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 ≥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.

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.
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. 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. 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. The use of POCUS in the ED has been rapidly increasing because it is safe, reliable, non-invasive, rapid, and repeatable at the bedside.

The first ultrasound protocol for undifferentiated shock was published in 2004; 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. 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. 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.

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. We established the enrolment criteria for this study based on clinical feasibility and previous literature: (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

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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.

![Diagram of THIRD protocol](image)

**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
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/hemorrhage, 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, 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.
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.
THIRD bedside ultrasound protocol

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

<table>
<thead>
<tr>
<th>Shock type based on THIRD protocol</th>
<th>Shock type based on final clinical diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolaemic (n=32)</td>
<td>Hypovolaemic</td>
</tr>
<tr>
<td>Hypovolaemic (n=32)</td>
<td>30</td>
</tr>
<tr>
<td>Cardiogenic (n=21)</td>
<td>0</td>
</tr>
<tr>
<td>Distributive (n=33)</td>
<td>0</td>
</tr>
<tr>
<td>Obstructive (n=5)</td>
<td>0</td>
</tr>
<tr>
<td>Mixed (n=21)</td>
<td>0</td>
</tr>
<tr>
<td>Total, No. (%)</td>
<td>30 (26.8%)</td>
</tr>
</tbody>
</table>

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*

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

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. 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. After a decade of rapid development, nearly half of EDs in China have dedicated bedside ultrasound equipment. 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
Since its initial use in 2001 by Rose et al., the RUSH protocol is one of the most frequently used POCUS protocols for undifferentiated shock. Multiple studies have shown that the kappa index of the RUSH protocol–based ultrasound diagnosis and the final clinical diagnosis is approximately 0.7. The RUSH protocol is used to find ultrasound abnormalities in three major aspects of a patient’s physiology, including ‘pump, tank, and pipe’. Unlike the RUSH protocol or other existing POCUS shock protocols (eg, ACES, UHP, or FATE), 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.

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.

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.

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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