

Management of Sternal Wound Infection—Determinants of Length of Stay and Recurrence of Infection after Muscle Flap Coverage

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Abstract

Aim The aim of this study was to define determinants of length of hospital stay (LOS) longer than mean and recurrence of infection (ROI) after complete healing of patients with deep sternal wound infections (DSWI).

Patients and Methods In this observational study, we included 303 patients (155 females and 148 males, with mean age of 68 years) treated from 2016 to 2020 at the Department of Plastic Surgery of the HELIOS Klinik Krefeld, Germany. All patients received extensive necrosectomy, repetitive negative pressure therapy, and final transplantation of a pectoral musculocutaneous flap. In the German diagnosis-related group (DRG)-system, the mean inpatient LOS depends on the number of surgical procedures and is longer in those with four or more surgical procedures (DRG I02B) and shorter in those with fewer procedures (DRGs I02C and I02D). The determinants which have a significant effect on LOS longer than mean and ROI after complete healing were identified by estimating a logistic regression model. The effect of the different calculated determinants was quantified as odds ratio. To measure the discriminant ability of the model between patients, we determined a receiver operating characteristic curve. The fit of the model was quantified by comparing predicted probabilities of the model with empirical probabilities of the data. The goodness of fit was then measured by applying the Hosmer–Lemeshow test.

Results Among patients in DRG I02B ($n = 246$), the variable clopidogrel and therapeutic anticoagulation was the most important determinant for a longer LOS, with an odds ratio of 5.83 (95% CI = 0.83/40.80). Female sex and renal insufficiency also prolonged LOS. Applying this analysis to the patients with group DRG groups I02C and I02D ($n = 57$), none of these parameters were predictive. The variable immunosuppression was the most important determinant for ROI ($n = 49$) (OR = 4.67; 95% CI = 1.01/21.52). Body mass index also played a role, but with a much smaller influence.

Conclusion There are specific risk factors for LOS longer than mean and ROI in patients with DSWI that can be identified on admission. Addressing these risk factors, if possible, could reduce the rate of patients with LOS longer than mean and ROI.

Keywords

- ▶ deep sternal wound infections
- ▶ clopidogrel
- ▶ anticoagulation
- ▶ immunosuppression
- ▶ body mass index

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Introduction

Deep sternal wound infections (DSWIs) are a serious complication following sternotomy for cardiothoracic surgery. "Conventional" treatment provides debridement and secondary closure or closed catheter irrigation.¹ Risk factors for the development of DSWIs after median sternotomy include diabetes, obesity, chronic obstructive pulmonary disease, osteoporosis, tobacco use, reoperation, prolonged intensive care unit stays, and use of assistive devices.² The Pairolero classification of infected median sternotomies divides wounds into three types based on duration and clinical findings.^{3,4} Type I infections occur within the first week after sternotomy and typically have serosanguineous drainage but no cellulitis, osteomyelitis, or costochondritis and type II infections, which occur during the second to fourth weeks after sternotomy and usually involve purulent drainage, cellulitis, and mediastinal suppuration. Costochondritis is rare, but osteomyelitis is frequent. Type III infections occur months to years after sternotomy and typically involve chronic draining sinus tracts and localized cellulitis. Although mediastinitis is rare, osteomyelitis, costochondritis, and/or retained foreign bodies are often present.

Treatment ranges from antibiotics and a single-stage operation, debridement of all necrotic tissues with removal of all foreign materials and exposed cartilage in subtotal sternotomy and muscle flap coverage, as also noted in the current S3 guidelines on the management of mediastinitis after cardiac surgery.⁴⁻⁷ After radical infection repair by subtotal sternotomy and defect coverage by a muscle flap, some patients develop a new wound healing disorder, which often leads to reoperation and prolonged hospitalization.^{8,9}

Treatment of these patients is time-consuming and recurrence of infection cannot be excluded in any case.

The aim of this study was to define determinants of length of hospital stay and recurrence of infection after complete healing of patients with DSWI to identify at admission patients who are likely to have a length of stay (LOS) above the mean LOS or recurrence of infection (ROI).

Patients and Methods

The Department of Plastic Surgery of the HELIOS Klinik Krefeld is specialized in the treatment of patients with DSWI, and patients come from a major part of western Germany. From 2016 to 2020, 303 patients were treated. All patients received detailed documentation of their medical history, a clinical examination, determination of blood values, and bacterial infection. Initial treatment started with extensive debridement and necrosectomy (► **Table 1**). In all patients, the sternum was subtotally removed. Repetitive negative pressure therapy was given until the tissue was prepared for transplantation of a pectoral musculocutaneous flap. In total, 155 patients were female and 148 were male (mean age was 68 years). Six patients died in the hospital during treatment due to myocardial infarction and sepsis. The median inpatient LOS was 43 days.

Determinants of Length of Stay Longer than Mean Length of Stay

Mean LOS was 43 days and ranged from 16 to 168 days. We were interested in determining that if there are any determinants at the time of hospital admission that are associated with an LOS longer than the mean LOS calculated by the German diagnosis-related group (DRG) system.

Table 1 Patients' characteristic by admission to hospital separated by the endpoint

	102B (n = 246)	102C/102D (n = 57)	ROI (n = 49)
Age (mean ± SD)	67.7 ± 9.4	69.3 ± 9.4	66.5 ± 9.4
Females, n (%)	123 (50.0)	32 (56.1)	31 (63.3)
Diabetes mellitus, n (%)	134 (54.5)	30 (52.6)	27 (55.1)
Hypertension, n (%)	236 (95.9)	55 (96.5)	49 (100)
Renal insufficiency, n (%)	120 (48.8)	32 (56.1)	30 (61.1)
Obesity, n (%)	185 (75.2)	39 (68.4)	36 (73.5)
Smoking, n (%)	92 (37.4)	30 (52.6)	22 (44.9)
Prior resternotomy, n (%)	26 (10.6)	3 (5.3)	5 (10.2)
Anemia, n (%)	228 (92.7)	53 (93.0)	47 (95.9)
CRP, n (%)	245 (99.6)	57 (100)	49 (100)
Hypoalbuminemia, n (%)	165 (67.1)	37 (64.9)	33 (67.3)
Immunosuppression, n (%)	15 (6.1)	3 (5.3)	6 (12.2)
Prophylactic anticoagulation, n (%)	144 (58.5)	32 (56.1)	28 (57.1)
Prophylactic anticoagulation and clopidogrel, n (%)	50 (20.3)	6 (10.5)	8 (16.3)
Therapeutic anticoagulation, n (%)	102 (41.5)	25 (43.9)	21 (42.9)
Therapeutic anticoagulation and clopidogrel, n (%)	18 (7.3)	0	3 (6.1)

Abbreviations: CRP, C-reactive protein; ROI, recurrence of Infection; SD, standard deviation.

Depending on the intensity of treatment and the number of surgical procedure, all patients were categorized into three DRGs with different LOS.

DRG I02B ($n=246$): Patients in this group had four or more surgical procedures and mean LOS in the DRG-system was calculated as 39.5 days (lower borderline 12 and upper borderline 58 days).

DRG I02C and I02D ($n=57$): Patients in this group had less than four surgical procedures. In the I02C group, mean LOS was calculated as 31.6 days (10–50 days). LOS days in the I02D group were 27.6 days (8–46 days). The grouping was based on the DRG system from the year 2020.

Determinants of Recurrence of Infection after Healing

ROI requiring revision during the same hospital stay was defined as “necessity to perform a new surgical debridement, abscess drainage or transplantation days after primary healing of the pectoral muscle flap.” It occurred in 49 patients (31 females and 18 males). The median LOS was 58 days in this group.

Included Variables

Variables included in the analyses are listed in ► **Table 1**. Body mass index (BMI) was classified according to the World Health Organization classification into normal weight up to a BMI of 24.9 and overweight above 25. Smoking was assigned as a risk factor for those who consumed nicotine at the time of their disease.

Arterial hypertension was considered a risk factor when there was the use of at least one antihypertensive drug.

In addition, the presence of chronic renal insufficiency was included as a risk factor. The severity of renal failure was not considered in detail. At a glomerular filtration rate of 89 or less on the day of hospitalization, the kidney was considered to have reduced function

Further, the presence of hypalbuminemia (albumin less than 3.5 g/L), anemia (hemoglobin [Hb] value less than 14 g/dL in men and less than 12.3 g/dL in women), elevated C-reactive protein (CRP; value greater than 0.5 mg/dL), and diabetes mellitus (taking oral antidiabetics or insulin or Hba1c greater than 6.5% on hospital admission) at inpatient admission was investigated.

The use of angiotensin-converting enzyme inhibitors, calcium antagonists, and immunosuppressant drugs was also studied. The medication at the inpatient admission of the patient was examined.

In addition, perioperative anticoagulation was examined in more detail. A total of four groups were formed for this purpose: one group in which patients received only prophylactic anticoagulation with heparin or enoxaparin, one group in which patients additionally received clopidogrel, one group in which patients were therapeutically anticoagulated with heparin or enoxaparin, and one in which patients received clopidogrel and therapeutic anticoagulation.

Other potential risk factor included the performance of re sternotomy during the initial cardiac surgery procedure.

Statistical Methods

The aim of our statistical analysis was to determine a logistic regression model for the dependent variables LOS above mean LOS and ROI after complete healing. Furthermore, we wanted to quantify the fit of our models and the ability to discriminate between the patients.

In the case of the dependent variable ROI after complete healing, we split the entire sample of 303 patients randomly into two subgroups of 152 patients (subgroup 1) and 151 patients (subgroup 2).

The logistic regression model was then estimated for subgroup 1. For this model identification, we applied three different types of variable selection, namely forward, backward, and stepwise selection. The model with the lowest value of the Akaike information criterion was chosen.¹⁰ For the dependent variable ROI after complete healing and subgroup 1, the explanatory variables BMI and immunosuppression were identified as the most important determinants.

The fit of our calculated model was then analyzed based on subgroup 2. For this purpose, we determined the average over the predicted probabilities of the event ROI after complete healing (for every patient) in the deciles of subgroup 2. We also calculated the relative inference for this event for the same deciles, stated as observed values. The observed and the predicted values were plotted, to check if they differ greatly from each other. The goodness of this model fit was quantified by applying the Hosmer–Lemeshow test.

The variables BMI and immunosuppression were then used to calculate a logistic regression model for the entire patient population, so for all 303 patients.

The identically procedure was used for analyzing the determinants of the dependent variable I02B, with a sample size of 246 patients. The identified explanatory variables are gender, therapeutical anticoagulation and clopidogrel, clopidogrel, and renal insufficiency defined by glomerular filtration rate. The identified explanatory variables which we used for the logistic regression for I02B were also applied to determine the logistic regression models for I02C and I02D. The samples of I02C and I02D were not randomly split into two subgroups, since the sample sizes of I02C and I02D consist only of 57 patients, which is too small for sample splitting.

All surveys were performed with the approval of the relevant ethics committee, in accordance with national law and in accordance with the declaration of Helsinki of 1975 (in the current, revised version). All participating patients or their legal guardians gave consent before inclusion into the trial. All statistical procedures were calculated via SAS 9.4.

Results

► **Table 1** shows the patients' characteristics separated for the different groups (endpoint: I02B, endpoint: I02C/I02D, endpoint: ROI after complete healing).

Table 2 Odds ratio (OR) of the determinants of an LOS longer than mean in patients grouped in DRG I02B in subgroup 1

Effect	OR	95% Wald confidence limits	
Gender, female vs. male	2.17	1.0	4.74
Clopidogrel +_therapeutic anticoagulation, yes vs. no	5.83	0.83	40.80
Clopidogrel, yes vs. no	0.25	0.06	0.99
Renal insufficiency, yes vs. no	1.04	0.69	1.56

Abbreviation: LOS, length of stay.

Among patients in the DRG I02B ($n = 246$) treated with four or more surgical procedures, mean LOS defined by the DRG system is 39.5 days. In total, 132 patients had a longer LOS than mean. In the multivariate analysis, the variable clopidogrel and therapeutic anticoagulation, which was present in 7.3% of patients, was the most important determinant for a LOS longer than mean with an odds ratio of 3.56 (95% CI = 1.03/12.26) in the overall group and of 5.83 (95% CI = 0.83/40.80; ► **Table 2**) in the subgroup 1. Female gender and renal insufficiency also prolonged LOS. The results of the Hosmer–Lemeshow test are shown in ► **Table 3**. ROC curve (► **Fig. 1**) and model fit (► **Fig. 2**) showed the discriminatory power of the model as well as the goodness of fit to the data. The area under the curve (AUC) was 0.62, and the p -value of the Hosmer–Lemeshow test was 0.83 so that the null hypothesis “observed and predicted values are equal” could not be rejected.

Applying this analysis to the patient group in DRG I02C and I02D ($n = 57$), none of this parameter was predictive. Applying it to the patients with the endpoint ROI after complete healing ($n = 49$), the variables therapeutic anti-coagulation, renal insufficiency, and gender had a much lower impact.

Doing a new separate analysis in these patients, ROI after complete healing showed that the variable immunosuppression, which was present in 12.2% of the patients, is the most important determinant with an odds ratio of 4.67 (95% CI: 1.01/21.52) in the subgroup and an odds ratio of 3.03 (95% CI:

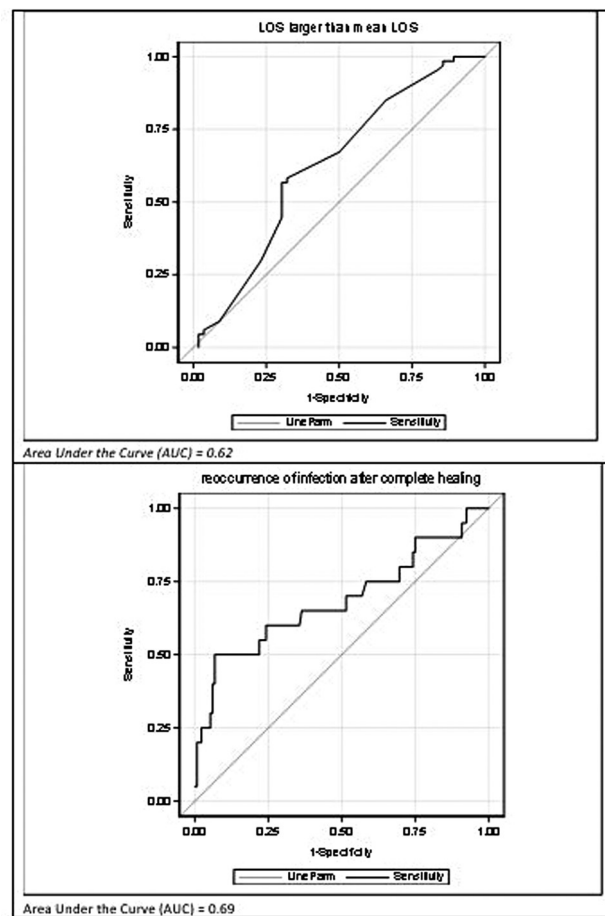


Fig. 1 ROC curve predicting events based on our model for the LOS longer than mean LOS (upper) and ROI after healing (lower).

1.07/8.59) in the overall group. Obesity was relevant too, but with a much lower impact. Odds ratio was 1.10 (95% CI: 1.03/1.17) in the subgroup. The result of the Hosmer–Lemeshow test is shown in ► **Table 4**. The p -value of the Hosmer–Lemeshow test was 0.34 so that the null hypothesis “observed and predicted values are equal” could not be rejected. Although the p -value was not as large as for I02B, it indicated that the fit is not too bad. The ROC curve had an AUC of 0.69.

Table 3 Hosmer–Lemeshow test including determinants of ► **Table 5** in subgroup 2

Decentile	Sum	LOS longer than mean		LOS not longer than mean	
		Observed	Predicted	Observed	Predicted
1	14	4	5.17	10	8.83
2	15	9	6.91	6	8.09
3	15	6	7.07	9	7.93
4	14	7	6.77	7	7.23
5	9	6	4.81	3	4.19
6	23	13	13.64	10	9.36
7	23	13	13.92	10	9.08
8	10	7	6.70	3	3.30

Abbreviation: LOS, length of hospital stay.

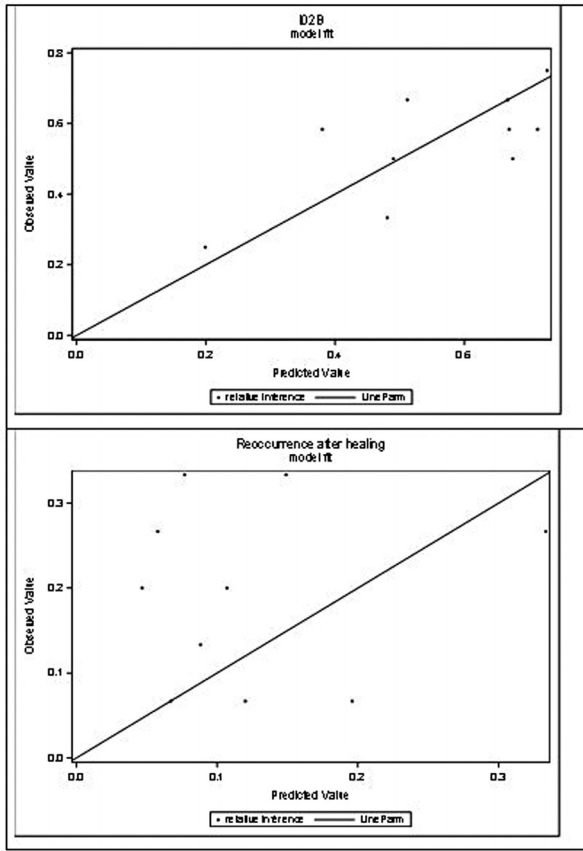


Fig. 2 Model fit predicting events based on our model for the LOS longer than mean LOS (upper) and ROI after healing (lower).

Discussion

Our analysis shows that already at admission there are specific determinants of an LOS longer than mean and

much fewer specific determinants of ROI after healing in patients presenting with DSWI. Modifying these determinants should have an impact on LOS longer than mean and ROI after complete healing.

DSWI is a rare but potentially devastating complication of median sternotomy performed in cardiac surgery. The incidence of DSWI is reported to be between 0.2 and 3%.⁶ Obesity, bilateral internal mammaria artery grafts plus diabetes, prolonged operative time, ICU treatment > 5 days, reexploration, and the need for repeated blood transfusions in the early postoperative period are reported as predictors for DSWI.^{2,4,11,12} Pectoralis muscle flaps are the workhorse for complex sternal wound coverage, but complications after flap reconstruction for DSWIs remain high. In a retrospective study including 119 cases from 2007 to 2008, end-stage renal disease and vertical rectus abdominis myocutaneous reconstruction were associated with the complicated postoperative course in these patients.⁵

In addition to the literature, our analysis examines for the first time determinants of LOS longer than mean and ROI after complete healing among patients send to the hospital for DSWI. In fee-for-service countries like Germany, reimbursement becomes more and more important for hospitals. An LOS longer than mean and an early ROI after complete healing during in-hospital stay are important factors that reduce profit and thus threaten the existence of the hospital. The question is whether these determinants can effectively be addressed before admission.

Pech et al analyzed the treatment of 130 patients treated by latissimus flap to cover sternal wounds between 2009 and 2015 retrospectively.⁷ The reoperation rate because of wound healing problems was 21.5% and bleeding complications leading to reoperation occurred in 10.8% of all patients. In this setting, high dose therapy with danaparoid/fondaparinux was a significant risk factor for bleeding complications

Table 4 Hosmer–Lemeshow test for ROI in subgroup 2

Decentile	Sum	Surgical revision because of ROI		No surgical revision because of ROI	
		Observed	Predicted	Observed	Predicted
1	15	1	1.98	14	13.02
2	15	5	2.32	10	12.68
3	16	1	2.68	15	13.32
4	17	3	3.03	14	13.97
5	15	3	2.78	12	12.22
6	15	4	2.89	11	12.11
7	15	1	3.00	14	12.00
8	15	4	3.13	11	11.87
9	15	2	3.27	13	11.73
10	13	5	3.92	8	9.08
Hosmer and Lemeshow goodness-of-fit test					
Chi-quadrat		DF		Pr > ChiSq	
9.07		8		0.34	

Abbreviation: ROI, recurrence of infection.

Table 5 Included variables and their definitions

Step	Variable	Definition
1	Diabetes mellitus	Oral antidiabetics or insulin or HbA1c greater than 6.5% on hospital admission
2	Hypertension	Use of at least one antihypertensive drug at inpatient admission
3	Renal insufficiency	Glomerular filtration rate of 89 or less on the day of hospitalization
4	Obesity	Body mass index greater than/ equal to 25 on the day of hospitalization
5	Smoking	Nicotine consumption at the time of the disease
6	Resternotomie	As part of the initial cardiac surgery procedure
7	Anemia	Hb value less than 14 g/dL in men and less than 12.3 g/dL in women on the day of hospitalization
8	CRP	CRP value greater than 0.5 mg/dL on the day of hospitalization
9	Hypoalbuminemia	Albumin less than 3.5 g/L on the day of hospitalization
10	Immunosuppression	Yes or no at inpatient admission
11	Prophylactic anticoagulation	Prophylactic anticoagulation with heparin or enoxaparin
12	Prophylactic anticoagulation and clopidogrel	Yes or no at inpatient admission
13	Therapeutical anticoagulation	Therapeutical anticoagulation with heparin or enoxaparin at inpatient admission
14	Therapeutical anticoagulation and clopidogrel	Therapeutical anticoagulation with heparin or enoxaparin and clopidogrel at inpatient admission
15	LOS	Length of hospital stay
16	ROI	Recurrence of infection

Abbreviation: CRP, C-reactive protein.

needing reoperation. The LOS longer than the mean of patients in our study taking clopidogrel and therapeutically dosed heparin was also most likely attributable to bleeding complications. In particular, stepwise subtotal resection of the sternum may provoke postoperative bleeding requiring revision, thus increasing the number of surgical procedures until final defect coverage and prolonging the LOS. Prolonged LOS due to renal failure is most likely due to the disease itself. Indeed, multiple studies have shown that the presence of renal insufficiency has no influence on the development of mediastinitis and sternal osteomyelitis.^{11,13} In particular, number of days for hemodialysis and complications due to renal insufficiency, such as electrolyte imbalance or the development of peripheral edema and interstitial pulmonary edema, can significantly prolong the duration of hospitalization.¹⁴ Women make up the majority of the collective in our study with 51%. The composition of our collective is thus different from that in other large studies, in which the proportion of women is significantly underrepresented.^{15,16} Previously, female sex had been described only as an independent risk factor for increased lethality in the setting of cardiac surgery.¹⁶ Our data now show that female sex is also a risk factor for prolonged hospitalization in the setting of treatment for severe sternal osteomyelitis with four or more operations until defect coverage.

However, contrary to what has been demonstrated in several other studies, our data do not show an increased ROI requiring revision after defect coverage in the female sex and thus coincides, for example, with the study results of Spindler et al.¹⁷ We were unable to demonstrate the consid-

eration that lateral traction forces of large mammaries lead to wound healing problems requiring revision.^{18,19}

In our study, obesity and immunosuppressant use played a statistically relevant role in the ROI requiring revision after defect coverage by pectoralis major flap surgery. Just as Kozlow et al²⁰ and Pech et al⁷ demonstrated in their study, we also assume that the increased incidence of ROI after defect coverage can be explained by an increased traction force on the flap plastic due to the massive overweight. Nevertheless, not the obesity but the use of immunosuppressants is the main determinant for ROI in our study. In the group of patients considered for ROI in our collective only six (12.2%) took immunosuppressants: every 6 with chronic obstructive pulmonary disease. Elevated glucocorticoid levels, whether endogenous or exogenous, affect wound healing.¹⁸ Systematic glucocorticoid therapy results in increased granulation tissue formation and decreased wound contraction.²¹ Various animal studies show that wound healing is inhibited by glucocorticoids in a dose-dependent manner, particularly in the perioperative and early phases of wound healing.²² Several clinical studies can also demonstrate this effect,²³ just like our study now.

The final question is whether the described determinants can be addressed before admission to reduce the rate of patients with LOS longer than mean and ROI. From the three determinants female sex, clopidogrel and therapeutic anticoagulation and renal insufficiency, only clopidogrel and therapeutic anticoagulation could actively be changed, depending on the timing of treatment. Only clopidogrel is mentioned in our study as we already change prasugrel and

ticagrelor to clopidogrel before hospital admission. With the changing recommendations in the guidelines in the last years²⁴ in some patients on therapeutic anticoagulation, we ask the cardiologist to stop clopidogrel earlier today. The same comes true for immunosuppressants. These are only 8% of the admitted patients and already today we discuss the necessity of this therapy in each patient.

Overall, with the knowledge of risk factors that prolong LOS longer than mean, it would be additionally desirable to adapt the DRG system in Germany to the multimorbid patients with mediastinitis. However, recent years have shown that the refinancing of critically ill patients with mediastinitis is becoming increasingly difficult and that the DRG system is far from adapting.

Limitation

Although the analysis is based on detailed data regarding patients' characteristics, comorbidities, and treatment, it is a retrospective and monocentric study. The endpoint LOS above mean is very specific for the German DRG system and might not be relevant in other health systems. In addition, the study did not take into account whether the patients were undergoing complex intensive care or were being treated in the normal ward. The risk factor for DWSI reported in the literature is bilateral internal mammaria artery grafts. We did not consider initial surgical techniques which could also have an impact on musculocutaneous flap healing.

In conclusion, our study is the first to examine risk factors and complications that prolong recumbency in the setting of sternal osteomyelitis. These data can be used to further determine the risk of complications preoperatively based on gender, pre-existing conditions, and medication use. They help to explain prolonged and severe courses of disease and can also be used for a differentiated assessment of courses of disease. Nonetheless, this study encourages consideration of the risk factors for prolonged hospitalization in the treatment of sternal osteomyelitis. Addressing risk factors could reduce LOS and lower costs.

Conflict of Interest

None declared.

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