Impact of rapid identification and phenotypic results on outcomes in patients with Gram-negative bacteremia

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Background

- Bloodstream infections are associated with significant morbidity and healthcare expenditures.[1,2]
- Nearly one-half of all cases are caused by Gram-negative bacilli, and their management is a growing challenge due to increasing antimicrobial resistance.[3]
- A critical determinant of clinical outcome involves timely and effective antimicrobial therapy.
  - Risk of mortality increases 7.6% with each hour delaying administration in septic shock.[4]
  - 1 in 5 patients receive ineffective empiric therapy.[5]
  - Ineffective empiric therapy is independently associated with increased risk of mortality, regardless of the presence or absence of resistance, sepsis, or septic shock.[5]
- Broad-spectrum antibiotics, such as antipseudomonal β-lactams, improve the odds of adequate coverage but carry the risk of causing collateral harm.
  - Empiric use for >48 hours is an independent risk factor for new *Clostridioides difficile* infection (CDI).[6]
  - Risk of emerging antimicrobial resistance increases 4% with each additional day of exposure.[7]
- Rapid diagnostic tests enable earlier organism identification, clinical intervention, and are associated with improved clinical outcomes and reduced hospital costs compared to conventional methods.[8,9]
- Accelerate Pheno™ is a new system that provides both organism identification and antimicrobial susceptibility results within 8 hours.

Objective

To evaluate the impact of Accelerate Pheno™ on clinical, economic, and antimicrobial stewardship outcomes in patients with Gram-negative bacteremia.

Methods

- IRB-approved single center, pre-post quasi-experimental study
- Retrospective chart review of data from patient medical records
  - November 2nd–January 31st 2019–2020 (historical group)
  - November 2nd–February 27th 2020–2021 (intervention group)
- Inclusion Criteria
  - Admitted inpatients ≥18 years of age
  - Positive blood culture with *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., *Citrobacter* spp., *Serratia marcescens*, *Pseudomonas aeruginosa,* or *Acinetobacter baumannii*
- Exclusion Criteria
  - Pregnant
  - Positive blood culture with the same organism and source within 7 days
  - Positive blood culture with >1 organism
  - Palliative care, hospice care, or death before susceptibilities result

Outcomes

Primary

- Time to targeted antibiotic therapy (TTT)

Secondary

- Time to first intervention following Gram stain (TFI-GS), organism identification (TFI-ID), and antimicrobial susceptibility test results (TFI-AST)
- Days of antipseudomonal therapy (Antipseudomonal DOT)
- Antibiotic intensity score at 96 hours following Gram stain result (AIS)
- Hospital and ICU length of stay (LOS, ICU-LOS)
- Hospital-acquired CDI
- In-hospital all-cause mortality
- Hospital costs for antibiotics and microbiology tests

Statistical Analysis

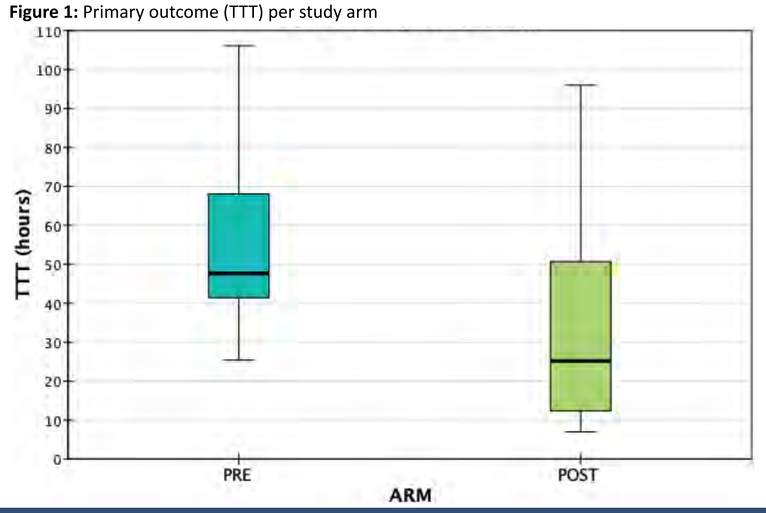
With alpha set *a priori* at 0.05, achieving 80% power to detect a 10-hour decrease in time to targeted therapy required a sample size of 132 patients per study arm.[10] Statistical testing was performed with the Mann-Whitney U test for all nonparametric continuous data and with the Chi-square or Fisher's exact test for all nominal data.

Results

Table 1: Baseline Characteristics

Characteristic	PRE (n = 64)	POST (n = 54)	*P* value
Age, median years (IQR)	73 (65–79)	73 (63–80)	0.87
Male sex, n (%)	35 (55)	31 (57)	0.77
Hospitalization in prior 30 days, n (%)	12 (19)	11 (20)	0.83
Pitt bacteremia score, median (IQR)	1 (0–2)	2 (1–3)	< 0.05
ESBL isolate, n (%)	3 (5)	8 (15)	0.06
ID consulted, n (%)	51 (80)	42 (78)	0.8
Pharmacist intervention, n (%)	30 (47)	33 (61)	0.12
Recommendation rejected, n (%)	1 (3)	6 (18)	0.06

Figure 1: Primary outcome (TTT) per study arm



Results (continued)

Table 2: Primary and Secondary Outcomes

Outcome	PRE (n = 64)	POST (n = 54)	*P* value
TTT, median h (IQR)	48 (41–69)	25 (12–51)	< 0.05
TFI-GS, median h (IQR)	0.8 (0.2–2.0)	0.7 (0.2–1.6)	0.86
TFI-ID, median h (IQR)	3.1 (0.5–6.0)	1.3 (0.8–12.3)	0.68
TFI-AST, median h (IQR)	4.8 (2.8–27.1)	8.1 (1.8–16.0)	0.19
Antipseudomonal DOT, median days (IQR)	2 (0–3)	1 (0–4)	0.84
AIS, median (IQR)	5 (3–8)	5 (3–8)	0.81
Hospital LOS, median days (IQR)	4 (3–6)	5 (3–7)	0.26
ICU LOS, median days (IQR)	3 (2–4)	3 (1–5)	0.82
Hospital-acquired CDI, n (%)	1 (2)	2 (4)	0.6
In-hospital all-cause mortality, n (%)	4 (6)	5 (9)	0.73
Antibiotic costs, median (IQR)	$86 (66–143)	$108 (59–213)	0.4
Microbiology costs†, median	$103	$135	< 0.05

† Values are adjusted to reflect the relative cost difference rather than actual costs

Discussion

- Higher Pitt bacteremia score and numerically higher incidence of ESBL infection in the post-implementation group may have impacted secondary outcome results, but the study was not powered to detect a difference.
- Limitations of this study include the small sample size between groups, microbiology laboratory and pharmacy workflow causing delayed reporting of and response to overnight results, and unknown COVID-19 status.

Conclusions

Time to targeted therapy was reduced with Accelerate Pheno™, but the addition of intentional measures for stewardship intervention is needed to take full advantage of the system's capabilities.

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