MALDI-TOF alone *versus* MALDI-TOF combined with real-time antimicrobial stewardship intervention on time to optimal antimicrobial therapy in patients with positive blood cultures

Maya Beganovic, Pharm.D., MPH,[1] Sarah M. Wieczorkiewicz, Pharm.D., BCPS (AQ-ID)[1]
[1]Department of Pharmacy, Advocate Lutheran General Hospital/Advocate Children's Hospital Park Ridge

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

Advocate Lutheran General Hospital

Inspiring medicine. Changing lives.

BACKGROUND

- Bloodstream infections (BSI) associated with high rates of morbidity and mortality
- Delays in antimicrobial therapy result in poor clinical outcomes
- Traditional organism identification methods are time-consuming

Matrix Assisted Laser Desorption Ionization- Time of Flight (MALDI-TOF)

- Utilizes mass spectrometry to rapidly and accurately identify isolated organisms
- Reduces time to identification by 1.2-1.5 days
- Improved clinical and financial outcomes when combined with antimicrobial stewardship interventions

METHODS

- Single-center, pre-post quasi-experimental study
- Included adult and pediatric patients with positive blood culture(S)
- Excluded patients transferred to ALGH with active BSI, and patients that expired prior to culture result

Primary objective

- Time to optimal antimicrobial therapy (TTOT)

Secondary objectives

- Time to effective antimicrobial therapy (TTET)
- In-hospital all-cause mortality
- Hospital and ICU length of stay (LOS)
- Time to microbiologic clearance
- Recurrent bacteremia within 30 days of antimicrobial discontinuation
- Antimicrobial length of therapy

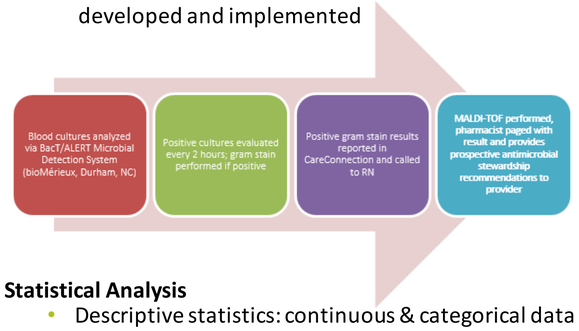
Workflow Prior to Intervention

- No guidelines for positive blood culture management

METHODS

Workflow Post-Intervention

- Guidelines for positive blood culture management developed and implemented



Statistical Analysis

- Descriptive statistics: continuous & categorical data
- Two-tailed *p*-value of <0.05 considered statistically significant in all analyses
- Sample size of 40/group to achieve 80% power

RESULTS

Table 1: Baseline Demographics

Demographic	Pre-Intervention (n=116)	Intervention (n=123)	*p*-value
Age, y, mean ± SD	58.33 ± 28.3	63.5 ± 23.4	0.219
Adults, y, mean ± SD (n)	68.43 ± 17.8 (97)	68.59 ± 16.4 (113)	0.946
Pediatrics, y, mean ± SD (n)	6.78 ± 7.5 (19)	6 ± 6.5 (10)	0.783
Gender [Female, n (%)]	63 (54.3)	66 (53.7)	0.920
Clinical Status, n (%)			
General medicine, n (%)	77 (66.3)	82 (66.7)	0.962
Intensive Care Unit, n (%)	39 (33.6)	41 (33.3)	0.962
Hospice or palliative care, n (%)	12 (10.3)	22 (17.9)	0.095
PITT Bacteremia Score, mean ± SD	1.91 ± 1.96	2.39 ± 2.44	0.096
Hemodynamic instability requiring vasopressors, n (%)	20 (17.2)	19 (15.4)	0.708
Charlson Comorbidity Index	4.81 ±3.76	**5.15**± 3.47	0.468
Number of risk factors for MDRO*, n (%)			
0	23 (19.8)	27 (21.9)	0.558
1	29 (25)	39 (31.7)	
2	29 (25)	29 (23.6)	
3	21 (18.1)	20 (16.3)	
4	10 (8.6)	7 (5.7)	
5	4 (3.4)	1 (0.8)	

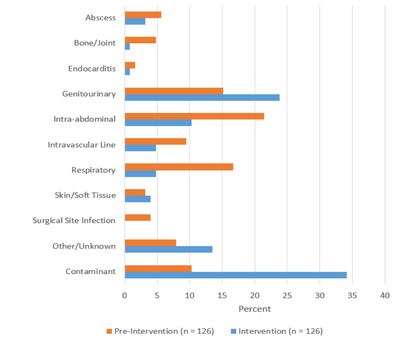
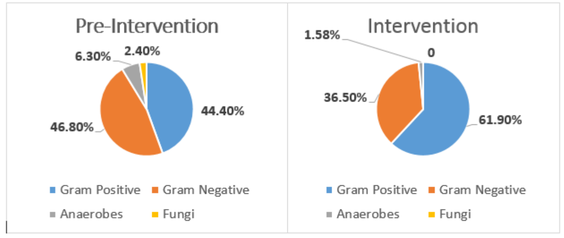


Figure 1: Source of Positive Blood Culture

RESULTS



Organism	Pre-Intervention n = 126	Intervention n = 126	*p*-value
Gram Positive, n (%)	56 (44.4)	78 (61.9)	0.005
Gram positive Infection, n (%)	43 (76.8)	35 (44.9)	0.340
Gram positive Contaminant, n (%)	13 (23.2)	43 (55.1)	<0.001
Gram Negative, n (%)	59 (46.8)	46 (36.5)	0.097

Figure 2: Organism Distribution

Table 2: Primary Endpoint Outcomes

Outcome	Pre-Intervention (n = 126)	Intervention (n = 126)	*p*-value
Overall TTOT, h ± SD	75.17 ± 59.5	43.06 ± 35.3	<0.001
TTOT Gram +, h ± SD (Infection, n)	64.04 ± 63.3 (43)	41.61 ± 44.9 (35)	0.082
TTOT Gram +, h ± SD (Contaminant, n)	48.21 ± 37.1 (13)	11.75 ± 23.7 (43)	<0.001
TTOT Gram -, h ± SD (n)	71.83 ± 61.5 (59)	35.98 ± 30.9 (46)	<0.001

Table 3: Secondary Endpoint Outcomes

Outcome	Pre-Intervention	Intervention	p-value
Time to effective therapy, h, ± SD (n)	16.8 ± 19.59 (113)	12.15 ± 17.2 (83)	0.082
Clinical Outcomes			
In-hospital all-cause mortality, n (%)	12/116 (10.3)	15/123 (12.2)	0.805
Gram Positive Infection, n (%)	3/116 (2.6)	8/123 (6.5)	0.256
Gram Negative Infection, n (%)	6/116 (5.2)	7/123 (5.7)	0.860
Overall time to microbiologic clearance, h, ± SD	55.07 ± 45.6	42.49 ± 46.2	0.059
Gram Positive Infection, h, ± SD	58.49 ± 56.1	53.94 ± 62.8	0.595
Gram Negative Infection, h, ± SD	51.13 ± 31.2	34.51 ± 26.5	<0.001
Overall hospital LOS, d, ± SD	15.03 ± 22.7	9.02 ± 7.3	0.021
Gram Positive Infection, d, ± SD	14.64 ± 10.5	10.31 ± 7.89	0.002
Gram Negative Infection, d, ± SD	15.40 ± 30.1	7.90 ± 6.7	0.027
Overall ICU LOS, d, ± SD	4.30 ± 14.0	1.22 ± 3.8	0.053
Gram Positive Infection, d, ± SD	1.43 ± 4.2	1.32 ± 3.5	0.846
Gram Negative Infection, d, ± SD	5.55 ± 18.3	1.19 ± 4.13	0.035
Overall recurrence of same bacteremia, n (%)	4 (3.5)	1 (1.2)	0.255
Gram Positive Infection, n (%)	0	0	---
Gram Negative Infection, n (%)	4 (3.5)	1 (1.2)	0.255
Overall length of antimicrobial therapy, d, ± SD	18.57 ± 11.95	15.93 ± 11.11	0.117
Gram Positive Infection, d, ± SD	24.30 ± 16.0	18.97 ± 14.8	0.018
Gram Negative Infection, d, ± SD	14.25 ± 5.5	13.20 ± 4.5	0.156

RESULTS

Table 4: Financial Outcomes

	Pre-Intervention	Intervention	Difference	*p* value
Average LOS	15.03	9.02	- 6.01	0.021
Average Direct Costs	$28,677	$15,784	- $12,893	0.010
			Projected annual cost savings	$6,291,784

CONCLUSIONS

- Optimal therapy approximately 1.3 days earlier in the intervention group
- TTOT for Gram-positive infections not statistically significant however, trend toward faster optimization
- Empiric antimicrobials discontinued faster for contaminated cultures
- Rapid de-escalation for Gram-negative infections with reduction in anti-pseudomonal agents
- Reduced LOS, faster microbiologic clearance, and reduced antimicrobial exposure
- Healthcare dollars saved may help to justify pharmacist FTE to sustain intervention

Future Directions

- Evaluate the combination of rapid identification methods with genetic testing for resistance
- Expand program to other sites within our 12-hospital system

LIMITATIONS

- Small sample size may have contributed to lack of difference in some of the secondary outcomes including mortality
- Not controlled for organism distribution
- Labor-intensive for one person
- Narrowing therapy challenging without susceptibility reports
  - Concern for MDROs
  - Unable to identify genetic mutations

ACKNOWLEDGEMENTS

The authors would like to acknowledge Dr. Mike Costello, Technical Director of Microbiology at ACL Laboratories and Ina Zamfirova and Sarah Kozmic, Research Coordinators, Patient Centered Outcomes Research at the Russell Institute for Research and Innovation for their assistance with this project.