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Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Carriage and MRSA Surgical Site Infections in Patients Undergoing Colorectal Surgery: A Cohort Study in Two Centers

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Abstract

Background: Surgical site infections (SSIs) after colorectal surgery usually are caused by commensal intestinal bacteria. Methicillin-resistant *Staphylococcus aureus* (MRSA) may be responsible for additional SSI-related morbidity. The aim of this retrospective cohort study was to describe the epidemiology of SSIs caused by MRSA after colorectal surgery in two tertiary-care centers, one in Geneva, Switzerland (G), and the other in Chicago, Illinois (C).
Methods: Adult patients undergoing colorectal resections during periods of universal screening for MRSA on admission were identified retrospectively. Demographic characteristics, surgery-related factors, and occurrence of MRSA SSI were compared in patients with and without MRSA carriage before surgery.
Results: There were 1,069 patients (G = 194, C = 875) with a median age of 67 years fulfilling the inclusion criteria. Of these, 45 patients (4.2%) had a positive MRSA screening result within 30 days before surgery (G = 18, C = 27; $p < 0.001$). Ten patients (0.9%; G = 6, C = 4) developed MRSA SSI, detected a median of 17.5 days after surgery, but only two of them were MRSA-positive before surgery. Nine of the 45 MRSA carriers identified by screening received pre-operative prophylaxis with vancomycin (G 6/18, C 3/27), and 17 of these patients (37.8%; G 7/18, C 10/27) were started on MRSA decolonization therapy before surgery. Pre-operative administration of either decolonization or vancomycin was not protective against MRSA SSI ($p = 0.49$).
Conclusion: Methicillin-resistant *S. aureus* seems to be an infrequent cause of SSI after colorectal resections, even in MRSA carriers. Systematic universal screening for MRSA carriage prior to colorectal surgery may not be beneficial for the individual patient. Post-operative factors seem to be important in MRSA infections, as the majority of MRSA SSIs occurred in patients negative for MRSA carriage.

About one in five patients undergoing colorectal surgery will develop a surgical site infection (SSI) [1,2]. Whereas *Staphylococcus aureus* is the most common pathogen responsible for SSIs after clean surgery, the majority of SSIs after colorectal interventions are caused by the aerobic and anaerobic commensal flora of the colon [1–3]. Regimens for peri-operative antibiotic prophylaxis in colorectal surgery do not cover methicillin-resistant *S. aureus* (MRSA) and offer various degrees of coverage for methicillin-sensitive *S. aureus* and other gram-positive pathogens [4]. Even if the relative frequency of *S. aureus* as the cause of SSI in colorectal surgery is low, it might still be responsible for a substantial number of SSIs, as the overall rate of SSI is much higher after colorectal surgery than after other types of surgery, but this has been investigated rarely [5]. The objective of this study was to describe the epidemiology of MRSA carriage and MRSA SSIs among patients undergoing colorectal interventions during periods of active screening for MRSA on admission.

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Table 1. Characteristics and Study-Relevant Policies of the Two Study Centers

	Geneva	*Chicago*
Time period	September 2005–May 2006	January 2006–September 2008
Number of hospitals	One	Three
Setting	Primary and tertiary-care hospital	Two tertiary-care and one community hospital
Number of colorectal interventions per year	About 420	About 370
Recommended antibiotic prophylaxis in colorectal surgery	Third-generation cephalosporin + metronidazole	Second-generation cephalosporin + anaerobic coverage
Prophylaxis with additional oral antibiotics?	No	No
Vancomycin recommended in guidelines for MRSA positive patients undergoing colorectal surgery	Yes	Yes
Agent used for disinfection of the surgical site	Povidone–iodine + alcohol	Povidone–iodine, iodine Povacrylex + isopropyl alcohol, or chlorhedixine gluconate + alcohol
Type of screening	Active	Active
Screening technique	PCR (in-house)[6]	PCR (commercial)[7]
Screening sites	Anterior nares, perineal region, and other sites (catheter insertion sites, skin lesions, or urine) when indicated clinically	Anterior nares
Routine decolonization for MRSA carriers recommended	Yes	Yes
Surveillance of surgical site infection	In the context of a prospective study	Routine surveillance

PCR = polymerase chain reaction.

Patients and Methods

This retrospective study collected data from two centers, one in Switzerland (Geneva = G) and one in the United States (Chicago = C). Table 1 shows the general characteristics of the two centers. All adult patients undergoing colorectal resections in the two hospitals during a period when active screening for MRSA was performed on admission, and who had an MRSA screening test performed within 30 d before surgery, were included. Patients undergoing abdominal surgery that did not involve the resection of at least a portion of the colon were excluded.

In Geneva, data on MRSA colonization and MRSA infection were obtained in the context of a prospective study [6]. During a nine-month period, patients admitted for abdominal surgery were screened systematically for MRSA [6]. For MRSA-positive patients, additional information was extracted prospectively from medical charts.

The second center is a four (at the time of the study three)-hospital university-affiliated organization in Chicago where active screening for MRSA has been performed since 2005 [7]. Demographic characteristics, surgery-related information, and MRSA screening results were extracted from the electronic medical records for all patients undergoing colorectal resections during a 33-month period.

Patients were considered to be MRSA positive before surgery if a positive MRSA screening test was retrieved within 30 d of surgery. In both centers, patients were assessed for the occurrence of MRSA SSI using criteria established by the U.S. Centers for Disease Control and Prevention [8]. The Institutional Review Boards of the participating hospitals approved the MRSA screening studies and related analyses.

Variables in the baseline comparison between centers were analyzed by χ^2 test, Fisher exact test, *t*-test, or Wilcoxon rank sum test, as appropriate. A two-sided p value of < 0.05 was considered statistically significant. All analyses were performed using Stata version 11 (Stata Corp, College Station, TX).

Results

We identified 1,069 patients (G = 194, C = 875) undergoing colorectal resections during the study. Median age (67 years in both centers), the proportion of female patients (G 50.0%, C 54.5%), the percentage of patients with American Society of Anesthesiologists (ASA) scores ≥ 3 points (G 42.9%, C 43.0%), and the median length of surgery (G 125 min, C 130 min) were not significantly different in the two centers. Patients in Geneva were more likely to have emergency procedures (G 30.9%, C 18.1%; $p < 0.001$), had a longer median post-operative length of stay (G 12 d, C 6 d; $p < 0.001$), and had a higher in-hospital mortality rate (G 5.2%, C 2.4%; $p = 0.04$) but were less likely to have laparoscopic surgery (G 22.3%, C 53.7%; $p < 0.001$) and had a lower median body mass index (G 24.5 kg/m^2, C 26 kg/m^2; $p = 0.01$).

Overall, 45 patients (4.2%) had a positive MRSA screening result within 30 days before surgery (G = 18, C = 27; $p < 0.001$). These patients were significantly older, had a higher mortality rate, were less likely to have had laparoscopic surgery, and had a shorter median length of surgery than patients without a positive MRSA screening result before surgery (Table 2).

Ten patients (0.9%; G = 6, C = 4) developed MRSA SSI, but only two of them were identified as MRSA-positive before

Table 2. Comparison of Patients with and without Positive Methicillin-Resistant *Staphylococcus aureus* Screening Results before Surgery

	MRSA carriage[a]	*No MRSA carriage*	P *value*
Patients	45	1,024	
Median age (years)	72.5	66	0.03
Female (%)	24 (53.3)	550 (53.7)	NS
ASA score ≥ 3 points (%)	22 (52.4)	430 (42.6)	NS
Start of MRSA decolonization before surgery (%)	17 (37.8)	NA	–
Peri-operative anti-MRSA prophylaxis with vancomycin (%)	9 (20)	NA	–
Emergency surgery	11 (24.4)	206 (20.2)	NS
Laparoscopic surgery	15 (33.3)	498 (48.7)	0.04
Length of surgery (min; median; IQR)	90 (70–160)	130 (90–190)	0.04
MRSA SSI (%)	2 (4.4)	8 (0.8)	NS
LOS after surgery in days (median; IQR)	7 (5–14)	6 (4–10)	NS
In-hospital death (%)	6 (13.3)	25 (2.4)	< 0.001

[a]Positive MRSA screening test on day of surgery or up to 30 days before day of surgery.

ASA = American Society of Anesthesiologists; IQR = interquartile range; LOS = length of stay; MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not available; NS = not statistically significant ($p > 0.05$); SSI = surgical site infection.

surgery. Neither of these patients received peri-operative prophylaxis with vancomycin or was started on decolonization therapy before surgery. The MRSA SSI rate may have been higher in pre-operative MRSA carriers than in non-carriers (4.4/100 procedures vs. 0.8/100 procedures; $p = 0.06$). An MRSA SSI was detected a median of 17.5 d after surgery (range 5–29 days). Five MRSA SSIs were classified as organ-space (G 3, C 2), four were deep incisional (G 3, C 1), and one was superficial incisional (C 1). Five of the 10 MRSA SSIs were monomicrobial (G 4, C 1). In two instances, *Enterococcus* spp. was a co-pathogen of doubtful importance; and in three instances, Enterobacteriaceae also were isolated, once in combination with *S. milleri* and once with viridans streptococci/*Candida* spp.

Nine of the 45 patients with a positive pre-operative MRSA screening result received pre-operative prophylaxis with vancomycin (G 6/18, C 3/27); none of them developed a MRSA SSI. Seventeen of the 45 patients (37.8%; G 7/18 C 10/27) were started on MRSA decolonization therapy before surgery. Again, none of them developed a MRSA SSI. Six patients received both types of intervention, and 25 had neither. Among the 45 patients with known pre-operative MRSA colonization, pre-operative administration of either decolonization or vancomycin was not protective against MRSA SSI ($p = 0.49$). The median real-life turnaround time for the polymerase chain reaction (PCR) test is about 24 h in both hospitals, and PCR tests are not performed at night. Of the 45 MRSA carriers, 30 had surgery within 2 d of admission, so carrier information was not always available at the time of surgery.

Discussion

In this two-center cohort study, MRSA was responsible for relatively few SSIs after colorectal surgery. Although the observed rate of 0.9 MRSA SSIs/100 procedures is similar to the rate observed in clean surgery, these infections likely represent a small proportion of all SSIs after colorectal surgery [3,6]. Indeed, the overall SSI rate after colorectal surgery was 7.8/100 procedures for Chicago during the study period, and although similar data are not available from Geneva for the study time frame, 2008–2009 surveillance data found a colorectal SSI rate of 19.1/100 procedures. Other trials of SSI in colorectal surgery have reported similar findings. For instance, a multicenter trial of 602 patients evaluating the effect of gentamicin-collagen sponges on the rate of SSI after colorectal interventions observed a rate of 1.4 MRSA SSIs/100 procedures [2]. A multicenter drug trial in 1,002 patients undergoing colorectal surgery found a rate of 0.4 MRSA SSIs/100 procedures [1]. Although the MRSA SSI rate was higher in known preoperative carriers versus non-carriers, the fact that eight of the ten MRSA SSIs in this study occurred in patients MRSA-free before surgery suggests that post-operative factors play an important role in MRSA infections [6, 9].

Systematic, universal screening for MRSA carriage prior to colorectal surgery may not be beneficial. Therefore, the decision to screen patients for MRSA carriage before colorectal surgery should be more individualized (taking into account the presence of specific risk factors for colonization in patients at high risk of SSI) [10]. However, MRSA carriage obviously has implications that go beyond the individual patient, because the detection of MRSA carriers even without reduction of the individual risk of SSI may have some ecologic benefit (e.g., implementation of contact precautions to reduce the probability of nosocomial MRSA transmission).

Half of all detected MRSA SSIs were monomicrobial. Although this is unusual for SSIs after colorectal surgery as a whole, it might be more common for SSIs caused by pathogens such as MRSA that are not part of the usual intestinal flora and often are acquired by exogenous skin contamination [11–13]. The median time from surgery to detection of the MRSA SSI was 17.5 days in our study, which is longer than the median of 10 days reported for all colorectal SSIs [14,15]. Again, this might indicate the role of post-operative, exogenous contamination of surgical sites with MRSA. Because of the small number of MRSA SSIs, this result should, however, be interpreted with caution.

We noted several important differences between the centers that might reflect differences between the Swiss and U.S. health-care systems (length of stay), study populations (body mass index, emergency interventions), and local practices (use of laparoscopy vs. open surgery). It is interesting that significantly more patients in Chicago underwent laparoscopic

surgery, which has been suggested to reduce SSI rates in colorectal surgery [16]. The higher MRSA carriage rate in Geneva might be explained at least partly by differences in screening sites and screening techniques.

It is generally accepted that vancomycin prophylaxis is indicated for known MRSA carriers or patients with a history of MRSA carriage undergoing high-risk clean surgery [17]. The effect of adding vancomycin to the usual antibiotic prophylaxis for known MRSA carriers is less clear with regard to colorectal surgery. In our cohort, vancomycin prophylaxis was used inconsistently for MRSA carriers, despite being recommended in both centers in addition to the usual prophylactic regimen. In most cases, this non-compliance might have been attributable to the unavailability of the MRSA screening result before surgery. Furthermore, it is possible that physicians are less aware of the recommendation to add vancomycin for pre-operative MRSA carriers to the prophylactic regimen used routinely in colorectal surgery. However, our study was underpowered to assess the efficacy of vancomycin prophylaxis for the prevention of MRSA SSI in colorectal surgery. A study published in 1990 comparing aztreonam with cefotaxime (both in combination with metronidazole) as prophylactic agents in 154 patients undergoing elective colorectal surgery found higher rates of SSI caused by gram-positive agents (notably *Staphylococcus* spp.) in the aztreonam group, suggesting that coverage of methicillin-sensitive *S. aureus* might be important [18]. A recent retrospective study of patients having undergone clean or clean-contaminated surgery (not only colorectal) at a single U.S. healthcare center identified vancomycin prophylaxis as a risk factor for post-operative MRSA conversion, but the study did not consider post-operative factors and is thus difficult to interpret [19].

Our study has several limitations. The data on MRSA SSIs from Geneva were obtained in the context of a prospective clinical trial, whereas the other center relied on routine surveillance. It therefore is possible that SSIs were more likely to be detected in Geneva. In addition, the two centers used different PCR assays and screening sites, and the molecular epidemiology of MRSA is likely to be different; the impact of these differences may be difficult to predict. A further limitation is that the outcome of interest (MRSA SSI) was too rare to allow a multivariable risk factor analysis to identify protective factors. A study pursuing that aim would require thousands of patients. Finally, we did not document the microbiological etiology of non-MRSA SSI.

In summary, this study suggests that MRSA SSIs are relatively infrequent after colorectal surgery. Systematic, universal screening for MRSA carriage prior to colorectal surgery may not be beneficial for the individual patient. The efficacy of vancomycin and decolonization strategies in preventing SSI in MRSA carriers undergoing colorectal surgery merits further investigation. This study suggests, however, that these measures alone will not be effective without other infection control strategies, as post-operative contamination seems to play a crucial role in SSIs.

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