Lack of Correlation Between Clinical Parameters of Sepsis and Molecular Strain Typing in *Staphylococcus aureus*

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Introduction

Sepsis is a systemic, deleterious host response to infection which may lead to acute organ dysfunction and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). Severe sepsis and septic shock are major healthcare problems, affecting millions of people each year and increasing in incidence (1).

Staphylococcus aureus is an important human pathogen. Pulsotype strain USA300 (ST8-MRSA-SCC*mec*IV) is the predominant CA-MRSA strain in North America. It is a major cause of skin and soft tissue infection and also may be associated with severe sepsis and septic shock (2-4). However, Lam et. al. found that the development of septic shock associated with MRSA bacteremia was independently correlated with baseline severity of illness, presence of acute renal failure, and SCC*mec* type II (5). A recent meta-analysis also found a lack of association between USA300 sepsis and mortality (6).Given this background we sought to analyze if any correlations existed between *S. aureus* strain molecular typing with the clinical parameters of sepsis from patients enrolled in the Alberta Sepsis Network.

Materials and Methods

Patient selection: Patients were identified through the University of Calgary Data Haven SepsisNet environment. Between Sep 2009 and Dec 2012, 28 *S. aureus* isolates which possessed matched clinical data including admitting APACHE II score and maximum SOFA score were recovered from Calgary Laboratory Services.

Molecular characterization: Isolates were analyzed using multiple techniques including: pulsed field gel electrophoresis (PFGE) after digestion with *SmaI* (7), agr typing (8), SCC*mec* typing (9), Staphylococcal protein A (SPA) typing (10), multilocus sequence typing (MLST) (11), and testing for the presence of Panton-Valentine leukocidin (PVL) (12).

Clinical parameters:

APACHE II: Acute Physiology and Chronic Health Evaluation II is a severity-of-disease classification system (13). It is computed to an integer score from 0 to 71 based on several measurements, higher scores correspond to more severe disease and a higher risk of death. It is one of several ICU scoring systems and is applied within 24 hours of admission of a patient to ICU.

SOFA score**:** The sequential Organ Failure Assessment (SOFA) score (14), is a scoring system to determine the extent of a person's organ function or rate of failure. It is based on six different scores, one each for respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems. Both the mean and highest SOFA scores are predictors of outcome. An increase in SOFA score during the first 24 to 48 hours in the ICU predicts a mortality rate of at least 50% . Scores less than 9 give a predictive mortality of 33% while above 11 can be close to or above 95%. It is one of several ICU scoring systems and is used to track a patient's status during the stay in ICU.

Statistical methods**:** Single-factor ANOVA was used to determine whether methicillin resistant or sensitive, different agr, spa, ST, or PFGE types were associated with clinical severity of sepsis .

Fig. 1 *S. aureus* isolates (n=28) genetically characterized using PFGE, *agr* typing, SCC*mec* typing, *spa* typing, presence of PVL, and MLST

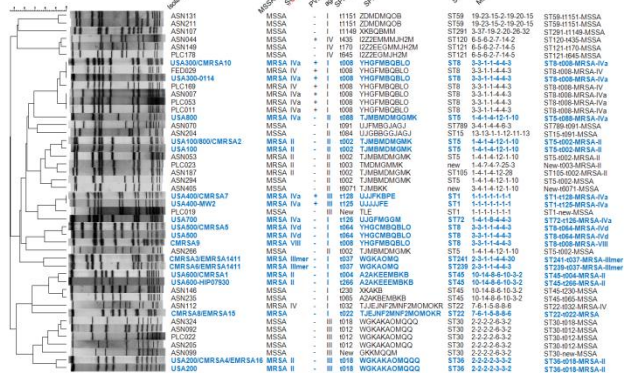


Fig.2 Constitution of 28 *S. aureus* isolates

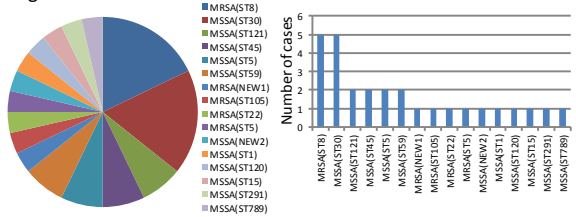
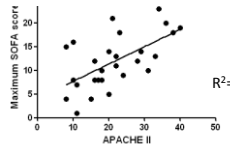


Fig. 3 Clinical parameters of 28 cases demonstrating a moderate positive relationship between APACHE II and maxSOFA score



R^2= 0.3711, P=0.0007

Fig.4 Correlation between clinical parameter and different epidemiologic/molecular characteristics: (A) MLST type; (B) spa type; (C) agr type; (D) presence or absence of PVL; (E) MRSA vs. MSSA; (F) different SCC*mec* type for MRSA strains.

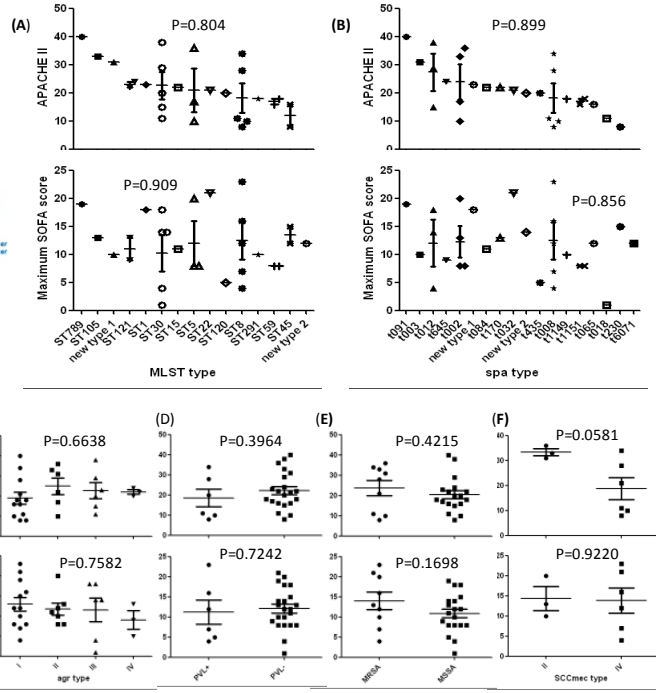


Table 1. summary of P values

	MLST type	Spa type	Agr type	PVL+vs.. PVL -	MSSA vs.. MRSA	SCC*mec* type
APACHE II	P=0.804	**P=0.899**	**P=0.6638**	**P=0.3964**	**P=0.4215**	**P=0.0581**
Maximum SOFA score	P=0.909	**P=0.856**	**P=0.7582**	**P=0.7242**	**P=0.1698**	**P=0.9220**

Summary & Discussion

1. ST8-MRSA (USA300) and ST30-MSSA were the major *S. aureus* strains causing sepsis in our population
2. A relationship exists between APACHE II and maximum SOFA score
3. We found no correlation for *Staphylococcus aureus* sepsis clinical parameters of severity of illness in an intensive care unit population and molecular strain characterization (MLST, spa, agr, presence of PVL, MRSA or MSSA, and SCC*mec* type)

References

1.Dellinger et al., *Crit Care Med*, 2013;
2.Seybold, et al. *Clin Infect Dis.* 2006;
3.Kreisel, et al. *Diagn Microbiol Infect Dis.* 2011;
4. Kempker, et al. *J Infect*. 2010;
5. Lam, et al. *Int J Infect Dis.* 2012;
6.Rajeshwari et al. *Infect Control Hosp Epidemiol*.2014;
7.Mulvey et al., *J Clin Microbiol*.2001;
8.Peacock et al., *Infect Immun*. 2002;
9. Zhang et al., *J Clin Microbiol*. 2005
10.Harmsen et al., *J Clin Microbiol*. 2003
11.Enright et al., *J Clin Microbiol*. 2000
12.McClure et al., *J Clin Microbiol*. 2006
13. Knaus et al., *Crit Care Med*. 1985
14.Vincent et al., *Intensive Care Med*. 1996