



Abstract

Background: Centralization of laboratory testing has resulted in a system where limited diagnostic testing occurs onsite where the patient is being treated and most diagnostic testing is performed at a centralized laboratory. Positive blood cultures collected and incubated at the satellite laboratory receive a Gram stain and rapid identification via genotypic testing before transport to the centralized laboratory for identification and AST. This transportation step can result in a delay of actionable results that may impact clinical decisions, including antimicrobial therapy adjustments. We analyzed the theoretical impact of decentralization via rapid phenotypic AST.

Materials/Methods: This multicenter retrospective cohort study included adult patients with GN-BSI across three hospitals within the same health system. All three hospitals completed Gram stain and BioFire RDT on-site; standard-of-care (SOC) AST by MicroScan was performed at the centralized laboratory. Turnaround times were measured from index blood-culture collection to Gram stain, RDT, SOC AST, and theoretical Q-linea ASTar. We analyzed the data to determine accuracy and time to results as well as the potential clinical impact by using the DOOR-MAT analysis, defined by mean score (+ standard deviation) and proportion who received desirable therapy.

Results: We enrolled 118 patients with Gram-negative BSIs. The comparison SOC AST showed ASTar having 96.0% essential agreement, 93.7% categorical agreement and 1.6% very major errors. The average time from blood culture collection to Gram stain was 16.6 + 14.8 hours, with SOC AST being 67.7 + 17.6 hours and the theoretical time to ASTar with a decentralized approach was 23.4 + 17.9 hours. DOOR-MAT was determined for 85 patients with Enterobacteriales BSI. Mean DOOR-MAT scores increased from 55 (+33) with empiric therapy to 86 (+25) with targeted therapy, $p < 0.001$. The proportion of patients with desirable antimicrobial therapy increased from 27% (n = 23) to 76% (n = 65) with targeted therapy, $p < 0.001$.

Conclusions: Rapid phenotypic AST with Q-linea ASTar can decrease time to results with a decentralized approach and can increase appropriate use of antimicrobial therapy.

Background

- Gram-negative bloodstream infections (BSI) remain a major cause of morbidity and mortality, necessitating timely optimization of antimicrobial therapy.
- Many large hospital systems have centralized diagnostic testing such that minimal microbiological testing occurs at the local level. In the University of Maryland Medical System, blood cultures are incubated at the satellite laboratory and, if positive, a Gram stain and rapid molecular test are performed prior to sending the bottle(s) to the University of Maryland Medical Center microbiology laboratory.
- Hospitals increasingly rely on rapid diagnostic platforms—such as BioFire BCID2, MicroScan AST, and QLinea ASTar—to shorten time to organism identification and susceptibility results.
- Transport of blood culture bottles to the central laboratory result in delayed culturing, which ultimately can result in a delay in final organism identification and AST results.
- Rapid antimicrobial susceptibility testing (rAST) methods, such as the QLinea ASTar present an opportunity to decrease the time not only to AST results but also to the administration of appropriate antimicrobial therapies.
- This study examines the comparability between SOC AST testing at the centralized laboratory to results produced by the QLinea ASTar rAST instrument as well as the theoretical impact of ASTar rAST on desirable antimicrobial therapy decisions through a DOOR-MAT analysis.
- Results will help determine if decentralized rAST can lead to improved patient outcomes for Gram negative BSI.

Methods

- Design:** Retrospective, multicenter observational review including adult inpatients with Gram-negative bacteremia across three University of Maryland Medical System hospitals in the state of Maryland (one centralized academic hospital, two decentralized community hospitals).
- Study Population:** Adults with positive blood cultures for Gram-negative organisms on-panel for Qlinea ASTar.
- Data Sources:** Electronic health record—extracted data for patient demographics, clinical care course, timestamps for index blood culture, Gram stain, BCID2 RDT, MicroScan AST, and antibiotic therapy changes.
- Discarded blood samples were prospectively collected and run on Qlinea ASTar.
- Discordant susceptibility results were run in triplicate utilizing broth microdilution. Modal values were considered the true result and used for adjudication.
- A representative sample of clinical cases (N = 50) of Enterobacteriales BSI were placed in a (Quatrics Provo, UT) survey with de-identified clinical case vignettes including BCID2 RDT and Qlinea ASTar AST asking providers antibiotic therapy choice based on the available data. Choices were then compared across a DOOR-MAT matrix for categorization and scoring (figure below)
- Outcome Measures:** Time to Gram stain, BCID2 RDT, MicroScan AST, and theoretical time to ASTar results, time to antibiotic changes, categorical and essential agreements between ASTar results and MicroScan AST results, DOOR-MAT categories and average scores four stages of antibiotic therapy decisions: empiric, BCID2 RDT, MicroScan AST, and theoretical Qlinea ASTar AST.
- Analytical Approach:** Descriptive statistics of time-to-event metrics, antibiotic stewardship actions, and resistance phenotype distributions across hospital sites and infection sources.
- DOOR-MAT Matrix and Scoring System**

Empiric or Targeted Antibiotic	AST Susceptibility Profile							DOOR MAT Scoring System
	S-S-S-S	R-S-S-S	R-R-S-S	R-R-R-S-S	R-R-R-R-S	R-R-R-R-R	R-R-R-R-R	
Cefazolin, Ampicillin/Sulbactam	S	R	R	R	R	R	R	100 Desirable treatment
Ceftriaxone	S	S	R	R	R	R	R	50 Potentially appropriate
Cefepime, Ceftazidime, Piperacillin/Tazobactam	S	S	S	R	R	R	R	50 Appropriate but broad
Meropenem, Ertapenem	S	S	S	S	R	R	R	25 Overtreatment
Ceftazidime/Avibactam, Meropenem/Vabroactam	S	S	S	S	S	S	R	0 Undertreatment

Results

Table 1. Demographics and Clinical Characteristics of Enrolled Patients

Variable	N = 118 (%)	Variable	N = 118 (%)	Variable	N = 118 (%)
Age: Mean (SD)	65.4 (16.0)	Severely immunocompromised	23 (19.7%)	ID consult at collection	56 (48.3%)
Age: Median [IQR]	68.5 [56.0, 76.8]	Sepsis (not shock)	40 (33.8%)	Septic shock	34 (29.1%)
Hospital		Previous MDR GNR (12 m)		Acuity Level	
UMMC	50 (42.4%)	Diagnostic Culture	6 (5.1%)	Medical Floor	38 (32%)
BWMC	39 (33.1%)	Surveillance Culture	1 (0.8%)	Intensive Care Unit	25 (21%)
SMC	29 (24.6%)			Emergency Department	24 (20%)
				Intermediate Care Unit	23 (19%)
				Trauma Center	8 (7%)

GNR = Gram-negative rod; MDR = Multidrug resistant; IQR = Interquartile range; SD = Standard deviation

Table 2. Organism Distribution and Susceptibility Testing Agreement Between MicroScan and ASTar Methods

Organism	N	CA	EA	mE	ME	VME
<i>Acinetobacter baumannii</i>	1	100	100	0	0	0
<i>Enterobacter cloacae</i> complex	9	95.31	94.53	0.78	3.91	0
<i>Escherichia coli</i>	59	93.81 (95.08)	96.61 (97.71)	3.9 (3.65)	0.85 (0.76)	1.44 (0.51)
<i>Klebsiella aerogenes</i>	2	100	100	0	0	0
<i>Klebsiella oxytoca</i>	4	89.19 (94.59)	93.24 (95.95)	5.41 (2.70)	0	5.41 (2.70)
<i>Klebsiella pneumoniae</i>	21	97.24	99.75	2.51	0	0.25
<i>Proteus mirabilis</i>	5	93.62 (94.68)	94.68	1.06 (0)	4.26	1.06
<i>Pseudomonas aeruginosa</i>	13	87.37 (88.42)	89.47	9.47	2.11 (1.05)	1.05
<i>Serratia marcescens</i>	4	79.69 (87.50)	81.25 (89.06)	6.25	0	14.06 (6.25)
Combined organisms	118	93.77 (95.02)	96.14 (97.10)	3.62 (3.33)	1.01 (0.92)	1.59 (0.72)

N = number; CA = Categorical agreement; EA = Essential agreement; mE = Minor errors; ME = Major errors; VME = Very major errors. All values except N are percentages. Values in () indicate new values following broth microdilution adjudication.

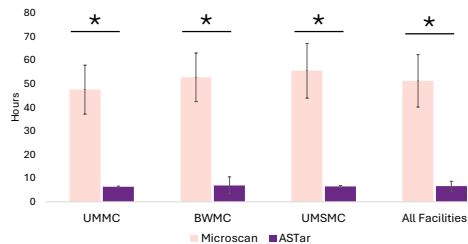


Figure 1. Use of ASTar for susceptibility testing would result in drastically decreased turn-around times to AST results. MicroScan result times were measured from positive Gram stain result until susceptibility result. ASTar result times were determined from the total runtime of the test as recorded by the instrument. Student's t test was performed and a p value < 0.01 is denoted by an *.

Table 3. DOOR-MAT Cohort (N = 100 Enterobacteriales)

Variable	N (%)
Hospital	
UMMC (academic)	35 (35%)
BWMC (community)	38 (38%)
Shore (community)	27 (27%)
Age, years (mean ± SD)	66.0 ± 16.8
Acuity	
Floor	36 (36%)
ED	22 (22%)
Intensive Care Unit/Trauma	17 (17%)
Intermediate Care Unit	25 (25%)
Sepsis	
Sepsis	56 (56%)
Septic Shock	29 (29%)
Immunocompromised Status	14 (14%)
Source of Bacteremia	
Urinary tract	54 (54%)
Unknown	13 (13%)
Skin and soft tissue	5 (5%)
Pulmonary	10 (10%)
Other	2 (2%)
Intra-abdominal	11 (11%)
Endovascular/catheter	5 (5%)
Previous MDR GN	4 (4%)
ID Consult	42 (42%)

AST Resistance Profiles

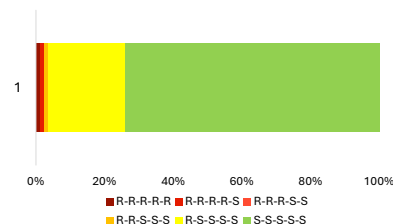


Figure 2. Breakdown of antimicrobial susceptibility profile (by MicroScan) for Enterobacteriales cohort. Accounting for post-hoc discrepancy analysis.

DOORMAT Categories

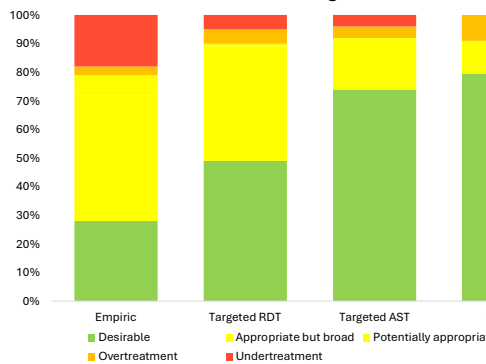


Figure 3. Breakdown of DOOR-MAT categories for desirability of antibiotic therapy choices. Empiric to Targeted AST collected from EMR-extracted chart review. ASTar antibiotic choices collected from theoretical decisions based on clinical case review. The mean (+SD) DOOR-MAT score for each phase were Empiric = 55 (+32.7), BCID2 RDT = 72.1 (+29.2), MicroScan AST = 86.5 (+25.5), ASTar = 92.5 (+23.8).