41 outliers with possible influence on the analysis. These were removed from the dataset and a new multivariate analysis was performed on a dataset with a total of 11,141 patients and 148 cases of DSWI. This analysis was performed to evaluate the influence of outliers on the results of the multivariate analysis. When comparing the results from the two multivariate analysis we found that diabetes was now a significant risk factor after removal of outliers, with OR = 1.55 and CI:1.05–2.26, all other variables remained unchanged in terms of significance after the removal of outliers.

To evaluate the difference in survival between patient with and without DSWI Kaplan Meier plot was produced and can be seen in Fig. 1. A log-rank-test were performed, and it showed a significant difference $(p = 1^{-15})$ in survival in the two groups.

Next patients were divided into two new groups according to the type of surgery they underwent.

The two groups were comprised of patients who underwent either a surgery that included a CABG or a non-CABG surgery. The incidence of DSWI in the two groups can be found in Table 4. Multivariate analyses were performed on the two groups with a reduces number of variables.

Table 2

Univariate analyses of risk factors for deep sternal wound infection.

Variable	Category	No DSWI (n = 10,993)	DSWI (n = 189)	p-value
Treatment for high Cholesterol	No	4401(40 %)	57(30.2 %)	
	Yes	6592(60 %)	132(69.8 %)	0.0064
Treatment for high blood pressure	No	4717(42.9 %)	65(34.4 %)	
	Yes	6276(57.1 %)	124(65.6 %)	0.0196
Diabetes	No	9154(83.3 %)	135(71.4 %)	
	Yes	1839(16.7 %)	54(28.6 %)	2.4E-05
Known arrhythmia ^a	No	9512(86.5 %)	144(76.2 %)	
	Yes	1481(13.5 %)	45(23.8 %)	5.68E-05
LVEF ^b	>30 %	10,376(94.4 %)	165(87.3 %)	
	<30 %	617(5.6 %)	24(12.7 %)	5.75E-05
BMI^{c}	<25	3523(32 %)	37(19.6 %)	
	>25-30	4760(43.3 %)	77(40.7 %)	0.03186
	>30-35	2063(18.8 %)	48(25.4 %)	0.00031
	>35-40	551(5%)	23(12.2 %)	3.04E-07
Gender	>40 Male	96(0.9 %) 8257(75.1	4(2.1 %) 145(76.7	0.01019
	Female	%) 2736(24.9	%) 44(23.3	0.612
Age groups (years)	<60	^{%)} 2531(23 %)	%) 27(14.3 %)	
	60–69	3642(33.1 %)	66(34.9 %)	0.02118
	70–79	4145(37.7 %)	88(46.6 %)	0.00188
COPD ^d	>80 No	675(6.2 %) 9834(89.5	8(4.3 %) 148(78.3	0.79487
	Yes	%) 1159(10.5	%) 41(21.7	1.85E-06
ECC duration (minutes) ^e	mean	%) 110.8	%) 132.1	1.11E-07
Reoperation	No	9987(90.8 %)	149(78.8	11112 07
	Yes	1006(9.2 %)	40(21.2 %)	6.23E-08
Blood transfusion during surgery (liter)	Mean	0.22	0.82	3.32E-09
Blood transfusion in intensive care unit (Liter)	Mean	0.57	3.2	1.67E-12
CABG ^g	No	3824(34.8 %)	50(26.5 %)	
	Yes	7169(65.2 %)	139(73.5 %)	0.0177
Aortic valve replacement	No	7010(63.8 %)	125(66.1 %)	
	Yes	3983(36.2 %)	64(33.9 %)	0.502
Known peripheral atherosclerosis	No	9925(90.3 %)	145(76.7 %)	
	Yes	1068(9.7 %)	44(23.3 %)	3.21E-09
Current smoking	No	8601(78.2 %)	130(68.8 %)	
	Yes	2392(21.8 %)	59(31.2 %)	0.00202
Active endocarditis	No	10,799(98.2 %)	185(97.9 %)	
	Yes	194(1.8 %)	4(2.1 %)	0.717

Table 2 (continued)

Variable	Category	No DSWI (n = 10,993)	DSWI (n = 189)	p-value
Previous open-heart surgery	No	9087(82.7 %)	136(72 %)	
	Yes	1906(17.3 %)	53(28 %)	0.000157
Duration of intubation	Mean	18.4	97.53	6.9E-15

^a The dominating arrhythmia type was atrial fibrillation but other types of arrhythmias also occurred.

^b Left ventricular ejection fraction prior to surgery.

^c Body mass index.

^d Chronic obstructive pulmonary disease.

e Extracorporeal circulation.

^f Acute reoperation caused by bleeding, tamponade, or ischemia.

^g Coronary artery bypass grafting.

Table 3

Multivariate analysis of risk factors for deep sternal wound infection.

Variable	OR	95 % CI	p-Value
Treatment for high cholesterol	1.2624	0.8923-1.8064	0.194467
Treatment for high blood pressure	1.0227	0.7377-1.4291	0.893875
Diabetes	1.4023	0.9845-1.9731	0.056136
Known arrhythmia ^a	1.7021	1.1678-2.4377	0.004527
LVEF ^b	1.6548	1.0165-2.5829	0.033535
BMI 25–30 ^c	1.6605	1.1157-2.5155	0.014170
BMI 30–35 ^c	2.3455	1.4946-3.7103	0.000227
BMI 35–40 ^c	3.6048	2.0121-6.3329	1.07E - 05
BMI 40+ ^c	3.6993	1.0300-10.2016	0.022186
Age 60–69	1.6396	1.0345-2.6711	0.040200
Age 70–79	1.9521	1.2332-3.1849	0.005543
Age 80+	1.4159	0.5809-3.1151	0.410829
COPD ^d	1.7741	1.2134-2.5387	0.002274
ECC duration (minutes) ^{e,h}	0.8873	0.6340-1.3448	0.551874
Reoperation ^f	1.6308	1.0567-2.4493	0.022238
Blood transfusion during surgery (liter)	1.0870	1.0086 - 1.1653	0.020501
Blood transfusion in intensive care unit	1.0330	1.0091 - 1.0578	0.005186
(liter)			
CABG ^g	1.2860	0.8946-1.8754	0.182052
Known peripheral atherosclerosis	1.8226	1.2475-2.6137	0.001432
Current smoking	1.6861	1.1971-2.3503	0.002360
Previous open-heart surgery	1.2902	0.8499-1.9214	0.221501
Duration of intubation (hours) ^h	1.3308	1.1159–1.5731	0.001087

^a The dominating arrhythmia type was Atrial fibrillation but other types of arrhythmias also occurred.

^b Left ventricular ejection fraction prior to surgery.

^c Body mass index.

^d Chronic obstructive pulmonary disease.

^e Extracorporeal circulation.

^f Acute reoperation caused by bleeding, tamponade, or ischemia.

^g Coronary artery bypass grafting,

^h Log transformed.

The results can be found in Tables 5 and 6.

For the CABG group the following significant variables were found; Known arrhythmia (OR = 1.67; CI:1.04–2.59), Body Mass Index 25–30 (OR = 1.99; CI:1.21–3.39), Body Mass Index 30–35 (OR = 3.33; CI:1.95–5.86), Body Mass Index 35–40 (OR = 5.03; CI:2.52–9.93), Age 70–79 (OR = 1.99; CI:1.18–3.49), Chronic Obstructive Pulmonary Disease (OR = 1.81; CI:1.15–2.75), Reoperation (OR = 1.96; CI:1.19–3.14), Known peripheral atherosclerosis (OR = 1.71; CI:1.11–2.57), Current smoking (OR = 1.89; CI:1.28–2.75) and Duration of intubation (OR = 1.35; CI:1.09–1.64).

For the non-CABG group, the following significant variables were found; Body Mass Index >40 (OR = 4.74; CI:0.94–17.6), Blood transfusion in surgery (OR = 1.12; CI:0.99–1.25), Blood transfusion in intensive care unit (OR = 1.06; CI:1.02–1.11), Known peripheral atherosclerosis (OR = 2.57; CI:1.10–5.48).

Red: no DSWI Blue: DSWI



Fig. 1. Kaplan Meier plot of the difference in survival between patients with and without a DSWI.

Table 4

Incidence of infection in patients that have undergone a procedure including a CABG and for patients with a non-CABG procedure.

Procedure type	No DSWI (n = 10,993)	DSWI (n = 189)	Incidents
CABG+	7169	139	1,90 %
Non-CABG	3824	50	1,29 %

Table 5

Multivariate analysis of risk factors for deep sternal wound infection for patients undergoing a procedure that includes CABG.

Variable	OR	95 % CI	p-Value
Diabetes	14,349	0.9715-2.0876	0.06358
Known arrhythmia ^a	1.6731	1.0386-2.5999	0.02733
LVEF ^b	1.6605	0.9504-2.7526	0.06035
BMI 25–30 ^c	1.9902	1.2145-3.3874	0.00819
BMI 30-35 ^c	3.3335	1.9501-5.8628	1.63E - 05
BMI 35-40 ^c	5.0297	2.5189-9.9308	3.39E-06
BMI 40+ ^c	2.1219	0.1145-11.0380	0.47582
Age 60–69	1.5000	0.8894-2.6193	0.13908
Age 70–79	1.9968	1.1851-3.4955	0.01179
Age 80+	1.0984	0.3109-3.0315	0.86834
COPD ^d	1.8129	1.1596-2.7508	0.00676
Reoperation ^e	1.9644	1.1904-3.1357	0.00613
Blood transfusion during surgery (liter)	1.0639	0.9620-1.1603	0.17145
Blood transfusion in intensive care unit (liter)	1.0217	0.9861-1.0555	0.19848
Known peripheral atherosclerosis	1.7059	1.1075-2.5656	0.01245
Current smoking	1.8896	1.2835-2.7540	0.00106
Duration of intubation (hours) ^f	1.3526	1.0962-1.6485	0.00367

^a The dominating arrhythmia type was atrial fibrillation but other types of arrhythmias also occurred.

^b Left ventricular ejection fraction prior to surgery.

^c Body mass index.

^d Chronic obstructive pulmonary disease.

^e Acute reoperation caused by bleeding, tamponade, or ischemia.

^f Log transformed.

4. Discussion

The aim of this study was to identify risk factors associated with the development of DSWI after OHS.

Multivariate analysis of risk factors for deep sternal wound infection for patients
undergoing a non-CABG procedure.

Variable	OR	95 % CI	p- Value
Diabetes	1.7628	0.7831-3.6554	0.1455
Known arrhythmia ^a	1.8514	0.9787-3.4181	0.0521
LVEF ^b	1.5764	0.5085-3.9162	0.3731
BMI 25–30 ^c	1.2574	0.6243-2.5759	0.5227
BMI 30-35°	0.9121	0.3336-2.2669	0.8487
BMI 35-40°	1.8669	0.5571-5.3151	0.2694
BMI 40+ ^c	4.7403	0.9362-17.6042	0.0327
Age 60–69	2.5432	1.0055-7.4340	0.0625
Age 70–79	2.3268	0.9363-6.7799	0.0889
Age 80+	2.4031	0.5777-9.1859	0.2006
COPD ^d	1.7081	0.7851-3.4296	0.1512
Reoperation ^e	1.0286	0.3826-2.3674	0.9510
Blood transfusion during surgery (liter)	1.1248	0.9949-1.2542	0.0432
Blood transfusion in intensive care unit	1.0564	1.0165-1.1132	0.0159
(liter)			
Known peripheral atherosclerosis	2.5741	1.1026-5.4816	0.0198
Current smoking	1.0530	0.4638-2.1672	0.8943
Duration of intubation (hours) ^f	1.2236	0.8793-1.6486	0.2062

^a The dominating arrhythmia type was atrial fibrillation but other types of arrhythmias also occurred.

^b Left ventricular ejection fraction prior to surgery.

^c Body mass index.

Table 6

^d Chronic obstructive pulmonary disease.

^e Acute reoperation caused by bleeding, tamponade, or ischemia.

^f Log transformed.

Previous studies have sought to do the same with varying results. The relatively low incidence of DSWI makes it hard to accumulate enough cases to conduct advanced analyses using an observational study design. Furthermore, the nature of DSWI makes it impossible to conduct randomizes controlled studies. Studies are therefore mainly based on retrospective cohorts. This specific study was conducted with data drawn from the Western Danish Heart Registry, which composes a potentially big margin for error since data are mostly manually reported, resulting in a risk of errors when entering information into the database. In our study this resulted in a large number of entries having to be removed before analysis, because of missing entries or unreliable data. However, after the careful removal of irregular entries we consider our data of generally high quality, as a previous study evaluated the WDHR and concluded that that the data registry was valid with an overall low error rate and would therefore be well suited for use in epidemiological studies [16].

The majority of the current literature identifies a few significant risk factors in their multivariate analyses, from a large pool of variables, such as diabetes, COPD, obesity, prolonged intubation time, and CABG. In our study, we manage to confirm many of the previously found risk factors in our multivariate analysis of the full cohort, with a total number of 11 risk factors associated to the development of DSWI after OHS. Our excessed findings are probably due to our larger number of patients with DSWI in a historically large cohort, making the statistical power of the study greater than previous studies on the subject. Dividing our cohort into subgroups according to procedure-type significantly reduces our statistical power, although we still produce statistically significant results, on some of the known risk factors, the decreasing number of patients in the two groups affects the analysis substantially, increasing our confidence intervals for the significant results, therefore the results should be interpreted with care.

Although, no new associations have been found, our study was able to confirm almost all the previously detected factors in a single heartsurgery population. Only a few earlier detected risk factors were not significant in our study, such as male gender and extracorporeal circulation (ECC) time. This could be due to the fact that these might be indirect risk factors of the patient's risk, since male gender is known to be associated with both diabetes, COPD and arteriotic arteriosclerosis, while increased ECC-time may be an in-direct risk factor for more severe disease in the patient population such as multiprocedural surgeries and endocarditis etc. Therefore, not surprisingly was ECC time a significant risk factor for DSWI in the univariate analysis, while not in the multivariate analysis. Further, prolonged ECC time often results in increased transfusion requirements [17,18], which was found to be a significant risk factor for DSWI in both the univariate and the multivariate analysis. ECC time may therefore present as a confounder in the univariate analysis.

Transfusions, both during and after surgery, were associated with increased risk of DSWI, and since this is a factor that, to some extent, is amendable, it should be a focus point when dealing with patients undergoing OHS. We found an increased risk of DSWI for the age group 60–69 and 70–79 years, but not for the 80+ group. This discrepancy is most likely related to the low number of patients in the 80+ group and we expect that this group would have increased risk of DSWI if the sample size was bigger.

Surprisingly, we initially found no association between diabetes and DSWI in the multivariate analysis even though diabetes is a well-known risk factor for surgical infections [19]. A limitation of this study is the rather large number of outliers that affected the final analysis. A second multivariate analysis was therefore performed to investigate the influence of the outliers on the result. After removal of the outliers the multivariate analysis revealed an association between diabetes and DSWI while all other factors remained unchanged in regard to significance. Therefore, we find that the lack of significance is probably due to suppression by the outliers, and recommend relying on the conclusions of previous studies, that diabetes is a risk factor.

Regarding survival after a DSWI, as expected we see a lower survival rate in patients who have develop a DSWI. The significant difference in survival develops during the first few months after the primary surgery, and then levels out to a point where the two curves develop a parallel trend. Thus, our results suggest, that if a patient survives the initial infection, it's complications, and treatment, the survival rate is no different than in patients without a DSWI.

When considering the relative impact for the individual risk factors in the development of DSWI, it is difficult to identify prime movers, due to relatively similar effect sizes and overlapping CI. However, when looking at baseline characteristics, BMI shows the highest point estimate (OR: BMI > 40 compared to ref. = 3.6993), but other factors such as smoking, peripheral atherosclerosis, COPD and diabetes are also important in the development of DSWI.

Although a postoperative factor such as reoperation are statistically indistinguishable from BMI due to overlapping CI, practical considerations concerning reoperation may make BMI the superior choice for intervention.

5. Conclusion

The overall conclusion of the study is that the development of DSWI is multifactorial and pinpointing specific variables as the main cause is difficult. This study can point out areas that needs considerations in the quest to eliminate DSWI. Though some baseline variables such as diabetes, COPD and age cannot be changed, others such as BMI, arrhythmia and smoking, are factors that can be improved or prevented. Reductions in BMI could be a point of focus when trying to reduce the risk of infection.

Ethical statement

The regional ethics board in the regions of southern Denmark evaluated the study and found no approval necessary, because the data where drawn from a quality database.

Funding

This project did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- C.A. Milano, K. Kesler, N. Archibald, D.J. Sexton, R.H. Jones, Mediastinitis after coronary artery bypass graft surgery: risk factors and long-term survival, Circulation. 92 (8) (1995) 2245–2251.
- [2] A.S. Omran, A. Karimi, S.H. Ahmadi, S. Davoodi, M. Marzban, N. Movahedi, et al., Superficial and deep sternal wound infection after more than 9000 coronary artery bypass graft (CABG): incidence, risk factors and mortality, BMC Infect. Dis. 7 (2007).
- [3] M. De Feo, A. Renzulli, G. Ismeno, R. Gregorio, A. Della Corte, R. Utili, et al., Variables predicting adverse outcome in patients with deep sternal wound infection, Ann. Thorac. Surg. 71 (1) (2001) 324–331.
- [4] F.D. Loop, B.W. Lytle, D.M. Cosgrove, S. Mahfood, M.C. McHenry, M. Goormastic, et al., Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care, Ann. Thorac. Surg. 49 (2) (1990) 179–187. Feb. Available from: https://linkinghub.elsevier.com/retrieve/p ii/000349759090136T. Feb. Available from:.
- [5] R. Wouters, F. Wellens, H. Vanermen, R. De Geest, I. Degrieck, F. De Meerleer, Sternitis and mediastinitis after coronary artery bypass grafting. Analysis of risk factors, Texas Hear. Inst. J. 21 (3) (1994) 183–188. Available from: http://www.nc bi.nlm.nih.gov/pubmed/8000263. Available from:.
- [6] A.A. Juhl, S. Hody, T.S. Videbaek, T.E. Damsgaard, P.H. Nielsen, Deep sternal wound infection after open-heart surgery: a 13-year single institution analysis, Ann. Thorac. Cardiovasc. Surg. 23 (2) (2017) 76–82. Available from: https://www jstage.jst.go.jp/article/atcs/23/2/23_oa.16-00196/_article. Available from:.
- [7] R. Baillot, D. Cloutier, L. Montalin, L. Côté, F. Lellouche, C. Houde, et al., Impact of deep sternal wound infection management with vacuum-assisted closure therapy followed by sternal osteosynthesis: a 15-year review of 23 499 sternotomies, Eur. J. Cardiothorac. Surg. 37 (4) (2010) 880–887.
- [8] P. Munoz, A. Menasalvas, J.C.L.B. de Quiros, M. Desco, J.L. Vallejo, E. Bouza, Postsurgical Mediastinitis: a case-control study, Clin. Infect. Dis. 25 (5) (1997) 1060–1064. Nov. Available from: https://doi.org/10.1086/516068. Nov. Available from:.
- [9] E. Matros, S.F. Aranki, L.R. Bayer, S. McGurk, J. Neuwalder, D.P. Orgill, Reduction in incidence of deep sternal wound infections: random or real? J. Thorac. Cardiovasc. Surg. 139 (3) (2010) 680–685.
- [10] L. Pan, R. Mo, Q. Zhou, D. Wang, Deep sternal wound infection after cardiac surgery in the Chinese population: a single-centre 15-year retrospective study, J. Thorac. Dis. 9 (9) (2017) 3031–3037. Sep. Available from: http://jtd.amegroups. com/article/view/15342/12708. Sep. Available from:.
- [11] F. Filsoufi, J.G. Castillo, P.B. Rahmanian, S.R. Broumand, G. Silvay, A. Carpentier, et al., Epidemiology of deep sternal wound infection in cardiac surgery, J. Cardiothorac. Vasc. Anesth. 23 (4) (2009) 488–494. Aug. Available from: htt ps://linkinghub.elsevier.com/retrieve/pii/S1053077009000421. Aug. Available from:.
- [12] W.J. Mauermann, P. Sampathkumar, R.L. Thompson, Sternal wound infections, Best Pract. Res. Clin. Anaesthesiol. 22 (3) (2008) 423–436.
- [13] P.J. Robinson, B. Billah, K. Leder, C.M. Reid, Factors associated with deep sternal wound infection and haemorrhage following cardiac surgery in Victoria, Interact. Cardiovasc. Thorac. Surg. 6 (2) (2006) 167–171. Dec 1. Available from: htt ps://doi.org/10.1510/icvts.2006.132191. Dec 1. Available from:.
- [14] J. Lu, Risk factors for sternal wound infection and mid-term survival following coronary artery bypass surgery, Eur. J. Cardio Thorac. Surg. 23 (6) (2003) 943–949. Jun. Available from: https://doi.org/10.1016/S1010-7940(03)00137-4. Jun. Available from:.
- [15] T.B. Ferguson, B.G. Hammill, E.D. Peterson, E.R. DeLong, F.L. Grover, A decade of change—risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990–1999: a report from the STS National Database Committee and the Duke Clinical Research Institute, Ann. Thorac. Surg. 73 (2) (2002) 480–489. Feb. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0003497 501033392, Feb. Available from:.
- [16] L.A. Rasmussen, H.E. Bøtker, L.O. Jensen, J. Ravkilde, L. Riber, P.H. Nielsen, et al., Quality assurance of the Western Denmark Heart Registry, a population-based healthcare register, Dan. Med. J. 64 (10) (2017). Oct. Available from: http://www. ncbi.nlm.nih.gov/pubmed/28975887. Oct. Available from:.
- [17] J.B. Williams, B. Phillips-Bute, S.D. Bhattacharya, A.A. Shah, N.D. Andersen, B. Altintas, et al., Predictors of massive transfusion with thoracic aortic procedures involving deep hypothermic circulatory arrest, J. Thorac. Cardiovasc. Surg. 141 (5)

L. Gundestrup et al.

(2011) 1283–1288. May. Available from: https://linkinghub.elsevier.com/retrieve

- /pii/S002252231001175X. May. Available from:.
 [18] K. Karkouti, R. O'Farrell, T.M. Yau, W.S. Beattie, Prediction of massive blood transfusion in cardiac surgery, Can. J. Anesth. 53 (8) (2006) 781-794. Aug. Available from: https://doi.org/10.1007/BF03022795. Aug. Available from:.
- [19] E.T. Martin, K.S. Kaye, C. Knott, H. Nguyen, M. Santarossa, R. Evans, et al., Diabetes and risk of surgical site infection: a systematic review and meta-analysis, Infect. Control Hosp. Epidemiol. 37 (1) (2016) 88–99. Jan 27. Available from: htt ps://www.cambridge.org/core/product/identifier/S0899823X15002494/type/ journal_article. Jan 27. Available from:.