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Use of PCR/electrospray ionization mass spectrometry for rapid identification and antibiotic treatment adaptation in patients suffering from sepsis

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Background: Sepsis is a life-threatening dysregulated host response to infection. Fast and early diagnostics are crucial for appropriate treatment of the underlying infection.

Material/methods: We analyzed blood from critically ill patients with new onset of sepsis using both conventional gold standard methods (VITEK, MALDI-TOF) and a new culture-independent PCR/electrospray ionization mass spectrometry (PCR/ESI-MS) technology (IRIDICA; Abbott Molecular, Des Plaines, IL). Associated IRIDICA reagents included a high-volume bead-beating

platform (IRIDICA BB), automated DNA extraction and PCR set-up platform (IRIDICA SP), PCR thermocycler (IRIDICA TC), automated amplicon desalting and DNA debulking platform (IRIDICA DS), automated electrospray ionization mass spectrometer (IRIDICA MS), and a control and analysis computer (IRIDICA AC). We used the IRIDICA BAC BSI Assay for pathogen analysis, consisting of a pre-filled PCR reaction strip encompassing 18 primer pairs in 16 wells, targeting broadly conserved bacterial and *Candida* genes and 4 specific antibiotic resistance markers (*mecA*, *vanA*, *vanB* and bla_{KPC}). Provided software performed signature matching between detected base compositions and multilocus species-specific signatures derived through analysis of type strains or surveys of whole-genome data from GenBank.

Results: We report 5 cases from an ongoing clinical observational study protocol. Patient 1 was admitted with sepsis following partial liver resection. Empiric antibiotic treatment was started with meropenem/vancomycin. Conventional blood culture grew *E. faecalis*. IRIDICA analysis additionally *detected P. denticola, F. nucleatum, C. freundii* and *K. oxytoca*. Patient improved following initial antibiotic treatment. Patient 2 suffered from sepsis associated with acute leukemia. Empirical treatment was started with meropenem/voriconazol/linezolid/aciclovir. Chest x-ray revealed pneumonia, conventional blood cultures remained negative. IRIDICA showed *E. faecium with vanA* and *S. haemolyticus*. Treatment was not de-escalated due to patient's underlying condition. Patient improved and was discharged after 33 days. Patient 3 developed sepsis 14 days after coronary bypass grafting. Empirical antibiotic treatment was started with piperacillin/tazobactam/ciprofloxacin. Antibiotic treatment was de-escalated to flucoxacillin/ciprofloxacin after detection of *S. aureus* by IRIDICA. Focus was not found, patient improved under adapted antibiotic treatment. Patient 4 underwent a surgical procedure for spondylodiscitis due to a known *S. aureus* infection. Postoperatively, patient was given flucoxacillin/clindamycin which was escalated due to high fever and sepsis to piperacillin/tazobactam. After renewed detection of *mecA* negative *S. aureus* by IRIDICA, antibiotic treatment was again deescalated to flucoxacillin/clindamycin. However, patient died because of intraspinal empyema. Patient 5 suffered from an intraabdominal abscess following hemicolectomy. He was started on linezolid after detection of *E. faecium* in IRIDICA and improved clinically.

Conclusions: In the reported cases, IRIDICA BAC BSI assay provided additional early pathogen identification in culture negative specimens. These reports lead to modification and/or optimization of antibiotic treatment as appropriate. The IRIDICA system might be helpful for early adapted treatment choices and antibiotic stewardship programs