Quantitative detection of bacterial DNA in whole blood in bloodstream infection

av

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Abstract

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This thesis aims to increase the knowledge on how quantitative PCR can be used in the diagnostics of bloodstream infections, with an emphasis on quantitative elements.

In Papers I and II, we evaluated quantitative data from two commercial PCR tests for pathogen detection directly in blood, Magicplex Sepsis (I) and SeptiFast (II), from patients with suspected sepsis. We found that high quantification cycle (Cq) values, indicating low DNA loads, were associated with findings of pathogens with doubtful clinical relevance, whereas low Cq values, indicating high DNA loads, were correlated with sepsis and septic shock, as well as with positive blood culture results.

In Paper III, we aimed to study the bacterial DNA load during *Staphylococcus aureus* bacteremia, in relation to different clinical factors. For this purpose, we developed a droplet digital PCR (ddPCR) for precise DNA quantification, targeting *S. aureus* specifically. We found that a high initial *S. aureus* DNA load was associated with laboratory markers for immune dysregulation as well as with sepsis, endocarditis, and mortality.

In Paper IV, we aimed to develop a tool for repeated DNA quantification during bloodstream infection. For this purpose, we optimized a ddPCR, targeting the universal bacterial 16S rDNA, and performed a comparison with species-specific ddPCRs on spiked blood, and on clinical samples. The performance of the 16S rDNA ddPCR was adequate, and we found that a high 16S rDNA load was associated with sepsis and mortality.

In conclusion, our results indicate that the pathogen DNA load in blood plays an important role in the clinical picture in BSI. In future research on molecular BSI diagnostics, studies on DNA loads and clearance should be included.

*Keywords*: bloodstream infection, bacteremia, sepsis, DNA load, quantitative PCR, droplet digital PCR, 16S rDNA

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