Hospital acquired vancomycin resistant enterococci in surgical intensive care patients – a prospective longitudinal study

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Abstract

**Background:** Vancomycin resistant enterococci (VRE) occur with enhanced frequency in hospitalised patients. This study elucidates the prevalence of VRE on admission among surgical intensive care unit (SICU) patients, whether these patients are at special risk for VRE acquisition and which risk factors support this process.

**Methods:** Patients admitted to SICUs of the University Hospital Münster were examined during August–October 2017. VRE screening was performed within 48 h after admission and directly prior to discharge of patients. In parallel risk factors were recorded to estimate their effect on VRE acquisition during SICU stay.

**Results:** In total, 374 patients (68% male) with a median age of 66 years were admitted to one of the SICUs during the investigation period. Of all, 336 patients (89.8%) were screened on admission and 268 (71.7%) on discharge. Nine patients were admitted with previously known VRE colonisation. Twelve (3.6%) further patients were VRE positive on admission. During ICU stay, eight (3.0%) additional patients turned out to be VRE colonised. Risk factors found to be significantly associated with VRE acquisition were median length of stay on the ICU (14 vs. 3 days; \(p = 0.01\)), long-term dialysis (12.5% vs. 2.0% of patients; \(p = 0.05\)), and antibiotic treatment with flucloxacillin (28.6% vs. 7.2% of patients; \(p = 0.01\)) or piperacillin/tazobactam (57.1% vs. 26.6% of patients; \(p = 0.01\)).

**Conclusions:** SICU patients are not at special risk for VRE acquisition. Previous stay on a SICU should therefore not be considered as specific risk factor for VRE colonisation.

**Keywords:** Vancomycin resistant enterococci, Hospital-acquisition, Risk factors, Surgical intensive care patients

Background

Enterococci are an emerging pathogen in hospitalised patients [1]. These pathogens ubiquitously occur in the hospital environment and show a high tenacity on inanimate surfaces [2–4]. As a result, enterococcal infections emerge with a rising frequency. Additionally, enterococci have the ability of acquiring resistances to multiple antimicrobial agents and the capacity to transfer resistances to other pathogens via mobile genetic elements [5–7]. For this reason the prevalence of vancomycin resistant enterococci (VRE) has increased intensively [1]. Vancomycin resistance is associated with enhanced mortality, e.g. among patients with enterococcal blood stream infections [8]. Within hospital settings prevention of VRE transmission is therefore a major objective.

Infection control strategies to control VRE vary, depending on local guidelines. Usually bundle strategies are applied to prevent transmission of VRE between two patients [9]. These include contact precautions, intensified disinfection strategies, the usage of personal protective equipment and active surveillance [10, 11]. In this context, screening strategies are controversially discussed [12]. Both, generalised screening and a risk-adaptive screening, are possible approaches. Regarding the latter, the question arises, which patient groups should be included. Acquisition of VRE in critical ill patients has been associated with prolonged duration of hospital stay, previous hospitalisations, antibiotic...
treatment, long-term dialysis and immunosuppression [13–15]. Surgical intensive care patients host a variety of these risk factors, although not explicitly mentioned as risk clientele. Whether surgical intensive care patients per se are at a special risk to acquire VRE and should therefore be included in a risk adapted screening upon subsequent admission to a hospital has not yet been investigated. The present work addresses these questions and investigates risk factors making a VRE acquisition more probable.

Methods
Clinical setting and infection control measures
The 1500-bed University Hospital Münster comprises four interdisciplinary SICUs, hosting abdominal-, trauma-, neuro-, vascular- and thoracic-surgery patients. In total, capacity of all ICUs is 43 beds at its maximum distributed over 26 patient rooms.

Routinely, screening for multidrug-resistant organisms includes an admission-screening for methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Gram-negative bacteria according to the national German guidelines is established [16, 17]. After coincidental detection of VRE in screening swabs and clinical samples of SICU patients, a prospective investigation was initiated, concentrating on VRE acquisition during a stay on a SICU.

Extended hygiene measures in case of VRE detection include contact isolation in a separate room; cohorting of multiple VRE patients is possible. Sanitary facilities are strictly separated and staff is instructed to wear personal protective equipment in case of entering a patient room, consisting of gloves, and gowns. Surface cleaning disinfection was performed once a day.

Detection of risk factors for VRE acquisition
During the 2-month study period (August – October 2017), risk factors for VRE acquisition were prospectively recorded during the entire in-patient stay. These risk factors included demographic data (age, gender), the duration of stay on the respective SICU, underlying diseases (haemato-oncological, immunosuppressive diseases [e.g. autoimmune-disease, malignancies, HIV-infection, immunomodulatory drug treatment], hepatic insufficiency, liver transplantation, renal insufficiency, long-term dialysis) and medication (systemic glucocorticoid and antibiotic treatment) attributed to VRE acquisition and previous contacts to the healthcare system (admission from a foreign or domestic hospital, admission from an (in-house) ICU) [13–15, 18]. Patients with a pre-existing VRE status were not included in the analysis, in order to detect risk factors of VRE acquisition on the SICU ward.

VRE screening, culture, antibiotic resistances, PCR testing methods
VRE screening was performed upon patients’ admission on the SICU as well as upon discharge of patients from the SICU in order to detect VRE acquisition during SICU stay. Hospital-acquired VRE was defined as acquisition > 48 h after hospitalisation on the SICU. All VRE not acquired during SICU stay were defined as pre-existing VRE. Swabs were obtained rectally (5 cm ab ano) (Trans-wab® m40 compliant, mwe, Corsham, Wiltshire, UK) and subsequently streaked onto chromogenic selective agar (VRESelect™, Biorad, Hercules, California, USA). Suspected colonies were confirmed via MALDI-TOF-MS (Bruker Corporation, Bremen, Germany). Susceptibility testing was performed in accordance with the current European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards for clinical breakpoints (version 7.0) using the VITEK® 2 system (BioMérieux, Nürtingen, Germany). Vancomycin resistance was confirmed by the detection of vanA, vanB, vanC1 and vanC2/3 using the GenoType Enterococcus system (Hain Lifescience, Nehren, Germany). Additionally, subsequent whole genome sequence-based typing confirmed presence of van--genes in these isolates.

Whole genome sequence-based typing
In order to elucidate the clonal relationship of VRE-strains, isolates were compared genetically via whole genome sequencing (WGS) using the Illumina MiSeq platform (Illumina Inc., San Diego, USA) and laboratory procedures as described previously [19]. Coding regions were compared in a gene-by-gene approach (core genome multilocus sequence typing, cgMLST) using the SeqSphere+ software version 4.1 (Ridom GmbH, Münster, Germany) [20]. To visualize the clonal relationship a minimum-spanning tree was generated using the same software. Genotypes that differed in ≤3 cgMLST targets were rated as closely related and highly suspected for a hospital-acquired transmission. For backwards compatibility with classical molecular typing, i.e. MLST, the MLST sequence types (ST) were extracted from the WGS data in silico.

Statistical analysis
All data are expressed as absolute numbers or percentage, if not stated otherwise. Independent risk factors were determined in a two-step analysis. First, a univariate analysis was performed, selecting potential risk factors. Chi-Square test was used for categorical and the two-sided student’s t-test for comparison of numerical data. Second, a logistic regression was performed to ascertain the independency of risk factors. Statistical significance was declared at $p \leq 0.05$. 

Kampmeier et al. Antimicrobial Resistance and Infection Control (2018) 7:103
**Results**

**Screening adherence, acquired VRE, genotypes**

Table 1 shows the detailed results of screening data. Of 374 admitted patients, 336 were screened on admission and 268 on discharge respectively, not considering patients with a confirmed VRE status prior to admission or discharge. In total eight hospital-acquired VRE could be detected. Of all pre-existing VRE (on admission), six presented a \(\text{vanA}\), four a \(\text{vanB}\) and one both genotypes. Of all hospital-acquired VRE, one hosted a \(\text{vanA}\) and seven a \(\text{vanB}\) genotype.

**Antimicrobial resistance expressions**

In total, 29 VRE isolates of 26 patients (one patient was readmitted twice and one patient once) were tested for antimicrobial resistance expressions. Table 2 gives a detailed overview of tested substances.

**Whole genome sequence-based typing and VRE transmission**

Of all 29 isolates 25 were subjected to whole genome sequencing. In patients with repetitive VRE detections and the same antimicrobial resistance expression, only the first isolate was undertaken the sequencing procedure. One isolate was not sequenced. Analysing the MLST ST of all sequenced isolates, ST117 was most prevalent (64.0%) followed by ST80 (24.0%) and ST721 (11.0%) (see also Table 2). A genetical comparison with the help of the cgMLST scheme, based on 1423 genes present in all isolates, revealed six clusters, comprising two, three, five and six isolates respectively (Fig. 1). Two of these clusters contain genotypes of pre-existing isolates and isolates detected in both screenings. Six out of eight VRE isolates (204, 283, 291, 314, 361, 372) detected in patients on discharge, who were previously tested negative for VRE on admission, are genetically closely related to isolates detected in other patients, suggesting a transmission of one VRE clone on ward in these cases (see also Fig. 2). The other two isolates (300, 302) detected on discharge are genetically unrelated to other isolates, which can be attributed to selection of VRE e.g. via antibiotic application in these patients or a false-negative screening result on admission.

**Discussion**

Control of VRE is an emerging topic, patients and healthcare workers have to cope with. An important aspect for prevention of transmission is the early recognition of VRE via screening strategies. Here, the question was addressed, whether SICU patients acquire VRE during their stay and which factors put them at special risk for acquisition. VRE acquisition rate (3.0%) on the SICU was lower than the initial prevalence (3.6%) on admission of all patients. Additionally, no hospital-acquired infection but only colonisations occurred. Distribution of detected \(\text{van}\)-genotypes and MLST ST (\(\text{vanB}\)-genotype and ST117 were most prevalent) are thereby in accordance with national results and trends published for German healthcare institutions recently [21]. In contrast to another retrospective study investigating hospital-acquired VRE, where the acquisition rate was 28.6%, on different wards including surgical and internal ICUs and lacking a generalised VRE screening, acquisition of VRE in our investigation was comparably low [22]. Further investigations on haemato-oncological patients revealed one third of these patients to develop hospital-acquired VRE [18]. SICU patients should per se not be considered as a specific risk clientele for VRE acquisition in comparison with these patients.

**Table 1** Screening data of SICU-admitted patients \((n = 374)\) during August to October 2017

| Screening result | Positive | Negative | Total |
|------------------|----------|----------|-------|
|                  | \(\text{vanA}\) genotype | \(\text{vanB}\) genotype | \(\text{vanA}\) and \(\text{vanB}\) genotype |
| Pre-existing VRE | 6 (66.7%) | 3 (33.3%) | 0 (0%) |
| Screening on admission | 0 (0%) | 11 (3.3%) | 1 (0.3%) |
| Screening on discharge | 1 (0.4%) | 7 (2.6%) | 0 (0%) |
Table 2 Collection dates, van-genotypes, MLST sequence types and antimicrobial resistance expression of VRE strains detected in SICU patients. Each row represents a single patient.

| Isolate no. | Collection date | Positive result | MLST ST | van - genotype | AMP | SAM | AX | AMC | PRL | TPZ | IPM | CIP | LEV | VAN | TEC | QD | TGc | LNZ | CN-HLR | S-HLR |
|-------------|-----------------|-----------------|---------|----------------|-----|-----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-------|
| 001         | 15/08/2017      | On admission    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | r   | –    | –     |
| 123         | 01/09/2017      | Pre-existing    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | +   | –    | –     |
| 021         | 07/07/2017      | Pre-existing    | ST721   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 119         | 31/08/2017      | Pre-existing    | ST721   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | +   | –    | –     |
| 143         | 04/09/2017      | Pre-existing    | ST721   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 025         | 02/07/2017      | Pre-existing    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 076         | 25/08/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 085         | 02/08/2017      | Pre-existing    | ST721   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | +   | –    | –     |
| 126         | 05/09/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 189         | 12/09/2017      | On admission    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 204         | 26/09/2017      | On discharge    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 235         | 20/09/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 248         | 27/03/2017      | Pre-existing    | ST721   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 251         | 22/09/2017      | On admission    | NS      | vanA + B       | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | +   | –    | –     |
| 256         | 22/09/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 283         | 02/10/2017      | On discharge    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 291         | 05/10/2017      | On discharge    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 300         | 04/10/2017      | On discharge    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 302         | 25/10/2017      | On discharge    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 314         | 13/10/2017      | On discharge    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 330         | 06/10/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 335         | 04/10/2017      | Pre-existing    | ST80    | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 338         | 09/10/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 348         | 11/10/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 351         | 11/10/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 352         | 02/04/2013      | Pre-existing    | ST117   | vanA           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | +    | –     |
| 361         | 22/10/2017      | On discharge    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 366         | 13/10/2017      | On admission    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |
| 372         | 30/10/2017      | On discharge    | ST117   | vanB           | t   | t   | r  | r   | r   | r   | r   | r   | r   | s   | s   | s   | –   | –    | –     |

MLST: Multilocus sequence typing; AMP: Ampicillin; SAM: Ampicillin/sulbactam; AX: Amoxicillin; AMC: Amoxicillin/clavulanic acid; PRL: Piperacillin; TPZ: Piperacillin/tazobactam; IPM: Imipenem; CIP: Ciprofloxacin; LEV: Levofloxacin; VAN: Vancomycin; TEC: Teicoplanin; QD: Quinopristin/dalfopristin; TGC: Tigecyclin; LNZ: Linezolid; CN-HLR: Gentamicin-high level resistance; S-HLR: Streptomycin-high level resistance; r: Resistant, s: Susceptible, +: positive, -: negative, NS: not sequenced.
Nevertheless, since hospital-acquired VRE colonizations occurred in our patients, risk factors supporting a VRE acquisition in this group of patients were assessed. Here, the median duration of stay, long-term dialysis and the antibiotic treatment with flucloxacillin or piperacillin/tazobactam were found to be the predominant risk factors. These data correspond with previously investigated risk factors and certainly cannot be considered independently but presuppose each other [23, 24], as also verified by the multivariate analysis. Other risk factors that were found to play an important role in VRE acquisition in other patient clientele could not be verified for our SICU patients. Here, the attributed risk of VRE acquisition after cephalosporin treatment needs to be mentioned. Due to perioperative antibiotic prophylaxis standards, especially referring to cardiac surgery patients, approximately 60% of all admitted patients received cefuroxime; however, this did not lead to an increased VRE acquisition rate. This is noteworthy, since cephalosporine use promotes selection of enterococci and thereby VRE due to intrinsic resistance mechanisms. Nevertheless, previous studies could confirm, that cephalosporine use per se during hospitalization does not result in an enhanced VRE carriage [14]. Interestingly, since the duration of application of flucloxacillin and piperacillin/tazobactam did not vary significantly among the hospital-acquired VRE and the non VRE group, the present results suggest that few antibiotic applications can be sufficient to potentially select VRE. The impact of relatively low numbers of antibiotic administrations on selection of certain pathogens corroborates similar findings for the selection of Clostridium difficile [25].
Previous contacts to VRE confirmed patients are often mentioned as a major risk factor in VRE acquisition [26]. Considering the present core genome analysis of isolates, transmission of VRE on ward could not explicitly be excluded in some cases. This may be due to the transmission of this pathogen on inanimate surfaces in advance to the final diagnosis of the VRE status. Hence in case of a confirmed VRE status, adequate basic and, if necessary, intensified hygienic measures consisting of bundle strategies including contact precautions, usage of personal protective equipment, appropriate disinfection strategies, screening of contact patients and antibiotic stewardship should be implemented to avoid transmissions as good as possible.

Our study has limitations. First, the study period was relatively short. Additional risk factors might have been revealed in case of a longer study period. Moreover, distribution of detected MLST ST in found VRE could have been different. Second, we evaluated risk factors promoting VRE carriage, e.g. flucloxacillin and piperacillin/tazobactam application, but did not investigate the pathophysiological background. Future (prospective) studies are needed to reveal underlying mechanisms. Nevertheless, our findings are in accordance with results published previously [27]. Environmental sampling was not performed during the present study, which could have uncovered the role of inanimate surfaces in VRE transmission, especially in cases of clonality of isolates. Another limitation is the problem of screening sensitivity. Here, only one rectal swab was applied on admission and on discharge respectively, which can lead underestimation of VRE prevalence. However, since screening was performed the same way on admission and on discharge, acquisition rate of VRE during SICU stay can still be assessed precisely.
Conclusion

Compared to patient clienteles previously investigated [23, 28–30], SICU patients per se are not at higher risk of VRE acquisition if hygiene measures are applied as recommended. If a risk adapted screening policy is applied as practised in other national institutions [22], stay on a SICU should not be considered as a risk factor for screening upon admission to a healthcare facility.

Abbreviations
SICU: Surgical intensive care unit; VRE: Vancomycin resistant enterococci

Table 3 Characteristics and risk factors of admitted surgical intensive care patients with and without hospital-acquired VRE

| Characteristic                                    | All admitted patients (n = 374) | Patients with acquired VRE (n = 8) | Patients without acquired/ pre-existing VRE (n = 345) | p-value |
|--------------------------------------------------|---------------------------------|-----------------------------------|------------------------------------------------------|---------|
| Demographic data                                 |                                 |                                   |                                                      |         |
| Median age (years)                               | 66 (range: 14–91)               | 71.5 (range: 50–78)               | 65 (range: 14–91)                                    | 0.43    |
| Male gender                                      | 254 (67.9%)                     | 4 (50.0%)                         | 241 (69.9%)                                         | 0.23    |
| Median duration of stay (days)                   | 3 (range: 1–45)                 | 14 (range: 7–30)                  | 3 (range: 1–45)                                     | 0.01    |
| Underlying disease/treatment                     |                                 |                                   |                                                      |         |
| Haemato-oncological disease                      | 62 (16.6%)                      | 1 (12.5%)                         | 58 (16.8%)                                          | 0.74    |
| Immunosuppressive disease                        | 71 (19.0%)                      | 1 (12.5%)                         | 66 (19.1%)                                          | 0.63    |
| Hepatic insufficiency                            | 17 (4.5%)                       | 0 (0%)                            | 15 (4.3%)                                           | 0.55    |
| Liver transplantation                             | 8 (2.1%)                        | 0 (0%)                            | 8 (2.3%)                                            | 0.66    |
| Renal insufficiency                              | 51 (13.6%)                      | 2 (25.0%)                         | 41 (11.9%)                                          | 0.26    |
| Long-term dialysis                               | 10 (2.7%)                       | 1 (12.5%)                         | 7 (2.0%)                                            | 0.05    |
| Systemic glucocorticoid treatment                | 36 (9.6%)                       | 1 (12.5%)                         | 32 (9.2%)                                           | 0.76    |
| Antibiotic treatment                             | 218 (58.3%)                     | 7 (87.5%)                         | 207 (60.0%)                                         | 0.11    |
| Ampicillin                                       | 7 (3.2%)                        | 0 (0%)                            | 4 (1.9%)                                            | 0.76    |
| Amoxicillin                                      | 14 (6.4%)                       | 0 (0%)                            | 13 (3.9%)                                           | 0.58    |
| Flucloxacillin                                   | 20 (9.2%)                       | 2 (28.6%)                         | 15 (7.2%)                                           | 0.01    |
| Piperacillin/tazobactam                          | 62 (28.4%)                      | 4 (57.1%)                         | 55 (26.6%)                                          | 0.01    |
| Cefuroxime                                       | 130 (59.6%)                     | 1 (14.2%)                         | 127 (61.4%)                                         | 0.16    |
| Ceftriazone                                      | 7 (3.2%)                        | 0 (0%)                            | 3 (1.4%)                                            | 0.79    |
| Meropenem                                        | 41 (18.8%)                      | 2 (28.6%)                         | 36 (17.4%)                                          | 0.19    |
| Clindamycin                                      | 7 (3.2%)                        | 0 (0%)                            | 7 (3.4%)                                            | 0.68    |
| Daptomycin                                       | 8 (3.7%)                        | 0 (0%)                            | 5 (2.4%)                                            | 0.73    |
| Linezolid                                        | 3 (1.4%)                        | 0 (0%)                            | 3 (1.4%)                                            | 0.79    |
| Rifampicin                                       | 13 (6.0%)                       | 0 (0%)                            | 10 (4.8%)                                           | 0.63    |
| Erythromycin                                     | 7 (3.2%)                        | 0 (0%)                            | 6 (2.9%)                                            | 0.71    |
| Vancomycin                                       | 19 (8.7%)                       | 0 (0%)                            | 16 (7.7%)                                           | 0.53    |
| Fosfomycin                                       | 7 (3.2%)                        | 0 (0%)                            | 6 (2.9%)                                            | 0.71    |
| Trimethoprim/Sulfamethoxazole                    | 6 (2.8%)                        | 0 (0%)                            | 6 (2.9%)                                            | 0.71    |
| Metronidazole                                    | 8 (3.7%)                        | 0 (0%)                            | 7 (3.4%)                                            | 0.68    |
| Previous contact to healthcare system            |                                 |                                   |                                                      |         |
| Admission from a foreign hospital                | 1 (0.3%)                        | 0 (0%)                            | 1 (0.3%)                                            | 0.88    |
| Admission from a domestic hospital               | 188 (50.2%)                     | 5 (62.5%)                         | 173 (50.0%)                                         | 0.49    |
| Admission from an intensive care unit            | 90 (24.1%)                      | 4 (50.0%)                         | 76 (22.0%)                                          | 0.06    |

Statistical significance was declared at $p \leq 0.05$ (see italicized entries)

Table 4 Multivariate analysis: risk factors associated with VRE acquisition

| Risk factors ($p \leq 0.05$) | Odds Ratio | 95% CI |
|------------------------------|------------|--------|
| Duration of stay             | 0.90       | 0.84–0.96 |
| Long-term-dialysis           | 0.08       | 0.01–1.10 |
| Flucloxacillin treatment     | 0.09       | 0.01–0.60 |
| Piperacillin/tazobactam treatment | 0.24       | 0.05–1.13 |
Authors' contributions
SK and AK: Conception and design of the study, acquisition, analysis and interpretation of data, drafting article. LMC and DK: Acquisition, analysis and interpretation of data, revising article critically. CE, AG and HF: Interpretation of data, revising article critically. AM: Conception and design of the study, interpretation of data, revising article critically. All authors have seen and approved the final version of the manuscript.

Ethics approval and consent to participate
All strategies and investigations were performed in accordance with the recommendations for cluster detections of nosocomial infections of the legally assigned institute for infection control and prevention (Robert Koch Institute). Present analysis was performed after cluster of VRE in SICU patients. Formal consent was therefore not required.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 4 April 2018 Accepted: 14 August 2018
Published online: 23 August 2018

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