


Associations of Hospital Length of Stay with Surgical Site Infections

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Published online: 5 July 2018
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Abstract

Background Surgical site infections (SSI) are a major cause of morbidity and mortality in surgical patients. Postoperative and total hospital length of stay (LOS) are known to be prolonged by the occurrence of SSI. Preoperative LOS may increase the risk of SSI. This study aims at identifying the associations of pre- and postoperative LOS in hospital and intensive care with the occurrence of SSI.

Methods This observational cohort study includes general, orthopedic trauma and vascular surgery patients at two tertiary referral centers in Switzerland between February 2013 and August 2015. The outcome of interest was the 30-day SSI rate.

Results We included 4596 patients, 234 of whom (5.1%) experienced SSI. Being admitted at least 1 day before surgery compared to same-day surgery was associated with a significant increase in the odds of SSI in univariate analysis (OR 1.65, 95% CI 1.25–2.21, $p < 0.001$). More than 1 day compared to 1 day of preoperative hospital stay did not further increase the odds of SSI (OR 1.08, 95% CI 0.77–1.50, $p = 0.658$). Preoperative admission to an intensive care unit (ICU) increased the odds of SSI as compared to hospital admission outside of an ICU (OR 2.19, 95% CI 0.89–4.59, $p = 0.057$). Adjusting for potential confounders in multivariable analysis weakened the effects of both preoperative admission to hospital (OR 1.38, 95% CI 0.99–1.93, $p = 0.061$) and to the ICU (OR 1.89, 95% CI 0.73–4.24, $p = 0.149$).

Conclusion There was no significant independent association between preoperative length of stay and risk of SSI while SSI and postoperative LOS were significantly associated.

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Introduction

Surgical site infections (SSI) are a common threat to surgical patients [1, 2]. As many as 5% of all patients who undergo surgery will experience SSI in spite of a variety of efforts to prevent them. SSI are associated with increased morbidity and mortality rates [3–5]. Furthermore, they are known to cause prolongation of hospital stays which also impact health care costs [6–8]. The association between SSI and total as well as postoperative hospital stays is well documented by a large body of observational evidence [3–5, 7, 9–14]. Since the common hypothesis is that the infection occurs during surgery at the surgical site, it has been assumed that SSI cause the prolongation of the hospital stay. However, the hospital environment is a known source of bacterial contamination in many settings, and therefore, being discharged earlier after surgical procedures may decrease the risk of SSI.

In terms of preoperative length of stay (LOS), some reports have suggested that this is per se associated with an increased risk of SSI compared to same-day surgery [15–21]. One study showed a striking association between increasing delays of elective coronary artery bypass grafts, colectomies and lung resections on one hand and infectious complications on the other hand [18]. Importantly, there seems to be no study reporting associations between both pre- and postoperative hospital and intensive care unit (ICU) LOS and SSI risk in a population of general, orthopedic trauma and vascular surgical patients.

The aim of this study was to examine the associations between the length of both pre- and postoperative hospital and ICU stays with the occurrence of SSI. This could help determine the need to shorten hospitalization times.

Methods

Setting

This is an observational cohort study. The dataset stems from a multicenter randomized controlled trial (RCT) [22] designed to determine the optimal timing of surgical antimicrobial prophylaxis. Data were therefore collected prospectively between February 2013 and August 2015 at the University Hospital of Basel and the hospital of Aarau, two tertiary referral centers in Switzerland.

Patients

All inpatients aged 18 years or older who underwent general, vascular and orthopedic trauma surgery with surgical antimicrobial prophylaxis (SAP) indicated according to

Center for Disease Control (CDC) standards [2] were eligible. In more detail, procedures analyzed in this study included upper and lower gastrointestinal, hepatobiliary and pancreatic procedures for both malignant and benign diseases; breast resections including oncoplastic procedures and axilla dissections for breast cancer; thyroid and adrenal surgery; bariatric surgery; both open and endoscopic inguinal, femoral, ventral and inner hernia repairs; aortoiliac, carotid, upper and lower extremity arterial and AV access surgery; major amputations; any osteosynthetic procedures of the shoulder, pelvis, upper and lower extremities; shoulder, elbow, hip, knee and ankle joint replacement procedures as well as surgery to remove osteosynthetic materials.

Exclusion criteria were outpatient surgery, contraindication for cefuroxime and/or metronidazole, preexisting antibiotic therapy within 14 days prior to surgery, cognitive impairment, combined operations including other than the above specified surgical departments and emergency procedures with planned incision within 2 h after indicating the procedure. Wound class 4 was also an exclusion criterion; however, because this can at times only be defined intraoperatively, few patients with wound class 4 were still included and—according to intention-to-treat principles—remained in the analysis. Hence, these few patients also remained in the analysis set for this study.

The complete study protocol of the RCT was previously published [23]. The study was approved by the local ethics committees and all patients signed an informed consent.

Justification for pre- and postoperative ICU admissions

Reasons to be admitted to the ICU preoperatively differed between surgical divisions. In orthopedic trauma surgery, the main indication was life-threatening conditions in polytraumatized patients, e.g., thoracic and cranial injuries. In vascular surgery, the main indication for preoperative ICU admissions was the surveillance of patients with either symptomatic aortic aneurysms or complicated aortic dissections between admission and surgery. No general surgical patients were admitted to the ICU preoperatively.

Postoperatively, all vascular surgical patients undergoing arterial procedures are routinely admitted to the ICU. Orthopedic trauma patients were mainly admitted to the ICU postoperatively after being taken for surgery either directly from the emergency room with life-threatening injuries or from a preoperative ICU admission. General surgical patients were mainly admitted to the ICU postoperatively after long procedures associated with hypothermia and prolonged ventilation.

Endpoints

The endpoint of this study was the occurrence of SSI within 30 days after surgery. SSI were defined according to CDC criteria [2]. In-hospital SSI were diagnosed by the surgical team and members of the RCT study team that was responsible for registration of SSI for the purpose of this study. Diagnoses of SSI registered by the investigators could not be overruled by the clinical team. Follow-up after discharge from the hospital was performed by trained members of the RCT study team. Patients were contacted by phone 30 days after surgery. In case of suspected SSI, charts from the outpatient clinics were reviewed and primary care physicians were contacted for additional information. After five unsuccessful attempts to contact patients, they were considered lost to follow-up. All diagnoses of SSI were validated by a board-certified infectious diseases specialist.

Statistical analysis

All analyses were performed using R version 3.4.0 (2017-04-21).

Investigating the association of LOS and ICU stay on the probability of SSI was based on logistic regression models.

We first examined the probability of SSI by preoperative LOS used as a continuous variable alongside a dummy variable indicating any preoperative hospitalization. Next, we compared patients with >1 day to those with 1 day of preoperative hospitalization and in addition compared patients with any preoperative hospitalization to those undergoing same-day surgery.

Preoperative ICU admission was examined as a single binary predictor in case there was preoperative hospitalization.

Graphical descriptions of the probability of SSI by preoperative LOS were produced using two different methods. First, the probability of SSI was calculated for each day of preoperative hospitalization, except the longest hospitalization times were combined to allow a minimum of 50 patients per group. Second, preoperative LOS was categorized to groups as suggested by Vogel et al. [18] (0, 1, 2–5, 6–10 and 11–16 days).

Following the first steps, we added pre-defined potential confounders to the analysis model. All the confounders were included in the model alongside their interactions with both preoperative LOS and preoperative ICU admission. Interaction terms were removed from the model if they failed to improve model fit measured as a reduction in Akaike's information criterion (AIC) of $\Delta \geq 2$.

In the final model, we added postoperative LOS and ICU admission to both the models with and without the remaining potential confounders.

Results are reported as odds ratios (OR) and 95% confidence intervals (CI). For continuous variables, these refer to a per unit increase. For categorical variables, they refer to the comparison with a reference level, generally the most frequent category of the variable.

In this analysis, ASA classification and wound class were taken as continuous variables. Also, age was centered on its mean and LOS was centered on the relevant median.

Results

In total, 5175 patients were analyzed in the RCT on the timing of surgical antimicrobial prophylaxis. All patients were followed up in hospital, but 579 were lost to follow-up before day 30. Therefore, 4596 patients were analyzed. Baseline characteristics are presented in Table 1. A total of 234 patients (5.1%) experienced SSI. In total, 1895 patients (41.2%) underwent same-day surgery, while 2701 (58.8%) were admitted to the hospital one or several days before surgery. Out of 4596 patients, 58 patients (1.3%) were admitted to the ICU preoperatively and 729 patients (15.9%) were admitted to the ICU postoperatively.

Table 2 shows several logistic regression models examining total and preoperative LOS and ICU stays as predictors for SSI. In the simplest model including only preoperative admission, a 65% increase in the odds of SSI compared to same-day surgery (OR 1.65, 95% CI 1.25–2.21, $p < 0.001$) was found. In contrast, being admitted more than 1 day compared to 1 day preoperatively did not result in a significant increase in the odds of SSI (OR 1.08, 95% CI 0.77–1.50, $p = 0.658$). This is also explained by the graphical depiction in Fig. 1. It shows that while the probability of experiencing SSI increases from 0 to 2 preoperative days, this trend becomes less clear with longer LOS. Similarly, considering preoperative LOS in categories, the probability of SSI does not increase beyond a preoperative stay of 1 day. In those patients admitted to hospital preoperatively, being in the ICU preoperatively further increased the odds of SSI although this was not statistically significant (OR 2.19, 95% CI 0.89–4.59, $p = 0.057$).

A multiple logistic regression model was fit with the predictors from the previous models and pre-specified potential confounders and effect modifiers. All interactions were removed from the model because almost all of them reduced, while none substantially improved the model fit. The results of the model are presented in Fig. 2. Both preoperative admission and preoperative ICU admission remained associated with increased odds of SSI; however,

Table 1 Patient characteristics, stratified by outcome

	No SSI ^a	SSI ^a	<i>p</i>
<i>n</i>	4362	234	
Male sex <i>n</i> (%)	2340 (53.6)	147 (62.4)	0.007
Age—years (mean (SD ^b))	57.0 (18.6)	62.7 (15.7)	<0.001
LOS ^c (d) (median [IQR ^d])	5.00 [3.00, 9.00]	13.00 [7.00, 24.75]	<0.001
Preoperative (median [IQR])	1.00 [0.00, 1.00]	1.00 [0.00, 1.00]	0.001
Postoperative (median [IQR])	4.00 [2.00, 7.00]	11.00 [5.00, 23.00]	<0.001
Pre-op ICU ^e LOS (d) (median [IQR])	1.00 [1.00, 2.00]	2.00 [1.00, 4.50]	0.177
Post-op ICU LOS (d) (median [IQR])	1.00 [1.00, 1.00]	1.00 [1.00, 7.00]	<0.001
Preoperative LOS, categorical			0.014
0 days	1824 (41.8)	71 (30.3)	
1 day	1724 (39.5)	108 (46.2)	
2–5 days	571 (13.1)	40 (17.1)	
6–10 days	179 (4.1)	11 (4.7)	
11–16 days	64 (1.4)	4 (1.7)	
ASA ^f class			<0.001
1	802 (18.4)	16 (6.8)	
2	2345 (53.8)	90 (38.5)	
3	1169 (26.8)	122 (52.1)	
4	44 (1.0)	6 (2.6)	
Wound class			<0.001
I	3437 (79.0)	139 (59.4)	
II	677 (15.6)	63 (26.9)	
III	191 (4.4)	24 (10.3)	
IV	48 (1.1)	8 (3.4)	
Surgical department			<0.001
General	2117 (48.5)	155 (66.2)	
Trauma	1693 (38.8)	39 (16.7)	
Vascular	552 (12.7)	40 (17.1)	
Diabetes <i>n</i> (%)	402 (9.2)	35 (15.0)	0.005
BMI ^g (kg/m ²) (mean(SD))	27.1 (6.4)	28.2 (7.2)	0.007
Urgent procedure (<i>n</i> (%))	819 (18.7)	32 (13.7)	0.063
Duration of surgery (median [IQR])	1.47 [0.98, 2.23]	2.60 [1.58, 3.91]	<0.001
Steroid treatment	100 (203)	7 (3.0)	0.641
Urgent hospitalization	1715 (39.3)	63 (26.9)	<0.001

Comparison of continuous variables is by *t* test or Wilcoxon's rank-sum test if strongly skewed; Categorical variables are compared by Chi-square test or Fisher's exact test as appropriate

^aSSI surgical site infection

^bSD standard deviation

^cLOS length of stay

^dIQR interquartile range

^eICU intensive care unit

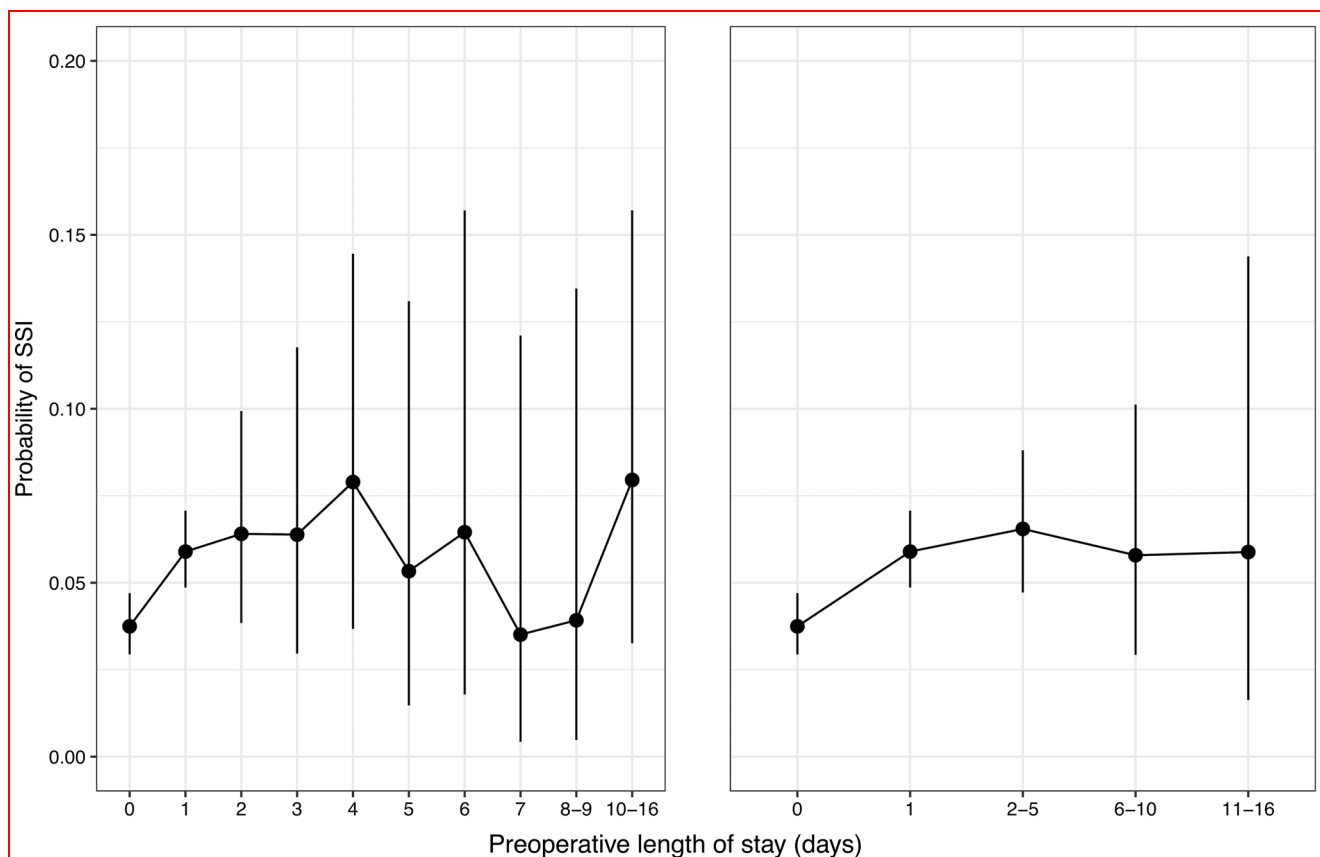
^fASA American Society of Anesthesiologists

^gBMI body mass index

this was now less pronounced and, in terms of preoperative admission, no longer significant (OR 1.38, 95% CI 0.99–1.93, *p* = 0.061 and OR 1.89, 95% CI 0.73–4.24, *p* = 0.149, respectively).

Table 2 Logistic regression models exploring preoperative LOS and ICU stay as predictors of SSI

Model	OR ^a [95% CI ^b]	<i>p</i>	AIC ^c
Total LOS ^d	1.12 [1.11, 1.14]	<0.001	1610.13
Preoperative admission yes versus no	1.65 [1.25, 2.21]	<0.001	1840.92
Preoperative LOS			1842.73
Any versus none	1.67 [1.25, 2.25]	<0.001	
>1 versus 1	1.08 [0.77, 1.50]	0.658	
Preoperative admission & preoperative ICU ^e stay			1839.91
Preoperative admission	1.61 [1.21, 2.16]	0.001	
Preoperative ICU stay	2.19 [0.89, 4.59]	0.057	

^aOR odds ratio^bCI confidence interval^cAIC Akaike information criterion^dLOS length of stay^eICU intensive care unit**Fig. 1** Probability of SSI depending on preoperative LOS. SSI surgical site infection, LOS length of stay. Left: Probability of SSI for each day of preoperative hospitalization, except the longest

hospitalization times were combined to allow a minimum of 50 patients per group. Right: Probability of SSI depending on preoperative LOS—categorized as suggested by Vogel et al

Adding postoperative LOS and postoperative ICU admissions to the previous models changed the effects of the preoperative predictors significantly (Table 3). In the

model containing only the admission variables, the previously strong effects of the preoperative predictors were virtually lost, while the postoperative LOS (OR 1.14, 95%

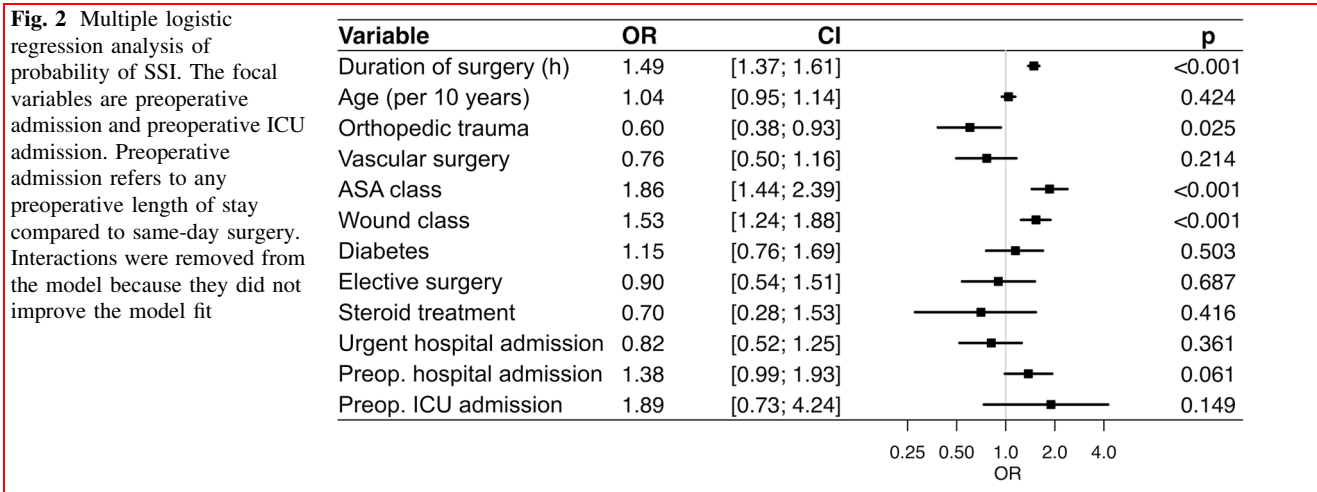


Table 3 Logistic regression models including pre- and postoperative variables

Variable	OR ^a [95% CI ^b]	p	AIC ^c
Logistic regression model including pre- and postoperative variables of interest			1569.76
Preoperative admission	0.93 [0.68, 1.28]	0.650	
Preoperative ICU ^d stay	1.39 [0.52, 3.20]	0.477	
Postoperative LOS ^e	1.14 [1.12, 1.15]	<0.001	
Postoperative ICU stay	1.60 [1.15, 2.21]	0.005	
Multiple logistic regression model including confounders			1504.64
Preoperative admission	1.12 [0.79, 1.58]	0.529	
Preoperative ICU stay	1.61 [0.58, 3.87]	0.323	
Postoperative LOS	1.12 [1.10, 1.14]	<0.001	
Postoperative ICU stay	0.86 [0.58, 1.26]	0.434	
Duration of surgery (h)	1.20 [1.09, 1.32]	<0.001	
Age (per 10 years)	0.96 [0.87, 1.06]	0.385	
Orthopedic trauma department	0.48 [0.30, 0.75]	0.002	
Vascular surgery department	0.90 [0.57, 1.41]	0.654	
ASA class	1.53 [1.17, 1.99]	0.002	
Wound class	1.30 [1.04, 1.62]	0.019	
Diabetes	1.08 [0.70, 1.62]	0.734	
Elective surgery	0.84 [0.49, 1.43]	0.517	
Steroid treatment	0.63 [0.23, 1.48]	0.325	
Urgent hospital admission	0.70 [0.44, 1.09]	0.125	

^aOR odds ratio

^bCI confidence interval

^cAIC Akaike information criterion

^dICU intensive care unit

^eLOS length of stay

CI 1.12–1.15, $p < 0.001$) and ICU admissions (OR 1.60, 95% CI 1.15–2.21, $p = 0.005$) were now strongly and significantly associated with the odds of SSI. In the multiple logistic regression model including the pre- and postoperative variables and potential confounders, the

association between postoperative LOS and the odds of SSI remained virtually unchanged (OR 1.12, 95% CI 1.10–1.14, $p < 0.001$), while postoperative ICU admission lost its association with the odds of SSI (OR 0.86, 95% CI 0.58–1.26, $p = 0.434$).

Last, a linear regression model showed that preoperative hospitalization was associated with a 1.76-fold increase in the postoperative LOS (95% CI 1.69–1.86, $p < 0.001$).

Discussion

To our knowledge, this is the first study that reports the associations of both pre- and postoperative LOS and ICU admissions with SSI in a population of general, orthopedic trauma and vascular surgery. We report three main findings.

First, we found that throughout a number of simple logistic regression models, when tested both alone and together with preoperative ICU admission, preoperative hospital admission compared to same-day surgery was significantly associated with increased odds of experiencing SSI which seem to be further increased with preoperative ICU admissions. The latter association between preoperative ICU admissions and SSI risk was not statistically significant due to a very wide 95% confidence interval. This is most likely because of the low number of patients who were admitted to the ICU preoperatively (1.2% of all patients and 2.1% of those patients who were admitted to hospital preoperatively). Therefore, it is likely that with a higher percentage of patients admitted to the ICU preoperatively, this association would become statistically significant. This assumption is backed by the existing literature where in hospitalized patients, ICU admission, ICU stay in days and mechanical ventilation were all identified as independent risk factors for health care-associated infections [24].

The above-mentioned associations between preoperative hospital admission and SSI did not remain significant when adding known or potential confounders in more complex models. This highlights the importance of considering strong SSI risk factors, such as duration of surgery and ASA class, in multivariable analyses in this field. These findings partially contradict the existing literature reporting that preoperative inpatient stay is clearly associated with increased odds of experiencing SSI [15–21]. In the study reported by Vogel et al. [18] that was performed in the USA, patients who were admitted before surgery had specific reasons to be, and factors associated with delayed surgery after hospital admission included age >80 years, congestive heart failure, chronic pulmonary disease and renal failure. In contrast, early admission is still a common practice in Switzerland and accepted by both patients and health care providers, even in the absence of specific reasons, and hence, there was a much higher percentage of patients being admitted one or several days prior to surgery in the present study. This could explain why in the present

study preoperative hospitalization was less strongly associated with increased odds of SSI.

Second, the length of preoperative stay was not significantly associated with the probability of SSI. This was true when considering preoperative LOS as a continuous variable, but also when using the same categories as Vogel et al. did. This finding is again in contradiction to the existing literature stating that increasing preoperative LOS is associated with increasing odds of SSI. Vogel et al. showed that SSI rates after coronary artery bypass grafting (CABG) and colon resections significantly increased with preoperative LOS [18]. One possible explanation for this difference is the selection of differing surgical subspecialties in this analysis and the one mentioned above. While the present analysis includes general, orthopedic trauma and vascular surgery patients, Vogel et al. included CABG procedures as well as colon and lung resections. Furthermore, it could be argued that the hospital environment in our study poses a lesser risk to the patient compared to that of the USA due to the near-absence of multiresistant bacteria in our setting. In this study, only eight multi-drug-resistant pathogens were found out of a total of 128 isolated pathogens (6.3%) as reported in the publication of the underlying RCT [22], while in an earlier analysis from one of the two study centers, there was not a single case of SSI caused by multi-drug-resistant pathogens [25]. Meanwhile, in the USA, as many as 17% of severe SSI have been reported to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA) alone [26]. Therefore, it may be less likely in our setting for patients being admitted preoperatively to get in contact with multi-drug-resistant bacteria and to not receive the appropriate surgical antimicrobial prophylaxis needed to cover them. Last, due to the lower numbers of patients with more than 2 days of preoperative hospitalization, the estimation of SSI rates for those patients becomes less reliable as can be seen from the wide confidence intervals.

Third, when specifically adding postoperative LOS and ICU admissions to the various models, the associations between preoperative LOS and ICU admission with SSI were weakened, and in the multivariate model, postoperative LOS was the only factor that remained significantly associated with SSI. This association is well known. We had no possibility to include the exact dates of diagnosis of infection and admissions to the ICU in our analyses and, therefore, we cannot further explore the causal relationships of these associations. However, the common interpretation is that the occurrence of SSI increases hospital and ICU LOS. Therefore, adding both a potential predictor (preoperative admission) and a potential outcome (postoperative LOS and ICU admission) to a model may subject it to misinterpretation. This is also supported by the results of our simple linear regression model showing that

preoperative hospitalization had a strong multiplicative effect on the postoperative LOS and hence that preoperative admission and postoperative LOS are highly associated with each other.

The results of this study are highly relevant. While preoperative hospitalization is a common practice in many countries, same-day surgery represents a current economic trend worldwide that may have an impact on patient satisfaction and quality of life. Although our data suggest that preoperative inpatient stay is associated with increased odds of SSI, this seems confounded by multiple factors, questioning its relevance and causative direction.

This study has multiple strengths. First, all variables were collected in a strictly prospective manner within a RCT with stringent quality control [22]. The highly significant associations of known risk factors and odds of SSI in the multiple logistic regression models highlight the validity of our data. Second, this study includes the full set of patients who were randomized in the underlying RCT and for whom outcomes were known, reducing potential selection bias. Third, the large sample size allowed the present analysis to be performed with high power. Fourth, the inclusion of patients from a wide variety of surgical specialties increases the generalizability of our findings.

We acknowledge, however, the presence of several limitations to this study. First, this study was exposed to all inherent bias of an observational design. Second, due to the design of the underlying RCT, this study includes only patients who received surgical antimicrobial prophylaxis before surgery. It cannot be ruled out that this alters the effect of LOS and ICU admissions on the occurrence of SSI compared to patients who do not receive surgical antimicrobial prophylaxis. On the other hand, both patients undergoing such procedures and those procedures per se are usually neither prone to high rates of nosocomial infections nor inpatient or ICU stays, and therefore, this limitation may not be of great importance.

In conclusion, the present results confirm the known association between SSI and postoperative LOS, while preoperative hospitalization was not independently associated with the odds of SSI.

Acknowledgements This work was financially supported by the Swiss National Foundation, the “Kantonsspital Aarau”, the “Gottfried und Julia Bangerter-Rhyner-Stiftung”, the University of Basel, the “Freiwillige Akademische Gesellschaft Basel”, and the “Nora van Meeuwen-Haefliger-Stiftung”.

Compliance with ethical standards

Conflict of interest None of the authors has any potential or real conflicts of interest to report.

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