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The MRSA-import in ICUs is an important predictor for the occurrence of nosocomial MRSA cases

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Abstract

Nosocomial infections with methicillin-resistant Staphylococcus aureus *(MRSA) account for increased morbidity, mortality and healthcare costs in critically ill patients worldwide. The intensive care unit (ICU) component of the German surveillance system for nosocomial infections (Krankenhaus-Infektions-Surveillance-System, KISS) has been supplemented with a module targeting the surveillance of multiresistant pathogens [Multiresistente Erreger (MRE)-KISS] in order to account for the increasing burden of antibiotic-resistant bacteria. The aim of this study was to assess the association between structural and organizational characteristics of ICUs and the number of nosocomial MRSA cases. Data were derived from routine data collected in the frame of the national surveillance system of nosocomial infections (ICU- and MRE-KISS) from January 2007 to December 2008 and from a questionnaire inquiring about structure and process parameters. One hundred and forty ICUs performing active screening have been included. Process parameters such as isolation of MRSA patients, decolonization procedures and introduction of MRSA alert systems have been implemented by the majority of the ICUs, whereas the application mode of screening procedures and pre-emptive isolation measures is heterogeneous. Multivariable analysis using negative binominal regression models shows that a stay on a medical ICU has a protective effect (incidence rate ratio, 0.42; 95% confidence interval, 0.24–0.74; p = 0.003), whereas the imported MRSA incidence is significantly associated with the number of nosocomial MRSA cases (incidence rate ratio, 1.74; 95% confidence interval, 1.23–2.45; p = 0.002). Structure and process parameters do not show any effect. ICU type and imported MRSA incidence should be considered for benchmarking between hospitals.*

Introduction

Nosocomial infections with multiresistant bacteria, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), play an increasing role in the hospital care of critically ill patients [1]. In Germany, the percentage of MRSA in relation to *Staphylococcus aureus* isolates derived from blood cultures increased from 9% in 1999 to 20% in 2002 [2]. However, in recent years the proportion of MRSA-positive isolates appears to have stagnated in German hospitals, probably due to enhanced infection control measures [3,4].

Cross-transmission by direct contact, such as hands of healthcare workers and visitors and a contaminated environment (e.g. equipment), is an important and preventable cause of the spread of MRSA in hospitals. In order to prevent and control nosocomial MRSA infections, a comprehensive strategy comprising surveillance of nosocomial infections and the spread of MRSA, personal and institutional hygiene measures, surveillance of antibiotic resistance and usage and measures to ensure prudent antibiotic use (e.g. antibiotic stewardship programmes) is necessary [5].

In Germany, a national surveillance system for nosocomial infections has been introduced (Krankenhaus-Infektions-Surveillance-System, KISS) in 1997 [6]. Nosocomial infections in ICUs were recorded in the ICU component of KISS (ICU-KISS). In 2003, ICU-KISS has been supplemented by the multiresistant microorganisms module [Multiresistente Erreger (MRE)-KISS] in order to account for

the growing impact of multiresistant bacteria [7]. Besides infection control and prevention practices, structural parameters of ICUs and hospitals, such as size and type of hospitals and ICUs, the equipment in single bedrooms and ventilator places, may have an influence on the frequency of nosocomial MRSA cases. So far, a systematic investigation of the effect of structural factors on hospital MRSA acquisition has rarely been performed. The aim of this study is to obtain data on structural and organizational characteristics of ICUs participating in ICU- and MRE-KISS and to analyse the association of these factors with the number of nosocomial MRSA cases. Data are derived from routine surveillance reports combined with a structured questionnaire from 140 German ICUs participating in ICU- and MRE-KISS in 2007/2008.

Methods

Monthly recorded numbers of patients, patient days, device days (ventilator, central venous catheter and urinary tract catheter) and patient-based MRSA cases were derived from routine data collected in the frame of the national surveillance system of nosocomial infections (ICU- and MRE-KISS) from January 2007 to December 2008.

In March 2008, a web-based questionnaire was sent out to all ICUs participating in ICU- and MRE-KISS to collect information on structural characteristics and measures for prevention and infection control. From 275 ICUs, 185 (67.3%) questionnaires were completed.

Only those 140 ICUs that perform active screening for MRSA have been included in the analysis, in order to allow for the estimation of nosocomial MRSA acquisition.

The recorded data comprise the following.

- Structural type and size of hospitals and ICUs, geographical region, parameters: and number of ventilator places, single bedrooms and ICUs per hospital.
- Process length of stay, device utilization and MRSA prevention parameters: rate, employed staff, proportion of short stayers (≤48 h), implementation of an MRSA alert system, screening for MRSA on admission, type of screening performed (patients at high risk of MRSA, or all patients), time point of screening, pre-emptive isolation, isolation of confirmed MRSA patients, and decolonization measures.

The following definitions have been used.

- MRSA every patient in whom MRSA has been detected at any body site case: during his/her stay on the ICU, irrespective of whether the patient presents with symptoms of infection or is merely colonized.
- Nosocomial detection of MRSA more than 48 h after admission to the ICU, MRSA case: either as a result of the performance of screening cultures or the investigation of clinical samples.
- detection of MRSA within 48 h after admission to the ICU. Imported MRSA case:
- number of MRSA cases/1000 patients. MRSA incidence density:
- number of nosocomial MRSA cases/1000 patient-days. Nosocomial MRSA incidence density:
- number of imported MRSA cases/100 patients. Imported MRSA incidence:
- Device number of device days/100 patient-days. These rates utilization rate: are calculated separately for invasive ventilation, central venous catheters (CVC) and urinary tract catheters (UTC).
- number of actually employed staff/patient/day/shift. Staff-patient ratio:

Data analysis

The results of descriptive analysis are presented as summary measures appropriate to the data type and distribution. For categorial variables data are expressed in numbers and percentages, and for continuous variables in means and standard deviation (SD) if the variables showed a normal distribution or in medians with interquartile ranges (IQR) for non-normally distributed variables.

Univariate and multivariable analysis has been performed to identify independent risk factors for nosocomial MRSA cases. A negative binominal regression model has been used to estimate the association of the number of nosocomial MRSA cases with the parameters. The log number of patient days was treated as an offset in the model. As the magnitude of the variance of the outcome parameter indicates overdispersion and the dispersion parameter alpha of the likelihood ratio test, which differs significantly from zero, also confirms the presence of overdispersion, negative binominal regression has been used instead of poisson regression. Comparison with a zero inflated model using the Vuong test did not show any advantage over negative binominal regression.

For multivariable analysis a stepwise forward approach has been applied, which considered all variables with a p-value of <0.25 in univariable analysis. The p-value for retention of a covariate in the model was 0.05 to identify independent risk factors.

Comparisons between ICU types and between different hospital sizes have been performed by using the Kruskal–Wallis test and the Wilcoxon rank sum test, respectively.

Calculations have been performed using Stata version 9.

Results

In 140 ICUS, coming from all major geographical regions in Germany, a total of 228 703 patients, accounting for 852 835 patient days, have been treated in 2007/2008. From 4279 MRSA cases 3496 (81.7%) were contracted from outside the hospital and 783 (18.3%) were classified as nosocomial in the ICU.

MRSA situation

The numbers and rates of MRSA in the ICUs are shown in Table 1. Stratification by ICU type shows that medical ICUs exhibit significant ($p = 0.02$) lower numbers of nosocomial MRSA cases/month (median, 0.07; IQR, 0–0.33) as compared with interdisciplinary (median, 0.17; IQR, 0.04–0.42) and surgical ICUs (median,: 0.29; IQR, 0.10–0.54) and show a lower incidence density of nosocomial MRSA cases ($p = 0.006$) as well, presenting with a median incidence of nosocomial MRSA/1000 patient-days of 0.24 (IQR, 0–0.82) in contrast to interdisciplinary and surgical ICUs, which show a median value of 0.64 (IQR, 0.26–1.50) and 0.93 (IQR, 0.41–1.45), respectively. Comparison of the MRSA parameters stratified by hospital size (hospitals ≤1000 beds and hospitals >1000 beds) reveals a higher MRSA incidence density and a higher incidence of imported MRSA in large hospitals >1000 beds (Wilcoxon rank sum test, $p < 0.001$ and $p < 0.001$, respectively), whereas the nosocomial MRSA incidence densities do not show any differences (Wilcoxon rank sum test, $p = 0.34$).

Structural and organizational characteristics

Structural and organizational characteristics of the ICUs are shown in Table 2. The largest proportion of the participating hospitals was classified as academic teaching hospitals (50%). The hospitals were broadly evenly distributed over the main geographical regions in Germany. Ninety-five (67.9%) hospitals have 1000 beds or less and 65 (46.4%) participating ICUs are classified as interdisciplinary. While 51 (36.4%) ICUs screen all patients, 89 (63.6%) ICUs restrict screening to patients at particular risk, including previously known MRSA patients and contact patients. The majority (86.4%) of the ICUs perform screening at the patient's admission, while only a smaller proportion (27.9%) applied screening at regular intervals during their stay. Twenty (14.3%) ICUs combine both strategies. From the 51 ICUs screening all patients, only 14 (27.4%) perform prophylactic isolation measures. In contrast, most ICUs arrange single room isolation of MRSA patients.

Association of nosocomial MRSA cases with structure, process and MRSA-prevention measures of the ICUs

The results of univariate analysis to assess the association between nosocomial MRSA cases and structure, process and MRSA-prevention measures of the ICUs are shown in Table 2. Medical ICUs showed a significantly lower number of nosocomial MRSA cases than interdisciplinary and surgical ICUs. The incidence rate ratio (IRR) for nosocomial MRSA cases was 0.48 (95% confidence interval (CI), 0.31–0.74) compared with interdisciplinary ICUs. Teaching hospitals and 'other hospital types' experience a lower number of nosocomial MRSA cases than university hospitals, but not statistically significantly lower. Similiarly, hospital size does not appear to be related to the number of nosocomial MRSA cases, while ICU sizes of ≥12 beds are associated with more nosocomial MRSA cases (IRR = 1.49; 95% CI, 1.04–2.13). Increased application of devices such as UTCs was associated with a higher rate of nosocomial MRSA cases. The higher incidence of imported MRSA (>0.94) is associated with a 1.8-fold increase in the rate of nosocomial MRSA cases, compared with the lower incidence of imported MRSA.

Multivariable analysis (Table 3) confirms that type of ICU and incidence of imported MRSA cases were independent risk factors for nosocomial MRSA acquisition. The adjusted IRR for medical ICUs, compared with interdisciplinary ICUs, was 0.42 (95% CI, 0.24–0.74) and for ICUs with an incidence of imported MRSA cases greater than the median was 1.74 (95% CI, 1.23–2.46) as compared with those with imported MRSA incidences lower than the median.

Discussion

Multivariable analysis shows that the incidence of imported MRSA is significantly associated with the number of nosocomial MRSA cases in ICUs and that stay on medical ICUs has a protective effect. The latter result does not contradict former studies, which found surgical ICUs to be at particular risk of presenting with high MRSA infection rates [8,9]. The lower number of nosocomial MRSA cases in medical ICUs is probably due to differences in patient characteristics between conservative and surgical medicine with respect to gender, age, underlying diseases, severity of disease, frequency of invasive procedures and antibiotic therapy. Patient-level risk factors have been extensively investigated in former studies [10–12].

The incidence of imported MRSA cases showed a highly significant association with nosocomial MRSA cases, which is plausible because with the increase of the MRSA-positive reservoir the probability of transmission to other patients rises. This result is confirmed by several other studies, which showed that colonization pressure is an independent risk factor for hospital MRSA acquisition [13–15]. In order to account for this close relationship some authors proposed using adjusted MRSA transmission rates for intra- and interhospital comparisons [16,17]. This has to be considered with caution, as the measures characterizing colonization pressure might be strongly influenced by the screening policy of the hospitals [18].

In multivariable analysis none of the structural parameters showed an association with the number of nosocomial MRSA cases. Previous data on the relationship of structural properties of hospitals and ICUs with MRSA acquisition rates are scarce. Grammatico-Guillon *et al.* [8] investigated the relationship of MRSA prevalence and infection control indicators in French hospitals in 2005/2006. They found that private for-profit hospitals present with the lowest MRSA prevalence, but this could be explained by the specific patient population. Hospital ownership has not been considered in the present study. Mears *et al.* [19] found a relationship between availability of single bedrooms and nosocomial MRSA rates, which could not be confirmed in the present study. Another study shows merely descriptive data [20]. The overall negative results imply that probably other factors, which have not been considered in the present study, such as patient-level characteristics, may play a more important role in determining the amount of nosocomial MRSA cases. Another reason might be that hospitals participating in MRE-KISS are too homogenous to detect any differences.

Process-indicators of infection control and prevention measures also did not yield a significant effect in multivariable analysis, which is mainly due to the design of the study, which enables an analysis of the actual situation but does not allow estimating the temporal relationship of dependant and independent

variables. Nevertheless, the data give insight into the current situation and provide a basis for the evaluation of future developments.

Descriptive data show that a wide range of hospital and ICU types and sizes from all major regions of Germany are represented. Most of the infection control and prevention measures are implemented in the majority of the ICUs. Screening and pre-emptive isolation practices, which have been investigated in more detail, provide a more heterogeneous picture. Regarding general organizational factors, such as staff-patient ratio, portion of short-stayers and MRSA-specific infection control measures, no significant differences between ICU types have been seen.

Despite the overall impression of a similar approach in combating the hospital spread of MRSA, underlying heterogeneities can not be excluded. As standardized definitions are missing, the question regarding screening of patients at risk does not specify which patients should be considered to be at risk. As ICUs use individual risk definitions, a positive answer comprises different screening strategies. Additionally, there is no information on other determinants of screening policy, such as the site of screening, which influences the yield of MRSA cases [21,22]. Similarly, staff-patient ratio is an important determinant of hospital staff policy, but reflects only one component of a multifaceted entity. Several other factors, such as bed occupancy and workload, should be considered in order to provide a more comprehensive picture [23].

Another limitation of the study regards the different screening policies, which might result in misclassification. As only 27.9% of the ICUs screen for MRSA at regular intervals (e.g. two fixed days a week), an underestimation of the nosocomial transmission rate has to be assumed. On the other hand, those ICUs that do not screen at admission (13.6%) but perform screening at regular intervals might overlook imported MRSA cases and misclassify imported MRSA cases as hospital acquired.

As the response rate in the study was 67.3% and after exclusion of the non-screeners only 50.9% participants remained, selection bias has to be considered and representativity of the study population for all screening ICUs participating in MRE-KISS can not be warranted. Furthermore, hospitals and ICUs deciding to participate in ICU- and MRE-KISS might differ systematically from those that do not take part in a surveillance system. Thus, the representativity for all German ICUs is difficult to assess.

Another important point to consider is the size of the study. As the study sample is relatively small, it can be assumed that the power is not sufficient to detect small differences. For future studies efforts should be made to enhance the participation rate.

Compliance with infection control procedures, one aspect known to have substantial influence on the effectivity of infection control interventions, has not been addressed in the study [24,25]. Hence, appraisal of the study results should take account of this problematic factor. In this context it should also be kept in mind that the variables that have been included in the study represent only a proportion of the whole spectrum of infection control measures aiming to prevent nosocomial infections as well as the spread of multiresistant pathogens. Thus, there may be several confounding and/or interacting factors, which may not have been considered but nevertheless make an essential contribution to the outcome-measure.

In conclusion, multivariate analysis did not reveal any risk factors or protective effects originating from the structural set-up of hospitals and ICUs and from organizational interventions targeting prevention and control of the spread of MRSA. Nevertheless, it could be shown that medical ICUs experience lower nosocomial MRSA case rates than the other ICU types and that the imported MRSA incidence is si

gnificantly associated with higher numbers of nosocomial MRSA cases. This point should be considered when benchmarking between hospitals.

Transparancy Declaration: The authors declare that they have no conflict of interests in relation to this work.

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Tables

Table 1. Cases and rates of methicillin-resistant *Staphylococcus aureus* (MRSA) in the 140 intensive care units (ICUs), stratified by type of ICU

Parameter	All ICUs median (IQR)	Interdisciplinary ICUs median (IQR)	Medical ICUs median (IQR)	Surgical ICUs median (IQR)	p-value [a]
Number of MRSA cases per month (*n*/month)	1.0 (0.35–1.96)	0.79 (0.41–1.75)	0.92 (0.33–2.04)	1.38 (0.63–2.08)	0.330
Number of nosocomial MRSA cases per month (*n*/month)	0.16 (0.04–0.47)	0.17 (0.04–0.42)	0.07 (0–0.33)	0.29 (0.10–0.54)	0.020
Incidence density of MRSA [b]	3.66 (1.51–6.10)	3.34 (1.30–5.71)	2.94 (1.07–6.06)	3.94 (2.36–6.48)	0.500
Incidence density of nosocomial MRSA [c]	0.59 (0.15–1.35)	0.64 (0.26–1.50)	0.24 (0–0.82)	0.93 (0.41–1.45)	0.006
Incidence of imported MRSA [d]	0.94 (0.35–2.22)	0.68 (0.36–1.58)	0.94 (0.27–2.65)	1.24 (0.50–2.48)	0.380
Median days to nosocomial MRSA case (days)	13.0 (9.0–18.0)	13.0 (9.0–17.5)	14.5 (5.0–19.5)	12.0 (9.0–18.0)	0.990

[a] Kruskal–Wallis rank test.
[b] Incidence density of MRSA, number of MRSA/1000 patient days.
[c] Incidence density of nosocomial MRSA, number of nosocomial MRSA/1000 patient days.
[d] Incidence of imported MRSA, number of imported MRSA/100 patients.

Table 2. Summary of structure, process and MRSA parameters in 140 intensive care units (ICUs) and their association with the number of nosocomial MRSA cases: univariate negative binomial regression model

Characteristic	Number (%)	Incidence rate ratio (95%CI[a])	p-value
Structure parameters			
Type of ICU			
Interdisciplinary	65 (46.4)	Reference	0.001
Medical	34 (24.3)	0.48 (0.31–0.74)	
Surgical	41 (29.3)	1.09 (0.74–1.63)	
Size of ICU			
≤12 beds	78 (55.7)	Reference	0.030
>12 beds	62 (44.3)	1.49 (1.04–2.13)	
Type of hospital			
University	29 (20.7)	Reference	0.490
Teaching	70 (50.0)	0.75 (0.45–1.20	
Other	41 (29.3)	0.83 (0.50–1.40)	
Size of hospital			
<1000 beds	95 (67.9)	Reference	0.542
≥1000 beds	45 (32.1)	1.13 (0.77–1.65)	
Geographical region			
East	33 (23.6)	Reference	0.611
South-east	31 (21.1)	0.74 (0.44–1.25)	
South-west	22 (15.7)	1.18 (0.66–2.10)	
North	21 (15.0)	0.95 (0.53–1.69)	
West	33 (23.6)	1.02 (0.61–1.70)	
Number of ICUs in the hospital			
1–2	77 (55.0)	Reference	0.881
3–13	63 (45.0)	0.97 (0.68–1.40)	
Percentage of single bedrooms/all ICU beds (median, IQR) 20.7 (11.8–36.9)			
≤21%		Reference	0.562
>21%		1.11 (0.78–1.6)	
Number of ventilation places/all ICU beds (median, IQR) 80.0 (50.0–100)			
≤80		Reference	0.620
>80		1.09 (0.77–1.57)	
Staff-patient ratio[b] (median, IQR) 0.93 (0.79–1.06)			
≤0.93		Reference	0.42
>0.93		0.86 (0.60–1.24)	

(Continued on next page)

Portion of short stayers			
<1/3	50 (35.7)	Reference	0.342
1/3–2/3	77 (55.0)	0.78 (0.52–1.12)	
≥2/3	13 (9.3)	1.01 (0.54–1.92)	
Process parameters			
Length of stay in days (median, IQR) 3.8 (2.9–5.1)			
≤4		Reference	0.262
>4		1.23 (0.86–1.78)	
CVC rate[c] (mean, SD) 68.1 (18.0)			
<55.4		Reference	0.050
55.4–70.6		1.28 (0.78–2.13)	
70.7–81.1		2.00 (1.21–3.29)	
>81.1		1.28 (0.78–2.11)	
UTC rate[d] (mean, SD) 80.4 (13.7)			
<73.8		Reference	0.001
73.9–82.9		1.96 (1.18–3.25)	
83.0–89.9		2.62 (1.59–4.34)	
>89.9		2.33 (1.41–3.89)	
Invasive ventilation rate[e] (mean, SD) 40.0 (17.1)			
<26.7		Reference	0.110
26.8–38.3		1.38 (0.82–2.32)	
38.4–50.8		1.78 (1.07–2.97)	
>50.8		1.72 (1.03–2.87)	
MRSA parameters			
Incidence of imported MRSA[f] (median, IQR) 0.94 (0.35–2.22)			
≤0.94		Reference	0.001
>0.94		1.81 (1.28–2.55)	
Alert system for MRSA			
No	18 (12.9)	Reference	0.708
Yes	122 (87.1)	1.11 (0.64–1.93)	
Screening			
Of risk patients[g]	89 (63.6)	Reference	0.560
Of all patients	51 (36.4)	1.03 (0.90–1.19)	
Timepoint of screening			
At admission only	101 (72.1)	Reference	0.255
Regularly only	19 (13.6)	1.21 (0.72–2.06)	
At admission and regularly	20 (14.3)	1.50 (0.91–2.46)	
Pre-emptive isolation of all patients on ICUs screening all admitted patients			
No	37 (72.6)	Reference	0.190
Yes	14 (27.4)	1.50 (0.82–2.71)	
Single room isolation of MRSA patients			
No	10 (7.1%)	Reference	0.463
Contact precautions only	118 (84.3)	0.72 (0.37–1.39)	
Single room isolation	12 (88.6)	0.57 (0.24–1.39)	
Decolonization of MRSA patients			
No	10 (7.6)	Reference	0.980
Mupirocin only	26 (19.7)	0.93 (0.42–2.07)	
Mupirocin and antiseptic washings	96 (72.7)	0.93 (0.46–1.89)	

[a] CI, confidence interval.
[b] Staff-patient ratio, number of staff/patient/day/shift.
[c] CVC rate, central venous catheter-rate; number of CVC-days/100 patient-days, quartiles.
[d] UTC rate, urinary tract catheter rate; number of UTC-days/100 patient days, quartiles.
[e] Invasive ventilation rate, number of invasive ventilation-days/100 patient-days, quartiles.
[f] Incidence of imported MRSA, number of imported MRSA/100 patients.
[g] For example, patients with chronic wounds, previous stay in a healthcare facility and other risk factors.