Assessing the clinical impact of rapid pathogen identification and antimicrobial susceptibility testing provided by the ASTar system from Q-linea

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Background

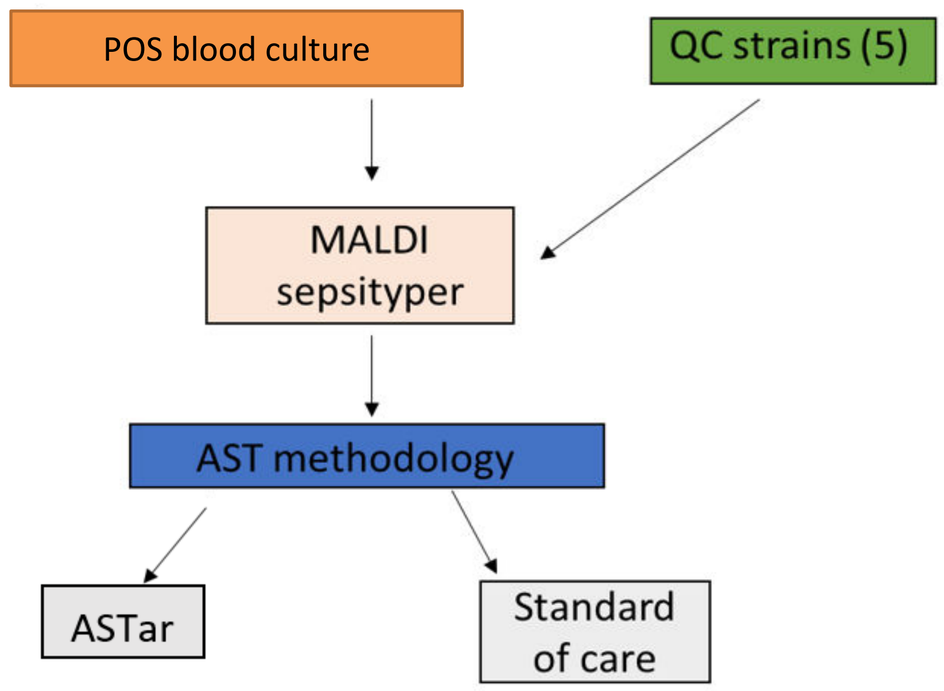
Sepsis is one of the leading causes of deaths worldwide. It is defined as a potentially fatal infection of the bloodstream and in severe cases is characterised by an overactivation of the body's immune response, which can result in severe organ dysfunction. In 2017, sepsis was reported to be responsible for 20% of worldwide deaths and there were 48.9 million reported cases. Treatment of blood stream infections that can lead to sepsis is time-critical and therefore requires rapid empirical broad-spectrum antibiotics to be administered. At this point in the patient timeline there is much diagnostic uncertainty, so samples are collected as part of the differential diagnosis including blood cultures. Using traditional culture-based techniques the clinical laboratory can take at least two days for blood culture identification (ID) and antimicrobial sensitivity testing (AST) results to become available. Rapid ID and AST of microorganisms cultured from blood is essential for optimising management of patients with sepsis. During bloodstream infections, rapid adaptation of empirical treatment according to the microorganism identified is essential to decrease mortality. Clinical outcomes are influenced by timeliness of appropriate antimicrobials and investigations for source control. *Escherichia coli* is the most prevalent Gram-negative (GN) pathogen followed by other species of *Enterobacterales*. *Staphylococcus aureus, Streptococcus pneumoniae* and coagulase–negative staphylococci are the most frequently isolated Gram-positive (GP) bacteria but isolation of the latter often reflect contamination from skin flora during the sampling process. The aim of the present study was to assess the microbiological performances of a new rapid blood culture AST assay, the Q-linea ASTar system versus the current standard of care.

Materials/Methods

A prospective study was designed to investigate the analytical performance and clinical impact of the rapid AST generated by the ASTar System versus our standard of care EUCAST disc diffusion. We processed signal positive blood cultures from **57** septic patients in ITU and on admission to ED and determined the analytical performance and theoretical clinical impact of these potential early interventions.

Standard of care was 24 hour direct disc diffusion from the culture bottle + saline, disc selection was based on Sepsityper MALDI ID and read the next day using EUCAST clinical breakpoints. The ASTar method as per manufacturers guidelines.

Clinical impact analysis was provided by Consultant Microbiologists in our department after reviewing clinical notes and the rapid AST result and then decided whether the following were applicable: Optimisation of treatment, Reduction of overall antibiotic use, Narrowing of antibiotic spectrum, IV to oral switch, Infection control intervention or No change.



Results

Escherichia coli	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Proteus mirabilis*	*Citrobacter koseri*	*Enterobacter* spp.	ESβL	CPE
36	11	3	5	1	1	4	3

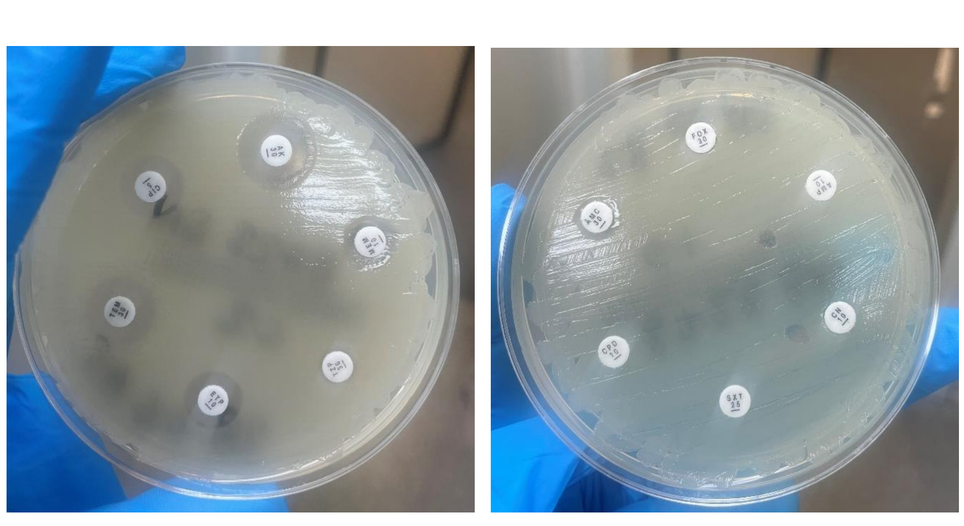
ASTar vs SoC (n= **57** signal positive BCs, **717** antibiotic data points**)**

Categorical Agreement (S, I, R)	Very Major Error (VME)	Major Error (ME)	Minor Error (MiE)
98.19% [704/717]	**0.42%** [3/717]	**0.84%** [6/717]	**0.56%** [4/717]

R, resistant; S, susceptible; I, intermediate (potentially susceptible at higher dose). **Very major error** (false susceptibility) indicates that the isolates were susceptible by ASTar and resistant by the reference method; **Major error** (false resistance), indicates that the isolates were resistant by ASTar diffusion and susceptible by the reference method and **minor error** indicates that the isolates were intermediate by ASTar and resistant or susceptible by reference.

Clinical Impact	Blood cultures
Optimisation of treatment	**14**
Reduction of overall antibiotic use	**5**
Narrowing of antibiotic spectrum	**9**
IV to oral switch	**0**
Infection control intervention	**7**
No change	**10**

The results above show good concordance with the lab SOC AST assays. To have confidence in the new assay we would expect to have error rates below 1.5% for VME and MEs. This in turn gives confidence in acting on the rapid results. We calculated 45 different theoretical clinical interventions based on rapid results. To complement categorial AST results the ASTar assay also includes MICs. Having this rapid detail can lead to further optimisation of treatment.



Disc diffusion plates with an NDM CPE *K. pneumoniae* and ASTar MIC results

Antimicrobial	MIC (mg/L)	Interpret
Amoxicillin-clavulanic acid	>32	R[1]
Piperacillin-tazobactam	256	R
Cefazolin	>16	R
Cefepime	32	R
Cefotaxime	>128	R[2]
Cefoxitin	>64	POS[3]
Ceftazidime	>64	R
Ceftazidime-avibactam	>32	R
Ceftolozane-tazobactam	>32	R
Ceftriaxone	>128	R[2]
Cefuroxime	>64	R[1]
Ertapenem	2	R
Meropenem	2	S[2]
Aztreonam	64	R
Ciprofloxacin	4	R[4]
Levofloxacin	1	I[4]
Amikacin	4	S[5]
Gentamicin	32	R
Tobramycin	32	R
Colistin	0.5	S[6]
Trimethoprim-sulfamethoxazole	>8	R

Conclusion

The ASTar system represents an exciting innovative platform with potential for significantly decreasing the interval to antimicrobial optimisation in blood stream infections. The potential clinical impact is greatest in pathogens with unpredictable antibiograms like those we encounter locally in our Gram-negative pathogens. It's impressive performance is also combined with ease-of-use and low hands-on-time for the lab technician which are benefits that are often overlooked.

The demonstrable rapid clinical interventions can deliver significant benefits for individual patients and healthcare organisations in terms of quality of care, patient safety, antimicrobial stewardship and infection prevention measures.

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