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Original Article

Identifying patients at high risk for multidrug-resistant organisms after hospitalization abroad

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Abstract

Objectives: We quantified the percentage of multidrug-resistant organism (MDRO) carriers among repatriated patients. We identified factors associated with MDRO carriage, and we evaluated the yield of MDRO detection per screened body site.

Design: Retrospective cohort study.

Setting: A tertiary-care center in Switzerland.

Patients: Adult patients after a stay in a healthcare institution abroad.

Methods: Patients were screened for MDRO carriage. Standard sites, including nose and throat, groins, and (since mid-2018) rectum, and risk-based sites (wounds, urine, tracheal secretion) were sampled. MDROs were defined as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), extended-spectrum β-lactamase (ESBL)– and carbapenemase-producing Enterobacterales (CPE), multidrug-resistant (MDR) Enterobacterales, and MDR nonfermenting gram-negative rods. Risk factors for MDRO carriage were assessed using multivariate logistic regression.

Results: Between May 2017 and April 2019, 438 patients were screened and 107 (24.4%) tested positive for an MDRO, predominantly ESBL-producing and MDR Enterobacterales. Risk factors for MDRO colonization were the length of stay in hospital abroad, antibiotic treatment with 'Watch' and 'Reserve' antibiotics, and region of hospitalization abroad. Rectal swabs had the highest yield for detecting patients with MDR intestinal bacteria, but nose/throat and groins, or wound samples were more sensitive for MRSA or nonfermenting gram-negative organisms, respectively.

Conclusions: We identified risk factors for MDRO carriage and body sites with the highest yield for a specific MDRO, which might help to target screening and isolation and reduce screening costs.

The number of patients colonized or infected with multidrug-resistant organisms (MDROs), such as carbapenemase-producing Enterobacterales (CPE) or vancomycin-resistant *Enterococcus* (VRE), is rapidly and continuously increasing.[1,2] Nevertheless, MDRO prevalence rates differ between countries, and northern and central European countries generally have lower prevalence.[3,4] Various studies have found that, among other reasons, globalization, trade, and travel drive global MDRO spread.[5,6] Accordingly, new resistance mechanisms can be traced back to their probable place of origin across the globe, exemplified by the gene encoding for colistin resistance *mcr-1*.[7]

Until the COVID-19 pandemic, international travel was increasing and each year >1 billion people traveled for professional, social, and recreational purposes.[8] Additionally, medical tourism has been a more recent and increasing phenomenon.[9] Intentionally or not, some travelers find themselves hospitalized in a foreign country due to illness, accident, or elective medical care. As a result, repatriation to a healthcare institution in their home country is often required, as evidenced by an increase of repatriations to a Swiss level-1 trauma center between 2000 and 2011.[10] Because hospitalization in high-prevalence regions is commonly known as a risk factor for MDRO colonization,[11–18] patients repatriated from hospitals abroad pose a considerable risk of introducing MDROs into the receiving hospital.

To prevent the in-hospital spread of MDROs, hospitals in low-prevalence regions often look after the repatriated patients with

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pre-emptive isolation precautions and screening for MDRO carriage.[16,19] However, only a handful of studies have assessed risk factors for MDRO carriage in patients who received medical care abroad. Also, little is known about body sites yielding the highest MDRO colonization in such patients. A better understanding of these factors could help to estimate the individual risk of a repatriated patient and to perform more cost-effective admission screening. We quantified the prevalence of patients with MDRO among patients repatriated to a Swiss tertiary-care hospital, identified risk factors for MDRO carriage, and evaluated the relevance of the screened body sites regarding MDRO carriage.

Methods

Study setting and design

The university hospital in Zurich (USZ) is a tertiary-care center with 950 beds in Switzerland with ~40,000 annual admissions. Patients treated in healthcare facilities abroad within the previous 3 months and for >12 hours cumulatively are managed with pre-emptive contact isolation precautions and are screened for MDRO on admission. This retrospective cohort study included all patients who received MDRO admission screening after repatriation between May 2017 and April 2019. Patients aged <18 years and patients with known MDRO colonization were excluded.

Admission screening and MDRO definition

In this study, MDROs included methicillin-resistant *Staphylococcus aureus* (MRSA), VRE, CPE, extended-spectrum β-lactamase (ESBL)–producing Enterobacterales, multidrug-resistant (MDR) Enterobacterales, and MDR nonfermenting gram-negative rods. MDR was defined as resistance to at least 3 of 5 classes of antibiotics: piperacillin-tazobactam, third- and fourth-generation cephalosporins, carbapenems, aminoglycosides, and fluoroquinolones (Supplementary Table 1 online).

MDRO admission screening included swabbing the 'standard' sites—nose and throat, groins, and (since May 2018) rectum—within the first 24 hours after admission. Additionally, as a 'risk-based' expansion of the standard sites, wounds were swabbed if present and accessible, urine and tracheal secretions were sampled if the patient had an indwelling urinary catheter or an endotracheal (or tracheostomy) tube, respectively. Clinical samples (eg, blood cultures) were taken at the discretion of the care team and were included in the analysis if they were taken within the first 24 hours after admission, assuming that these isolates were certainly externally acquired (Supplementary Table 2 online).

Microbiological methods

Microbiologic samples were processed in the clinical microbiology laboratory of the USZ Institute of Medical Microbiology. Groins, risk-based screening sites, and clinical samples were screened for all MDROs. Nose/throat samples were screened for all MDROs except VRE. Rectal samples were screened for all MDROs except MRSA. In general, antimicrobial susceptibility testing (AST) was performed by disc diffusion according to EUCAST guidelines[20,21] and as previously described.[22] Species identification of all potential pathogens was performed using matrix-assisted laser desorption ionization–time-of-flight mass spectrometry (MALDI-TOF MS, Bruker Daltonics, Bremen, Germany) with the direct transfer-formic acid method.[23] Detailed microbiologic screening methods for all MDROs are described in Supplementary Table 3 (online).

Data collection and definitions

Demographic data, MDRO screening results, and data about hospital stay abroad (eg, length, antibiotic treatment, ward affiliation) were gathered by an in-depth review of electronic medical records, including reports from foreign hospitals. Geographical regions were clustered to northwestern Europe, southeastern Europe, North America, South America, Africa, and Asia.[28] Antibiotic use in hospitals abroad was classified into categories of 'Access', 'Watch' and 'Reserve' antibiotics according to the World Health Organization (WHO) AWaRe classification database 2019 (Supplementary Table 2 online).[29]

The analysis was conducted as part of a quality improvement project and received a waiver from the Zurich Cantonal Ethics Commission regarding the necessity for a formal ethical evaluation (no. Req-2019-00454).

Statistical analysis

We used χ^2 tests to test differences in categorical variables. For comparison of continuous variables, we used the Student t test. The relationship between the screening outcome (MDRO carrier) and potential risk factors were analyzed using univariate and multivariate logistic regression. Due to the large number of risk factors, multicollinearity between them, and the limited number of observations, we reduced the number of risk factors in the multivariate model by bidirectional elimination based on Akaike information criterion (AIC) starting with the full model including all risk factors. All statistical analysis was conducted in R version 4.0.3 software (R Foundation for Statistical Computing, Vienna, Austria).

Results

The patient population included 438 individuals (Table 1). A total of 286 (65.3%) patients were male, most (n = 202, 46.1%) belonged to the age category of 50–70 years, and were repatriated from countries within Europe (n = 310, 70.8%), predominantly from southeast Europe (n = 212, 48.4%). The median length of hospital stay abroad was 6 days (interquartile range [IQR], 3–11 days), and 258 patients (58.9%) received antibiotic treatment abroad. Also, 128 patients (29.2%) needed treatment in the ICU, 108 patients (24.7%) underwent surgery, and 58 patients (13.2%) needed both ICU and surgery.

Overall, 107 MDRO carriers were identified, corresponding to 24.4% of repatriated patients. The most frequently identified MDROs were ESBL-producing bacteria (n = 80, 18.3%), followed by MDR Enterobacterales (n = 56, 12.8%). In total, 13 patients (3.0%) carried MRSA, 20 patients (4.6%) carried VRE, 13 patients (3.0%) carried CPE, and 19 patients (4.3%) carried MDR nonfermenting gram-negative isolates. Table 2 shows the percentage of patients colonized with an MDRO per geographic region. The most frequently isolated ESBL-producing bacteria were *Escherichia coli* (48 isolates) and *Klebsiella pneumoniae* (38 isolates) (Supplementary Table 4 online). Among the patients with an MDRO, 64 patients (59.8%) carried only 1 MDRO, 31 patients (29.0%) carried 2 MDROs, and 12 patients (11.2%) carried 3 or more MDROs. In 6 (1.3%) of 438 patients with negative admission screening, an MDRO was identified only during hospitalization in the USZ. Another 8 patients were identified to carry an additional MDRO. Of these 14 patients (3.2%), 9 were identified within 1 week, with a median of 4 days (IQR, 3–5 days), and the remaining 5 patients were discovered much later during hospitalization.

Table 1. Patient Characteristics and Risk Factor Analysis for MDRO Colonization

Variable	Patients (n=438), No. or Indicated Otherwise	MDRO Carriers (n=107, 24.4%) No. (%) or Indicated Otherwise	Non-MDRO Carriers (n=331, 75.6%), No. (%) or Indicated Otherwise	Odds Ratio (95% CI) in Univariate Analysis	P Value in Univariate Analysis	Adjusted Odds Ratio (95% CI) in Multivariate Analysis	P Value in Multivariate Analysis
Age							
<30 y	41	11 (27)	30 (73)	1			
30–50 y	86	22 (26)	64 (74)	0.94 (0.41–2.24)	.881		
50–70 y	202	49 (24)	153 (76)	0.87 (0.42–1.94)	.728		
>70 y	109	25 (23)	84 (77)	0.81 (0.36–1.9)	.619		
Sex							
Male	286	66 (23)	220 (77)	1			
Female	152	41 (27)	111 (73)	1.23 (0.78–1.93)	.367		
Affiliation							
Surgery	185	39 (21)	146 (79)	1			
Medicine	253	68 (27)	185 (73)	1.38 (0.88–2.17)	.164		
Region of hospital stay abroad							
Northwestern Europe	98	10 (10)	88 (90)	1		1	
Southeastern Europe	212	43 (20)	169 (80)	2.24 (1.11–4.91)	**.032**	1.82 (0.87–4.11)	.127
North America	22	6 (27)	16 (73)	3.3 (1–10.25)	**.041**	1.97 (0.52–6.94)	.297
Africa	20	8 (40)	12 (60)	5.87 (1.92–18.02)	**.002**	3.87 (1.19–12.54)	**.023**
Asia	70	31 (44)	39 (56)	6.99 (3.22–16.35)	**<.001**	4.03 (1.72–10.02)	**.002**
South America	14	9 (64)	5 (36)	15.84 (4.61–61.16)	**<.001**	7.73 (1.99–33.28)	**.004**
Australia and Oceania[a]	2	0 (0)	2 (100)	0 (NA–1.3×10^37)	.984	–	–
ICU stay abroad							
No ICU stay	310	68 (22)	242 (78)	1			
ICU stay	128	39 (30)	89 (70)	1.56 (0.98–2.47)	.060		
Surgery abroad							
No surgery abroad	330	73 (22)	257 (78)	1			
Surgery abroad	108	34 (31)	74 (69)	1.62 (0.99–2.61)	.051		
Antibiotic therapy abroad							
No antibiotic therapy	180	20 (11)	160 (89)	1		1	
Antibiotic therapy: 'Access' category only	39	9 (23)	30 (77)	2.4 (0.96–5.66)	.051	1.22 (0.41–.29)	.707
Antibiotic therapy: 'Watch' or 'Reserve' categories, or unknown category	219	78 (36)	141 (64)	4.43 (2.62–7.77)	**<.001**	2.85 (1.59–5.28)	**.001**
Direct transfer[b]							
No	75	23 (31)	52 (69)	1			
Yes	356	82 (23)	274 (77)	0.68 (0.39–1.19)	.163		
Length of stay abroad, mean d (SD)	8.73 (9.4)	13.4 (13.0)	7.3 (7.4)	1.71 (1.42–2.09)[c]	**<.001**	1.44 (1.17–1.79)[c]	**.001**
Rectal sampling							
Not taken	221	46 (21)	175 (79)	1		1	
Taken	217	61 (28)	156 (72)	1.49 (0.96–2.32)	.076	2.12 (1.27–3.59)	**.005**
Urine sampling							
Not taken	281	59 (21)	222 (79)	1			
Taken	157	48 (31)	109 (69)	1.66 (1.06–2.58)	**.026**		

(Continued)

Table 1. (*Continued*)

Variable	Patients (n=438), No. or Indicated Otherwise	MDRO Carriers (n=107, 24.4%) No. (%) or Indicated Otherwise	Non-MDRO Carriers (n=331, 75.6%), No. (%) or Indicated Otherwise	Odds Ratio (95% CI) in Univariate Analysis	P Value in Univariate Analysis	Adjusted Odds Ratio (95% CI) in Multivariate Analysis	P Value in Multivariate Analysis
Tracheal secretion sampling							
Not taken	402	94 (23)	308 (77)	1			
Taken	36	13 (36)	23 (64)	1.85 (0.88–3.75)	.093		
Wound sampling							
Not taken	308	65 (21)	243 (79)	1			
Taken	130	42 (32)	88 (68)	1.78 (1.12–2.82)	**.013**		
Blood culture sampling							
Not taken	330	72 (22)	258 (78)	1			
Taken	108	35 (32)	73 (68)	1.72 (1.06–2.77)	**.027**		

Note. AWaRe, 'Access', 'Watch', 'Reserve' classification of antibiotics according to the WHO; CI, confidence interval; ICU, intensive care unit; log, logarithm; MDRO, multidrug-resistant organism; SD, standard deviation; WHO, World Health Organization.
Antibiotic consumption was classified into 'Access', 'Watch' and 'Reserve' categories defined by the WHO AWaRE classification; unknown antibiotic consumption was grouped with categories 'Watch' and 'Reserve'. Bold indicates statistical significance.
[a]Australia and Oceania is not included in the multivariate logistic regression analysis due to low patient number.
[b]Information of 8 patients was missing and not included in the analysis.
[c]The continuous predictor 'length of stay abroad' is log-transformed for our uni- and multivariate analysis, ie, odds ratio with respect to a doubling of the length of stay abroad.

Table 2. Type of Multidrug-Resistant Organism (MDRO) and Percentage of Carriers per Geographic Region

MDRO	Africa (n=20), No. (%)	Asia (n=70), No. (%)	North America (n=22), No. (%)	NW Europe (n=98), No. (%)	SE Europe (n=212), No. (%)	South America (n=14), No. (%)	Australia and Oceania (n=2), No. (%)	All Countries (n=438), No. (%)
Total MDROs	8 (40.0)	31 (44.3)	6 (27.3)	10 (10.2)	43 (20.3)	9 (64.3)	0 (0.0)	107 (24.4)
MRSA	0 (0.0)	4 (5.7)	1 (4.6)	1 (1.0)	6 (2.8)	1 (7.1)	0 (0.0)	13 (3.0)
VRE	0 (0.0)	4 (5.7)	1 (4.6)	3 (3.1)	11 (5.2)	1 (7.1)	0 (0.0)	20 (4.6)
CPE	1 (5.0)[a]	5 (7.1)[b]	0 (0.0)	0 (0.0)	6 (2.8)[c]	1 (7.1)[d]	0 (0.0)	13 (3.0)
ESBL-producing Enterobacterales	8 (40.0)	27 (38.6)	3 (13.6)	5 (5.1)	28 (13.2)	9 (64.3)	0 (0.0)	80 (18.3)
MDR Enterobacterales	7 (35.0)	16 (22.9)	2 (9.1)	3 (3.1)	20 (9.4)	8 (57.1)	0 (0.0)	56 (12.8)
MDR nonfermenting gram-negatives	2 (10.0)	8 (11.4)	1 (4.6)	0 (0.0)	6 (2.8)	2 (14.3)	0 (0.0)	19 (4.3)

Note. CPE, carbapenemase-producing Enterobacterales; ESBL, extended-spectrum β-lactamase; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; NW, northwest; SE, southeast; VRE, vancomycin-resistant enterococci; No., number of patients carrying an MDRO per geographic region; 'Total MDROs' includes all listed MDROs.
[a]1 OXA-48–type carbapenemase.
[b]3 NDM-1–type carbapanemase, 1 VIM-type carbapanemase, 1 OXA-like–type carbapenemase.
[c]3 OXA-48–type carbapanemase, 2 NDM-1–type carbapanemase, 1 KPC-type carbapenemase.
[d]1 KPC-type carbapenemase.

The results of our risk factor analysis are shown in Table 1. Factors significantly associated with MDRO colonization were the length of stay in hospital abroad, antibiotic treatment with 'Watch' and 'Reserve' antibiotics, and region of hospitalization. Because rectal screening was introduced during our study period and was expected to increase the number of positive screenings, we included it as a covariate in the analysis. Rectal screening was associated with MDRO detection.

Figure 1 illustrates the yield of screening sites for MDRO detection. Of the standard screening sites, rectal samples showed the highest percentage of MDRO positivity. Of the risk-based screening sites, tracheal secretion had the highest yield to detect an MDRO. The rectal swab had the highest detection rate (83.6%; 95% confidence interval [CI], 71.9%–91.9%) for the respective MDRO in a patient identified as an MDRO carrier, with >80% for intestinal bacteria such as MDR and ESBL Enterobacterales, CPE, and VRE. MRSA was most often revealed in nose/throat and groin samples. Nonfermenting gram-negative organisms were mainly identified in tracheal secretion or wound samples. Up to mid-2018, groin samples were used as an approximation to gut colonization. A comparison of the yield of the rectal and groin sampling sites showed that VRE and Enterobacterales were more often identified in rectal samples, but groin samples did rarely identify microorganisms not detected in rectal swabs (Fig. 2).
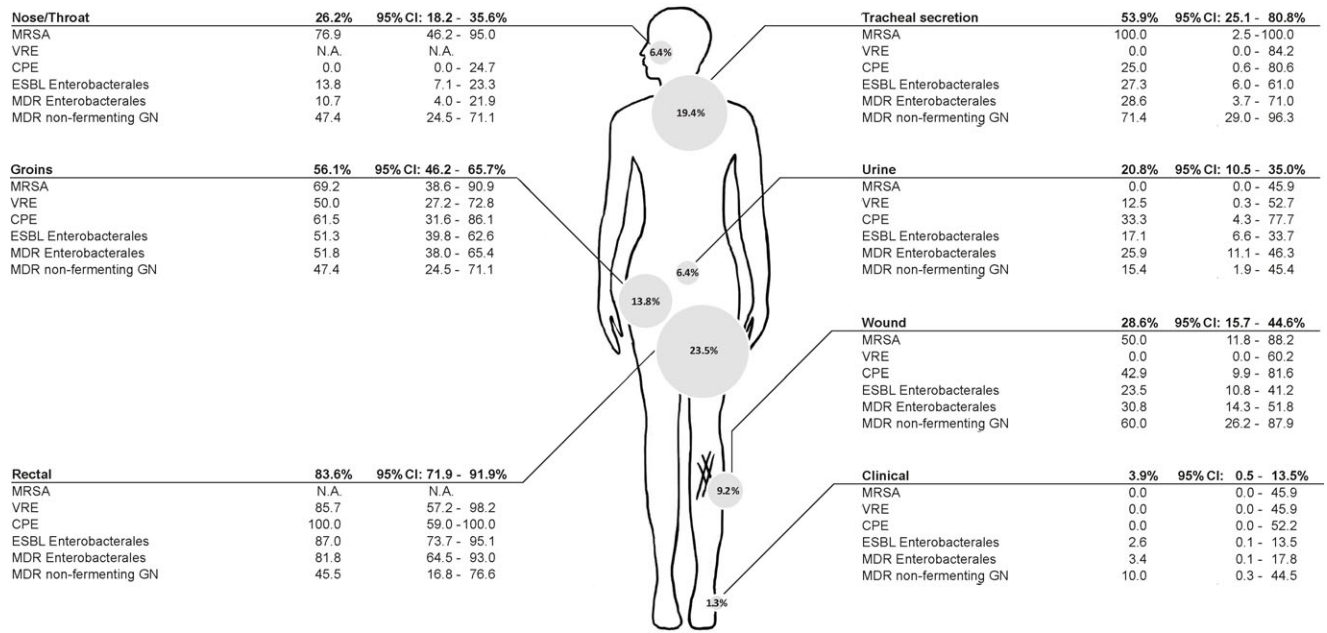
Fig. 1. MDRO detection per body site. The numbers in gray circles and its size represent the percentage of screening positivity rate for any MDRO in all patients per sampling site. Listed sampling sites and numbers in bold font are percentages of positive sites in diagnosed MDRO carriers and—in regular font—the percentage of positive sites in carriers of the specific organism. Note. CI, Confidence Interval; CPE, carbapenemase-producing Enterobacterales; ESBL, extended-spectrum β-lactamase; MDR, multidrug-resistant; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.
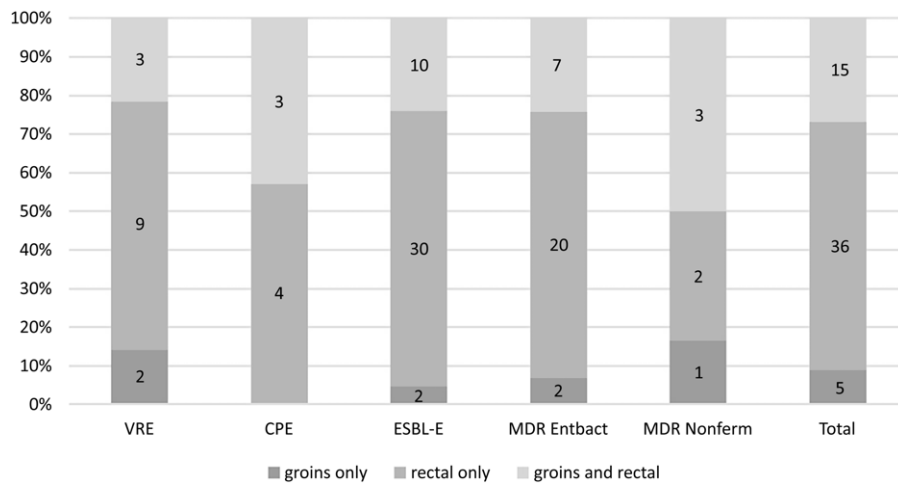

Fig. 2. Comparison of MDRO detection in rectal and groin samples. This figure compares groin and rectal samples of 5 single MDROs and 'total' (all 5 separately depicted MDROs). 'Groins only': MDROs were detected in groin but not rectal samples. 'Rectal only': MDROs were detected in rectal but not groin samples. 'Groins and rectal': MDROs were detected in both rectal and groin samples. Numbers in bars are absolute numbers of positive screening sites. Note. CPE, carbapenemase-producing Enterobacterales; Entbact, Enterobacterales; ESBL-E, extended-spectrum β-lactamase-producing Enterobacterales; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; Nonferm, nonfermenting gram-negative organisms; VRE, vancomycin-resistant enterococci.

Figure 3 shows the positivity rate over time of patients identified with and without considering rectal screening results. After the introduction of rectal screening, a considerable proportion of MDRO carriers were identified by rectal screening only. Simultaneously, the percentage of MDRO carriers identified by other screening sites dropped from 28.1% to 13.4% ($P < .001$), and this change was mainly driven by a decrease in ESBL Enterobacterales in groin swabs from 21.2% to 8.3% ($P < .001$) (data not shown). A comparison of patient groups with and without rectal screening (ie, roughly before and after introduction of rectal screening) showed that patients with rectal swabs received 'Watch', 'Reserve' or antibiotics of unknown category less often (44.7 vs 55.2%; $P = .028$). Also, these patients were less often directly transferred to the USZ (78.0 vs 87.1%; $P = .013$). The remaining exposures were comparable (Supplementary Table 5).

Discussion

In patients repatriated to a Swiss tertiary-care center between 2017 and 2019, 107 (24.4%) of patients carried an MDRO. The most common MDROs were ESBL-producing Enterobacterales and MDR Enterobacterales, followed by VRE and MDR nonfermenting gram-negative isolates. The overall highest chance to detect Enterobacterales and VRE was in the rectal swab. MRSA was most often identified by nose/throat or groin swab. Nonfermenting gram-negative isolates were identified in wound or tracheal secretion samples. Another 14 patients were identified with a new MDRO during their hospital stay and thus might have been missed by the admission screening. Risk factors for MDRO colonization were the length of hospital stay abroad, antibiotic treatment with 'Watch' and 'Reserve' antibiotics, and geographic region of previous hospitalization.
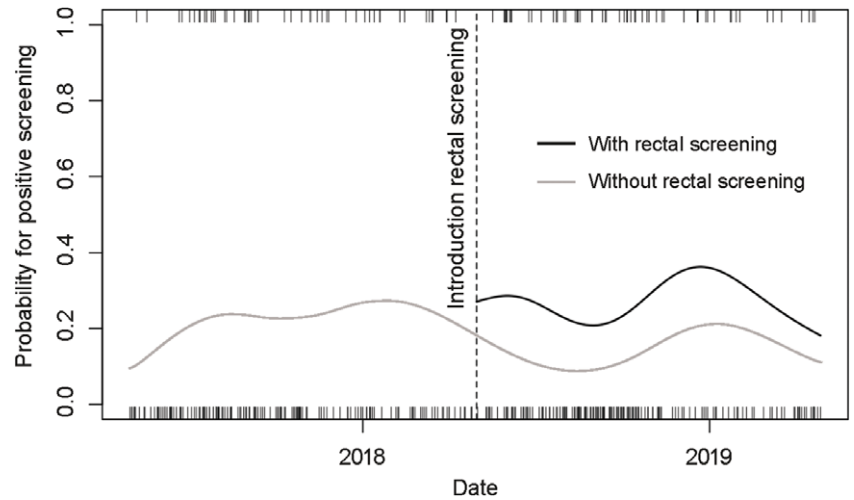
Fig. 3. Positivity rates of admission screening with and without rectal samples. The black line shows the positivity rate of patients with rectal screening, which was newly introduced after mid-2018. The gray line shows the positivity rate of patients without rectal screening or without taking into consideration the results of rectal screening if executed. Ticks along the lower axis indicate a negative screened patient; along the upper axis they indicate a positive screened patient.

The rate of 24.4% MDRO carriers identified in our hospital is slightly higher than the rates reported in earlier studies from Switzerland. Nemeth et al,[12] who analyzed patients admitted to our hospital in 2009–2011, reported a rate of 17% MDRO carriers, but their study varied from the current study in not including rectal screening and not considering VRE as an MDRO.[12] Kaspar et al,[18] analyzing patients repatriated to a tertiary-care hospital in Bern, Switzerland, in 2012–2013, found a rate of 18% MDRO carriers by applying a comparable screening methodology and definition of patients at risk. However, this study also did not include VRE as an MDRO.[18] In comparison, a large study from Finland by Khawaja et al. found almost 30% of MDRO carriers in patients from 2010–2013.[17] The difference in these positivity rates could be attributed to the higher percentage of patients from high-risk countries and the consistent application of rectal screening. Notably, admission screening results for MDRO remarkably differ depending on MDRO definition, the screening sites, the microbiological methods applied, and the exposures of the included patient population.

To focus on screening and pre-emptive isolation for patients at high risk for MDRO carriage, we sought to identify factors associated with MDRO colonization. We identified 3 relevant risk factors. First, the country from which the patient was repatriated was a risk factor. Compared to northwestern Europe, the risk for MDRO colonization tended to be higher in patients from southeastern Europe and North America (without reaching statistical significance) as well as patients from Asia, Africa, and South America. This finding roughly mirrors the epidemiologic situation of antibiotic resistance in these world regions[3,4,30] and is in line with the findings of other studies.[11,14,17] Second, antibiotic therapy with 'Watch' and 'Reserve' antibiotics almost tripled the odds of carrying an MDRO. Other studies have also identified antibiotics as a risk factor.[11,13–15,17,18] However, our study was unique in distinguishing between different antibiotic categories according to the WHO AWaRe classification.[29] Therapy with the 'Access' group of antibiotics only was not associated with MDRO colonization, and this finding was rather unexpected because all antibiotics are expected to cause selective pressure. The association of 'Watch' and 'Reserve' categories of antibiotics with MDRO carriage might be due to administering these antibiotics to patients with known MDRO colonization or infection. Furthermore, this association might be an indicator for prolonged antibiotic treatment (a prerequisite for MDRO selection), or the antibiotics might have been used empirically if local epidemiology required it. In our model, we corrected only for the last factor by including the geographic region of previous hospitalization in the multivariable model. Third, as previously shown,[11,13] we identified prolonged length of stay, and thus prolonged exposure to the local epidemiology, as an independent risk factor for MDRO colonization. Patient-specific parameters like age and sex were not associated with MDRO carriage. However, our study included only adults and thus was not designed to confirm the finding of Khawaja et al[17] that small children are at highest risk. In contrast to other studies, a stay in the ICU and surgery were not predictors for MDRO colonization.[13,14,17,18]

We assessed the most relevant screening sites for MDRO detection and found that rectal screening alone identified >80% of patients with colonization with ESBL-producing or MDR Enterobacterales, CPE, and VRE, which is in line with other studies.[31–35] Until mid-2018, our hospital chose a screening method without a rectal sample to screen mainly for MRSA carriage and for colonization with MDR gram-negative pathogens at sites relevant for bacterial spread such as the skin, wounds, or urine in patients with catheters. Nevertheless, with the increasing prevalence of CPE and VRE, the necessity arose to include a rectal swab to increase detection rates for these highly relevant pathogens. Rectal swabs more than doubled the detection of Enterobacterales and enterococci compared to groin swabs. Peculiarly, in parallel to the implementation of rectal screening, groin positivity rates decreased. A patient population at lower risk (cf, indicated by lower numbers of patients receiving 'Watch' or 'Reserve' antibiotics and patients directly transferred to USZ) might partly explain this decrease, but we cannot exclude a change in bedside groin sampling technique or other unknown factors.

Even for intestinal bacteria, screening sensitivity can be further improved by swabbing sites other than the rectum. Van Prehn et al[34] showed that 14% of ESBL carriers were not identified by the rectal sample but by testing other sites like the urogenital region, respiratory tract, and pus. For patients with MRSA, our study showed that the nose/throat and groin samples were both positive in 60%–70% of all positive patients, but swabbing single sites such as nares or skin may overlook a considerable percentage of carriers,[36,37] and other sites like wounds are worth sampling.[36,38] For MDR nonfermenting gram-negative rods, literature is scarce, and our results suggest both standard and risk-based sampling of multiple sites to help detect these pathogens. Importantly, even

with the extensive sampling we applied, another 1.3% of MDRO carriers were detected during their hospital stay. This finding could be due to an acquisition of MDRO while staying in our hospital, but in our low-prevalence region, a false-negative admission screening is probably equally likely. For instance, >50% of rectal screens are negative in VRE-colonized patients[39]; therefore, a certain percentage of other MDRO probably are missed, too. Repetitive screening might overcome this issue and is already performed in other institutions.[15] Rectal swabs could be quality tested, either by visual inspection for stool on the swab or with microbiologic methods to confirm intestinal flora.

This study had several limitations. It had a single-center design with a specific patient population and a center-specific definition of MDRO, which limits the generalizability of our results. Second, the data were collected retrospectively, and most information about hospitalization abroad was gathered from discharge reports, which sometimes included superficial information only. Moreover, despite the effort to exclude patients with known colonization with an MDRO, the carrier status was often not given and thus was assumed to be negative. Therefore, MDRO acquisition may have occurred before hospitalization abroad.

In conclusion, we identified a high percentage of almost 25% of repatriated patients as MDRO carriers. Certain patients are colonized more often, and a screening based on risk factors might be more cost-effective than a universal screening of all repatriated patients. Additionally, choosing the screening spectrum specific to the anticipated pathogen per site might further reduce the costs of an admission screening. Our manuscript can guide both the targeted screening of at-risk patients and the selection of screening spectrum per site. However, the decision about the targeted screening sensitivity resides with the admitting hospital, bearing in mind the potential downsides of extensive screening, especially antibiotic overtreatment.

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