ORIGINAL ARTICLE

Venous Congestion Assessed by Venous Excess Ultrasound (VExUS) and Acute Kidney Injury in Children with Right Ventricular Dysfunction

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Abstract

Background: Right ventricular dysfunction (RVD) is a complication following congenital cardiac surgery in children and can lead to systemic venous congestion, low cardiac output, and organ dysfunction. Venous congestion can be transmitted backwards and adversely affect encapsulated organs such as the kidneys.

Primary objective: To investigate the association between systemic venous congestion, as estimated by Venous Excess Ultrasound (VExUS), and the occurrence of acute kidney injury (AKI) in children with RVD following congenital heart surgery. Secondary objectives included comparing changes in VExUS scores after initiating treatment for RVD and venous congestion.

Methods and results: This was a prospective observational study in children with RVD. The VExUS study was performed on day 1, day 2, and day 3 and categorized as VExUS-1, VExUS-2, and VExUS-3. Among 43 patients with RVD and dilated inferior vena cava, 19/43 (44%), 10/43 (23%), and 12/43 (28%) were VExUS-2 and VExUS-3, respectively. There was an association between severe RVD and elevated pulmonary artery systolic pressures and a VExUS score >2. A significant association was observed between central venous pressure (CVP) measurements and VExUS. Among 31 patients with a high VExUS score >2, 18 (58%) had AKI. Additionally, improvement in CVP and fluid balance was associated with improving VExUS scores following targeted treatment for RVD.

Conclusion: VExUS serves as a valuable bedside tool for diagnosing and grading venous congestion through ultrasound Doppler. An elevated VExUS score was associated with the occurrence of AKI, and among the components of VExUS, portal vein pulsatility may be useful as a predictor of AKI.

Keywords: Acute kidney injury, Children, Right ventricular dysfunction, Venous congestion, Venous excess ultrasound.

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Highlights

- In patients with right ventricular dysfunction, venous congestion can be assessed by a venous excess ultrasound (VExUS) exam at the bedside.
- A VExUS score >2 is associated with acute kidney injury (AKI) following congenital heart surgeries.
- VExUS provides insight to optimize reno-protective strategies in patients with ventricular dysfunction.

Introduction

Right ventricular dysfunction (RVD) following surgery for congenital heart disease (CHD) in children remains an important complication associated with elevated filling pressures, low cardiac output (CO), organ dysfunction, and mortality.[1] Traditionally, managing hemodynamics in these children has centered around fluid management and the use of vasoactive agents to maintain CO and arterial blood pressures. Both low CO and elevated systemic venous pressures can contribute to reduced organ perfusion. However, elevated venous pressures are often overlooked. Elevated venous pressures are transmitted backward to organs, raising capillary hydrostatic pressure and impeding blood flow, especially in encapsulated organs such as the kidneys.[2] The development of acute kidney injury (AKI) postoperative cardiac surgery can be multifactorial, such as prolonged cardiopulmonary bypass time, low CO, nephrotoxic drugs, and sepsis (yuan). Systemic venous congestion and elevated filling may also be important. Studies in adults have demonstrated that elevated venous pressure primarily drives kidney dysfunction rather than diminished CO.[3] Altered portal

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and intrarenal venous flow have been demonstrated to predict AKI in postoperative CHD patients.[4] The Venous Excess Ultrasound (VExUS) score, a grading tool that evaluates inferior vena cava (IVC), hepatic, portal, and renal venous flow patterns using pulsed-wave Doppler ultrasound, has emerged as a semiquantitative measure of venous congestion. An elevated VExUS score indicating severe congestion has demonstrated a greater positive likelihood ratio for predicting AKI compared to central venous pressure (CVP) in adults after cardiac surgery. While there are reports in adult literature,[4,5] there is a lack of pediatric data evaluating the association of venous congestion with AKI. The primary objective of this study was to evaluate the association between VExUS and the occurrence of AKI in children with RVD after surgery for CHD.

Methods

We conducted this prospective observational study in children aged 1 month to 17 years in a pediatric cardiac intensive care unit in a tertiary care hospital between June 2021 and March 2022. The study protocol was approved by an independent ethics committee (IRB: ACH-DNB-003/01-21). Informed consent was obtained from the parents/guardians for study participation. The study was conducted in accordance with the 1964 Declaration of Helsinki.

Study Population

We included children with RVD and dilated IVC in whom VExUS could be performed after corrective cardiac surgery. Children with residual or uncorrected lesions, single ventricle physiology, preexisting established AKI, need for preoperative invasive ventilation, vasopressor/inotropes, and preoperative cardiac arrest were excluded. Children with poor acoustic windows were also excluded.

Ultrasound Measurements

Ultrasound evaluation was performed at the bedside by either of the authors RN or AK, both of whom were certified in advanced ultrasound. A portable echocardiography machine (Philips Affiniti 50, Amsterdam, the Netherlands) with a C 6-2 (2–6 MHz) curved array and C 8–5 (5–8 MHz) curved transducers was used. Patients were positioned supine with their heads elevated at 30°. The evaluation began by assessing the IVC. B-mode images of the IVC and aortic images were obtained in the transverse plane. The maximum diameters of the aorta and IVC were measured. The size of the IVC varies with age. We used the IVC/aortic diameter ratio established for children.[6] The IVC was considered dilated if the IVC/aorta ratio was greater than 0.83 in infants <1 year, 0.92 (1–4 years), 0.9 (4–7 years), 1.07 (7–10 years), 1.11 (10–13 years), and 1.22 (13–16 years). Patients who had RVD based on the criteria described below and a dilated IVC were included in the study.

For the assessment of Doppler studies, the transducer was positioned transversely in the right hypochondrium to perform hepatic vein Doppler (HVD) and portal vein Doppler (PVD) as described previously.[4] The technique of Doppler imaging and the grading of Doppler waveforms are described in SDC: (Fig. 1).[4] To mitigate respire-phasic variation, three readings were averaged.

When venous Doppler demonstrated a mildly abnormal pattern, VExUS was grade I, grade II, and III when one or more than two venous Doppler patterns were severely abnormal, respectively.[7]

Following the initial echocardiogram and VExUS evaluation on postoperative day 1, examinations were repeated on day 2 and day 3. The association of VExUS with AKI was done on day 2. Therapeutic decisions such as vasoactive agents, diuretics, dialysis, pulmonary vasodilators, and other treatments options were based on clinical exams, echocardiography, and laboratory findings, and the treating team was unaware of the VExUS findings.

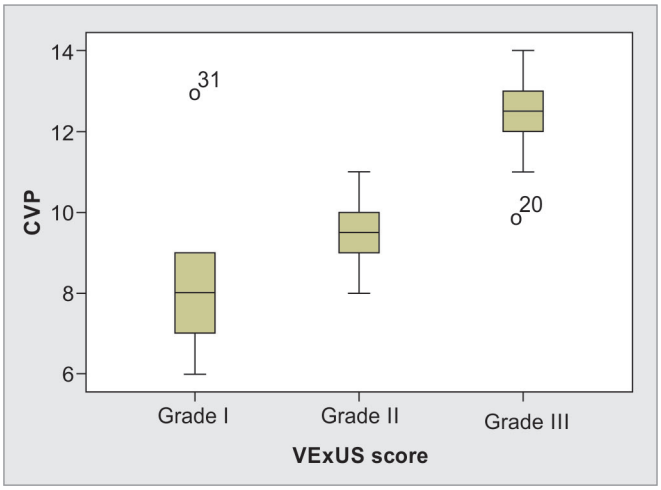

Fig. 1: CVP central venous pressure

Definition(s)

There are several ways to quantify RVD, each with its own strengths and limitations. We used the tricuspid annular peak systolic excursion (TAPSE) because it is reproducible and easy to perform.[8] The TAPSE reflects the longitudinal systolic displacement of the lateral annulus during systole and is measured by M-mode. With an increasing degree of RVD, the tricuspid annular excursion progressively decreases, and age-appropriate TAPSE values <1 SD, <2 SD, and <3 SD was considered mild, moderate, and severe RVD, respectively.[9]

The estimation of the pulmonary artery systolic pressures (PASP) was based on the peak velocity of the tricuspid regurgitant velocity (TRV) jet. The simplified Bernoulli equation using continuous wave (CW) Doppler to assess RVSP [Right Ventricular Systolic Pressures (RVSP) = $4 \times (TRV)^2 + CVP$)]. CVP measurements were performed using methods. RVSP was used as a surrogate of PASP in the absence of RV outflow tract (RVOT) obstruction. PASP was considered high if RV pressures were >36 mm Hg.[10,11]

Left ventricular (LV) dysfunction was considered if ejection fraction was <55%.[12]

AKI was defined and staged by the pRIFLE criteria.[13] AKI stages 1, 2, and 3, corresponding to risk, injury, and failure, respectively, were determined based on a percentage decline in creatinine clearance of 25%, 50%, or 75%, respectively.[14] We preferred the pRIFLE criteria because it is the most sensitive test for detecting AKI.[15]

Data Collection

Demographics and hemodynamic parameters, including mean CVP, echocardiographic recording of left ventricular ejection fraction (LVEF), TAPS, tricuspid regurgitation, pulmonary artery systolic pressures (PASP), and VExUS readings, were captured on postoperative day 1, day 2, and day 3. Cardiopulmonary-bypass and aortic cross-clamp duration, cumulative fluid balance, serum creatinine levels, and the need for vasoactive agents, mechanical ventilation, and renal replacement therapy were recorded.

Study Outcomes

The primary objective of this study was to determine the association between venous congestion as estimated by VExUS and the occurrence of AKI in postoperative children with RVD after CHD repair. The secondary objective was to compare the change in VExUS score after the initiation of treatment for RVD and venous congestion.

Statistical Analysis

Statistical analysis was performed by SPSS, version 19 (Chicago, 2019). The normality of the data was assessed by Shapiro–Wilk test. Continuous variables were expressed as the mean (standard deviation) or median (interquartile range). Group comparison was performed using ANOVA for normally distributed data and Kruskal–Wallis test for non-normally distributed data. Categorical variable data were expressed as frequency (percentages). To study the association between VExUS and echocardiography and VExUS and AKI, a Chi-square test was used. VExUS and CVP were compared using ANOVA.

A p-value < 0.05 was considered significant. Receiver operating curve (ROC) was generated to evaluate components of VExUS in predicting AKI. The sensitivity and specificity of VExUS in predicting AKI were calculated.

Results

During the study period, 43 children were included (SDC Fig. 2). The baseline characteristics and clinical data are represented in Table 1.

Ultrasound Assessment, Association with Echo Parameters, and CVP (Table 2)

At the initial evaluation, VExUS–1, –2, and –3 scores were documented in 10/43 (23%), 12/43 (28%), and 19 (44%) children, respectively. Notably, prolonged cardiopulmonary bypass (CBP) times were associated with VExUS-3 (VExUS-3, 218 min [189–245] vs VExUS-2, 136 min [97.5–162], $p < 0.001$). The association between VExUS and echocardiographic parameters is described in Table 2 and SDC (Fig. 3). The VExUS-3 was observed in all 19 patients with moderate-severe RVD ($p < 0.001$). There was a significant association between high PASP and VExUS (VExUS-2: 2/12 vs VExUS-3: 14/19, $p < 0.001$). The association of VExUS with LV systolic and diastolic dysfunction was not significant.

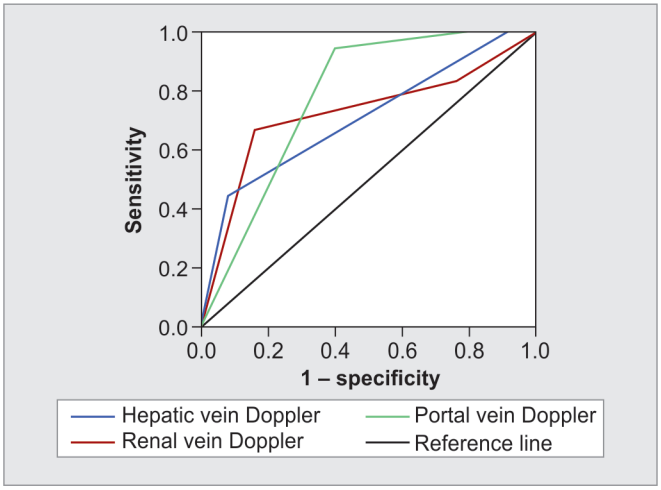

Fig. 2: ROC receiver operative curve. An elevated CVP > 8 mm Hg was observed in 11/12 patients with VExUS-2 and 19/19 patients with VExUS-3, $p < 0.001$). Patients with VExUS-2 and VExUS-3 exhibited median CVP of 9 mm Hg and 12 mm Hg, respectively (Fig. 1). The mean difference between CVP and VExUS-3 was 4.26 mm Hg (95% CI: 2.99–5.53, $p < 0.001$). Furthermore, a clear correlation existed between VExUS-3 grade and positive fluid balance

Table 1: Demographics and baseline characteristics according to VExUS

Variables	*VExUS-1*	*VExUS-2*	*VExUS-3*	*p-value*
Number of patients (*n*%)	10 (24%)	12 (29.3%)	19 (46.3%)	
Age (months) Median (IQR)	24 (10–25%)	121 (2.5–31%)	12 (6–26%)	0.2
Gender: Female (*n*%)	7 (70%)	7 (58.3%)	8 (42%)	0.33
CBP (minutes) Median (IQR)	127 (98–168%)	136 (97.5–162%)	218 (189–245%)	<0.001
Cross clamp time (min) median (IQR)	93.5 (73–106%)	93 (58–117%)	106 (81–130%)	0.6
HR (BPM) Median (IQR)	144 (135–154%)	136 (130–150%)	140 (140–154%)	0.5
SBP (mm Hg) Median (IQR)	80 (69–98%)	77 (70–88%)	70 (60–80%)	0.16
MBP (mm Hg) Median (IQR)	51 (46–68%)	54 (47–63%)	45 (40–50%)	0.09
Hypotension SBP<5th centile (*n*%)				
Intubated (*n*%)	7 (70%)	12 (100%)	18 (94.7%)	0.04
RVD (*n*%)	1 (10%)	1 (8.3%)	19 (100%)	<0.001
LV dysfunction (EF%)	50 (40–56%)	50 (45–55%)	50 (40–50%)	0.38
LV diastolic dysfunction (*n*%)	6 (60%)	6 (42%)	13 (68%)	0.33

CBP, cardiopulmonary bypass; EF, ejection fraction; IQR, interquartile range; LV, left ventricle; MBP, mean blood pressures; RVD, right ventricular dysfunction; SBP, systolic blood pressures; VExUS, venous excess ultrasound

Table 2: Association of venous excess ultrasound score with and echocardiographic parameters and central venous pressure

	VExUS-1 (n = 12)	*VExUS-2 (n = 12)*	*VExUS-3 (n = 19)*	*p-value*
Right ventricular dysfunction (moderate and severe)	1 (4.8%)	1 (4.85%)	19 (90.5%)	<0.001
High pulmonary artery systolic pressures (PASP)	1 (5.5%)	2 (11.8%)	14 (82.4%)	<0.001
LV dysfunction: EF <55%	7 (24.1%)	7 (24.1%)	15 (51.7%)	0.358
Diastolic dysfunction E/e'	7 (28%)	5 (20%)	13 (52%)	0.339
Hepatic vein Doppler				
Normal	2 (100%)	0	0	<0.001
Mild abnormality	10 (32%)	12 (38%)	9 (9%)	
Severe abnormality	0	0	10 (100%)	
Portal vein Doppler				
Normal	5 (100%)	0	0	<0.001
Mild abnormality	7 (63.6%)	4 (36%)	0	
Severe abnormality	0	8 (29%)	19 (70%)	
Renal vein Doppler				
Normal	6 (66%)	1 (11%)	2 (22%)	<0.001
Mild abnormality	6 (33%)	11 (61%)	1 (5%)	
Severe abnormality	0	0	16 (100%)	
CVP >8 mm Hg	4 (11.8%)	11 (32%)	19 (55%)	<0.001
CVP mm Hg, mean (SD)	8 (1.90)	9.5 (0.9)	12.26 (0.99)[a]	<0.001[b]
Positive fluid balance (>10%), *n*%	0	6 (26%)	17 (73%)	<0.001

[a]mean difference: 4.26 mm Hg between VExUS-3 and VExUS-1 (95% CI: 2.99–5.53); [b]$p < 0.001$ VExUS-3 vs VExUS-1; CVP, central venous pressure; EF, ejection fraction; SD, standard deviation; VExUS, venous excess ultrasound

Table 3A: Association of VExUS with kidney function

	AKI	
Variables	*Yes*	*No*
VExUS-1	0	12 (100%)
VExUS-2	3 (25%)	9 (75%)
VExUS-3	15 (78%)	4 (21%)[a]
HVD1	0	2 (100%)
HVD2	10 (32%)	21 (69%)
HVD3	8 (80%)	2 (20%)
PVD1	0	5 (100%)
PVD2	1 (9%)	10 (90%)
PVD 3	17 (63%)	10 (37%)
RVD1	3 (33%)	6 (66%)
RVD2	3 (16%)	15 (83%)
RVD3	12 (75%)	4 (25%)[d]

[a]$p < 0.001$ VExUS-3 vs VExUS-2; [d]$p < 0.002$ VExUS-3 vs VExUS-2; AKI, acute kidney injury; HVD, hepatic vein Doppler; PVD, portal vein Doppler; RVD, renal vein Doppler; VExUS, venous excess ultrasound score

Table 3B: Sensitivity and sensitivity of VExUS in predicting AKI

	Value (%)	*95% CI*
Sensitivity	83.3%	58–96
Specificity	84%	63–95
Positive likelihood ratio	5.1	2.0–13
Positive likelihood ratio	0.2	0.07–0.5
Positive predictive value	78.9%	59–90
Negative predictive value	87.5%	71–95

CI, confidence interval

Association of VExUS Grading with AKI (Tables 3A and B)

Among 19 patients with VExUS-3, 15 patients had AKI, compared to 3/12 patients with VExUS-2, $p < 0.001$. The area under the ROC for the prediction of AKI was 0.70, 0.77, and 0.72 for HVD, PVD, and RVD, respectively (Fig. 2). The sensitivity and specificity of VExUS in predicting AKI were 83% and 84%, respectively, with a positive likelihood ratio of 5.1.

Change in VExUS Score with Treatment (SDC Table 1)

On day 3, patients were characterized into two groups of "improving" and "no change," determined by the VExUS score transition from VExUS-3 to VExUS-2/VExUS-1 or VExUS-2 to VExUS-1. A significant association was observed between fluid balance and improvement in CVP with improvement in VExUS grade, $p < 0.001$.

Discussion

Among children with RVD following CHD surgery, there was an association of venous congestion as assessed by VExUS and AKI. Following supportive treatment for RVD, including decongestive therapies, we observed a decrease in the VExUS score as well as a reduction in CVP and pulmonary artery systolic pressures.

Right ventricular dysfunction is a common occurrence following congenital heart surgery and may lead to organ dysfunction.[16] We observed a significant association between RVD and higher VExUS scores. Portal flow alteration, a component of VExUS, has previously been shown to be associated with RVD in adults following cardiac surgery.[17] Similarly, in our study, all children with severe RVD and VExUS-3 had high portal vein pulsatility (>30%). Challenges in assessing RV function in the immediate postoperative period due to limited access and acoustics can be mitigated by incorporating

easily performed portal vein Doppler.[18] Moreover, portal vein pulsatility has been reported to have superior predictive value over echocardiographic parameters in identifying RVD-related complications[17] and may serve as an alternative diagnostic tool for RVD. Long cardiopulmonary bypass times could explain the high VExUS score, considering the increased incidence of RVD. This highlights the potential utility of VExUS in assessing fluid status in this setting.[19]

Central venous pressure measurements may reflect both RVD and circulating volume.[20] Our study established an association between VExUS and CVP, underscoring the utility of VExUS as a marker for evaluating venous congestion. These findings align with a recently published pediatric study.[21]

Traditionally, renal hypoperfusion secondary to hypotension ± low CO has been incriminated as the central cause of AKI risk. Venous congestion as a cause of AKI has not been previously described in children except following surgery for univentricular hearts and Fontan completion.[22]

High systemic venous pressures can negatively impact organs, particularly capsulated organs such as the kidneys, and cause AKI. The incidence of AKI in cardiac surgical patients varies between 10 and 30%.[23] We observed AKI in 41% of patients with VExUS scores of >2. While both abnormal portal and renal vein Doppler were predictive of AKI, portal vein Doppler demonstrated superior performance when compared to other components of VExUS. Studies in adults have shown intrarenal vein flow abnormalities rather than portal vein pulsatility are associated with AKI.[4]

Venous congestion can increase intracapsular pressure and interstitial edema, hampering both venous and lymphatic outflow.[24] Additionally, cardiopulmonary bypass and fluid overload can damage the endothelial glycocalyx and worsen interstitial edema.[25] As a consequence, renal perfusion pressure, determined by the inflow and outflow gradients, can be severely affected by low CO when coupled with a high CVP from RVD ± fluid overload.[26] Implementing measures to optimize right ventricular function can ameliorate venous congestion. In our cohort, we observed improved CVP and VExUS using combination therapy including inotropes, negative fluid balance, and pulmonary vasodilators, all of which may have been helpful to improve RV function and thereby enhance renal perfusion. Reports in adult patients have reported improvement in portal vein pulsatility when inhaled pulmonary vasodilators were employed, suggesting the potential benefits of such interventions in managing venous congestion and its associated complications.[27]

Limitations

This is a small, single-center study focusing on cardiac surgical patients and cannot be extrapolated to other critically ill children. We used the pRIFLE classification, which has demonstrated superior performance compared to the Acute Kidney Injury Network (AKIN) criteria or Kidney Disease: Improving Global Outcomes (KDIGO) criteria for diagnosing AKI.[28] However, substantial disparities in staging leading to variations in the incidence of AKI have been reported with pRIFLE compared to other criteria.[29] We did not examine other potential confounding variables, such as hypotension, that could contribute to AKI. Larger studies are required to establish the cause-and-effect relationship between the various risk factors in this high-risk cohort and to determine whether a change in VExUS is a suitable therapeutic target.

Conclusion

In pediatric postoperative cardiac surgery patients with right ventricular function, VExUS score may be a useful predictor of AKI. The potential effectiveness of tailoring treatment strategies to reverse abnormal venous flow patterns in order to prevent organ dysfunction warrants further evaluation.

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