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The VExUS score and mortality in patients with Acute Kidney Injury: findings from a multidisciplinary prospective study

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Abstract

Aim: The utility of the venous excess ultrasound (VExUS) score in predicting mortality remains uncertain in acute kidney injury (AKI) patients. **Material and methods**: This was a post-hoc study involving 246 AKI patients presenting to a tertiary care emergency department. Venous ultrasound assessments were conducted to determine the VExUS score. Cox regression analysis was used to identify predictors of 6-month mortality. **Results**: The study found no significant association between the VExUS score and 6-month mortality in AKI patients in the regression analyses. However, in the subgroup analyses, VExUS grades 2-3 were associated with lower survival rates in the cardiorenal subgroup (HR: 3.98 [95% CI: 1.33–11.93]), and in AKI grade 1 (HR: 4.07 [95% CI: 1.74–9.49]). This association was not present in other AKI subgroups. The predictors of mortality included higher age (OR: 1.024; 95% CI 1.005-1.043), malignancy (OR: 2.186; 95% CI 1.408-3.392), lower systolic blood pressure (OR: 0.990; 95% CI 0.982-0.998), elevated pulse (OR: 1.013; 95% CI 1.005-1.022), and higher lactate levels (OR: 1.210; 95% CI 1.097-1.334). **Conclusion**: The VExUS score did not predict 6-month mortality in the general cohort of AKI patients in the emergency department. However, VExUS grades 2-3 were associated with lower survival rates in the cardiorenal subgroup and patients with AKI grade 1.

Keywords: acute kidney injury; emergency medicine; organ congestion; venous Doppler; VExUS

Introduction

The coexistence of venous congestion and organ dysfunction constitutes a critical concern in the management of critically ill patients. Among various forms of organ dysfunction, acute kidney injury (AKI) holds particular significance, with extensive research dedicated to understanding the impact of fluid overload on patient outcomes in AKI management [1,2]. Recent findings from a meta-analysis underscore a notable association between fluid overload and mortality in AKI patients, encompassing both sepsis and nonsepsis cohorts [3]. However, the literature presents a heterogeneous landscape, with some studies supporting a clear correlation between fluid overload and impaired renal recovery, while others yield conflicting results [2,3].

Fluid overload is conventionally characterized by an accumulation of fluid surpassing 10% of baseline body weight or a positive daily fluid balance [3]. While these metrics are applicable for patients under continuous monitoring, they pose logistical challenges in settings such as the emergency department (ED) or early hospitalization. In response, the identification of venous congestion through bedside ultrasound has emerged as a promising strategy for critical care practitioners. The venous excess ultrasound (VExUS) score, initially devised as an indirect indicator of venous congestion in cardiac surgery patients [4], has garnered attention for its potential in predicting AKI development [5]. Nevertheless, the literature on the association between this novel score and adverse outcomes in AKI patients remains limited, with only a handful of studies exploring this relationship [6,7].

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This study aims to elucidate the connection between the VExUS score, serving as a surrogate marker of venous congestion, and mortality among ED patients with AKI. Furthermore, we endeavour to explore this association across different AKI subgroups.

Material and methods

Study design and participants

This study constitutes a post-hoc analysis derived from a multidisciplinary prospective observational study aimed at identifying etiological subgroups of AKI [8]. The study was conducted in a tertiary care ED between July 2021 and October 2022. Institutional ethical approval was obtained under protocol number 14.06.2021-550, and the trial was registered on ClinicalTrials.gov (NCT04948710). Written consent was obtained from patients or their relatives.

Participants included individuals aged 18 years and above who were diagnosed with AKI during weekday daytime hours by an emergency physician, following the criteria established by the Kidney Disease: Improving Global Outcomes (KDIGO). AKI was defined as either a 50% or greater increase in serum creatinine from baseline, a rise in serum creatinine of at least 0.3 mg/dL within a span of 2 days, or urine output of less than 0.5 mL/kg/hour for 6 hours [9].

Exclusion criteria encompassed patients with end-stage renal disease, renal or liver transplants, liver malignancy, cirrhosis, cardiac arrest, pregnancy, referral from another hospital after initiation of treatment, postrenal AKI, and refusal to provide consent. Additionally, patients who had already received more than 500 mL of parenteral fluids or more than 40 mg of furosemide were excluded due to the potential influence of fluid therapy and diuretics on venous Doppler patterns.

The subgroups of AKI

Etiological subgroups of AKI were delineated through a meticulous three-stage diagnostic process involving collaboration between nephrologists and emergency physicians [8]. Initially, upon presentation at the ED, all AKI patients underwent consultation with nephrology. Subsequently, in weekly deliberations, a nephrologist and an emergency physician worked jointly to ascertain AKI subtypes by scrutinizing patients' electronic records, which encompassed medical histories, laboratory results, formal radiological tests, and biopsy findings. Upon completion of patient recruitment, all data underwent a comprehensive review utilizing the aforementioned methodology. Throughout this diagnostic assessment, researchers remained blinded to bedside ultrasound examinations. Ultimately, etiological subgroups were categorized as hypovolemia, cardiorenal, systemic vasodilation, renal, and mixed/unknown.

AKI grades were classified according to the KDIGO criteria; grade 1 denoted a rise in creatinine of ≥1.5-1.9 times baseline, grade 2 signified a rise in creatinine of ≥2–2.9 times baseline, and grade 3 indicated a rise in creatinine of ≥3 times baseline.

Additionally, documentation included whether patients underwent emergency hemodialysis (HD) within 24 hours of admission or not.

Ultrasound assessment

Ultrasound evaluations of the venous system for the VExUS score were performed by an experienced emergency physician with a minimum of eight years of bedside ultrasound practice. The parameters assessed included the inferior vena cava (IVC) and the hepatic, portal, and intrarenal veins. The imaging protocol commenced with a renal ultrasound to rule out postrenal causes, followed by capturing images and video clips during periods of calm respiration or at the end of expiration.

The diameter of the IVC was measured in the subcostal view with the patient in the supine position at 2.0 to 3.0 cm from the junction with the right atrium, using the long-axis view [10]. Imaging of the hepatic, portal, and intrarenal veins was performed from the mid-axillary line in the right coronal plane. The hepatic vein flow pattern was assessed as close to the IVC as feasible, portal vein flow was measured from the level of the main portal vein whenever possible, and renal blood flow was recorded from the most distal flow visible on Doppler, avoiding the main renal vessels after switching to the renal presets [8]. In cases where interpretation was considered difficult, multiple images were taken from each region to enhance the accuracy of the measurements.

Doppler pattern evaluation entailed identifying severe abnormalities, including a reversed systolic phase in the hepatic vein, a pulsatility fraction exceeding 50% in the portal vein, and a discontinuous pattern with only a diastolic phase in the intrarenal vein. Subsequently, the VExUS score was graded into four categories based on IVC measurements and Doppler patterns [4] (fig 1). Finally, these images underwent external review by one of the developers of the VExUS score.

Logiq S7 (GE Medical Systems, Milwaukee, Wisconsin) equipped with a 2–5 MHz convex transducer, was used for ultrasound examinations.

Statistical analysis

The collected data were analyzed using SPSS software version 21 (IBM Corp., Chicago, IL, USA) and MedCalc version 15.8 (MedCalc Software bvba, Ostend, Belgium). Continuous variables were presented as median values and interquartile ranges (IQRs), while cat-

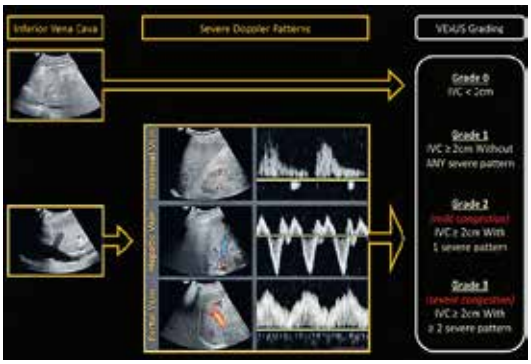

Fig 1. Interpretation of the venous excess ultrasound (VExUS) score. If inferior vena cava (IVC) is <2 cm, it indicates VExUS grade 0; if IVC is >2 cm, it suggests VExUS grades 1-3 based on the number of severe organ Doppler patterns.

egorical variables were summarized as frequencies. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Statistical differences between groups for continuous variables were determined using the Mann–Whitney U test, whereas categorical variables were compared using Pearson's $\chi 2$ test or Fisher's exact test. Odds ratios (ORs) were reported with corresponding 95% confidence intervals (95% CIs), and statistical significance was defined as a critical α value of 0.05.

Kaplan–Meier estimation was utilized to generate observed survival curves for the VExUS score, and hazard ratios (HRs) were calculated for 6-month mortalities. Univariate and multivariate Cox regression analyses were employed to assess the predictive relationship between 6-month mortality and parameters, including the VExUS score, AKI subtypes, AKI grading, demographics, vitals, laboratory tests, and emergency HD within 24 hours. Parameters with values <0.1 in univariate analysis were included in multivariate analysis. In cases where parameters exhibited high correlation factors, only one was included in the analysis.

Results

During the study period, a total of 246 AKI patients were included after applying the exclusion criteria (fig 2). The median age was 74 years (IQR: 65-83), with males comprising 45.1% of the cohort. Mixed/unknown was the most common etiological subtype, accounting for 41.9% of cases. AKI grade 3 was observed in 24% of patients, and the rate of emergency HD was 12.6%. The most prevalent hemodynamic sonographic finding was VExUS grade 0, observed in 68.7% of cases, followed by grade 1 (15.9%), grade 2 (6.1%), and grade 3 (9.3%). The six-month mortality rate was 39.4%. Detailed patient characteristics are presented in Table I.

Kaplan–Meier analyses revealed similar survival rates at six months across four VExUS grades for all AKI patients (p=0.186) (fig 3, Appendix Table I). Grouping of VExUS grades, as 0-1 and 2-3, didn't change survival rates (p=0.062) (fig 3, Appendix Table II).

Cox regression analysis (significance level: p<0.001) identified age (OR: 1.024; 95% CI 1.005-1.043), malignancy (OR: 2.186; 95% CI 1.408-3.392), systolic blood pressure (OR: 0.990; 95% CI 0.982-0.998), pulse (OR: 1.013; 95% CI 1.005-1.022), and lactate (OR: 1.210;

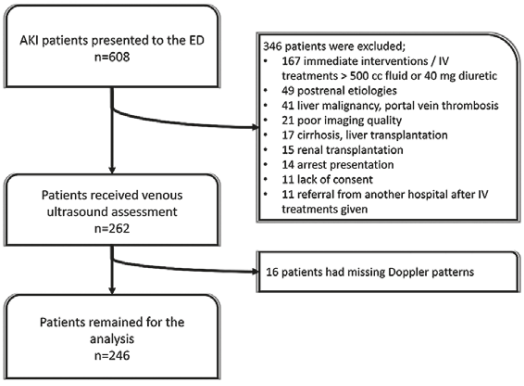

Fig 2. Flow chart of the study

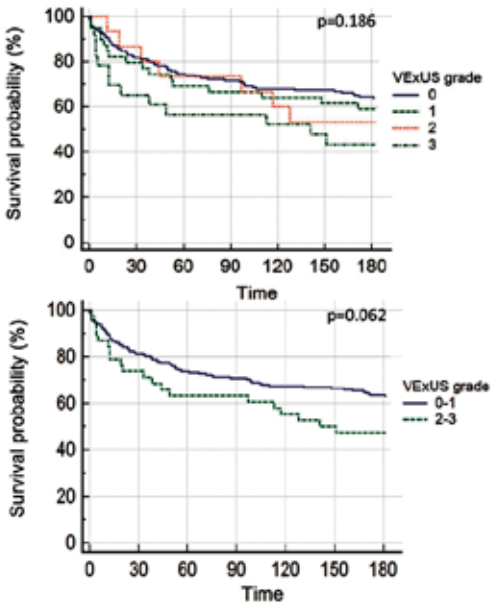

Fig 3. Survival curves of the VExUS score for 6-month mortality

Table I. Comparison of AKI patients regarding mortality status

Parameters	Total n=246	Mortality present n=97	Mortality absent n=149	p
Male gender, n (%)	111 (45.1)	41 (42.3)	70 (47)	0.468
Age, median (IQR)	74 (65-83)	78 (66-86)	72 (63-81.3)	0.022
Comorbidities, n (%)				
Hypertension	174 (70.7)	67 (69.1)	107 (71.8)	0.644
Diabetes mellitus	94 (38.2)	31 (32)	63 (42.3)	0.103
Coronary artery disease	64 (26)	22 (22.7)	42 (28.2)	0.336
Congestive heart failure	54 (22)	28 (28.9)	26 (17.4)	0.035
COPD	29 (11.8)	10 (10.3)	19 (12.8)	0.562
Chronic kidney disease	69 (28)	28 (28.9)	41 (27.5)	0.818
Dementia	22 (8.9)	14 (14.4)	8 (5.4)	0.015
Cerebrovascular disease	31 (12.6)	16 (16.5)	15 (10.1)	0.138
Malignancy	70 (28.5)	36 (37.1)	34 (22.8)	0.015
Vitals, median (IQR)				
Systolic	119 (100-138)	111 (91-130)	126 (107-143)	0.002
Diastolic	70 (60-84)	67 (60-85)	72 (62-82)	0.058
Pulse	94 (80-110)	101 (80-118)	91 (80-105)	0.005
Saturation	94 (88-96)	90 (83-95)	95 (90-96)	<0.001
AKI subtypes, n (%)				
Hypovolemia	96 (39)	25 (25.8)	71 (47.7)	<0.001
Cardiorenal	23 (9.3)	13 (13.4)	10 (6.7)	0.078
Renal	11 (4.5)	4 (4.1)	7 (4.7)	1.000
Systemic vasodilatation	13 (5.3)	8 (8.2)	5 (3.4)	0.094
Mixed-unknown	103 (41.9)	47 (48.5)	56 (37.6)	0.091
AKI Grade, n (%)				
1	114 (46.3)	38 (39.2)	76 (51)	0.161
2	73 (29.7)	31 (32)	42 (28.2)	
3	59 (24)	28 (28.9)	31 (20.8)	
Emergency HD, n (%)	31 (12.6)	19 (19.6)	12 (8.1)	0.008
Laboratory, median (IQR)				
Creatinine	2 (1.6-3.1)	2.2 (1.7-3.2)	2 (1.6-2.9)	0.130
GFR	26 (16.8-36)	24 (15-33.5)	28 (19-37)	0.075
BUN	50 (36-77)	61.8 (41-98)	45 (35-66)	<0.001
Potassium	4.4 (3.8-5.1)	4.5 (3.8-5.3)	4.3 (3.8-5)	0.356
Sodium	136 (132-139)	136 (132-140)	135 (132-138)	0.297
Lactate	1.7 (1.1-2.4)	1.8 (1.2-2.9)	1.6 (1.1-2.2)	0.018
Chlore	102 (97-106)	103 (97-106)	102 (98-106)	0.859
IVC maximum, median (IQR)	15 (12-21)	15 (11-22)	15 (12-20)	0.543
VExUS grade, n (%)				
0	169 (68.7)	61 (62.9)	108 (72.5)	0.265
1	39 (15.9)	16 (16.5)	23 (15.4)	
2	15 (6.1)	7 (7.2)	8 (5.4)	
3	23 (9.3)	13 (13.4)	10 (6.7)	
VExUS group, n (%)				
0-1	208 (84.6)	77 (79.4)	131 (87.9)	0.070
2-3	38 (15.4)	20 (20.6)	18 (12.1)	

COPD, chronic obstructive pulmonary disease; HD, hemodialysis

95% CI 1.097-1.334) as predictors for 6-month mortality (Table II).

AKI subgroups and mortality

The log-rank test was performed for two VExUS groups and mortality among various AKI subgroups. In the cardiorenal subgroup, VExUS grades 2-3 were associated with lower survival rates (HR: 3.98 [95% CI: 1.33–11.93]). Survival rates were similar between VExUS grades 0-1 and 2-3 for other etiological subgroups. Within each AKI grade, VExUS grades 2-3 were associated with decreased survival only in AKI grade 1 (HR: 4.07 [95% CI: 1.74–9.49]). Survival rates were also similar in patients requiring emergency HD.

Table II. Cox regression analysis for 6-month mortality in AKI

Parameters	OR (%95 CI)	p
Age	1.024 (1.005-1.043)	0.013
Malignancy	2.186 (1.408-3.392)	<0.001
Systolic blood pressure	0.990 (0.982-0.998)	0.016
Pulse	1.013 (1.005-1.022)	0.003
Lactate	1.210 (1.097-1.334)	<0.001

Discussion

This study investigated the relationship between venous ultrasound findings indicative of organ congestion and mortality in AKI patients in the ED. The regression analysis found that the VExUS score, serving as an indirect marker of organ congestion, did not exhibit a significant association with mortality in this cohort. In the subgroup analyses, there was a notable relationship between the VExUS score and mortality, specifically in patients with AKI grade 1 and cardiorenal AKI. However, this association was not present in other AKI etiological subgroups or the administration of emergency HD.

The existing literature on the relationship between the VExUS score and mortality in AKI patients is limited. A prospective cohort study by Beaubien-Souligny et al examined severe AKI patients and found that individual ultrasound parameters of congestion and the VExUS score at enrolment were not associated with major adverse kidney events at 30 days in the intensive care unit (ICU). However, the VExUS score was linked to 90-day mortality, with patients having a VExUS grade ≥2 often presenting with cardiovascular diagnoses at a rate of 80% [6]. Despite sharing similar methodological aspects, the outcomes of this study and the present study diverged. Several factors could contribute to these disparate findings. Firstly, differences in clinical settings, such as ICU versus ED, likely played a significant role. These settings exhibit distinct causes of AKI; ICU-related AKI is frequently driven by cardiovascular and sepsis diagnoses, while ED-related AKI commonly arises from hypovolemic conditions. Secondly, variations in AKI grades for enrollment may have influenced outcomes. While the ICU study focused on severe AKI cases, the current study included all AKI grades in the ED setting. However, this discrepancy may be less impactful, as our findings indicate a relationship between the VExUS score and mortality only in AKI grade 1 rather than grades 2 or 3.

The use of the VExUS score has been explored in various clinical settings [11,12]. For instance, a randomized controlled study by Islas-Rodríguez et al investigated whether VExUS-guided decongestant therapy enhances kidney function recovery (KFR) in patients with cardiorenal syndrome. Interestingly, while survival at 90 days and KFR were similar between VExUS-guided and control groups, the study found that VExUS-guided therapy doubled the odds of achieving successful decongestion [7]. Conversely, in a quasi-experimental study, Rihl et al. observed that patients with severe AKI in the ICU who experienced a reduction in their VExUS scores within 48 hours exhibited lower in-hospital mortality rates compared to those whose scores did not decrease [13]. On the other hand, Andrei et al. reported no association between the VExUS score and 28-day mortality or AKI in the ICU [14]. In the literature, some other ultrasound parameters were used to predict mortality in AKI [15,16]. Given these conflicting findings, additional data are warranted to fully leverage ultrasound examination, including the VExUS score, in predicting mortality in AKI patients.

According to subgroup analysis results, the significant difference in survival despite the small number of patients in the cardiorenal subgroup of the present study highlights the potential of the VExUS score to aid in risk stratification and management decisions in these patients. Higher VExUS scores were also associated with decreased survival in AKI grade 1. This result may be primarily due to the higher rate of venous congestion ultrasound findings and the prevalence of patients with cardiorenal diagnoses in AKI grade 1 (Appendix Table III-IV). We concluded that consistent with the initial publication of the VExUS score and supported by other studies, the score is more effective in predicting cardiorenal syndrome and determining prognosis [4,5,8].

In the present study, Cox regression analysis revealed several factors associated with 6-month mortality, including higher age, the presence of malignancy, lower systolic blood pressure, elevated pulse, and higher lactate levels. These findings are consistent with those reported by Gross et al, who identified age ≥65 years and the presence of cardiovascular disease, dementia, heart failure, and malignancy as correlates of 90-day mortal-

ity in patients with community-acquired AKI [17]. These results underscore the multifactorial nature of mortality prediction in AKI and highlight the importance of considering various clinical and demographic factors in risk stratification and management decisions.

There are several limitations to consider in this study. Firstly, it is a single-center study, which may limit the generalizability of the findings to other settings or populations. Additionally, the enrolment of patients was restricted to weekday daytime hours, potentially introducing selection bias. However, despite these constraints, the study included the highest number of AKI patients with VExUS scores reported in the literature to date over a one-year study period. Another limitation pertains to the subgroup analyses, where the number of patients decreased for analysis. This reduction in sample size could lead to over- or under-estimation of the results and may limit the robustness of subgroup-specific conclusions.

Despite these limitations, the study provides valuable insights into the relationship between the VExUS score and mortality in AKI patients, adding to the growing body of literature on this topic. Future studies incorporating larger, multicenter cohorts and employing standardized enrolment procedures could address some of these limitations and provide further clarity on the utility of the VExUS score in predicting outcomes in AKI.

Conclusion

Our study found that the VExUS score, utilized as a sonographic tool to assess venous congestion, did not demonstrate a significant association with 6-month mortality among AKI patients in the ED. This lack of association persisted across various AKI subgroups. Notably, the only observed relationship between the VExUS score and mortality emerged in patients with AKI grade 1 and cardiorenal AKI subgroups.

Conflict of interest: none

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