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ORIGINAL ARTICLE

Interplay of nasal and rectal carriage of *Staphylococcus aureus* in intensive care unit patients

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Abstract

The aim of this study was to investigate the relationship between nasal and rectal *Staphylococcus aureus* carriage in intensive care unit (ICU) patients and the occurrence of ICU-acquired infections related to *S. aureus* carriage. Three hundred and ninety-five patients admitted in ICU were screened for *S. aureus* nasal and rectal carriages and followed to record *S. aureus* infections during their stay. *S. aureus* strains were genotyped by arbitrarily primed PCR, spa-typing, microarray and whole genome sequencing. At ICU admission, 112 of 363 (30.9%) patients carried *S. aureus* including 61 (16.8%) exclusive nasal carriers, 40 (11.0%) combined nasal and rectal carriers and 11 (3.0%) exclusive rectal carriers. The 152 *S. aureus* isolates from nasal and rectal swabs belonged to 19 clonal complexes (CCs). Patients colonized in both nose and rectum harboured different strains in at least 40% of cases according to arbitrarily primed PCR data. Nasal carriers of CC5 *S. aureus* had an increased risk of rectal carriage (RR = 1.85, $P < .05$). *S. aureus* nasal and rectal carriage was a risk factor of *S. aureus* ICU-acquired infection (RR = 4.04; 95%CI [1.38–11.76]). Incidence rates of endogenous ICU-acquired infections in exclusive nasal carriers, exclusive rectal carriers and in both nasal and rectal carriers were 0.08 (5/61), 0.09 (1/11) and 0.03 (1/40), respectively ($p = 0.47$). Rectal swabbing increased the detection of *S. aureus* carriage and revealed an important diversity of *S. aureus* strains in ICU patients. Further studies are needed to understand how *S. aureus* rectal carriage increases the risk of endogenous ICU-acquired infections.

Keywords *Staphylococcus aureus* · Colonization · Nose · Rectum · Staphylococcal infections · Intensive care unit

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Introduction

Staphylococcus aureus colonizes the skin and mucosal membranes of approximately one third of human beings [1–3]. Nasal colonization is a well-established risk factor of different types of *S. aureus* infections in all populations that have been studied [2]. In most cases, the *S. aureus* strains isolated from the nose and the infection site(s) are indistinguishable but the mechanisms of colonization-related infection (i.e. endogenous infection with the strain of carriage) are poorly understood [2]. Still, there is a lack of evidence to define whether *S. aureus* reaches preferentially the site of infection by contamination from the cutaneous site or by translocation through mucosal membrane [4]. The latest data indicate that the mean prevalence of *S. aureus* colonization is 24% and 14% in the nose and intestinal tract, respectively [1, 2]. Compared with the *vestibulum nasi*, which is the main site of carriage in humans, the gastro-intestinal tract also needs to be considered as an important reservoir of *S. aureus* in humans. However, most studies about *S. aureus* intestinal colonization conducted in the past decades have focussed on methicillin-resistant *S. aureus* (MRSA), and the role of methicillin-susceptible *S. aureus* (MSSA) intestinal carriage in colonization-related infection has been largely neglected. To the best of our knowledge, only a few epidemiological studies comparing nasal and intestinal carriage showed that *S. aureus* intestinal colonization could be an additional risk factor for *S. aureus* infections [5–7]. More recent data showed that a particular clone of *S. aureus* (i.e. ST228 MRSA) could be linked with lasting colonization of the intestinal tract [8]. Together, these results suggest that the *S. aureus* intestinal reservoir could play a significant role in colonization-related infections and outbreaks. Besides, *S. aureus* decolonization based on topical application of mupirocine and chlorhexidine for preventing *S. aureus* colonization-related infection did not reduce the intestinal colonization rate [9] and antibiotics-based decolonisation could not be recommended due to the risk of emergence of multidrug-resistant bacteria. Thus, prevention strategies taking into account intestinal *S. aureus* reservoir could help reduce colonization-related *S. aureus* infections, especially in surgical or critically-ill patients.

In order to better understand the relationship between *S. aureus* nasal and intestinal colonization whatever the susceptibility to methicillin, we conducted a prospective study in a cohort of ICU patients that aimed to investigate (i) the prevalence of *S. aureus* nasal and intestinal colonization, (ii) the clonality of *S. aureus* strains isolated in both sites and (iii) the risk of colonization-related infections during hospitalization in ICU.

Material and methods

Patient and sample collection The study took place at the University Hospital of St-Etienne, France, between February and July 2013 in the three adults ICUs including a nephrological unit of 6 beds, a polyvalent medical and surgical unit of 12 beds and one emergency medical unit of 15 beds. Patients were enrolled prospectively and sampled at admission in ICU using nasal and rectal swabs (eSwab 480 CE, Copan, Brescia, Italy). *S. aureus* infections were collected prospectively by the intensive care physicians during the patients' ICU stays. ICU-acquired infections were defined according to the surveillance definition of health care-associated infection in acute care settings elaborated by Centres for disease control and the National Healthcare Safety Network standards [10]. All medical records of infected patients were reviewed independently by both an infectious disease (EBN) and an infection control (JG) specialists. *S. aureus* infection was defined as ICU-acquired if it occurred more than 48 h after patient's admission in the ICU. Acquired-infections were considered endogenous if the strain responsible for infection shared both the same spa-type and the same microarray profile as the one(s) found in nasal and/or rectal swabs sampled before the occurrence of infection.

Microbiological methods Nasal and rectal swabs were plated on *S. aureus* chromogenic agar (BBL CHROMAgar Staph aureus, Becton Dickinson, France) by using the EasySpiral Dilute instrument (Interscience, St-Nom-la-Bretèche, France) and incubated at 36 °C for 48 h. The Scan1200 plate reader (Interscience) was used to quantify *S. aureus* loads [11]. Clinical specimens were plated on blood agar (COS ref.: 43049, bioMérieux, France) and incubated at 36 °C for at least 48 h. All presumptive colonies were identified by MALDI-TOF MS according manufacturer recommendations (Microflex LT, Bruker, Bremen, Germany).

Genotyping of *S. aureus* strains *S. aureus* strains were analysed by arbitrarily-primed PCR [12], spa-typing [13] and DNA microarray (*S. aureus* Genotyping Kit v2.0, Alere, France) [14]. Clonal complexes (CC) of *S. aureus* strains were assigned by using the results of DNA microarray [14]. Microarray data and spa-types were analysed with BioNumerics software v7.6 (Applied Maths, Sint-Martens-Latem, Belgium). To analyse more closely the relationship between strains isolated from two patients colonized at both nasal and rectal sites and who presented *S. aureus* infection, Illumina 300 bp paired-end whole genome shotgun sequencing was performed as previously described [15]. Core genome single-nucleotide polymorphism (SNP) analysis and pairwise distance matrices were produced with Snippy v4.2.1 (https://github.com/tseemann/snippy), by using the rectal strain sequence as reference. *S. aureus* strains isolated from within

a single individual were considered as unrelated when pairwise SNPs were greater than 40 [16].

Statistical methods Statistical analysis was performed using SPSS software (IBM SPSS v20.0, Chicago, IL, USA) and MedCalc statistical software v18.11 (MedCalc Software bvba, Ostend, Belgium). Chi-squared and Fisher's exact tests were used to compare categorical variables. Mann–Whitney *U* test was used to compare continuous variables. *p* values below 0.05 were considered as statistically significant. Minimum spanning tree was computed with BioNumerics v7.6 (Applied Maths, Sint-Martens-Latem, Belgium).

Ethical statement This study was approved by an Institutional Review Board ("Comité de Protection des Personnes Sud-Est I" No 2012-28) and by the National Security Agency of Medicines and Health Products.

Results

Patient population From the 400 patients enrolled, 363 were analysed in this study (Fig. 1). The sex ratio (M/F) was 1.6; the mean (±SD) age was 61 ± 16 years and the median (range) of Simplified Acute Physiologic Score II was 38 (6–115).

***S. aureus* nasal and rectal carriage** At ICU admission, 112 of 363 (30.9%) patients carried *S. aureus*: 61 (54.5%) were exclusive nasal carriers including 6 MRSA carriers, 40 (35.7%) were co-carriers (i.e. carriers of *S. aureus* in both nose and rectum) including 2 MRSA carriers, and 11 (9.8%) were exclusive rectal carriers. Thus, rectal swab improved the detection of *S. aureus* carriage by 10% (11/112). The characteristics of the studied population, according to *S. aureus* carriage status, are described in Table 1. Except for the risk of acquired infection (see below), characteristics of patients were similar between *S. aureus* carriers and non-carriers. Notably, exposure to antimicrobials with activity against *S. aureus* was similar between *S. aureus* carriers and non-carriers (Table 1).

At inclusion, the mean (±SD) *S. aureus* load was significantly higher in nasal specimens (5.1 ± 2.2 log CFU/swab) than in rectal specimens (3.3 ± 1.3 log CFU/swab) ($p < 0.0001$) (Fig. 2a). The mean (±SD) *S. aureus* nasal loads were 5.6 ± 2.1 and 4.7 ± 2.2 log CFU/swab in co-carriers and in sole nasal carriers, respectively ($p = 0.053$) (Fig. 2b). The mean (±SD) *S. aureus* rectal loads were 3.4 ± 1.3 and 3.1 ± 1.4 CFU/swab in co-carriers and in sole rectal carriers, respectively ($p = 0.6$) (Fig. 2c).

Genetic diversity of *S. aureus* strains The 152 *S. aureus* isolates recovered from nasal and rectal swabs belonged to 20 clonal complexes (CCs). Sixteen (10.5%) isolates were meticillin-resistant including 14 isolates belonging to CC8 (Lyon clone, EMRSA-2) and two isolates belonging to CC22 (EMRSA-15) (Fig. 3).

Arbitrarily primed PCR showed that strains recovered from patients with combined nasal and rectal *S. aureus* carriages are different between the two sites in 16 patients out of 40 (40%). In other words, the rectal sampling improved the recovery of *S. aureus* strains colonizing humans up to 24% (27/112).

Interestingly, nasal carriers of *S. aureus* strains belonging to CC5 have been found to have an increased risk of *S. aureus* rectal carriage (RR = 1.85, 95%CI [1.14–3.02]). No other

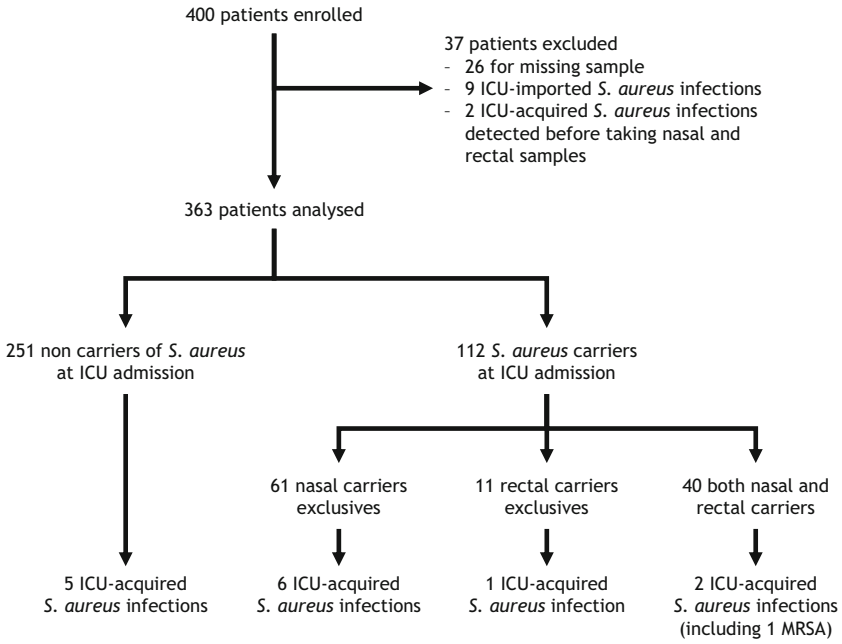

Fig. 1 Flowchart: study design and distribution of the studied population in the three adult ICUs of the University hospital of St-Etienne, France

Table 1 Characteristics of patients admitted in ICUs according to their *S. aureus* carrier state

	S. aureus carriers at ICU admission *n* = 112 (%)	Non *S. aureus* carriers at ICU admission *n* = 251 (%)	*P* value
Type of ICU			
Medical and surgical	55 (49.1)	111 (44.2)	ns
Emergency medical	38 (33.9)	81 (32.3)	ns
Nephrological	19 (17.0)	59 (23.5)	ns
Sex ratio (M/F)	1.8	1.5	ns
Age (mean ± SD)	60 ± 17	62 ± 15	ns
SAPSII[a] (mean ± SD)	42 ± 22	41 ± 20	ns
S. aureus acquired infections	9 (8.0)	5 (2.0)	< 0.05
Bacteremia[b]	6 (5.4)	1 (0.4)	< 0.01
Pneumonia (incl. VAP)	3 (2.7)	4 (1.6)	ns
Antimicrobial treatment with activity against *S. aureus* before nasal and rectal samplings	45 (40.2)	112 (44.6)	ns

[a] Simplified acute physiologic score II

[b] Including four cases of catheter-related bacteremia in carrier group and one case non-carrier group

VAP ventilator-associated pneumonia

clonal complex was found to influence the risk of associated rectal carriage (Table 2).

S. aureus acquired infections Fourteen ICU-acquired *S. aureus* infections, including one due to MRSA, were diagnosed during the study period and are summarized in Table 3. Nine *S. aureus* infections occurred in carriers and 5 in non-carriers. *S. aureus* carriage was significantly associated with the occurrence of *S. aureus* ICU-acquired infections (RR = 4.30; 95% CI [1.41–13.14]). Overall, the density incidence of ICU-acquired *S. aureus* infections was 2.2 per 1000 ICU-days, respectively, 4.66 and 1.1 per 1000 ICU-days in *S. aureus* carriers and non-carriers ($p < 0.01$). The median (interquartile range) of infection onset after ICU admission was 16 (11 to 19) and 12 days (3.75 to 27.5) in carriers and non-carriers, respectively ($p = 0.39$).

S. aureus infections occurring in carriers were due to their endogenous strain in 8 out of 9 cases (Table 3). Incidence rates of endogenous infections were, respectively, 0.08 (5/61), 0.09 (1/11) and 0.03 (1/40) in exclusive nasal carriers, exclusive rectal carriers and in both nasal and rectal carriers ($p = 0.47$). One patient (case no. 6) acquired a *S. aureus* bloodstream infection related to a femoral arterial-catheter and had a previous rectal colonization with high bacterial load (10^5 CFU/swab) and no *S. aureus* nasal colonization (Table 3). Two patients (cases number 9 and 10) were found to carry *S. aureus* in the nose and in the rectum and acquired *S. aureus* after ICU admission (Table 3). Briefly, in case no. 8, *S. aureus* isolates recovered from the nose and the rectum harboured similar DNA microarray profiles and as little as 6 SNPs (> 97% reference genome mapped). On the one hand, the strain isolated in blood culture showed a deletion of 2 spa repeats compared to the nasal and rectal isolates using spa-typing method. On the other hand, whole genome sequencing showed 894 and 896 pairwise SNPs compared to the nasal and rectal isolates respectively. In case no. 9, *S. aureus* isolates

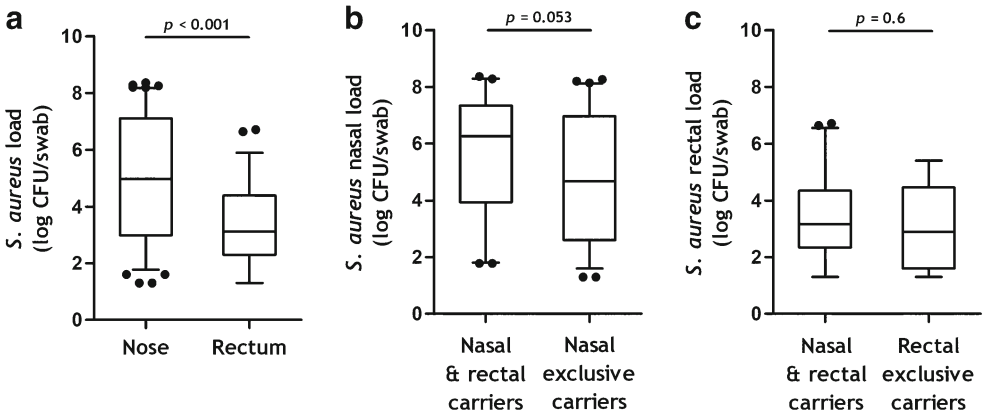

Fig. 2 *S. aureus* loads recovered from nasal and rectal specimens of the 363 patients included in the study (**a**), from nasal specimens of co-carriers and nasal carriers sole (**b**) and from rectal specimens of co-carriers and rectal carrier sole (**c**)

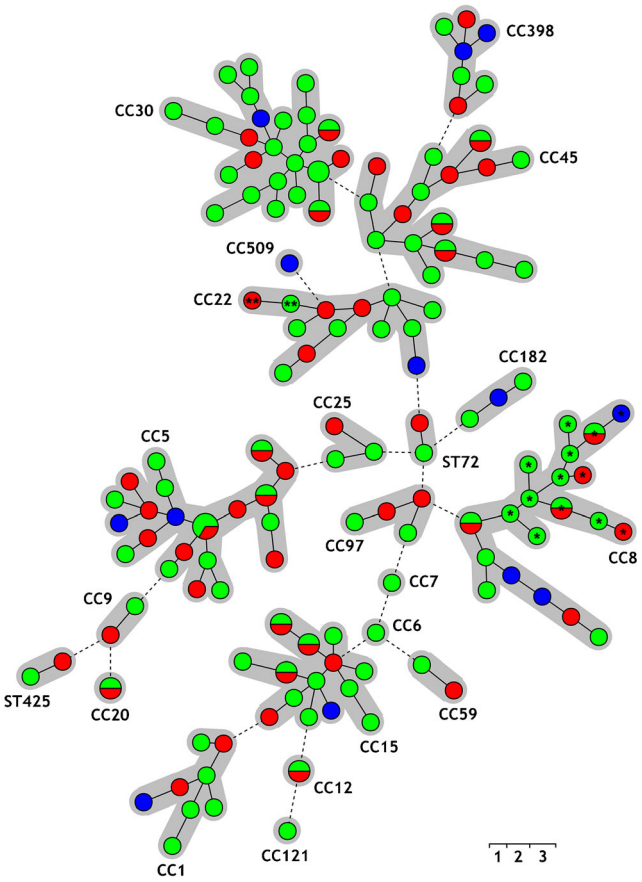

Fig. 3 Minimum spanning tree based on DNA microarray analysis of 165 *S. aureus* isolates recovered from nose (green), rectum (red) and infection site (blue) in intensive care unit patients. Clonal complexes (CC) or sequence type (ST) assigned by microarray analysis are highlighted in light grey. The node size represents the number of isolates according to the scale given. *CC8-MRSA-IV [sea+], Lyon Clone/UK-EMRSA-2. **CC22-MRSA-IV [fnbB-,sec/l-], UK-EMRSA-15/Barnim EMRSA

grown from the nasal swabs, rectal swabs and blood culture shared the same spa-type and similar DNA microarray profiles, and harboured no more than 9 pairwise SNPs (Table 3).

Discussion

In ICU patients, we found a prevalence of nasal (28%) and rectal (14%) carriages very similar to other settings [1, 2] despite frequent exposure to antimicrobial drugs with activity against *S. aureus* in this population. Exclusive rectal carriage occurred rarely in our cohort (3%), which confirms the results found in other populations [1, 17]. Although nasal carriage was more frequent than rectal carriage, we found that the incidence of endogenous infection in exclusive rectal carriers is similar to those observed in exclusive nasal carriers. To date, few is known about the risk of infection related to colonization at other sites than the nose. In this prospective cohort, we reported a well-documented case of endogenous infection in a patient with exclusive rectal carriage (see case 6; Table 3) and 2 other cases of endogenous *S. aureus* infections occurring in patients colonized at both sites (cases 8 and 9; see Table 3). Previously, two studies reported three cases of *S. aureus* infections in *S. aureus* exclusive rectal carriers. However, molecular typing of colonization and infection strains was not performed and the time between colonization and the occurrence of infection was not specified [6, 18]. Additionally, Szumowski et al. showed that MRSA perianal colonization was associated with skin and soft tissue infection (SSTI) but they did not compare perianal and SSTI isolates [7]. Squier et al. reported that patients with both rectal and nasal carriage were significantly more likely to develop *S. aureus* infection than those with nasal carriage only in ICU but they failed to find infection in exclusive rectal carriers [5]. Here, in the case of bacteremia occurring in an exclusive rectal carrier, it can be hypothesized that the catheter proximity to the colonized site and the high bacterial load in the rectum led to the occurrence of a bloodstream infection. For the two other cases, since strains of colonization were similar, it is impossible to know which site of colonization was at the origin of the infection. In case 8, the strain isolated from the blood culture was considered as different from those

Table 2 Risk of *S. aureus* rectal carriage in ICU patients according to the clonal complex of the *S. aureus* nasal carriage strain

Clonal complex of *S. aureus* nasal isolate (no. of patients)	Relative risk of rectal carriage	95% confidence interval	*P* value
CC30 (21)	1.11	0.63–1.95	ns
CC8 (15)	0.82	0.38–1.75	ns
CC5 (12)	1.85	1.14–3.02	< 0.05
CC45 (12)	1.31	0.70–2.44	ns
CC15 (11)	0.87	0.38–1.96	ns
CC22 (8)	0.94	0.37–2.38	ns
CC398 (3)	0.31	0.02–4.13	ns
CC1 (5)	0.49	0.08–2.89	ns
CC97 (2)	1.27	0.31–5.18	ns
Others CCs (12)	0.60	0.22–1.65	ns

Table 3 Characteristics of patients with *S. aureus* infections acquired in ICU (among carriers and non carriers)

Case no. (ID)	Age/ gender	Comorbidities	Admission diagnosis	SAPS II	Type of infection	Outcome	Delay between admission and infection (days)	*S. aureus* positive specimen(s)	Clonal complex (CC)[c]	Spa-type	Repeat succession
1 (008)	71/F	Arterial hypertension Abdominal aortic aneurysm	Meningeal haemorrhage	44	Bloodstream infection	Discharge	28	Nasal swab[a] Blood culture	CC398 CC398	t1250 t1250	08-16-02-25-02-25 08-16-02-25-02-25
2 (014)	62/M	Chronic obstructive pulmonary disease	Necrotizing Myositis Respiratory failure	41	Ventilator-associated pneumonia	Death	12	Nasal swab[a] Tracheal aspirates	CC22 CC22	t852 t852	11-19-12-21-17-34-24-34-22-25 11-19-12-21-17-34-24-34-22-25
3 (120)	63/F	Kidney transplantation Systemic lupus Arterial hypertension Atrial fibrillation	Haemorrhagic stroke	25	Ventilator-associated pneumonia	Discharge	16	Nasal swab[a] Tracheal aspirates	CC7 CC398	t091 t571	07-23-21-17-34-12-23-02-12-23 08-16-02-25-02-25-34-25
4 (150)	71/M	Arterial hypertension Atrial fibrillation	Respiratory failure	50	Catheter related bloodstream infection	Discharge	44	Nasal swab[a] Blood culture	CC8 CC8	t008 t008	11-19-12-21-17-34-24-34-22-25 11-19-12-21-17-34-24-34-22-25
5 (340)	62/F	Mesenteric artery aneurysm Anxio-depressive syndrome	Heart attack	44	Bloodstream infection	Death	4	Nasal swab[a] Blood culture	CC8 CC8	t190 t190	11-17-34-24-34-22-25 11-17-34-24-34-22-25
6 (343)	50/M	–	Subarachnoid haemorrhage	15	Femoral arterial-catheter related bloodstream infection	Discharge	11	Rectal swab[a] Blood culture	CC1 CC1	t127 t127	07-23-21-16-34-33-13 07-23-21-16-34-33-13
7 (366)	53/M	–	Multiple injuries due to a road accident	39	Ventilator-associated pneumonia	Death	16	Nasal swab[a] Tracheal aspirates	CC182 CC182	t493 t493	04-34-17-66-32-17-23-24 04-34-17-66-32-17-23-24
8 (399)	58/M	Pulmonary embolism	Pneumonectomy due to sarcoma Lower limb ischaemia	39	Bloodstream infection	Discharge	29	Nasal swab[a] Rectal swab[a] Blood culture	CC5 CC5 CC5	t539 t539 t062	26-23-17-34-17-12-17-16 26-23-17-34-17-12-17-16 26-23-17-12-17-16
9 (400)	50/M	Cirrhosis Arterial hypertension	Status epilepticus	70	Catheter related bloodstream infection	Discharge	16	Nasal swab[a] Rectal swab[a] Blood culture[b]	CC8 CC8 CC8	t008 t008 t008	11-19-12-21-17-34-24-34-22-25 11-19-12-21-17-34-24-34-22-25 11-19-12-21-17-34-24-34-22-25
10 (113)	19/M	–	Suicide attempt Facial injury	11	Pneumonia	Discharge	14	Tracheal aspirates	CC30	t4322	04-44-33-31-12-16-34-12-25-22-22-34
11 (256)	67/M	Chronic obstructive pulmonary disease Aortic aneurysm Cerebral vascular accident Chronic alcoholism	Acute pancreatitis	22	Catheter related bloodstream infection	Discharge	68	Blood culture	CC5	t045	26-17-20-17-12-17-16

Table 3 (continued)

Case no. (ID)	Age/ gender	Comorbidities	Admission diagnosis	SAPS II	Type of infection	Outcome	Delay between admission and infection (days)	*S. aureus* positive specimen(s)	Clonal complex (CC)[c]	Spa-type	Repeat succession
12 (260)	73/M	–	Aortic dissection	48	Pneumonia	Discharge	12	Tracheal aspirates	nd	nd	
13 (322)	47/M	Arterial hypertension Hypothyroidism	Head injury Occupational accident	37	Ventilator-associated pneumonia	Discharge	3	Tracheal aspirates	CC509	t489	49-13-23-05-34-34-33-34
14 (383)	52/M	Cervical myelopathy Meniscectomy	Spinal cord injury tetraplegia Occupational accident	33	Ventilator-associated pneumonia	Discharge	4	Tracheal aspirates	CC15	t084	07-23-12-34-34-12-12-23-02-12-23

[a] Carriage isolate sites

[b] MRSA strain responsible for infection

[c] Clonal complex was assigned by microarray genotyping (*S. aureus* genotyping kit V2.0, Alere)

nd not done because missing strain

recovered from the nose and the rectum of this patient given the large number of pairwise SNPs observed. In this case, the delay of infection occurred 29 days after ICU admission, which could be enough to let the bacteria adapt to the host [19]. In case 9, WGS sequencing showed that the strain isolated in blood culture and those isolated from nasal and rectal sites were closely related, and despite the use of high-throughput method for investigation [20], it was not possible to determine whether nasal or rectal colonization originated the infection. Both cases of bacteremia might be related to rectal carriage. As we observed here, the combination of colonization sites is also associated to a high *S. aureus* bacterial load and then could potentially facilitate staphylococcal infections, increasing the risk of device contamination [18]. These observations evoke that the rectal reservoir could play a role in autoinfection [21]. The combination of colonization sites is probably associated to a dispersion of *S. aureus* colonization on the body (skin and mucosa) and in the environment of the patient [18]. Additionally, Senn et al., who reported a large outbreak of *S. aureus* colonization, suggested that the *S. aureus* rectal strain plays the role of a stealthy superbug able to maintain a long-term hospital outbreak by cross-transmission [8]. In our work, the genotyping of the 165 *S. aureus* isolates revealed a great diversity within patients indicating that no or few cross-transmissions occurred in the ICUs. Interestingly, we showed that strains belonging to CC5 seem to be more implicated in rectal carriage, notably when the patient was co-colonized with this clone in nose and rectum compared to other clones. The ST228 was already related to rectal carriage in an outbreak of *S. aureus* colonization [8].

Staphylococcus aureus is one of the most frequent causes of infections in the ICU [22–24] and we confirmed that *S. aureus* carriage is a risk factor for *S. aureus* ICU-acquired infections. This risk factor had been largely described previously for MRSA carriage [22, 25–29] but not so extensively for MSSA carriage [30, 31]. In recent studies [22, 25–30, 32], the relative risk of acquisition of *S. aureus* infections in ICU associated with *S. aureus* nasal or throat carriage ranged from 2.5 to 17.8 and our data are in concordance to previous findings. In fact recently, studies showed that screening patients for MRSA carriage at ICU admission is a valuable tool for guiding decision to treat ICU-acquired infections [27, 28]. We highlighted in the present work that not only MRSA carriage but also MSSA carriage could have an impact on the risk of infection in ICU as also showed by Paling et al. in a post hoc analysis of two cohort studies in critically ill patients [32]. Interestingly, molecular typing of *S. aureus* strains in ICU-patients harbouring combined nasal and rectal carriage showed that approximately half of them were colonized with two different strains of *S. aureus*. Similarly, we reported that *S. aureus* naso-pharyngeal carriers harboured two different strains in approximately half of cases in a cohort of haemodialysis patients [33]. These results suggest that

S. aureus carriers could harbour two or three different strains in the nose, the throat and the rectum in hospitalized patients exposed to colonization pressure and antimicrobial drugs [34]. Therefore, screening *S. aureus* carriage at ICU admission, for whatever methicillin resistance profile, would allow physicians, especially among patients with pneumonia, to adapt a probabilistic antibiotic treatment for patients according to the antimicrobial drug susceptibility of their *S. aureus* carriage strain with potential antimicrobial stewardship implications [35]. The prevention of *S. aureus* (MSSA and MRSA) endogenous infections may also be questioned in further studies since a recent meta-analysis showed that mupirocin decolonization was protective against *S. aureus* infections among adult ICU patients [36].

There are some limitations to our study. First, patients have been enrolled in 2013 and the study data may not represent the present situation. In the present work, we did not investigate other reservoirs as the study was observational without additional sampling of the patients. Additionally, because of the high rate of patients exposed to antimicrobial drugs, the prevalence of *S. aureus* carriage was probably underestimated and not reliable to determine the *S. aureus* nasal carrier status, as described by our team [37, 38] when we investigated the relationship between persistent and non-persistent carriers and the risk of developing a ICU-acquired *S. aureus* infection. However, this study is relevant in a population of ICU patients because of the frequent prescription of antibiotics in all ICUs.

Conclusion

This study confirms that nasal colonization by *S. aureus* is an important risk factor for *S. aureus* ICU-acquired infections and suggests that *S. aureus* rectal carriage could be an additional risk factor for infection. Rectal swabbing could improve the detection of an unrecognized *S. aureus* strain. Screening of *S. aureus* carriage in ICU patients, for whatever methicillin resistance profile, may help the prescription of antibiotics. Further studies are needed to better understand the role of the different reservoirs of *S. aureus* strains and their clinical impact on the risk of *S. aureus* infection, notably in ICUs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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