BESTFIT-T3: A Tiered Monitoring Approach to Persistent/Recurrent Paediatric Septic Shock – A Pilot Conceptual Report

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Abstract

Objective: Persistent shock (PS) or recurrent shock (RS) after initial fluids and vasoactives can be secondary to myriad complex mechanisms, and these patients can have a high mortality. We developed a noninvasive tiered hemodynamic monitoring approach which included, in addition to basic echocardiography, cardiac output monitoring and advanced Doppler studies to determine the etiology and provide targeted therapy of PS/RS.

Design: Prospective observational study.

Setting: Tertiary Care Pediatric Intensive Care Unit, India.

Methods: A pilot conceptual report describing the clinical presentation of 10 children with PS/RS using advanced ultrasound and noninvasive cardiac output monitoring. Children with PS/RS after initial fluids and vasoactive agents despite basic echocardiography underwent BESTFIT + T3 (**B**asic **E**chocardiography in **S**hock **T**herapy for **F**luid and **I**notrope **T**itration) with lung ultrasound and advanced 3-tiered monitoring (T1-3).

Results: Among 10/53 children with septic shock and PS/RS over a 24-month study period, BESTFIT + T3 revealed combinations of right ventricular dysfunction, diastolic dysfunction (DD), altered vascular tone, and venous congestion (VC). By integrating information obtained by BESTFIT + T1-3 and the clinical context, we were able to modify the therapeutic regimen and successfully reverse shock in 8/10 patients.

Conclusion: We present our pilot results with BESTFIT + T3, a novel approach that can noninvasively interrogate major cardiac, arterial, and venous systems that may be particularly useful in regions where expensive rescue therapies are out of reach. We suggest that, with practice, intensivists already experienced in bedside POCUS can use the information obtained by BESTFIT + T3 to direct time-sensitive precision cardiovascular therapy in persistent/recurrent pediatric septic shock.

Keywords: Basic Echocardiography in Shock Therapy for Fluid and Inotrope Titration, Diastolic dysfunction, Persistent shock, Right ventricular dysfunction, Venous excess ultrasound (VExUS).

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Introduction

Several reports, including our own, have suggested that basic echocardiography (BESTFIT = **B**asic **E**chocardiography in **S**hock **T**herapy for **F**luid and **I**notrope **T**itration) and invasive arterial monitoring in pediatric septic shock can provide crucial information which can fine-tune hemodynamic management.[1] However, a few patients may have several physiological derangements not established by basic echocardiogram, and remain in PS or exhibit RS with worsening hemodynamics and progressive multiorgan failure. Refractory or PS is a lethal manifestation of cardiovascular failure defined by an inadequate cardiovascular response to high doses of multiple vasopressor-inotrope therapies.[2]

The optimal diagnostic and therapeutic approach to refractory shock remains inadequate with a paucity of evidence/guidelines, given that this condition is poorly represented in large clinical trials and is associated with extremely poor survival (<10%).[3,4]

We developed a noninvasive, bedside tiered hemodynamic monitoring approach termed as BESTFIT + T3. While BESTFIT interrogates the heart, IVC, and lungs, T3 includes echo-Doppler studies with detailed RV and DD assessment, noninvasive CO monitoring, and venous Doppler imaging. This comprehensive approach can systematically evaluate the entire hemodynamic system encompassing the heart, arterial, and venous systems to determine the etiology and provide targeted therapy of PS/RS.

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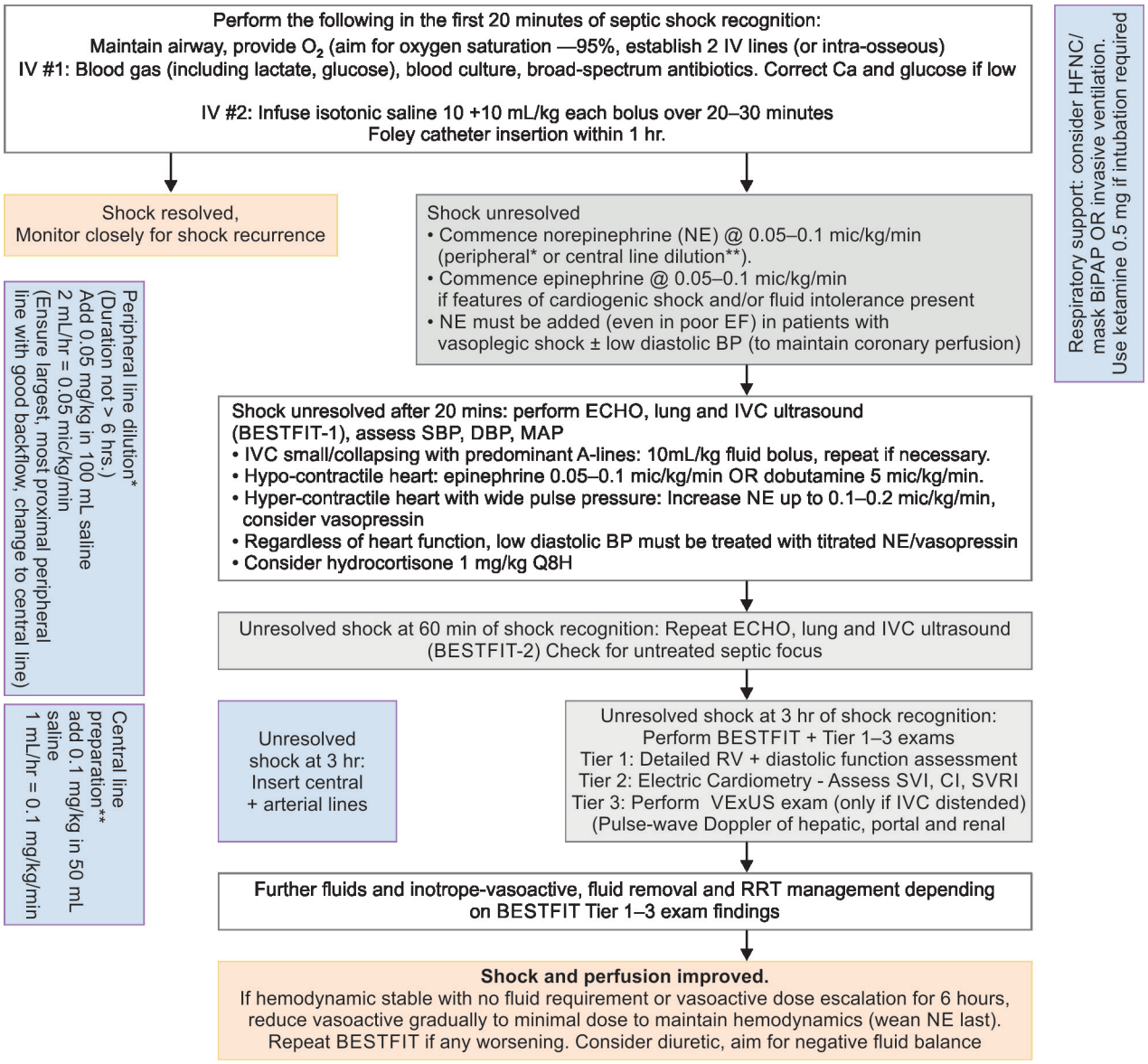
A strong evidence base for comprehensive hemodynamic monitoring that integrates cardiac function, arterial tone, and VC is limited, although there are emerging competency-based training modules in the adult population.[5]

Our intention is to describe our unit's pilot conceptual approach to this challenging group of children rather than discuss the evidence for each component of monitoring.

Methods

We prospectively studied children aged 1 month to 16 years with suspected or confirmed septic shock over 24 months from December 2018 to December 2020 in Chennai, India, who

Flowchart 1: Pediatric septic shock treatment pathway. O_2, oxygen; BESTFIT, Basic Echocardiography in Shock Therapy for Fluid and Inotrope Titration; ECHO, echocardiography; IVC, inferior vena cava; $ScvO_2$, central venous oxygen saturation; PRBC, packed red blood cells; RV, right ventricle; CI, cardiac index; SVI, stroke volume index; SVRI, systemic vascular resistance index; VExUS, venous excess ultrasound; RRT, renal replacement therapy



received initial septic shock interventions as per our unit protocol (Flowchart 1). This article describes the management of patients with PS/RS (see definitions below) despite initial treatment.

Written informed consent was obtained from the parents/guardians prior to enrolment, and the study was approved by the Ethics Committee of Apollo Hospital (ACH-C-S-04/01-20).

Standard supportive therapy included empiric broad-spectrum antibiotics within 1 hour of septic shock recognition and source control where indicated.

A BESTFIT exam was performed within 60 minutes of the first fluid bolus (FB), aiming to rapidly screen for tamponade, cardiac function, inferior vena cava (IVC) dimensions with respirophasic variations along with lung ultrasound to gauge fluid tolerance and guide FB decisions.[1]

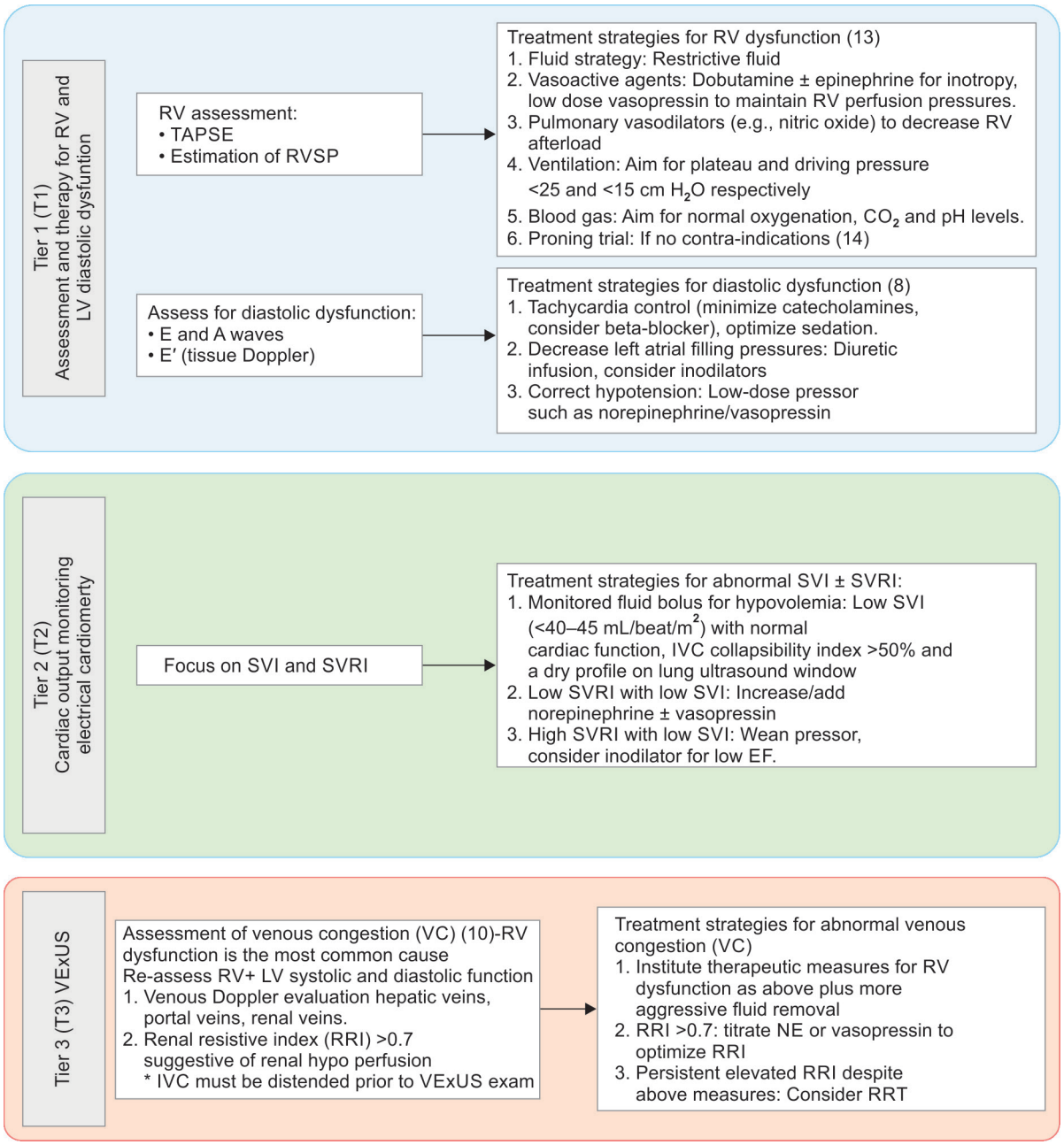
The monitoring was performed by one of the two authors, both of whom were formally trained and certified in Basic and Advanced point-of-care-ultrasound (POCUS). However, we did not perform any test of inter- and intraobserver agreement analysis.

Cardiovascular supportive therapy was instituted based on the initial BESTFIT exam findings and our institutional protocol (Flowchart 1).

If shock was unresolved, a second BESTFIT exam was performed within 60 minutes of the first exam and treatment further fine-tuned.

Persistent shock was defined by the presence of >2 features of hypoperfusion (hypotension, tachycardia, poor peripheral perfusion, low urine output, high lactates)[6] not explainable by other causes for 3 hours despite therapy based on two BESTFIT examinations.

Flowchart 2: Tier 1–3 examination and treatment strategies for persistent or recurrent shock. TAPSE, tricuspid annular plane systolic excursion; RVSP, right ventricular systolic pressure; SVI, stroke volume index; SVRI, systemic vascular resistance index; IVC, inferior vena cava; NE, norepinephrine; VExUS, venous excess ultrasound; RRI, renal resistive index; RRT, renal replacement therapy



Recurrent shock (RS) was defined as recurrence of shock after at least 48 hours of initial cardiovascular stability.

Among children with PS or RS, three further tiered hemodynamic monitoring modalities (T1-3) were sequentially performed (Flowchart 2). T1-2 exams were performed together in 5–7 minutes, while T-3 monitoring could be completed in 4–5 minutes.

We excluded moribund patients, those with inadequate echocardiographic or EC signals and in whom experienced monitoring personnel were unavailable.

Tier-1 examination (T-1) composed of two parts

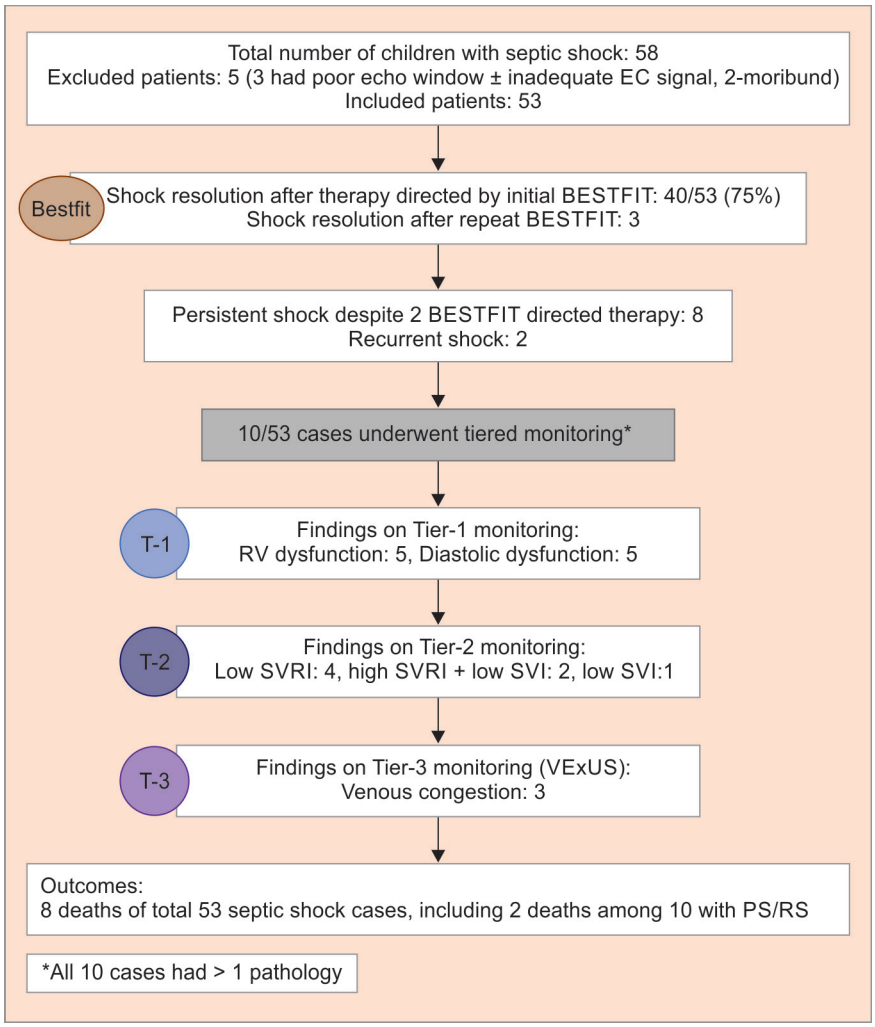
- *Right ventricular (RV) assessment*

Although "eyeballing" of the RV size and function was part of the initial BESTFIT exam, if the RV dysfunction was deemed to be contributing to the hemodynamic derangement, a more detailed assessment was performed, focusing mainly on tricuspid annular peak systolic excursion (TAPSE) for quantifying RV dysfunction.[7]

- *Left ventricular diastolic dysfunction (LV-DD)*

Left ventricular diastolic dysfunction (LV-DD) was assessed by examining the mitral annular-inflow Doppler flow velocities in apical four-chamber view (E and A waves) and lateral mitral-annular tissue Doppler imaging (E′).[8]

Flowchart 3: Inclusions, findings on BESTFIT T1-3 monitoring and outcome. EC, electrical cardiometry; BESTFIT+, basic Echo to titrate fluids and Inotropes + lung USG; RV, right ventricle; LV, left ventricle; VExUS, venous excess ultrasound; SVRI, systemic vascular resistance; SVI, stroke volume index; PS, persistent shock; RS, recurrent shock



Tier-2 examination (T-2) comprised noninvasive CO monitoring using the EC device (Osypka-Medical, Germany) which can be applied even on spontaneously breathing patients without invasive lines.[9] We documented the following cardiac index (CI), stroke volume index (SVI), and systemic vascular resistance index (SVRI). We preferred SVI rather than CI measurements since CO values are often maintained in normal range by compensatory tachycardia even when SVI is low.

Tier-3 examination (T-3)

T-3 exam uses venous Doppler or VExUS (**V**enous **E**xcess **U**ltra**S**ound) to assess for organ and VC,[10] and was performed only in patients with a dilated IVC.[11] T-3 was assessed in three locations: portal veins, hepatic veins, and intrarenal vessels.[12]

Change in Cardiovascular Therapy Following BESTFIT+T3

Among patients with PS/RS, we integrated information obtained by serial clinical examination BESTFIT and T1-T3 exams to provide physiologically directed stepwise changes in cardiovascular therapy (Flowcharts 1 and 2). Therapeutic measures for RV dysfunction, DD, abnormal vascular tone, and venous congestion including fluid regimen, vasoactives, and other strategies are described in Flowchart 2.[8,13,14]

Results

During the study period of 58 children with septic shock, 5 were excluded and 53 children were included in the study (Flowchart 3). Forty of 53 patients (75%) improved with a fluid and vasoactive-inotrope regimen based on BESTFIT-1 exam, and shock resolved in another three children after the BESTFIT-2 directed therapy. Eight children continued to exhibit features of PS and two developed RS despite initial BESTFIT-guided therapy and are described below. Table 1 describes demographics, circulatory pathophysiology, BESTFIT + T3-directed changes in therapy and outcomes.

Case #1 was a laboratory-confirmed dengue shock and hypotensive PS despite two BESTFIT exams. T1-2 exams revealed RV systolic dysfunction and low SVRI (rather than the expected high SVRI in dengue shock). Blood cultures grew *Klebsiella* spp. confirming bacterial etiology for vasodilatory shock. Norepinephrine was initiated (NE) infusion along with supportive therapy for dengue shock. T-3 monitoring demonstrated features

Table 1: Demographics, BESTFIT findings, tiered monitoring, and outcome

s# PS/RS	*Age/sex PRISM PELOD, PMR*	*BESTFIT findings and therapy*	*Tiered monitoring (T1-3) and change in therapy*	*Shock resolution (hour) outcome*
1 PS	12 years/M 19 34, 42.8%	Dengue shock with *Klebsiella* bacteremia. *BESTFIT:* LVEF 60%, IVC full. *Rx:* NE + Epi	T1: RV dysfunction T2: SVRI low T3: PVP 30%, renal venous congestion, high RRI. *Rx:* NE increased, vasopressin commenced, fluid removal via CRRT	16 hours after T1-3 exam. Survived
2 RS	14 years/F 32 22, 10.8%	Leukemia with invasive *candida* sepsis. Recurrent hypotensive shock after 48 hours. *BESTFIT:* LVEF 40% *Rx*: NE + epi + vaso	T1: RV dysfunction, LV diastolic dysfunction T2: SVRI high, SVI low *Rx*: Epi and NE discontinued, low dose vasopressin continued, milrinone added. CRRT for diuretic-resistant fluid overload	22 hours after T1-2 exam. Survived
3 RS	8 months/M 24 13, 2.3%	*Pseudomonas* bacteremia *BESTFIT:* LVEF 55%, B lines + *Rx*: NE + epi Shock recurrence with pulmonary edema requiring re-intubation.	T1: Diastolic dysfunction T2: Normal *Rx*: Dobutamine and epinephrine discontinued. Milrinone and diuresis initiated. HR control with beta-blocker	Successful second extubation. Survived
4 PS	5 months/F 19 21, 20.8%	*Staphylococca*l pneumonia *BESTFIT:* LVEF 70% *Rx*: FB, NE	T1: Diastolic dysfunction + RV dysfunction T2: SVRI high, low SVI *Rx*: Milrinone and diuresis. NE discontinued	16 hours after T1-2 Survived
5 PS	7 months/F 28 18, 32%	*Klebsiella* sepsis, gut focus *BESTFIT:* LVEF 60%, IVC full. *Rx*: NE	T1: RV dysfunction T2: Normal T3: HVD: Systolic (S) >Diastolic (D), PVP 40%, RRI 0.7. *Rx*: Milrinone, epinephrine, vasopressin, PEEP titration, inhaled nitric oxide, CRRT for diuretic-resistant positive fluid balance	Inadequate response Died on day 6
6 PS	2 months/M 10 15, 18%	*Klebsiella* pneumonia, ARDS *BESTFIT:* LVEF 65%, IVC full *Rx*: NE, milrinone	T1: RV dysfunction T2: Normal T3: HVD: Systolic (S) wave reversal, PVP 40% *Rx*: Milrinone up-titrated, epinephrine + vasopressin started, diuresis increased. PEEP titration, inhaled nitric oxide started	26 hours after T3 exam. Survived
7 PS	8 months/M 15 10, 12.9%	Pyelonephritis, *Klebseilla* spp. *BESTFIT:* LVEF 40% *Rx*: FB, NE, epi	T1: Normal T2: SVRI low *Rx*: Epi continued, NE infusion carefully up-titrated with serial clinical, EC and Echo monitoring	12 hours after T2 exam. Survived
8 PS	4 years/F 36 22, 26%	*E. coli* sepsis, GI focus *BESTFIT:* LVEF 30% *Rx*: NE, epi	T1: Diastolic dysfunction T2: SVRI low *Rx*: Epi stopped, Milrinone and diuresis started, NE increased, Vasopressin added	36 hours after T2 exam. Survived
9 PS	6 years/F 26 23 32.3%	Neutropenic sepsis, Adenovirus pneumonia *BESTFIT:* LVEF 35%, *Rx*: NE, epi, vaso	T1: Diastolic dysfunction T2: SVRI low *Rx*: Epinephrine and NE dose decreased, added vasopressin + Levosimendan, Fluid removal by CRRT	Inadequate response Died on day 7
10 PS	15/M 13 25 8.5%	*Klebsiella* sepsis, ALL neutropenic sepsis. *BESTFIT:* EF 25%, IVC full, B lines++ *Rx*: NE, Epi	T1: Normal T2: SVI low *Rx*: Red cell transfusion for low $ScvO_2$ and SVI. NE discontinued, diuresis.	28 hours after T2 exam. Survived

BESTFIT+, **B**asic **E**chocardiography in **S**hock **T**herapy for **F**luid and **I**notrope **T**itration + lung ultrasound; CRRT, continuous renal replacement therapy; EC, electric cardiometry; Echo, echocardiography; Epi, epinephrine; FB, fluid bolus; HVD, hepatic venous Doppler; IVC, inferior vena cava; LVEF, left ventricular ejection fraction; NE, norepinephrine; POCUS, point of care ultrasound; PVP, portal vein pulsatility; RRI, renal resistive index; RV, right ventricle; Rx, treatment; $ScvO_2$, central venous saturations; SVI, stroke volume index; SVRI, systemic vascular resistance index; Vaso, vasopressin; VExUS, venous excess ultrasound

of systemic venous congestion and high renal-resistance index (RRI 0.8). Continuous renal replacement therapy (CRRT) was commenced for diuretic-resistant renal failure and gross fluid overload. T1-3 monitoring in this patient not only prompted the earlier recognition of bacterial sepsis and early antibiotic initiation, but also directed intensified therapy of RV dysfunction and VC. Following this targeted management, his circulatory and metabolic parameters improved.

Case #2 was a patient with RS who demonstrated worsening shock and organ dysfunction 48 hours after initial improvement, for whom ECMO was considered. T1-2 monitoring showed combined LV systolic and DD, low SVI and high SVRI. Catecholamines were

discontinued, and noncatecholamine vasoactives (milrinone and vasopressin) were initiated targeting perfusion parameters and low-normal MAP along with controlled fluid removal via CRRT. Her circulatory status and oxygenation recovered steadily, and she could be extubated in 5 days.

Case #3 also had combined LV systolic and DD at initial presentation. His cardiac function and perfusion improved well enabling discontinuation of supports and extubation on day-4. However, he required to be re-intubated and ventilated with higher vasoactive and ventilatory support owing to RS and pulmonary edema. Repeat BESTFIT + T1 monitoring demonstrated recurrence of DD. Shock resolution and a successful second extubation were facilitated by initiation of therapy for DD including tachycardia control with low-dose beta-blocker.

Case #4 had hypotensive vasodilatory shock and normal LV systolic function. MAP normalized with NE titration. However, he remained in PS with episodic pulmonary edema, and T1-2 exam demonstrated moderate RV dysfunction, DD, low SVI with elevated SVRI. With this information, NE infusion was decreased to target low-normal MAP and SVRI, milrinone was added for RV inotropy and LV lusitropy, and furosemide infusion dose was increased. The changed therapeutic regime resulted in improved SVI and biventricular function, as well as better lung mechanics permitting successful extubation.

Cases #5 and #6 presented with septic shock unresponsive to initial fluid boluses and inotropes (NE, NE + milrinone). BESTFIT + T-1 monitoring demonstrated normal LV systolic function and a congested IVC and RV dysfunction with TR, while T-2 monitoring was noncontributory. Both patients remained in unresolved PS despite receiving diuresis, vasoactives, and adjusted ventilator settings to optimize RV function. T-3 monitoring revealed persistent VC, TR features on hepatic Doppler, a pulsatile portal vein, and renal congestion. In addition, renal Doppler exam in Case #5 demonstrated a RRI of 0.7 indicative of advanced VC.

In both patients, vasopressin and epinephrine were initiated to increase RV support and more aggressive fluid removal including CRRT in Case #5 was instituted. While Case #6 recovered fully, Case #5 remained in PS and died.

Cases #7, 8, 9 had similar initial BESTFIT exams and therapy and were placed on epinephrine + NE infusions for hypotensive vasodilatory shock and LV systolic dysfunction. T-1 and T-2 monitoring demonstrated additional DD in case #8 and 9, with low SVRI in all three patients despite NE infusion. Considering the risk of further worsening of the LV systolic impairment with escalated pressors, cautious increase in NE, addition of low-dose vasopressin, and serial monitoring of clinical perfusion markers, SVI and SVRI via EC along with LV systolic and diastolic function via echo was performed. This strategy resulted in steady improvement in MAP and diastolic BP, which provided opportunities for initiating diuresis and addition of noncatecholamine inodilator (milrinone). The circulatory status normalized in Case #7 and 8, and all vasoactive as well as ventilatory supports were discontinued over the next 36 hours.

However, in Case #9, vasoplegia with low DBP and MAP was refractory, her heart function continued to be sluggish, and weaning from ventilatory and RRT support was not possible on account of persistent organ failure: the patient expired on day-7.

Case #10 had PS with poor LV systolic function + low SVI on T-2 monitoring and anemia (Hb 7.1 gm/dL). His perfusion parameters including SVI improved with weaning of pressor, red cell transfusion, and an inodilator (milrinone) infusion.

Discussion

We present our unit experience with 10 cases of pediatric septic shock with PS/RS. We propose that a few life-threatening diagnoses exist that are difficult to make clinically or even with BESTFIT examination, and these can be detected with advanced ultrasound and noninvasive CO monitoring. We briefly outline the circulatory abnormalities as well as changes in therapy detected and directed by BESTFIT + T3 examinations and demonstrate that this novel approach was successful in providing more precise therapy and reversing PS/RS in 8/10 patients.

However, while noninvasive, high-yield, and relatively inexpensive, these advanced imaging modalities can only be powerful if the bedside intensivist has a deep understanding of the strengths and limitations of each modality, an ability to integrate the information within the clinical context as well as a clear grasp of cardiovascular physiology and supportive regimens.[15]

The intensivist experienced in bedside POCUS is well-positioned to progress to real-time BESTFIT + T3 to fine-tune not just fluids and vasoactive-inotrope infusions, but also other ICU therapies with important cardio-respiratory interactions such as mechanical ventilation, sedation, and patient position.

Common Pathophysiologic Aberrations in Our Cohort

Coexisting Pathophysiology and Therapeutic Conflict

The commonest reason for PS/RS in our series was coexisting circulatory pathophysiology requiring diametrically opposite hemodynamic treatments and posing therapeutic conflict. For instance, Cases #7, 8, 9 had poor LV systolic function (necessitating afterload-lowering inodilators) coexisting with vasodilatory shock (needing afterload-raising pressors to maintain perfusion pressures). Similarly, Cases #2, 3, 8, and 9 had co-existence of LV systolic and DD; in these cases, commonly used catecholamine-inotropic therapy of the former can lead to worsening of the latter.[16] Moreover, in patients with unresolved shock, clinicians often tend to give more fluid, more inotropes, and more pressors without clear indications, further compounding the continuing circulatory instability and making it exceedingly challenging to tease out the cause and effect of PS.

Right Ventricular Dysfunction

Acute RV dysfunction is well reported to have significant hemodynamic impact and mortality in adults[17] but sparsely reported in pediatric septic shock,[18] and in our cohort, was seen in 10% of all septic shock and in 5/10 cases of PS/RS. The thin-walled RV functions best as a "volume-pump" rather than a "pressure-pump," and undergoes rapid potentially lethal decompensation with acute increases in afterload, as might typically occur when a patient ventilated with high airway pressures receives fluid loading for hypotension/hypoperfusion as in Case #6. Because of the integrated relationship of the RV and LV pumps, both in series and working in parallel, RV decompensation leads to dilation and interventricular septal shift. This decreases LV filling and cardiac

output, setting off a rapid downward spiral with further decreases in RV perfusion and function.[13]

Diastolic Dysfunction

Similar to RV dysfunction, DD is also underrecognized, being reported in 33–41% in pediatric sepsis[19] and was present in 5/53 (10%) and 5/10 (50%) of the entire septic shock cohort and PS/RS, respectively. Diastolic dysfunction has greater mortality than systolic dysfunction,[20] and typically presents with tachycardia, low CO, and flash pulmonary edema.[8] Catecholamines with prominent beta-1 adrenergic effects (dopamine, dobutamine, epinephrine) can result in tachycardia which decreases time for ventricular relaxation and worsen DD further because the adverse chronotropic effect of beta-1 stimulation (shortened ventricular filling time) outweighs the lusitropic effect of beta-1 effect.[21]

Abnormal Vascular Tone

Altered vascular tone is common in patients with persistent shock; however, clinical examination may be unreliable to differentiate between a low vs high SVRI state.[1]

PS in patients #7, 8, and 9 was due to persistent hypodynamic LV with low SVRI despite epinephrine and norepinephrine infusions. Cautious up-titration of pressor and inotrope infusions while monitoring trends in clinical perfusion markers, along with objective measures of SVI, LVEF, and SVRI is important to maintain the balance of optimal perfusion pressures with preserved LV function.[22,23]

Venous Congestion

Hemodynamic management has always focused on the arterial side with the venous aspect being mostly disregarded. Venous congestion or venous excess is a relatively new concept that is gaining recognition in critically ill adults where volume accumulation occurs secondary to mismatch between venous return and cardiac output.[24] Venous congestion is often underrecognized and underdiagnosed and is an area of critical care ultrasound that can provide great value in fluid management.

Heart disease (RV or LV systolic and LV-DD), lung disease, and fluid overload can cause venous congestion, as high pressure anywhere downstream of the veins will result in high venous pressures.[25] Venous congestion can lead to tissue hypoperfusion and organ dysfunction due to a reduced gradient for organ perfusion; VC may be particularly detrimental when CO is also reduced.[26]

Venous congestion first manifests on ultrasound as IVC dilatation and then as flow abnormalities in the great veins (hepatic, portal, and renal veins) when assessed with PW Doppler. Assessment of this is termed as Venous Excess UltraSound (VExUS).

There is growing recognition of the utility of Doppler ultrasound to detect and treat VC in adult critically adults, but no reports of VExUS in pediatric septic shock. Although seemingly daunting at first glance, VExUS is a logical extension of POCUS. With adequate training and practice, POCUS-trained pediatric intensivists can perform hepatic, portal, and renal Doppler reasonably well such that the VC may be diagnosed at early stages of abnormal flow patterns.

Limitations

This is a small case series of a single-center experience of hemodynamic optimization in a group of extremely sick patients. BESTFIT-T3 requires an advanced skillset with greater proficiency in image generation, image interpretation, and clinical integration. Although this approach lacks a strong evidence base, we found that a systematically applied BESTFIT-T3 approach was useful to manage persistent/recurrent shock in our unit.

Regarding the EC device, while extensively studied in children, the device has limitations in accuracy, and it has not been validated in pediatric septic shock. The choice of EC was based on pragmatic reasons, including rapid deployment even in nonintubated patients, safety, noninvasiveness, cost, and no interobserver variability. Moreover, our treating team has a good understanding of its strengths/limitations, with two recent studies using this device.[9,27]

A recent pediatric meta-analysis reviewed the validity of electrical bioimpedance-based noninvasive CO-monitoring compared with thermodilution and echocardiography, and demonstrated no significant difference between the means of compared devices (except in neonatal stroke-volume). The authors concluded that electrical velocimetry devices may be acceptable for use in pediatrics, but the validity in neonates remains uncertain.[28]

Conclusion

A significant proportion of children with septic shock can have complicated interconnected pathophysiology that requires information beyond that provided by BESTFIT.

In this pilot conceptual report, we have described our unit experience with a tiered monitoring approach to clarify the underlying etiology of persistent or recurrent pediatric septic shock, as well as a physiologically driven cardiovascular treatment regimen that was helpful in 8/10 children with PS or RS. Further studies will be helpful to determine whether the novel BESTFIT-T3 approach is helpful to provide precision cardiovascular therapy in such patients.

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