

Methicillin-Resistant *Staphylococcus aureus* SCCmec Type and Its Association with Clinical Presentation, Severity, and Length of Stay among Patients with Complicated Skin and Skin Structure Infections

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Abstract

Data from a prospective, randomized, open-label, active-controlled, multicenter, Phase 4 study comparing oral or intravenous linezolid with intravenous vancomycin for treatment of complicated skin and soft-tissue infections caused by methicillin resistant *Staphylococcus aureus* was used to determine the association between staphylococcal cassette chromosome *mec* (SCCmec) type and patient's clinical presentation, infection severity, intravenous therapy duration and length of stay (LOS). Compared to SCCmec types I, II, and III, SCCmec type IV, PVL+ was associated with more frequent presentation of abscesses, lower severity scores, and shorter intravenous therapy duration and LOS in both treatment groups.

Keywords

MRSA, SCCmec Type, Infection Severity, Length of Stay

1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important pathogen associated with complicated skin and soft-tissue infections (cSSTIs). MRSA isolates are classified according to the type of staphylococcal cassette chromosome *mec* (SCC*mec*), with SCC*mec* types I, II, and III associated with healthcare-associated MRSA and SCC*mec* type IV associated with community-associated MRSA (CA-MRSA). Most CA-MRSA isolates obtained from cSSTIs in the United States carry the gene encoding Panton-Valentine leukocidin (PVL). We sought to determine the impact of SCC*mec* type on clinical presentation, severity of the cSSTI, and healthcare resource utilization among patients that were enrolled in an international Phase 4 study designed to compare the clinical and microbiological outcomes and safety of linezolid and vancomycin for the treatment of culture-confirmed MRSA-cSSTIs [1]. (This study was presented at 111th General meeting of the American Society of Microbiology, New Orleans, LA, May 21-24, 2011).

2. Methods

The parent study was approved by the local Institutional Review Board at each site and informed consent was obtained from each study participant. A total of 545 MRSA isolates were evaluated from specimens obtained by fine-needle aspiration, tissue biopsy, or collection of debridement tissue from patients with cSSTIs. Superficial swabs of infection or wound sites were not allowed. MRSA was identified by local laboratories using routine methods, and isolates were submitted to a central laboratory for SCC*mec* typing (I–IV) and PVL-encoding genes screen using a multiplex polymerase chain reaction (PCR) as previously described [2].

We defined CA-MRSA as SCC*mec* type IV, PVL positive strain [3]. Patients were treated with linezolid 600 mg orally or intravenously every 12 hours or vancomycin 15 mg/kg of body-weight intravenously every 12 hours, with dose adjustment based on trough levels and creatinine clearance, for up to 28 days. Baseline variables were collected at screening to calculate Wilson severity score, a validated test to assess patient risk and predict clinical outcome (cure or failure) [4]. Length of hospital stay (LOS) analysis used Kaplan Meier survival techniques. It was based on the daily hospital location data and was censored at end of study. Duration of intravenous therapy was compared using the Student t test. Statistical analyses were performed using SAS v.8.2 (SAS Institute, Cary, NC, www.sas.com).

3. Results

SCC*mec* type IV accounted for 69.0% (376/545) of cSSTIs MRSA isolates. In total, 54.1% (295/545) of isolates were CA-MRSA as defined by SCC*mec* type IV, PVL+. Most were from the United States and subsequently characterized as USA300 sequence type 8 (ST8) [2]. Thirty-one percent (169/545) of MRSA isolates were SCC*mec* type I, II, or III. CA-MRSA was most commonly associated with an abscess presentation (Table 1). SCC*mec* types I to III were most commonly seen with surgical wound infections (Table 1).

SCC*mec* type IV PVL+ had lower Wilson severity scores (23.8) compared with patients with SCC*mec* types I (38.0), II (45.5), III (33.7) and IV, PVL– (40.6) ($p < 0.05$ for each pairwise comparison). In the linezolid treatment group, SCC*mec* type IV, PVL+ was associated with a shorter mean intravenous antibiotic treatment duration and shorter length of hospital stay which were statistically significant when compared to SCC*mec* type I to III and type IV, PVL– (Table 2). In the vancomycin treatment group, patients with SCC*mec* type IV, PVL+ had statistically significant shorter length of hospital stay compared with SCC*mec* types I to III and type IV, PVL–. Compared to SCC*mec* type I, there was a statistically significant shorter mean intravenous antibiotic treatment duration for SCC*mec* type IV, PVL+ in patients treated with vancomycin (Table 2).

4. Discussion

Although some studies have shown that SCC*mec* II is associated with a higher mortality rate compared to the other SCC*mec* types [5], we have previously shown no significant difference between the type of SCC*mec* and clinical cure and mortality among patients with MRSA cSSTIs [6]. This has also been confirmed by other studies [7] [8]. However, an association between length of stay (LOS) and SCC*mec* type has been reported by other authors. Davis *et al.* showed that the mean length of stay was significantly longer for SCC*mec* II/III (18 days) than for SCC*mec* IV (10 days) [8]. We found similar results with MRSA SCC*mec* type IV, PVL+ being associated with a shorter length of stay compared with SCC*mec* types I to III and type IV, PVL–. The long LOS

Table 1. Clinical characteristics of study patients by SCCmec type.

Clinical presentation	MRSA SCCmec Type, n (%)					Total (N = 545)
	I (N = 48)	II (N = 88)	III (N = 33)	IV, PVL- (N = 81)	IV, PVL+ (N = 295)	
Surgical wound	35 (72.9)*	35 (39.8)*	14 (42.4)*	26 (32.1)*	10 (3.4)	120 (22.0)
Abscess	2 (4.2)*	8 (9.1)*	4 (12.1)*	11 (13.6)*	255 (86.4)	280 (51.4)
Infected burn	0	2 (2.3)	3 (9.1)*	3 (3.7)*	1 (0.3)	9 (1.7)
Trauma wound infection	2 (4.2)	6 (6.8)	1 (3.0)	5 (6.2)	8 (2.7)	22 (4.0)
Decubitus ulcer	0	3 (3.4)	4 (12.1)*	3 (3.7)	2 (0.7)	12 (2.2)
Diabetic ulcer	2 (4.2)	21 (23.9)*	5 (15.2)*	11 (13.6)*	6 (2.0)	45 (8.3)
Infected skin ulcer, other	5 (10.4)*	10 (11.4)*	1 (3.0)	17 (21.0)*	0	33 (6.1)
Other**	2 (4.2)	3 (3.4)	1 (3.0)	5 (6.2)	13 (4.4)	24 (4.4)

MRSA, methicillin-resistant *Staphylococcus aureus*; SCCmec, staphylococcal cassette chromosome *mec*; PVL, Pantone-Valentine leukocidin. * $p < 0.05$ versus IV PVL+; Fisher exact test. Because of rounding, some values may not add up to 100%. **Includes infected skin ulcer, trauma wound infection, decubitus ulcer and infected burn.

Table 2. Resource utilization by SCCmec type.

Treatment Outcomes	MRSA SCCmec Type				
	I	II	III	IV, PVL-	IV, PVL+
Days, Mean (SE)					
Linezolid					
Length of IV therapy ^{ab}	(N = 25) 6.4 (0.89)*	(N = 28) 5.7 (0.80)*	(N = 13) 7.9 (0.96)*	(N = 20) 6.3 (0.94)*	(N = 72) 4.0 (0.33)
Length of IV therapy (All)	(N = 25) 6.4 (0.89)*	(N = 50) 3.2 (0.60)*	(N = 15) 6.9 (1.09)*	(N = 38) 3.3 (0.71)*	(N = 142) 2.0 (0.24)
Length of stay ^a	(N = 24) 10.8 (1.39)*	(N = 27) 8.2 (0.97)*	(N = 13) 12.7 (1.87)*	(N = 20) 13.6 (1.53)*	(N = 71) 5.8 (0.60)
Length of stay (All)	(N = 25) 10.9 (1.34)*	(N = 50) 7.6 (0.76)*	(N = 15) 12.3 (1.86)*	(N = 38) 13.7 (1.11)*	(N = 142) 4.4 (0.40)
Vancomycin					
Length of IV therapy	(N = 23) 12.0 (0.86)*	(N = 38) 10.6 (0.64)	(N = 18) 10.8 (0.82)	(N = 43) 9.3 (0.48)	(N = 153) 9.4 (0.31)
Length of stay	12.6 (1.33)*	9.1 (1.05)*	12.8 (1.39)*	14.3 (1.06)*	5.6 (0.42)

^aPatients who started on IV linezolid study therapy are included in this analysis. ^bThree patients who started on oral therapy and received IV during their course of therapy are included in this analysis. * $p < 0.05$ versus IV PVL+; one-way analysis of variance. IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; SCCmec, staphylococcal cassette chromosome *mec*; PVL, Pantone-Valentine leukocidin; SE, standard error.

for SCCmec IV reported by Davis *et al.* might have been due to the presence of PVL- strains which have a longer LOS compared to the PVL+ strains as seen in our study. This is consistent with a lower Wilson severity score found in SCCmec type IV, PVL+ compared the other SCCmec types and may be partially explained by MRSA SCCmec type IV, PVL+ being associated with abscesses, which are often less severe than other types of cSSTIs.

PVL has been linked to cSSTIs [9], however its presence in these infections has not been associated with worse outcomes. Bae *et al.* reported that patients with cSSTIs caused by PVL+ MRSA strain were more likely to achieve cure than patients with PVL- MRSA strain infections (91.6% vs. 80.7%) [10]. We obtained similar results in that SCCmec type IV, PVL+ strains were associated with a lower severity score and shorter LOS than PVL- strains. The higher Wilson severity score seen with non-SCCmec type IV might be related with the higher involvement of surgical wound infection which is an independent risk factor for worse outcome in this scoring system [4]. Similarly, the longer LOS of non-SCCmec type IV is most likely due to the higher Wilson severity scores in these patients.

5. Conclusion

Although CA-MRSA cSSTIs are on the rise, the data from this prospective Phase IV clinical trial suggest these infections are associated with a less severe type of cSSTI and shorter LOS compared with the non-CA-MRSA infection.

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Abbreviations

MRSA: Methicillin-resistant *Staphylococcus aureus*
CA-MRSA: community-associated methicillin-resistant *Staphylococcus aureus*
cSSTIs: complicated skin and soft-tissue infections
SCC*mec*: staphylococcal cassette chromosome *mec*
PVL: Panton-Valentine leukocidin
LOS: length of hospital stay
PCR: polymerase chain reaction