

Assessment of the clinical impact of rapid identification with same-day phenotypic antimicrobial susceptibility testing (Accelerate Pheno™ system) on the management of bloodstream infections in adult patients with antibiotic stewardship intervention: A retrospective observational study.

Kathrin Ehren¹, Arne Meißner², Nathalie Jazmati¹, Julia Ertel¹, Norma Jung³, Janne Vehreschild³, Martin Hellmich⁴, Harald Seifert¹

¹Institute for Medical Microbiology, Immunology and Hygiene, University Hospital of Cologne, Cologne, Germany, ²Department of Hospital Hygiene and Infection Control, University Hospital of Cologne, Cologne, Germany, ³Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany, ⁴Institute of Medical Statistics and Computational Biology, University Hospital of Cologne, Cologne, Germany

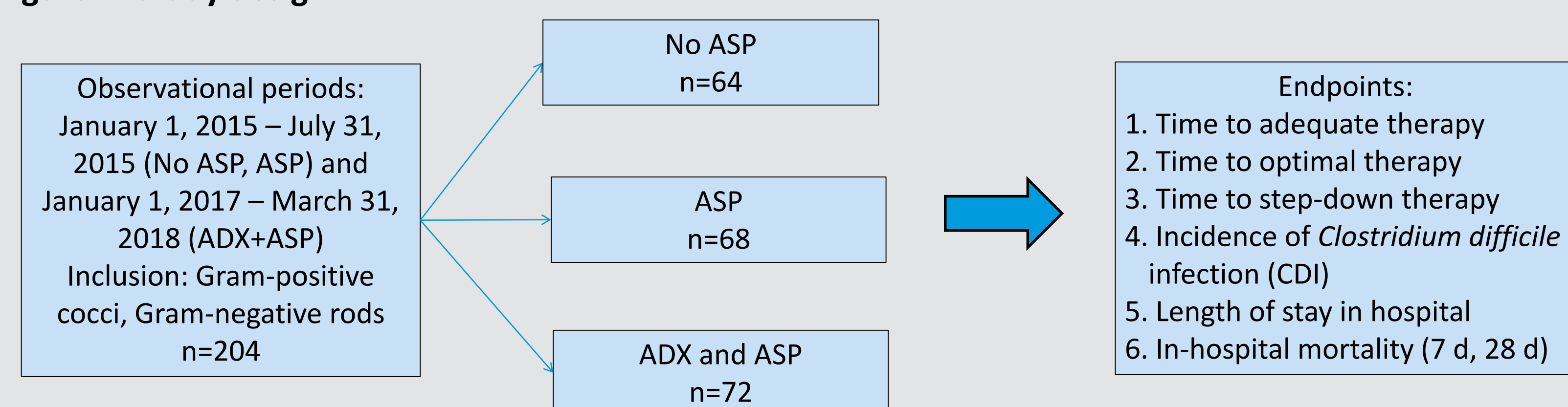
Background

- Rapid initiation of appropriate antimicrobial therapy is crucial in managing severe infections [1]
- Timely availability of microbiological results is essential to enable early targeted antimicrobial therapy
- Effective antimicrobial stewardship program (ASP) improves patient outcomes in bloodstream infections [2]
- Accelerate Pheno™ system (Accelerate Diagnostics, Tucson, Arizona, USA) (ADX) is a novel technology for rapid identification (<1.5hrs) and phenotypic antimicrobial susceptibility testing (~7hrs) [3] directly from positive blood cultures
- The impact of ADX on the clinical management and patient outcome still is unclear

Methods

- Retrospective before and after observational study at the University Hospital of Cologne (1464 beds), observational periods January 1, 2015 – July 31, 2015 and January 1, 2017 – March 31, 2018
- Three groups were compared:
 - (1) Conventional microbiological diagnostics without ASP (“no ASP”), conventional diagnostics including MALDI-TOF MS (Biotyper, Bruker Daltonics, Bremen, Germany), Vitek 2, and Etest (bioMérieux, Nürtingen, Germany)
 - (2) Conventional microbiological diagnostics with ASP intervention (including chart review, physical examination and recommendation for therapy after Gram stain result) (“ASP”)
 - (3) ADX (in addition to conventional standard) with ASP (“ADX and ASP”)

Figure 1: Study design



Abbreviations: ASP, Antimicrobial stewardship program; ADX, AcceleratePheno™ System.

Results

- 204 patients met inclusion criteria (No ASP n=64; ASP=68; ADX and ASP=72), no difference in clinical and demographic characteristics
- ADX decreased time from positive blood culture to microorganism identification (ID) (median: No ASP 24.2 hours; ASP 25.2 hours; ADX and ASP 12.5 hours; p<0.001) and time to susceptibility testing (AST) (median: No ASP 44.1 hours; ASP 43.8 hours; ADX and ASP 17.6 hours; p<0.001)
- ASP intervention alone improved the proportion of patients on optimal therapy within 48 hours after Gram stain (62.5% vs. 80.9%; p<0.05; p-value not shown in Table 2)
- ADX improved time from Gram stain to optimal antimicrobial therapy (median: ASP 11 hours; ADX and ASP 7 hours; p=0.044) and time to-step down therapy (median: ASP 27.8 hours; ADX and ASP 12 hours; p=0.018), no effect on time to adequate therapy could be shown

Table 1: Microbiological and clinical findings

Species	Total	No ASP	ASP	ADX and ASP
<i>Escherichia coli</i>	50 (24.5%)	14 (21.9%)	18 (26.5%)	18 (25%)
<i>Klebsiella</i> spp.	21 (10.3%)	8 (12.5%)	5 (7.4%)	8 (11.1%)
<i>Enterobacter cloacae</i>	11 (5.4%)	5 (7.8%)	1 (1.5%)	5 (6.9%)
Other <i>Enterobacteriaceae</i>	15 (7.5%)	4 (6.4%)	5 (7.4%)	6 (8.4%)
<i>Pseudomonas aeruginosa</i>	12 (5.9%)	3 (4.7%)	5 (7.4%)	4 (5.6%)
<i>Staphylococcus aureus</i>	51 (25%)	16 (25%)	22 (32%)	13 (18.1%)
<i>Enterococcus faecium</i>	25 (12.3%)	7 (10.9%)	5 (7.4%)	13 (18.1%)
<i>Enterococcus faecalis</i>	15 (7.4%)	6 (9.4%)	5 (7.4%)	4 (5.6%)
Others	4 (2%)	1 (1.6%)	2 (3%)	1 (1.4%)
Source of Infection	Total	No ASP	ASP	ADX and ASP
Urinary tract	62 (30.4%)	17 (26.6%)	22 (32.4%)	23 (31.9%)
Intra-abdominal	39,0 (19.1%)	10 (15.6%)	14 (20.6%)	15 (20.8%)
Intravascular catheter	29 (14.2%)	12 (18.8%)	8 (11.8%)	9 (12.5%)
Skin/skin structure	21 (10.3%)	5 (7.8%)	8 (11.8%)	8 (11.1%)
Respiratory tract	13 (6.4%)	7 (10.9%)	4 (5.9%)	2 (2.8%)
Endocarditis	4 (2%)	4 (6.3%)	0 (0%)	0 (0%)
Central nervous system	1 (0.5%)	0 (0%)	0 (0%)	1 (1.4%)
Unknown	23 (11.3%)	7 (10.9%)	5 (7.4%)	11 (15.3%)
Acquisition	Total	No ASP	ASP	ADX and ASP
Hospital	152 (74.5%)	49 (76.6%)	51 (75%)	52 (72.2%)

Abbreviations: ASP, Antimicrobial stewardship program; ADX, AcceleratePheno™ System.

Table 2: Timing of antimicrobial therapy and outcome

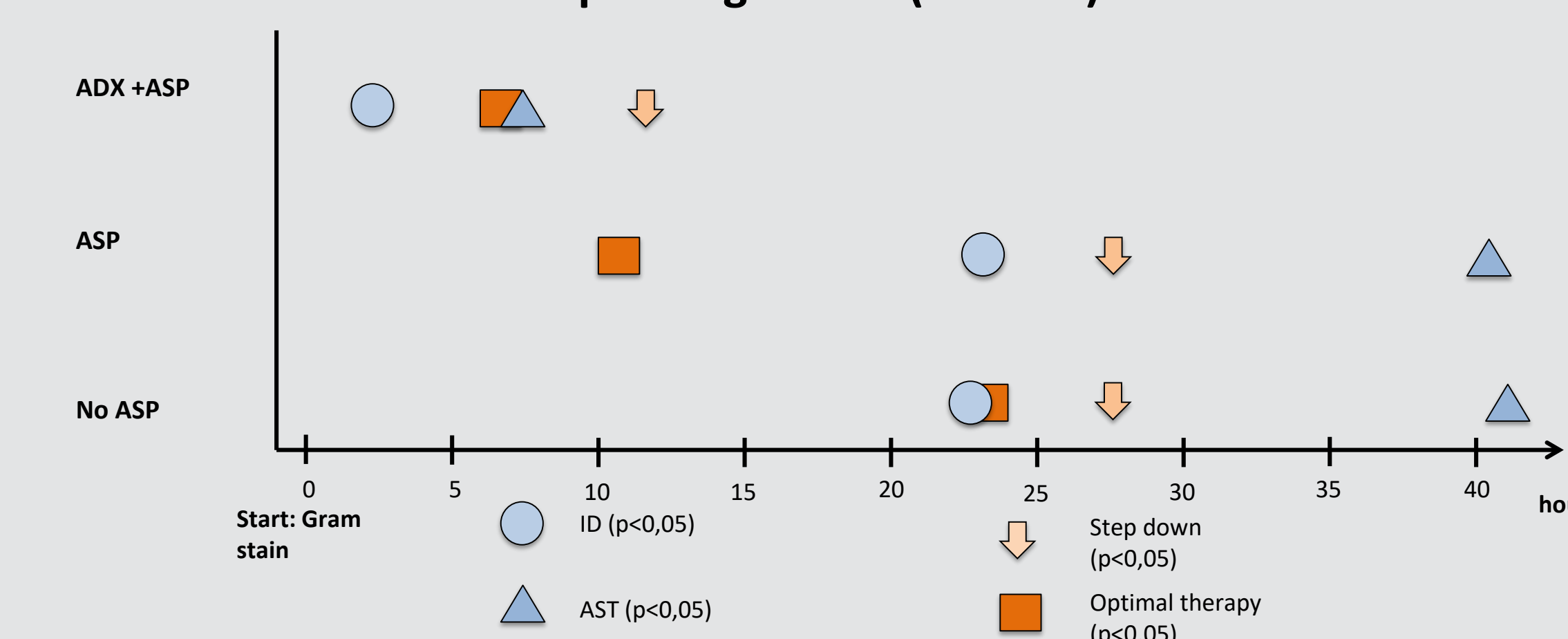
	Total	No ASP	ASP	ADX and ASP	p-value ^c
Time to adequate therapy (h) ^a , median (IQR)	0 (0-3.4)	0 (0-4)	0 (0-4)	0 (0-3.3)	.446
Valid N	200	62	67	71	.
Time to optimal therapy (h) ^b , median (IQR)	9.25 (0-27.5)	23 (0.8-31.6)	11 (0-31)	7 (0-13.3)	.044
Valid N	163	44	57	62	.
Time to step down (h) ^a , median (IQR)	25 (8.5-33.3)	27.5 (23.5-34)	27.8 (11-44.5)	12 (7.5-25.5)	.018
Valid N	87	19	38	30	.
Optimal therapy within 48 hours ^a	156 (76.5%)	40 (62.5%)	55 (80.9%)	61 (84.7%)	.547
CDI	11 (5.4%)	3 (4.7%)	2 (2.9%)	6 (8.3%)	.170
Length of stay ^b (d), median (IQR)	26 (15-43.5)	27.5 (15-42.5)	25 (6-40.5)	26 (14-46.5)	.758
In-hospital mortality d7	4 (2%)	1 (1.6%)	1 (1.5%)	2 (2.8%)	.593
In-hospital mortality d28	33 (16.2%)	10 (15.6%)	9 (13.2%)	14 (19.4%)	.322

Abbreviations: ASP, Antimicrobial stewardship program; ADX, AcceleratePheno™ System; CDI, *Clostridium difficile* infection. ^a: from Gram stain, ^b: after blood culture draw, ^c: p-values from Pearsons chi square test and Kruskal Wallis test for comparison of ASP/ASP+ADX.

Conclusion

- ADX significantly reduced time to ID and AST by more than 11 and 26 hours, respectively
- In combination with ASP intervention ADX significantly reduced time to optimal therapy by 4 hours (ASP) and 16 hours (No ASP), time to step-down was reduced by 15.8 hours (ASP) and 15.5 hours (No ASP)
- ASP intervention alone improved the proportion of patients on optimal therapy within 48 hours from 62.5% to 80.9%
- Additional ADX in an advanced technology setting had no impact on the time to institution of adequate antimicrobial therapy
- Earlier optimal therapy and especially earlier step-down helps to reduce broad spectrum antimicrobial therapy in the context of emerging antimicrobial resistance

Figure 2: Timeline conventional vs. rapid diagnostics (median)



Abbreviations: ASP, Antimicrobial stewardship program; ADX, AcceleratePheno™ System; ID, identification; AST antimicrobial susceptibility testing.

References

1. Kumar, A., et al., *Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*. Crit Care Med, 2006. **34**(6): p. 1589-96.
2. Barlam, T.F., et al., *Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America*. Clin Infect Dis, 2016. **62**(10): p. e51-77.
3. Pancholi, P., et al., *Multicenter Evaluation of the Accelerate PhenoTest BC Kit for Rapid Identification and Phenotypic Antimicrobial Susceptibility Testing Using Morphokinetic Cellular Analysis*. J Clin Microbiol, 2018. **56**(4).