

# Impact of Rapid Organism Identification via Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Combined with Antimicrobial Stewardship Team Intervention in Adult Patients With Bacteremia and Candidemia

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## Background:

- Bloodstream infections (BSI) are still associated with high morbidity/mortality
- Timely pathogen identification is crucial for optimal antimicrobial therapy and enables early streamlining (targeted, narrow-spectrum treatment)
- MALDI-TOF accurately identifies most bacterial and yeast species. In addition, time to organism identification can be decreased by 1.2-1.5 days compared to conventional methods.
- Antimicrobial stewardship teams (AST) providing real-time review and intervention can improve patient outcome compared to reporting of microbiology results alone.
- **Study objective:** to assess the impact of rapid pathogen identification with MALDI-TOF combined with AST intervention on outcomes in patients with BSI.

## Methods:

- Single-center, pre-post, quasi-experimental study at the University of Michigan Hospitals and Health System.
- Inclusion criteria:
  - Intervention group: >18a and BSI with organism identified via MALDI-TOF between 01.09 and 30.11.2012
  - Control group: >18a; BSI with organism identified via conventional methods between 01.09 and 30.11.2011
- Exclusion criteria : Patient transferred from outside hospital with active BSI ; BSI with organisms not validated for identification by MALDI-TOF (Mycobacteria, Nocardia, anaerobic organisms, molds).
- Microbiology workflow:
  - Both arms: reporting of Gram stain between 6:00 AM and 11:30 PM; Resistance testing with VITEK-2, Etest, disk diffusion or broth microdilution
  - Control: conventional identification between 6:00 AM and 11:30 PM (mainly VITEK-2)
  - Intervention: positive blood cultures were subcultured to solid media and incubated overnight; MALDI-TOF identification
- AST Intervention :
  - Intervention : real-time electronic notification between 6:00 AM and 11:30 PM in addition to 24 hour email notification. Evidence- based antibiotic recommendations at time of Gram stain, organism identification, and resistance testing results. Review of medical records
  - Control : real-time intervention only for patients with yeast on Gram stain (7:00 AM to 5:00 PM, Monday to Friday) ; reviewed patients on restricted antibiotics and gave advice.
- **Clinical outcomes:** 30-day all-cause mortality, ICU and hospital length of stay following BSI, microbiologic clearance, 30-day readmission for recurrent BSI with same organism ; CNS and other skin flora deemed to be a contaminant were excluded from clinical outcomes analysis.
- **Microbiologic outcomes :** time to effective and to optimal antimicrobial therapy

- **AST outcome** : recommendations, acceptance rate, timing of intervention in relation to Gram stain, identification and resistance testing.
- Statistics:
  - Kaplan-Meier survival analysis with log-rank test
  - Stratified analysis for gram-positive, yeast and gram- negative organisms
  - Unconditional logistic regression analysis to evaluate for factors associated with mortality.

## Results:

- Figure 1: 256 vs. 245 BSI in final clinical outcome analysis
- Table 1 (baseline characteristics): control group older (59 vs. 56a), less often chemotherapy (15 vs. 22%) and endocarditis (3.5 vs. 7.3%)
- Table 2 (microbiologic characteristics) : control group with less MRSA (3.7 vs. 9.7%) ; 50% gram positive organisms, 20% polymicrobial and 7% yeast.
- Figure 2 : intervention group with shorter time to organism identification (56 vs 84 h) AND time to resistance testing results (77 vs. 87 h)
- Figure and Table 3 (clinical outcomes) : intervention group with reduced 30-day all-cause mortality (13 vs. 20%), length of stay in ICU (8 vs. 15 d) and rate of BSI recurrence with same organism (2 vs. 6%).
- Microbiologic outcomes : intervention group with shorter time to effective (20 vs. 30 h) and optimal therapy (47 vs. 90 h)
- No effect on time to microbiologic clearance!
- Stratified analysis : improved survival mainly in gram-negative BSI (8 vs. 25%).
- Table 5 (multivariate analysis) : malignancy, bone marrow transplantation, ICU status, older age associated with mortality. Trend between improved survival and accepted ATS intervention.
- AST :
  - 90% of recommendations were accepted
  - Interventions : 38% after reporting of resistance testing results (mainly narrowing cover), 36% at organism identification (mainly discontinuing unnecessary tx), and 26% at time of Gram stain (mainly broadening/initiating cover)
  - Spectrum broadening necessary only in 9 patients

## Discussion:

- Largest study to evaluate clinical impact of MALDI-TOF combined with AST
- Combination of AST **AND** early organism identification resulted in reduced mortality
- Limitations:
  - Quasi-experimental study (no randomization)
  - Not possible to dissect effects of ATS vs. MALDI-TOF (are both necessary ?)
  - Impact of AST interventions greatest after reporting of Gram stain – hence MALDI-TOF impact questionable ;
  - Extensive manpower required – 8:00 AM to 5:00 PM equivalent ?
  - Impact of MALDI-TOF identification directly from blood cultures ?

**Conclusion** : AST have significant impact on patient outcomes and appropriate utilization of antimicrobial therapy. The role of rapid identification with MALDI-TOF remains to be determined.