

THIRD bedside ultrasound protocol for rapid diagnosis of undifferentiated shock: a prospective observational study

P Geng, B Ling, Y Yang, Joseph Harold Walline, Y Song, M Lu, H Wang, Q Zhu, D Tan *, J Xu

ABSTRACT

Introduction: It is clinically challenging to differentiate the pathophysiological types of shock in emergency situations. Here, we evaluated the ability of a novel bedside ultrasound protocol (Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection [THIRD]) to predict types of shock in the emergency department.

Methods: An emergency physician performed the THIRD protocol on all patients with shock who were admitted to the emergency department. All patients were closely followed to determine their final clinical diagnoses. The kappa index, sensitivity, specificity, positive predictive value, and negative predictive value were calculated for the initial diagnostic impression provided by the THIRD protocol, compared with each patient's final diagnosis.

Results: In total, 112 patients were enrolled in this study. The kappa index between initial impression and final diagnosis was 0.81 (95% confidence interval=0.73-0.89; $P<0.001$). For hypovolaemic, cardiogenic, distributive, and obstructive types of shock, the sensitivities of the THIRD protocol were 100%, 100%, 93%, and 100%, respectively; the sensitivity for a 'mixed' shock aetiology was 86%. The negative predictive value of the THIRD protocol for all five types of shock was $\geq 96\%$.

Conclusion: Initial diagnostic judgements determined using the THIRD protocol showed

favourable agreement with the final diagnosis in patients who presented with undifferentiated shock. The THIRD protocol has great potential for use as a bedside approach that can guide the rapid management of undifferentiated shock in emergency settings, particularly for patients with obstructive, hypovolaemic, or cardiogenic shock.

Hong Kong Med J 2022;28:383–91

<https://doi.org/10.12809/hkmj219648>

¹ P Geng ^{*, MD}

¹ B Ling ^{*, MM}

¹ Y Yang, MM

² JH Walline, MD

¹ Y Song, MM

¹ M Lu, MD

¹ H Wang, MM

¹ Q Zhu, MM

¹ D Tan ^{*, MD}

³ J Xu, MD

¹ Department of Emergency Medicine, Clinical Medical College of Yangzhou University, Northern Jiangsu People's Hospital, Yangzhou, China

² Accident and Emergency Medicine Academic Unit, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

³ Department of Emergency Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China

[#] The first two authors contributed equally to this work

* Corresponding author: tandingyu1981@163.com

This article was published on 29 Sep 2022 at www.hkmj.org.

New knowledge added by this study

- Differentiating shock types in emergency situations is clinically challenging. We sought to assess the ability of a novel bedside ultrasound protocol (Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection [THIRD]) in predicting shock aetiology. Shock aetiology determined using the THIRD protocol showed acceptable agreement with the final diagnosis of shock in critically ill emergency department patients.
- The THIRD protocol demonstrated very high negative predictive values when it was used to evaluate patients with hypovolaemic, cardiogenic, distributive, and obstructive shock.
- The THIRD protocol showed least sensitivity for evaluation of mixed aetiology shock.

Implications for clinical practice or policy

- Our findings support incorporation of the THIRD protocol into routine emergency department assessment of patients with undifferentiated shock to help guide early treatment.
- Additional clinical assessments should be conducted to confirm a diagnosis of mixed shock made using the THIRD protocol.

THIRD床旁超聲方案用作快速診斷原因不明 休克：前瞻性觀察研究

耿平、凌冰玉、楊燕、華林傑、宋應豪、陸明峰、王暉暉、
朱慶程、談定玉、徐軍

引言：在緊急情況下區分休克的病理生理類型在臨床上具挑戰性。本文旨在評估一種新型床旁超聲方案（THIRD方案：填塞/張力性氣胸、心臟、下腔靜脈、呼吸系統、深部靜脈血栓/主動脈夾層）預測急症科區分休克類型的能力。

方法：急症科醫生對所有被急症科收治的休克患者進行THIRD方案，並進行密切跟進以確定他們的最終臨床診斷。計算由THIRD方案作出初步診斷的kappa指數、敏感性、特異性、陽性預測值和陰性預測值，並與每位患者的最終診斷比較。

結果：納入112名患者。初步診斷和最終診斷之間的kappa指數為0.81（95%置信區間=0.73-0.89； $P<0.001$ ）。對於低血容量性、心源性、分佈性和阻塞性休克類型，THIRD方案的敏感性分別為100%、100%、93%和100%；混合型休克病因的敏感性為86%。THIRD方案對所有五種休克的陰性預測值均達96%或以上。

結論：使用THIRD方案對原因不明休克患者的初步診斷與最終診斷結果一致。THIRD方案是具潛力的床旁指導方案，針對緊急情況下原因不明休克患者的快速管理，特別是對於阻塞性、低血容量性或心源性休克患者。

Introduction

Undifferentiated shock is a common presenting condition in the emergency department (ED) which requires timely and effective interventions. The rapid and accurate differentiation of possible shock aetiologies is essential for reducing morbidity and mortality in critically ill patients with shock.¹ Patients with undifferentiated shock in the ED often have an acute onset of severe illness, unstable vital signs, a limited medical history, and sparse physical examination findings.² Point-of-care ultrasound (POCUS) has a crucial role in the management of undifferentiated shock because it is the only visual imaging tool that can provide real-time information concerning the key elements of haemodynamics.^{3,4} The use of POCUS in the ED has been rapidly increasing because it is safe, reliable, non-invasive, rapid, and repeatable at the bedside.⁵

The first ultrasound protocol for undifferentiated shock was published in 2004⁶; since then, several additional protocols have been developed. The results of multiple studies have provided evidence that POCUS can help to differentiate the cause of hypotension, identify the most immediate life-threatening conditions, improve diagnostic certainty, and optimise treatment.^{7,8} The ‘Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection’ (THIRD) bedside

ultrasound protocol was published in 2017; it is the first POCUS protocol for undifferentiated shock in emergency medicine in mainland China.⁹ Compared with the ‘Rapid Ultrasound for Shock and Hypotension’ (RUSH) protocol, the THIRD protocol has been reported to significantly increase physician trainee self-confidence when diagnosing undifferentiated shock.¹⁰

The THIRD protocol is now widely accepted and regularly used by emergency physicians in China; to our knowledge, the protocol has not been validated in any studies thus far. This study was conducted to examine the effectiveness and accuracy of the THIRD protocol as an early and rapid bedside approach for the investigation of undifferentiated shock in emergency settings. We hypothesised that THIRD early diagnostic predictions would not demonstrate significant inconsistency with the final clinical diagnosis.

Methods

Enrolment

This single-centre prospective observational study enrolled patients with shock who presented to the emergency intensive care unit (EICU) section of the ED at a large, urban, tertiary teaching hospital between October 2017 and May 2019. The ED of the hospital has approximately 240 000 visits per year, and >800 patients annually are admitted to the 15-bed EICU for extended management. Shock was defined as acute circulatory failure which led to inadequate cellular oxygen utilisation.¹¹ We established the enrolment criteria for this study based on clinical feasibility and previous literature^{12,13}: (1) age >18 years and <95 years; (2) systolic blood pressure <90 mmHg or shock index (pulse/systolic blood pressure) >1.0, confirmed after ≥ 3 measurements during the first assessment; and (3) at least one of the following symptoms or signs of hypoperfusion: altered mental status (eg, syncope, delirium, or unresponsiveness), respiratory distress, oliguria, severe fatigue or discomfort, skin mottling, elevated blood lactate, and severe chest pain or abdominal pain. Patients with the following conditions were excluded from the study: (1) a pre-existing ‘hypotensive’ state recorded in past medical history or reported by the patient; (2) transfer from another hospital with a known diagnosis of shock type; and (3) no definite diagnosis of shock established during hospitalisation, despite plenary discussion of their clinical data.

Point-of-care ultrasound technique

The POCUS is routinely performed in all hemodynamically unstable patients in our EICU. In this study, an independent emergency physician with specific competence in emergency ultrasound

performed the THIRD protocol evaluation upon patient arrival (Fig 1). The physician had completed a 20-hour emergency ultrasound workshop including the THIRD protocol and had 3 years of experience with >300 ultrasound examinations per year. The physician was unaware of the history of present illness or any other diagnostic test results; the pathophysiological diagnosis of shock was made

based on ultrasound findings (Table 1). Ultrasound evaluation was performed with a Philips® Sparq ultrasound device routinely used in the EICU. This ultrasound system contains a high-frequency 4-12 MHz linear probe, a 2-6 MHz curvilinear probe, and a 2-4 MHz cardiac probe.

The THIRD protocol is divided into the following five parts.

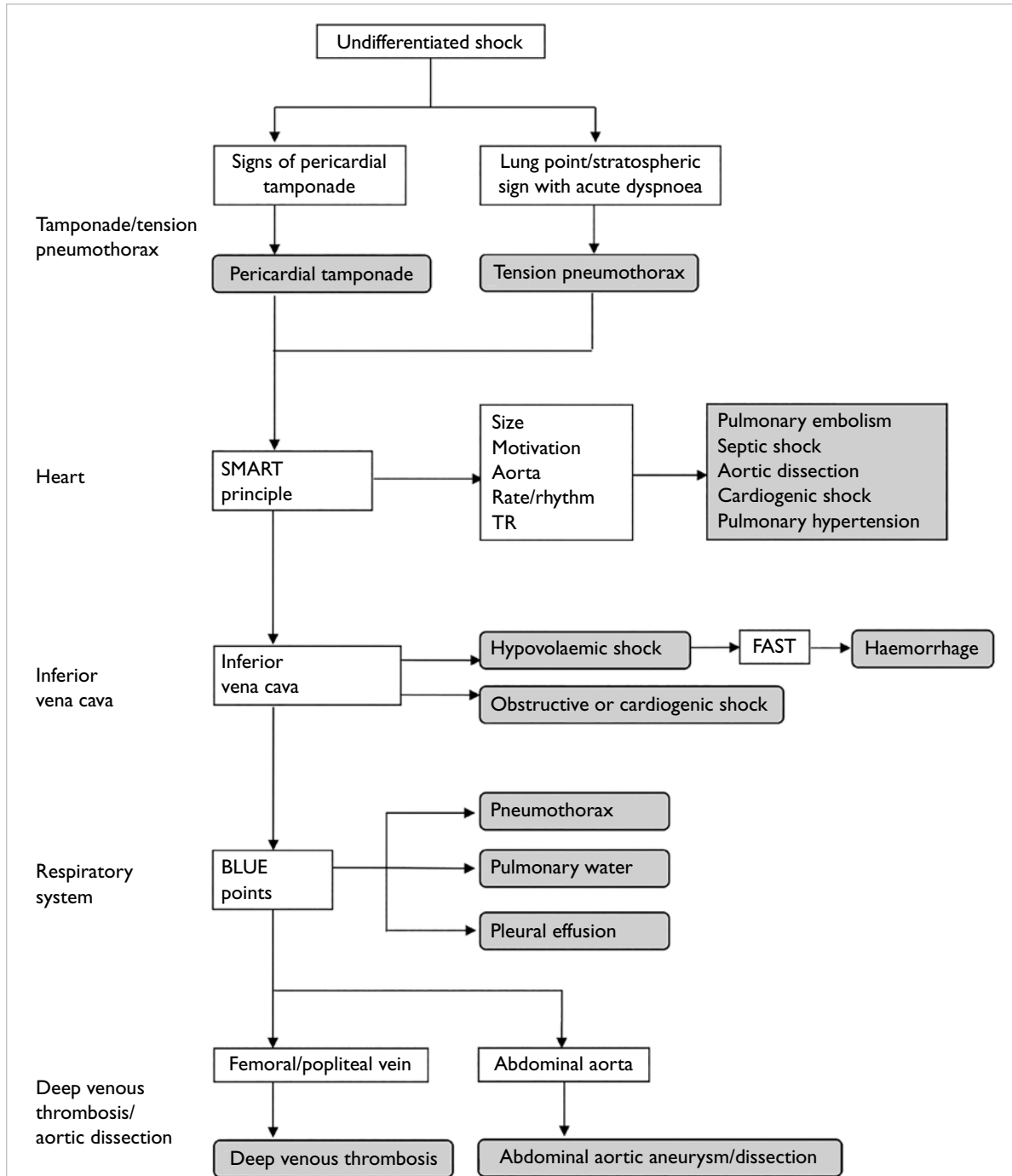


FIG 1. THIRD protocol for bedside ultrasound evaluation of undifferentiated shock

Abbreviations: BLUE = Bedside Lung Ultrasound in Emergency; DVT = deep venous thrombosis; FAST = Focused Assessment with Sonography for Trauma; SMART = Size, Motivation, Aorta, Rhythm/rate, Tricuspid regurgitation; THIRD = Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection; TR = tricuspid regurgitation

TABLE 1. THIRD protocol: possible ultrasound findings in shock

Ultrasound pattern	Diagnosis	Tamponade/ tension pneumothorax	Heart					IVC	Respiratory system		DVT or dissection
			Size	Motivation	Aorta	Rhythm/ rate	TR		Pulmonary water	Pleural effusion	
Obstructive	Cardiac tamponade	Pericardial effusion	Right heart collapse	Oscillating heart	-	Tachycardia	-	Dilation	-	-	-
	Tension pneumothorax	Stratosphere sign/lung point	Limited observations					Dilation	-	-	-
	Pulmonary embolism	-	D-sign	-	-	Tachycardia	+	Dilation	-	-	±DVT
Hypovolaemic shock	Haemorrhagic shock	-	Decreased	Hyperdynamic	-	Tachycardia	-	Collapsed	-	±	-
	Aortic aneurysm	-	±Decreased	Hyperdynamic	±	±	-	Narrow	-	-	Dilated aorta
	Aortic dissection	±Pericardial effusion	±Decreased	±Valve regurgitation	Expanded aortic root; intimal flap	±	-	Narrow	-	-	Intimal flap
Cardiogenic	Arrhythmia	-	-	-	-	+	-	-	±B lines	-	-
	AMI	-	-	Regional wall motion abnormality	-	±	-	-	±B lines	-	-
	Heart failure	-	±Increased	Hypodynamic	-	±	-	±Dilation	B lines	±	-
Distributive	Septic shock	-	-	Hyperdynamic*	-	±	-	±Narrow	A/B lines	±	-

Abbreviations: AMI = acute myocardial infarction; DVT = deep venous thrombosis; IVC = inferior vena cava; THIRD = Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection; TR = tricuspid regurgitation
 * Can be hypodynamic in late sepsis

TABLE 2. SMART procedure for focused cardiac ultrasound assessment

Evaluation aspect	Main evaluation components
S: Size	Size, shape, and proportions of the left and right sides of the heart Thickness of the ventricular wall
M: Motivation	Global cardiac systolic function Amplitude and coordination of ventricular wall motion Segmental or diffuse ventricular wall motion abnormalities
A: Aorta	Aortic root diameter and aortic intimal continuity Presence of intimal flap
R: Rhythm/rate	Abnormal rhythm or frequency
T: Tricuspid regurgitation	Flow velocity of tricuspid regurgitation and pulmonary artery pressure

Tamponade or tension pneumothorax: First, the subcostal cardiac view is used to determine the presence of any pericardial effusion; then, evidence of right atrial or right ventricular diastolic collapse or cardiac oscillation is assessed to identify signs of pericardial tamponade-related shock. Second, the bilateral anterior thorax in the mid-clavicular lines is explored to identify pleural sliding, the ‘seashore’ sign, A lines, and B lines. If the above signs are not found and a ‘stratosphere’ sign or lung point is identified, tension pneumothorax-related obstructive shock is suspected.

Heart: The SMART (Size, Motivation, Aorta, Rhythm/rate, Tricuspid regurgitation) procedure is used to assess the heart size, shape, and wall motion; aortic diameter; presence of an aortic intimal flap; cardiac rhythm and rate; and presence of tricuspid regurgitation on the parasternal long-axis, parasternal short-axis, and apical four-chamber views. These assessments help to clarify the cause and type of shock with respect to cardiac function (Table 2).

Inferior vena cava: The subcostal longitudinal acoustic window is used to localise the inferior vena cava. The diameter and respiratory variation rate of the inferior vena cava are measured to estimate central venous pressure, assess right heart function and overall blood volume, and evaluate indirect evidence of shock caused by hypovolaemia, right heart failure, pulmonary embolism, or pulmonary hypertension.

Respiratory system: Lung ultrasound assessment is performed using a symmetrical three-point technique to identify common lung ultrasound signs (eg, pleural fluid, pleural sliding, A lines, B lines, shred sign, and lung rockets). These signs are indicators of shock caused by lung consolidation, massive pleural effusion/haemorrhage, or other aetiologies such as pulmonary oedema.

Deep venous thrombosis or aortic dissection: The acoustic windows of the bilateral symmetrical inguinal areas and popliteal fossae are used to detect

and assess the compressibility of the femoral veins and popliteal veins; these assessments facilitate the identification of deep vein thromboses. Because pulmonary emboli are commonly associated with deep venous thrombosis from the lower extremities, this ultrasound technique is an indirect test for shock caused by pulmonary emboli. Scans of the abdominal aorta in horizontal sections of the peritoneal trunk, superior mesenteric artery, and renal artery are then conducted to determine whether aortic dissection or aneurysm is present.

Clinical evaluation and final diagnosis

Upon admission to the EICU, the following information was recorded for all enrolled patients: demographic data, co-morbidities, APACHE II (acute physiology and chronic health evaluation II) score, need for mechanical ventilation, and physiological data (eg, mean arterial pressure, shock index, lactate level, and central venous oxygen saturation). All patients were closely followed to confirm their final diagnosis of shock. A panel of three board-certified physicians (D Tan, emergency physician; J Ye, radiologist; and J Zhang, cardiologist) established the diagnosis of shock type based on all relevant clinical data including history of present illness, signs, auxiliary examination results. Disagreements concerning diagnosis were resolved using a majority vote approach. Patients were excluded if their diagnosis could not be agreed upon by at least two physicians.

Statistical analysis

Statistical analysis was performed using SPSS (Windows version 21; IBM Corp., Armonk [NY],

United States). Sample size calculations were performed prior to enrolment; to detect a protocol accuracy of >90% using the kappa method and considering an anticipated 10% rate of exclusion or dropout,¹⁴ at least 100 patients were required. Thus, we planned a sample size of >110 patients in this study. We calculated the kappa index between the diagnosis of shock type according to the THIRD protocol and the final diagnosis of shock. Additionally, we separately assessed the kappa agreement and reliability indices (sensitivity, specificity, positive predictive value [PPV] and negative predictive value [NPV]) of the THIRD protocol for each type of shock. For this analysis, we excluded patients without a definite final diagnosis of shock type.

Results

Patient characteristics and final clinical diagnoses

In total, 120 patients were enrolled; eight patients were excluded prior to the analysis (two patients had a history of hypotension in their previous medical records, three patients were transferred from another hospital with a known diagnosis of shock type, and three patients did not have a definite final diagnosis of shock type) [Fig 2]. In the final sample size of 112 patients, 54% were men, with a mean age of 66.5 ± 13.5 years and a mean arterial pressure of 51.2 ± 10.9 mmHg at presentation to the EICU. The mean duration of a complete THIRD protocol evaluation was 9.1 ± 1.5 minutes. The baseline characteristics of enrolled patients are shown in Table 3. The final charted clinical diagnoses of the 112 patients are reported in Table 4.

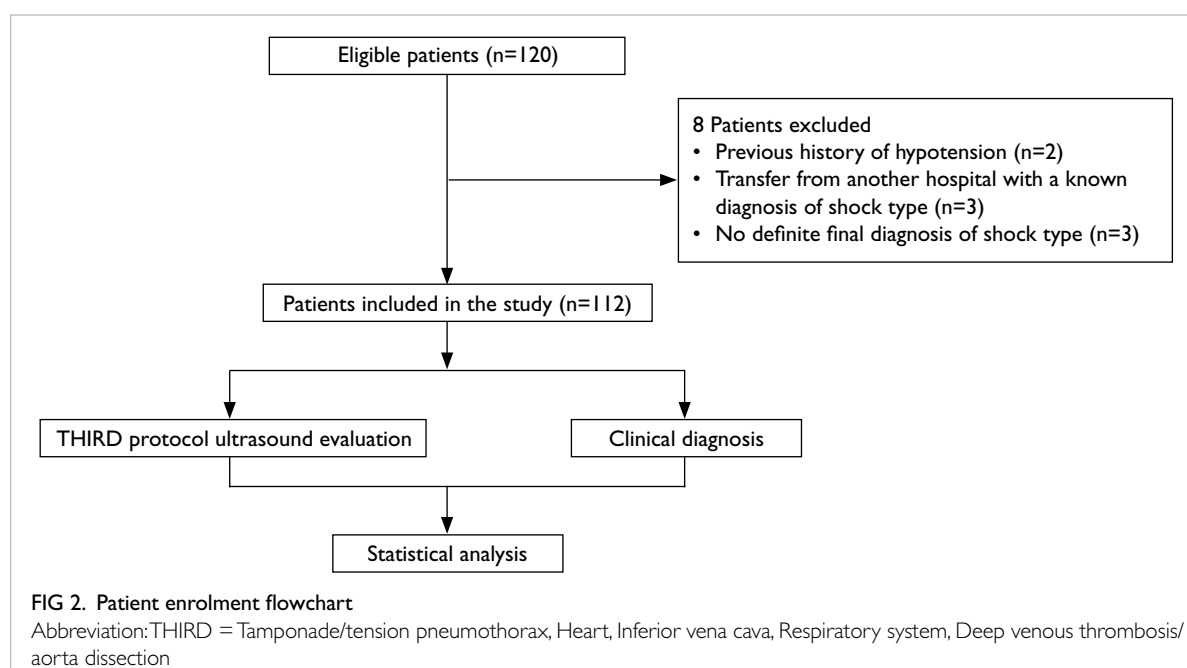


TABLE 3. Baseline characteristics of enrolled patients (n=112)*

Characteristic	Value
Male sex	60 (53.6%)
Age, y	66.5 ± 13.5
Co-morbidities	
Diabetes mellitus	36 (32.1%)
Hypertension	51 (45.5%)
Coronary artery disease	27 (24.1%)
Chronic liver disease	8 (7.1%)
Chronic kidney disease	13 (11.6%)
Cerebrovascular disease	21 (18.8%)
Malignancy	4 (3.6%)
Mechanical ventilation	89 (79.5%)
APACHE II score (0-71)	17.6 ± 4.2
Mean arterial pressure, mmHg	51.2 ± 10.9
Lactate, mmol/L	8.3 ± 5.1
Shock index (normal range: 0-0.5)	1.7 ± 0.5
Central venous oxygen saturation, %	58.6 ± 6.7

Abbreviation: APACHE II = acute physiology and chronic health evaluation II

* Data are shown as No. (%), unless otherwise specified

TABLE 4. Final charted clinical diagnoses of 112 patients with symptomatic undifferentiated shock at presentation*

Final clinical diagnosis	No. (%)
Sepsis	42 (37.5%)
Pulmonary	26 (23.2%)
Bloodstream	8 (7.1%)
Urinary	2 (1.8%)
Gastrointestinal	3 (2.7%)
Biliary tract	3 (2.7%)
Multiple injury	23 (20.5%)
Intoxication	15 (13.4%)
Acute heart failure	8 (7.1%)
Acute coronary syndrome	7 (6.3%)
Severe acute pancreatitis	5 (4.5%)
Acute gastrointestinal bleeding	3 (2.7%)
Pericardial effusion	3 (2.7%)
Spinal shock	3 (2.7%)
Pulmonary embolism	2 (1.8%)
Cachexia	1 (0.9%)

* Data are shown as No. (%)

The final clinical diagnoses of the 112 patients, based on chart assessment by the three auditors and the THIRD protocol evaluation results, are shown in Table 5. The most common type of shock in our study was distributive shock (36 patients, 32.1%).

The kappa index for general agreement between final clinical diagnosis and the type of shock identified using the THIRD protocol was 0.81 (95% confidence interval=0.73-0.89; P<0.001) for all patients. Table 6 shows the kappa index, sensitivity, specificity, PPV, and NPV of the THIRD protocol for determining each type of shock among patients with definite final diagnoses.

Hypovolaemic shock

Using the THIRD protocol, 32 patients had a diagnosis of hypovolaemic shock. The causes of hypovolaemic shock were traumatic bleeding (n=23), sepsis (n=2), acute gastrointestinal bleeding (n=3), cachexia (n=1), and pancreatitis (n=1). The remaining two patients included in the 32 patients were misdiagnosed with hypovolaemic shock based on their ultrasound findings, but the final clinical diagnoses were mixed shock (n=1) and distributive shock secondary to sepsis (n=1) [97.3% specificity and 95% PPV].

Cardiogenic shock

Using the THIRD protocol, 21 patients had a diagnosis of cardiogenic shock. Of them, 19 patients had a final clinical diagnosis of cardiogenic shock due to decompensated heart failure (n=8), acute myocardial infarction (n=7), and intoxication (n=4). The final clinical diagnosis for the remaining two patients was mixed aetiology shock (97.83% specificity and 90.9% PPV). The agreement between ultrasound findings and the final diagnosis was 92% (P<0.001) for cardiogenic shock.

Distributive shock

Using the THIRD protocol, 33 patients were diagnosed with distributive shock. Of them, 30 patients had a final clinical diagnosis of sepsis (concurrent pneumonia [n=26], concurrent cholangitis [n=2], concurrent urinary tract infections [n=2]) and three patients had a final clinical diagnosis of neurogenic aetiologies. Three other patients had a final clinical diagnosis of distributive shock, who were initially misdiagnosed using the THIRD protocol with hypovolaemic (n=1) and mixed aetiology shock (n=2). The agreement between ultrasound findings and the final diagnosis was 89% (P<0.001) for distributive shock.

Obstructive shock

Using the THIRD protocol, five patients were diagnosed with obstructive shock, and all five of them had a final clinical diagnosis of obstructive shock (cardiac tamponade [n=3], large, acute pulmonary embolism [n=2]). The agreement between ultrasound findings and the final diagnosis was 100% (P<0.001) for obstructive shock.

TABLE 5. Prevalences of types of shock based on final clinical diagnosis and THIRD protocol evaluation*

Shock type based on THIRD protocol	Shock type based on final clinical diagnosis				
	Hypovolaemic	Cardiogenic	Distributive	Obstructive	Mixed
Hypovolaemic (n=32)	30	0	1	0	1
Cardiogenic (n=21)	0	19	0	0	2
Distributive (n=33)	0	0	33	0	0
Obstructive (n=5)	0	0	0	5	0
Mixed (n=21)	0	0	2	0	19
Total, No. (%)	30 (26.8%)	19 (17.0%)	36 (32.1%)	5 (4.5%)	22 (19.6%)

Abbreviation: THIRD = Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection

* Data are shown as No. (%), unless otherwise specified

TABLE 6. Reliability indices and kappa agreement values of the THIRD protocol for each individual shock subtype*

	Shock type based on final clinical diagnosis				
	Hypovolaemic (n=30)	Cardiogenic (n=19)	Distributive (n=36)	Obstructive (n=5)	Mixed (n=22)
Sensitivity	100%	100%	92.86%	100%	85.71%
Specificity	97.3%	97.83%	100%	100%	98.94%
PPV	95%	90.9%	100%	100%	94.74%
NPV	100%	100%	97.67%	100%	96.81%
Kappa (95% CI; P value)	0.92 (0.83-0.98; P<0.001)	0.92 (0.82-0.95; P<0.001)	0.89 (0.78-0.92; P<0.001)	1 (1-1; P<0.001)	0.82 (0.76-0.89; P<0.001)

Abbreviations: 95% CI = 95% confidence interval; PPV = positive predictive value of THIRD protocol for determining each type of shock; NPV = negative predictive value of THIRD protocol for determining each type of shock; Kappa = index of agreement between the diagnosis of shock type based on THIRD protocol and the final clinical diagnosis; THIRD = Tamponade/tension pneumothorax, Heart, Inferior vena cava, Respiratory system, Deep venous thrombosis/aorta dissection

* Data are shown as percentages, unless otherwise specified

Mixed aetiology shock

Using the THIRD protocol, 21 patients were diagnosed with mixed aetiology shock. Of them, 19 had a final clinical diagnosis of mixed aetiology shock (sensitivity of 90.4%). The remaining two patients were misdiagnosed with mixed aetiology shock; the final clinical diagnosis was distributive shock (n=2). Three other patients had a final clinical diagnosis of mixed aetiology shock, who were initially misdiagnosed using the THIRD protocol with hypovolaemic (n=1) or cardiogenic shock (n=2). The THIRD protocol had the lowest agreement (82%, P<0.001) with the final diagnosis for mixed aetiology shock.

Discussion

In this prospective study, the primary diagnosis after implementation of the THIRD protocol in patients with undifferentiated shock was highly concordant with the final clinical diagnosis. The protocol was highly effective in guiding the rapid bedside management of undifferentiated shock in emergency settings, particularly for patients with obstructive,

hypovolaemic, or cardiogenic shock.

Point-of-care ultrasound is the only tool available at the bedside that can rapidly reveal acute pathophysiology and establish key diagnoses to guide targeted interventions.¹⁵ As in other disciplines, POCUS has been commonly used in emergency medicine; it is an essential skill for emergency physicians. In mainland China, bedside ultrasound has been used in EDs since 2006, mainly for guidance during vascular puncture procedures and for the assessment of free intraperitoneal fluid.¹⁶ After a decade of rapid development, nearly half of EDs in China have dedicated bedside ultrasound equipment.¹⁷ The applications of POCUS have gradually expanded to undifferentiated hypotension, shortness of breath, chest pain, sepsis, and cardiac arrest, as well as other clinical manifestations.

To our knowledge, the THIRD protocol is the first ultrasound protocol for assessment of undifferentiated shock in mainland China, and this is the first study to validate the effectiveness and accuracy of the protocol. This study demonstrated favourable general agreement between the final clinical diagnosis of shock and the results of this early

bedside ultrasound assessment ($\kappa=0.81$). Similar to the RUSH protocol,¹³ the highest agreements were observed in patients with hypovolaemic, cardiogenic, and obstructive shock (κ values of 0.92, 0.92, and 1.00, respectively). The NPVs for these shock types were all 100%, suggesting that the THIRD protocol can reliably exclude these types of shock. Clinically significant hypovolaemia, cardiac dysfunction, cardiac tamponade, pulmonary embolism, and tension pneumothorax are readily identifiable on ultrasound; the corresponding signs facilitate rapid diagnosis and ensure minimal delays in life-saving interventions for these conditions.^{4,18}

The sensitivity, NPV, and κ values of the THIRD protocol were lower for distributive or mixed shock than for the other three types of shock. Sepsis was the main cause of distributed shock in our study; high cardiac output with reduced vascular resistance is the main pathophysiological feature of this type of shock.¹⁹ A plausible explanation for this pathophysiological feature is that a hyperdynamic heart is not specific to distributive shock, and a decrease in vascular resistance lacks specific ultrasound signs. Our protocol had the least sensitivity and agreement for mixed aetiology shock. Considering this increased uncertainty, caution is advised when making a diagnosis of a 'mixed' type of shock.

Since its initial use in 2001 by Rose et al,²⁰ POCUS has been increasingly used in the management of patients with undifferentiated shock in the ED. Furthermore, >15 ultrasound protocols for hypotension have been developed since 2001.⁷ These protocols consist of items such as echocardiography, transthoracic scanning, evaluation of the inferior vena cava and aorta, assessment of free fluid in the abdominal cavity, and detection of deep vein thrombosis. The overall goal of these protocols is to provide a comprehensive and practical approach for the classification of clinical syndromes that involve circulatory failure—syndromes which lack specificity and may have substantially different possible treatments—into four specific and manageable types of shock.

The RUSH protocol is one of the most frequently used POCUS protocols for undifferentiated shock.²¹ Multiple studies have shown that the κ index of the RUSH protocol-based ultrasound diagnosis and the final clinical diagnosis is approximately 0.7.^{13,14,22} The RUSH protocol is used to find ultrasound abnormalities in three major aspects of a patient's physiology, including 'pump, tank, and pipe'.²³ Unlike the RUSH protocol or other existing POCUS shock protocols (eg, ACES,²⁴ UHP,²⁰ or FATE²⁵), each letter of the THIRD protocol represents a specific ultrasound assessment. The THIRD protocol is easy for clinicians to remember and can be used as a practical checklist for ultrasound examination

during the management of patients with shock. This might explain why trainees had greater confidence and performance when using the THIRD protocol than when using the RUSH protocol in a training curriculum.¹⁰

There were some limitations in this study. First, we did not exclude certain patients, such as patients with traumatic injuries or gastrointestinal bleeding. However, trauma and gastrointestinal bleeding are common among patients who present to our ED, and the inclusion of these patients ensures that our shock assessment is consistent with real-world emergency settings. Second, we did not compare the THIRD protocol with other protocols, such as the RUSH protocol; thus, we cannot conclusively state whether the THIRD and RUSH protocols are equally effective. Third, we did not assess the impact of the THIRD protocol on subsequent treatment. In a previous study, 24.6% of patients had a statistically significant change in their management after a POCUS protocol examination.¹²

In conclusion, this study demonstrated that the initial diagnostic judgements obtained using the THIRD protocol in the ED are consistent with the final diagnosis in patients who present with undifferentiated shock. The findings in this study encourage the incorporation of the THIRD protocol into routine ED assessment of patients with undifferentiated shock to help guide early interventions. The impact of the THIRD protocol on the outcomes of patients with shock, as well as comparisons of the effectiveness and accuracy of the THIRD protocol with other POCUS protocols, should be the focus of future studies.

Author contributions

Concept or design: P Geng, B Ling, J Xu, D Tan.

Acquisition of data: B Ling, Y Song, H Wang, Q Zhu, Y Yang, M Lu.

Analysis or interpretation of data: Y Song, H Wang, Q Zhu, Y Yang, M Lu.

Drafting of the manuscript: B Ling, JH Walline, D Tan, P Geng. Critical revision of the manuscript for important intellectual content: D Tan, JH Walline, J Xu, P Geng.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

The authors declare that they have no competing interests.

Acknowledgement

We are grateful to J Ye and J Zhang for their contributions to establish the diagnosis of shock type in this study.

Funding/support

This work was supported by the Rui E Special Fund for Emergency Medicine Research (R2017003), the Yangzhou

Science and Technology Development Plan (YZ2018090), the Yangzhou Phase III ‘Talent Cultivation Program’ Support Project (2018034), the Hospital-Level Support Project of Northern Jiangsu People’s Hospital (yzucms2018943), and the Hospital-Level Support Project of Northern Jiangsu People’s Hospital (fcjs201708, fcjs201842).

Ethics approval

This study protocol was approved by the Institutional Ethics Committee of Northern Jiangsu People’s Hospital (Ref: fcjs2017008). Written informed consent was obtained from all patients (or next of kin, if the patient was unable to provide informed consent). The study was registered in the Chinese Clinical Trial Registry (Ref: ChiCTR2000031072).

References

- Hiemstra B, Eck RJ, Keus F, van der Horst IC. Clinical examination for diagnosing circulatory shock. *Curr Opin Crit Care* 2017;23:293-301.
- Goodwin M, Ito K, Gupta AH, Rivers EP. Protocolized care for early shock resuscitation. *Curr Opin Crit Care* 2016;22:416-23.
- Sasmaz MI, Gungor F, Guven R, Akyol KC, Kozaci N, Kesapli M. Effect of focused bedside ultrasonography in hypotensive patients on the clinical decision of emergency physicians. *Emerg Med Int* 2017;2017:6248687.
- Koster G, van der Horst IC. Critical care ultrasonography in circulatory shock. *Curr Opin Crit Care* 2017;23:326-33.
- Whitson MR, Mayo PH. Ultrasonography in the emergency department. *Crit Care* 2016;20:227.
- PRISM Investigators; Rowan KM, Angus DC, Bailey M, et al. Early, goal-directed therapy for septic shock—a patient-level meta-analysis. *N Engl J Med* 2017;376:2223-34.
- Mok KL. Make it SIMPLE: enhanced shock management by focused cardiac ultrasound. *J Intensive Care* 2016;4:51.
- Alpert EA. The ABCDs of ResUS—Resuscitation ultrasound. *Cureus* 2019;11:e4616.
- Unexplained shock emergency ultrasound clinical practice expert consensus group. Expert consensus on emergency ultrasound practice for unexplained shock [in Chinese]. *Chin J Emerg Med* 2017;26:498-506.
- Shi D, Liu J, Xu J, Zhu H, Yu X. Evaluation of a new goal-directed training curriculum for point-of-care ultrasound in the emergency department: impact on physician self-confidence and ultrasound skills. *Eur J Trauma Emerg Surg* 2021;47:435-44.
- Cecconi M, De Backer D, Antonelli M, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med* 2014;40:1795-815.
- Shokoohi H, Boniface KS, Pourmand A, et al. Bedside ultrasound reduces diagnostic uncertainty and guides resuscitation in patients with undifferentiated hypotension. *Crit Care Med* 2015;43:2562-9.
- Ghane MR, Gharib MH, Ebrahimi A, et al. Accuracy of rapid ultrasound in shock (RUSH) exam for diagnosis of shock in critically ill patients. *Trauma Mon* 2015;20:e20095.
- Volpicelli G, Lamorte A, Tullio M, et al. Point-of-care multiorgan ultrasonography for the evaluation of undifferentiated hypotension in the emergency department. *Intensive Care Med* 2013;39:1290-8.
- Sun JT. New advances in emergency ultrasound protocols for shock. *J Med Ultrasound* 2017;25:191-4.
- Vincent JL, De Backer D. Circulatory shock. *N Engl J Med* 2013;369:1726-34.
- Shi D, Walline JH, Yu X, Xu J, Song PP, Zhu H. Evaluating and assessing the prevalence of bedside ultrasound in emergency departments in China. *J Thorac Dis* 2018;10:2685-90.
- Bernier-Jean A, Albert M, Shiloh AL, Eisen LA, Williamson D, Beaulieu Y. The diagnostic and therapeutic impact of point-of-care ultrasonography in the intensive care unit. *J Intensive Care Med* 2017;32:197-203.
- Russell JA. Vasopressor therapy in critically ill patients with shock. *Intensive Care Med* 2019;45:1503-17.
- Rose JS, Bair AE, Mandavia D, Kinser DJ. The UHP ultrasound protocol: a novel ultrasound approach to the empiric evaluation of the undifferentiated hypotensive patient. *Am J Emerg Med* 2001;19:299-302.
- Keikha M, Salehi-Marzizarani M, Soldoozi Nejat R, Sheikh Motahar Vahedi H, Mirrezaie SM. Diagnostic accuracy of rapid ultrasound in shock (RUSH) Exam; a systematic review and meta-analysis. *Bull Emerg Trauma* 2018;6:271-8.
- Ghane MR, Gharib M, Ebrahimi A, et al. Accuracy of early rapid ultrasound in shock (RUSH) examination performed by emergency physician for diagnosis of shock etiology in critically ill patients. *J Emerg Trauma Shock* 2015;8:5-10.
- Perera P, Mailhot T, Riley D, Mandavia D. The RUSH exam: Rapid Ultrasound in SHock in the evaluation of the critically ill. *Emerg Med Clin North Am* 2010;28:29-56, vii.
- Atkinson PR, McAuley DJ, Kendall RJ, et al. Abdominal and Cardiac Evaluation with Sonography in Shock (ACES): an approach by emergency physicians for the use of ultrasound in patients with undifferentiated hypotension. *Emerg Med J* 2009;26:87-91.
- Sordillo LA, Pu Y, Pratavieira S, Budansky Y, Alfano RR. Deep optical imaging of tissue using the second and third near-infrared spectral windows. *J Biomed Opt* 2014;19:056004.