Clinical Impact of Expedited Pathogen Identification and Susceptibility Testing for Gram-negative Bacteremia and Candidemia Using the Accelerate Pheno™ System

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ABSTRACT

Background:

Inappropriate initial antibiotic therapy (IIAT) for sepsis increases mortality. Fast diagnostic tests providing earlier identification (ID) of pathogens and antimicrobial susceptibility testing (AST) have the potential to improve mortality and antimicrobial stewardship. The Accelerate Pheno™ system (AXDX) is a newly FDA cleared fast diagnostic testing system that provides ID and AST for Gram-positive and Gram-negative bacteria (GNB) and ID for Candida bloodstream isolates.

Methods:

From 4/14/2016-6/1/2017, blood cultures from unique patients in the ED or medical ICU at Barnes-Jewish Hospital signaling positive and Gram-stain positive for GNB or yeast were eligible for inclusion. Standard-of-care (SOC) diagnostics were conducted in parallel with AXDX, though AXDX could be delayed up to 8 hours depending on research technician availability. Differences in time to ID and AST between SOC and AXDX were determined. Clinical outcomes included appropriateness of initial empiric antimicrobial therapy, potential for early antimicrobial de-escalation with AXDX, and mortality.

Results:

Of 429 screened blood cultures, 153 met inclusion criteria; 125 had organisms that were on-panel for AXDX, 110 GNB and 15 *C. glabrata* or *C. albicans*. For GNB, mean time from blood culture positivity to ID and AST using SOC was 22.4 and 53.5 hours, respectively, and 1.4 and 12.7 hours using AXDX (from time AXDX started). For *Candida* spp., mean time to ID was 17.1 hours faster for AXDX. Antimicrobial de-escalation or a change to appropriate antimicrobials was possible based on AXDX testing in 70.6% of patients. A total of 32 (25.6%) patients received IIAT. In-hospital mortality was higher (45.2%) in the IIAT group than in those receiving appropriate initial antibiotics (11.8%), p<0.001.

Conclusions:

The Accelerate Pheno™ system is a novel fast diagnostic that significantly reduces the time to ID and AST for GNB and ID of *Candida* spp. bloodstream infections, with the potential to impact clinical outcomes. Prospective clinical trials are needed to evaluate the impact of this new system on clinical outcomes and antimicrobial stewardship.

INTRODUCTION

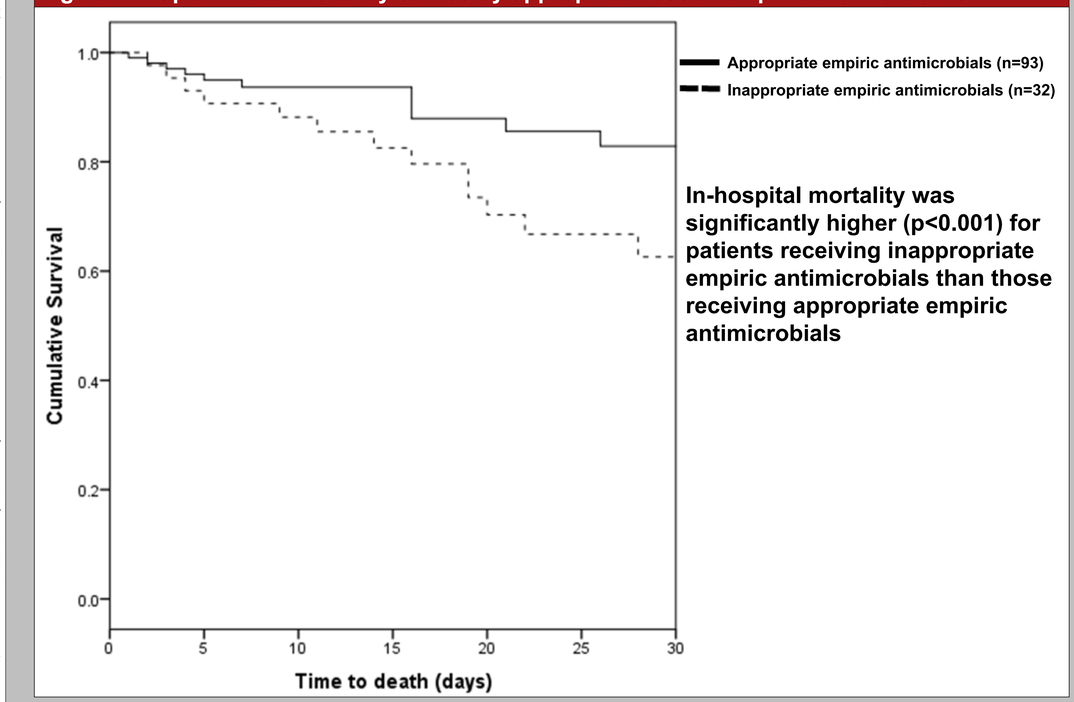
- **Delays in appropriate antimicrobial therapy for sepsis lead to poor clinical outcomes**
- **Earlier results of identification and antimicrobial susceptibility testing has the potential to reduce time to appropriate antimicrobials and improve antimicrobial stewardship**

METHODS

- **Design: Prospective cohort from Barnes-Jewish Hospital, a 1250 bed academic medical center in St. Louis, MO**
- **Study period: 4/14/2016-6/1/2017**
- **Inclusion criteria: ED or ICU patient with a blood culture signaling positive and Gram stain positive for GNB or yeast**
- **Exclusion criteria: age ≤18. Blood cultures meeting above criteria but signaling positive >8 hours before a research technologist was available**
- **Endpoints: time to ID and AST, in-hospital mortality, length of hospital and ICU stay, duration of mechanical ventilation**
- **Statistical methods:**
- **Univariate analysis was performed by chi-square or Fischer's exact test where appropriate for categorical values**
- **Student's t-test or Mann-Whitney U test was used where appropriate for continuous variables**
- **Kaplan-Meier analysis with log-rank test was used for mortality**

RESULTS

Figure 1: Kaplan-Meier mortality curves by appropriateness of empiric antimicrobials



In-hospital mortality was significantly higher (p<0.001) for patients receiving inappropriate empiric antimicrobials than those receiving appropriate empiric antimicrobials

Figure 2: Hospital length of stay by appropriateness of empiric antimicrobials

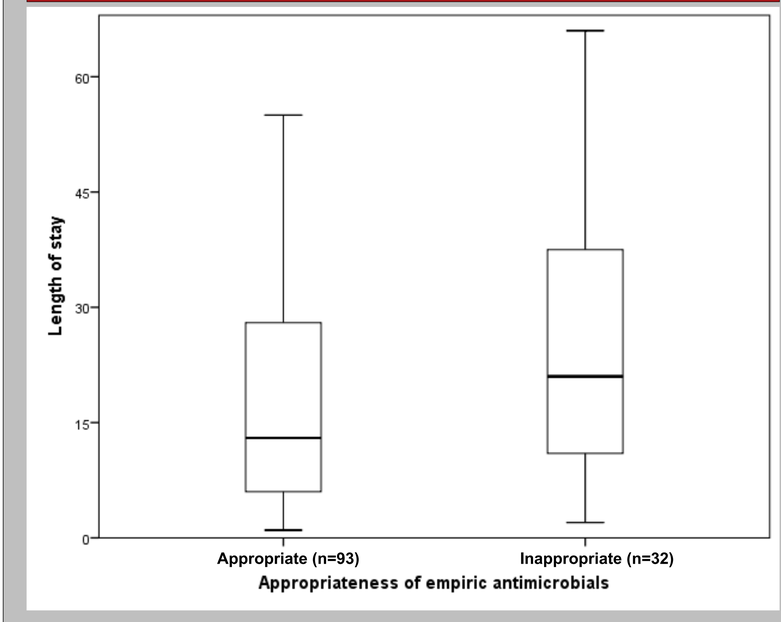


Table 1: Baseline characteristics of the patients with on-panel organisms

	Received appropriate antimicrobials (n=93)	Received inappropriate antimicrobials (n=32)	p-value
Age	62 ± 14.2	59.3 ± 13.8	0.34
Underlying malignancy	45 (48.4)	18 (56.3)	0.44
Coronary artery disease	25 (26.9)	7 (21.9)	0.58
Diabetes mellitus	25 (26.9)	10 (31.3)	0.64
Renal replacement therapy	12 (12.9)	6 (18.8)	0.42
Hospitalized in last 6 months	55 (59.1)	23 (71.9)	0.2
APACHE II score	17.1 ± 5.1	21.3 ± 5.3	<0.001
Recent mechanical ventilation	16 (20.0)	16 (35.6)	0.06
Use of vasopressors during hospitalization	33 (35.5)	18 (56.3)	0.04
Gram-negative isolate	89 (95.7)	21 (65.6)	<0.001
Yeast isolate	4 (4.3)	11 (34.4)	<0.001
Polymicrobial culture	10 (10.8)	3 (9.4)	1
Discharge home	57 (69.5)	9 (50.0)	0.19
LOS	12 [5.5-28]	21 [9-37]	0.027
ICU LOS	0 [0-4]	4 [0-18]	0.010
In-hospital mortality	11 (11.8)	14 (45.2)	<0.001
Duration of mechanical ventilation	0 [0-2.5]	1 [0-7]	0.004

APACHE: acute physiology and chronic health evaluation; ICU: intensive care unit; LOS: length of stay.

Table 2: Timing of ID and AST for SOC and AXDX for all organisms

	SOC (hours)	AXDX (hours)
Time from blood culture positivity to AXDX initiation	N/A	8.7 ± 2.86
Time from blood culture positivity to ID[a]	22.4 ± 12.3	10.0 ± 2.9
Time from AXDX initiation to ID[b]	N/A	1.4 ± 0.02
Time from blood culture positivity to AST[a]	53.5 ± 8.8	20.1 ± 15
Time from AXDX initiation to AST[a]	N/A	12.7 ± 17.4

[a]For organisms not on panel, time to ID and AST for SOC were substituted.
[b]Only calculated for on panel organisms.
All times reported as ± one standard deviation.
AST: antimicrobial susceptibility testing; AXDX: Accelerate Pheno™ System; ID: identification; SOC: standard of care.

CONCLUSIONS

- **The Accelerate Pheno™ system is a novel fast diagnostic that significantly reduces the time to ID and AST for GNB and ID of *Candida* spp. bloodstream infections, with the potential to impact clinical outcomes.**
- **Prospective clinical trials are needed to evaluate the impact of this new system on clinical outcomes and antimicrobial stewardship.**

ACKNOWLEDGMENTS

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