European Journal of Clinical Microbiology & Infectious Diseases (2023) 42:1163–1172
https://doi.org/10.1007/s10096-023-04650-5

ORIGINAL ARTICLE

Prevention of ICU-acquired infection with decontamination regimen in immunocompromised patients: a pre/post observational study

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Received: 22 May 2023 / Accepted: 7 August 2023 / Published online: 19 August 2023

Abstract

Purpose Although the proportion of immunocompromised patients admitted to the ICU is increasing, data regarding specific management, including acquired infection (ICU-AI) prophylaxis, in this setting are lacking. We aim to investigate the effect of multiple-site decontamination regimens (MSD) in immunocompromised patients.

Methods We conducted a prospective pre-/post-observational study in 2 ICUs in Bretagne, western France. Adults who required mechanical ventilation for 24 h or more were eligible. During the study period, MSD was implemented in participating ICUs in addition to standard care. It consists of the administration of topical antibiotics (gentamicin, colistin sulfate, and amphotericin B), four times daily in the oropharynx and the gastric tube, 4% chlorhexidine bodywash once daily, and a 5-day nasal mupirocin course.

Results Overall, 295 immunocompromised patients were available for analysis (151 in the post-implementation group vs 143 in the pre-implementation group). Solid organ cancer was present in 77/295 patients while immunomodulatory treatments were noticed in 135/295. They were 35 ICU-AI in 29/143 patients in the standard-care group as compared with 10 ICU-AI in 9/151 patients in the post-implementation group ($p < 0.001$). In a multivariable Poisson regression model, MSD was independently associated with a decreased incidence of ICU-AI (incidence rate ratio = 0.39; 95%CI [0.20–0.87] $p = 0.008$). There were 35/143 deaths in the standard-care group as compared with 22/151 in the post-implementation group ($p = 0.046$), this difference remained in a multivariable Cox model (HR = 0.58; 95CI [0.34–0.95] $p = 0.048$).

Conclusion In conclusion, MSD appeared to be associated with improved outcomes in critically ill immunocompromised patients.

Keywords Critical care · Pneumonia · Bacteremia · Mortality · Acquired infection · Immunodepression · Selective decontamination of the digestive tract

Introduction

Despite improvement in survival of immunocompromised patients admitted to the ICU [1, 2], this population still has a poor outcome, including high ICU-acquired infection (ICU-AI) incidence but also higher mortality than immunocompetent patients [1, 3]. Noteworthy, a previous study reported that ICU-AI in immunocompromised patients decreases survival, suggesting that ICU-AI prevention may improve outcomes [4]. Multiple-site decontamination (MSD) is a selective decontamination regimen that has been associated with decreased ICU-AI incidence in critical patients, but also with decreased mortality in some specific settings [5, 6]. Although the proportion of immunocompromised patients admitted to the ICU is increasing, data regarding specific management,

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including ICU-AI prophylaxis, in this setting are lacking and previous studies regarding selective decontamination were conducted in the previous century [7–9]. Interestingly, this population is at higher risk of nonbacterial infection, such as pulmonary aspergillosis or viral reactivation [4, 10], this type of micro-organisms being not directly targeted by MSD. We aim to investigate the effect of MSD in immunocompromised patients and hypothesized that MSD might improve outcomes through a decrease in ICU-AI incidence.

Patients and methods

Patients and setting

We conducted an ancillary analysis of a prospective pre/post observational study in 2 medico/surgical ICUs in Bretagne, western France. Anticipating a change in daily practice with MSD implementation in participating ICUs, an observational study with prospective collection of data has been conducted as reported elsewhere [11]. From 1 January 2020 until 31 December 2022, all adults who required mechanical ventilation for 24 h or more were eligible with the exception of those with liberty deprivation, pregnant women, and patients younger than 18 years old who were excluded from the study. Follow-up was pursued until ICU discharge or death, whichever occurs first.

Ethics

The study protocol received approval from the Rennes Hospital ethics committee (comité d'éthique du CHU de Rennes avis 19–52). Patients or closest relatives were informed of the anonymous prospective collection of the data and had the possibility not to participate in the study. In case of refusal, the data were not collected accordingly. This manuscript follows the STROBE statement for reporting cohort studies.

Intervention

As of May 5, 2021 (Saint-Brieuc), and June 1, 2021 (Vannes), MSD was implemented in participating ICUs in addition to standard care for the prevention of acquired infections in patients with expected intubation duration > 24 h. Patients admitted after the implementation date received MSD and constituted the post-implementation group (from 5 May 2021 to 31 December 2022, in Saint-Brieuc and from June 1, 2021, to December 31, 2022, in Vannes), whereas those admitted earlier, even when they were still hospitalized in the ICU after the implementation date, received standard-care and constituted standard-care group (from 1 January 2023 to 5 May 2021 in Saint-Brieuc and from 1 January 2023 to 1 June 2021 in Vannes). MSD is a variant of selective digestive decontamination, which consists of the administration of topical antibiotics including gentamicin (543 mg per day), colistin sulfate (400 mg per day), and amphotericin B (2 g per day), four times daily in the oropharynx and the gastric tube, 4% chlorhexidine bodywash once daily and a 5-day nasal mupirocin course without intravenous antibiotics [6, 11].MSD was applied in intubated patients with an expected intubation duration > 24 h from admission and during the full length of mechanical ventilation duration.

Strategies for ICU-AI prevention and diagnosis

Strategies for VAP and BSI prevention were left at each ICU's discretion but they were no modifications of practices during the study period with the exception of MSD implementation in concerned ICUs. Standard care strategy for ICU-AI prevention was applied during both pre- and post-implementation periods and consists of a bundle of care that included semi-recumbent positioning (depending on its feasibility and tolerance), specific oral care with tooth brushing and mouth washing every 6 h and 4 times daily cuff pressure monitoring. There was no specific protocol for ulcer prophylaxis. Catheter dressings were performed with dry sterile compresses and were changed weekly or sooner in case of bleeding or spotting.

VAP diagnosis was systematically associated with a pulmonary sample that can be an endotracheal aspiration, a broncho-alveolar lavage, or a distally protected sample. During the study period, physicians were asked to complete a checklist for each VAP suspicion in order to collect data (clinical, biological, and radiological findings) for VAP classification by the dedicated team in each center [12].

Patients were classified as having possible, putative, probable, or proven aspergillosis according to the AspICU, Influenza-associated pulmonary aspergillosis (IAPA), and COVID-19-associated pulmonary aspergillosis (CAPA) criteria when indicated [13–15] (Supplementary Fig 1).

ICU-acquired infections diagnoses were prospectively recorded by an external committee that was not blinded to the pre- or post-intervention study period. Herein, ICU-AI diagnosis was suspected by the treating physician but the final diagnosis was confirmed by a dedicated member of the nosocomial infection committee (CLIN) in each hospital. The CLIN was composed of a microbiologist, infectiologist, and physician including a member of the intensive care unit in each hospital.

In all participating ICUs, patients were screened for MDRO rectal carriage at admission, weekly afterward, and at discharge on rectal swabs. As described elsewhere, patients with no prior colonization (no colonization at admission) who tested positive for MDRO on either rectal screening or on a blood or respiratory sample were considered as having MDRO acquisition [16].

Definition

Immunodepression was considered in patients with ongoing solid organ neoplasia (active or in remission for less than 5 years), haematological malignancy, severe neutropenia (< 0.5 G/L) acquired immunodeficiency syndrome, organ transplant or taking immunosuppressive drugs including long term steroids > 10 mg prednisolone per day during > 28 days) [4, 17].

Each center had a CLIN for the prevention and prospective census of ICU-AI and applied the recommendations of the French Society for Hospital Hygiene for the prevention and treatment of infection (available at https://sf2h.net/publications/actualisation-precautions-standard-2017). Infection was considered acquired in the ICU when it was diagnosed 48 h after admission and was not incubating on admission. ICU-AI was diagnosed by the treating physician. BSI was defined as a positive blood culture occurring 48 h or more after admission. Regarding common skin contaminants, 2 positive blood cultures drawn on separate occasions were required [18]. The diagnosis of VAP was considered in patients ventilated for 48 h or more and until 48 h after extubation and was based on clinical signs (fever, purulent sputum, hypoxia), radiological findings (new infiltrate on chest-X-ray or CT scan), and leukocytosis [19]. All VAPs were bacteriologically confirmed. Respiratory samples for VAP diagnosis were performed either using fiberoptic bronchoalveolar lavage or endotracheal aspiration, according to local practices. The threshold for lung samples positivity was 104 cfu/mL for BAL and 105 cfu/mL for tracheal aspirate. Microorganisms responsible for infection were considered as MDRO according to the European Society of Clinical Microbiology and Infectious Disease definition [20].

Primary and secondary endpoints

The primary endpoint was ICU-AI incidence and the secondary endpoints were specific VAP and BSI incidences as well as ICU mortality. Finally, we aim to describe the microbiology of ICU-AI episodes in both groups.

Statistical analysis

Statistical analysis was performed with the statistical software R 4.1.1. Categorical variables were expressed as percentages and continuous variables as median and interquartile range (IQR). The chi-square test and Fisher exact test were used to compare categorical variables and the Man-Whitney U test or the Wilcoxon for continuous variables.

Predictors of acquired infections were estimated using a uni- and multivariable Poisson regression model while predictors of ICU death were analyzed using a uni- and multivariable Cox proportional hazard model and Kaplan–Meier survival curves with log-rank test.

In order to account for competing events such as discharge from the ICU alive, a second analysis using uni (Model 1) and multivariable (Model 2) competitive risk analysis was used to estimate the probability of developing ICU-AI. A third Fine and Gray model (Model 3) was finally performed to analyze the association between exposure and VAP with extubation being a competing event with VAP onset. Using the "cmprsk" package, we performed a fine and gray model to estimate the sub-distribution hazard ratio (sdHR). A multivariable Cox proportional hazard model was used for survival analysis. Variables associated with events (either BSI or death) with a p value < 0.2 in univariate analysis were included in a multivariable model. Of note, for outcome comparison, only the first BSI was taken into account.

Since SAPS II includes age, collinearity is present between this variable and the variable age. To go through, the variable included in the multivariable analysis consisted of SAPS II with the exception of the age component. Multivariable analyses were performed with the inclusion of non-redundant variables associated with the event (ICU-AI or death) with a p value < 0.2 in the univariate analysis. There were no missing data in the dataset. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Results

Population

Overall, 1654 patients were admitted to participating ICUs during the study period, of whom 758 were not intubated or remained < 24 h in the ICU. Among the 896 remaining patients, 601 were considered immunocompetent, giving 295 immunocompromised patients available for analysis (143 in the pre-implementation group vs 151 in the post-implementation group) (Fig. 1). Age was 68 years [60–73], 61% were male, the main reason for admission was medical (88%) and SAPS II was 48 [34–62]. Solid organ cancer was the main reason for immunosuppression (53%), with a majority of lung cancer (75/156), urological cancer (52/156), hepatobiliary cancer (36/156), and breast cancer (35/156). Immunomodulatory treatments were noticed in 135 patients (46%) including 64/135 with recent chemotherapy and 61/135 with immunotherapy for auto-immune or auto-inflammatory disease. Fifty-nine patients (20%) were admitted with neutropenia < 0.5 G/L, 51 (17%) patients had hematological malignancy and 23 (8%) had solid organ transplantation. Seven (2%) patients were colonized with a MDRO at admission (6 ESBL-PE

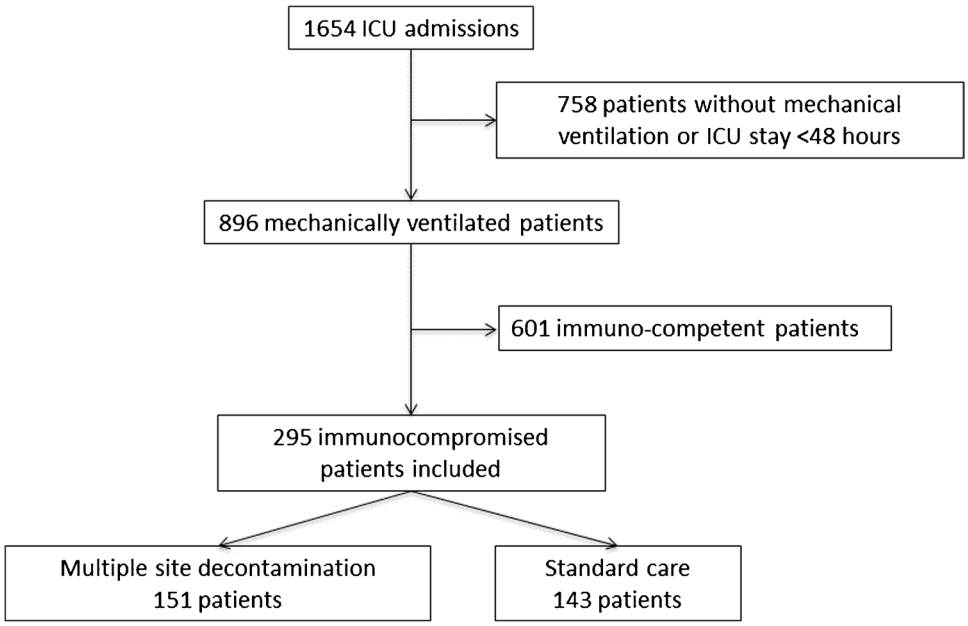


Fig. 1 Flow chart

and 1 vancomycin-resistant Enterococcus). Length of stay was 7 days [4–13] and 57 patients (19%) died in the ICU. Baseline characteristics at ICU admission did not differ between patients admitted before MSD implementation (pre-implementation group) and after implementation (MSD/ post-implementation group) (Table 1).

Acquired infections

They were 35 ICU-AI (25 VAP and 10 BSI) in 29 patients (20%) (corresponding to 1 671 patient days) in the standard-care group as compared with 10 ICU-AI (4 VAP and 6 BSI) in 9 patients (6%) (corresponding to 1440 patient days) in the post-implementation group ($p < 0.001$ for ICU-AI, $p < 0.001$ for VAP and $p = 0.377$ for BSI) (Table 1) (Supplementary Figure 1).

In a multivariable Poisson regression model, MSD was independently associated with a decreased incidence of ICU-AI (incidence rate ratio [IRR] = 0.39; 95%CI [0.20–0.87] $p = 0.008$). Conversely, COVID-19 (IRR = 1.85; 95%CI [1.04–1.30] $p = 0.036$), vascular catheter (IRR = 4.94; 95%CI [1.19–20.39] $p = 0.027$) and immunomodulatory treatment (IRR = 1.91; 95%CI [1.08–3.68] $p = 0.027$) were associated with an increased risk (Table 2). In a second model taking into account discharge from ICU as a competing risk using a Fine and Gray model, results were similar with a decreased risk of ICU-AI in patients receiving MSD (sdHR = 0.40 95%CI [0.19–0.84] $p = 0.015$). Similarly, a decreased risk of VAP was observed in model 3 (competing risk analysis with extubation being the competing event of VAP) (Supplementary Table 1).

There were no differences in the distribution of microorganisms responsible for ICU-AI between groups (Table 3). Interestingly, 9/38 patients with ICU-AI had pulmonary *Aspergillosis*, making this micro-organism as frequent as non-fermenting Gram-negative *Bacilli*. *Enterobacteriaceae* were present in 8/39 patients, coagulase-negative *Staphylococci* in 5/39.

Finally, 7 patients in the pre-implementation period vs 2 patients in the post-implementation period acquired a MDRO colonization while in the ICU ($p = 0.096$).

Survival

There were 35/143 deaths in the standard-care group as compared with 22/151 in the post-implementation group ($p = 0.046$) (Table 1 and Fig. 2). This difference remained in a multivariable Cox proportional hazard model (HR = 0.58; 95CI [0.34–0.95] $p = 0.048$) (Table 3). Conversely, higher SAPS II (without age component) (HR = 1.02; 95%CI [1.00–1.03] $p = 0.008$) and higher age (HR = 1.03 [1.00–1.07] $p = 0.020$) were associated with poor outcome (Table 4).

In a second model assessing the association between ICU-AI and death, patients with ICU-AI had a higher risk of death with time (HR = 1.89; [1.00–3.51] $p = 0.049$) (Supplementary Table 2).

Discussion

In the present study involving critically ill immunocompromised patients, we observed a decreased incidence of ICU-AI, especially VAP, associated with a higher survival rate in patients treated with MSD.

Table 1 Baseline characteristics and outcomes of study patients

Variables	Standard care $n=143$	Multiple site decontamination $n=151$	p value
Year of admission			<0.001
2020 – no. (%)	91 (63.6)	0 (0.0)	
2021 – no. (%)	52 (36.4)	65 (43.0)	
2022 – no. (%)	0 (0.0)	86 (57.0)	
Age, year	69 [61.61—72]	68 [60—73]	0.605
Male – no. (%)	83 (58.0)	98 (64.9)	0.276
Simplified acute physiology score II	49 [34—62]	48 [34—61]	0.627
Reason for admission			0.076
Scheduled surgery– no. (%)	4 (2.8)	11 (7.3)	
Urgent surgery– no. (%)	6 (4.2)	12 (7.9)	
Medical – no. (%)	133 (93.0)	128 (84.8)	
Trauma*– no. (%)	5 (3.5)	4 (2.6)	0.934
COVID-19– no. (%)	27 (18.9)	20 (13.2)	0.247
Localization before admission			0.331
Other ICU– no. (%)	8 (5.6)	4 (2.6)	
Home– no. (%)	86 (60.1)	100 (66.2)	
Acute care ward– no. (%)	49 (34.3)	47 (31.1)	
Early management			
Systemic antibiotic at admission – no. (%)	97 (67.8)	96 (63.6)	0.519
Vascular catheter – no. (%)	91 (63.6)	107 (70.9)	0.232
Immunodepression			
Immunomodulatory treatment – no. (%)	72 (50.3)	63 (41.7)	0.172
Active solid organ malignancy – no. (%)	77 (53.8)	79 (52.3)	0.884
Solid organ transplant – no. (%)	7 (4.9)	16 (10.6)	0.109
Hematological malignancy	26 (18.2)	25 (16.6)	0.831
Neutropenia < 0.5 G/L	28 (19.6)	31 (20.5)	0.954
MDRO colonization at admission	4 (2.8)	3 (2.0)	0.717
Outcomes			
In ICU death– no. (%)	35 (24.5)	22 (14.6)	0.046
Death at day 30 – no. (%)	34 (23.8)	18 (11.9)	0.012
Length of stay, days	7 [4-14]	6 [4-11]	0.088
Length of mechanical ventilation, days	7 [3-15]	4.50 [2-10]	0.103
ICU-acquired infection– no. (%)	29 (20.3)	9 (6.0)	<0.001
Ventilator-associated pneumonia– no. (%)	25 (17.5)	4 (2.6)	<0.001
Bloodstream infection– no. (%)	10 (7.0)	6 (4.0)	0.377
MDRO acquired infection – no. (%)	1 (0.7)	0	-
MDRO colonization acquisition – no. (%)	7 (4.9)	2 (1.3)	0.096

ICU intensive care unit, *COVID-19* SARS-COV 2 associated infection disease, *MDRO* multi-drug resistant microorganisms

*Among the immunocompromised patients included, the main reason for ICU admission could be secondary to trauma

In recent decades, the management of immunosuppression has become a daily issue for physicians in general but particularly in the ICU [21]. The rise of patients with deficient immune systems had led to an increase in the need for ICU admission for these specific populations. The landscape of immunosuppression has evolved with a lower proportion of uncontrolled HIV patients, while new immunosuppressive treatments have emerged and are increasingly used [22, 23]. In addition, the increasing number of solid organ transplantation and recent advances in the field of hematological malignancies have contributed to improved survival for these patients but also increase the risk of life-threatening events making this population particularly at risk for needing ICU admission [2, 22, 24]. Beyond these epidemiological shifts, these

Table 2 Risk factors for acquired infection (Poisson regression test)

	Univariable			Multivariable		
Variables	IRR	95%CI	*p* value	IRR	95%CI	*p* value
Age, per supplementary year	0.99	0.97–1.02	0.56			
Male (vs female)	1.64	0.90–3.02	0.11	1.49	0.78–2.81	0.22
Reason for admission						
Scheduled surgery	0.37	0.05–2.67	0.32			
Urgent surgery	0.66	0.16–2.72	0.57			
Medical	Ref	Ref	Ref			
Trauma	0.85	0.21–3.50	0.82			
COVID-19	2.04	1.19–3.51	0.009	1.85	1.04–3.30	0.036
Localization before admission						
Other ICU	1.49	0.57–3.90	0.41	0.61	0.22–1.67	0.38
Home	Ref	Ref	Ref			
Acute care ward	1.60	0.92–2.79	0.096	1.29	0.71–2.35	0.40
Simplified acute physiology score II, per 1-point increment	1.01	0.99–1.02	0.24			
Early management						
Vascular catheter	5.62	1.37–23.08	0.016	4.94	1.19–20.39	0.027
Systemic antibiotic at admission	0.96	0.52–1.76	0.89			
Immunodepression						
Immunomodulatory treatment	2.30	1.32–4.01	0.003	1.91	1.08–3.38	0.025
Active solid organ malignancy	0.72	0.42–1.22	0.23			
Solid organ transplant	1.67	0.71–3.89	0.24			
Hematological malignancy	1.22	0.64–2.30	0.55			
Neutropenia < 0.5 G/L	1.11	0.56–2.21	0.76			
Multiple Site Decontamination	0.29	0.15–0.56	< 0.001	0.39	0.20–0.78	0.008

ICU intensive care unit, *COVID-19* SARS-COV 2 associated infection disease

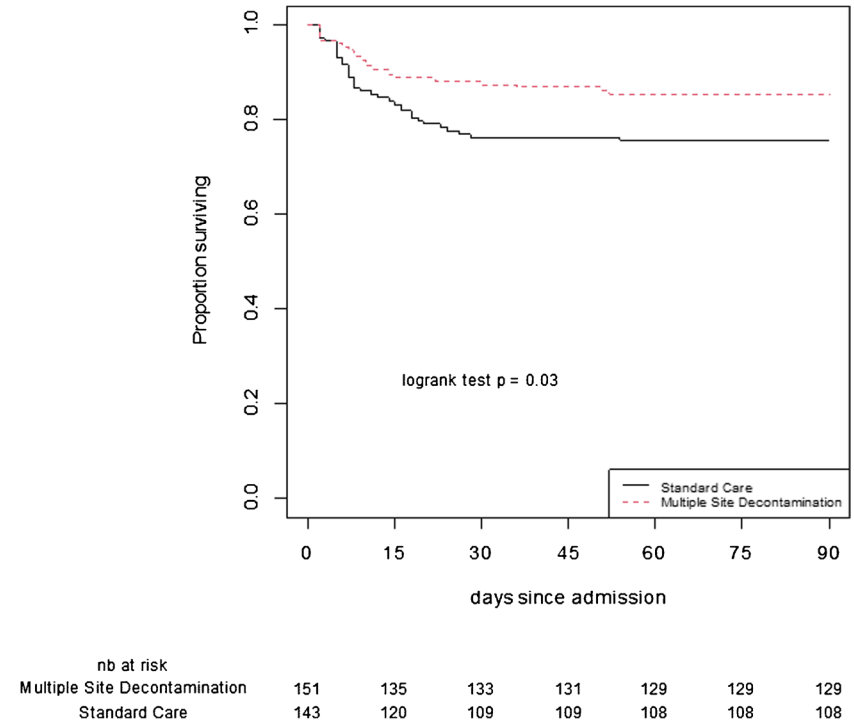
Table 3 Data regarding ICU-AI

Variables	Standard care $n=29$	Multiple site decontamination $n=9$	*p* value
Time from admission to first AI, days	9 [4-14]	7.50 [4-12]	0.734
Pulmonary Aspergillosis– no. (%)	6 (20.7)	3 (30.0)	0.867
Non-fermenting Gram-negative Bacilli – no. (%)	7 (24.1)	2 (20.0)	1.000
Enterobacteriaceae– no. (%)	6 (20.7)	2 (20.0)	1.000
Staphylococcus aureus– no. (%)	4 (13.8)	0 (0.0)	0.525
Streptococcus sp. – no. (%)	2 (6.9)	0 (0.0)	0.983
Enterococcus sp. – no. (%)	2 (6.9)	1 (10.0)	1.000
Coagulase-negative *Staphylococcus*– no. (%)	2 (6.9)	3 (30.0)	0.182

AI acquired infection

patients are characterized by their severity, which is reflected in higher mortality rates and longer ICU lengths of stay, increasing exposure to nosocomial infections [3, 4].

Although a recent study reported similar ICU-AI incidence in immunocompromised patients than in non-immunocompromised patients, the impacts of those infections on the fate of immunocompromised patients deserve to be highlighted [4, 18]. The compromised host immune response as well as pathogen-involved specificities may contribute to this higher mortality in these patients. Impaired host response may result in an atypical clinical presentation (absence of fever, torpid course), while pre-existing disease may result in radiological abnormalities (pulmonary infiltrates), making the rapid diagnosis of ICU-acquired infections a challenge. As a result, diagnosis and treatment of these infections are often delayed [24]. In



nb at risk							
Multiple Site Decontamination	151	135	133	131	129	129	129
Standard Care	143	120	109	109	108	108	108

Fig. 2 Cumulative incidence of ICU-AI in both groups

addition, the higher proportion of multidrug-resistant bacteria and the broader spectrum of pathogens involved may lead to inappropriate empirical treatments [4, 25]. Therefore, strategies to prevent nosocomial infections should be particularly considered in these patients.

Selective digestive decontamination was initially investigated in patients with hematological diseases and in liver recipients because these patients were at-risk of nosocomial infections [7–9]. Moreover, among the unrestricted ICU population, the assessment of selective decontamination regimen has evidenced its effectiveness in preventing ICU-acquired infections [26]. However, due to concerns about rebound infection on cessation of SDD, such a strategy is no longer used in those patients. Although recommended in recent guidelines as a validated strategy to prevent VAP, implementation of selective decontamination in intensive care units remains low [27]. Among factors contributing to the low widespread of this strategy the fear of antimicrobial resistance, may participate in such a poor compliance with current guidelines. However, a study assessing this issue evidenced the absence of the effect of selective decontamination regimens on multidrug-resistant bacteria colonization and acquired infections [13, 28, 29]. Noteworthy, a previous study conducted in participating ICUs reported lower consumption of high-risk promoting resistance antibiotics when MSD was implemented [11]. This may explain the favorable impact of MDRO acquisition with MSD implementation [13, 28].

The high proportion of fungi (reaching nearly 24% of the pathogens involved) in patients with VAP is remarkable. Invasive fungal infections are a common cause of ARDS in immunocompromised populations [30] and immune disorders have been reported as a risk factor for ICU-acquired pulmonary aspergillosis [10, 31], prompting broad screening for these pathogens in immunocompromised populations.

To our knowledge, our study is the first to evaluate decontamination strategies in critically ill immunocompromised populations. However, some limitations must be acknowledged. First, as our study was conducted in adult intensive care units located in western France, where the prevalence of multidrug-resistant bacteria is low, our results may not be generalizable to other settings. Moreover, the long-term impacts of MSD on both environmental and individual ecology remain a crucial issue. Herein, although we did not observe any impact on MDRO acquisition, the sample size precludes a strong conclusion. Second, the heterogeneous entity of immunosuppression may warrant a granular analysis of the effect of preventive strategies in these different settings. Furthermore, the definition of immunocompromised is challenging, in the present study we used a definition that was previously used in ICU patients. However, as immunosuppressive drugs are evolving, the definition of immunocompromised patients must also evolve and could be debated. Third, although the frequency of colonization with MDR-resistant bacteria in immunosuppressed patients has

Table 4 Risk factors for death in the ICU (Cox proportional hazard model)

Variables	Univariable			Multivariable		
	HR	95%CI	*p* value	HR	95%CI	*p* value
Age, per supplementary year	1.04	1.01–1.07	0.008	1.03	1.00–1.07	0.020
Male (vs female)	0.96	0.57–1.64	0.89			
Reason for admission						
Scheduled surgery	0.28	0.04–2.05	0.23			
Urgent surgery	0.25	0.03–1.79	0.21			
Medical	ref	ref	Ref			
Trauma	2.83	1.02–7.83	0.045	2.61	0.93–7.32	0.067
COVID-19	1.41	0.75–2.67	0.29			
Localization before admission						
Other ICU	0.00	0.00–inf	0.99			
Home	ref	ref	Ref			
Acute care ward	1.12	0.65–1.92	0.68			
Simplified acute physiology score II without age component*, per 1-point increment	1.02	1.01–1.04	< 0.001	1.02	1.00–1.03	0.008
Early management						
Vascular catheter	2.57	1.30–5.08	0.007	1.58	0.75–3.30	0.22
Systemic antibiotic at admission	1.01	0.58–1.77	0.96			
Immunodepression						
Immunomodulatory treatment	1.22	0.73–2.06	0.45			
Active solid organ malignancy	0.84	0.50–1.42	0.52			
Solid organ transplant	1.46	0.63–3.40	0.38			
Hematological malignancy	0.64	0.29–1.43	0.28			
Neutropenia < 0.5 G/L	0.74	0.36–1.50	0.40			
Multiple site decontamination	0.56	0.33–0.96	0.034	0.58	0.34–0.95	0.048

ICU intensive care unit, *COVID-19* SARS-COV 2 associated infection disease. * Since SAPS II include age, collinearity is present between this variable and the variable age. To go through, the variable included in the present analysis consisted of SAPS II at the exception of the age component

recently been shown to be lower than in other populations [17], the effects of MSD on colonization with MDR-resistant bacteria have not been evaluated. Finally, the study design (pre-post design without randomization, unblinded assessment of ICU-AI cases) precludes any conclusion to be drawn. The follow-up of included patients was limited to ICU stay, accordingly, the long-term impact of SDD on patients' outcomes could not be assessed (particularly potential invasive fungal infection rebound on withdrawal of SDD). Randomized controlled trials are needed to properly study the effects of MSD in these specific populations.

In conclusion, in ICU immunocompromised patients, MSD appeared to be associated with improved outcomes including a decreased incidence of ICU-AI, especially VAP.

The burden of ICU-acquired infections on the fate of critically-ill immunocompromised patients emphasizes the need for preventive strategies.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10096-023-04650-5.

Acknowledgements The Authors thank Florence MASSART and Brendan STOY for their help in the English writing of the article.

Author contribution All authors participated in the acquisition of data. NM, FR, and PF participated in the conception and design of the study, and NM performed the analysis and interpretation of data. NM and FR drafted the article, and all authors finally approved the submitted version.

Data availability The datasets generated during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval The study protocol received approval from the Rennes Hospital ethics committee (comité d'éthique du CHU de Rennes avis 19–52).

Consent to participate Patients or closest relatives were informed of the anonymous prospective collection of the data and had the possibility not to participate in the study. In case of refusal, the data were not collected accordingly.

Competing interest The authors declare no competing interests.

References

1. van Vliet M, Verburg IWM, van den Boogaard M et al (2014) Trends in admission prevalence, illness severity and survival of haematological patients treated in Dutch intensive care units. Intensive Care Med 40:1275–1284. https://doi.org/10.1007/s00134-014-3373-x
2. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA Cancer J Clin 68(1):7–30. https://doi.org/10.3322/caac.21442
3. Mokart D, Pastores SM, Darmon M (2014) Has survival increased in cancer patients admitted to the ICU? Yes. Intensive Care Med 40:1570–1572. https://doi.org/10.1007/s00134-014-3433-2
4. Moreau AS, Martin-Loeches I, Povoa P, Salluh J, Rodriguez A, Thille AW, Diaz Santos E, Vedes E, Lobo SM, Mégarbane B, MoleroSilvero E, Coelho L, Argaud L, Sanchez Iniesta R, Labreuche J, Rouzé A, Nseir S, TAVeM Study Group (2018) Impact of immunosuppression on incidence, aetiology and outcome of ventilator-associated lower respiratory tract infections. Eur Respir J 51(3):1701656. https://doi.org/10.1183/13993003.01656-2017
5. Massart N, Reizine F, Fillatre P, Seguin P, La Combe B, Frerou A, Egreteau PY, Hourmant B, Kergoat P, Lorber J, Souchard J, Canet E, Rieul G, Fedun Y, Delbove A, Camus C (2022) Multiple-site decontamination regimen decreases acquired infection incidence in mechanically ventilated COVID-19 patients. Ann Intensive Care 12(1):84. https://doi.org/10.1186/s13613-022-01057-x
6. Camus C, Bellissant E, Sebille V et al (2005) Prevention of acquired infections in intubated patients with the combination of two decontamination regimens. Crit Care Med 33(2):307–314. https://doi.org/10.1097/01.ccm.0000152224.01949.01
7. de Jong PJ, de Jong MD, Kuijper EJ, van der Lelie H (1993) The value of surveillance cultures in neutropenic patients receiving selective intestinal decontamination. Scand J Infect Dis 25(1):107–113
8. E.O.R.T.C. (1982) Gnotobiotic Project Group: a prospective cooperative study of antimicrobial decontamination in granulocytopenic patients. Comparison of two different methods. Infection 10(3):131–8. https://doi.org/10.1007/BF01640762
9. Bow EJ, Rayner E, Scott BA, Louie TJ (1987) Selective gut decontamination with nalidixic acid or trimethoprim-sulfamethoxazole for infection prophylaxis in neutropenic cancer patients: relationship of efficacy to antimicrobial spectrum and timing of administration. Antimicrob Agents Chemother 31(4):551–557. https://doi.org/10.1128/AAC.31.4.551
10. Schauwvlieghe AFAD, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Van Tienen C, Lagrou K, Verweij PE, Van de Veerdonk FL, Gommers D, Spronk P, Bergmans DCJJ, Hoedemaekers A, Andrinopoulou ER, van den Berg CHSB, Juffermans NP, Hodiamont CJ, Vonk AG, Depuydt P, Boelens J, Wauters J, Dutch-Belgian Mycosis study group (2018) Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. Lancet Respir Med 6(10):782–792. https://doi.org/10.1016/S2213-2600(18)30274-1
11. Massart N, Dupin C, Legris E, Fedun Y, Barbarot N, Legay F, Wattecamps G, Le Gall F, La Combe B, Bouju P, Frerou A, Muller L, Rieul G, Fillatre P (2023) Multiple-site decontamination in mechanically ventilated ICU patients: A real-life study. Infect Dis Now 53(3):104666. https://doi.org/10.1016/j.idnow.2023.104666
12. Massart N, Dupin C, Mari A et al (2021) Clinician involvement for ventilator-associated pneumonia surveillance resulted in higher than expected incidence rate reported with implication for attributable mortality. Infect Dis (Lond) 53(2):154–157. https://doi.org/10.1080/23744235.2020.1839129
13. Blot SI, Taccone FS, Van den Abeele AM, Bulpa P et al (2012) A clinical algorithm to diagnose invasive pulmonary aspergillosis in critically ill patients. Am J Respir Crit Care Med 186(1):56–64. https://doi.org/10.1164/rccm.201111-1978OC. (Erratum in: Am J Respir Crit Care Med. 2012 Oct 15;186(8):808)
14. Verweij PE, Rijnders BJA, Brüggemann RJM et al (2020) Review of influenza-associated pulmonary aspergillosis in ICU patients and proposal for a case definition: an expert opinion. Intensive Care Med 46(8):1524–1535. https://doi.org/10.1007/s00134-020-06091-6
15. Koehler P, Bassetti M, Chakrabarti A et al (2021) Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. Lancet Infect Dis 21(6):e149–e162. https://doi.org/10.1016/S1473-3099(20)30847-1
16. Massart N, Camus C, Benezit F, Moriconi M, Fillatre P, Le Tulzo Y (2020) Incidence and risk factors for acquired colonization and infection due to extended-spectrum beta-lactamase-producing Gram-negative bacilli: a retrospective analysis in three ICUs with low multidrug resistance rate. Eur J Clin Microbiol Infect Dis 39(5):889–895. https://doi.org/10.1007/s10096-019-03800-y
17. Kreitmann L, Vasseur M, Jermoumi S, Perche J, Richard JC, Wallet F, Chabani M, Nourry E, Garçon P, Zerbib Y, Van Grunderbeeck N, Vinsonneau C, Preda C, Labreuche J, Nseir S (2023) Relationship between immunosuppression and intensive care unit-acquired colonization and infection related to multidrug-resistant bacteria: a prospective multicenter cohort study. Intensive Care Med 49(2):154–165. https://doi.org/10.1007/s00134-022-06954-0
18. Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F et al (2012) Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med 38(12):1930–1945
19. Leone M, Bouadma L, Bouhemad B et al (2018) Hospital-acquired pneumonia in ICU. Anaesth Crit Care Pain Med 37(1):83–98. https://doi.org/10.1016/j.accpm.2017.11.006
20. Magiorakos AP, Srinivasan A, Carey RB et al (2012) Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 18(3):268–281. https://doi.org/10.1111/j.1469-0691.2011.03570.x
21. Harpaz R, Dahl RM, Dooling KL (2016) Prevalence of Immunosuppression Among US Adults, 2013. JAMA 316(23):2547–2548. https://doi.org/10.1001/jama.2016.16477
22. Azoulay É, Castro P, Maamar A, Metaxa V, de Moraes AG, Voigt L, Wallet F, Klouche K, Picard M, Moreau AS, Van De Louw A, Seguin A, Mokart D, Chawla S, Leroy J, Böll B, Issa N, Levy B, Hemelaar P, Fernandez S, Munshi L, Bauer P, Schellongowski P, Joannidis M, Moreno-Gonzalez G, Galstian G, Darmon M, Valade S, Nine-I investigators (2021) Outcomes in patients treated with chimeric antigen receptor T-cell therapy who were admitted to intensive care (CARTTAS): an international, multicentre, observational cohort study. Lancet Haematol 8(5):e355–e364. https://doi.org/10.1016/S2352-3026(21)00060-0
23. Toffart AC, Meert AP, Wallet F, Gibelin A, Guisset O, Gonzalez F, Seguin A, Kouatchet A, Delaunay M, Debieuvre D, Duchemann B, Rousseau-Bussac G, Nyunga M, Grimaldi D, Levrat A, Azoulay E, Lemiale V (2023) ICU admission for solid cancer patients treated with immune checkpoint inhibitors. Ann Intensive Care 13(1):29. https://doi.org/10.1186/s13613-023-01122-z
24. Timsit JF, Sonneville R, Kalil AC, Bassetti M, Ferrer R, Jaber S, Lanternier F, Luyt CE, Machado F, Mikulska M, Papazian L, Pène F, Poulakou G, Viscoli C, Wolff M, Zafrani L, Van Delden C (2019) Diagnostic and therapeutic approach to infectious diseases in solid organ transplant recipients. Intensive Care Med 45(5):573–591. https://doi.org/10.1007/s00134-019-05597-y
25. Florescu DF, Sandkovsky U, Kalil AC (2017) Sepsis and Challenging Infections in the Immunosuppressed Patient in the Intensive Care Unit. Infect Dis Clin North Am 31(3):415–434. https://doi.org/10.1016/j.idc.2017.05.009

26. de Smet AM, Kluytmans JA, Cooper BS et al (2009) Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med 360(1):20–31. https://doi.org/10.1056/NEJMoa0800394
27. Roquilly A, Chanques G, Lasocki S, Foucrier A, Fermier B, De Courson H, Carrie C, Danguy des Deserts M, Gakuba C, Constantin JM, Lagarde K, Holleville M, Blidi S, Sossou A, Cailliez P, Monard C, Oudotte A, Mathieu C, Bourenne J, Isetta C, Perrigault PF, Lakhal K, Rouhani A, Asehnoune K, Guerci P, Tran Dinh A, Chousterman B, Cupaciu A, Dahyot-Fizelier C, Bellier R, Au Duong J, Mansour A, Morel J, Beauplet G, Vibet MA, Feuillet F, Sébille V, Leone M (2021) Implementation of French recommendations for the prevention and the treatment of hospital-acquired pneumonia: a cluster-randomized trial. Clin Infect Dis. 73(7):e1601-e1610. https://doi.org/10.1093/cid/ciaa1441
28. Camus C, Sauvadet E, Tavenard A et al (2016) Decline of multidrug-resistant Gram negative infections with the routine use of a multiple decontamination regimen in ICU. J Infect 73(3):200–209. https://doi.org/10.1016/j.jinf.2016.06.007
29. de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, Vroom MB, Dankert J, Kesecioglu J (2003) Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet 362(9389):1011–1016. https://doi.org/10.1016/S0140-6736(03)14409-1
30. Azoulay E, Russell L, Van de Louw A, Metaxa V, Bauer P, Povoa P, Montero JG, Loeches IM, Mehta S, Puxty K, Schellongowski P, Rello J, Mokart D, Lemiale V, Mirouse A, Nine-i Investigators (2020) Diagnosis of severe respiratory infections in immunocompromised patients. Intensive Care Med 46(2):298–314. https://doi.org/10.1007/s00134-019-05906-5
31. Gangneux JP, Dannaoui E, Fekkar A, Luyt CE, Botterel F, De Prost N, Tadié JM, Reizine F, Houzé S, Timsit JF, Iriart X, Riu-Poulenc B, Sendid B, Nseir S, Persat F, Wallet F, Le Pape P, Canet E, Novara A, Manai M, Cateau E, Thille AW, Brun S, Cohen Y, Alanio A, Mégarbane B, Cornet M, Terzi N, Lamhaut L, Sabourin E, Desoubeaux G, Ehrmann S, Hennequin C, Voiriot G, Nevez G, Aubron C, Letscher-Bru V, Meziani F, Blaize M, Mayaux J, Monsel A, Boquel F, Robert-Gangneux F, Le Tulzo Y, Seguin P, Guegan H, Autier B, Lesouhaitier M, Pelletier R, Belaz S, Bonnal C, Berry A, Leroy J, François N, Richard JC, Paulus S, Argaud L, Dupont D, Menotti J, Morio F, Soulié M, Schwebel C, Garnaud C, Guitard J, Le Gal S, Quinio D, Morcet J, Laviolle B, Zahar JR, Bougnoux ME (2022) Fungal infections in mechanically ventilated patients with COVID-19 during the first wave: the French multicentre MYCOVID study. Lancet Respir Med 10(2):180–190. https://doi.org/10.1016/S2213-2600(21)00442-2