EDITORIAL

VExUS Score: Making Waves in an Ocean but Still a Mirage in the Desert

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Systemic venous congestion is a significant clinical problem that can lead to organ dysfunction with an increase in morbidity and mortality. The trajectory of acutely resuscitated or chronic critically ill patient is often punctuated by pathophysiological changes of organ failure which are attributable to hypo perfusion due to systemic venous congestion. These organ failures result in an increased length of stay in the intensive care unit (ICU), prolonged duration of mechanical ventilation, use of renal replacement therapy, increased morbidity and short-term mortality. The venous excess ultrasound (VExUS) score has emerged as a tool to address this challenge. It documents organ congestion in the larger context of systemic venous congestion. It is a dynamic measure which tracks systemic venous congestion and decongestion in real time and hence helps monitor and titrate the contribution of systemic venous congestion towards end organ hypo perfusion.

Since the original description of VExUS by Beaubien-Souligny et al. for successfully predicting acute kidney injury (AKI) in a cohort of cardiac surgical patients, there has been a surge of studies to extrapolate use of VExUS in predicting AKI in different subsets, especially in those with cardio renal syndrome and in the critically ill.[1–4] The performance of VExUS in predicting AKI in cardio renal syndrome and its resolution with decongestion is clinically significant.[3] However, this predictive value is not consistently significant in the general critically ill patient.[4,5] This difference stems from the fact that systemic venous congestion is an important component of the pathophysiology of AKI in the patient with cardiorenal syndrome as compared to the general critically ill patient where the pathophysiology of AKI is multifactorial.

The study by Khan et al. is a single center prospective observational study that enrolled 30 carefully selected general non-cardiac critically ill patients, excluding those with cardiac disease, pre-existing AKI, chronic kidney and chronic liver disease. The authors investigated the hypothesis that VExUS score could identify patients at risk for AKI in this cohort. The primary outcome was to assess the association between serial VExUS scores and the development of AKI as per the acute kidney injury Network (AKIN) criteria. The secondary outcomes were the correlation between VExUS scores and fluid balance, P/F ratio, duration of mechanical ventilation, ICU length of stay, Glasgow outcome score, and 30-day mortality. VExUS scoring was done at admission, and daily for six days or until AKI developed, whichever occurred first.[6]

In this small sample size with robust statistical analyses, the authors report a high incidence of AKI (73%). They attribute this high incidence of 73% as compared to the 22% reported by Andrei et al. to their inclusion of patients on rising vasopressor support, while the latter group excluded patients of shock not responding to vasopressors.[5] Most patients had stage I AKI (43%). The incidence of mild congestion was 41%, moderate congestion was 47%, and severe congestion 11% in the AKI group. The mean VExUS scores were significantly higher in the AKI group as compared to the non-AKI group on day 2, day 3, and day 5 of ICU stay with the receiver operating characteristic (ROC) analysis demonstrating a strong ability for VExUS score to distinguish between patients with and without AKI on day 2 and day 3. Logistic regression did not reveal any significant correlation between the VExUS scores on day 2 and day 3 and the development of AKI. There was a moderative positive correlation between VExUS score and fluid balance on day 2 and day 3. There were no significant correlations between VExUS scores and any other variable.[6] The results were similar to Andrei et al. who in a cohort of 145 general ICU patients did not demonstrate any significant association between the VExUS scores and development of AKI or 28-day mortality but discordant with the results of Beaubien-Souligny et al. who demonstrated a significant correlation between severe congestion on VExUS scoring and 30-day mortality in a cohort of patients with severe AKI as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) stage II or higher. This difference was attributed to a higher number of patients with severe congestion in the latter study.

The small sample size of 30 against 173 screened subjects highlights the first challenge in performing VExUS scoring. Most studies on VExUS exclude patients at both extremes of the clinical spectrum. The less severely ill do not qualify for VExUS scoring while

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the most severely ill are excluded by study design, e.g., refractory shock, anticipated to survive less than 48 hours, on mechanical circulatory support, and pre-existing organ failure.[4,5,7] This translates into the fact that studies capture only the intermediate quartile of sickness, limiting the generalizability and performance of the score. There is also a consistent dropout in the number of patients undergoing ultrasound as studies progress due to development of AKI (primary end point achieved), correction of fluid balance or initiation of vasopressors by the treating physician (pragmatic study design), poor echo window precluding full assessment, ICU discharge, and death. This attrition ensures that the study does not capture deteriorating patients and is restricted to patients who remain in the quartile of intermediate degree of sickness.

The size of inferior vena cava (IVC) as the dichotomous factor for initiating VExUS scoring is in itself contentious. The size of IVC varies with body mass index being smaller in Asians, as well as with disease pathology, e.g., raised intra-abdominal pressure (small IVC) highlighting the fact that IVC $\geq$ 2 cms may not be present despite systemic venous congestion.[8] Individual Doppler components of the score like portal venous pulsatility and interlobar renal vein flow pattern in themselves perform better and have a significant correlation with systemic venous congestion and their ability to predict AKI questioning the very basis of integrating the role of IVC and that too in a dichotomous rule in or rule out manner.[9,10]

The correlation of VExUS score with fluid balance is not uniformly distributed across the entire range of fluid overload. VExUS score correlates better with fluid balance when there is a significant daily or cumulative fluid overload. The association of VExUS score with mortality is significant in the presence of moderate or severe congestion as compared to the presence of mild congestion.[4,5] In the study by Khan et al. there was a significant positive correlation between fluid balance on day 2 and 3 for the entire cohort with the VExUS score. There was however no significant difference in the daily and cumulative fluid balance between those who developed AKI as compared to those who did not develop AKI, except for day 3 where the fluid balance was significantly higher in the AKI group. The VExUS score did not have any predictive value for AKI. This highlights the fact that fluid balance and VExUS score may not have a predictive value for AKI when the predominant pathophysiology of AKI is not systemic venous congestion, as was seen in this subset of non-cardiac critically ill patients. The VExUS score was not significantly different between survivors and non-survivors, again highlighting the fact that it performs best when there is significant difference in fluid balance between the groups. This profile is expected in patients with severe congestion, as in cardiac failure and severe AKI.

Venous excess ultrasound score is only one indicator of systemic venous congestion and has to be interpreted in the context of other signs of congestion like transduced central venous pressure (CVP), left heart filling pressures (E/e'), and the lung ultrasound score, together with evaluation of left and right ventricular systolic and diastolic function. Excluding patients with cardiac function at baseline is not helpful either as a variable percentage of patients develop sepsis related myocardial dysfunction or stress cardiomyopathy or acute cor pulmonale during the course of critical illness and their contribution to the score may be falsely attributed to fluid overload rather than to cardiac dysfunction. This will preclude a response to decongestion warranting the management of the underlying cause, e.g., titrating inotrope support, optimizing positive end expiratory pressure (PEEP), or initiating pulmonary vasodilator therapy. Hence, VExUS score is best done as part of a comprehensive critical care echocardiography hemodynamic assessment. Studying VExUS score in isolation is akin to driving a car with one wheel.

Adding to this complex picture is the fact that critically ill patients may not have a stable hemodynamic trajectory and may need fluid resuscitation and alteration of dose of vasopressors. The coexistence of a fluid responsive and venous congestion state makes it more difficult to titrate fluid therapy. In the study by Munoz et al. there was no association between fluid balance at diagnosis and the presence of venous congestion signals. The venous congestion signals were equally distributed in the fluid responsive and non-responsive group, but the VExUS score was significantly higher in the fluid non-responsive group. The prevalence of fluid responsiveness and venous congestion were similar among patients with normal and abnormal capillary refill time. Thus, a patient with normal capillary refill time who is fluid non-responsive and has venous congestion will benefit from decongestion while a patient with an abnormal capillary refill time who is fluid responsive but has venous congestion will require additional resuscitation strategies such as inotrope, vasopressor, inodilator, and titration of mechanical ventilation settings.[7] The episodes of hypotension and the fluid loading as well as adjustment of dose of vasoactive agent or settings of mechanical ventilator or reduction of intra-abdominal pressure all alter the VExUS score and need to be integrated into the logistic regression analysis for yielding the predictive value of VExUS score for AKI.

There is a requirement of technical expertise to get high quality images and record the Doppler waveforms in an appropriate ECG gated manner. There are several confounders which alter the VExUS pattern of congestion, yielding false positive and false negative results. There is always a percentage of patients who do not have good echo window to permit a full venous waveform analysis.[11]

In conclusion, VExUS scoring definitely makes waves in an ocean since it performs well in the severely congested patient but is a mirage in the desert as it does not retain its predictive value in the mildly congested patients. Despite its limitations, the VExUS score holds promise as a valuable tool for assessing venous congestion, guiding therapy, and improving patient outcomes, if used in conjunction with other clinical information and assessment tools. Future large-scale, prospective studies are needed to refine the scoring system, address technical challenges, and confirm its impact on clinical outcomes across diverse patient subsets.

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