DISTRIBUTION OF ACUTE AND CHRONIC KIDNEY DISEASES ACROSS CLINICAL PHENOTYPES FOR SEPSIS

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BACKGROUND & OBJECTIVE

Sepsis is the most common cause of acute kidney injury (AKI) in critically ill patients. Four clinical phenotypes (alpha, beta, gamma, delta) of sepsis have been described using routine clinical data. Biomarkers of kidney stress, tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7), have been proposed to aid AKI staging together with KDIGO criteria since [TIMP-2]•[IGFBP7]>2.0 is associated with worse outcome. Our **objective** was to investigate the distribution of AKI, chronic kidney disease (CKD), AKI-on-CKD, and acute kidney disease (AKD) across the four phenotypes.

METHODS

We performed a secondary analysis of a randomized clinical trial (ProCESS) including patients with early septic shock enrolled in 31 sites in the US. Each patient was assigned to one of the four phenotypes. After excluding patients with end-stage kidney disease and missing data, we determined the rates of: *a) AKI* within the first 24 hours from enrollment (stage 2 or 3 or stage 1 with [TIMP-2]•[IGFBP7]>2.0); *b) CKD; c) AKI-on-CKD; d) AKD*, for patients with *AKI*, defined as persistence of AKI at any KDIGO stage on day 7 following enrollment. The Chi-square test was used to compare distributions between phenotypes.

TABLE. DISTRIBUTION OF KIDNEY DISEASES ACROSS THE FOUR CLINICAL PHENOTYPES FOR SEPSIS

	Total (N. 1090)	Alpha (N. 364)	Beta (N. 238)	Gamma (N. 313)	Delta (N. 175)	*P**
AKI	543 (49.8%)	94 (25.8%)[a]	168 (70.6%)[b]	145 (46.3%)[c]	136 (77.7%)[b]	<0.001
CKD	387 (35.5%)	117 (32.1%)[a]	125 (52.5%)[b]	89 (28.4%)[a]	56 (32%)[a]	<0.001
AKI-on-CKD	196 (18.0%)	26 (7.1%)[a]	90 (37.8%)[b]	38 (12.1%)[a]	42 (24%)[c]	<0.001
AKD	237 (21.7%)	28 (7.7%)[a]	84 (35.3%)[b]	54 (17.3%)[c]	71 (40.6%)[b]	<0.001

*If overall p<0.05, pairwise comparisons between phenotypes was performed using Bonferroni correction. Values in the same row not sharing the same superscript letter are significantly different at adjusted p<0.05.

RESULTS

Among 1090 eligible patients, 543 (49.8%) patients had *AKI*. Across sepsis phenotypes, the rates of *AKI* varied highest in the delta and beta phenotypes (77.7% and 70.6%, respectively), and lowest in the alpha phenotype (25.8%, overall p<0.001). The highest rates of *CKD* and of *AKI-on-CKD* were found in the beta phenotype (52.5% and 37.8% respectively, both p<0.001). *AKD* occurred most often in the delta phenotype (40.6%) and least often in alpha (7.7%).

CONCLUSION

AKI was significantly more common among patients with beta and delta phenotypes. However, the beta phenotype had a higher level of underlying CKD that predisposed to new AKI. Alpha and gamma phenotypes not only had lower rates of AKI, but these cases were less likely to progress to AKD.

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