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Pediatric Profound Dengue Shock Syndrome and Use of Point-of-Care Ultrasound During Mechanical Ventilation to Guide Treatment: Single-Center Retrospective Study, 2013–2021

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OBJECTIVES: Profound dengue shock syndrome (DSS) complicated by severe respiratory failure necessitating mechanical ventilation (MV) accounts for high case fatality rates among PICU-admitted patients. A major challenge to management is the assessment of intravascular volume, which can be hampered by severe plasma leakage and the use of MV.

DESIGN: Retrospective cohort, from 2013 to 2021.

PATIENTS: Sixty-seven children with profound DSS supported by MV, some of whom underwent bedside point-of-care ultrasound (POCUS) for assessment and monitoring of hemodynamics and fluid administration.

SETTING: PICU of the tertiary Children's Hospital No. 2 in Vietnam.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: We analyzed data clinical and laboratory data during PICU stay. In particular, during use of MV (i.e., at times 0-, 6-, and 24-hr after commencement) and fluid resuscitation. The primary study outcome was 28-day in-hospital mortality, and the secondary outcomes were associations with changes in hemodynamics, blood lactate, and vasoactive-inotrope score (VIS). Patients had a median age of 7 years (interquartile range, 4–9). Use of POCUS during fluid management (39/67), as opposed to not using (28/67), was associated with lower mortality (6/39 [15%] vs. 18/28 [64%]; difference 49 % [95% CI, 28–70%], $p < 0.001$). Use of POCUS was associated with lower odds of death (adjusted odds ratio 0.17 [95% CI, 0.04–0.76], $p = 0.02$). The utilization of POCUS, versus not, was associated with greater use of resuscitation fluid, and reductions in VIS and pediatric logistic organ dysfunction (PELOD-2) score at 24 hours after MV and PICU discharge.

CONCLUSIONS: In our experience of pediatric patients with profound DSS and undergoing MV (2013–2021), POCUS use was associated with lower odds of death, a higher volume of resuscitation fluid, and improvements in the blood lactate levels, VIS, and PELOD-2 score.

KEYWORDS: dengue; dengue shock syndrome; mechanical ventilation; point-of-care ultrasound

Profound dengue shock syndrome (DSS) is a severe complication of dengue infection in hospitalized dengue-infected children (1). We know from modeling in a 1999–2009 cohort that profound DSS is a potentially fatal complication that occurs during the critical phase of dengue infection in patients with recurrent and decompensated DSS episodes (1). In the absence of timely and appropriate management, the in-hospital mortality rate of DSS in a 2015 cohort of adults was 23.1% (2), and in a 2015–2019 cohort of children, it was 25.6% (3).

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RESEARCH IN CONTEXT

- Historically, mechanically ventilated children with profound dengue shock syndrome (DSS) have high case fatality rate.
- The utilization of bedside point-of-care ultrasound (POCUS) can be used to improve assessment of hemodynamics.
- Here, we report our single-center experience of using POCUS to guide fluid therapy in mechanically ventilated children with profound DSS.

In this context, in 2022, we reported two pediatric patients of profound DSS with severe plasma leakage, requiring mechanical ventilation (MV) (4). These patients underwent bedside point-of-care ultrasonography (POCUS) to assess intravascular volume and cardiac function, and to identify the presence of any pericardial-pleural effusions or ascites. We now extend these preliminary observations with a full retrospective summary of our experience of POCUS-based interventions in our 2013–2021 cohort of MV children with profound DSS. Our primary hypothesis is to test whether this practice is associated with improved 28-day in-hospital mortality. The secondary hypothesis is whether during POCUS-based intervention there was an associated change with improved hemodynamics, blood lactate concentration, vasoactive-inotrope score (VIS), and pediatric logistic organ dysfunction (PELOD-2) score.

MATERIALS AND METHODS

Our retrospective study called "Impact of point-of-care ultrasound (POCUS) utilization on outcomes in mechanically ventilated children with profound dengue shock syndrome" was approved by the Scientific Committee and institutional review board of Children Hospital No. 2, Ho Chi Minh City, Vietnam (approval number 367/QD-BVND2) on March 15, 2023. The study was conducted in accordance with Good Clinical Practice and the 1975 Declaration of Helsinki.

Study Design and Participants

Our Children's Hospital (No. 2, Ho Chi Minh City) in Vietnam is one of the three largest tertiary referral pediatric hospitals in southern Vietnam. We identified a retrospective cohort (January 2013 to December 2021) by using the hospital electronic database and the *International Classification of Diseases* 10-CM code numbers for severe DSS (A97.2). The inclusion criteria were: 1) admission to the PICU, 2) laboratory-confirmed dengue infection, 3) presence of profound DSS who required MV, and 4) age < 18 years. Of a total of 25,944 confirmed dengue hospitalized patients, we identified 67 who met our inclusion criteria (**Fig. S1**, http://links.lww.com/PCC/C452).

In this cohort, dengue infection was defined using the 2009 World Health Organization (WHO) criteria for laboratory confirmation of the diagnosis using the dengue-IgM antibody test or the nonstructural 1 antigen test (5). Profound DSS was defined as meeting the following two groups of criteria: 1) first, being treated with greater than or equal to two colloid boluses during fluid resuscitation for the first sign of compensated DSS, or having greater than or equal to two episodes of recurrent shock, or being given colloid resuscitation for decompensated DSS plus other episodes of DSS recurrence later on, and/or 2) second, fluid management with colloid combined with inotropes to sustain hemodynamic stability (1).

Patient Management

In the period 2013–2021, there was no international guidance detailing the management of children with profound DSS, even in the 2009 WHO dengue guidelines (5). However, at our center, over the 2013–2021 period, our practice in children with profound DSS was based on 2011 national dengue guidelines from the Vietnamese Ministry of Health (**Fig. S2**, http://links.lww.com/PCC/C452). This treatment protocol suggests using the following parameters to guide fluid administration: central venous pressure (CVP), invasive blood pressure, cardiac functions, serum albumin, and hematocrit level. Most importantly, CVP measurement is considered the cornerstone for assessing intravascular volume and guiding fluid and vasopressor use.

Placement of a central venous catheter for CVP measurement is an invasive procedure, with high risk of severe bleeding in profound DSS patients. Additionally, CVP values may be substantially altered—and therefore unreliable—during respiratory cycle-induced

changes in intrathoracic pressure caused by MV. CVP may also be altered by the presence of a pleural and pericardial effusion. Therefore, in patients with profound DSS (given that CVP measurement was either contraindicated or unreliable) our practice was to carry out POCUS to assess intravascular volume, cardiac function, and any effusions, and to guide fluid resuscitation and inotropes. Over the period 2013–2021, all POCUS studies were performed by one operator (VTL, a senior intensivist and Head of PICU in infectious diseases, and certified in advanced cardiac sonography).

The structured protocol for POCUS-based intervention included the following assessment to guide fluid resuscitation and vasopressor use: 1) state of inferior vena cava (IVC) as being either normal, collapsed, or distended, and 2) state of ventricular filling and cardiac ejection fraction (%) (**Fig. S3**, http://links.lww.com/PCC/C452).

Study Outcomes

Our primary outcome was 28-day in-hospital mortality. The secondary outcomes were changes in hemodynamics, blood lactate concentration, VIS, and PELOD-2 score.

Data and Measurements

Case report forms were used to record data from the medical paper-based records of the 67 patients in our cohort. Clinical and laboratory variables of interest were collected from various timepoints, including at the start of MV and when there was POCUS-guided fluid resuscitation (i.e., at 6- and 24-hr after POCUS-based fluid management, and PICU discharge).

The 28-day in-hospital mortality was calculated from hospital admission to the occurrence of patient death. Severe bleeding was defined according to the 2009 WHO dengue guidelines (5). The VIS was used to evaluate the degree of hemodynamic support (6). The PELOD-2 score was used to assess and compare the severity of organ dysfunction (7).

Statistical Analyses

Continuous variables were summarized as medians and interquartile ranges (IQRs). Categorical variables are presented as numbers (*n*) and percentages (%). Two-sided, two-sample *t* tests were used to compare means of continuous variables. The Chi-square test and adjusted Fisher exact test were used to compare categorical variables. Logistic regression models with and without adjustments for covariables including severe bleeding, severe hepatic transaminases, blood lactate level, and VIS at starting MV were used to study the associations between POCUS-guided fluid intervention and 28-day in-hospital mortality. Point estimates are reported with 95% CIs. These adjusted covariables were chosen, based on dengue pathogenesis and our clinical knowledge. We also used the conservative Bonferroni-corrected p values with a significance level less than 0.01, accounting for multiplicity adjustment of pairwise comparisons of hemodynamics, fluid administration, blood lactate level, and VIS at various timepoints (i.e., at the initiation of MV and POCUS performance, and at 6- and 24-hr after MV and POCUS-guided fluid resuscitation, and at PICU discharge) (8). The remaining statistical significance was set at p values of less than 0.05. The R statistical software (version 4.2.2; Boston, MA) was used for all analyses.

RESULTS

In the period 2013–2021, we identified 67 PICU-admitted children with profound DSS requiring MV who met inclusion criteria. The clinical and laboratory characteristics, and outcomes of these patients at the timepoint of initiating MV, before POCUS was performed, are summarized in **Table 1**. Overall, median patient age was 7 years (IQR 4–9), and 35 of 67 (52%) were male patients. Notably, 40 of 67 patients (60%) presented with severe bleeding, and it occurred more frequently in the no-POCUS than POCUS group (21/28 [75%] vs. 19/39 [49%], mean difference 26% [95% CI, 2.3–45.3%], $p = 0.03$). There were substantial elevations in hepatic transaminases and severe coagulation disorders, with greater severity in no-POCUS than POCUS group. The median serum lactate was 4.4 (IQR, 2.0–7.3) mmol/L, and higher lactate levels were observed in the no-POCUS group (a median of 7.2 [IQR, 3.3–10.7]) than POCUS group (a median of 3.0 [IQR, 1.7–6.5]). For all studied patients, the median cardiac troponin I was 0.15 (IQR, 0.04–1.66) ng/mL, and the median VIS was 38 (IQR, 10–140). Markedly higher VIS were observed in patients who did not undergo POCUS (a median of 115 [IQR, 25–385]) than

TABLE 1.
Characteristics and Discharge Outcomes of Children With Profound Dengue Shock Syndrome at the Start of Mechanical Ventilation, Before Point-of-Care Ultrasound Was Used

Characteristics	All Patients (*n* = 67)	POCUS (*n* = 39)	No-POCUS (*n* = 28)
Age, median (IQR), yr	7 (4–9)	7 (5–9)	7 (3–10)
Male, *n* (%)	35 (52)	22 (56)	13 (46)
Underlying diseases, *n* (%)	4 (6)	4 (10)	0 (0)
Severe bleeding, *n* (%)	40 (60)	19 (49)	21 (75)
Systolic shock index, median (IQR of beats/min/mm Hg)	1.4 (1.2–1.7)	1.5 (1.3–1.7)	1.4 (1.2–1.7)
Diastolic shock index, median (IQR of beats/min/mm Hg)	2.13 (1.71–2.73)	2.11 (1.71–2.5)	2.2 (1.88–2.92)
WBC count, median (IQR) × 10^9/L	5.78 (4.17–10.61)	5.29 (4.19–9.18)	6.78 (3.87–12.8)
Hemoglobin, median (IQR) g/dL	13.8 (11.1–15.1)	13.4 (11–15.6)	13.9 (11.7–15)
Peak hematocrit, median (IQR) (%)	45 (38–48)	45 (37–50)	46 (38–47)
Nadir hematocrit, median (IQR) (%)	35 (30–42)	38 (32–42)	33 (28–41)
Platelet cell count, median (IQR) × 10^9/L	34 (20–52)	34 (21–50)	37 (16–53)
AST, median (IQR), IU/L	991 (302–3,763)	665 (288–2,659)	1,652 (546–6,511)
ALT, median (IQR), IU/L	382 (135–1,442)	279 (97–868)	823 (242–1,734)
INR, median (IQR)	2.1 (1.7–2.8)	1.9 (1.7–2.6)	2.3 (1.9–3.0)
Serum lactate, median (IQR), mmol/L	4.4 (2.0–7.3)	3.0 (1.7–6.5)	7.2 (3.3–10.7)
Serum creatinine, median (IQR), μmol/L	51 (41–88)	47 (39–60)	70 (46–127)
Troponin I, median (IQR), ng/mL	0.15 (0.04–1.66)	0.15 (0.04–0.66)	1.43 (0.05–4.91)
Vasoactive-inotrope score, median (IQR)	38 (10–140)	20 (5–50)	115 (25–385)
Duration of vasopressor support, median (IQR), d	2 (1–5)	2 (1–3)	3 (1–6)
Length of PICU stay, median (IQR), d	7 (5–12)	8 (6–13)	6 (3–9)
Length of hospital stay, median (IQR), d	13 (7–22)	15 (11–24)	7 (3–17)
In-hospital mortality, *n* (%)	24 (36)	6 (15)	18 (64)

ALT = alanine aminotransferase, AST = aspartate aminotransferase, INR = international normalized ratio, IQR = interquartile range, POCUS = point-of-care ultrasound.
Summary statistics are median (IQR) for continuous variables and frequency (%) for categorical variables.

in those who intervened with POCUS (a median of 20 [IQR, 5–50]). Overall, the median length of hospital stay was 13 days (IQR, 7–22) and that of PICU stay was 7 days (IQR, 5–12). The median duration of vasopressor support was 2 days (IQR, 1–5). Noticeably, the POCUS group had longer PICU and hospital stays, and shorter days of vasopressor support than the no-POCUS group. Taken together, these data might reflect the higher mortality in the no-POCUS than POCUS groups (as presented in **Fig. S4**, http://links.lww.com/PCC/C452).

28-Day In-Hospital Mortality

Overall, 24 of 67 patients (36 %) in the cohort died. POCUS-based fluid management, as opposed to no-POCUS, was associated with lower proportion of mortality (6/39 [15%] vs. 18/28 [64%], mean difference of 49% [95% CI, 28–70%], $p < 0.001$). Both univariate and adjusted multivariable analyses showed that being in the POCUS group was associated with improved survival of patients, as shown in **Table 2**. The use of POCUS was associated with lower odds of mortality,

TABLE 2.
Associations Between the Point-of-Care Ultrasound, as Opposed to the No-Point-of-Care Ultrasound Designation, and Odds of Mortality

Fatal Outcome	POCUS ($n = 39$)	No-POCUS ($n = 28$)	Crude OR[a] (95% CI)	p^a	Adjusted OR[b] (95% CI)	p^b
Yes, *n* (%)	6 (15)	18 (64)	0.10 (0.03–0.32)	< 0.001	0.17 (0.04–0.76)	0.02
No, *n* (%)	33 (85)	10 (36)				

OR = odds ratio, POCUS = point-of-care ultrasound.

[a]Crude OR and *p* values from univariate model.

[b]The OR and *p* values from multivariable logistic analysis were adjusted for severe bleeding, severe hepatic transaminases, blood lactate level, and vasoactive-inotrope score at starting mechanical ventilation.

with an adjusted odds ratio of 0.17 (95% CI, 0.04–0.76), $p = 0.02$.

POCUS Findings at the Start of Mechanical Ventilation

Bedside POCUS findings of the cohort, presented in **Table 3** were available in 37 of 39 patients (two had missing POCUS data). Abdominal and pleural effusions were present in almost all patients undergoing POCUS. Among the studied patients, only one had reduced ejection fraction. IVC collapse and poor filling of the ventricles were present in 28 of 37 studied patients (76%). Nonetheless, distention of the IVC was observed in 9 of 37 children (24%). Of these nine patients with IVC distention, it was accompanied by adequate ventricular filling in five patients, and by poor ventricular filling in the other four patients.

TABLE 3.
Point-of-Care Ultrasound Findings at the Time of Starting Mechanical Ventilation and Intensive Care Fluid Resuscitation

Point-of-Care Ultrasound Features	Patients (*n*)	Statistics
IVC collapse and poor filling of ventricles	37	28 (76)
IVC distention and adequate filling of ventricles	37	5 (13)
IVC distention and poor filling of ventricles	37	4 (11)
Preserved ejection fraction (> 50 %)	37	36 (97)
Reduced ejection fraction (< 50 %)	37	1 (3)
Pleural effusion	37	37 (100)
Abdominal ascites	37	37 (100)

IVC = inferior vena cava.

Summary statistic is frequency (%). Data were missing in two of the total 39 patients in point-of-care ultrasound cohort.

Comparisons in Hemodynamics, Fluid Administration, Blood Lactate, VIS, and PELOD-2 Score in POCUS and No-POCUS Groups

At the initiation of MV, despite higher VIS and blood lactate in no-POCUS group, when compared with the POCUS group, we failed to identify any association with systolic shock index (**Table 4**). After 24-hr of MV, there was an associated improvement in the VIS in the POCUS group, but not in the no-POCUS group (POCUS: mean difference 33 [95% CI, 15–52, $p < 0.001$]; vs. no-POCUS: mean difference 148 [95% CI, 26–270, $p = 0.02$]), (as presented in **Figs. 1, *A*** and ***B*)**. Additionally, at the start of MV and 24 hours later, there was an association between POCUS grouping and blood lactate level; and at both timepoints no-POCUS group had higher lactate levels. On paired data analyses between the start of MV and 24 hours later, we failed to find an associated change in lactate level in either group (POCUS: mean difference –0.2 mmol/L [95% CI, –1.8 to 1.4, $p = 0.83$]; and no-POCUS: mean difference –1.6 mmol/L [95% CI, –4.9 to 1.8, $p = 0.34$]). The dynamic variations of blood lactate within 24 hours post-MV were analyzed and presented in SDC **Figure S6** and **Table S1** (http://links.lww.com/PCC/C452). Markedly, the no-POCUS cohort had persistently elevated blood lactate levels and impaired clearance function, while the POCUS group experienced constantly lower blood lactate concentrations and better clearance capacity.

TABLE 4.
Comparisons in Hemodynamics, Fluid Administration, and Vasoactive-Inotrope Score

Parameters	POCUS ($n = 39$)	No-POCUS ($n = 28$)	p[a]
Systolic shock index			
Shock index at timing of MV (beats/min/mm Hg)	1.5 (1.33–1.65)	1.41 (1.15–1.66)	0.67
Shock index at 24 hr after MV and fluid resuscitation (beats/min/mm Hg)	0.95 (0.76–1.12)	0.73 (0.59–0.86)	< 0.001
Pocus-based fluid amounts given to patients			
Total fluid is given during first 06 hr on starting MV (mL/kg)	53 (36–70)	43 (35–59)	0.21
Total fluid is given within 24 hr after starting MV (mL/kg)	185 (71–227)	85 (55–142)	< 0.01
Vasoactive-inotrope score			
VIS at the initiation of MV	20 (5–50)	115 (25–385)	< 0.01
VIS at 6 hr after MV and fluid resuscitation	10 (0–30)	26 (20–55)	< 0.01
VIS at 24 hr after MV and fluid resuscitation	5 (0–20)	60 (0–200)	< 0.01
VIS at PICU discharge or death	0 (0–0)	140 (0–345)	0.02
Blood lactate concentration			
Lactate level at the initiation of MV (mmol/L)	3.0 (1.7–6.5)	7.2 (3.3–10.7)	< 0.01
Lactate level at 24 hr after MV and fluid resuscitation (mmol/L)	2.9 (1.4–5.7)	8 (3.6–14)	< 0.01
PELOD-2 score			
PELOD-2 at the timing of starting MV	8 (6–9)	10 (8–17)	< 0.001
PELOD-2 at 24 hr after fluid resuscitation and MV	7 (6–9)	13 (7–19)	< 0.001
PELOD-2 at discharge or death	2 (0–4)	11 (1–23)	< 0.001

MV = mechanical ventilation, OR = odds ratio, PELOD-2 = pediatric logistic organ dysfunction score, POCUS = point-of-care ultrasound, VIS = vasoactive-inotrope score.

[a]*p* values withdrawn from two-sample *t* test and complete-case analysis.

Summary statistics are median (interquartile range) for continuous variables and frequency (%) for categorical variables. The Bonferroni-corrected *p* values were all set at the significance level of less than 0.01 for multiple pairwise comparisons.

Regarding fluid resuscitation, we failed to identify the use of POCUS and an associated difference in fluid administration within 6 hours since starting MV. However, by 24 hours, there was an associated greater volume of fluid resuscitation in the POCUS group, as opposed to the no-POCUS group (185 [IQR 71–227] vs. 85 [IQR 55–142] mL/kg, $p < 0.01$) (Table 4). Lastly, there were significant differences in PELOD-2 score between POCUS and no-POCUS groups at various timepoints: at MV, 24 hours post-MV, and at PICU discharge (Table 4). Particularly, POCUS cohort showed marked improvement in PELOD-2 score at PICU discharge compared with the baseline (mean difference 3.7 [95% CI, 1.1–6.3], $p < 0.01$) (**Fig. 1*C***), in contrast to poorer conditions in the no-POCUS cohort (mean difference –2.6 [95% CI, –7.4 to 2.3], $p = 0.28$) (**Fig. 1*D***).

DISCUSSION

Profound DSS is observed in the late stage of critical dengue-infected patients with multiple episodes of recurrent hypotensive shock (2). Our study shows that in our 2013–2021 experience, such children requiring MV had a high in-hospital mortality of 36% (95% CI, 25–49%). These data are consistent with other adult and pediatric cohorts (2, 3). In this context, over 9 years we have used POCUS in caring for 39 pediatric patients with profound DSS, accounting for 58% of all patients with DSS that we encountered in our PICU. Using POCUS (rather than not) in DSS patients is associated with greater volumes of fluid resuscitation administered in the first 24 hours after initiation of MV, and there was also a fall in vasopressor use in this same period. In

AT THE BEDSIDE

- In our experience of managing critically ill children with profound DSS requiring mechanical ventilation, POCUS-guided fluid resuscitation, rather than not was associated with lower odds of death.
- During PICU care, use of POCUS at the time of fluid resuscitation was associated with improvements in hemodynamics, blood lactate levels, and vasoactive-inotrope score.
- The utility of POCUS to individualize fluid resuscitation in mechanically ventilated patients with profound DSS warrants prospective evaluation.

retrospect, being selected for use of POCUS during profound DSS management was associated with lower odds of mortality, at least a 10% reduction.

Institutional POCUS training focusing on PICU patients was reported as early as 2015 (9), and the clinical applicability of POCUS has been increasingly shown to improve pediatric critical care (10). In parallel with the evolution of POCUS, we used POCUS in 39 children with profound DSS during pediatric intensive care at our tertiary hospital since 2017. The distribution of patients with profound DSS managed with POCUS, is shown in **Figure S5** (http://links.lww.com/PCC/C452). A recent report of a Malawian pediatric cohort showed a high prevalence of left ventricular systolic dysfunction among hospitalized children with severe febrile illness and elevated serum lactate levels, which were detected by cardiac POCUS (11). However, there was no statistically significant association between heart dysfunction and in-hospital mortality, likely because of limited study power. Consequently, both the Malawian cohort and our study highlighted the practical need for POCUS applicability in emergency and pediatric intensive care. POCUS offers many modalities across a spectrum of disciplines, demanding proficient performers and standardized training programs to ensure accuracy and patient safety (12).

Significantly, two main targets for fluid resuscitation in profound DSS cohort are compensation for ongoing fluid leakage and appropriate decompression of the distended abdominal cavity. Effusions and elevated intra-abdominal pressure may reduce the accuracy of many modalities of fluid response assessments in children (13, 14). In patients with intra-abdominal hypertension, dynamic heart-lung interaction indices such as pulse pressure variation and stroke volume variation remain valid in the absence of low-tidal volume, cardiac arrhythmias, and spontaneous breathing activity (15). However, these methods are limited by indeterminate cutoff points and the common practice of low-tidal volume to prevent ventilator-associated lung injuries in pediatric patients. Likewise, the reliability of the passive leg-raising test diminishes in the presence of high intra-abdominal pressure (13, 16). The central principle in managing patients with severe DSS is to ensure sufficient blood perfusion to vital organs with minimal fluid administration (5). Patients with severe DSS may present with highly increased intra-abdominal pressure, and a collapsed IVC may signify precardiac obstruction due to pressure (4, 17, 18). Our study showed that approximately three-quarters of patients had IVC collapse and poor filling of ventricles, while 11% of children had IVC distention and poor filling of ventricles. This indicated that dengue obstructive shock syndrome occurred early in the abdominal cavity, and a late stage was observed in the cardiac chambers (4). Poor filling of ventricles with preserved ejection fraction was notably present in most patients, which could be a result of combined causes, including: 1) obstruction of the IVC due to drastically increased pressures in the intra-abdominal, pleural, and pericardial cavities, 2) severe plasma leakage, and 3) reduced afterload due to systemic vasodilation. Consequently, our patients experienced prolonged dengue shock and multiple organ failures due to reduced hemoperfusion (ischemia). Notably, the POCUS patient cohort received greater volumes of fluid resuscitation in the first 24 hours after MV initiation and fewer vasopressors (lower VIS) than the comparable no-POCUS group. Hence, interventions with less fluid and higher vasopressor administration could possibly lead to poorer survival outcomes among patients without POCUS. In the presence of dengue obstructive shock syndrome, particularly in patients on MV, fluid demand rather than vasopressors is needed. That is to state more inotropy and/or less fluid administration can aggravate prolonged dengue shock. Simultaneously, abdominal decompression is critical for recovering the blood return to the heart. Notably, the end-diastolic volumes of both ventricles are decreased when the intrathoracic

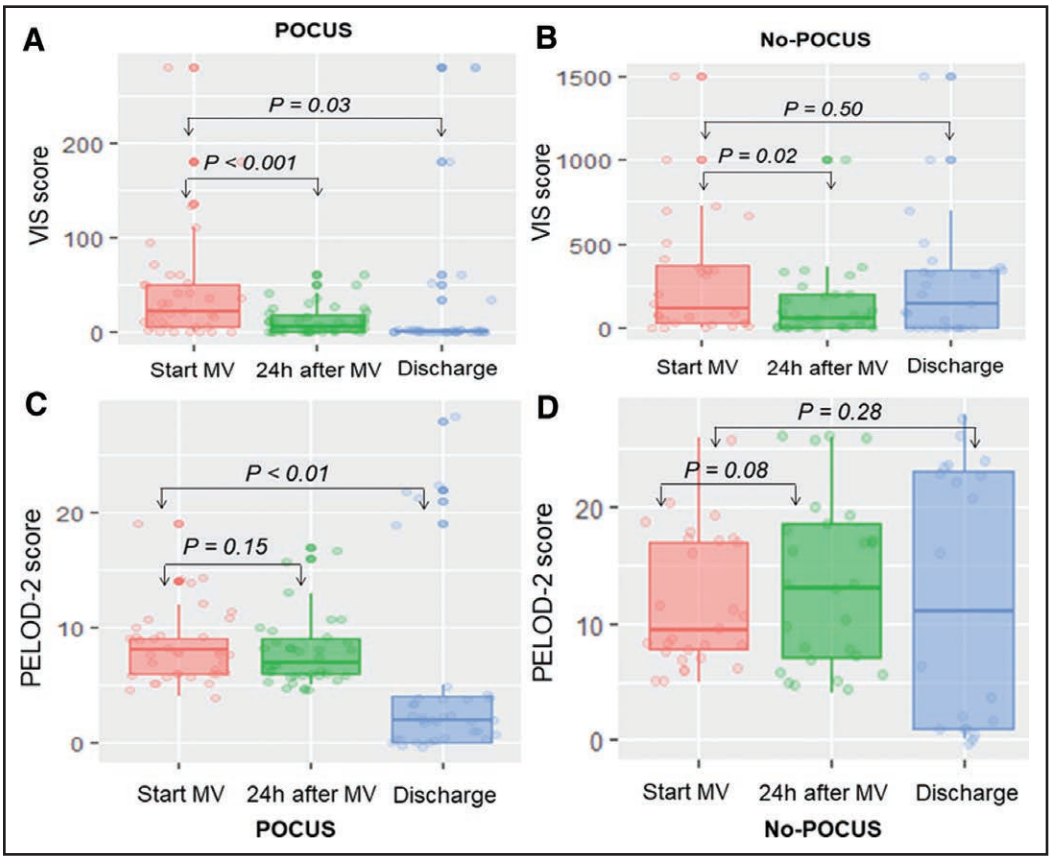

Figure 1. Serial-paired *t* tests in vasoactive-inotropic score (VIS) and pediatric logistic organ dysfunction (PELOD-2) score at various timepoints: at the initiation of mechanical ventilation (MV), 24 hours after MV plus fluid resuscitation, and at PICU discharge. In particular, the point-of-care ultrasound (POCUS) cohort showed significant improvements in VIS (**A**) and PELOD-2 (**C**) scores at 24 hours post-MV and at PICU discharge compared with baseline levels (at MV initiation). In contrast, the comparable no-POCUS group experienced deterioration in both the VIS (**B**) and PELOD-2 (**D**) scores at PICU discharge compared with baseline levels.

pressure increases (19, 20). Hence, interventions to reduce intrathoracic pressure significantly improve ventricular volume, ejection fraction, and cardiac output (21). Therefore, we propose a sensible approach that includes 1) continued fluid administration to ensure preload adequacy, 2) early abdominal paracentesis for decompression in the presence of dengue obstructive shock syndrome, and 3) vasoconstrictors for systemic vasodilation due to multiple organ failure.

Additionally, in this study, we acknowledged that non-POCUS patients presented with more severe disease (higher blood lactate score and VIS and more liver injury) at baseline (MV) than the POCUS group. However, the 24-hour progression post-MV in both groups raises several important points. First, whether fluid demand or vasopressors are more significant in patients with profound DSS. The aforementioned pathophysiology shows that higher inotropy can potentially harm patients with prolonged DSS, and fluid administration is more essential than vasopressors. Second, whether ischemia or impaired clearance explains the deterioration in patients without POCUS. Our study data showed that both PELOD-2 score and clearance were persistently poorer in the no-POCUS group than in the POCUS group during PICU stay. The 24-hour dynamic changes in PELOD-2 and lactate clearance suggest that ischemia is more predominant than impaired clearance. In profound DSS patients, decreased effective arterial blood volume was a critical factor, and a greater volume of resuscitated fluid can improve hemoperfusion to vital organs, increasing patient's survival outcome.

Our study has several limitations inherent to the nature of a single-center, retrospective cohort design with small sample size and unstandardized collections of clinical and laboratory data during hospitalization. Most significantly, differences in manifestations between the POCUS and no-POCUS patients at the outset necessitate prudent interpretation of our results.

Further investigation in prospective cohorts with an appropriate study design and well-defined interventions is essential to elucidate this knowledge gap. A standardized POCUS protocol for patients with profound DSS is necessary for practicality in the PICU. Our study results pave the way for the utility of POCUS in individualizing fluid resuscitation in mechanically ventilated patients with profound DSS.

CONCLUSIONS

Mechanically ventilated children with profound DSS who underwent POCUS-based fluid interventions had better survival outcomes. POCUS use was associated with a higher volume of resuscitation fluid and improvements in the blood lactate levels, VIS, and PELOD-2 score.

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REFERENCES

1. Lam PK, Tam DT, Dung NM, et al: A prognostic model for development of profound shock among children presenting with dengue shock syndrome. *PLoS One* 2015; 10:e0126134
2. Chen CM, Chan KS, Yu WL, et al: The outcomes of patients with severe dengue admitted to intensive care units. *Medicine (Baltim)* 2016; 95:e4376
3. Sachdev A, Pathak D, Gupta N, et al: Early predictors of mortality in children with severe dengue fever: A prospective study. *Pediatr Infect Dis J* 2021; 40:797–801
4. Nguyen TT, Le NT, Nguyen NM, et al: Clinical features and management of children with dengue-associated obstructive shock syndrome: A case report. *Medicine (Baltimore)* 2022; 101:e31322
5. Dengue: *Guidelines for Diagnosis, Treatment, Prevention and Control: New Edition*. Geneva, World Health Organization, 2009
6. McIntosh AM, Tong S, Deakyne SJ, et al: Validation of the vasoactive-inotropic score in pediatric sepsis. *Pediatr Crit Care Med* 2017; 18:750–757
7. Leteurtre S, Duhamel A, Salleron J, et al; Groupe Francophone de Réanimation et d'Urgences Pédiatriques (GFRUP): PELOD-2: An update of the PEdiatric logistic organ dysfunction score. *Crit Care Med* 2013; 41:1761–1773
8. Armstrong RA: When to use the Bonferroni correction. *Ophthalmic Physiol Opt* 2014; 34:502–508
9. Conlon TW, Himebauch AS, Fitzgerald JC, et al: Implementation of a pediatric critical care focused bedside ultrasound training program in a large academic PICU. *Pediatr Crit Care Med* 2015; 16:219–226
10. Conlon TW, Kantor DB, Su ER, et al: Diagnostic bedside ultrasound program development in pediatric critical care medicine: Results of a national survey. *Pediatr Crit Care Med* 2018; 19:e561–e568
11. Bensman RS, Berrens Z, Mkaliainga T, et al: Prevalence of cardiac dysfunction in Malawian children with severe febrile illness. *Pediatr Crit Care Med* 2022; 23:493–501
12. Maxson IN, Su E, Brown KA, et al; Pediatric Research Collaborative on Critical Ultrasound (PeRCCUS), a subgroup of the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network: A program of assessment model for point-of-care ultrasound training for pediatric critical care providers: A comprehensive approach to enhance competency-based point-of-care ultrasound training. *Pediatr Crit Care Med* 2023; 24:e511–e519
13. Beurton A, Monnet X, Teboul JL: Assessment of fluid responsiveness in patients with intraabdominal hypertension. In: *Annual Update in Intensive Care and Emergency Medicine*. Vincent JL (Ed). Cham, Springer, 2018
14. Monnet X, Shi R, Teboul JL: Prediction of fluid responsiveness. What's new? *Ann Intensive Care* 2022; 12:46
15. Lee JH, Kim EH, Jang YE, et al: Fluid responsiveness in the pediatric population. *Korean J Anesthesiol* 2019; 72:429–440
16. Goldsmith AJ, Shokoohi H, Loesche M, et al: Point-of-care ultrasound in morbidity and mortality cases in emergency medicine: Who benefits the most? *West J Emerg Med* 2020; 21:172–178
17. Cheatham ML: Abdominal compartment syndrome: Pathophysiology and definitions. *Scand J Trauma Resusc Emerg Med* 2009; 17:10
18. Gottlieb M, Davenport DV, Adams S, et al: Current approach to the evaluation and management of abdominal compartment syndrome in pediatric patients. *Pediatr Emerg Care* 2019; 35:874–878
19. Vaska K, Wann LS, Sagar K, et al: Pleural effusion as a cause of right ventricular diastolic collapse. *Circulation* 1992; 86:609–617
20. Verhoeff K, Mitchell JR: Cardiopulmonary physiology: Why the heart and lungs are inextricably linked. *Adv Physiol Educ* 2017; 41:348–353
21. Wang Z, Cai QZ, Ban CJ, et al: Improved heart hemodynamics after draining large-volume pleural effusion: A prospective cohort study. *BMC Pulm Med* 2018; 18:62