Master of Medicine

Clinical and microbiological characteristics of hospital-acquired methicillin-resistant *Staphylococcus aureus* bacteremia caused by community-associated PVL-negative ST72-SCC*mec*IV strain

Panton-Valentine leucocidin 음성 지역사회 관련 메티실린 내성 황색포도알균에 의한 병원 내 혈류감염의 임상적, 미생물학적 특징에 관한 연구

The Graduate School
of the University of Ulsan
Department of Medicine
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Clinical and microbiological characteristics of hospital-acquired methicillin-resistant *Staphylococcus aureus* bacteremia caused by community-associated PVL-negative ST72-SCC*mec*IV strain

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A Master's Thesis

Submitted to
the Graduate School of the University of Ulsan
For the Degree of

Master of Medicine
by
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Seoul, Korea
February 2021

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February 2021

ABSTRACTS

Background: ST72-SCCmecIV, a community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strain in Korea, originated in the community and has been spreading in the healthcare settings. Herein, we describe the clinical and microbiological characteristics of patients with hospital-acquired MRSA bacteremia (MRSAB) caused by community-associated strains.

Methods: We analyzed hospital-acquired MRSAB cases caused by ST72-SCC*mec*IV using a prospective cohort of patients with SAB at in a tertiary hospital in Korea from July 2008 to December 2018. We compared the clinical and microbiological characteristics of ST72-SCC*mec*IV with ST5-SCC*mec*II, a representative hospital-associated genotype strain.

Results: Of the 1782 *S. aureus* bacteremia (SAB) cases, 629 (35.3%) were hospital-acquired MRSAB. Of the 629 isolates, 431 (68.5%) were ST72-SCC*mec*IV and 152 (24.2%) were ST5-SCC*mec*II. Patients with ST72-SCC*mec*IV were younger than those with ST5-SCC*mec*II and less likely to have a history of recent surgery, antibiotic treatment, nasal MRSA colonization, and central venous catheter placement. Compared with ST5-SCC*mec*II, ST72-SCC*mec*IV isolates were more likely to have vancomycin MICs $\leq$ 1.0 mg/L ($p <$ 0.001). Osteoarticular infection as the primary site infection [7.2% (11/152) vs. 1.4% (6/431)] was more common in patients with ST72-SCC*mec*IV. There were no significant differences in the rate of recurrence ($\leq$ 90 days), persistent bacteremia ($\geq$ 7 days), and 30- and 90-day mortality rates between the two groups.

Conclusion: After adjusting for potential confounders, ST72-SCC*mec*IV in hospital-acquired infections was significantly associated with osteoarticular infections. Mortality rates between the ST72-SCC*mec*IV and ST5-SCC*mec*II groups were not significantly different.

Keywords: Methicillin-resistant *Staphylococcus aureus*, Panton-Valentine Leukocidin-negative, hospital-acquired infection, bacteremia, outcome

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) exhibits enhanced virulence and causes a wide range of infections from mild to life-threatening conditions in both the hospital and community settings. Historically, MRSA infections have primarily occurred among hospitalized patients. However, a growing number of community-associated MRSA (CA-MRSA) infections have recently emerged worldwide [1, 2] and new MRSA strains, often called CA-MRSA strains, have been isolated. As such, their virulence factors have not yet been completely established. CA-MRSA strains present different characteristics from those of the traditional hospital-associated MRSA (HA-MRSA) strains [3].

S. aureus can evade the host innate immunity [4] and may secrete toxins such as Panton-Valentine leukocidin (PVL), which is lytic to human neutrophils and has pro-inflammatory effects [5]. The distribution and prevalence of dominant CA-MRSA clones and PVL gene status vary among countries [3]. In the United States, CA-MRSA isolates are mostly attributed to the single-clone sequence type (ST) 8 (pulsotype USA 300) possessing PVL [6, 7]. In South Korea, ST72-SCC*mec*IV is the major CA-MRSA clone [8, 9] and is distinct compared with other clones in Asia or those international [10]. Particularly, unlike the PVL-positive CA-MRSA isolates from Western countries, ST72-SCC*mec*IV isolates do not carry the PVL gene. This PVL-negative ST72-SCC*mec*IV CA-MRSA strain first emerged in the community and has been spreading in the healthcare settings [11-13]. However, there have only been a few reports on hospital-acquired MRSA bacteremia (MRSAB) caused by ST72-SCC*mec*IV [14-16].

We thus evaluated the clinical and microbiological characteristics and outcomes of Korean patients with MRSAB caused by ST72-SCC*mec*IV and compared them with those caused byST5-SCC*mec*II, a representative HA-MRSA genomic strain in Korea.

METHODS

Study design and patients

This prospective cohort study was conducted at the Asan Medical Center (Seoul, Republic of Korea) from July 2008 through December 2018. This 2,700-bed institution is a university-affiliated teaching hospital that provides both primary and tertiary care. All adult patients with *S. aureus* bacteremia (SAB) were prospectively enrolled and observed for 90 days. SAB cases were reviewed by infectious disease (ID) experts within 2 or 3 days after the identification of *S. aureus* in blood culture tests. ID experts recommended the following routine as protocol. Follow-up blood cultures were performed every 2 to 3 days until the patient tested negative. Echocardiography and fundoscopic examination were recommended to detect cardiac vegetation and endophthalmitis, respectively. It is also recommended that vancomycin through concentrations were monitored and maintained at 15–20 mg/L in patients with SAB. Patients were excluded from the analysis if they had polymicrobial bacteremia, had been discharged before obtaining positive blood culture results, or had SAB within the previous 3 months. Demographic characteristics, underlying diseases or conditions and their severity, severity of bacteremia, place of infection, initial source of SAB, presence of a central venous catheter (CVC) or other prosthetic devices, patient management, and clinical outcomes were recorded. The Charlson Comorbidity Index (CCI) was used to measure the composite score of severity of preexisting comorbidities [17]. A positive culture from a patient who had been hospitalized for ≥ 48 h was defined to be hospital-acquired bloodstream infection [18]. Within this SAB cohort, hospital-acquired MRSAB cases caused by ST72-SCC*mec*IV and ST5-SCC*mec*II strains were selected and analyzed. This study was approved by the Asan Medical Center Institutional Review Board (approval number 2013-0234).

Laboratory and microbiological data

All *S. aureus* isolates were identified using the standard methods. The first blood isolate obtained from the patient was used for microbiological and molecular assessments. The minimum inhibitory concentration (MIC) of vancomycin was determined using the broth microdilution method. All isolates underwent vancomycin susceptibility testing according to the Clinical and Laboratory Standards Institute (CLSI) guideline with the inclusion of 1.5 mg/L dilution [19-21]. Antimicrobial susceptibilities were determined using the MicroScan system (Dade Behring, West Sacramento, CA, USA) and the standard criteria of the CSLI. Polymerase chain reaction of the *mec*A gene was performed to confirm methicillin resistance. δ-Hemolysin activity was used to determine *agr* functionality as described previously [22]. PVL genes, the staphylococcal cassette chromosome *mec* (SCC*mec*) type, and the multilocus sequence type (MLST) were identified as previously described [23-27]. MLST allele names and STs were derived from the MLST database (http://www.mlst.net).

Data collection and information on variables

Data of the following variables were obtained from all patients: age, sex, underlying diseases or conditions, recent surgery history, history of immunosuppressive therapy, presence or absence of medical devices, primary site of infection, metastatic infection, antibiogram results, patient management, and clinical outcome. The site of infection was determined based on clinical, radiological, and bacteriological investigations. Infective endocarditis was defined according to the modified Duke criteria [28]. We classified bacteremia without an identifiable site of infection as primary bacteremia. Prosthetic devices included orthopedic devices, cardiovascular electronic devices, prosthetic valves, and

vascular grafts. Septic shock was defined as sepsis with persistent hypotension that requires vasopressors to maintain mean arterial pressure ≥ 65 mmHg, and lactate level ≥ 2 mmol/L despite adequate fluid resuscitation [29]. Recurrent bacteremia was defined as SAB occurrence within 90 days of resolution of the first episode, whereas persistent bacteremia was defined as SAB lasting at least 7 days.

Statistical analysis

Pearson's χ-square test or Fisher's exact test was used to analyze the categorical variables, whereas Student's *t*-test and the Mann–Whitney *U*-test were used to analyze normally and non-normally distributed continuous variables, respectively. Univariate and multivariate analyses using logistic regression models were performed to identify the independent risk factors for crude mortality. All variables with $p < 0.05$ in univariate analysis and additional variables of clinical importance, such as age, sex, underlying diseases, and sequence type, were included in the multivariate logistic regression model. Odds ratios and their 95% confidential intervals (CIs) were calculated. All p values were two-tailed, and $p < 0.05$ were considered statistically significant. Data were analyzed using SPSS v21.0 (IBM Co., Armonk, NY, USA).

RESULTS

Study population

We found 1,782 SAB cases, comprising 924 (51.9%) MRSA and 629 (35.3%) hospital-acquired MRSA bacteremia. Of the 629 isolates, 431 (68.5%) were ST72-SCC*mec*IV and 152 (24.2%) were ST5-SCC*mec*II. Therefore, we analyzed 583 hospital acquired MRSAB cases.

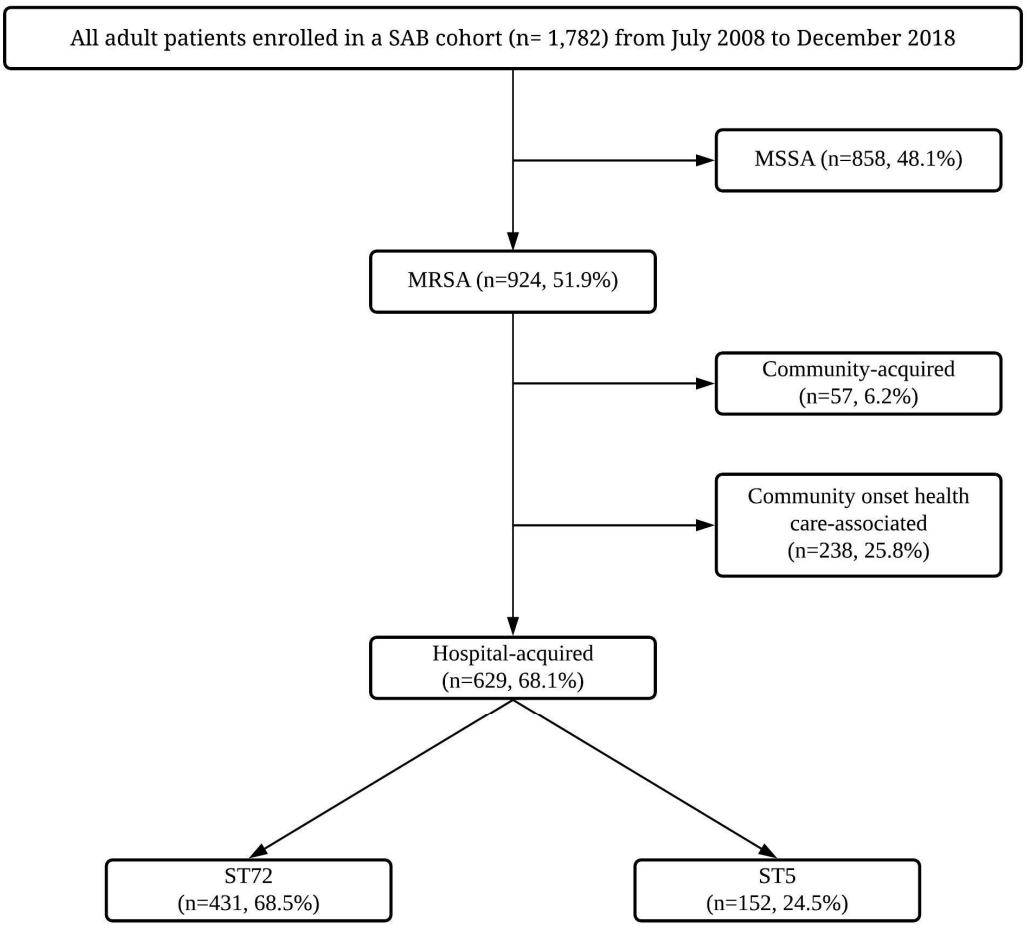

Figure 1. Flow chart of patient disposition

Patient characteristics

The clinical characteristics of 583 patients with hospital-acquired MRSAB caused by ST72-SCC*mec*IV and ST5-SCC*mec*II strains are summarized in Table 1. Patients with ST72-SCC*mec*IV were younger than those with ST5-SCC*mec*II (median age: 63 vs. 65; $p = 0.013$) and had hematologic malignancy more frequently (13.8% [21/152] vs. 4.6% [20/431]). There were no significant differences in the frequency of other underlying diseases and CCI between the two groups. Meanwhile, patients with ST72-SCC*mec*IV were less likely to have a history of recent surgery (27% [41/152] vs. 39.9% [172/431]; $p = 0.004$), prior antibiotic treatment (within 1 month; 41.4% [63/152] vs. 86.5% [373/431]; $p < 0.001$), nasal MRSA colonization (16.4% [25/152] vs. 45.2% [195/431]; $p < 0.001$), and central venous catheter placement (17.7% [68/152] vs. 73.5% [317/431]; $p = 0.001$). The ST72-SCC*mec*IV strain caused more frequent osteoarticular infections than ST5-SCC*mec*II (7.2% [11/152] vs. 1.4% [6/431]; $p = 0.001$). Intravascular catheter-related infections were more common in the ST5-SCC*mec*II group (43.4% [66/152] vs. 52.9% [228/431]; $p = 0.044$). There were no significant differences on the frequency of metastatic infections and vancomycin use as definitive antibiotic therapy between the two groups.

Table 1. Clinical characteristics of adult patients with hospital-acquired MRSAB (*n* = 583)

Characteristic	ST5 (*n* = 431)	ST72 (*n* = 152)	*p*
Age (years), median (IQR)	65 (55–73)	63 (50–71)	0.013
Male	285 (66.1)	87 (57.2)	0.050
Underlying diseases			
Solid cancer	199 (46.2)	65 (42.8)	0.468
Hematologic malignancy	20 (4.6)	21 (13.8)	<0.001
Diabetes mellitus	131 (30.4)	47 (30.9)	0.904
Liver cirrhosis	64 (14.8)	26 (17.1)	0.508
End-stage renal disease	33 (7.7)	14 (9.2)	0.545
Chronic pulmonary disease[a]	18 (4.2)	3 (1.3)	0.096
Heart failure	22 (5.1)	8 (5.3)	0.939
Hypertension	171 (39.7)	56 (36.8)	0.538
Solid organ transplantation	40 (9.3)	10 (6.6)	0.306
CCI, median (IQR)	3 (2–5)	2 (2–5)	0.821
CCI > 4	114 (26.5)	38 (25.0)	0.726
Predisposing condition			
Recent surgery[b]	172 (39.9)	41 (27.0)	0.004
Prior antibiotic treatment [b]	373 (86.5)	63 (41.4)	<0.001
Nasal MRSA colonization[c]	195 (45.2)	25 (16.4)	<0.001
Immunosuppressive treatment[b]	136 (31.6)	52 (34.2)	0.547
Central venous catheter	317 (73.5)	68 (17.7)	<0.001
Non-catheter prosthetic devices[d]	58(13.5)	22 (14.5)	0.754
Septic shock[e]	62 (14.4)	22 (14.5)	0.979
Primary site of infection			
Intravascular catheter-related	228 (52.9)	66 (43.4)	0.044
Pneumonia	47 (10.9)	13 (8.6)	0.412
Surgical site infection	36 (8.4)	13 (8.6)	0.939
Osteoarticular infection	6 (1.4)	11 (7.2)	<0.001
Skin and soft tissue infection	12 (2.8)	5 (3.3)	0.750
Infective endocarditis	4 (0.9)	4 (2.6)	0.121
Other	45 (10.4)	12 (7.9)	0.363
Unknown (primary bacteremia)	51 (11.8)	23 (15.1)	0.294
Metastatic infection	55 (12.8)	21 (13.8)	0.740

Eradicable foci	271 (62.9)	87 (57.2)	0.219
Focus removed	255 (94.1)	72 (82.8)	<0.001
Definitive antibiotic treatment			
Vancomycin	352 (81.7)	122 (80.3)	0.702
Teicoplanin	108 (25.1)	41 (27.0)	0.642

Data are presented as the number of patients (%), unless otherwise indicated.

IQR, interquartile range; CCI, Charlson Comorbidity Index.

[a] Includes COPD and BE.

[b] During the previous month.

[c] Positive result of the nasal swab test performed within 48 hours after confirmation of positive blood culture.

[d] Includes pacemaker/ICD (8 patients), prosthetic heart valves (20 patients), orthopedic devices (21 patients), and vascular grafts (27 patients).

[e] Sepsis with persistent hypotension that requires vasopressors to maintain mean arterial pressure ≥65 mmHg, and lactate ≥2 mmol/L despite adequate fluid resuscitation.

Microbiologic characteristics

The microbiological characteristics and antibiotic susceptibilities of MRSA strains are summarized in Table 2. Most of the ST5-SCC*mec*II isolates (96.1%) have *agr* dysfunction, whereas most of the ST72-SCC*mec*IV isolates (90.1%) possess *agr* function. ST72-SCC*mec*IV isolates exhibited lower vancomycin MIC distribution and were less likely to be resistant to various classes of antibiotics, including clindamycin, ciprofloxacin, erythromycin, fusidic acid, gentamicin, and rifampicin, than ST5-SCC*mec*II isolates (Table 2).

Table 2. Microbiologic characteristics of 583 MRSA isolates causing bloodstream infections

Characteristic	ST5 (*n* = 431)	ST72 (*n* = 152)	*p*
agr dysfunction	414 (96.1)	15 (9.9)	<0.001
Vancomycin MIC by BMD			
≤ 1.0 mg/L	302 (70.1)	136 (89.5)	<0.001
1.5 mg/L	117 (27.1)	15 (9.9)	<0.001
≥ 2.0 mg/L	12 (2.8)	1 (0.7)	0.127
Resistance to			
Clindamycin	422 (97.9)	33 (21.7)	<0.001
Ciprofloxacin	427 (99.1)	13 (8.6)	<0.001
Erythromycin	426 (98.8)	39 (25.7)	<0.001
Fusidic acid	372 (86.3)	2 (1.3)	<0.001
Gentamicin	339 (78.7)	14 (9.2)	<0.001
Rifampin	41 (9.5)	2 (1.3)	0.001
Trimethoprim/sulfamethoxazole	9 (2.1)	1 (0.7)	0.243

MIC, minimum inhibitory concentration; BMD, broth microdilution method

Treatment and outcomes

Table 3 compares the treatment outcomes of patients with ST72-SCC*mec*IV or ST5-SCC*mec*II isolates. Those with ST5-SCC*mec*II isolates were more likely to receive medical care in the intensive care unit (35.7% [154/431] vs. 12.5% [19/152]; $p < 0.001$). However, there were no significant differences in terms of 30- and 90-day mortality and persistent (≥ 7 days) and recurrent bacteremia between the two groups. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors for mortality (Table 4).

In univariate analyses, high CCI (> 4), accompanying septic shock and pneumonia as site of infection were significantly associated with 30-day mortality, whereas underlying hypertension was negatively correlated with 30-day mortality. Vancomycin MICs were not associated with 30-day mortality. In addition, the ST72-SCC*mec*IV strain had no significant effect on mortality.

In multivariate analyses, after controlling for several confounders and including other significant variables, there was no significant difference in 30-day mortality between the ST72-SCC*mec*IV and ST5-SCC*mec*II groups. CCI > 4 (adjusted odds ratio [aOR], 3.17; 95% CI, 1.84–5.45), accompanying septic shock (aOR, 3.05; 95% CI, 1.76–5.29), pneumonia as the site of infection (aOR, 3.25; 95% CI, 1.75–6.03), and underlying hypertension (aOR, 0.41; 95% CI, 0.24–0.71) were independently associated with 30-day mortality.

Table 3. Clinical outcomes of 583 adult patients with hospital-acquired MRSAB

Outcome	ST5 (*n* = 431)	ST72 (*n* = 152)	*p*
ICU	154 (35.7)	19 (12.5)	<0.001
Mortality (within 30 days)	91 (21.1)	24 (15.8)	0.156
Mortality (within 90 days)	147 (34.1)	41 (27.0)	0.106
Persistent bacteremia ≥ 7 days	75/429 (17.5)	18/145 (12.4)	0.152
Recurrent bacteremia within 90 days[a]	20 (4.6)	4 (2.6)	0.284

Table 4. Univariate and multivariate analyses of risk factors associated with 30-day mortality in 583 adult patients with hospital-acquired MRSAB

Risk factor	Univariate analysis		Multivariate analysis [a]	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age ≥ 65 years	1.04 (0.69–1.57)	0.836	1.36 (0.84–2.22)	0.217
Male	0.94 (0.62–1.43)	0.765	0.83 (0.52–1.31)	0.421
Underlying solid cancer	1.35 (0.90–2.03)	0.148	0.91 (0.53–1.56)	0.721
Hematologic malignancy	1.34 (0.64–2.83)	0.438	1.69 (0.72–3.96)	0.171
Diabetes mellitus	0.81 (0.51–1.27)	0.353	1.03 (0.61–1.76)	0.905
Liver cirrhosis	1.60 (0.96–2.70)	0.074	1.42 (0.78–2.58)	0.250
End-stage renal disease	0.69 (0.30–1.59)	0.388	0.94 (0.37–2.41)	0.895
Chronic pulmonary disease[b]	1.37 (0.49–3.86)	0.548	1.37 (0.42–4.44)	0.603
Heart failure	1.02 (0.41–2.55)	0.969	0.77 (0.28–2.18)	0.627
Hypertension	0.49 (0.31–0.77)	0.002	0.41 (0.24–0.71)	0.001
Solid organ transplantation	0.64 (0.28–1.46)	0.291	0.53 (0.21–1.36)	0.185
CCI > 4	2.63 (1.71–4.04)	<0.001	3.17 (1.84–5.45)	<0.001
Septic shock	2.89 (1.75–4.77)	<0.001	3.05 (1.76–5.29)	<0.001
Intravascular catheter-related	0.84 (0.56–1.27)	0.406		
Pneumonia	3.44 (1.96–6.02)	<0.001	3.25 (1.75–6.03)	<0.001
Surgical site infection	0.44 (0.17–1.13)	0.088		
Osteoarticular infection	0.25 (0.03–1.89)	0.178		
Skin and soft tissue infection	0.25 (0.03–1.89)	0.178		
Infective endocarditis	1.36 (0.27–6.84)	0.707		
Unknown (primary bacteremia)	0.94 (0.51–1.75)	0.852		
Metastatic infection	1.43 (0.81–2.51)	0.217		
Eradicable foci	0.85 (0.45–1.03)	0.066		
Removal of eradicable focus	0.47 (0.21–1.08)	0.077		
MRSA genotype				
ST5-SCCmecⅡ	1	NA	1	NA
ST72-SCCmecⅣ	0.70 (0.43–1.15)	0.158	0.65 (0.38-1.11)	0.217
agr dysfunction	1.56 (0.94–2.56)	0.083		
Vancomycin MIC by BMD				

≤1.0 mg/L	1	NA
1.5 mg/L	0.93 (0.57–1.52)	0.771
≥2.0 mg/L	0.72 (0.16–3.22)	0.677

OR, odds ratio; CI, confidence interval; CCI, Charlson Comorbidity Index; NA, not applicable; ST, sequence type; SCC, staphylococcal cassette chromosome; MIC, minimal inhibitory concentration; BMD, broth microdilution.

[a] Multivariate analysis included age, sex, underlying diseases, and variables showing significant differences ($p < 0.05$) in univariate analysis.

[b] Includes COPD and BE.

DISCUSSION

In this study, we evaluated the clinical characteristics and outcomes of patients with hospital-acquired MRSAB caused by ST72-SCC*mec*IV, a representative PVL-negative, CA-MRSA strain in Korea, by comparing with those by ST5-SCC*mec*II, a representative HA-MRSA strain in Korea. The ST72-SCC*mec*IV strain was significantly associated with osteoarticular infections, and ST72-SCC*mec*IV isolates were more likely to have vancomycin MICs ≤ 1.0 mg/L than ST5-SCC*mec*II. Mortality and recurrence rates were not significantly different between the two groups.

The proportion of osteoarticular infection as the primary site of infection was significantly high for ST72-SCCmecIV infections. According to a previous study by Lee *et al*., who analyzed CA-MRSA bacteremia cases and compared them with CA-MSSA, bone and joint infections were independent risk factors for CA-MRSA caused by ST72-SCC*mec*IV [30]. In another study on MRSAB, ST72-SCC*mec*IV isolates caused osteoarticular infection more frequently than ST5-SCC*mec*II [13]. ST72-SCC*mec*IV is thus suggested to play a role in the predominance of osteoarticular infections in patients with CA-MRSA bacteremia. In this current study, we strictly controlled for potential confounding factors and only included hospital-acquired infections such that the place of acquisition would not affect the outcome. Even after controlling confounders, ST72-SCC*mec*IV was significantly associated with osteoarticular infection, indicating that it is a strain-specific characteristic of ST72-SCC*mec*IV.

Furthermore, we found that ST72-SCC*mec*IV isolates were more likely to have vancomycin MICs ≤ 1.0 mg/L than the ST5-SCC*mec*II isolates. MIC values of CA-MRSA clones are usually lower than those of HA-MRSA clones [31]. Because only hospital infections were analyzed, this study was consistent with previous studies. Several studies have shown that a

high vancomycin MIC is associated with worse clinical outcomes [32-34]. In our study, however, increased vancomycin MICs were not associated with mortality.

Whether there are differences in the mortality associated with infections caused by CA-MRSA and HA-MRSA strains remains controversial [2, 35-38]. Previous studies on found that mortality associated with infections caused by ST72-SCC*mec*IV was similar or lower than that by ST5-SCC*mec*II or other comparative HA-MRSA strains [13, 16]. In this study, we controlled the potential confounding factors and included only hospital-acquired SAB for a more accurate comparison. As a result, mortality was not significantly different between the two groups. Although ST72-SCC*mec*IV may be more virulent in theory, the real-world outcome is complex. The exact reasons have not been elucidated; however, we attribute this to three factors. First, a previous study revealed that strain-specific virulence factors such as staphylococcal superantigen genes, including *sel*, *sec*, and *tst,* which are less commonly found in ST72-SCC*mec*IV isolates, might contribute to higher mortality in ST5-SCC*mec*II infections [13]. Second, because vancomycin MICs in the ST5-SCC*mec*II group were higher, its bactericidal activity is reduced. Lastly, the percentage of patients with recent surgery or CVC presence was higher in the ST5-SCC*mec*II group than in the ST72-SCC*mec*IV group. Overall, the ST72-SCC*mec*IV strain might be more virulent itself as it caused bacteremia in the absence of these prerequisites. Given this, mortality may be more related to the patient's comorbidities and site of acquisition rather than the strain itself.

Our study had some limitations. First, patients included those only from a single hospital; therefore, our findings may not be entirely representative of CA-MRSA strains in Korea. Second, because our comparative analysis only included hospital-acquired infections and excluded community-acquired infections, our findings cannot be generalized to all ST72-SCC*mec*IV strains. Thus, further studies are needed to clarify the role of PVL and to identify the virulence factors in the ST72-SCC*mec*IV strain.

CONCLUSION

In conclusion, osteoarticular infection was more frequently observed in hospital-acquired MRSAB caused by ST72-SCC*mec*IV than those by ST5-SCC*mec*II. The ST72-SCC*mec*IV strain was not associated with worse clinical outcomes, including 30-day mortality, 90-day mortality, persistent bacteremia, and recurrence, when compared with ST5-SCC*mec*II.

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국문요약

Panton-Valentine leucocidin 음성 지역사회 관련 메티실린 내성 황색포도알균에 의한 병원 내 혈류감염의 임상적, 미생물학적 특징에 관한 연구

이윤우

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연구 배경: SCC*mec* type4, Sequence type 72 (ST72-SCC*mec*IV)는 한국의 대표적인 지역사회 관련 methicillin-resistant *Staphylococcus aureus* (community-associated MRSA, CA-MRSA) 균주이고, Panton-Valentine leucocidin (PVL) 음성이라고 알려져 있으나, 그 임상적 특징에 대하여는 잘 알려져 있지 않다. ST72-SCC*mec*IV에 의하여 발생한 병원 내 혈류 감염의 임상적 특징, 사망의 위험인자, 예후를 대표적인 병원관련 균주 (HA) ST5-SCC*mec*II MRSA와 비교하여 알아보고자 하였다.

연구 방법: 2008년 7월부터 2018년 12월까지 서울아산병원에서 성인 환자 중

S.aureus bacteremia가 확인된 환자들을 전향적으로 등록하여 90일 동안 관찰하는 코호트를 구축하였고, 이 코호트에서 ST72-SCC*mec*IV와 ST5-SCC*mec*II 균주에 의한 병원내 혈류 감염 증례만을 최종 선정하여 후향적 연구를 진행하였다.

연구 결과: 총 1782 건의 *S.aureus* bacteremia (SAB)가 있었고, 629 건이 병원관련 MRSA 혈류감염에 해당하였다. ST72-SCC*mec*IV는 432 건으로 68.5%를 차지하였고, ST5-SCC*mec*II가 152 건으로 24.5% 였고, 이들 583 건이 최종적으로 분석대상이 되었다. ST72-SCC*mec*IV MRSA 환자들은 ST5-SCC*mec*II MRSA 환자들에 비교하여 연령 중앙값이 낮았으며, 최근 수술력, 최근 항생제 사용력, 중심정맥관을 가지고 있는 경우, 비강 집락 양성인 경우가 유의하게 적었다. ST72-SCC*mec*IV MRSA에서 Vancomycin MIC가 더 낮은 경향을 보였고, MIC 1.0 mg/L의 비율이 ST72-SCC*mec*IV MRSA에 비하여 유의하게 높았다 (p <0.001). ST72-SCC*mec*IV 군에서 골관절 감염의 빈도가 유의하게 높았다 [7.2% (11/152) vs. 1.4% (6/431)]. 두 군 간 재발, 지속성 균혈증 (≥ 7일), 30일 사망률, 90일 사망률에는 유의한 차이가 없었다.

연구 결론: 병원내 MRSAB에서 ST72-SCC*mec*IV MRSA는 ST5-SCC*mec*II MRSA에 비교하여 골관절 감염을 더 자주 일으키고, 재발, 지속성 균혈증 (≥ 7일), 30일 사망률, 90일 사망률에는 유의한 차이가 없다.

중심 단어: 메티실린 내성 황색포도알균, Panton-Valentine Leukocidin-음성, 병원 감염, 균혈증