Influence of Antimicrobial Stewardship and Molecular Rapid Diagnostic Test on Antimicrobial Prescribing for ESBL- and Carbapenemase-producing Bacteria in Bloodstream Infections

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Background

- **Gram-negative bloodstream infections** are associated with significant morbidity and mortality, often resulting in life-threatening organ dysfunction.
- *E. coli* and *K. pneumoniae* demonstrate increasing resistant mechanisms including **extended-spectrum beta-lactamases** (ESBL) and ***Klebsiella pneumoniae* carbapenemases** (KPC).
- **Molecular rapid diagnostic tests** (mRDT) may expedite time to optimal antimicrobial therapy and lessen burdens of ESBL- and carbapenemase-producing bacteria in bloodstream infections (BSI).

Figure 1. mRDT and CONV workflow

Organism detection from gram stain:
VERIGENE®: ~2.5 hours
Conventional microbiological methods: >30 hours

Study purpose: To evaluate if the addition of mRDT to standard antimicrobial stewardship practices (mRDT + ASP) decreased the time to optimal antimicrobial therapy for patients with ESBL- and carbapenemase-producing *E. coli* and *K. pneumoniae* BSI compared to conventional microbiological methodologies and ASP intervention (CONV + ASP).

Methods

Retrospective, parallel cohort study from February 2014 – July 2019

mRDT + ASP

CONV + ASP

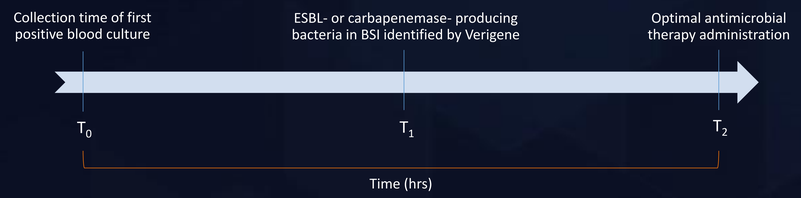
Inclusion

- ≥18 years of age and admitted to the hospital
- Blood culture positive with ESBL- or carbapenemase-producing organism
- Available susceptibility results

Exclusion

- Polymicrobial BSI
- Transferred in from OSH with positive blood culture
- Bone marrow or solid organ transplant recipient
- Cancer or febrile neutropenia
- Incarcerated
- Enrolled in a concomitant research study
- Died before culture results

Figure 2. Primary outcome of time to optimal antimicrobial therapy*



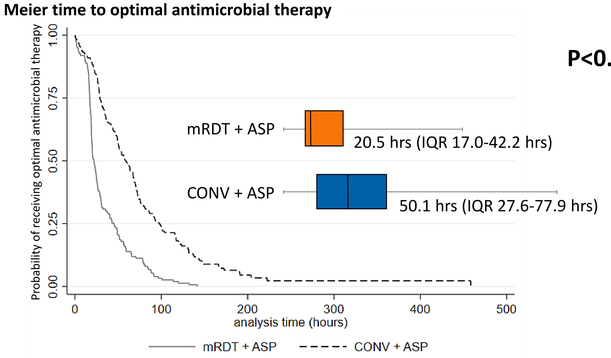
Secondary outcomes

- Time to microbial clearance**
- All-cause hospital mortality
- 30-, 60- and 90-day readmission rates
- *Clostridioides difficile* rates

*Time to optimal therapy = (T_2-T_0). Optimal therapy was defined as a carbapenem for ESBL-producing bacteria in BSI and ceftazidime-avibactam or at least one drug active in-vitro with the most-narrow spectrum for carbapenemase-producing bacteria in BSI.
**Time to microbial clearance defined as the time from index blood culture collection to the time of collection of the first negative blood culture or hospital discharge.
ŦData presented as no. (%) or median (IQR) unless specified otherwise

TAKE-HOME POINTS

Figure 5. Kaplan Meier time to optimal antimicrobial therapy



In patients with ESBL- or carbapenemase-producing bacteria in bloodstream infections, mRDT + ASP significantly decreased the time to optimal antimicrobial therapy and microbial clearance compared to CONV + ASP.

Study strengths

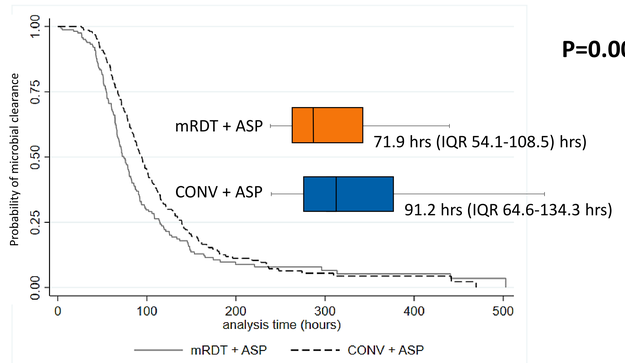
- Multicenter study with large sample size of ESBL- and KPC-producing organisms
- Established ASP at each site throughout study period
- Similar time to optimal therapy at CONV + ASP site compared to mRDT site prior to mRDT implementation[4]

Study limitations

- Retrospective, non-blinded, chart review
- Practice site variation cannot be excluded between academic medical centers
- CONV + ASP had significantly more infectious diseases consults
- Piperacillin-tazobactam excluded as optimal therapy based on MERINO trial data[5]

Antimicrobial stewardship programs can use these data to help justify the need for mRDT to quickly identify patients and promote optimal antimicrobial therapy in patients with ESBL- or carbapenemase-producing *E. coli* and *K. pneumoniae* BSI.

Figure 6. Kaplan Meier time to microbial clearance



Results

Figure 3. Patient allocation schema

Table 1. Baseline CharacteristicsŦ

	mRDT + ASP n = 164	CONV + ASP n = 214	P value
Age, mean ±SD	59.5 ± 15.7	62.9 ± 16.9	0.054
Female sex	71 (43.3)	95 (44.4)	0.100
Race/ethnicity			
Black	79 (48.2)	58 (27)	0.189
Non-Hispanic white	76 (46.3)	143 (66.8)	0.096
Hispanic	9 (5.5)	9 (4.2)	0.254
Beta-lactam allergy	33 (20.1)	35 (16.4)	0.301
NH/LTC residence	36 (22)	41 (19.2)	0.562
Charlson comorbidity index, mean ±SD	6.1 ± 3.4	5.6 ± 2.9	0.275
Pitt Bacteremia score, mean ±SD	3.1 ± 2.4	3.4 ± 2.7	0.439
Immunosuppressive medication within previous 30 days	13 (7.9)	13 (6.1)	0.453
Surgical procedure within previous 30 days	34 (20.7)	41 (19.2)	0.103
Gram-negative infection within previous 6 months	79 (48.2)	87 (40.7)	0.139
History of ESBL-resistant Enterobacteriaceae infection	54 (32.9)	61 (28.5)	0.759
History of carbapenemase-resistant Enterobacteriaceae infection	6 (3.7)	2 (0.9)	0.084
Hospital-acquired infection	84 (51.2)	94 (43.9)	0.233
Infectious Diseases consult	57 (34.8)	176 (82.2)	<0.001

Figure 4. Source of BSIŦ

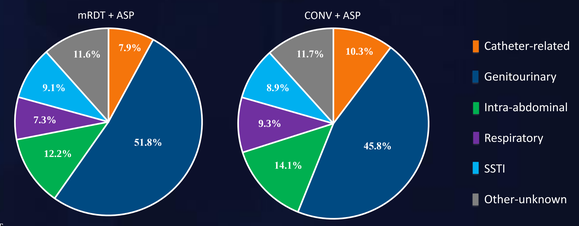


Table 2. Secondary outcomesŦ

	mRDT + ASP n = 164	CONV + ASP n = 214	P value
All-cause hospital mortality	13 (8.2)	29 (13.6)	0.088
Hospital length of stay	4 days (IQR 3-5 days)	12 days (IQR 7-23 days)	0.465
Infection-related length of stay	3 days (IQR 2-4 days)	4 days (IQR 3-5 days)	<0.001
Readmission rates			
30-day	45 (27.4)	43 (20.1)	0.094
60-day	60 (36.6)	60 (28.7)	0.093
90-day	63 (38.4)	68 (31.8)	0.179
Clostridioides difficile rate	10 (6.1)	7 (3.3)	0.189
Hospital charges	$114,649.59 (IQR 51,123.32-114,649.49)	$88,218.40 (IQR 47,372,44-209,913.35)	0.711
Infection-related charges	$43,488.94 (IQR 28,388.69-68,269.46)	$39,695.220 (IQR 28,361.69-59,978.75)	0.960

1. Huang AM et al. *Clin Infect Dis*. 2013;57(9):1237-1245.
2. Sullivan et al. *J Clin Microbiol* 2014.
3. Pettit et al. *J Infect Dis Epidemiol* 2019;5(1):069.
4. Sothoron C et al. *J Clin Microbiol* 2015;53.
5. Harris et al. *JAMA* 2018;320.