ORIGINAL ARTICLE

Factors associated with methicillin-resistant coagulase-negative staphylococci as causing organisms in deep sternal wound infections after cardiac surgery

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Abstract

Established preoperative antibiotic prophylaxis in cardiac surgery is ineffective against methicillin-resistant coagulase-negative staphylococci (CoNS). This case–control study aimed to determine factors predicting deep sternal wound infections due to methicillin-resistant CoNS. All cardiac surgery patients undergoing sternotomy between June 2009 and March 2013 prospectively documented in a Swiss tertiary care center were included. Among 1999 patients, 82 (4.1%) developed deep sternal wound infection. CoNS were causal in 36 (44%) patients, with 25/36 (69%) being methicillin resistant. Early reintervention for noninfectious causes (odds ratio (OR) 4.3; 95% confidence interval (CI) 1.9–9.5) was associated with methicillin-resistant CoNS deep sternal wound infection. Among CoNS deep sternal wound infection, perioperative antimicrobial therapy (p 0.002), early reintervention for noninfectious causes (OR 7.9; 95% CI 0.9–71.1) and time between surgery and diagnosis of infection over 21 days (OR 10.8; 95% CI 1.2–97.8) were associated with methicillin resistance. These findings may help to better tailor preoperative antimicrobial prophylaxis.

Keywords: Cardiac surgery, coagulase-negative staphylococci, methicillin resistance, sternotomy, surgical site infection
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Introduction

Surgical site infections (SSI) in cardiac surgery with midline sternotomy remain a major challenge. Reported incidence varies between 2% and 14% for all SSI and between 2% to 4% for deep sternal wound infections. Deep sternal wound infections have a substantial impact on morbidity and mortality and are associated with considerable costs [1–8]. Several risk factors for deep sternal wound infection have been described, either related to comorbidities (e.g. diabetes and obesity) or interventions (e.g. duration of surgery and reintervention) [1,9–12].

The most common etiologic pathogens are *Staphylococcus aureus,* coagulase-negative staphylococci (CoNS) and Gram-negative bacteria [4,7,13–15]. In one study, infection control interventions have been successful in reducing the rate of sternal SSI caused by *S. aureus,* while the incidence of deep sternal wound infection attributable to CoNS has not declined in parallel [7].

Known risk factors for sternal SSI due to CoNS are length of hospital stay before surgical intervention, duration of surgery and reintervention at the same surgical site [15]. Intraoperative, presumably airborne, transmission of CoNS from healthcare workers to patients has been shown to occur [16,17]. In addition, there is evidence that CoNS from clinical specimens are closely related to one another at a hospital, interhospital or even interregional level [18,19].

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Factors associated with methicillin resistance in CoNS causing deep sternal wound infection in patients with heart surgery involving sternotomy have not been defined yet. Understanding these factors is important for infection control and antibiotic prophylaxis policy, as routine prophylaxis recommended by official guidelines does not cover SSI caused by methicillin-resistant bacteria [20]. Furthermore, empirical antimicrobial treatment in the case of an infection could be more targeted in cases with presence of known risk factors. We aimed to address this question by analysing a large prospective cohort of cardiac surgery patients with midline sternotomy from a major Swiss university-affiliated tertiary care center.

Methods

Setting

The University Hospital Zurich is a tertiary care center with 942 beds. In 2012, 1166 patients underwent cardiac surgery, including coronary artery bypass graft procedures, valve repairs and replacements, heart transplantation and placement of implantable cardiovascular devices, e.g. aortic grafts and ventricular assist devices. Cefuroxime 1.5 g provided intravenously with repetition every 8 hours in case of prolonged surgery is the standard antibiotic prophylaxis for initial surgery and reintervention.

Surveillance of SSI

All consecutive patients undergoing heart surgery at the University Hospital Zurich are included prospectively in the surveillance protocol of the Swissnoso Surgical Site Infection Surveillance Module (http://www.swissnoso.ch/), which is based on the US Centers for Disease Control and Prevention definitions [21]. As a modification to the latter, sternal osteitis is considered a deep incisional SSI even in the absence of concomitant mediastinitis (http://www.swiss-noso.ch/wp-content/uploads/2009/05/2_-D-30-09-2013_D_Teilnehmerhandbuch_VERSION-UPDATE_SEPTEMBER-20132.pdf).

Importantly, the protocol includes rigorous postdischarge surveillance. All patients are contacted by phone 1 month after the surgical intervention, or after 1 year if an implant, i.e. sternal plate, wire cerclage, valve repair or replacement, was involved. If suspicion for SSI arises, the case is further discussed with the treating physician.

The data collected for each patient included the following: sex, age, days between admission and surgery, timing of preoperative antibiotic prophylaxis, body mass index (BMI), wound contamination class, American Society of Anesthesiologists (ASA) score, intervention exceeding 75th percentile of duration cut point [22] and reintervention. National Nosocomial Infections Surveillance scores were calculated [22]. In case of SSI, the depth of the infection, i.e. superficial incisional, deep incisional or organ/space, and the causing organisms were recorded.

Case definition

All consecutive patients undergoing coronary artery bypass graft procedures, valve repairs and replacements, or placement of implantable cardiovascular devices, e.g. aortic grafts, ventricular assist devices, between 1 June 2009 and 30 September 2013 were included, with the exception of minimally invasive interventions. SSI surveillance was suspended between 1 January 2011 and 31 March 2011.

Deep sternal wound infection was defined according to the Swissnoso Surgical Site Infection Surveillance Module definitions (http://www.swiss-noso.ch/wp-content/uploads/2009/05/2_-D-30-09-2013_D_Teilnehmerhandbuch_VERSION-UPDATE_SEPTEMBER-20132.pdf). In brief, deep sternal wound infection had to become manifest within 1 year after surgery and had either to be confirmed by a treating physician *or* to be present with purulent drainage of the deep incisional compartment or spontaneous wound dehiscence together with pain, redness or temperature >38°C *or* a positive bacterial culture from a deep tissue sample. Mediastinitis was deep sternal wound infection with cultural, histologic or macroscopic evidence of mediastinal involvement. Postoperative endocarditis was not considered a deep sternal wound infection.

Besides the clinical criteria, CoNS etiology of deep sternal wound infection required either a monoculture of CoNS from at least one deep tissue sample. In polymicrobial deep sternal wound infection, CoNS was only considered when additional pathogens were *Propionibacterium acnes* or appeared in follow-up cultures only. Antibiotic susceptibility was reported for the first CoNS isolated from the wound. Susceptibility testing was done on Müller-Hinton agar (Becton-Dickinson, Franklin Lakes, NJ, USA) using MacFarland 0.5 from overnight cultures followed by incubation at 35°C for 16 to 18 hours. The disc diffusion method according to Kirby-Bauer was applied for susceptibility testing (http://www.eucast.org/antimicrobial_susceptibility_testing/disk_diffusion_methodology/) using discs from i2a (Montpellier, France). Inhibition zone diameters were determined and recorded in the automated Sirweb/Sirscan system (i2a) and interpreted according to EUCAST 1.3 guidelines from the European Committee on Antimicrobial Susceptibility Testing using their breakpoint tables for interpretation of minimum inhibitory concentrations and zone diameters, versions 1.3 and 2.0 (http://www.eucast.org/antimicrobial_susceptibility_testing/previous_versions_of_tables/).

Additional variables

For cases of CoNS with deep sternal wound infection, a retrospective chart review was performed and the following additional information extracted: perioperative antibiotic treatment, defined as a course of therapeutic antibiotic not for deep sternal wound infection (this had to be started, continued or stopped in the 4 weeks before surgery until 2 weeks after surgery); diabetes mellitus, defined by any long-term oral or injectable antidiabetic medication before surgery; and uni- or bilateral internal mammary artery grafting.

Definition of factors evaluated for methicillin resistance

Factors were defined as preoperative (sex, age, length of hospital stay before surgery, BMI, diabetes, ASA score, time between antimicrobial prophylaxis and incision, contamination class), intraoperative (duration of surgery and calculated *t* score, grafting of bilateral internal mammary artery, grafts using a venous bypass), perioperative (perioperative antibiotic as defined above) and postoperative (latency to diagnosis of deep sternal wound infection, early reintervention within 1 month for noninfectious complication).

Statistical analysis

For descriptive analyses, we used the chi-square or Fisher's exact test, as appropriate, for categorical data and the Mann-Whitney *U* test for continuous variables. Univariable logistic regression analysis was applied to calculate odds ratios (OR) with 95% confidence intervals (CI) in order to determine risk factors for infection with methicillin-resistant CoNS in patients with sternotomy and differences between infections with methicillin-resistant CoNS and methicillin-sensitive CoNS. A log-rank test was used to compare time to diagnosis in patients with methicillin-resistant CoNS and methicillin-sensitive CoNS.

We used SPSS Statistics software, version 22 (IBM, Armonk, NY, USA), for statistical analyses. A p value of <0.05 was considered statistically significant.

Ethics approval

SSI surveillance is considered to be a quality improvement project and is therefore exempt from ethical approval. All patients were informed on the SSI surveillance at admission and had the possibility to opt out.

Results

We followed 2044 patients who underwent sternotomy between 1 June 2009 and 1 March 2013. As a result of incomplete documentation, 45 patients were excluded. Of the remaining 1999 patients, 82 (4.1%) were diagnosed with a deep sternal wound infection. In 36 (44%) cases, CoNS was the causative microorganism and in 25/36 (69%) cases, CoNS were methicillin resistant (Fig. 1). In 10/82 cases, *S. aureus* was found to be the causative organism, while none of them was methicillin resistant. Patient characteristics are shown in Table 1.

No difference was seen in pre- and intraoperative characteristics between patients with methicillin-resistant CoNS and the remainder of the study patients. Reintervention within 30 days for noninfectious causes was the only factor associated with deep sternal wound infection due to methicillin-resistant CoNS compared to patients without deep sternal wound infection or those with deep sternal wound infection due to other pathogens (OR 4.26; 95% CI 1.9–9.5; p 0.001).

Among patients with CoNS deep sternal wound infections, perioperative therapeutic antibiotic treatment was associated with methicillin resistance, as was consecutive reintervention for noninfectious complications (Table 1).

Time from surgery to diagnosis of deep sternal wound infection differed between cases with methicillin-sensitive CoNS (median, 16 days) and cases with methicillin-resistant CoNS (median, 23 days; $\chi 2$ [df 1] 4.37; p 0.037). Moreover, diagnosis of deep sternal wound infection after 21 days was strongly associated with methicillin-resistant CoNS (OR 10.8; 95% CI 1.2–97.8; p 0.016; Fig. 2).

Among the 82 patients with deep sternal wound infection, 15 (18%) had mediastinitis, which corresponds to 0.8% of all 1999 patients. Among the 36 cases with CoNS deep sternal wound infection, 6 (17%) had mediastinitis.

Although all CoNS tested were susceptible to vancomycin, methicillin-resistant CoNS were more often resistant to trimethoprim/sulfamethoxazole (13/25; 52%) than methicillin-sensitive CoNS (1/11; 9% p 0.016), while no difference was found in resistance rates to clindamycin in methicillin-resistant CoNS than in methicillin-sensitive CoNS (12/25; 48% vs. 2/11; 18%; p 0.09).

Discussion

Our study suggests that in cardiac surgery with midline sternotomy, early surgical reintervention for noninfectious complications is associated with deep sternal wound infection due to methicillin-resistant CoNS. Among patients with CoNS deep sternal wound infections, perioperative antibiotic therapy, early surgical reintervention for noninfectious causes and occurrence of deep sternal wound infection >21 days after surgery were associated with methicillin resistance.

To our knowledge, our study is the first to evaluate factors associated with methicillin resistance in deep sternal wound infection in terms of causing CoNS. The strict SSI surveillance

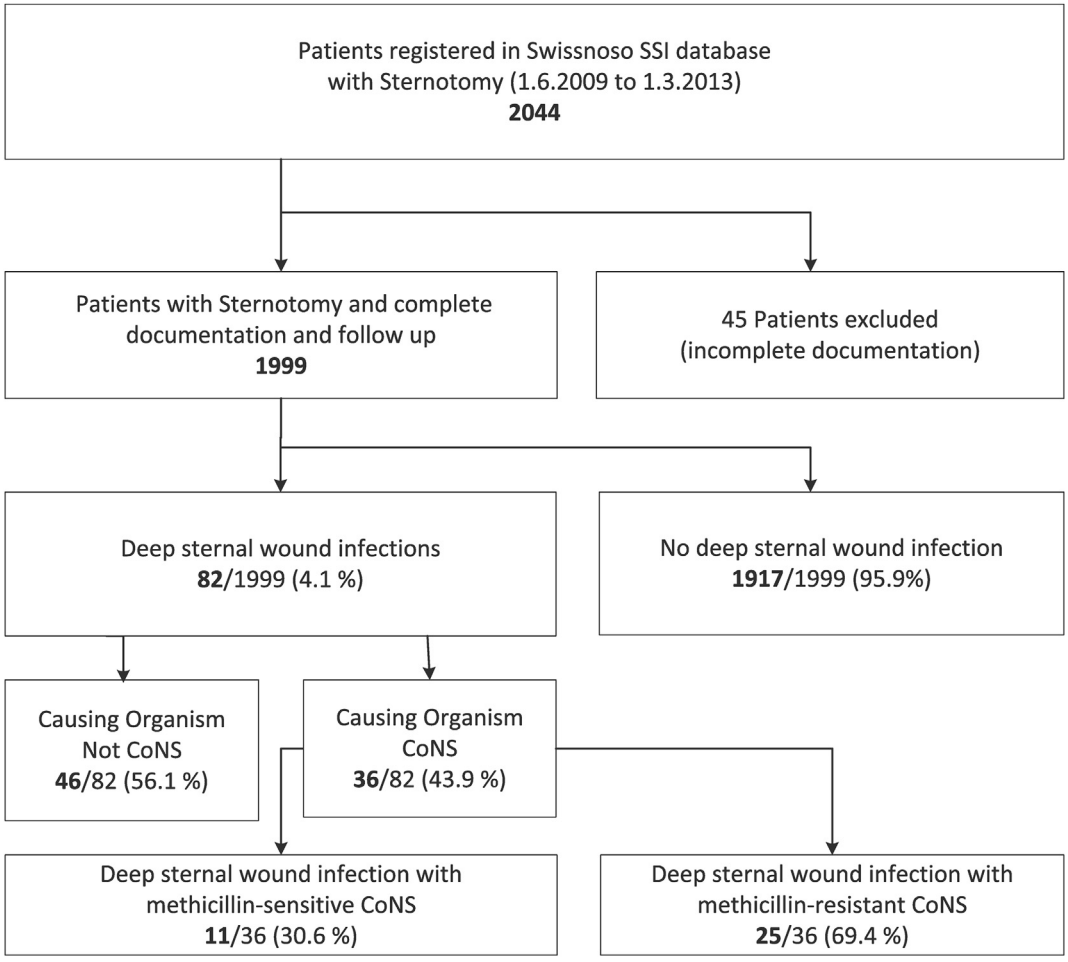

FIG. 1. Included and excluded study cases and controls. SSI, surgical site infection; CoNS, coagulase-negative staphylococci.

program guarantees high and representative data quality for sternotomy patients, which is also reflected in the high follow-up rate of 98%. The drawbacks of our study were the retrospective analysis and the inherently limited number of infectious outcomes. Therefore, performance of a multivariable regression analysis was not possible.

Early reintervention is a well-established risk factor for deep sternal wound infection [15]. These patients usually have a longer preoperative hospital stay, and as a consequence, they might be colonized with methicillin-resistant CoNS rather than methicillin-sensitive CoNS [23]. Moreover, reintervention wound healing might be compromised as a result of scarring, which increases the overall infection rate. Because reintervention is frequently an emergent procedure and the chest has already been opened before, standard aseptic procedure may be challenged. Hypothetically, methicillin-resistant CoNS could gain access to deep spaces during reintervention.

Among patients with CoNS deep sternal wound infections, the association of methicillin resistance and perioperative antibiotic is not surprising. A single dose of antibiotics has been shown to cause a marked increase of recovery of methicillin-resistant CoNS from a patient's skin [24]. This phenomenon has been observed before. One study of methicillin-resistant CoNS in cerebrospinal fluid shunt infection suggested that length of hospital stay before implantation was a risk factor and hypothesized a predisposition by previous antibiotic therapy [25]. Because perioperative antibiotic therapy was not recorded in the prospective data set, we were unable to conclude that perioperative antibiotic therapy was a risk factor for methicillin-resistant CoNS deep sternal wound infection among all study patients.

The time of diagnosis of methicillin-resistant and methicillin-sensitive CoNS infections was different. Twenty-one days after surgery, almost uniquely methicillin-resistant cases and not methicillin-sensitive cases were detected. A previous study examining early and late-onset mediastinitis observed differences in presenting clinical features and the microbial spectrum, but the authors did not report on differences in methicillin resistance of

TABLE 1. Patient characteristics

Characteristic	Methicillin-resistant CoNS[a]	Methicillin-sensitive CoNS[a]	Odds ratio[b]	p[b]	No methicillin-resistant CoNS[a]	Odds ratio[c]	P[c]
No. of patients	25	11			1974		
Preoperative factor							
Male sex	20/25 (80%)	9/11 (82%)	0.89	0.64	1421/1974 (72%)	1.58	0.248
Age, y	71 (38–81)	66 (48–85)	NA	0.84	68 (15–90)	NA	0.74
Time between admission and surgery, days	1 (1–8)	1 (1–4)	NA	0.84	1 (0–55)	NA	0.37
Time between preoperative antibiotic and incision, days	35 (0–125)[d]	35 (20–85)	NA	0.90	40 (0–1145)[e]	NA	0.59
Preoperative antibiotic within 1 hour before incision	21/25 (84%)	10/11 (91%)	0.53	0.59	1599/1974 (81%)	1.20	0.74
BMI, kg/m^2	30 (17–35)	29 (18–38)	NA	0.44	27 (14–71)	NA	0.18
Diabetes mellitus	10/25 (40%)	2/11 (18%)	3.0	0.19	ND		
ASA score	3 (3–4)	3 (2–4)	NA	0.15	3 (1–5)	NA	0.39
Contamination class of 1	25/25 (100%)	11/11 (100%)	NA		1935/1974 (98%)	NA	NA
Intraoperative factor							
ACBP with venous graft	9/25 (36%)	2/11 (18%)	2.53	0.25	651/1974 (33%)	1.12	0.47
ACBP with internal mammary artery	18/25 (72%)	5/11 (46%)	3.1	0.13	ND		
ACBP with bilateral internal mammary artery	6/25 (24%)	3/11 (27%)	0.84	0.57	ND		
Duration of surgery, minutes	246 (135–495)	250 (170–480)	NA	0.66	260 (25–970)	NA	0.48
NNIS score	1 (1–2)	1 (0–2)	NA	0.57	1 (0–3)	NA	0.28
Duration of surgery >75th percentile	11/25 (44%)	4/11 (36%)	1.38	.48	671/1974 (34%)	1.5	0.206
Perioperative factor							
Perioperative antibiotics	13/25 (52%)	0/11 (0%)	NA	0.002	ND		
Postoperative factor							
Reintervention ≤30 days after surgery for noninfectious causes	11/25 (44%)	1/11 (9%)	7.9	.043	305/1974 (15%)	4.26	.001
Latency between surgery and diagnosis of deep sternal wound infection with CoNS >21 days	13/25 (52%)	1/11 (9%)	10.8	0.016	NA		

Data are presented as *n*/*N* (%) or median (range).
ACBP, aortocoronary bypass; BMI, body mass index; CoNS, coagulase-negative staphylococci; ASA, American Society of Anesthesiologists; NNIS, National Nosocomial Infections Surveillance; NA, not applicable; ND, not determined.
[a]Patient groups according to occurrence and etiology of deep sternal wound infection.
[b]Odds ratio and p value comparing methicillin-resistant CoNS with methicillin-sensitive CoNS.
[c]Odds ratio and p value comparing methicillin-resistant CoNS with all study patients without methicillin-resistant CoNS.
[d]1/25 (4%) not determined before incision.
[e]121/1974 (6.1%) not determined before incision.

CoNS [26]. Possible hypotheses are decreased virulence of methicillin-resistant strains or a predisposition for postoperative wound contamination, with CoNS becoming increasingly resistant during the hospital stay [23]. These hypotheses could not be further evaluated because of the retrospective character of the analysis. Another possibility is that methicillin-resistant CoNS gain access to the wound only at reintervention, which could explain the delay. Because of the small number of study patients, multivariable analysis of the role of reintervention, perioperative antibiotic treatment and delay >21 days on methicillin-resistant CoNS was not possible. The later occurrence of methicillin-resistant CoNS infections can therefore hardly be used to curtail surgical prophylaxis, but it suggests that the chances of finding methicillin-sensitive CoNS in deep sternal wound infections diagnosed after 21 days after surgery are low.

Known risk factors for deep sternal wound infection—elevated BMI, diabetes, prolonged duration of surgery, collection of bilateral internal mammary artery [27]—did not differ between methicillin-sensitive and methicillin-resistant CoNS cases, possibly as a result of a lack of statistical power. The relatively high deep sternal wound infection incidence of 4.1% is explained by a strict surveillance method. Moreover, when applying the more conservative definition of deep sternal wound infection requiring proof of mediastinitis, the infection rate would be as low as 0.8%. We believe that for the purposes of this study, considering sternal osteitis alone as deep sternal wound infection was appropriate.

A meta-analysis demonstrated that glycopeptides alone are no more effective than β-lactams for the prevention of SSI, and its routine use has been discouraged [28]. Although the Society of Thoracic Surgeons suggests the use of one or two doses of a glycopeptide in cardiac surgery in combination with a β-lactam as prophylaxis in certain situations such as graft implantations [20], a more recent guideline by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America recommends the use of vancomycin in cardiac surgery only in the case of penicillin allergy [29]. Vancomycin use has been associated with an increase of vancomycin-resistant enterococci in many studies, even though when corrected for duration of hospitalization this association may be small [30]. Nevertheless, addition of glycopeptide prophylaxis should preferably be limited to a population at risk. This addition could be suitable as preoperative prophylactic antibiotic for reinterventions. If this would have been applied, 11 cases of methicillin-resistant CoNS could have potentially been avoided in 316 early reinterventions (3.5%; number needed to treat, 29). This is in contrast to potential avoidance of 25 cases of methicillin-resistant CoNS when applying a glycopeptide to the initial 1999 patients with

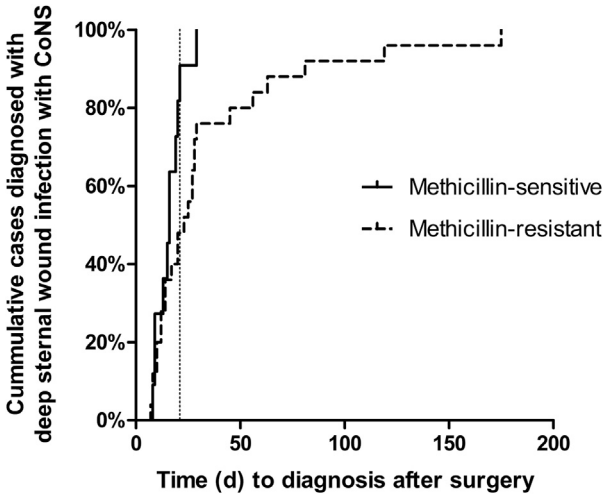

FIG. 2. Latency between surgery and diagnosis of deep sternal wound infection with CoNS. Cumulative events of deep sternal wound infection with methicillin-sensitive CoNS and methicillin-resistant CoNS according to latency (in days) between initial surgery and diagnosis. The dashed line indicates day 21. Diagnosis of deep sternal wound infection after this day was associated with methicillin resistance in etiologic CoNS (odds ratio 10.8; p 0.02). CoNS, coagulase-negative staphylococci.

sternotomy (1.3%; number needed to treat, 80). But because it is not likely that all methicillin-resistant CoNS infections would be avoided by a preoperative glycopeptide, the number needed to treat would realistically be higher.

Factors associated with methicillin resistance within CoNS cases (delayed diagnosis, perioperative antibiotic therapy) cannot be generalized to all patients. Thus, no suggestion for additional prophylaxis can be made.

In conclusion, we found that deep sternal wound infection with methicillin-resistant CoNS was associated with early reintervention. Among deep sternal wound infections with CoNS, methicillin resistance was associated with early reintervention and prior antibiotic treatment. A controlled prospective study is needed to understand if an addition of a glycopeptide as preoperative prophylaxis in this selected subpopulation of cardiac surgery patients would reduce the overall SSI rate and that due to CoNS, especially those with methicillin resistance. Further studies are also needed in regard to the pathophysiology of CoNS deep sternal wound infection to explain its delayed occurrence in those involving methicillin-resistant CoNS.

Conflict of interest

None declared.

References

[1] Lu JC, Grayson AD, Jha P, Srinivasan AK, Fabri BM. Risk factors for sternal wound infection and mid-term survival following coronary artery bypass surgery. Eur J Cardiothorac Surg 2003;23:943–9.
[2] Borger MA, Rao V, Weisel RD, et al. Deep sternal wound infection: risk factors and outcomes. Ann Thorac Surg 1998;65:1050–6.
[3] Toumpoulis IK, Anagnostopoulos CE, Derose Jr JJ, Swistel DG. The impact of deep sternal wound infection on long-term survival after coronary artery bypass grafting. Chest 2005;127:464–71.
[4] Sharma M, Berriel-Cass D, Baran Jr J. Sternal surgical-site infection following coronary artery bypass graft: prevalence, microbiology, and complications during a 42-month period. Infect Control Hosp Epidemiol 2004;25:468–71.
[5] Swenne CL, Lindholm C, Borowiec J, Carlsson M. Surgical-site infections within 60 days of coronary artery by-pass graft surgery. J Hosp Infect 2004;57:14–24.
[6] Mannien J, Wille JC, Kloek JJ, van Benthem BH. Surveillance and epidemiology of surgical site infections after cardiothoracic surgery in The Netherlands, 2002–2007. J Thorac Cardiovasc Surg 2011;141:899–904.
[7] Yavuz SS, Tarcin O, Ada S, et al. Incidence, aetiology, and control of sternal surgical site infections. J Hosp Infect 2013;85:206–12.
[8] Steingrimsson S, Gottfredsson M, Kristinsson KG, Gudbjartsson T. Deep sternal wound infections following open heart surgery in Iceland: a population-based study. Scand Cardiovasc J 2008;42:208–13.
[9] Stahle E, Tammelin A, Bergstrom R, Hambreus A, Nystrom SO, Hansson HE. Sternal wound complications—incidence, microbiology and risk factors. Eur J Cardiothorac Surg 1997;11:1146–53.
[10] Zacharias A, Habib RH. Factors predisposing to median sternotomy complications. Deep vs superficial infection. Chest 1996;110:1173–8.
[11] Ridderstolpe L, Gill H, Granfeldt H, Ahlfeldt H, Rutberg H. Superficial and deep sternal wound complications: incidence, risk factors and mortality. Eur J Cardiothorac Surg 2001;20:1168–75.
[12] Birkmeyer NJ, Charlesworth DC, Hernandez F, et al. Obesity and risk of adverse outcomes associated with coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. Circulation 1998;97:1689–94.
[13] Lepelletier D, Perron S, Bizouarn P, et al. Surgical-site infection after cardiac surgery: incidence, microbiology, and risk factors. Infect Control Hosp Epidemiol 2005;26:466–72.
[14] Mossad SB, Serkey JM, Longworth DL, Cosgrove 3rd DM, Gordon SM. Coagulase-negative staphylococcal sternal wound infections after open heart operations. Ann Thorac Surg 1997;63:395–401.
[15] Tegnell A, Aren C, Ohman L. Coagulase-negative staphylococci and sternal infections after cardiac operation. Ann Thorac Surg 2000;69:1104–9.
[16] Bitkover CY, Marcusson E, Ransjo U. Spread of coagulase-negative staphylococci during cardiac operations in a modern operating room. Ann Thorac Surg 2000;69:1110–5.
[17] Boyce JM, Potter-Bynoe G, Opal SM, Dziobek L, Medeiros AA. A common-source outbreak of *Staphylococcus epidermidis* infections among patients undergoing cardiac surgery. J Infect Dis 1990;161:493–9.
[18] Widerstrom M, Monsen T, Karlsson C, Wistrom J. Molecular epidemiology of meticillin-resistant coagulase-negative staphylococci in a Swedish county hospital: evidence of intra- and interhospital clonal spread. J Hosp Infect 2006;64:177–83.
[19] Gordon RJ, Miragaia M, Weinberg AD, et al. *Staphylococcus epidermidis* colonization is highly clonal across us cardiac centers. J Infect Dis 2012;205:1391–8.
[20] Engelman R, Shahian D, Shemin R, et al. The society of thoracic surgeons practice guideline series: antibiotic prophylaxis in cardiac

surgery, part II: antibiotic choice. Ann Thorac Surg 2007;83:1569–76.

[21] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital infection control practices advisory committee. Infect Control Hosp Epidemiol 1999;20:250–78.

[22] Emori TG, Culver DH, Horan TC, et al. National nosocomial infections surveillance system (NNIS): description of surveillance methods. Am J Infect Control 1991;19:19–35.

[23] Kuster SP, Ruef C, Zbinden R, et al. Stratification of cumulative antibiograms in hospitals for hospital unit, specimen type, isolate sequence and duration of hospital stay. J Antimicrob Chemother 2008;62:1451–61.

[24] Kernodle DS, Barg NL, Kaiser AB. Low-level colonization of hospitalized patients with methicillin-resistant coagulase-negative staphylococci and emergence of the organisms during surgical antimicrobial prophylaxis. Antimicrob Agents Chemother 1988;32:202–8.

[25] Etienne J, Charpin B, Grando J, Brun Y, Bes M, Fleurette J. Characterization of clinically significant isolates of *Staphylococcus epidermidis* from patients with cerebrospinal fluid shunt infections. Epidemiol Infect 1991;106:467–75.

[26] Mekontso Dessap A, Vivier E, Girou E, Brun-Buisson C, Kirsch M. Effect of time to onset on clinical features and prognosis of post-sternotomy mediastinitis. Clin Microbiol Infect 2011;17:292–9.

[27] Bryan CS, Yarbrough WM. Preventing deep wound infection after coronary artery bypass grafting: a review. Tex Heart Inst J 2013;40:125–39.

[28] Bolon MK, Morlote M, Weber SG, Koplan B, Carmeli Y, Wright SB. Glycopeptides are no more effective than beta-lactam agents for prevention of surgical site infection after cardiac surgery: a meta-analysis. Clin Infect Dis 2004;38:1357–63.

[29] Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013;70:195–283.

[30] Carmeli Y, Samore MH, Huskins C. The association between antecedent vancomycin treatment and hospital-acquired vancomycin-resistant enterococci: a meta-analysis. Arch Intern Med 1999;159:2461–8.