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Risk of acquiring multidrug-resistant Gram-negative bacilli from prior room occupants in the intensive care unit

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Abstract

The objective of this prospective cohort study was to determine whether admission to an intensive care unit (ICU) room previously occupied by a patient with multidrug-resistant (MDR) Gram-negative bacilli (GNB) increases the risk of acquiring these bacteria by subsequent patients. All patients hospitalized for >48 h were eligible. Patients with MDR GNB at ICU admission were excluded. The MDR GNB were defined as MDR *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and extended spectrum β-lactamase (ESBL) -producing GNB. All patients were hospitalized in single rooms. Cleaning of ICU rooms between two patients was performed using quaternary ammonium disinfectant. Risk factors for MDR *P. aeruginosa*, *A. baumannii* and ESBL-producing GNB were determined using univariate and multivariate analysis. Five hundred and eleven consecutive patients were included; ICU-acquired MDR *P. aeruginosa* was diagnosed in 82 (16%) patients, *A. baumannii* in 57 (11%) patients, and ESBL-producing GNB in 50 (9%) patients. Independent risk factors for ICU-acquired MDR *P. aeruginosa* were prior occupant with MDR *P. aeruginosa* (OR 2.3, 95% CI 1.2–4.3, p 0.012), surgery (OR 1.9, 95% CI 1.1–3.6, p 0.024), and prior piperacillin/tazobactam use (OR 1.2, 95% CI 1.1–1.3, p 0.040). Independent risk factors for ICU-acquired *A. baumannii* were prior occupant with *A. baumannii* (OR 4.2, 95% CI 2–8.8, p <0.001), and mechanical ventilation (OR 9.3, 95% CI 1.1–83, p 0.045). Independent risk factors for ICU-acquired ESBL-producing GNB were tracheostomy (OR 2.6, 95% CI 1.1–6.5, p 0.049), and sedation (OR 6.6, 95% CI 1.1–40, p 0.041). We conclude that admission to an ICU room previously occupied by a patient with MDR *P. aeruginosa* or *A. baumannii* is an independent risk factor for acquisition of these bacteria by subsequent room occupants. This relationship was not identified for ESBL-producing GNB.

Keywords: *Acinetobacter baumannii*, colonization, environmental contamination, extended spectrum β-lactamase, Gram-negative bacilli, multidrug-resistant bacteria, *Pseudomonas aeruginosa*, room cleaning
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Introduction

Multidrug resistant (MDR) bacteria are common among intensive care unit (ICU) patients. According to the results of a recent large international study performed in 1265 ICUs [1], infection was present in 51% of the 13 796 included patients. Infection was microbiologically confirmed in 69.8% of these patients, and MDR bacteria accounted for 44% of all bacteria. Patients with ICU-acquired infections related to MDR bacteria frequently receive inappropriate initial antibiotic treatment [2,3]. In addition, infections related to these bacteria are associated with increased morbidity and mortality [4,5].

Patients in the ICU are commonly exposed to broad-spectrum antimicrobial agents, and the ICU presents ample opportunities for the cross-transmission of MDR bacteria from patient to patient [6]. Environmental contamination with MDR bacteria occurs during the care of patients harbouring these bacteria [7,8]. Huang *et al.* [9] performed a 20-month retrospective multicentre study to determine the risk of acquiring resistant bacteria from prior room occupants. Among patients whose prior room occupant was positive for methicillin-resistant *Staphylococcus aureus* (MRSA), 3.9% acquired MRSA compared with 2.9% of patients whose prior room occupant was MRSA negative (OR 1.4, p 0.04). Among patients whose prior room occupant was positive for

vancomycin-resistant enterococci (VRE), these values were 4.5% and 2.8%, respectively (OR 1.4, p 0.02). Another recent study was performed during a 14-month period [10]. Weekly environmental cultures, and twice weekly patient surveillance cultures were performed in two ICUs. The authors found that prior room contamination, whether measured via environmental cultures or prior room occupancy by VRE-colonized patients, was highly predictive of VRE acquisition.

To the best of our knowledge, no study has evaluated the risk of acquiring MDR Gram-negative bacilli (GNB) from prior room occupants. However, these bacteria are frequently isolated in critically ill patients [1,11]. In addition, infections related to these bacteria are difficult to treat with frequent inappropriate initial antibiotic treatment, and high mortality and morbidity rates [3]. Therefore, we performed this prospective observational study to determine the relationship between colonization or infection with MDR GNB in prior room occupants and the risk of acquiring these bacteria by subsequent patients.

Patients and Methods

Study design

This prospective observational cohort study was conducted from December 2006 to December 2007. No informed consent was required by the local Institutional Review Board because of the non-interventional design of the study. Eligibility criteria included admission to the ICU during the study period, and length of ICU stay >48 h. Patients with colonization or infection related to MDR GNB at ICU admission were excluded.

Study population

The study was performed in a 30-bed medical and surgical ICU, including three ten-bed units. All ICU rooms were single beds. Healthcare workers did not share patient care between subunits. In addition, in each subunit the staff members were not responsible for specific ICU rooms. Cleaning of ICU rooms was performed at patient discharge using quaternary ammonium disinfectant. The infection control policy included isolation techniques, routine screening of MDR bacteria, written antibiotic treatment protocol, and continuous surveillance of nosocomial infections. In immunocompetent patients, isolation techniques were used for all patients at ICU admission, until receipt of screening results. Thereafter, these techniques were performed for all patients with infection or colonization related to MDR bacteria. Preventive isolation techniques were applied for all immunosuppressed patients. These techniques included use of protective gowns and gloves associated with adequate hand hygiene using alcohol-based hand rub formulations before and after patient contacts.

Routine screening of MDR bacteria was performed for all patients at ICU admission and weekly thereafter. This screening included nasal and rectal swabs. In addition, tracheal aspirate was performed in intubated or tracheotomized patients. Screening of MDR bacteria has been performed in our ICU as part of the infection control policy, and not for the purpose of this study. Other microbiological cultures were performed according to clinical status.

During the study period a quality audit was performed in 50 consecutive patients. Direct observation of healthcare workers was used by a student to assess compliance with disinfection protocol at patient discharge. A checklist of objects to clean was used to determine the percentage of objects cleaned at ICU discharge.

Data collection and definitions

All data on patient characteristics at ICU admission, and during ICU stay, were prospectively collected. The MDR GNB were defined as *Pseudomonas aeruginosa* resistant to ceftazidime or imipenem, *Acinetobacter baumannii*, and extended spectrum β-lactamase (ESBL) -producing GNB. The MDR GNB were defined as ICU-acquired if they were diagnosed >48 h after admission to ICU. A prior room occupant was considered as having the same MDR GNB as the next patient when any screening or diagnostic sample was positive for an MDR GNB that was subsequently isolated, on screening or diagnostic samples, in the next patient. Prior antibiotic treatment was defined as any antibiotic treatment during the 3 months preceding ICU admission. Colonization pressure was assessed daily, and was defined as the number of patients with MDR *P. aeruginosa*, *A. baumannii* or ESBL-producing GNB divided by the number of all patients in each ten-bed unit. McCabe score [12], chronic obstructive pulmonary disease [13] and immunosuppression [14] are defined elsewhere.

Statistical methods

SPSS 11.5 software (SPSS, Chicago, IL) was used for data analysis. Results are presented as number (percentage) for categorical variables. Distribution of quantitative variables was tested. Median values were 0 for several quantitative variables, because of their skewed distribution. Therefore, all quantitative variables are presented as mean ± SD. All p values were two-tailed. The statistical significance was defined as $p < 0.05$.

Univariate analysis was used to determine factors associated with ICU-acquired MDR *P. aeruginosa*, *A. baumannii* and

ESBL-producing GNB. Qualitative variables were compared using the Pearson chi-square test or the Fisher's exact test, as appropriate. Quantitative variables were compared using the Mann–Whitney *U*-test or the Student's *t*-test, as appropriate.

Multivariate analysis was used to determine factors independently associated with different ICU-acquired MDR *P. aeruginosa*, *A. baumannii* and ESBL-producing GNB. All predictors showing a p <0.1 association with ICU-acquired MDR bacteria in univariate analysis were incorporated in the multivariate logistic regression analysis. Potential interactions were tested. Clinical judgement was used to select the variable to introduce in the logistic regression model when an interaction was present between two variables. Odds ratios and 95% CI were calculated, as well as the Hosmer–Lemshow goodness-of-fit.

Exposure to risk factors for ICU-acquired MDR GNB was taken into account until the acquisition of MDR GNB, or until ICU discharge, in patients with and without ICU-acquired MDR GNB, respectively.

Results

Five hundred and eleven patients were eligible and were all included. Infection and colonization related to MDR GNB were diagnosed in 65 (79%) and 17 (20%) patients with *P. aeruginosa*, in 46 (80%) and 11 (19%) patients with *A. baumannii*, and in 42 (84%) and 8 (6%) patients with ESBL-producing GNB, respectively.

Patient characteristics are presented in Tables 1–4. Duration of mechanical ventilation and of ICU stay were significantly longer in patients with MDR *P. aeruginosa*, *A. baumannii* or ESBL-producing GNB compared with patients without these bacteria. Although ICU mortality was significantly higher in patients with MDR *P. aeruginosa* compared with patients without MDR *P. aeruginosa*, ICU mortality was similar in patients with and without *A. baumannii* or ESBL-producing GNB (Tables 2 and 4).

Several risk factors for ICU-acquired MDR *P. aeruginosa*, *A. baumannii* and ESBL-producing GNB were identified by univariate analyses, and are presented in Tables 1–4. Independent risk factors for ICU-acquired *P. aeruginosa* were prior occupant with MDR *P. aeruginosa*, surgery and prior use of piperacillin/tazobactam. Independent risk factors for ICU-acquired *A. baumannii* were prior occupant with *A. baumannii* and mechanical ventilation. Independent risk factors for ICU-acquired ESBL-producing GNB were tracheostomy and sedation (Table 5).

Time from ICU discharge of prior room occupants with MDR GNB to acquisition of these bacteria by subsequent patients was 5 ± 2 days, 6 ± 2 days and 20 ± 16 days in patients with *P. aeruginosa*, *A. baumannii* and ESBL-producing GNB, respectively. Although this time interval was significantly (p <0.001) shorter in patients with *P. aeruginosa* or *A. baumannii* with prior room occupant having the same MDR GNB compared with those without prior room occupant with the same MDR GNB, no significant difference (p 0.582) was found in this time interval between patients with ESBL-producing GNB with prior room occupant having

TABLE 1. Characteristics of patients with and without multidrug-resistant *Pseudomonas aeruginosa* (MDRPA) or *Acinetobacter baumannii* at intensive-care unit (ICU) admission

	ICU-acquired MDRPA				ICU-acquired *A. baumannii*			
	Yes (*n* = 82)	No (*n* = 429)	p value	OR (95% CI)	Yes (*n* = 57)	No (*n* = 454)	p value	OR (95% CI)
Age, years	60 ± 16	55 ± 19	0.040	NA	59 ± 16	56 ± 18	0.175	NA
Male gender	54 (65)	298 (69)	0.518	0.8 (0.5–1.3)	37 (68)	315 (69)	0.544	0.8 (0.4–1.4)
SAPS II	52 ± 19	44 ± 20	<0.001	NA	53 ± 18	44 ± 20	0.002	NA
LOD score	6.3 ± 3.7	5.2 ± 3.4	0.002	NA	6.4 ± 3.7	5.3 ± 3.4	<0.001	NA
Ultimately or rapidly fatal disease[a]	49 (59)	213 (49)	0.117	1.5 (.9–2.4)	34 (59)	228 (50)	0.206	1.4 (0.8–2.5)
Transfer from other wards	65 (79)	240 (55)	<0.001	3 (1.7–5.3)	39 (68)	266 (58)	0.197	1.5 (0.8–2.7)
Duration of hospitalization before ICU admission, days	7 ± 11	5 ± 9	<0.001	NA	5 ± 7	5 ± 10	0.137	NA
Category of admission								
Medical	44 (53)	330 (76)	<0.001	2.9 (1.8–4.7)	36 (63)	338 (74)	0.081	1.7 (0.9–3)
Surgical	38 (46)	99 (23)			21 (36)	116 (25)		
Comorbidities								
Diabetes mellitus	16 (19)	83 (19)	>0.999	1.01 (0.5–1.8)	12 (21)	87 (19)	0.724	1.1 (0.5–2.2)
COPD	21 (25)	116 (27)	0.892	0.9 (0.5–1.5)	11 (19)	126 (27)	0.206	0.6 (0.3–1.2)
Liver cirrhosis	1 (1)	14 (3)	0.484	0.3 (0.1–2.8)	4 (7)	11 (2)	0.074	3 (0.9–9.8)
Chronic dialysis	1 (1)	13 (3)	0.709	0.3 (0.1–3)	1 (1)	13 (2)	>0.999	0.6 (0.1–4.7)
Immunosuppression	20 (24)	88 (20)	0.461	1.2 (0.7–2.1)	16 (28)	92 (20)	0.172	1.5 (0.8–2.8)
Prior antimicrobial treatment	46 (56)	163 (38)	0.003	2.1 (1.3–3.4)	30 (52)	179 (39)	0.064	1.7 (0.9–2.9)

Data are *N*° (%) or mean ± SD. Results by univariate analysis. OR (95% CI) were only calculated for qualitative variables.
NA, not applicable; SAPS, simplified acute physiology score, LOD, logistic organ dysfunction; COPD, chronic obstructive pulmonary disease.
[a]According to McCabe score (Ref).

TABLE 2. Characteristics of patients with or without multidrug-resistant (MDR) *Pseudomonas aeruginosa* or *Acinetobacter baumannii* during intensive-care unit (ICU) stay

	ICU-acquired MDRPA				ICU-acquired *A. baumannii*			
	Yes (*n* = 82)	No (*n* = 429)	p value	OR (95% CI)	Yes (*n* = 57)	No (*n* = 454)	p value	OR (95% CI)
Prior room occupants with the same MDR GNB	21 (25)	64 (14)	0.023	1.9 (1.1–3.5)	16 (28)	36 (7)	<0.001	4.5 (2.3–8.9)
Colonization pressure, %	45 ± 15	43 ± 15	0.298	NA	51 ± 15	43 ± 14	0.003	NA
Room occupancy rate, %	97 ± 4	95 ± 5	0.041	NA	96 ± 6	95 ± 5	0.183	NA
Central venous catheter	78 (95)	323 (75)	<0.001	6.3 (2.3–17.9)	54 (94)	347 (76)	0.001	5.5 (1.7–18)
Arterial catheter	77 (93)	295 (68)	<0.001	6.9 (2.8–17.7)	53 (93)	319 (70)	<0.001	5.6 (1.9–15.9)
Urinary catheter	79 (96)	359 (83)	0.002	5.1 (1.6–16.7)	55 (96)	383 (84)	0.009	5.1 (1.2–21)
Tracheostomy	17 (20)	42 (9)	0.008	2.4 (1.3–4.5)	9 (15)	50 (11)	0.257	1.5 (0.7–3.2)
Sedation	74 (90)	289 (67)	<0.001	4.5 (2.1–9.6)	51 (89)	312 (68)	0.001	3.9 (1.6–9.2)
Antimicrobial treatment	78 (95)	352 (82)	0.002	4.2 (1.5–12)	55 (96)	374 (82)	0.004	5.9 (1.4–24.6)
Duration of antimicrobial treatment	15 ± 9	12 ± 10	0.002	NA	13 ± 9	15 ± 13	0.881	NA
Percentage of days in the ICU with antimicrobials	74 ± 32	65 ± 36	0.035	NA	68 ± 34	66 ± 35	0.674	NA
Penicillins	1 ± 6	3 ± 12	0.265	NA	4 ± 18	3 ± 12	0.886	NA
Amoxicillin-clavulanate acid	12 ± 26	22 ± 34	0.012	NA	16 ± 31	21 ± 34	0.227	NA
Piperacillin-tazobactam	41 ± 41	21 ± 34	<0.001	NA	39 ± 41	21 ± 34	<0.001	NA
Third-generation cephalosporins	8 ± 20	9 ± 23	0.690	NA	12 ± 26	9 ± 22	0.300	NA
Fourth-generation cephalosporins	3 ± 8	3 ± 13	0.067	NA	1 ± 7	4 ± 14	0.035	NA
Carbapenems	10 ± 22	5 ± 17	0.013	NA	5 ± 14	7 ± 19	0.495	NA
Fluoroquinolones	23 ± 32	17 ± 31	0.062	NA	29 ± 36	17 ± 30	0.012	NA
Aminoglycosides	18 ± 27	11 ± 23	0.001	NA	10 ± 19	13 ± 24	0.865	NA
Mechanical ventilation	76 (92)	327 (76)	0.001	3.9 (1.7–9.3)	56 (98)	346 (76)	<0.001	17.3 (2.6–126)
Duration of mechanical ventilation before MDRPA/*A. baumannii* acquisition or extubation, days[a]	19 ± 10	13 ± 11	<0.001	NA	16 ± 13	16 ± 15	0.290	NA
Total duration of mechanical ventilation, days	36 ± 23	13 ± 11	<0.001	NA	29 ± 22	16 ± 15	<0.001	NA
Length of stay before ICU-acquired MDRPA/*A. baumannii* or ICU discharge, days[a]	21 ± 15	15 ± 13	<0.001	NA	17 ± 14	18 ± 17	0.682	NA
Total duration of ICU stay, days	41 ± 27	15 ± 13	<0.001	NA	34 ± 24	18 ± 17	<0.001	NA
ICU-mortality	39 (47)	133 (31)	0.005	2 (1.2–3.2)	23 (40)	(32)	0.298	1.3 (0.7–2.4)

Data are *N°* (%) or mean ± SD. Results by univariate analysis. OR (95% CI) were only calculated for qualitative variables.
Exposure to risk factors was taken into account until MDRPA, or *A. baumannii* occurrence, and until ICU discharge in patients with and without these bacteria; respectively.
[a]In patients with MDRPA/*A. baumannii*, and patients without these bacteria; respectively.

the same bacterium compared with those without prior room occupant with ESBL-producing GNB (Fig. 1).

The quality audit performed during the study on 50 consecutive patients demonstrated that 56% of objects were correctly cleaned after ICU discharge. The most frequently incorrectly cleaned objects included room door knobs (45%), monitor screens (27%) and bedside tables (16%).

To determine the impact of colonization compared with infection on acquisition of MDR GNB by the next room occupant, we repeated all univariate and multivariate analyses in the subgroups of patients with colonization and infection. Similar results were found suggesting that the risk of acquiring MDR GNB did not differ according to the presence of colonization compared with infection in the prior room occupant (data not shown).

Discussion

The main results of our study are that admission to an ICU room previously occupied by a carrier of MDR *P. aeruginosa* or *A. baumannii* is an independent risk factor for acquisition of these bacteria by subsequent room occupants. However, this relationship was not identified for ESBL-producing GNB.

To the best of our knowledge, our study is the first to identify prior room occupant with MDR *P. aeruginosa* or *A. baumannii* as an independent risk factor for subsequent room occupants to acquire these bacteria. Previous studies found similar results with regard to MRSA, VRE and *Clostridium difficile* [9,10,15,16]. Our results suggest that the contamination of ICU rooms (e.g. surfaces and equipment) plays an important role in the spread of MDR *P. aeruginosa* and *A. baumannii*. Several studies have documented the contamination of sinks and sink drains by *P. aeruginosa* [17–19]. Other studies demonstrated that *A. baumannii* was isolated throughout the inanimate environment, on the beds of colonized patients and on nearby surfaces (e.g. on mattresses and bedside equipment), in hospital rooms (e.g. on floors, sinks, countertops and door handles), and in room humidifiers [7,20,21]. In addition, it has been demonstrated that MRSA, VRE and *A. baumannii* are readily transmitted from environmental surfaces to healthcare workers' hands [22–24]. However, many of these studies were performed in an outbreak setting [25]. In addition, few studies

TABLE 3. Characteristics of patients with or without intensive0care unit (ICU) -acquired extended spectrum β-lactamase (ESBL) -producing Gram-negative bacteria (GNB) at ICU admission

	ICU-acquired ESBL-producing GNB			
	Yes (*n* = 50)	No (*n* = 461)	p value	OR (95% CI)
Age	60 ± 12	56 ± 19	0.178	NA
Male gender	32 (64)	320 (69)	0.426	0.7 (0.4–1.4)
SAPS II	51 ± 21	45 ± 20	0.047	NA
LOD score	5.5 ± 3.6	5.4 ± 3.5	0.080	NA
Ultimately or rapidly fatal disease[a]	28 (56)	234 (50)	0.552	1.2 (0.6–2.2)
Transfer from other wards	35 (70)	270 (58)	0.131	1.6 (0.8–3.1)
Duration of hospitalization before ICU admission, days	4 ± 6	5 ± 10	0.176	NA
Category of admission				
Medical	36 (72)	338 (73)	0.876	1.1 (0.5–2)
Surgical	14 (28)	123 (26)		
Comorbidities				
Diabetes mellitus	10 (20)	89 (19)	0.852	1.1 (0.7–2.7)
COPD	17 (34)	120 (26)	0.241	1.4 (0.7–2.7)
Liver cirrhosis	2 (4)	13 (2)	0.650	1.4 (0.3–6.5)
Chronic dialysis	0	14 (3)	0.381	NA
Immunosuppression	12 (24)	96 (20)	0.587	1.2 (0.6–2.3)
Prior antimicrobial treatment	26 (52)	183 (39)	0.098	1.6 (0.9–2.9)

Data are *N*° (%) or mean ± SD. Results by univariate analysis. OR (95% CI) were only calculated for qualitative variables.
NA, not applicable; SAPS, simplified acute physiology score, LOD, logistic organ dysfunction; COPD, chronic obstructive pulmonary disease.
[a]According to McCabe score (Ref 12).

used molecular epidemiology (e.g. pulsed-field gel electrophoresis) [26].

One important limitation of our study is that environmental cultures were not performed to confirm the role of environmental contamination in MDR GNB transmission from prior room occupant to subsequent patient. However, the shorter time interval from ICU discharge to *P. aeruginosa* or *A. baumannii* acquisition in patients with prior room occupant having the same MDR GNB compared with those for whom the prior room occupant did not have the same MDR GNB indicates that environmental contamination is plausible. Another potential explanation of the findings is that the room itself did not transmit the pathogens, but that certain rooms were associated with specific staff members and that the staff members transmitted the organism from one patient to another. However, staff members were not responsible for specific ICU rooms. Molecular typing of all strains could have proved the similarity of MDR GNB strains between prior room occupant and subsequent patient. Unfortunately, molecular typing of all MDR GNB strains was not possible during the study period. In addition, this study was performed in a single centre so the results may not be generalizable to other centres.

Duration of survival of non-fermenting GNB has been reported to be as long as 48 h for *P. aeruginosa* on dry

TABLE 4. Characteristics of patients with or without intensive-care unit (ICU) -acquired extended spectrum β-lactamase (ESBL) -producing Gram-negative bacteria (GNB) during ICU stay

	ICU-acquired ESBL-producing GNB			
	Yes (*n* = 50)	No (*n* = 461)	p value	OR (95% CI)
Prior room occupants with ESBL-producing GNB	8 (16)	50 (10)	0.249	1.5 (0.6–3.5)
Colonization pressure	49 ± 11	43 ± 15	0.021	NA
Room occupancy rate	0.95 ± 0.05	0.95 ± 0.06	0.600	NA
Central venous catheter	49 (98)	352 (76)	<0.001	15.2 (2.1–111)
Arterial catheter	48 (96)	324 (70)	<0.001	10 (2.4–42.3)
Urinary catheter	50 (100)	388 (84)	<0.001	1.1 (1.1–1.2)
Tracheostomy	11 (22)	48 (10)	0.032	2.4 (1.2–5.1)
Sedation	48 (96)	315 (68)	<0.001	11.1 (2.7–46.4)
Antimicrobial treatment	49 (98)	383 (83)	0.003	9.9 (1.4–73.4)
Duration of antimicrobial treatment, days	20 ± 15	15 ± 12	0.005	NA
Percentage of days in the ICU with antimicrobials	75 ± 31	65 ± 36	0.066	NA
Penicillins	3 ± 12	3 ± 13	0.492	NA
Amoxicillin-clavulanate acid	21 ± 36	21 ± 33	0.298	NA
Piperacillin-tazobactam	31 ± 39	21 ± 34	0.030	NA
Third-generation cephalosporins	10 ± 24	8 ± 22	0.245	NA
Fourth-generation cephalosporins	6 ± 13	3 ± 13	0.001	NA
Carbapenems	15 ± 27	6 ± 17	0.027	NA
Fluoroquinolones	24 ± 30	18 ± 31	0.011	NA
Aminoglycosides	15 ± 23	12 ± 23	0.180	NA
Mechanical ventilation	47 (94)	355 (77)	0.003	4.7 (1.4–15.3)
Duration of mechanical ventilation before ESBL-producing GNB acquisition or extubation, days[a]	20 ± 14	16 ± 14	0.002	NA
Total duration of mechanical ventilation, days	28 ± 18	16 ± 15	<0.001	NA
Length of ICU stay before ESBL-producing GNB acquisition or ICU discharge, days[a]	23 ± 21	18 ± 17	0.060	NA
Total length of ICU stay, days	36 ± 26	18 ± 17	<0.001	NA
ICU-mortality	19 (38)	153 (33)	0.530	1.2 (0.6–2.2)

Data are *N*° (%) or mean ± SD. Results by univariate analysis. OR (95% CI) were calculated for only qualitative variables.
GNB, Gram-negative bacilli; ICU, intensive care unit; NA, not applicable.
Exposure to risk factors was taken into account until ESBL-producing GNB acquisition, or until ICU discharge, in patients with and without ESBL-producing GNB; respectively.
[a]In patients with and without ESBL-producing GNB, respectively.

TABLE 5. Independent risk factors for intensive care unit (ICU) -acquired multidrug-resistant (MDR) *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and extended spectrum β-lactamase (ESBL) -producing Gram-negative bacteria (GNB)

Risk factors	OR (95% CI)	p value
MDR *P. aeruginosa*		
Prior occupant with MDR *P. aeruginosa*	2.3 (1.2–4.3)	0.012
Surgery	1.9 (1.1–3.6)	0.024
Prior piperacillin/tazobactam use	1.2 (1.1–1.3)	0.040
A. baumannii		
Prior occupant with *A. baumannii*	4.2 (2–8.8)	<0.001
Mechanical ventilation	9.3 (1.1–83)	0.045
ESBL-producing GNB		
Tracheostomy	2.6 (1.1–6.5)	0.049
Sedation	6.6 (1.1–40)	0.041

Results by multivariate analysis. Hosmer–Lemeshow goodness-of-fit test, p 0.588, p 0.941, p 0.329 for MDR *P. aeruginosa*, *A. baumannii*, and ESBL; respectively. Model significance <0.005 for all multivariate analyses.
The following variables were not significant in the final model of risk factors for ICU-acquired MDR *P. aeruginosa*: age, simplified acute physiology score (SAPS II), logistic organ dysfunction (LOD) score, transfer from other wards, duration of hospitalization before ICU admission, prior antibiotic treatment, room occupancy rate, central venous catheter, arterial catheter, urinary catheter, tracheostomy, sedation, percentage of days in the ICU with amoxicillin-clavulanate acid, percentage of days in the ICU with piperacillin-tazobactam, percentage of days in the ICU with fourth-generation cephalosporins, percentage of days in the ICU with carbapenems, percentage of days in the ICU with fluoroquinolones, percentage of days in the ICU with aminoglycosides, mechanical ventilation, and length of ICU stay.
The following variables were not significant in the final model of risk factors for ICU-acquired *A. baumannii*: SAPS II, LOD, category of admission, prior antibiotic treatment, colonization pressure, central venous catheter, arterial catheter, urinary catheter, sedation, percentage of days in the ICU with piperacillin-tazobactam, percentage of days in the ICU with fourth-generation cephalosporins, percentage of days in the ICU with fluoroquinolones.
The following variables were not significant in the final model of risk factors for ICU-acquired ESBL-producing GNB: SAPS II, LOD, prior antibiotic treatment, colonization pressure, central venous catheter, arterial catheter, urinary catheter, percentage of days in the ICU with piperacillin-tazobactam, percentage of days in the ICU with fourth-generation cephalosporins, percentage of days in the ICU with carbapenems, percentage of days in the ICU with fluoroquinolones, mechanical ventilation, length of ICU stay

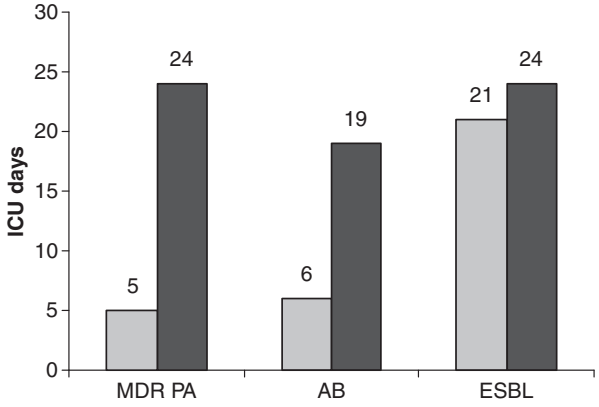

FIG. 1. Mean time from prior room occupant discharge to acquisition of multidrug-resistant Gram-negative bacteria (MDR GNB) in subsequent patients with and without prior room occupant having the same MDR GNB. Grey bars represent patients with prior room occupant having the same MDR GNB, black bars represent patients for whom prior room occupant did not have the same MDR GNB. MDRPA, MDR *Pseudomonas aeruginosa*; AB, *Acinetobacter baumannii*; ESBL, extended spectrum β-lactamase-producing GNB. p <0.001 for patients with *P. aeruginosa* or *A. baumanni* with prior room occupant having the same MDR GNB compared with patients without prior room occupant with the same MDR GNB, p 0.582 for patients with ESBL-producing GNB and prior room occupant with ESBL-producing GNB compared with those without prior room occupant with ESBL-producing GNB.

surfaces [27], and up to 33 days for *A. baumannii* on plastic laminate surfaces [28]. The absence of a relationship between colonization of prior room occupant with ESBL-producing GNB and acquisition of this GNB by the subsequent room occupant could be explained by the fact that survival of ESBL-producing GNB on inanimate surfaces is probably shorter compared with survival of *P. aeruginosa* and *A. baumannii* [29].

Cleaning of our ICU rooms was probably not efficient in eradicating MDR *P. aeruginosa* and *A. baumannii*. Two potential explanations could be provided. First, compliance with cleaning protocol was not optimal, as suggested by the quality audit performed during the study period. A recent multicentre study evaluated the thoroughness of terminal cleaning in 260 ICU rooms using a fluorescent targeting method [30]. Only 49.5% of surfaces were correctly cleaned. After intervention and multiple cycles of objective performance feedback to environmental services staff, thoroughness of cleaning improved to 82%. Second, our cleaning technique, using quaternary ammonium disinfectant, may not be efficient in eradicating MDR *P. aeruginosa* and *A. baumannii* [8]. New methods have recently been reported to improve cleaning of hospital rooms. A hydrogen peroxide dry-mist disinfection system was found to be significantly more effective than 0.5% sodium hypochlorite solution in eradicating *C. difficile* spores [31]. Hydrogen peroxide vapour decontamination also effectively eradicated important healthcare-associated pathogens such as MRSA, VRE, *A. baumannii*, *Serratia*, mycobacteria and viruses [32–35]. However, limitations of these studies included retrospective, observational or before–after designs, and the small number of patients included. In addition, the quality of the disinfecting process was not controlled during these studies. A recent study demonstrated that the novel automated ultraviolet radiation device significantly reduces *C. difficile*, VRE and MRSA contamination on commonly touched hospital surfaces [36]. Although innovative technologies may play a role in the environmental hygiene armamentarium, their logistical complexity, as well as the equipment and personnel costs of these interventions, makes it imperative that independent or consortium-sponsored, objectively controlled studies be undertaken to clarify the true role of these technologies [37].

Surgery and prior use of piperacillin/tazobactam were identified as independent risk factors for ICU-acquired MDR *P. aeruginosa*. Use of mechanical ventilation was identified as an independent risk factor for ICU-acquired *A. baumannii*. Tracheostomy and sedation were identified as independent risk factors for ICU-acquired ESBL-producing GNB. These results are in line with previous findings [38–45].

We conclude that admission to an ICU room previously occupied by a carrier of MDR *P. aeruginosa* or *A. baumannii* is an independent risk factor for the acquiring of these bacteria by subsequent room occupants. However, this relationship was not identified for ESBL-producing GNB. Future studies should determine the efficiency of new cleaning and disinfection methods on transmission of MDR GNB in critically ill patients.

Transparency Declaration

The authors have no potential conflicts of interest to declare and no involvement in any organization with a direct financial interest in the subject of the manuscript. There was no financial support.

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