Bloodstream and Skin Infection MRSA Isolates, 2019-2021: Strain Differences and Phylogenetic Clustering in a Single Health System

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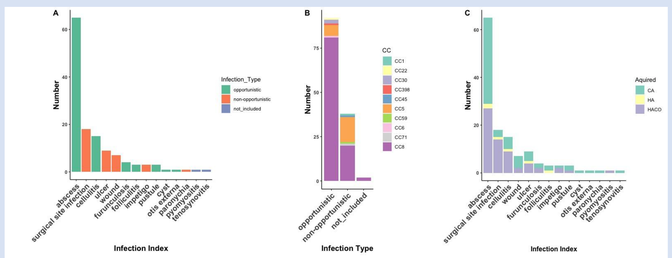
Introduction

S. aureus asymptomatically colonizes approximately 28-40% of the human population in the nares and is a common cause of skin and soft tissue infections (SSTI), bacteremia, endocarditis, and pneumonia. Colonization of patients has been associated with an increased risk of both bloodstream infections and SSTIs. To understand the relationship between SSTIs and bacteremia isolates, we performed WGS on SSTI and bacteremia MRSA strains from patients from two hospitals of the University of Pennsylvania from 2018-2020. We compared the phylogenetic structure of MRSA isolates from SSTIs and bloodstream infections. We then assessed whether these isolate genomes were closely associated, which would suggest recent transmission among study subjects. Within the SSTIs three clusters were identified. We also identified eight clusters containing strains from both SSTI and bacteremia cases, suggesting epidemiological overlap and spread of MRSA strains between patients with hospital and community-acquired MRSA infections within a single geographic area

Abscesses were the most common SSTI infection



Of the 132 patients with MRSA SSTI, abscesses were the most common presentation (n = 65), followed by surgical site infections (n= 18) and cellulitis (n= 15). If the SSTI occurred with no known major predisposing skin injury we referred to them as an opportunistic infections. The majority of the SSTI infections were determined to be opportunistic, 70% (92/132). There was no significant association between the epidemiologic classification of infection (CA, HA, HACO), and race, gender, the type of SSTI, or by opportunistic/non-opportunistic classification.

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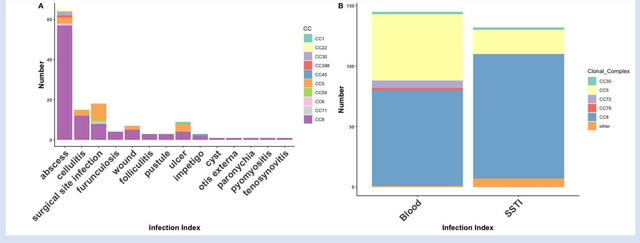
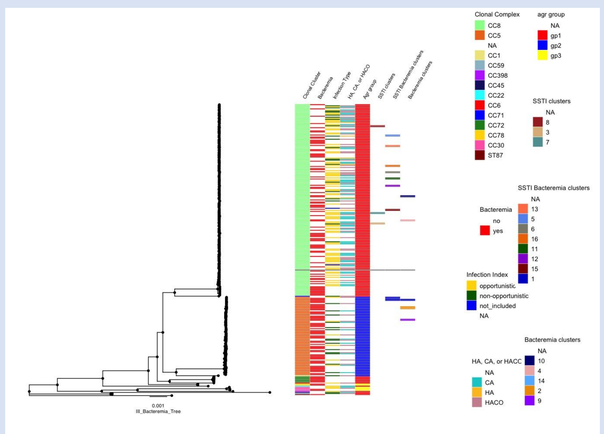
CC8 is enriched in SSTIs, while CC5 is enriched in Bacteremia



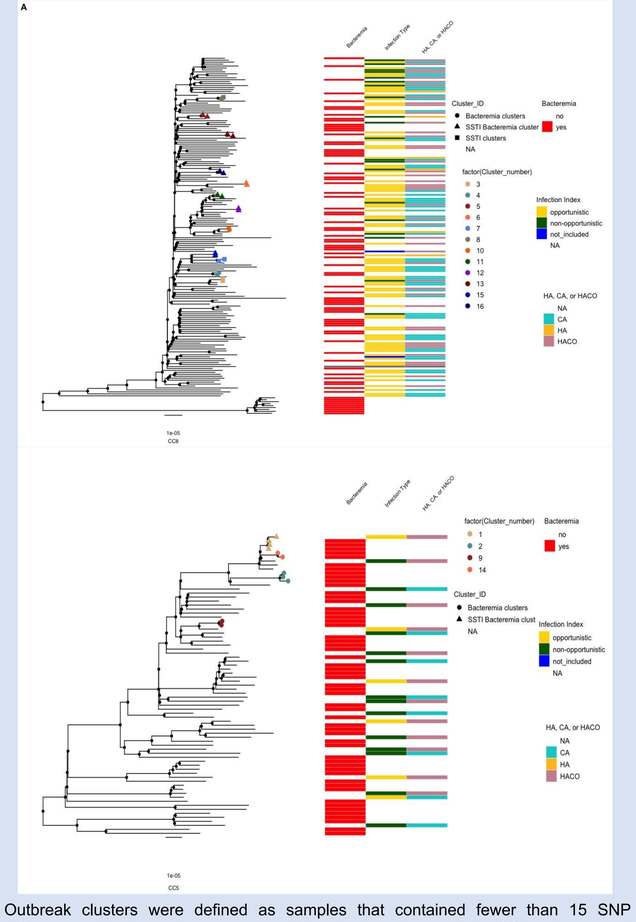
The 132 SSTI isolates were assigned to 14 STs and 10 Clonal Complexes while the bacteremia strains were assigned to 13 STs and 6 Clonal Complexes by genome-based multilocus sequence typing (MLST). Clonal complexes CC5 and CC8 were most common in the SSTIs (19/132, 14%, and 102/132, 77%) and bacteremia (55/145, 38%, and 79/145, 54%). CC8 was significantly overrepresented in the SSTI infections (103/132, 78%, p-value >0.01), with the majority of those infections being abscesses (57/80 71%). CC5 was overrepresented in the bacteremia strains (55/90, 61%, p-value >0.01).

Phylogenetic analysis of SSTI and Bacteremia isolates



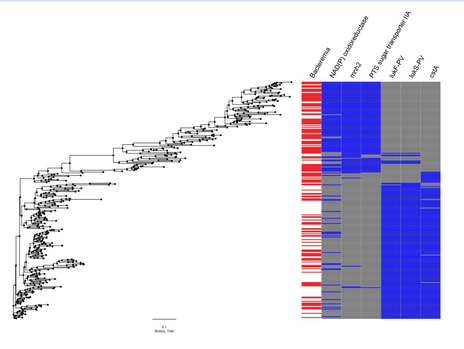
Isolates phylogenetically grouped together by Clonal Cluster, with CC8 being the largest clade. The *agr* types were also grouped together, with all CC8 strains being *agr* type 1 and CC5 strains being *agr* type 2.

Clustering based on SNP distances identify 16 clusters, 8 clusters overlap SSTI and Bacteremia



Outbreak clusters were defined as samples that contained fewer than 15 SNP differences. Eight clusters were identified that contained both SSTI strains and Bacteremia strains. Indicating that strains causing SSTI and bacteremia can be closely linked.

Genes associated with SSTI or Bacteremia infections



Using the GWAS program Scoary, preliminary data shows genes associated with SSTI or bacteremia. Genes *lukF-PV* and *lukS-PV* both associated with SSTIs, along with *cstA*. Genes associated with bacteremia included, *mnh2* a H+/Na+ antiporter, PTS sugar transport subunit IIA, and a NAD(P)/FAD dependent oxidoreductase.

Conclusions

The majority of SSTIs were caused by CC8, and SSTI strains were associated with the *lukF/S-PV* genes that are characteristic of USA300 strains. This suggests that USA300 strains are more predominate in skin infections than in bacteremia.

Eight outbreak clusters with fewer than 15 SNPs contained both SSTI and bacteremia strains. Indicating that strains that cause SSTI and bacteremia in different people located in a single geographical location may be closely linked.

Preliminary GWAS analysis found that *cstA*, a gene component of the *cst* operon that is activated under sulfide toxicity is associated with SSTIs. In contrast, genes associated with bacteremia included a a NAD(P)/FAD dependent oxidoreductase, and PTS sugar transport subunit IIA suggesting the possibility of distinctive metabolic characteristics of these strains.

Acknowledgements

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