Plasma concentrations of broad-spectrum beta-lactam antibiotics are significantly lower in critically ill patients with augmented renal clearance.

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INTRODUCTION:

- Appropriate dosing of beta-lactam antibiotics in critically ill patients is challenging.
- Augmented renal clearance (ARC) is considered an important cause of sub therapeutic plasma concentrations. However, data from large cohorts is lacking.

OBJECTIVES:

Correlate ARC and the steady-state plasma concentration of piperacilline/tazobactam (TZP) or meropenem (MER) in critically ill patients.

METHODS:

- Retrospective analysis of adult critically ill patients receiving continuous infusion of TZP or MER in UZ Gent between March 2016 and April 2019.
- Inclusion criteria: Admission to the intensive care unit (ICU), administration of TZP or MER in continuous infusion after an initial loading dose, age>18y and availability of a plasma concentration of the drugs studied.
- Exclusion criteria: Acute kidney injury, renal replacement therapy, and patients without a measured creatinine clearance (mCrCl) - based on an 8-hour urinary collection - at the moment of plasma sampling.
- Antimicrobial plasma concentrations were determined at steady state (>12 h continuous infusion) by liquid chromatography with tandem mass spectrometry. Measured concentrations were not disclosed to the treating physicians. Only one sample per antibiotic course was considered.
- ARC was defined as a mCrCl >130 mL/min.

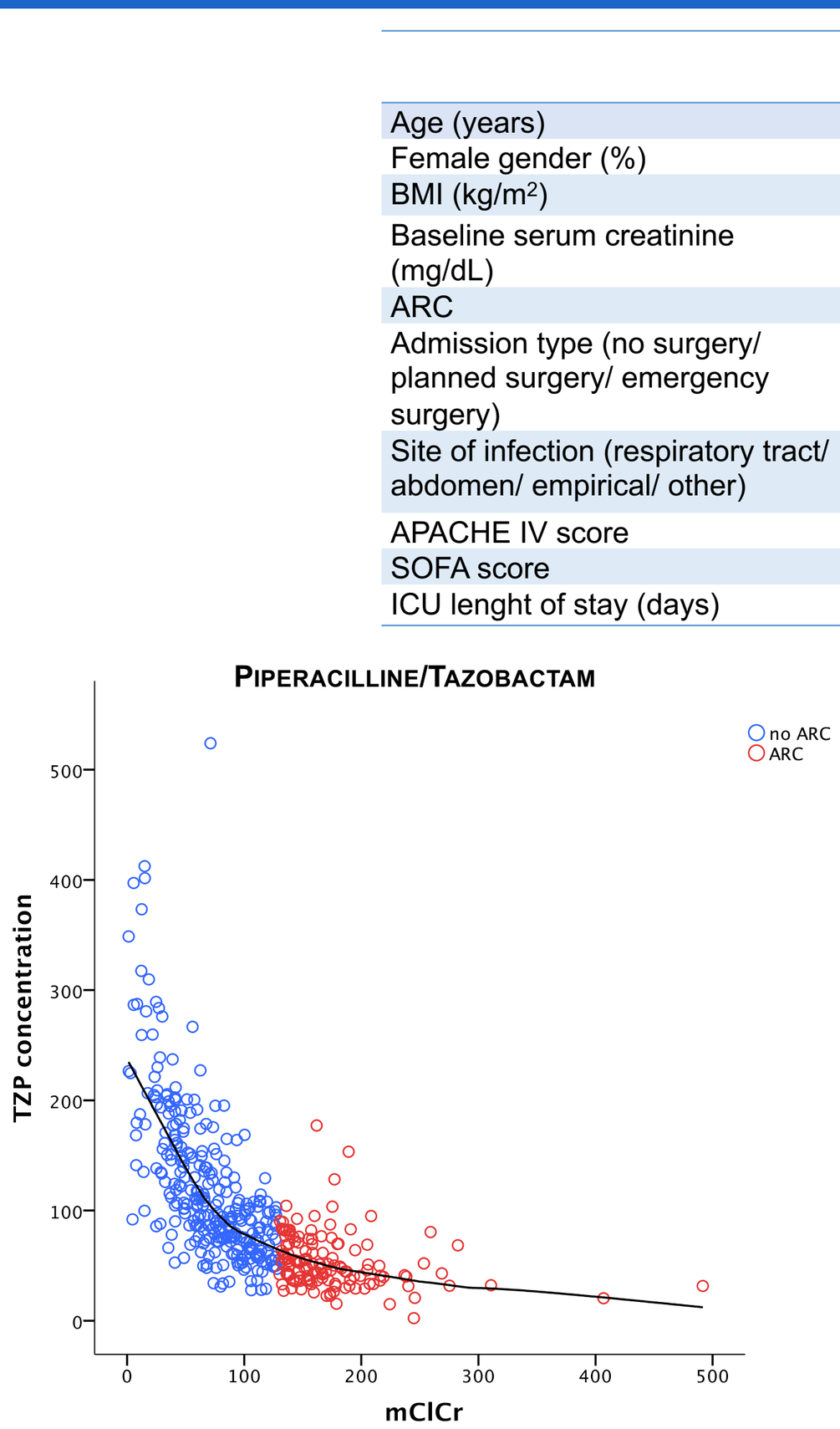
RESULTS:

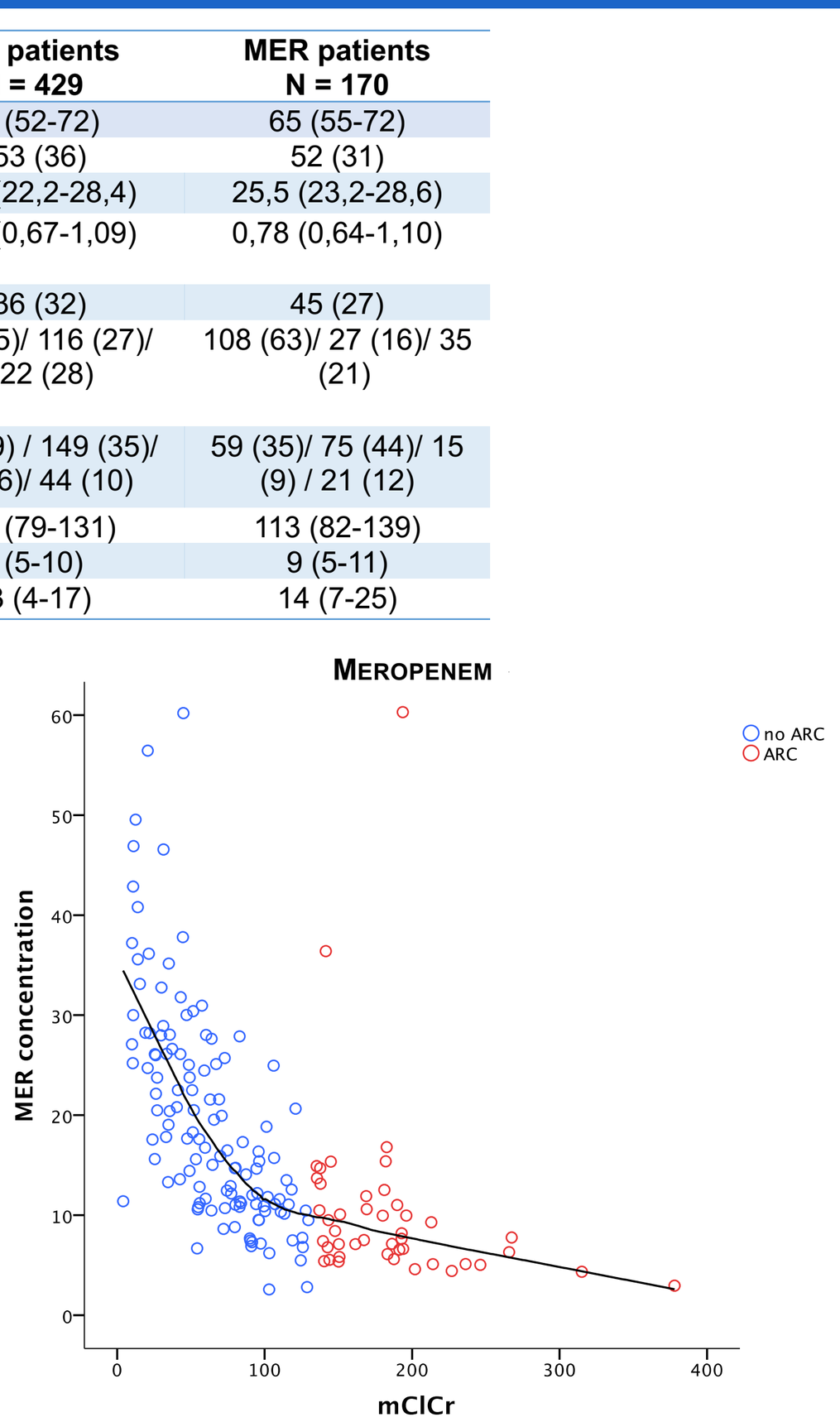
- Five hunderd and ninety-nine samples (72% TZP, 28% MER) from 545 ICU admissions, obtained from 531 individual patients.
- ARC was present in 32% of TZP patients and 27% of MER patients.
- There was a strong, negative correlation between mCrCl and TZP or MER concentration (rs = -0.769 and -0.749 respectively, p<0.001).
- When comparing patients with vs. without ARC, median TZP concentration was 48.6 (IQR 36.7-69.3) vs. 102.0 (IQR 74.5-151.9) mg/L, median MER concentration was 7.6 (IQR 5.7-11.5) vs. 16.7 (IQR 11.1-26.1) mg/L (both p<0.001).

There is a strong negative correlation between steady-state plasma concentrations of broad-spectrum beta-lactam antibiotics and mCrCl in critically ill patients.

Median TZP and MER plasma concentrations in patients with ARC were about half of the concentrations found in non-ARC patients.

	TZP patients N = 429	MER patients N = 170
Age (years)	63 (52-72)	65 (55-72)
Female gender (%)	153 (36)	52 (31)
BMI (kg/m^2)	25,0 (22,2-28,4)	25,5 (23,2-28,6)
Baseline serum creatinine (mg/dL)	0,83 (0,67-1,09)	0,78 (0,64-1,10)
ARC	136 (32)	45 (27)
Admission type (no surgery/ planned surgery/ emergency surgery)	191 (45)/ 116 (27)/ 122 (28)	108 (63)/ 27 (16)/ 35 (21)
Site of infection (respiratory tract/ abdomen/ empirical/ other)	166 (39) / 149 (35)/ 70 (16)/ 44 (10)	59 (35)/ 75 (44)/ 15 (9) / 21 (12)
APACHE IV score	105 (79-131)	113 (82-139)
SOFA score	7 (5-10)	9 (5-11)
ICU lenght of stay (days)	13 (4-17)	14 (7-25)





DISCLOSURES: None