The clinical and infection control impact of early MALDI-TOF identification of bacteria from positive blood cultures

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INTRODUCTION

- Identification of bacteria causing bacteraemia aids the making of clinical decisions on bacteraemia significance, likely source of infection and antimicrobial choice, as well as having infection control implications.
- Earlier microbiological diagnosis should therefore have a positive impact on patient outcomes and antimicrobial stewardship.[1]
- Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) is an established method for the identification of cultured bacterial isolates, with multiple methodologies for preparation of samples described.[2]
- We introduced a new standard operating procedure in our laboratory in which positive blood culture broths were spread and cultured for 4 hours before undergoing MALDI-TOF, with the aim to yield organism identification on day one, as opposed to our previous method which yielded results on day two.

OBJECTIVES AND METHODS

The objectives of this study were to answer the questions:

- Is the 4 hour MALDI-TOF clinically useful in real-world practice and if so, how?
- Is the 4 hour MALDI-TOF useful for all types of organism found on Gram staining?

Blood culture bottle broths underwent '4-hour MALDI-TOF identification' if they flagged positive overnight or before 11am on a weekday; all blood cultures flagging positive outside of this time period underwent MALDI-TOF the next day.

We collected data on all positive blood cultures from a three hospital-site NHS trust over a 30 day period, including the clinical impact of early microbiological diagnosis. Yeasts and Gram positive rods were excluded.

Data sources included laboratory work sheets of positive blood cultures, Gram stain results, MALDI-TOF results, as well as electronic microbiology clinical advice records.

RESULTS

- Over 30 consecutive days there were 280 positive blood cultures from 250 different patients.
- **109 (38.9%) cultures were eligible to undergo '4-hour MALDI-TOF', which proceeded successfully on 88 (80.7%) of cultures.**
- Reasons for ineligibility included time of positive flag, poor growth and mixed cultures.
- **Overall earlier organism identification was clinically useful in 35 of 88 (39.8%) of cultures that underwent 4-hour MALDI-TOF.**
- The most common reasons earlier organism identification was deemed clinically useful were earlier determination of 'doubtful clinical significance' of cultures (21 of 88 [23.9%]) and earlier instigation of an appropriate antibiotic (12 of 88% [13.6%]).
- **Earlier organism identification was most useful in Gram positive organisms with the appearance of Staphylococci on microscopy (27 out of 35 [75%]) and least useful in Gram negative bacilli (2 out of 34 [5.9%]).**

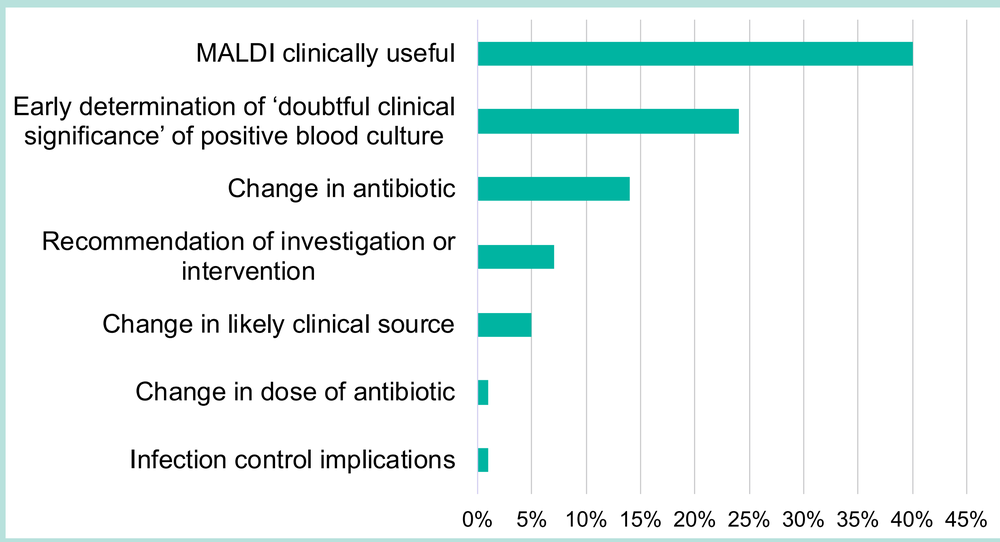

Figure 1: The proportion of blood cultures undergoing 4-hour MALDI-TOF in which earlier organism identification was clinically useful, including the ways in which early identification was useful.

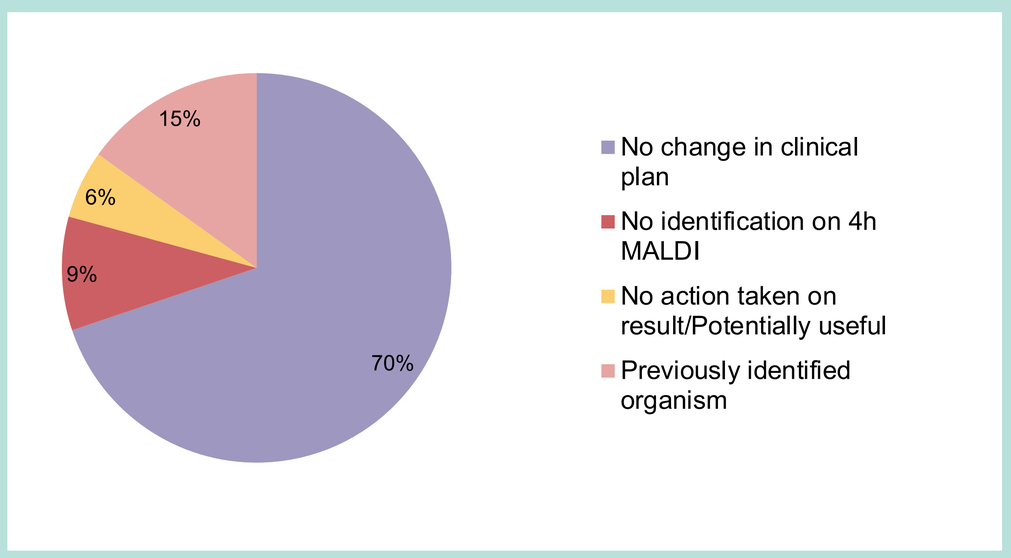

Figure 2: The reasons that 4-hour MALDI-TOF was not deemed clinically useful in 52 out of 88 positive cultures.

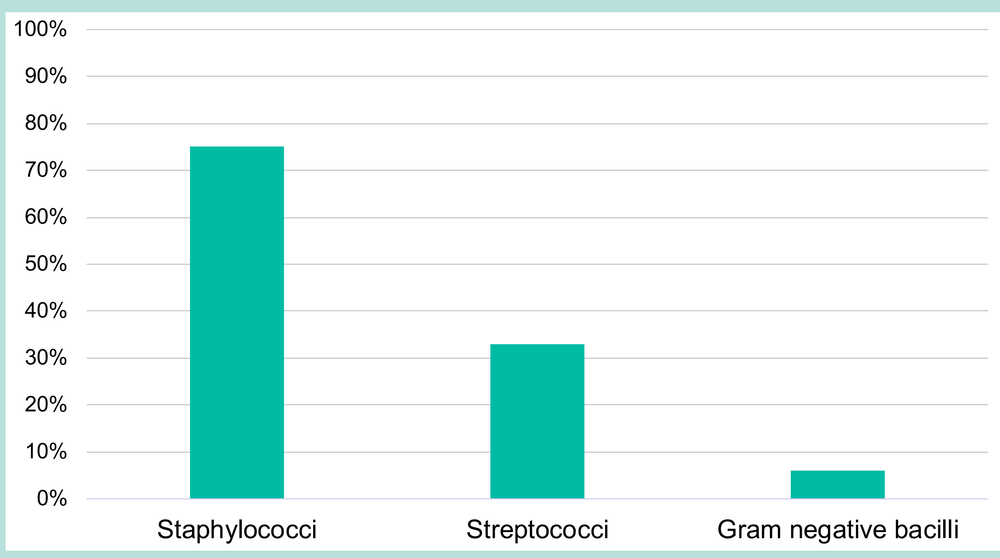

Figure 3: The proportion of blood cultures in which 4-hour MALDI was clinically useful, categorized into groups based on Gram stain appearance.

CASE EXAMPLES

Case example 1:

84F presented following a fall with a history of increasing shortness of breath. Clinically in fluid overload on arrival.
Patient became febrile so treated with co-amoxiclav for possible pneumonia.

Blood cultures: Gram positive cocci ?staphylococci
4h MALDI: *Staphylococcus aureus*

Antibiotics changed from co-amoxiclav to flucloxacillin.
Team advised to get echocardiogram and perform surveillance blood cultures.

Case example 2:

87F admitted with confusion and fevers.
History of penicillin allergy.
Initially treated with levofloxacin for possible pneumonia.

Blood culture: Gram positive cocci ?streptococci
4h MALDI: *Streptococcus pyogenes*

Patient reviewed and found to have hot, swollen right leg.
Antibiotics changed from levofloxacin to vancomycin.
Patient moved into side room for infection control.

Case example 3:

87M presented with lethargy and fever. Long-term catheter in situ.
Recent admission with treatment for UTI.
Treated with ertapenem for catheter-related UTI.

Blood culture: Gram negative bacillus
Catheter urine: Pseudomonas aeruginosa (cipro S; pip/taz I)
4h MALDI result: Pseudomonas aeruginosa

Patient changed from ertapenem to ciprofloxacin.

CONCLUSIONS

This analysis shows that early MALDI-TOF identification of bacteria is clinically useful in real-world practice.

The highest clinical utility came with Staphylococci, generally by allowing the earlier diagnosis of *Staphylococcus aureus* bacteraemia and the earlier determination of positive cultures being of doubtful clinical significance (in the case of most coagulase-negative Staphylococci).

There was far lower clinical utility with Gram negative bacilli, as most changes in treatment required results of antimicrobial susceptibility testing, rather than just microbiological diagnosis. However there were cases in which early identification did lead to a change in antimicrobials (e.g. early identification of *Pseudomonas aeruginosa* bacteraemia).

Overall early MALDI-TOF identification allows for successful triage and demand management within a busy clinical liaison service.

These results justify the continued use of this standard operating procedure and also allow prioritisation of workflow (i.e. towards Gram positive cocci rather than Gram negative bacilli) for days when resources are limited.

REFERENCES

1. French K, Evans J, Tanner H, Gossain S, Hussain A. The clinical impact of rapid, direct MALDI-TOF identification of bacteria from positive blood cultures. Plos One. 2016; 11(12).
2. Tanner H, Evans J T, Gossain S, Hussain A. Evaluation of three sample preparation methods for the direct identification of bacteria in positive blood cultures by MALDI-TOF. BMC Res Notes. 2017; 10:48.