
Comparing the Outcomes of Adults With Enterobacteriaceae Bacteremia Receiving Short-Course Versus Prolonged-Course Antibiotic Therapy in a Multicenter, Propensity Score-Matched Cohort.

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Hintergrund

Limited data bezüglich Therapiedauer gramnegativer Bakteriämie

- Guidelines?
 - Sanford: 10-14d
 - Uptodate: „duration of therapy should be determined by the clinical response of the patient in addition to the primary source and extent of infection“. „in most cases, the duration is [...] 7-14 days“
- Bisherige Studien (2): Meta-Analyse von 24 randomisiert kontrollierten Studien: 60% Kinder, 80% Bakteriämie durch Pneumonie/UTI, wenige health-care associated

1) *Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America*

2) HaveyTC, FowlerRA, DanemanN. Duration of antibiotic therapy for bacteremia: a systematic review and meta-analysis. Crit Care2011; 15:R267.

Fragestellung

- **Vergleich der Outcomes** von Erwachsenen mit einer Bakteriämie mit Enterobacteriaceae: **Short-course (6-10d) vs prolonged course (11-16d)**
 - **Primäres Outcome:** Mortalität innerhalb 30d nach Therapieende
 - **Sekundäre Outcomes:** Rezidivierende Bakteriämie (selber Erreger), *Clostridium difficile* infection, Nachweis von MDRGN-Bakterien innerhalb 30d nach Therapieende

Studiendesign / Methoden

- **Retrospektive Kohortenstudie an 3 „medical centers“** (John Hopkins Hospital, University of Maryland Medical Center, Hospital of the university of Pennsylvania), **2008-2014**
- **Einschluss:** ≥ 18 a, monomikrobielle Bakteriämie mit Enterobacteriaceae, Resistenzgerechte Therapie mit Dauer von 6-16d
- **1:1 propensity score matching → 385 Paare**

Studiendesign / Methoden

4,967 unique patients ≥ 18 years of age with Enterobacteriaceae bacteremia admitted to the three participating sites during the study period

Exclusions (not mutually exclusive)

- Polymicrobial bacteremia (n=789)
- Duration of therapy outside of the 6-16 day range (n=794)
- Discontinuation of antibiotic therapy due to transition to hospice care (n=211)
- Died while receiving antibiotic therapy (n=453)
- Failure to receive at least one agent with *in vitro* activity against the isolated organism from the time of culture obtainment to completion of therapy (n=541)
- Aminoglycoside monotherapy (n=39)
- Recipients of hematopoietic stem cell or solid organ transplantations (n=375)

1,769 patients met eligibility criteria

385 patients received short-course therapy (6-10 days)

1,384 patients received prolonged-course therapy (11-16 days)

1:1 propensity score matching

385 patients received short-course therapy (6-10 days)

385 patients received prolonged-course (11-16 days)

Baseline Characteristics of Hospitalized Adult Patients With Enterobacteriaceae Bacteremia Receiving Short (6–10 Days) or Prolonged Courses (11–16 Days) of Antibiotic Therapy



Characteristic	Whole Cohort		
	Short Course (n = 385)	Prolonged Course (n = 1384)	P Value
<u>Age, y, median (IQR)</u>	60 (46–69)	58 (46–69)	.20
<u>Female sex</u>	191 (49.6)	699 (50.5)	.76
Race/ethnicity			.13
White	196 (50.9)	647 (46.7)	.15
Black or African American	154 (40.0)	584 (42.2)	.44
Asian	11 (2.9)	62 (4.5)	.16
Latino	8 (2.1)	51 (3.7)	.12
Unknown or multiracial	16 (4.2)	40 (2.9)	.21

Table 1. The Pitt Bacteremia Score*

Criterion	Points	
Fever (oral temperature)	≤35°C or ≥40°C	2
	35.1–36.0°C or 39.0–39.9°C	1
	36.1–38.9°C	0
Hypotension	Acute hypotensive event with drop in systolic blood pressure > 30 mm Hg and diastolic blood pressure > 20 mm Hg	2
	or	
	Requirement for intravenous vasopressor agents	
Systolic blood pressure < 90 mm Hg	or	2
	Systolic blood pressure < 90 mm Hg	
Mechanical ventilation	2	
Cardiac arrest	4	
Mental status	Alert	0
	Disoriented	1
	Stuporous	2
	Comatose	4

* All criteria are graded within 48 hours before or on the day of first positive blood culture. The highest point score during that time is recorded.

Intensive care unit
bacteremia

	Short Course (n = 385)	Prolonged Course (n = 1384)	P Value
Preexisting medical conditions			
End-stage liver disease	35 (9.1)	87 (6.3)	.06
ESRD requiring dialysis	18 (4.7)	59 (4.3)	.73
Structural lung disease ^a	34 (8.8)	109 (7.9)	.54
CHF with an ejection fraction <45%	46 (11.9)	131 (9.5)	.15
Diabetes	96 (24.9)	325 (23.5)	.55
Immunocompromised ^b	127 (33.0)	523 (37.8)	.08
HIV	14 (3.6)	63 (4.6)	.44
Chemotherapy within 6 mo	93 (24.2)	419 (30.3)	.02
Absolute neutrophil count ≤100 cells/μL	24 (6.2)	108 (7.8)	.30
Immunomodulatory therapy or corticosteroids for ≥14 d	23 (6.0)	56 (4.0)	.01

Enterobacteriaceae Isolated in the Bloodstream of Hospitalized Adult Patients Between 2008 and 2014

Enterobacteriaceae	Entire Cohort (N = 1769)	Duration of Therapy in Matched Cohort	
		6-10 d (n = 385)	11-16 d (n = 385)
<i>Escherichia coli</i>	841 (47.5)	177 (46.0)	184 (47.8)
<i>Klebsiella</i> species	557 (31.5)	137 (35.6)	114 (29.6)
<i>Enterobacter</i> species	200 (11.3)	36 (9.4)	54 (14.0)
<i>Serratia</i> species	58 (3.3)	13 (3.4)	9 (2.3)
<i>Proteus</i> species	81 (4.6)	13 (3.4)	14 (3.6)
<i>Citrobacter</i> species	32 (1.8)	9 (2.3)	10 (2.6)

Data are presented as No. (%).

Results – Primary Outcome (Short vs. Long)

- 37 (9.6%) vs. 39 (10.1%) Todesfälle innerhalb 30d nach Therapieende [adjusted HR 1.0]

Thirty-Day All-Cause Mortality for Hospitalized Adult Patients With Enterobacteriaceae Bacteremia in a Propensity Score–Matched Cohort

Variable	Unadjusted HR (95% CI)	P Value	Adjusted HR ^a (95% CI)	P Value
Short-course therapy (6–10 d)	1.12 (.70–1.80)	.64	1.00 (.62–1.63)	.97
Urinary source	0.36 (.19–.67)	.001	0.49 (.26–.94)	.03
Pneumonia	3.06 (1.73–5.42)	<.001	1.60 (.85–3.02)	.15
Pitt bacteremia score	1.31 (1.21–1.42)	<.001	1.29 (1.17–1.43)	<.001
ICU on day 1 of bacteremia	2.38 (1.48–3.81)	<.001	0.99 (.56–1.76)	.98
End-stage liver disease	3.58 (2.05–6.06)	<.001	4.12 (2.30–7.39)	<.001
Immunocompromised status	1.03 (.63–1.70)	.89	1.40 (.83–2.36)	.21

Secondary Outcomes (Short vs. Long)

- **Episodes of recurrent bacteriemia:** 5 (1.3%) vs 9 (2.3%)
- **CDI:** 7 (1.8%) vs. 6 (1.6%)
- **MDRGN:** 17 (4.4%) vs. 28 (7.3%) [p=0.9]

Diskussion

Kein signifikanten Unterschied bezüglich Mortalität in den ersten 30d nach Therapie

Propensity Score

Limitationen:

- Propensitiy Score
- Geringe Fallzahl bez.
- Keine Angaben bez.:
- Short-course: Anteile

Covariates:

- Calendar year
- Hospital
- Age
- Preexisting conditions (end-stage kidney/-liver, structural lung disease, HF with EF <45%, DM, Immunocompromising conditions, Pitt bacteremia score, ICU-stay on day 1, source of bacteremia and source control measures)

Vielen Dank für die Aufmerksamkeit!



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Mechanical ventilation	2
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