ORIGINAL ARTICLE

Point-of-care ultrasound (POCUS) protocol for systematic assessment of the crashing neonate—expert consensus statement of the international crashing neonate working group

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Abstract

Sudden unexpected clinical deterioration or cardiorespiratory instability is common in neonates and is often referred as a "crashing" neonate. The established resuscitation guidelines provide an excellent framework to stabilize and evaluate these infants, but it is primarily based upon clinical assessment only. However, clinical assessment in sick neonates is limited in identifying underlying pathophysiology. The Crashing Neonate Protocol (CNP), utilizing point-of-care ultrasound (POCUS), is specifically designed for use in neonatal emergencies. It can be applied both in term and pre-term neonates in the neonatal intensive care unit (NICU). The proposed protocol involves a stepwise systematic assessment with basic ultrasound views which can be easily learnt and reproduced with focused structured training on the use of portable ultrasonography (similar to the FAST and BLUE protocols in adult clinical practice). We conducted a literature review of the evidence-based use of POCUS in neonatal practice. We then applied stepwise voting process with a modified DELPHI strategy (electronic voting) utilizing an international expert group to prioritize recommendations. We also conducted an international survey among a group of neonatologists practicing POCUS. The lead expert authors identified a specific list of recommendations to be included in the proposed CNP. This protocol involves pre-defined steps focused on identifying the underlying etiology of clinical instability and assessing the response to intervention.

Conclusion: To conclude, the newly proposed POCUS-based CNP should be used as an adjunct to the current recommendations for neonatal resuscitation and not replace them, especially in infants unresponsive to standard resuscitation steps, or where the underlying cause of deterioration remains unclear.

What is known?
• *Point-of-care ultrasound (POCUS) is helpful in evaluation of the underlying pathophysiologic mechanisms in sick infants.*

What is new?
• *The Crashing Neonate Protocol (CNP) is proposed as an adjunct to the current recommendations for neonatal resuscitation, with pre-defined steps focused on gaining information regarding the underlying pathophysiology in unexplained "crashing" neonates.*

• *The proposed CNP can help in targeting specific and early therapy based upon the underlying pathophysiology, and it allows assessment of the response to intervention(s) in a timely fashion.*

Keywords Crashing infant · Point-of-care ultrasound (POCUS) · Crashing Neonate Protocol (CNP) · Collapsed neonate · Collapsing neonate · Neonate

Abbreviations
AXR	Abdominal X-ray
CHD	Congenital heart disease
CNP	Crashing Neonate Protocol
CXR	Chest X-ray
LUS	Lung ultrasound

NICU   Neonatal intensive care unit
POCUS   Point-of-care ultrasound

Introduction

Point-of-care ultrasound (POCUS) refers to ultrasonography done at the bedside by the clinician caring for the patient [1]. It is performed in real time, with serial assessments longitudinally as required, to monitor disease progress and evaluate the response to interventions [2]. POCUS is a clinical tool applied to answer a practical specific question and guide critical care interventions, rather than a substitute for medical imaging performed and interpreted by diagnostic specialists (such as pediatric radiologists or cardiologists) [3]. A Crashing Neonate Ultrasound Protocol (CNP) could be used to assess any newborn needing or likely to need critical care, especially if the underlying cause is unknown. The routine use of POCUS has been suggested in clinical situations where the underlying mechanism of deterioration is unclear [3], and some authors have already proposed an algorithm for assessing life-threatening events in neonates admitted to the neonatal intensive care unit (NICU) such as SAFE/SAFER (Sonographic Assessment of Life-Threatening Events-Revised) protocol [4, 5].

A specific international working group of experts in POCUS was created to develop a screening protocol incorporating a quick bedside multiorgan ultrasound evaluation to understand the underlying mechanism of deterioration in a critically unwell newborn. The CNP protocol represents an expert consensus by POCUS key leaders, built on appropriate methodology, for the use of POCUS applications in the critically ill or crashing neonate in NICU. The proposed CNP is specifically designed for use in neonatal emergencies leading to significant cardiorespiratory instability and can be used in both term and pre-term neonates who are either "crashed" (needing resuscitation) or "crashing" (likely to need resuscitation if not stabilized soon) infants. CNP proposes a stepwise systematic targeted assessment with simple basic ultrasound views which are easily reproducible and can be learnt with a focused training, similar to the already established SAFE/SAFER in the newborn [5]. The CNP introduces a new approach with pre-defined steps focusing at assessing the underlying etiology for unresponsiveness to resuscitation, a sudden deterioration for unknown reason, or acute unexplained anemia/blood loss [6]. This protocol provides neonatal practitioners an opportunity to understand the ongoing multiorgan pathophysiology in real time as compared to the conventional blind "guessing" approach that often occurs in the absence of direct physiologic information. The CNP is focused on the evaluation of four vital organs most often compromised in the unstable neonate, as well as an assessment of central line-related complications. The protocol includes (a) Lung-POCUS assessment of pulmonary emergencies (pneumothorax, pleural effusion, or lung atelectasis); (b) Cardiac-POCUS assessment of shock and hemodynamic instability; (c) Cranial-POCUS assessment for acute brain hemorrhage; (d) Abdominal-POCUS assessment of peritoneal or subcapsular bleeding, gut injury, or bowel ischemia; and (e) assessment of central line-related complications by Central-Line POCUS [3, 7].
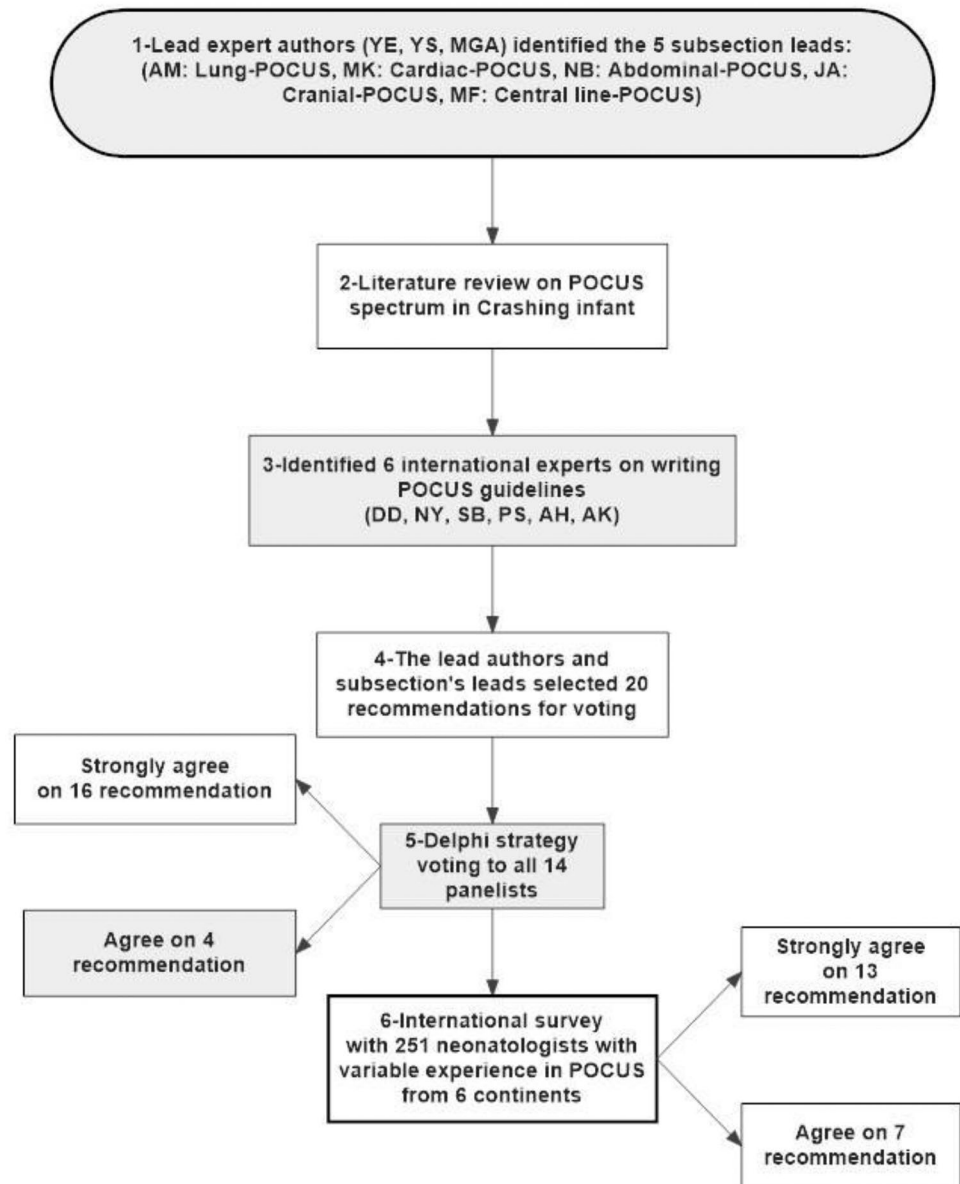
Methods

Steps of developing the consensus statement

We applied the following six steps in developing the consensus statement, as summarized in Fig. 1:

Step 1: Three lead expert authors in POCUS (YE, YS, and MGA) identified 5 subsection expert leaders (AM: Lung-POCUS, MK: Cardiac-POCUS, NB: Abdominal-POCUS, JA: Cranial-POCUS, MF: Central line-POCUS).

Step 2: The lead authors performed a literature review in the six main domains (general indications of CNP, Lung-POCUS, Cardiac-POCUS, Abdominal-POCUS, Cranial-POCUS, and central line-related complications). The level of evidence was assessed according to the published guidelines (GRADE) [8, 9].

Step 3: The lead authors together with the subsection leaders identified another 6 expert neonatologists who have significantly contributed with institutional guidelines and publications in the field of POCUS and/or developed POCUS training courses in the last 10 years. The selected experts were from Europe, USA, Canada, Asia, and Australia (DD, NY, SB, PS, AH, AK) and together formed a group of 14 panelists.

Step 4: The lead authors and subsection' leaders selected 20 recommendations for voting. The first 6 recommendations are general indications of the CNP protocol, 4 Lung-POCUS recommendations, 5 Cardiac-POCUS recommendations, 2 Abdominal-POCUS recommendations, one recommendation for each of Cranial and central line-related complications, and one related to the whole algorithm itself.

Step 5: *Step 5*: We applied a modified anonymous electronic Delphi strategy for the online voting process [10]. The Delphi method of voting was among the 14 panelists, each recommendation was graded to 5 grades of agreement: strongly agree, agree, neutral, disagree, and strongly disagree as described in RAND/ULCA published methodology of consensus agreement [11–13].

Step 6: The final step was an open anonymous survey to an international group of 251 neonatologists who are members of the "point of care ultrasound in neonatology association" (pocusneo.org) with a variable degree

Fig. 1 The flow diagram summarizing the six steps applied to reach the consensus agreement
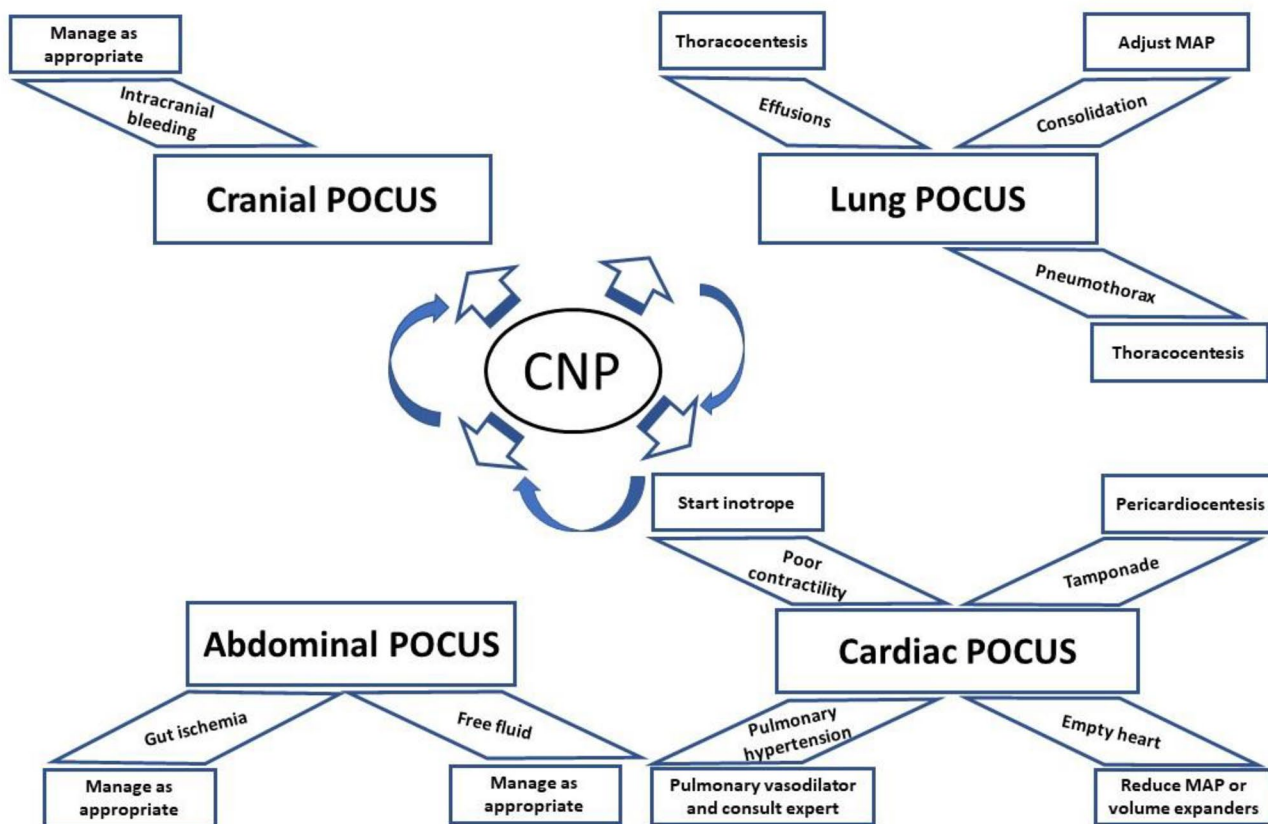

of experience in utilization of POCUS. The statement recommendations have been prepared according to the international Appraisal of Guidelines, Research and Evaluation (AGREE). Each recommendation is intended to be applied only in the neonatal population with unexplained deterioration as detailed in the protocol [14].

Steps of developing the CNP

The three lead experts met with the subsections leaders and developed the CNP considering the priority steps for assessment of neonate, parallel to neonatal resuscitation program (NRP) [15]. CNP starts with identifying the indication of the protocol as stated in the consensus agreement. The first priority of the NRP is assessment of adequate ventilation and the underlying lung pathology by Lung POCUS and then assessment of circulation by Cardiac POCUS [16, 17–21]. The next step is assessment of cranial hemorrhage by Cranial POCUS [22] followed by abdominal hemorrhage and gut injury on Abdominal POCUS [1, 23]. Then assessment of central line-related complication by Central line POCUS is recommended [24]. The algorithm of the CNP was refined many times before approving the final algorithm described in Fig. 2 by consensus agreement among all authors.

Fig. 2 Algorithm for multiorgan systematic assessment by ultrasound for any neonate not responding to the standard steps of resuscitation after birth or any time during NICU admission. The sequence and start point may be different according to the clinical presentation of the crashed or the crashing neonate

Results and discussion

A total of 20 recommendations on the use of POCUS in the crashing neonate were assessed. There was strong agreement among all the panelists on 16 recommendations and agreement on 4 recommendations, as detailed in Table 1. We included results of both the Delphi method of voting among the 14 expert panelists and the survey of POCUSNEO members (all members are practicing neonatologists and utilize POCUS in their clinical practice with variable expertise).

Recommendations for the general indications of the CNP in neonatal practice

1. *POCUS can provide helpful information when a neonate is not responding to the initial steps of resuscitation— agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: When a newborn is not responding to the initial steps of resuscitation (heart rate < 100, low arterial oxygen saturation (SpO2) < 85%

after effective positive pressure ventilation adequate oxygen therapy) with no identifiable cause clinically, the underlying cause is secondary to the cardiorespiratory systems in most of the cases as detailed in the next 2 Sects. [10–12].

2. *POCUS is helpful in evaluating infants with unexplained circulatory shock—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: In the presence of circulatory shock, defined as blood pressure less than the lower limit for corrected gestational age, POCUS is helpful in understanding the cause and mechanism of shock [26–28].

3. *POCUS is helpful in evaluating infants with unexplained lactic acidosis—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: Lactic acidosis is a marker of decreased oxygen delivery which could be due to hemodynamic instability, acute anemia, or severe hypoxia. Identifying the underlying cause can be a challenge without detailed multiorgan assessment using POCUS [25, 28, 29].

Table 1 Summary of recommendations for the Crashing Neonate Protocol with levels of agreements and quality of published evidence

POCUS section	Recommendation	Level of agreement		Quality of evidence (GRADE)
		Experts in POCUS $N=14$	Neonatologists $N=251$	
General-1	POCUS can provide helpful information when a neonate is not responding to the initial steps of resuscitation	Agree	Strongly agree	C
General-2	POCUS is helpful in evaluating neonates with unexplained circulatory shock	Strongly agree	Strongly agree	C
General-3	POCUS is helpful in evaluating neonates with unexplained lactic acidosis	Strongly agree	Strongly agree	C
General-4	POCUS evaluation is helpful in evaluation of worsening acute hypoxemia unresponsive to routine support	Strongly agree	Strongly agree	C
General-5	POCUS is helpful in assessing neonates with compromised peripheral perfusion, with decreased perfusion index or prolonged capillary refill time	Strongly agree	Strongly agree	C
General-6	POCUS is helpful in localizing a source of hemorrhage when there is an unexplained drop in hematocrit or hemoglobin	Strongly agree	Strongly agree	C
Lung-1	Lung POCUS is helpful to diagnose pneumothorax accurately in the crashing neonate	Strongly agree	Agree	B
Lung-2	Lung POCUS is helpful in diagnosis of pleural effusion in the crashing neonate	Strongly agree	Strongly agree	B
Lung-3	Lung POCUS is helpful in semi quantifying pleural effusion in the crashing neonate	Strongly agree	Strongly agree	D
Lung-4	Lung POCUS is helpful in diagnosis of lung consolidation in the crashing neonate	Strongly agree	Agree	B
Cardiac-1	Cardiac POCUS is helpful in diagnosis of pericardial effusion and pericardial tamponade in the crashing neonate	Strongly agree	Strongly agree	B
Cardiac-2	Cardiac POCUS is helpful in semi-quantification of pericardial effusion in the crashing neonate	Agree	Agree	C
Cardiac-3	Cardiac POCUS is helpful for rapid recognition of poor contractility in the crashing neonate	Agree	Agree	D
Cardiac-4	Cardiac POCUS is helpful in recognition of underfilling of the heart in the crashing neonate	Strongly agree	Strongly agree	D
Cardiac-5	Cardiac POCUS is helpful in recognition of pulmonary hypertension in the crashing neonate	Strongly agree	Agree	B
Cranial	Cranial POCUS is helpful in the assessment of intracranial hemorrhage in neonates with rapidly progressing anemia	Strongly agree	Strongly agree	A
Abdomen-1	Abdominal POCUS is helpful in the diagnosis of ascites or abdominal bleeding in the crashing neonate	Strongly agree	Agree	C
Abdomen-2	Abdominal POCUS is helpful in the diagnosis of gut injury in the crashing neonate	Agree	Agree	B
Line -POCUS	POCUS is helpful in identifying complications related to central lines in the crashing neonate	Strongly agree	Agree	C
Algorithm	Multiorgan assessment (Lung POCUS, Cardiac POCUS, Abdominal POCUS, Cranial POCUS, and Central Line POCUS) as one integrated algorithm is helpful in assessment of the crashing neonate with unknown etiology	Strongly agree	Strongly agree	C

4. *POCUS evaluation is helpful in evaluation of worsening acute hypoxemia unresponsive to routine respiratory support—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C):* Worsening hypoxemia unresponsive to routine respiratory support and positive pressure ventilation could be secondary to multiple pathophysiologic mechanisms related to parenchymal lung disease and/or cardiac con-

ditions, which may be difficult to diagnose without a detailed assessment using POCUS as explained in lung-POCUS subsection [4, 6, 7].

5. *POCUS is helpful in assessing infants with compromised peripheral perfusion, with decreased perfusion index or prolonged capillary refill time—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: Compromised peripheral per-

fusion can be an early sign of worsening hemodynamic instability or shock, and routine clinical examination has limitations in its ability to diagnose the underlying mechanism [28].
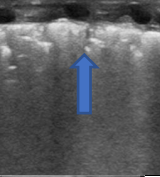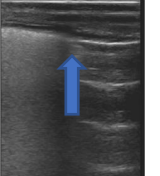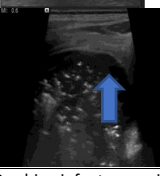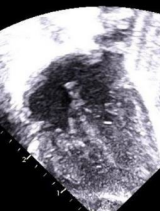
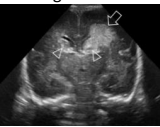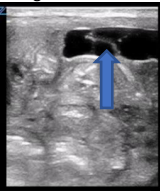6. *POCUS is helpful in localizing a source of hemorrhage when there is an unexplained drop in hematocrit or hemoglobin—strong agreement by the panelist and strong agreement by the neonatologists (quality of evidence C)*: Perinatal hemorrhage could be secondary to birth trauma, intraventricular hemorrhage in preterm infants, or spontaneous hemorrhage secondary to coagulopathy. Localizing the hemorrhage by ultrasonography is critical for planning medical intervention and is a time-sensitive indication [8–10].

Recommendations for applying Lung POCUS in the crashing infant

The use of lung ultrasound (LUS) in neonatal and pediatric intensive care has seen rapid growth over the past few years, both for clinical and research purposes [32, 33]. The recently published international guidelines on the use of POCUS provided evidence-based recommendations for diagnosis and monitoring of various lung conditions in critically ill children and neonates [1]. Lung POCUS is an ideal tool for use in emergency situations since it is quick, portable, repeatable, accurate, non-invasive, and radiation free and thereby offers a number of advantages for the clinician when compared with the chest X-ray (CXR) [34].

1. *Lung POCUS is helpful to diagnose pneumothorax accurately in the crashing neonate—strong agreement by the panelists and agreement by the neonatologists (quality of evidence B)*: Evidence from the adult, pediatric, and neonatal literature has shown that LUS has higher diagnostic accuracy (91% sensitivity and 98% specificity) when compared to CXR in detecting pneumothorax, and time to make the diagnosis is shorter [35–37]. Visualization of the following combined LUS patterns can accurately diagnose pneumothorax: (1) absence of "lung sliding sign" of the pleural line, (2) complete absence of B lines, i.e., only A-lines, (3) presence of a "lung point," and (4) presence of a stratosphere sign on M-mode imaging (Table 2B) [38]. Of note, evidence of pneumothorax on LUS should always be interpreted in the clinical context. Assessment of the lung point, which is the point of separation of the pleural leaflets and is seen at the point where normal sliding pleura meets the non-sliding segment, is specific of pneumothorax and can help in predicting pneumothorax size [36].

2. *Lung POCUS is helpful in diagnosis of pleural effusion in the crashing neonate—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence B)*: In a newborn with congenital effusion(s), such as those with congenital hydrothorax or chylothorax, may comprise ventilation, and a timely drainage of the effusion is often essential to allow expansion of the lung. Pleural effusion is also an uncommon, but serious complication of central lines, which are one of the mainstays of neonatal critical care in delivering infusions [39].

   Lung POCUS provides a quick and reliable information regarding presence of pleural fluid and has a high diagnostic accuracy, close to that of a CT scan and superior to CXR, with a 93% sensitivity and 96% specificity [40, 41]. The presence of effusion on lung POCUS is seen as a hypoechoic area between the pleural leaflets at the dependent costophrenic angle.

3. *Lung POCUS is helpful in semi-quantifying pleural effusion in the crashing neonate—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence D)*: Lung POCUS is an excellent tool to rule out or to detect large pleural effusion that may lead to acute decompensation or compromise resuscitation efforts [32, 42, 43]. Although it is easier to diagnose pleural effusion by ultrasound as compared to CXR, the quality of evidence is low on quantifying the volume of pleural effusion in neonates. Hence, for the clinical decision-making, it is better semi-quantified using categories of minimal, small, moderate, or large volume. It is estimated by measuring the distance at the site of maximum collection [40].

4. *Lung POCUS is helpful in diagnosis of lung consolidation in the crashing neonate—strong agreement by the panelists and agreement by the neonatologists (quality of evidence B)*: Lung consolidation is characterized by the presence of a non-aerated area or lung parenchyma filled with fluid [44, 45]. The most common causes are atelectasis, inflammatory processes, severe pulmonary edema, or acute pulmonary hemorrhage [46]. The sonographic appearance of a consolidated lung usually looks like an area with an abnormal pleural line and bronchograms (figure in Table 2A) [30, 47]. Meta-analysis of LUS studies on diagnosis of lung consolidation has shown a high sensitivity and specificity of 96% and 93%, respectively. LUS is superior to both CXR and laboratory tests, even when combined together [48]. In a crashing infant, lung POCUS may help in rapidly diagnosing consolidation and/or atelectasis, which looks like a solid organ-like resembling liver [49, 50].

Table 2 Case scenarios of crashing neonates with the ultrasound images and their interpretation and subsequent interventions

	Clinical scenario	Ultrasound image	Interpretation	Intervention
		Crashing infant scenarios diagnosed by Lung-POCUS		
A	Preterm infant with chronic lung disease, SpO2< 80% on FiO2 of 1 on Mechanical ventilation (MV)		Lung atelectasis with air bronchogram	adjust mean airway pressure
B	Late preterm required prolonged PPV after birth, SpO2< 85% and on FiO2 of 1 on MV		Pneumothorax with lung point (the arrow).	Tapping or needle aspiration of air
C	Term infant with hydrops fetalis not responding to resuscitation.		Pleural effusion (blue arrow) with lung consolidation	Urgent tapping
		Crashing infant scenarios diagnosed by Cardiac-POCUS		
D	Preterm 29 weeks, post abdominal surgery for NEC, with shock unresponsive to vasopressors		4 chamber view with severe underfilling of both ventricles	Volume expanders
E	Term infant born with severe hypoxemia due to meconium aspiration		Parasternal short axis view with dilated RV and paradoxical movement of the IVS signifying pulmonary hypertension	Initiation of inhaled nitric oxide as pulmonary vasodilator, consult for comprehensive echocardiogram
F	Preterm 25 weeks, with migration of central line		Subcostal view with pericardial effusion affecting myocardial performance.	Ultrasound guided pericardiocentesis and removal of central line
		Crashing infant scenario diagnosed by Cranial-POCUS		
G	Preterm 24 weeks with anemia and acidosis on day 3 of life		Cranial ultrasound with severe IVH; left parenchymal hemorrhage (arrow) and bilateral IVH (arrow heads)	Packed RBC transfusion, and serial follow up of cranial- POCUS
		Crashing infant scenarios diagnosed by Abdominal -POCUS		
H	Term infant post traumatic delivery with pallor		Abdominal ultrasound with fluids and debris.	Tapping of ascites and volume expansion (packed RBC transfusion if hemorrhagic ascites)
I	Preterm 32 weeks with abdominal distension and hemodynamics instability		Abdominal ultrasound showing pneumatosis intestinalis, absent peristalsis and ascites	Management according to NEC protocol

Recommendations for applying Cardiac POCUS in the crashing neonate

Cardiac POCUS was first described in the 1980s as a readily available, rapid, limited bedside examination performed by emergency physicians to enhance diagnostic capabilities and direct therapy [51]. In the event of acute decompensation, the goal of cardiac POCUS is to assess cardiac filling and function, pericardial effusion, and ventricular symmetry [52–54]. *Cardiac POCUS is not intended to be used as a screening tool for detection of congenital heart diseases (CHD)* [52]. However, when clinical urgency precludes a comprehensive echocardiographic assessment in a critically ill infant, utilization of standardized protocols by clinicians trained in cardiac POCUS may aid in recognition of abnormalities and help them in consulting a cardiac specialist earlier [1, 7, 55, 56]. CHD, such as outflow tract obstruction, may manifest as poor cardiac function, and recognition of an abnormal cardiac ultrasound may direct management and expedite a comprehensive cardiac evaluation [47].

1. *Cardiac POCUS is helpful in diagnosis of pericardial effusion and cardiac tamponade in the crashing neonate—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence B)*: One of the most immediate applications of cardiac POCUS in a crashing neonate is to rule out cardiac tamponade or a large pericardial effusion leading to cardiovascular instability [56, 58, 59]. Pericardial effusion can reliably be seen on cardiac POCUS by using multiple echocardiographic views. When cardiac tamponade is detected, POCUS can be used to guide pericardiocentesis, and ultrasound-guided pericardiocentesis is associated with a lower complication rate compared to the traditional landmark technique (figure in Table 2F) [59–61].

2. *Cardiac POCUS is helpful in semi-quantification of pericardial effusion in the crashing neonate—agreement by the panelists and agreement by the neonatologists (quality of evidence C)*: The decision to treat pericardial effusion should be made based upon the clinical significance, and ultrasound findings should be interpreted in the clinical context. Nagdev et al. assessed the importance of evaluating the movement of the right ventricle free wall and IVC size during respiratory cycle, and they reported a collapse of right ventricle free wall and absence of inspiratory collapse of IVC as reliable markers to diagnose significant pericardial effusion prior to development of shock [58].

3. *Cardiac POCUS can be used for rapid recognition of poor contractility in the crashing neonate—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: International

expert consensus statements highlighted the use of cardiac POCUS in pediatrics for assessment of cardiac function and filling [1]. The ability to rapidly identify and address cardiogenic shock can help in earlier initiation of appropriate treatment [62–65]. Qualitative assessment, rather than quantitative measurement of cardiac function from multiple views, including parasternal long and short axes and apical 4-chamber and subcostal view, is one of the primary goals of cardiac POCUS [52]. The use of cardiac POCUS in the hands of non-cardiologist clinicians trained in cardiac ultrasound enables them to differentiate normal and impaired contractility, with good interobserver correlation with cardiologists [66].

4. *Cardiac POCUS is helpful in recognition of underfilling of the heart in the crashing neonate—strong agreement by the panelists and strong agreement by the neonatologists (quality of evidence C)*: The use of clinical findings to guide fluid resuscitation in the neonate is challenging. The traditional markers such as capillary refill, central venous pressure, and tachycardia do not provide a definitive picture of fluid status [67]. The use of cardiac POCUS to evaluate volume status in a critically ill pediatric patient is recommended; however, in the mechanically ventilated neonates, recognition of preload can be challenging, and the findings should be interpreted in the clinical context. Assessment of the difference between end systolic and end diastolic volumes in the apical 4-chamber and parasternal long and short axis views by eyeballing for the filling volumes on 2D and M-Mode is useful for determining the need of fluid resuscitation (Table 2D) [1, 68].

5. *Cardiac POCUS is helpful in recognition of pulmonary hypertension in the crashing neonate—strong agreement by the panelists and agreement by the neonatologists (quality of evidence B)*: In a crashing infant, cardiac POCUS can be used to suspect or rule out moderate to severe pulmonary hypertension [69, 70]. While a detailed assessment of pulmonary hypertension or right ventricular function is out of the scope of cardiac POCUS, it can be utilized for the recognition and a focused evaluation of pulmonary hypertension and assessment of right ventricular function utilizing visual inspection and semi-quantitative assessment [54, 71].

In a crashing infant, pulmonary hypertension can be suspected when there is right ventricular hypertrophy and/or dilation in the presence of clinical suspicion such as persistent hypoxia and significant pre- and post-ductal saturation difference. In the presence of tricuspid regurgitation, pulmonary artery systolic pressure can be reliably estimated using cardiac POCUS [72, 73]. In the absence of tricuspid regurgitation, POCUS can be used for semi-quantitative assessment

of pulmonary hypertension by evaluating the interventricular septal position and movement at the end of systole and by assessing the flow direction and velocities across a patent ductus arteriosus and/or foramen ovale (figure in Table 2E) [69]. As stated previously, cardiac POCUS is not a screening tool for CHD, and recognition of abnormality warrants comprehensive cardiac evaluation to ensure a normal structured heart. Infants with suspected or established pulmonary hypertension should have a comprehensive echocardiographic evaluation by the specialist pediatric cardiologist or a neonatologist trained in performing targeted neonatal echocardiography.

Recommendations for applying Cranial POCUS in the crashing neonate

Cranial POCUS is helpful in assessment of intracranial hemorrhage in neonates with rapidly progressing anemia— strong agreement by the panelists, and strong agreement by the neonatologists (quality of evidence B): Cranial POCUS is the most common neuroimaging modality used in the NICU [62, 63]. In a crashing neonate, cranial POCUS enables the diagnosis of intraventricular, parenchymal, or large cerebellar hemorrhages. Cranial POCUS is usually performed through anterior fontanelle window; however, adding the mastoid fontanelle increases its reliability for diagnosing posterior fossa hemorrhages [74, 75]. Intraventricular hemorrhage (IVH) affects 20–40% of very preterm infants (born before 33 weeks' gestation) [65, 76]. Extensive IVH or parenchymal hemorrhage may present as a catastrophic event with apnea/bradycardia, hypotension, metabolic acidosis, a rapidly falling hematocrit, or seizures [66, 78]. Cranial POCUS can help in rapidly detecting IVH as per the Volpe or modified Papile classification (figure in Table 2I) [67, 77].

Recommendations for applying Abdominal POCUS in the crashing neonate

1. *Abdominal POCUS is helpful in the diagnosis of ascites or abdominal bleeding in the crashing neonate—agreement by the panelists, and agreement by the neonatologists (quality of evidence C)*: Ultrasound has a high sensitivity in assessing and localizing abdominal bleeding. While ultrasound cannot differentiate the nature of the fluid, free peritoneal or subcapsular fluid can represent blood in a patient with unexplained anemia or abdominal trauma [31]. Ultrasound can provide information regarding presence of blood in real time and can aid in therapeutic intervention such as ultrasound-guided abdominal paracentesis, mak-

ing it an excellent tool for use in neonatal emergencies [79, 80].

2. *Abdominal POCUS is helpful in the diagnosis of gut injury in the crashing neonate—agreement by the panelists, agreement by the radiologists, and agreement by the neonatologists (quality of evidence C)*: Ultrasound has been proven as an excellent imaging modality with a high sensitivity in assessing intestinal emergencies including gut ischemia secondary to shock [81, 82]. We recommend assessment of intestinal ischemic injury in any case of shock with unknown cause (figure in Table 2G) [1, 57]. In addition to gut ischemia, abdominal ultrasound can be performed in any infant suspected of having anemic shock due to traumatic abdominal bleeding (figure in Table 2H) [81].

Recommendations for applying Central Line POCUS in the crashing neonates

POCUS is helpful in identifying complications related to central lines in the crashing neonate—strong agreement by the panelists and agreement by the neonatologists (quality of evidence C): Several studies have questioned the accuracy of X-rays in assessing the line position accurately, reporting a discordance of 20–40% when compared to ultrasound assessment [83]. The anatomical position of the line can be viewed by X-ray, but identifying the intravascular position versus extravascular migration of the line needs either contrast study or ultrasound evaluation. With the available evidence, POCUS may be considered a standard of care for revealing central line tip position and catheter migration [84]. Furthermore, in neonates with acute clinical decompensation with impending cardiac arrest, where pericardial or pleural effusion are suspected due to central line malposition, radiological assessment is insufficient, and POCUS can reliably provide additional information in real time [60, 85, 86].

Integrated POCUS protocol for the crashing neonate

Multiorgan assessment (Lung POCUS, Cardiac POCUS, Abdominal POCUS, Cranial POCUS, and Central Line POCUS) as one integrated algorithm is helpful in assessment of the crashing neonate with unknown etiology— strong agreement by the panelists, and strong agreement by the neonatologists (B): The proposed protocol introduces a comprehensive approach using POCUS with pre-defined steps focused on the assessment of mechanisms of unresponsiveness to resuscitation, unexplained acute decompensation, or acute unexplained anemia/blood loss. CNP recommends using only focused ultrasound views, which are relatively easy to

practice and are reproducible, to detect specific pathologies [5]. Use of a POCUS-guided protocol in evaluation of a sick neonate provides an important opportunity for neonatal practitioners to identify the underlying pathophysiology in a crashing neonate in real time, replacing the empiric approach based upon clinical assessment [84]. This stepwise systematic assessment of the crashing neonate can be applied in any setting such as in the resuscitation room and NICU [5]. However, the sequence and the priority of the organ to be assessed might be different according to the clinical presentation [28]. Although this is the first consensus agreement statement on using POCUS to guide neonatal resuscitation, the practice in using POCUS during adult resuscitation is well established [5, 16].

If there is no response to resuscitation as per the neonatal resuscitation guidelines, we recommend using POCUS to identify the underlying pathology which may explain the reason for unresponsiveness to conventional measures, as demonstrated in the flow diagram (Fig. 2). This stepwise approach encompasses moving from organ to organ, considering the organ priorities as per the Neonatal Resuscitation Program (NRP) [5]. *First*, lung assessment includes assessing lung inflation for optimum ventilation and evaluation for the underlying pathologies such as lung collapse, pneumothorax, effusions [19, 45, 87, 88]. *Second*, cardiac assessment includes underfilling, poor contractility, pulmonary hypertension, and pericardial effusion [58, 89, 90]. If there is associated anemia or severe pallor, or suspicion of line migration, then cranial and abdominal POCUS should also be performed.

We acknowledge the limitations of POCUS-guided proposed protocol including the following: (1) Ultrasound is operator dependent, and the reliability of the images depends on the training and competency of the operator, quality of images, and the machine; (2) the operator needs to be trained in multiorgan assessment with completion of acceptable training in each module, so a clear institutional protocol for training and guidelines for practice should be considered; (3) CNP is time-sensitive and ideally needs a trained person being available in the NICU at any time; and (4) the level of evidence supporting the crashing neonate protocol is low to intermediate level (mostly B to C grade), and most studies supporting POCUS use are either observational or retrospective analysis type. An important next step would be to formally study the learning curve needed to apply the CNP protocol as a whole and/or each organ section.

Conclusion

The newly proposed protocol for the crashing neonate can be used as an adjunct to the current recommendations for neonatal resuscitation. The CNP protocol is proposed based upon preidentified steps focused on gaining information regarding pathophysiology in infants with unexplained clinical deterioration or those not responding to the standard resuscitation. In comparison to the currently used diagnostic aids, POCUS can provide valuable information in real time to answer a specific question relating to diagnosis or ruling out potential causes of deterioration. It can help in early diagnosis and facilitates targeting of specific intervention based upon the underlying pathophysiology in neonates, similar to the well-established application in pediatric and adult clinical practice.

Declarations

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