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ORIGINAL ARTICLE

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Adding vancomycin to perioperative prophylaxis decreases deep sternal wound infections in high-risk cardiac surgery patients

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Abstract

OBJECTIVES: Perioperative prophylaxis with cephalosporins reduces sternal wound infections (SWIs) after cardiac surgery. However, more than 50% of coagulase-negative staphylococci, an important pathogen, are cephalosporin resistant. The aim of this study was to determine the impact of adjunctive vancomycin on SWIs in high-risk patients.

METHODS: We conducted a pre- and postintervention study in an academic hospital. Preintervention (2010–2011), all patients received prophylaxis with 1.5 g of cefuroxime for 48 h. During the intervention period (2012–2013), high-risk patients additionally received 1 g of vancomycin. High-risk status was defined as body mass index $\leq$18 or $\geq$30 kg/m^2, reoperation, renal failure, diabetes mellitus, chronic obstructive pulmonary disease or immunosuppressive medication. Time series analysis was performed to study SWI trends and logistic regression to determine the effect of adding vancomycin adjusting for high-risk status.

RESULTS: A total of 3902 consecutive patients (n = 1915 preintervention and n = 1987 postintervention) were included, of which 1493 (38%) patients were high-risk patients. In the high-risk group, 61 of 711 (8.6%) patients had SWI before and 30 of 782 (3.8%) patients after the intervention. Focusing on deep SWI (DSWI), 33 of 711 (4.6%) patients had DSWI before and 13 of 782 (1.7%) patients afterwards; the absolute risk difference of 2.9% yielded a number-needed-to-treat of 34 to prevent 1 DSWI. Corrected for high-risk status, adding vancomycin significantly reduced the overall SWI rate (odds ratio 0.42, 95% confidence interval 0.26–0.67; P < 0.001) and the subset of DSWI (odds ratio 0.30, 95% confidence interval 0.14–0.62; P = 0.001). The rate of SWI in low-risk patients remained unchanged.

CONCLUSIONS: Adding vancomycin to standard antibiotic prophylaxis in high-risk patients significantly reduced DSWI after cardiac surgery.

Keywords: Cardiac surgery • Surgical site infection • Sternal wound infection • Antibiotic prophylaxis • Vancomycin

INTRODUCTION

A recently published landmark study determined the preventable proportion of the most common health care-associated infections and found surgical site infections to be preventable with evidence-based measures in more than 50% of cases [1]. Perioperative antimicrobial prophylaxis (PAP) is considered a key element among these preventive measures [2, 3], and the impact on surgical site infections is well documented for cardiac surgery [4]. First- or second-generation cephalosporins are the mainstay of PAP in this setting [5]. However, sternal wound infections (SWIs) after cardiac surgery are frequently caused by coagulase-negative staphylococci (CoNS), which, like methicillin-resistant *Staphylococcus aureus* (MRSA), are often resistant to standard antimicrobials used for prophylaxis. In our hospital, e.g. approximately 60% of CoNS isolates are beta-lactam resistant. Therefore, a number of trials have addressed the question whether 'switching' to non-cephalosporin compounds may provide additional risk reduction. In a recent meta-analysis, glycopeptides such as vancomycin were not found to be superior to cephalosporins, except for reducing infections due to MRSA or other methicillin-resistant staphylococci [6], thus reinforcing the conclusions of earlier systematic reviews [7, 8]. Another approach, 'combining' antibiotic prophylaxis (i.e. adding coverage for methicillin-resistant staphylococci to standard antibiotics) has been scrutinized in a handful of studies outside of cardiac surgery [9–11]. In cardiac surgery patients, Walsh *et al.* [12] targeted patients identified as MRSA carriers by adding vancomycin to their cefazolin prophylaxis and—along with other interventions such as intranasal mupirocin—documented a decrease in infections. Consequently, recent guidelines discourage routine

vancomycin prophylaxis but recommend that adjunctive vancomycin be considered in MRSA-colonized patients [5].

SWIs, albeit relatively rare events, remain a substantial cause for morbidity and mortality after cardiac surgery. They are costly for the health care system due to revision surgeries, antibiotic medication and prolonged hospitalization [13]. Certain factors confer an increased SWI risk, such as chronic obstructive pulmonary disease, diabetes mellitus and other procedure-related characteristics [14, 15]. Patients with these comorbid burden are likely to benefit most from optimized PAP.

The aim of this study was to determine the effect of adding vancomycin to standard cephalosporin PAP in a subset of high-risk patients undergoing cardiac surgery.

MATERIALS AND METHODS

Study design and patient population

This was a non-controlled pre- and postintervention study, which corresponds to an A1 level quality in study design [16]. We included consecutive adult patients who underwent cardiac surgery with midline sternotomy and cardiopulmonary bypass between 1 January 2010 and 31 December 2013 at our tertiary care centre hospital. In our area, the MRSA rate out of all clinical *Staphylococcus aureus* isolates was <5%. Exclusion criteria were age <18 years and allergy to the standard antibiotic cefuroxime. Eligible patients had to be identified by the Swiss Nosocomial Infection Surveillance Network (www.swissnoso.ch), which included all types of coronary artery bypass grafts, valve procedures and other cardiac surgeries with the exception of heart transplantations.

Routine perioperative management

For PAP in our institution, a 1.5-g dose of cefuroxime is applied intravenously within 60 min before surgical incision and continued 3 times daily for 48 h postoperatively. The operative site is first disinfected with an alcoholic povidone–iodine solution (Betaseptic®; Mundipharma Medical Company, Hamilton, Bermuda) and then covered with an iodine adhesive plastic sheet (Ioban®; 3M, Brookings, SD, USA) before skin incision and median sternotomy. Water-soluble bone haemostasis wax (Ostene®; Ceremed Inc, Los Angeles, CA, USA) is used for sternal haemostasis exclusively in cases of profuse bleeding. In most patients undergoing coronary artery bypass grafting, the internal thoracic artery is harvested as skeletonized graft. At the end of the procedure, chest tubes are placed in the mediastinum and the pericardial cavity. Sternal closure is performed with stainless steel wires, and the subcutaneous tissue and skin are closed using a running absorbable suture. Surgical gloves are changed immediately following sternotomy (by the lead surgeon) and before sternal closure (by the entire surgical team). Chest tubes are removed on postoperative day 1 or 2 depending on the amount of intraoperative blood loss.

Intervention

A 24-month preintervention period (1 January 2010–31 December 2011) was followed by the 24-month intervention period (1 January 2012–31 December 2013). The intervention consisted of adding vancomycin to routine cefuroxime prophylaxis in patients identified as high-risk patients (for definition, see section below 'Definitions'). Vancomycin was administered as a single 1-g intravenous dose, approximately 60 min before surgical incision. This decision to add vancomycin or not was based on preoperative evaluation by the clinical team meeting (cardiac surgeon, cardiologist and anaesthesiologist) in charge of perioperative patient management.

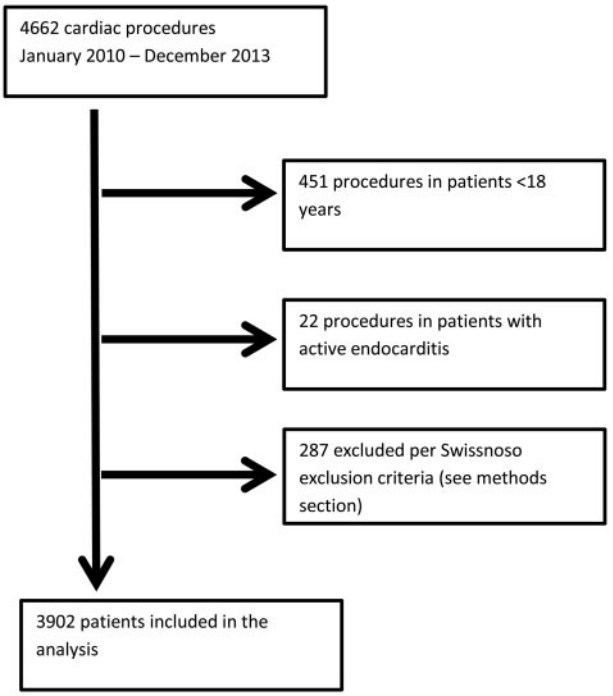

Figure 1: Flowchart.

Data collection

A data management team entered the perioperative data into an institutional registry and continuously checked for plausibility and correctness using a routine protocol. All records were matched with the hospital reimbursement system (SAP®; SAP SE, Walldorf, Germany) and operation planning system to ensure inclusion of all patients undergoing cardiac surgery in our institution. Data on preoperative risk factors, intraoperative details, postoperative complications and follow-up were extracted from this database for the analyses.

Information on PAP and infectious outcomes were taken from the infection prevention program's surveillance system. This surgical site infection (SSI) surveillance is performed within the framework of Swissnoso, the Swiss Nosocomial Infection Surveillance Network (www.swissnoso.ch), which follows the Centers for Disease Control and Prevention and National Healthcare Safety Network (NHSN) definitions (http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf). The surveillance team acquired the data from medical records, which served for ascertaining SSIs during the original admission. For the purpose of determining post-discharge SSIs, all patients were interviewed by telephone at 30 days and 12 months following the index cardiac surgery using a standardized questionnaire. All SSIs were validated by an infectious disease physician from our institution. This surveillance is subject to regular auditing by Swissnoso.

Table 1: Characteristics of cardiac surgery patients, stratified by risk category

	Low-risk patients ($n = 2409$)	High-risk patients		P-value[a]
		Before ($n = 711$)	After ($n = 782$)	
Age (years), mean ± SD	66.2 ± 11.8	64.5 ± 11.9	64.4 ± 11.6	0.88
Female, *n* (%)	630 (26)	202 (28)	223 (29)	0.96
Dyslipidaemia, *n* (%)	1558 (65)	519 (73)	558 (71)	0.45
BMI, mean ± SD	25.3 ± 2.7	30.3 ± 5.7	30.6 ± 5.2	0.18
Extracardiac arteriopathy, *n* (%)	434 (18)	204 (29)	208 (27)	0.37
Hypertension, *n* (%)	1644 (68)	567 (80)	630 (81)	0.73
Smoking, *n* (%)	1318 (55)	443 (62)	488 (62)	0.99
CCS class, *n* (%)				0.03
1	1387 (59)	367 (53)	460 (59)	
2	478 (20)	147 (21)	149 (19)	
3	289 (12)	129 (18)	105 (14)	
4	211 (9)	55 (8)	62 (8)	
NYHA class, *n* (%)				0.47
1	1038 (43)	238 (34)	244 (31)	
2	761 (32)	221 (32)	267 (34)	
3	470 (20)	198 (28)	211 (27)	
4	118 (5)	45 (6)	59 (8)	
Sinus rhythm, *n* (%)	2078 (86)	602 (85)	650 (83)	0.42
Logistic EuroSCORE, mean (range)	5.3 (0.7–39.4)	6.6 (0.9–48.7)	6.2 (0.8–51.5)	0.22
Last preoperative creatinine, mean (range)	81 (48–137)	91 (37–220)	89 (42–186)	0.95
High risk: BMI, *n* (%)	0 (0)	466 (66)	529 (68)	0.39
High risk: IDDM, *n* (%)	0 (0)	131 (18)	167 (21)	0.16
High risk: renal impairment, *n* (%)	0 (0)	31 (4)	19 (2)	0.04
High risk: immune suppression, *n* (%)	0 (0)	32 (5)	42 (5)	0.44
High risk: previous cardiac surgery, *n* (%)	0 (0)	134 (19)	146 (19)	0.93
High risk: COPD, *n* (%)	0 (0)	48 (7)	45 (6)	0.43

BMI: body mass index; CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; IDDM: insulin-dependent diabetes mellitus; NYHA: New York Heart Association.

[a]*P*-values relate to the high-risk patients only. For non-normally distributed variables, instead of the algebraic mean and the standard deviation, geometric means with reference ranges are shown. The *P*-values relate to the *t*-tests, the Kruskal–Wallis test or the χ^2 test, according to the type of data.

Definitions

The primary end-point was deep SWI (DSWI), as defined by Swissnoso (http://www.swissnoso.ch/wp-content/uploads/2009/05/14.10.2015_2_D-13–10-2015_D_Teilnehmerhandbuch_VERSION-UPDATE_OKTOBER_2015.pdf). Briefly, a DSWI had to occur within 1 year of cardiac surgery and fulfil ≥1 of the following 3 criteria: (i) purulent discharge from a deep incision; (ii) dehiscence of the incision or reopening of the incision, accompanied by temperature >38°C or by local pain/tenderness to palpation and (iii) abscess or deep infection as evidenced by means of revision surgery, pathology or radiology. Secondary end-points were SWI overall, length of hospital stay and in-hospital mortality.

In our population, high-risk patients were defined as those meeting one or more of the following criteria: body mass index ≤18 or ≥30 /kg/m^2, cardiothoracic reoperation, renal failure (eGFR <15 ml/min or haemodialysis dependent), insulin-dependent diabetes mellitus, chronic obstructive pulmonary disease GOLD III/IV or administration of immunosuppressive medication.

Statistical analysis

First, we investigated general trends in the quarterly infection rates (SWI and DSWI) by regressing the time interval on the observed infection rates in low-risk patients. Results were controlled for significant serial correlation using the Durbin–Watson method. Then, separate linear regression analyses were performed for the preintervention and the intervention period and compared with each other. We also included an interaction term for time and study period (displayed in Fig. 2). A logistic regression analysis was performed to quantify the overall effect of vancomycin on the risk of DSWI, adjusted for high-risk status.

We opted to analyse the data as 'intention to prophylax' rather than 'as prophylaxed'; however, we ran an analysis of 'as prophylaxed' for sensitivity purposes. Furthermore, we compared the baseline characteristics between high-risk patients who received versus patients who did not receive vancomycin. Logistic regression models were used to evaluate the association of each risk factor with SWI and DSWI and to determine the impact of the intervention on mortality. Negative binomial regression models with robust standard errors were used to investigate the association of vancomycin administration and the length of hospital stay, adjusted for high-risk status.

Data are displayed as means ± standard deviation, geometric means with reference ranges and numbers with percentages, as appropriate. The corresponding *P*-values have been calculated using the *t*-tests, the Kruskal–Wallis test and the χ^2 test, as appropriate. All *P*-values and confidence intervals (CIs) are 2-sided, with CI covering 95% of the data. We used the statistical package Stata 12 (STATA Corp., College Station, TX, USA) for all analyses.

Ethical approval

Approval for this study was obtained from the responsible ethical committee (Cantonal Ethics Committee, Canton of Bern, Switzerland).

Table 2: Operative data of cardiac surgery patients

	Low-risk patients ($n = 2409$)	High-risk patients		P-value[a]
		Before ($n = 711$)	After ($n = 782$)	
Vancomycin, *n* (%)	91 (4)	0 (0)	639 (82)	0.00
Procedure groups, *n* (%)				0.24
CAB alone	925 (38)	281 (40)	287 (37)	
CAB and valve	314 (13)	122 (17)	114 (15)	
CAB and valve and other	122 (5)	30 (4)	50 (6)	
CAB and other	101 (4)	34 (5)	37 (5)	
Valve alone	471 (20)	116 (16)	137 (18)	
Valve and other	349 (14)	76 (11)	103 (13)	
Other	127 (5)	52 (7)	54 (7)	
Perfusion time (min), mean ± SD	93 ± 43	95 ± 46	109 ± 55	0.00
Duration of operation (min), mean ± SD	213 ± 64	231 ± 74	239 ± 78	0.04
Urgency, *n* (%)				0.37
Emergency	266 (11)	60 (8)	60 (8)	
Urgent	288 (12)	90 (13)	83 (11)	
Elective	1855 (77)	561 (79)	639 (82)	
Procedure on the thoracic aorta, *n* (%)	432 (18)	104 (15)	135 (17)	0.17
Aortic valve, *n* (%)	966 (40)	274 (39)	327 (42)	0.20
Mitral valve, *n* (%)	339 (14)	77 (11)	88 (11)	0.80
Tricuspid valve, *n* (%)	73 (3)	21 (3)	30 (4)	0.35
Pulmonary valve, *n* (%)	2 (0)	8 (1)	8 (1)	0.85

CAB: coronary artery bypass.
[a]*P*-values relate to the high-risk patients only. For non-normally distributed variables, instead of the algebraic mean and the standard deviation, geometric means with reference ranges are shown. The *P*-values relate to the *t*-tests, the Kruskal–Wallis test or the χ^2 test, according to the type of data.

Table 3: Outcome data of cardiac surgery patients

	Low-risk patients ($n = 2409$)	High-risk patients		P-value[a]
		Before ($n = 711$)	After ($n = 782$)	
Deep sternal wound infection, *n* (%)	30 (1)	33 (5)	13 (2)	0.00
Sternal wound infection, *n* (%)	82 (3)	61 (9)	30 (4)	0.00
Perioperative MI, *n* (%)	66 (3)	17 (2)	28 (4)	0.18
Peak CKMB postoperatively, mean (range)	21 (4–108)	20 (4–108)	23 (4–142)	0.02
Peak TnT postoperatively, mean (range)	0.5 (0.1–3.4)	0.5 (0.1–3.1)	0.6 (0.1–4.2)	0.00
Renal, *n* (%)				0.13
Without dialysis	39 (2)	28 (4)	18 (2)	
New postoperative dialysis	23 (1)	14 (2)	21 (3)	
Peak creatinine postoperatively, mean (range)	90 (45–181)	109 (38–312)	104 (42–260)	0.30
ICU stay (days), mean (range)	1.2 (0.4–3.5)	1.4 (0.3–6.1)	1.4 (0.4–5.0)	0.70
IMC stay (days), mean (range)	1.6 (0.5–5.9)	1.9 (0.4–8.8)	1.8 (0.4–7.8)	0.27
Duration of hospitalization, mean (range)	8.9 (3.5–22.6)	10.3 (3.0–35.5)	10.1 (3.2–31.8)	0.94
Death, *n* (%)	47 (2)	21 (3)	20 (3)	0.64

CKMB: creatine kinase, MB subunit; ICU: intensive care unit; IMC: intermediate care; MI: myocardial infarction; TnT: Troponin T.
[a]*P*-values relate to the high-risk patients only. For non-normally distributed variables, instead of the algebraic mean and the standard deviation, geometric means with reference ranges are shown. The *P*-values relate to the *t*-tests, the Kruskal–Wallis test or the χ^2 test, according to the type of data.

RESULTS

A total of 4462 patients underwent cardiac surgery during the study period, 3902 of which were included in this study. Figure 1 depicts the flowchart with the details of patient inclusion. There were 1915 patients included in the preintervention period and 1987 in the postintervention period. Among these 3902 patients, 1493 (38%) patients were considered high-risk patients. Table 1 presents patient characteristics and risk factors for infection. There were no significant differences in the types of surgical procedures performed in high-risk versus low-risk patients (Table 2).

The overall SWI rate displayed a significant downwards trend across the entire patient cohort, with a quarterly decrease by -0.24% points (95% CI -0.37% to -0.11%, $P = 0.001$). Similarly, the DSWI rate dropped by -0.09% per quarter over the study period (CI -0.17% to -0.01%, $P = 0.03$). However, the preintervention period exhibited a minimal and non-significant rate change, both

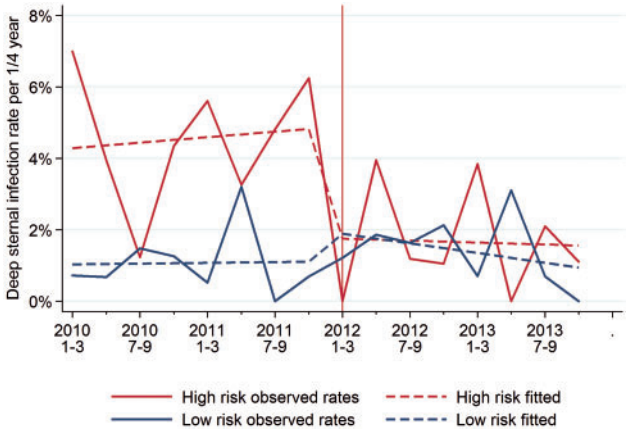

Figure 2: Deep sternal wound infection rates before and after the intervention. Rates are depicted for quarters (i.e. the first quarter of 2010 is represented as '1–3'). Observed rates represent crude data, and fitted curves are adjusted for time trends.

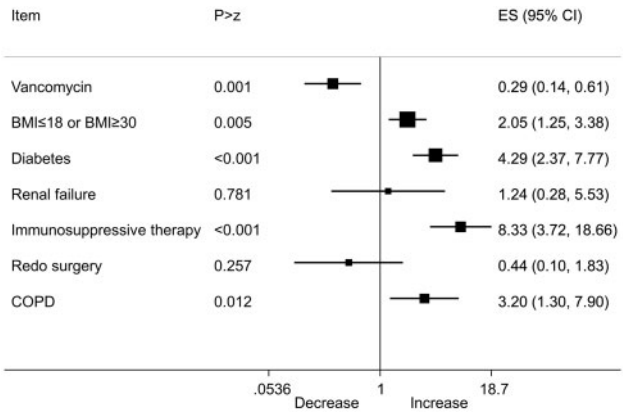

Figure 3: Association of risk factors with deep sternal wound infection, adjusted for vancomycin administration. ES: effect size.

for SWI overall (-0.22%, 95% CI -0.70 to 0.26; $P = 0.3$) and for DSWI (+0.01, 95% CI -0.27 to 0.29; $P = 0.9$); importantly, no changes were seen during the postintervention period, neither for SWI overall (-0.01%, 95% CI -0.35 to 0.33; $P = 0.9$) nor for DSWI (-0.10%, 95% CI -0.38 to 0.19; $P = 0.4$). These data reflect the instantaneous impact of the intervention. Restricting the analysis to low-risk patients, there was no significant decrease neither for SWI overall (-0.08%, 95% CI -0.29 to 0.13; $P = 0.4$) nor for the subset of DSWI (+0.02%, 95% CI -0.10 to 0.13; $P = 0.7$). In the group of high-risk patients, however, a significant decrease in both SWI overall (-0.49%, 95% CI -0.79 to -0.18; $P = 0.004$) and DSWI (-0.27, 95% CI -0.48 to -0.05; $P = 0.02$) was noted. Using shorter time intervals than quarters produced similar results (data not shown).

Overall, there were 91 SWIs in the high-risk group. Sixty-one (8.6%) SWIs were detected in 711 patients before and 30 (3.8%) SWIs in 782 patients during the intervention period, resulting in an odds ratio (OR) of 0.43 (95% CI 0.27–0.67, $P < 0.001$). Taking the entire study cohort and adjusting for high-risk status, the OR of adjunctive vancomycin prophylaxis with overall SWI rate was 0.42 (95% CI 0.26–0.67, $P < 0.001$).

Focusing on the DSWI subset among high-risk patients, we found 33 of 711 (4.6%) DSWI before and 13 of 782 (1.7%) DSWI during the intervention (Table 3), providing an OR of 0.35 (95% CI 0.18–0.67, $P = 0.001$). The absolute risk difference of 2.9% yielded a number-needed-to-treat of 34 (95% CI 21–84) to prevent 1 DSWI. Corrected for high-risk status, the intervention significantly reduced the rate of DSWI (OR 0.30, 95% CI 0.14–0.62; $P = 0.001$). Of note, the proportion of CoNS was 50% (19 of 38) before and higher, 87.5% (7 of 8), after the intervention. All except one of these isolates (which occurred pre-intervention) were methicillin resistant and would have benefited from vancomycin prophylaxis. To put this counterintuitive finding into context, one needs to understand that vancomycin was omitted for unknown reasons in the perioperative care of 4 of these 7 cases. In contrast, the infection rate in low-risk patients remained unchanged over the study period, with an OR of 0.86 (95% CI 0.55–1.34, $P = 0.5$) for SWI overall and an OR of 1.31 (95% CI 0.63–2.71, $P = 0.5$) for DSWI, respectively (Fig. 2).

The in-hospital mortality in high-risk patients was 3% ($n = 26$) during baseline and 2% ($n = 15$) in the intervention period. Vancomycin administration had no significant influence on mortality in the subset of high-risk patients (OR 0.77, CI 0.40–1.46; $P = 0.4$) nor in the entire cohort (OR 1.29, CI 0.78–2.13; $P = 0.3$). Similarly, length of hospital stay was unaffected by the intervention, both when adjusted for high risk (-0.03 hospitalization days, 95% CI - 0.15 to 0.09; $P = 0.6$) and when restricting the analysis to high-risk patients (-0.13 hospitalization days, 95% CI -0.27 to 0.02; $P = 0.09$).

In hindsight, not all high-risk patients seen in the intervention period received the intended prophylaxis (i.e. adjunctive vancomycin). Of the 782 patients classified as high risk, 143 (18%) patients did not receive vancomycin. Conversely, 91 of 730 (12%) patients who received vancomycin were not high-risk patients. This may have occurred due to breaks in the information chain surrounding the surgery, in particular, if a substitute cardiologist or housestaff was involved in the preoperative evaluation. In the 854 high-risk patients who did not receive vancomycin, 38 (4.4%) patients developed DSWI and in the 639 high-risk patients who received vancomycin, 8 (1.3%) DSWI occurred, yielding a number-needed-to-treat of 32 (95% CI 21–64) in the 'as prophylaxed' analysis.

All risk factors that constituted our definition of high risk, with the exception of renal impairment and cardiac reoperation, were independently associated with an increased risk for DSWI (Fig. 3). The need for immunosuppressive treatment conferred the highest risk of infection (OR 8.36, 95% CI 3.73–18.72), whereas diabetes mellitus (OR 4.29, 95% CI 2.36–7.77), COPD (OR 3.19, 95% CI 1.29–7.88) and elevated body mass index (OR 2.04, 95% CI 1.25–3.38) had lower but still significant impact on the DWSI rate. The same pattern was seen for SWI overall (data not shown). In addition, emergent surgery did not show any association with DSWI, neither in univariate analysis (OR 1.39, 95% CI 0.71–2.73) nor adjusted for all items that constituted high risk (OR 1.46, 95% CI 0.73–2.91).

DISCUSSION

In this pre- and postintervention study, vancomycin was added to the standard antibiotic prophylaxis in high-risk cardiac surgery patients. We were able to document a significant reduction of SWI in patients who received vancomycin. In terms of pathogenesis, this finding is not unexpected as CoNS, a major cause of SWI, are frequently methicillin resistant and thus not susceptible to standard antibiotics. We conclude that adjunctive vancomycin

prophylaxis prevented this pathogen from causing infections during the intervention period.

Our data document an impressive risk reduction during the intervention period, with 60% fewer SWI overall and 70% fewer DSWI among high-risk patients. The crude DSWI rate dropped from 4.6% to 1.7%. At the same time, low-risk patients (who received cefuroxime prophylaxis but not the intervention) experienced an unchanged SWI rate, which makes a sole time trend or other confounders unlikely. Except for the feedback of surveillance data to the surgical teams, no other preventive measures were taken during the study period, suggesting vancomycin as an effective addition to standard prophylaxis.

In the literature, very few studies have addressed the impact of combined prophylaxis in cardiac surgery. In 1 study, the SWI rate dropped from 11% to 5% after switching from cefazolin to a vancomycin–rifampin combination [17]. Another randomized trial compared the effect of administering vancomycin, gentamicin and rifampin on infection rates in a high-risk population (criteria were obesity, diabetes or bilateral thoracic artery harvesting) with standard cefuroxime. The infection rate was more than halved in the intervention arm (9% vs 25%), albeit the rate among the controls appeared quite high [18]. To our knowledge, no trial has been performed in cardiac surgery patients that investigated the coadministration of a beta-lactam antibiotic together with vancomycin, except for the one by Walsh *et al.* [12], which was focused on a subset of MRSA-colonized patients. Two studies in patients undergoing vascular surgery raised conflicting results [11, 19]. Shifting to studies that envisioned 'replacing' instead of 'combining' prophylactic agents, Garey *et al.* [20] performed an interrupted time series analysis in cardiac surgery, where the switch from cefuroxime to vancomycin was found to confer a reduction in SSIs (by 2.1 infections in 100 surgeries per month). The most pronounced effect was seen in the subset of infections due to cephalosporin-non-susceptible bacteria such as MRSA and CoNS. These findings are in line with another randomized study that compared vancomycin with cefazolin in patients undergoing cardiothoracic procedures detecting no difference in infection rates overall but in those caused by methicillin-resistant staphylococci (the rate of which dropped in the vancomycin group) [21].

In the absence of a preceding risk factor analysis in our cardiac surgery patients and without prior cost–benefit calculations, we specifically targeted the high-risk patients in this intervention study. Each individual factor included in our risk stratification had been reported as relevant in previous risk factor analyses [14]. In our *post hoc* analysis, however, we realized that not all characteristics were predictors of DSWI; neither chronic renal failure nor cardiac reoperation remained independent predictors for infection in the multivariable analysis (see Fig. 3). This is one of the limitations of our study. Of note, there are no studies to compare our specific set of risk factors for SWI.

Limitations

There are a number of other limitations in this non-controlled pre- and postintervention study. First, the administration of vancomycin was dependent on the preoperative team evaluation and, in addition, in the operating room on both the anaesthesiologist in charge and the cardiac surgeon. In a small percentage of patients, vancomycin was either given when not required (low-risk patients) or withheld when indicated (high-risk patients). In fact, 4 of the 7 high-risk patients with methicillin-resistant CoNS did not receive vancomycin in the intervention period. Therefore, our infection rates could have been even lower if all high-risk patients had correctly received vancomycin. In a subsequent 'as prophylaxed' analysis, we achieved a slightly more favourable number-needed-to-treat of 32 (95% CI 21–64), which seems to be realistic. Second, as a single-centre study, the generalizability of the result is limited. Third, we did not record subsequent colonization or infection with vancomycin-resistant organisms (e.g. enterococci), a potential detrimental effect of vancomycin overuse [22]; also, the very pathogens targeted with vancomycin may exhibit a vancomycin 'minimum inhibitory concentration creep' and become less susceptible to this prophylaxis. Maybe the most important drawback is that we were unable to show a decrease in coagulase-negative staphylococci, which may be explained by the fact that microbiological diagnosis was not a requirement in this NHSN-based surveillance programme.

CONCLUSION

In summary, to our knowledge, this is the first study that demonstrates the benefit of adding vancomycin to standard cephalosporin antibiotic prophylaxis in high-risk cardiac surgery patients. Our results support this combined prophylactic choice, which may not only confer a reduction in infection risk (and associated morbidity and mortality) for patients but also promises to save health care costs. Given that the excess costs of SWIs range from $10 000 to $20 000 and more, a reduction by 20 DSWIs (as witnessed here) promises even under conservative estimates a savings potential of approximately $300 000. In contrast, the administration of a single vancomycin dose per patient is unlikely to cost more than $100, which would have resulted in $80 000 expenses in the 800 high-risk patients we treated during the intervention period.

In clinical and economic respect, our findings, therefore, challenge the recommendation that vancomycin should not be routinely used for prophylaxis of surgical site infections [23]. In contrast, it should be considered as additional prophylaxis in high-risk patients undergoing cardiac surgery.

Conflict of interest: none declared.

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