Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common and problematic causes of bacterial skin and soft-tissue infections (SSTI). MRSA tends to form complex skin infections, furuncles, boils and abscesses. Many patients go on to have recurrent infections, requiring significant additional therapy to treat each infection as well as needing to undergo decolonization of the skin in order to remove the bacteria and try to prevent future infections. A test to distinguish patients at risk for recurrence can allow earlier more aggressive treatment for those at risk for recurrent infection. This can potentially reduce healthcare costs, prevent future hospital admissions and surgical procedures, and reduce loss of productivity experienced by patients suffering from multiple recurrences.

Methods. A genome-wide association study using the Affymetrix gene array was performed on 11 patients with confirmed recurrent MRSA SSTIs and 3 controls who never developed an SSTI despite confirmed heavy exposure to MRSA in order to identify single nucleotide polymorphisms (SNP) associated with recurrent MRSA. The 10 genes identified were then fully sequenced using an Illumina NextSeq 500 to identify additional SNPs.

Results. A total of 22 SNPs were found in 10 separate genes which distinguished patients with recurrent MRSA from patients without recurrent MRSA despite heavy exposure. The 10 genes are shown in Table 1 along with a representative SNP. The *P*-values for each individual SNP were between 3.5×10^{-5} and 1.2×10^{-7}.

Conclusion. This study provides the first evidence of a genetic risk for those patients who develop recurrent MRSA SSTIs. The majority of the genes involved are related directly to the skin, not to immune functions thus it appears the major risk factor for development of recurrent MRSA SSTI is related to the barrier function of the skin and not to an immune defect. Being able to determine which patients are at risk for recurrence at the time they first present with an MRSA SSTI would be of great help in preventing future recurrences, reducing morbidity and reducing healthcare costs.

Gene symbol	χ^2 p-value	Allele A	Allele B	Chr.	Cytoband
FAM129B	1.21E-07	A	C	9	q34.11
IGSF8	2.31E-06	A	G	1	q23.2
ADARB2	3.06E-05	A	G	10	p15.3
DCT	3.06E-05	C	T	13	q32.1
IGSF8	3.06E-05	C	T	1	q23.2
KANK4	3.06E-05	G	T	1	p31.3
LTF	3.06E-05	C	T	3	p21.31
RBM6	3.06E-05	C	G	3	p21.31
COL13A1	3.53E-05	A	G	10	q22.1
COL19A1	3.53E-05	C	T	6	q13

Table 1: Genes Identified as Linked to Recurrent MRSA

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1333. Utility of Admission Procalcitonin Level in Patients Presenting to the Hospital with Bloodstream Infection: Real-World Evidence from 250 US Hospitals

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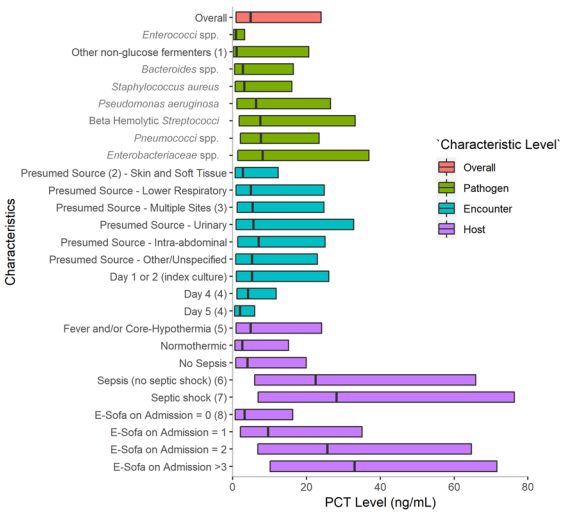
Background. Serum procalcitonin (PCT) may aid in early detection and treatment of bacterial bloodstream infections (BSI), yet evidence for this indication is inconclusive. We leveraged real-world data to examine biological variability in PCT across host and pathogen factors and its utility for ruling out BSI on admission.

Methods. PCT measurements within 24 hours of admission were examined in patients presenting with monomicrobial BSI to 250 hospitals in the *Cerner Healthfacts* Database. The reliability of admission PCT for ruling out BSI at hospital presentation was assessed using two different thresholds (<0.5 and <0.25ng/mL) and then stratifying results by presence vs. absence of sepsis (using CDC Adult Sepsis Event criteria), fever or hypothermia vs. normothermia, various presumed sources of BSI, and organism taxon.

Results. Between 2007 and 2017, PCT was measured on admission in 4,358/42,465 (10.3%) adults with BSI present on admission at 60 hospitals. Of these, 870 (20%) met CDC surveillance criteria for sepsis. The median admission PCT was 4.89 [0.93, 23.98] and varied by taxon, BSI source, patient temperature, and the presence and severity of sepsis; acute illness severity was the greatest driver of high PCT levels (Fig 1). Using a threshold of ≥ 0.50 ng/mL, the sensitivity of PCT for detection of BSI was 84% for all patients. Notably, BSI without sepsis was 4-fold more likely to yield a false negative PCT (<0.5ng/mL) than bacteremic sepsis. Sensitivity ranged from 77% with normothermia to 83% with fever/hypothermia ($P = 0.06$), between 81 and 88% across sources of BSI ($P = 0.13$) and more widely between 64 and 91% across taxa ($P = 0.02$). Enterococcal BSI was 2- and 4-fold more likely to have a falsely negative PCT than *S. aureus* or *S. pneumoniae* BSIs, whereas non-glucose fermenters other than *P. aeruginosa* had a 2 and 3-fold higher likelihood of being missed compared with *P. aeruginosa* and *Enterobacteriaceae* BSIs respectively (Fig 2). Pathogen-level variation in PCT sensitivity was also observed for BSI without sepsis (62–90%; $P = 0.02$) and upon using a stricter rule-out threshold of <0.25 ng/mL ($P = 0.01$).

Conclusion. PCT levels and the reliability of this test for ruling out bacteremia at hospital presentation varies by pathogen, presenting signs, and presence vs. absence of sepsis.

Figure 1: Distribution of Initial Procalcitonin Level by Pathogen and Host Characteristics

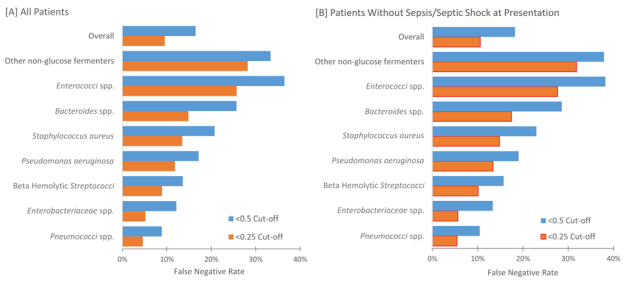


Boxes represent interquartile range and thick vertical lines within boxes represent median PCT level (ng/mL). 95% Confidence intervals and ranges are not presented for ease with data visualization.

(1) Other non-glucose fermenters include: *Achromobacter, Alcaligenes, Brevunidomonas, Burkholderia, Chryseobacterium, Comamonas, Flavimonas, other Pseudomonas and Acinetobacter spp. and S. maltophilia.*
(2) Presumed source derived from diagnosis codes based on established catgeories (Christensen KL et al. CID 2009)
(3) Any combination of sites skin and soft tissue, lower respiratory, urinary, and intra-abdominal
(4) Index PCT level was considered for all characteristics except Day 4 and Day 5 which represent subsequent PCT testing
(5) Fever defined as any temperature >100.3 F and core hypothermia as core temperature <95 F
(6) defined as infection (bacteremia) plus organ dysfunction by CDC Adult Sepsis Surveillance e-SOFA criteria (*Rhee C et al. Crit Care Med 2019)*
(7) defined as infection (bacteremia) and vasopressor dependent shock
(8) *Rhee C et al. Crit Care Med 2019*

Note: There was significant interspecies variability in median PCT level on admission tested by analysis of variance using a linear mixed model to account for hospital variation (p<0.001).

Figure 2: False Negative Rate of PCT by Pathogen in Overall BSI and BSI without Sepsis* at Presentation



Horizontal bars represent false negative rate [i.e. (1 – sensitivity) *100] of PCT on admission reported by bloodstream isolate taxon in blue for non-sepsis and orange for sepsis BSI cohorts. Using logistic regression with generalized estimating equations to account for hospital level variation
There was significant interspecies variability in false negative rate for the diagnosis of BSI on admission using PCT (p <0.05 for both< 0.25 and <0.5 cut offs) for both [A] overall BSI and [B] BSI without sepsis. The <0.25 and <0.5 ng/ml cut offs represent the most commonly utilized cut offs for PCT in respiratory infections and sepsis in the literature.

* defined as infection (bacteremia) plus organ dysfunction by CDC Adult Sepsis Surveillance e-SOFA criteria (*Rhee C et al. Crit Care Med 2019*) inclusive of vasopressor dependent shock

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