Impact of Multiplex PCR, MALDI-TOF, and Antimicrobial Stewardship on Antibiotic Use in a Pediatric Hospital

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Background

- ❑ Antibiotic resistance is a major public health threat
- ❑ Antimicrobial stewardship programs (ASPs) aim to optimize antibiotic use to limit resistance
- ❑ New rapid diagnostic techniques decrease time to organism identification
- ❑ Early pathogen identification ideally ➡ faster initiation of optimal antimicrobial therapy
- ❑ Limited data on impact of rapid diagnostics for:
  - Pediatric patients
  - Decreasing organism-drug mismatches
  - Decreasing unnecessary antimicrobial use

Study Objectives

For patients with positive blood cultures, determine impact of rapid diagnostics and ASP interventions on:

Aim #1	Time to initiation of optimal antimicrobial therapy (IDEAL and ACTUAL)
Aim #2	Time to initiation of effective antimicrobial therapy
Aim #3	Clinical outcomes

Methods

Study Design: Single-center, retrospective pre-post quasi-experimental observational study comparing antibiotic use for patients ≤21 years at Lurie Children's Hospital with positive blood cultures collected in 2012 and 2015. Includes gram-positive, gram-negative and fungal organisms

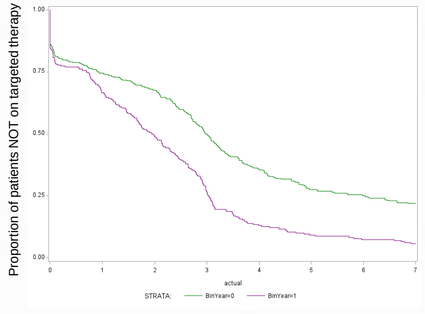
Exclusion Criteria: 1st positive culture drawn at outside hospital, death within 48 hours of culture collection, or blood cultures grew >1 organism within 7 days

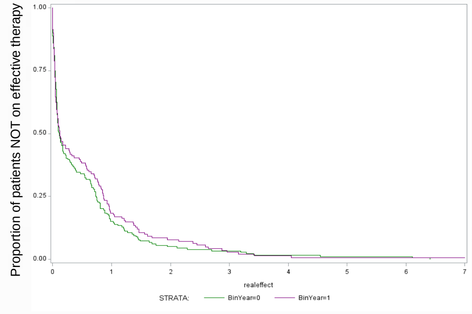
Data Collection: Demographic, clinical, pharmacologic, and microbiologic data collected retrospectively via patient chart reviews. Data reviewed by infectious diseases investigators to evaluate antibiotic decision-making.

Baseline Demographic	2012 N = 286 (%)	2015 N = 231 (%)	p-value*
Age	5.26	5.97	.176
Race:			.034
White	122 (42.7)	86 (37.2)	
African-American	55 (19.2)	35 (15.2)	
Asian	17 (5.9)	8 (3.5)	
Other or Unknown	92 (32.2)	102 (44.2)	
Gender - Male	152 (53.1)	136 (58.9)	.192
Congenital/Current Heart Disease - Yes	53 (18.5)	32 (13.9)	.154
Short gut syndrome - Yes	12 (4.2)	13 (5.6)	.451
Medically Complex -Yes	133 (46.5)	107 (46.3)	.967
Neonate <=2mo at time of Bcx - Yes	60 (21.0)	50 (21.6)	.854
Neutropenic with ANC <500 - Yes	55 (19.2)	40 (17.3)	.576
Immunocompromised- Yes	133 (46.5)	94 (40.7)	.186
Immune Status:			.211
Competent	153 (53.5)	137 (59.3)	
Hematologic Malignancy	53 (18.5)	33 (14.2)	
Non-Hematologic Malignancy	24 (8.4)	13 (5.6)	
SCT	20 (7.0)	19 (8.2)	
Solid Organ Transplant	18 (6.3)	8 (3.5)	
Other	18 (6.3)	21 (9.1)	
Central Line in Place at Time of Culture	172 (60.1)	119 (51.5)	.049
ID Officially Consulted-Yes	95 (33.2)	111 (48.1)	.001
Admission to ICU within 48hrs:			.280
No	167 (58.4)	141 (61.0)	
Yes	46 (16.1)	44 (18.0)	
Already in ICU	73 (25.5)	46 (19.9)	

Primary Outcomes	2012 N = 286	2015 N = 231	Mean Difference (95% CI)	p-value
Time to Organism ID (hours)	64.6	43.1	**21.5** (14.18, 28.8)	< .0001
Time to Optimal Therapy (days)	3.33	2.17	**1.163** (0.77, 1.56)	< .0001
Time to Effective Therapy (days)	0.53	0.61	**-0.08** (-0.29, 0.13)	.457

Graphs: Kaplan-Meier curves for time to optimal (left) and time effective therapy (right), with 2012 in green and 2015 in purple





Statistical Analysis

Chi-square, independent samples T-tests, and backward elimination stepwise multiple linear regression used for baseline demographics and clinical outcomes. Cox proportional hazards with backwards elimination and Kaplan Meier curves used for primary outcomes.

Clinical Outcomes Analysis	2012 N = 286	2015 N = 231	p-value*
Days of Hospitalization after +BCx	25.83	18.05	.014
Hours of Pressors for Bacteremia	15.595	4.484	.020
# of Pressors Used Within 7 Days	0.262	0.212	.427
# Days In ICU After +BCx	16.00	10.88	.087
Days Until Microbiologic Clearance	1.54	1.42	.258
C. difficile within 30days - Yes	18 (6.3)	16 (6.9)	.773
Unique # Abx Within 7 days	2.83	2.77	.641
Mortality within 30 days - Yes	11 (3.8)	14 (6.1)	.243
Recurrence within 30 days - Yes	9 (3.1)	4 (1.7)	.307
Clinically Worse within 24-72hrs - Yes	35 (12.2)	35 (15.2)	.336

Conclusions

Rapid diagnostics + ASP ➡ improved antibiotic decision-making in intervention period

- ❑ Earlier organism identification by mean of **21.5 hrs** (p=.000)
- ❑ Earlier initiation of optimal therapy by mean of **27.9 hrs** (p=.000)
- ❑ No difference in time to effective therapy (p = .457)

Intervention group's "hazard" of receiving optimal antibiotic therapy by 7 days is **1.74 times greater** than pre-intervention group (p <.0001)

1. Perez, K.K., et al., *Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs.* Arch Pathol Lab Med, 2013. **137**(9): p. 1247-54.
2. Huang, A.M., et al., *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.* Clin Infect Dis, 2013. **57**(9): p. 1237-45.
3. Perez, K.K., et al., *Integrating rapid diagnostics and antimicrobial stewardship improves outcomes in patients with antimicrobial-resistant Gram-negative bacteremia.* J Infect, 2014. **69**(3): p. 216-25.
4. Nagel, J.L., et al., *Impact of antimicrobial stewardship intervention on coagulase-negative Staphylococcus blood cultures in conjunction with rapid diagnostic testing.* J Clin Microbiol, 2014. **52**(8): p. 2849-54.