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Impact of contact isolation for multidrug-resistant organisms on the occurrence of medical errors and adverse events

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Abstract: Contact isolation of infected or colonised hospitalised patients is instrumental to interrupting multidrug-resistant organism (MDRO) cross-transmission. Many studies suggest an increased rate of adverse events associated with isolation. We aimed to compare isolated to non-isolated patients in intensive care units (ICUs) for the occurrence of adverse events and medical errors. *Methods:* We used the large database of the Iatroref III study that included consecutive patients from three ICUs to compare the occurrence of pre-defined medical errors and adverse events among isolated vs. non-isolated patients. A subdistribution hazard regression model with careful adjustment on confounding factors was used to assess the effect of patient isolation on the occurrence of medical errors and adverse events. *Results:* Two centres of the Iatroref III study were eligible, an 18-bed and a 10-bed ICU (nurse-to-bed ratio 2.8 and 2.5, respectively), with a total of 1,221 patients. After exclusion of the neutropenic and graft transplant patients, a total of 170 isolated patients were compared to 980 non-isolated patients. Errors in insulin administration and anticoagulant prescription were more frequent in isolated patients. Adverse events such as hypo- or hyperglycaemia, thromboembolic events, haemorrhage, and MDRO ventilator-associated pneumonia (VAP) were also more frequent with isolation. After careful adjustment of confounders, errors in anticoagulant prescription [subdistribution hazard ratio (sHR) = 1.7, $p = 0.04$], hypoglycaemia (sHR = 1.5, $p = 0.01$), hyperglycaemia (sHR = 1.5, $p = 0.004$), and MDRO VAP (sHR = 2.1, $p = 0.001$) remain more frequent in isolated patients. *Conclusion:* Contact isolation of ICU patients is associated with an increased rate of some medical errors and adverse events, including non-infectious ones.

Keywords Multidrug resistant bacteria · Isolation · Intensive care unit · Adverse events · Medical errors

Introduction

Antimicrobial resistance has reached such endemic levels that infection control programmes are now mandatory procedures in many centres. Means to prevent the spread of multidrug-resistant organisms (MDROs) have included the development of antimicrobial stewardship programmes, the promotion of hand hygiene and its improvement, the screening of patients at admission, and the use of strict barrier and isolation precautions. A number of infection control societies recommend mandatorily setting up and respecting standard and contact precautions for preventing

the transmission of MDROs such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin–resistant *Enterococcus* (VRE), and some gram-negative bacilli (GNB) [1–3]. However, although recommended and widely used in healthcare institutions to prevent transmission of MDROs, contact isolation measures and their global impact remain debated [4–7].

Recently, in a cluster-randomised trial conducted in the intensive care unit (ICU), some authors suggested that surveillance for MRSA and VRE colonisation as well as the expanded use of barrier precautions was not effective in reducing the transmission of these two MDROs [8]. Moreover, contact isolation in hospital wards has been associated with decreased patient-healthcare worker contact [9], an increased rate of depression and anxiety symptoms, decreased patient satisfaction with care [10], and a higher number of adverse events in patients on contact isolation [11].

So far, the global evaluation of the risk-benefit balance of the isolation of ICU patients remains controversial. During the Iatroref III study, we carefully monitored selected medication errors, adverse events and nosocomial infections. This study included two ICUs from the Iatroref III study where MDRO-related contact isolation of non-neutropenic, not graft-recipient patients was routinely performed on an individual patient basis and prospectively monitored.

Therefore, the purpose of this post hoc analysis is to assess the impact of isolation on the rate of medication errors and adverse events using the Iatroref III study data set.

Methods

This study was approved by the institutional review board of the Rhône-Alpes-Auvergne Clinical Investigation Centres, which waived the requirement for written informed consent. Patients eligible for the study are all patients from two centres extracted from the Iatroref III study [12, 13]. The Iatroref III study is a multicentre cluster-randomised study in consecutive patients older than 18 years, aiming to test the effects of three multifaceted safety programmes (MFSP). These programmes were designed to decrease insulin administration errors, anticoagulant prescription and administration errors, and errors leading to accidental removal of endotracheal tubes and central venous catheters, respectively. The Iatroref III study included all consecutive patients admitted during four predefined periods from January 2007 to January 2008 in three ICUs belonging to the Outcome Rea Study Group. The two centres that were eligible for the isolation study were those where patients were isolated for MDRO. Isolation was initiated when patients were suspected of or identified as carrying an MDRO or as being infected with one. One centre is within a university teaching hospital; the other is within a general hospital. Within this subset, patients were excluded if they had protective isolation for neutropenia or recent solid organ transplantation.

Patient characteristics were collected on Rhea ™ software (http://outcomerea.org/rhea/install), and medical error characteristics were entered in an add-on specifically designed for the study. The following data were collected: age, sex, the underlying diseases using the Knaus classification [14] admission category (medical, scheduled surgery, or unscheduled surgery), and the reason for ICU admission (with nine categories prospectively defined before the study, namely, respiratory, cardiac, or renal failure; coma, multiple organ failure, acute exacerbation of chronic pulmonary disease, monitoring, trauma, and scheduled surgery). The location of the patient prior to ICU admission was recorded, with transfer from wards defined as being within the same hospital or from another hospital. The Simplified Acute Physiology Score (SAPS II) [15] at admission and the Sequential Organ Failure Assessment (SOFA) score [16] were computed using the worst physical and laboratory data during the first 24 h in the ICU. The date and reason for contact isolation initiation were recorded. Patients who were MDRO carriers were isolated until the day of ICU discharge. Invasive procedures and medications (anticoagulants, vasopressor support, blood products, insulin, sedatives) used during the entire stay were listed. Lengths of stay in the ICU and acute-care hospital were recorded, as well as vital status at ICU and hospital discharge.

Specific incidences of adverse events were calculated as the ratio of the number of events on the number of days of ICU care where the patient was exposed to the risk of the specific event.

Medical errors targeted by the study

Medical errors were defined according to the Iatroref III study [13]; the three target safety indicators and their possible harm have been defined elsewhere [12]. The following events were prospectively recorded: accidental removal of a central venous catheter (Fig. 1) or accidental extubation [17, 18], hypernatremia >150 mmol/l [19], ventilator-associated pneumonia (VAP) [20] occurrence, error in insulin administration, error in anticoagulant administration, error in anticoagulant prescription, adverse events related to medication errors such as phlebitis, pulmonary embolism, haemorrhage requiring red blood cell transfusion, and hypo- and hyperglycaemia (Table 1).

Statistical analysis

Patients' characteristics were described using the frequency and percentage of qualitative variables, and the

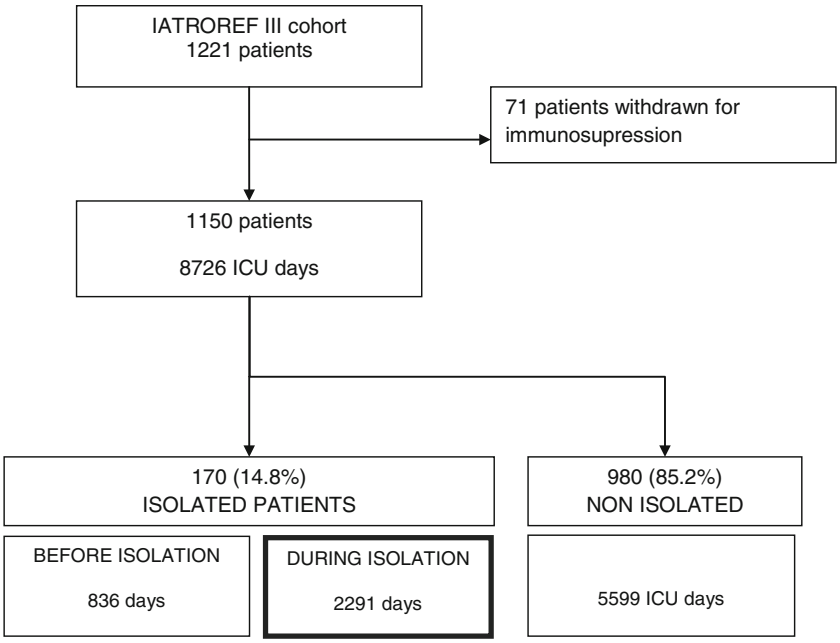

Fig. 1 Flow chart: the exposed population is in the *bold-line square*. (Isolated patients during isolation period)

Table 1 Definitions of selected medical errors

Selected medical errors	Definitions
Error in administering anticoagulant medication	Anticoagulant therapy is not administered as prescribed. The divergence may relate to the planning and/or execution of the prescription: drug choice, dosage, preparation and administration modalities, dosing times, or dosing intervals
Error in prescribing anticoagulant medication	Failure to comply with recommendations (scientific societies, department protocols, local drug committees) regarding the indications, dosage, administration modalities, contraindications, drug interactions, or laboratory monitoring of anticoagulant treatment
Error in administering insulin	Insulin therapy is not administered as prescribed (including as per department protocol). The divergence may relate to the planning and/or execution of the prescription: drug choice, dosage, or preparation and administration modalities
Accidental removal of a central venous catheter	Unplanned complete removal of a central venous catheter by the patient or by a healthcare worker during care or manipulation of the catheter
Accidental extubation	Unplanned extubation
Strict glucose control	4.4–6.1 mmol/l

mean and standard deviation (or median and quartiles) for quantitative ones.

Differences in specific incidence rates of adverse events/medical errors between the pre-isolation period and isolation period were tested using the Poisson regression model with the Pearson scale and robust sandwich variance to include intra-patient correlation.

We used subdistribution hazard models to account for discharge alive from the ICU as a competing event to experiencing medical errors or adverse event in the ICU [21]. This modelling took into account the indirect effect on mortality of a (potentially) extended stay due to the exposure. Isolation was treated as time-dependent exposition, changing from non-isolated to isolated status at the time of isolation. For each medical error or adverse event, models were adjusted for other clinically relevant confounders.

Models were applied to the entire cohort except for a few endpoints: for accidental removal of the endotracheal tube or catheter, analysis was restricted to intubated patient or patients with a central venous catheter at least once during the ICU stay. Errors on administering anticoagulant were restricted to patients with anticoagulants, ventilator-associated nosocomial pneumonia cases were restricted to ventilated patients, and errors in insulin administration were restricted to patients receiving insulin.

Every model was stratified by ICU centre. No correction for multiple testing was applied. The full statistical analysis was performed using SAS version 9.3, and models were fitted using PROC PHREG.

Results

A total of 1,221 patients were included in the two centres eligible for MDRO isolation study. The two centres were respectively an 18-bed medical ICU and a 10-bed medical/surgical ICU. The targeted nurse-to-bed ratios were 2.8 and 2.5 for both ICUs, but we did not collect daily nurse-to-bed ratio variability because of absenteeism of closed beds. Patients who were neutropenic or had had a graft transplant were excluded (171 patients, 5.8 %). Therefore, 1,150 (54 %) patients were eligible for the MDRO isolation study (Table 2). Among these patients, 170 (14.8 %) were isolated for MDRO carriage or infection during their ICU stay, whereas 980 (85.2 %) were not. The mean age of the study population was 62 years (±17 years), and the average SAPS was 43 (±21). Isolated patients were more often diagnosed for acute respiratory failure shock or multiorgan failure at admission than non-isolated patients. In the first 24 h following admission, they were more frequently treated with catecholamine and insulin and more frequently had central venous and arterial catheters.

Of the 170 isolated patients, 75 (44.1 %) had adverse events before isolation and 140 (82.4 %) during the isolation period.

Rates of medication errors or adverse events per patient are depicted in Table 3.

Specific incidences of adverse events associated with transfusion or VAP due to MDRO (Table 3) were higher during days under isolation compared to non-isolation days.

When we considered VAP, the specific incidence in non-isolated patients was 35.6 per thousand mechanical ventilation days, whereas, for isolated patients, the incidence was 72.1 per thousand before isolation and 65.9 per thousand under isolation. Interestingly, the increase in the incidence of VAP due to MDRO was the sole contributor to the increase in VAP incidence observed under isolation (Table 3).

Table 2 Patients' characteristics

Characteristics		All (n = 1,150)	Non-isolated patients (n = 980)	Isolated patients (n = 170)	P value
Characteristics at admission					
Age, mean (SD)		61.9 (17.6)	61.9 (17.9)	61.7 (16)	0.7
Gender	Male	686 (59.7)	570 (58.2)	116 (68.2)	0.01
	Female	464 (40.3)	410 (41.8)	54 (31.8)	
Type	Medical	947 (82.3)	825 (84.2)	122 (71.8)	<0.0001
	Emergency surgery	118 (10.3)	85 (8.7)	33 (19.4)	
	Scheduled surgery	85 (7.4)	70 (7.1)	15 (8.8)	
At least one chronic disease	Yes	446 (38.8)	356 (36.3)	90 (52.9)	<0.0001
Immunocompromised patient	Yes	105 (9.1)	82 (8.4)	23 (13.5)	0.03
Haemopathy	Yes	42 (3.7)	28 (2.9)	14 (8.2)	0.003
Metastatic cancer	Yes	8 (0.7)	5 (0.5)	3 (1.8)	0.9
AIDS	Yes	76 (6.6)	66 (6.7)	10 (5.9)	0.10
Diabetes	Yes	202 (17.8)	172 (17.8)	30 (17.6)	1
Symptoms at admission	Coma	211 (18.3)	191 (19.5)	20 (11.8)	0.009
	COPD exacerbation	42 (3.7)	34 (3.5)	8 (4.7)	
	Shock/multiorgan failure	266 (23.1)	213 (21.7)	53 (31.2)	
	Acute respiratory failure	254 (22.1)	208 (21.2)	46 (27.1)	
	Acute renal failure	63 (5.5)	57 (5.8)	6 (3.5)	
	Scheduled surgery/monitoring	309 (26.9)	273 (27.9)	36 (21.2)	
	Trauma	5 (0.4)	4 (0.4)	1 (0.6)	
Transfer from another ward	Yes	517 (45)	416 (42.4)	101 (59.4)	<0.0001
SAPS II (1), mean (SD)		43.4 (21.3)	42.9 (22)	46.6 (16.8)	0.0003
Bed occupancy rate at admission, [IQR]		0.9 [0.3]	0.9 [0.3]	1 [0.3]	0.36
Characteristics in the first 24 h					
MV	Yes	468 (40.7)	393 (40.1)	75 (44.1)	0.3
NIV	Yes	107 (9.3)	90 (9.2)	17 (10)	0.7
Arterial catheter	Yes	331 (28.8)	258 (26.3)	73 (42.9)	<0.0001
Central venous catheter	Yes	516 (44.9)	410 (41.8)	106 (62.4)	<0.0001
Urinary tract catheter	Yes	881 (76.6)	742 (75.7)	139 (81.8)	0.09
Vasopressors	Yes	352 (30.6)	285 (29.1)	67 (39.4)	0.007
Insulin administration	Yes	613 (53.3)	501 (51.1)	112 (65.9)	0.0004
Preventive and therapeutic anticoagulant used	Yes	497 (43.2)	431 (44)	66 (38.8)	0.24

Quantitative variables are expressed as mean (SD) or median [1st quartile; 3rd quartile] as appropriate; qualitative variables are expressed as frequency (percentage)

MV mechanical ventilation, *NIV* non-invasive ventilation

Table 3 Frequency (percentage) of patients with at least one adverse events and specific incidence of adverse events according to patients and days with or without isolation

	Adverse events	Non-isolated population 980 patients, 5,599 ICU days	Isolated population, 170 patients, 3,127 ICU days		*p* value $
			Before isolation 836 ICU days	During isolation 2,291 ICU days	
With accidental catheter removal or extubation	*n* Patients (%)	41 (4.2)	5 (2.9)	10 (5.3)	
	n Events/*n* days with tracheal tube or catheters (‰)	48/3,948 (12.2 ‰)	6/786 (7.6 ‰)	10/1,880 (5.3 ‰)	0.50
Anticoagulant administration error	*n* Patients (%)	31 (3.2)	5 (2.9)	7 (4.1)	
	n Events/*n* days with anticoagulant (‰)	33/4,080 (8.1 ‰)	5/653 (7.7 ‰)	10/1,717 (5.8 ‰)	0.67
Anticoagulant prescription error	*n* Patients (%)	66 (6.7)	5 (2.9)	19 (11.1)	
	n Events/*n* days with anticoagulant (‰)	99/4,080 (24.3 ‰)	6/653 (9.2 ‰)	35/1,717 (20.4 ‰)	0.13
Error prescribing or administering anticoagulant, prescription or administration error	*n* Patients (%)	88 (9.0)	9 (5.2)	24 (14.1)	
	n Events/*n* days with anticoagulant (‰)	132/4,080 (32.4 ‰)	11/653 (16.8 ‰)	45/1,717 (26.2 ‰)	0.31
Phlebitis/pulmonary embolism	*n* Patients (%)	26 (2.7)	5 (2.9)	10 (5.9)	
	n Events/*n* days with anticoagulant (‰)	32/4,080 (7.8 ‰)	5/653 (7.7 ‰)	15/1,717 (8.7 ‰)	0.98
Haemorrhage	*n* Patients (%)	24 (2.5)	7 (4.1)	8 (4.7)	
	n Events/*n* days with anticoagulant (‰)	32/4,080 (7.8 ‰)	8/653 (1.2 ‰)	8/1,717 (4.7 ‰)	0.38
Red blood cell transfusion (number of packs)	*n* Patients (%)	195 (19.9)	35 (20.6)	56 (32.9)	
	n Events/*n* days with anticoagulant (‰)	741/4,080 (181.6 ‰)	187/653 (286.3 ‰)	428/1,717 (249.3 ‰)	0.42
Insulin administration error	*n* Patients (%)	417 (42.5)	53 (31.2)	100 (58.9)	
	n Events/*n* days with insulin (‰)	3,259/4,071 (800.5 ‰)	812/692 (1,173.4 ‰)	1,808/1,794 (1,007.8 ‰)	0.40
Hypoglycaemia	*n* Patients (%)	168 (17.1)	33 (19.4)	53 (31.2)	
	n Events/*n* days with insulin (‰)	284/4,071 (69.8 ‰)	66/692 (95.4 ‰)	124/1,794 (69.1 ‰)	0.14
Hyperglycaemia	*n* Patients (%)	535 (54.6)	64 (37.6)	113 (66.4)	
	n Events/*n* days with insulin (‰)	1,720/4,071 (422.5 ‰)	252/692 (364.1 ‰)	767/1,794 (427.5 ‰)	0.14
ICU-acquired hypernatremia episode	*n* Patients (%)	23 (2.4)	6 (3.5)	5 (2.9)	
	n Events/*n* days in ICU (‰)	25/5,559 (4.5 ‰)	7/836 (8.4 ‰)	5/2,291 (2.2 ‰)	0.03
VAP	*n* Patients (%)	64 (6.5)	30 (17.6)	35 (20.6)	
	n Events/*n* days with intubation or tracheostomy (‰)	98/2,759 (35.5 ‰)	47/652 (72.1 ‰)	72/1,092 (65.9 ‰)	0.07
VAP (sensitive isolates)	*n* Patients (%)	56 (5.7)	17 (10)	22 (12.9)	
	n Events/*n* days with intubation or tracheostomy (‰)	80/2,759 (29.0 ‰)	28/652 (42.9 ‰)	34/1,092 (31.1 ‰)	0.06
VAP (resistant isolates)	*n* Patients (%)	16 (1.6)	16 (9.4)	19 (11.1)	
	n Events/*n* days with intubation or tracheostomy (‰)	18/2,759 (6.5 ‰)	19/652 (29.1 ‰)	38/1,092 (34.8 ‰)	0.65

VAP ventilation associated pneumonia, *Haemorrhage* haemorrhage > half of all blood volume, controlled and not controlled haemorrhages during puncture, digestive haemorrhage

$ Comparison of the incidence rate in isolated patients before vs. during isolation using Poisson regression with the Pearson scale and robust sandwich variance (intra-patient correlation)

The time-adjusted hazard ratio of errors in anticoagulant therapy prescription, in insulin administration, and of adverse events (hypo-, hyperglycaemia, haemorrhage, thromboembolic events) increased during isolation days. After adjustment of other risk factors, isolation remained associated with errors in anticoagulant prescription, hypo- and hyperglycaemia, and VAP due to MDRO (Table 4). Very similar results were obtained when comparing patients isolated on admission and patients not isolated. There was no significant difference in the effect of isolation on the occurrence of adverse events between the two centres.

Discussion

In this study, our purpose was to assess the frequency of adverse events according to the isolation status in an ICU cohort population. Medication errors and adverse events were prospectively collected by trained dedicated personnel on a large cohort of patients. After careful adjustment for confounding variables and use of appropriate time-adjusted models, hypoglycaemia, hyperglycaemia, error in anticoagulant prescription, and VAP due to MDRO were the five medication errors or adverse events observed significantly more often in isolated patients.

The presence of errors that could be avoided without having to examine the patient (e.g., insulin ordering depends on review of medical records and not on direct evaluation of the patient) could be considered surprising. Indeed, in the two ICUs, medical records were only available as paper charts located into the patient's room. Switching to electronic medical records available outside the room could be a potential benefit for reducing the occurrence of adverse events and needs to be further evaluated.

The risk-benefit ratio of isolation in the ICU is debated. Whereas a number of studies have suggested that isolation reduces the spread of multiresistant bacteria [7, 22], other studies have underlined the weakness of and potential bias associated with before-after studies [4, 23] that combine isolation with other interventions [24]. Several studies have reported significantly better control using surveillance cultures and contact precautions in the ICU [1, 7, 25].

Several studies [10, 11, 26, 27] performed in hospital wards outside of ICUs suggested that the use of isolation may cause patients to receive less medical attention and less healthcare worker-to-patient contact; may result in more frequent medical errors and adverse events, in delay of medical progress, and delay of discharge; and is associated with psychological stress and anxiety, and with decreased patient satisfaction with care [28].

Adverse events in patients under contact precaution (CP) have been evaluated in an historical-matched cohort reviewing charts for 150 patients under CP and 300 controls not under CP at two hospitals in North America. Two matched cohorts were retrospectively created with

Table 4 Risk of adverse events and medical errors according to isolation status

	Non-isolated patients 980 (100)	Isolated patients 170 (100)	Unadjusted sHR (95 % CI)	*p*	Adjusted sHR [95 % CI]	*p*[a]
Adverse events						
Accidental removal of endotracheal tube or catheter	41/784 (6.5)	14/148 (9.5)	1.2 (0.6–2.5)	0.6	1.3 (0.6–2.8)	0.5
Phlebitis/pulmonary embolism	26 980 (2.7)	15/170 (8.8)	2.8 (1.4–5.8)	0.004	1.8 (0.8–3.9)	0.15
Haemorrhage	24/980 (2.5)	15/170 (8.8)	2.4 (1.1–5.2)	0.03	1.5 (0.7–3.5)	0.3
Packed red blood cells administration (number of packs)	195/980 (19.9)	76/170 (44.7)	1.9 (1.4–2.7)	0.0001	1.3 (0.9–1.8)	0.2
Hypoglycaemia	168/980 (17.1)	74/170 (43.5)	1.9 (1.4–2.7)	0.0001	1.5 (1.0–2.1)	0.03
Hyperglycaemia	535/980 (54.6)	135/170 (79.4)	1.6 (1.2–2.0)	0.0004	1.5 (1.2–2.0)	0.002
Hypernatremia	23/980 (2.4)	11/170 (6.5)	1.3 (0.5–3.3)	0.6	0.7 (0.2–1.8)	0.4
VAP	64/497 (12.9)	50/125 (40)	1.2 (0.7–2.0)	0.5	1.1 (0.7–1.8)	0.7
VAP (sensitive isolates)	56/497 (11.3)	32/125 (25.6)	1.1 (0.6–1.9)	0.8	1.0 (0.6–1.8)	0.9
VAP (resistant isolates)	16/497 (3.2)	29/125 (23.2)	2.2 (1.4–3.4)	0.0005	2.1 (1.3–3.3)	0.002
Medical errors						
Anticoagulant prescription error	66/980 (6.7)	23/170 (13.5)	2.1 (1.2–3.5)	0.007	1.9 [1.1–3.3]	0.02
Anticoagulant administration error	31/705 (4.4)	12/148 (8.1)	1.3 (0.6–2.9)	0.5	1.0 [0.4–2.2]	0.9
Anticoagulant administration or prescription error	88/705 (12.5)	32/148 (21.6)	1.8 (1.1–2.8)	0.01	1.5 [0.9–2.5]	0.09
Insulin administration error administering insulin	417/711 (58.7)	118/158 (74.7)	1.2 (0.9–1.6)	0.2	1.0 [0.8–1.4]	0.8

sHR subdistribution hazard

[a] Systematic adjustment on age, transfer from another ward, type of patient, presence of chronic disease, immunosuppression, diabetes, symptoms on admission (multiple organ failure or shock; continuous monitoring, coma, respiratory failure), SAPS II score, ward occupational rate at admission

patients issued from general medicine or patients with congestive heart failure and adjusted on the CP exposure duration. This study showed that CP was associated with a decrease in vital sign recording and a decrease in medical and nurse daily recording of narrative notes. Isolation was also associated with a more than six-fold increase in the occurrence of preventable adverse events and with an eight-fold increase in supportive care failure (falls, pressure ulcers, fluid or electrolyte disorders) [11].

All these different studies have a number of limitations such as the limited number of patients included [27, 29], no or limited adjustment for the number of confounding factors, and an unclear total number of isolated patients. More importantly, it has never been tested in an ICU setting where a nurse-to-patient ratio of 1:2 is considered sufficient [11, 26]. Our results suggest that the association between isolation and non-infectious medical errors or adverse events exists also in the ICU setting.

In a recent study [30], the authors underline a decrease in the incidence of VAP in their ICU after implementing eight target recommendations, with most of them requiring close monitoring of the patient. In our study, after careful adjustment of the risk factors of VAP, isolation remained a risk factor solely for those VAPs due to MDRO. The increase in the cumulative incidence of VAP due to MDRO could either be due to a failure to maintain an appropriate strategy for prevention or be related to the MDRO carriage. Indeed, the increase in resistance of endogenous flora associated with MDRO carriage adds to the total burden of VAP [31] and likely explains the overall increase in the VAP rate.

Study limitations

The association shown between isolation measures and the increase in the risk of some medication errors and of some adverse events might have been related to the absence of control of other confounders that may influence the risk of events. We made a particular effort to adjust for potential confounders at ICU admission, but we cannot be sure that all confounders present at ICU admission or occurring between ICU admission and isolation have been taken into account.

The crude incidence of adverse events was paradoxically higher before that during isolation in isolated patients. This finding is explained by the fact that the daily number of adverse events in all patients (isolated and non-isolated) in the original IATROREF III study decreased with time during the ICU stay [12].

Another limitation is that our study was not designed to capture data related to the number of visits of healthcare staff to monitor and check the patient, the level of medical and nurse recording, or the patient's feelings about the isolation. We selected events previously demonstrated to be easy to measure and well defined. It still needs to be established that the selected adverse events are an appropriate surrogate of an increase in the overall rate of adverse events. Finally, although in our study we underlined an association between isolation and adverse events, it is unclear whether the observed results are markers of the severity of patient illness or are a direct consequence of isolation. However, we tried to adjust and take into account the numerous confounding variables as optimally as possible in order to draw the most realistic conclusions.

Conclusions

In this large study conducted in ICUs, isolation in the ICU was significantly associated with more medication errors and more adverse events. With regards to efficacy and therefore ethics, contact isolation measures for limiting the spread of MDRO should be limited and designed according to the individual risk and collective benefit to ensure the benefits outweigh the risks.

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