


Focused cardiac ultrasound in the early resuscitation of severe sepsis and septic shock: a prospective pilot study

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Abstract

Purpose Point-of-care ultrasonography has been increasingly used in the care of critically ill patients; however, reports on its use during active resuscitation are limited. The aim of this study was to investigate the true impact of focused cardiac ultrasound (FCU) during the management of sepsis with early (6-h) resuscitation.

Methods A prospective pilot observational study was conducted at an academic medical center from March 2011 through July 2012. Patients undergoing resuscitation for severe sepsis or septic shock were prospectively enrolled at medical and combined medical–surgical intensive care units. Patients underwent a 10-min FCU examination when echocardiography was not part of their care plan. FCU was performed by sonographers and interpreted by cardiologists to minimize risks of inadequate image acquisition and misinterpretation. Intensivists completed surveys on their diagnostic and therapeutic plans before and after receiving FCU information.

Results Of the 30 patients enrolled, 18 (60%) were male and the median age was 61 years [interquartile range (IQR) 50–71 years]. Median central venous oxygen saturation and lactate levels were 59.6% (IQR 53.1–66.2%) and 2.7 mmol/L (IQR 1.2–4.1 mmol/L), respectively. Clinical assessment by intensivists before FCU commonly failed to correctly estimate ventricular function; specifically, left ventricular in 12 patients [40%, 95% confidence interval

(CI) 25–58%] and right ventricular function in 15 patients (50%, 95% CI 33–67%). Intensivists' therapeutic plans changed in eight cases (27%, 95% CI 14–44%) after FCU information became available. The most common changes were fluid management and imaging tests. Intensivists' confidence in their therapeutic plans improved for 11 patients (37%, 95% CI 22–55%).

Conclusion FCU is a valuable examination tool during early resuscitation of severe sepsis and septic shock.

Keywords Point-of-care testing · Ultrasonography · Echocardiography · Sepsis · Critical care · Critical illness · Shock

Introduction

Severe sepsis and septic shock are among the most common admission diagnoses to the intensive care unit (ICU) [1, 2]. The 2012 Surviving Sepsis Campaign recommends protocolized quantitative resuscitation, such as early goal-directed therapy (EGDT) for initial patient management [1, 3]. Although many centers have adopted an EGDT strategy and achieved improved clinical outcomes [4, 5], a recent study suggests that mortality outcomes with EGDT or protocolized standard resuscitation were no different from those with usual care [6]. While various care improvements, such as use of lower hemoglobin for transfusion trigger and implementation of lung-protective strategies, have been implicated as reasons for the reduced benefit of EGDT or protocolized strategies [6–8], the increasing use of informal bedside echocardiography by emergency physicians and intensivists cannot be overlooked.

In the past decade, portable, small ultrasound platforms have been developed, and many noncardiologists have been

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trained in point-of-care ultrasonography [9–12]. The American Society of Echocardiography has recognized this trend and coined the term *focused cardiac ultrasound* (FCU) to describe a focused ultrasonographic examination of the cardiovascular system by a physician as an adjunct to the physical examination [10, 13]. The term *critical care echocardiography* was coined by American College of Chest Physicians and La Societe de Reanimation de Langue Francaise for goal-oriented cardiac ultrasonography that is performed and interpreted by intensivists at the bedside [12].

Despite this new practice and training trend in critical care, no reports have been published that robustly evaluate the role of ultrasonography using an ICU-based portable ultrasound machine during early (6-h) resuscitation of patients with severe sepsis and septic shock. The aim of this prospective pilot study was to test the utility of sonographer-performed, cardiologist-interpreted FCU using an ICU-based ultrasound machine. More specifically, our aim was to investigate the true impact of ultrasonographic information on sepsis resuscitation while minimizing the potential biases and concerns often raised about point-of-care ultrasonography, including inadequate image acquisition and misinterpretation when performed by inadequately trained providers. We hypothesized that the diagnostic impressions, therapeutic plans, and confidence levels of intensivists would be influenced by the FCU information. The primary outcomes of the study were the percentage change in intensivists' therapeutic plans and subjective confidence levels in their management after the release of ultrasonographic information. The percentage change in intensivists' impression on subtype of shock and accuracy of the intensivists' diagnostic assessment of ventricular function were also assessed.

Methods

Settings

This prospective pilot observational study was conducted in the medical and combined medical–surgical ICUs of an academic medical center from March 2011 through July 2012. The study was approved by the Mayo Clinic Institutional Review Board. Informed verbal consent was obtained from patients or their surrogates for study enrollment. Informed verbal consent was obtained from all participating intensivists.

Patient enrollment and definition of sepsis onset

Patients were screened using an electronic screening tool for the following criteria: (1) systolic blood pressure (sBP) of <90 mmHg after infusion of 20 mL/kg of crystalloid or 8 mL/kg of colloid; (2) serum lactate level of ≥ 4 mmol/L;

(3) initiation of an intravenous vasoactive or inotropic agent. Sepsis time 0 was defined separately for patients who were already in the ICU and those who were newly admitted to the ICU for the treatment of sepsis. For the former group, sepsis time 0 was the earliest time that any of the screening criteria were met; for the latter group, sepsis time 0 was defined as the time of admission to the ICU.

If one of the screening criteria was met, the patient's electronic medical records were further reviewed for enrollment eligibility. Inclusion criteria were (1) age ≥ 18 years; (2) fulfillment of two or more conditions of systemic inflammatory response syndrome in the setting of suspected infection [14]; (3) presentation within 6 h of sepsis time 0; (4) sBP of <90 mmHg after infusion of 20 mL/kg of crystalloid or 8 mL/kg of colloid, initiation of vasoactive or inotropic agent (regardless of sBP), or serum lactate level of ≥ 4 mmol/L; and (5) central venous oxygen saturation (ScVO₂) level of <70%, not ordered, or pending at the time of FCU examination.

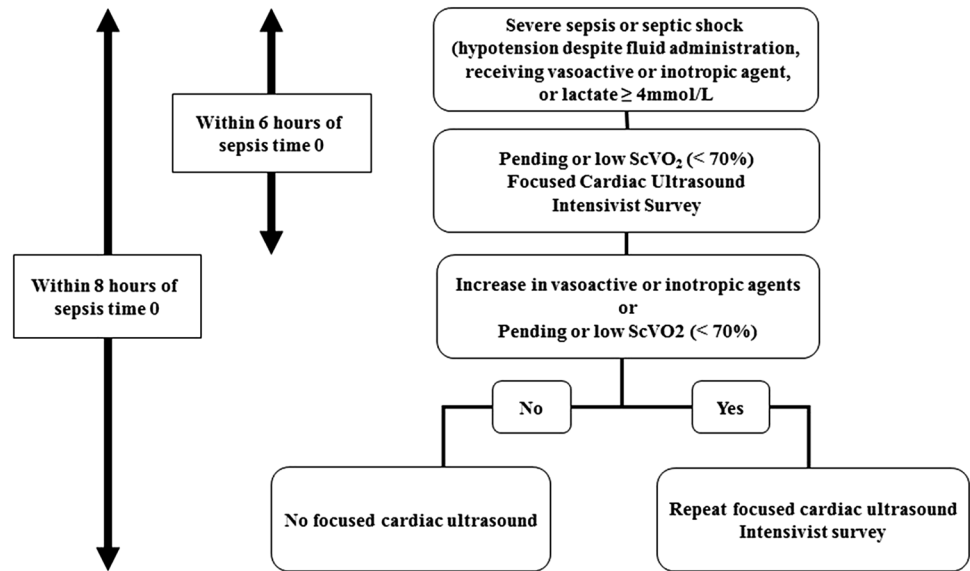
Exclusion criteria were (1) current hospitalization primarily due to trauma; (2) surgical procedure within 48 h of sepsis onset; (3) most recent ScVO₂ level of $\geq 70\%$ at any time before the initial FCU; (4) receiving or being scheduled for emergent echocardiography as part of medical care; (5) transfer from another medical center for sepsis treatment; (6) refusal to consent to use of medical records for research purposes; and (7) study eligibility met outside of normal business hours.

Study design

The study design is summarized in Fig. 1. Enrolled patients underwent FCU within 6 h after sepsis time 0. FCU was defined as a 10-min limited echocardiographic evaluation using an ICU-based portable ultrasound machine (M-Turbo; FUJIFILM SonoSite Inc. Bothell, WA).

FCU was performed by sonographers. Because the examination time was limited, the FCU evaluation followed a specific order: (1) subxiphoid four chambers without color Doppler; (2) subxiphoid four (or 5) chambers with color Doppler in mitral and tricuspid valves (aortic valve was optional); (3) subxiphoid inferior vena cava (IVC) with respiratory variation, measurement of maximal and minimal diameters; (4) parasternal long axis without color Doppler; (5) parasternal long axis with color Doppler in aortic and mitral valves; (6) parasternal short axis at papillary muscle level without color Doppler; (7) apical four chambers without color Doppler; and (8) apical four (or 5) chambers with color Doppler in mitral and tricuspid valve (aortic valve was optional). At least one motion image (6–10 s) for each step was digitally saved, regardless of image quality. If the color Doppler examination in the previous step was unremarkable, omission of a repeat color

Fig. 1 Summary of study protocol. *ScVO₂* Central venous oxygen saturation



Doppler in the subsequent steps was allowed. If the examination time exceeded 10 min, FCU was stopped.

Images were electronically transferred and immediately interpreted by a cardiologist. Interpretation and documentation of images proceeded as follows: visual categorical assessment of ventricular function (hyperdynamic; normal; mild, moderate, or severely decreased function), right ventricular size (normal; mild, moderate, or severe enlargement), IVC diameter and its respiratory collapsibility and collapsibility index [15], left ventricular wall motion abnormality, presence or absence of the McConnell sign (akinesia of the right ventricular mid free wall, with normal motion at the apex) [16], severe valvular abnormality, pericardial tamponade, image quality, and other notable pathologic findings. FCU reports were added to the electronic medical records to document justification for clinical decision-making.

Treating intensivists were asked to complete a survey immediately before the release of ultrasonographic information. The survey included questions regarding their estimation of ventricular function, subtypes of shock, therapeutic plans on fluid management, vasoactive and inotropic agents, transfusion, corticosteroid administration, imaging tests, procedures, consultation, *ScVO₂* measurements, and their confidence levels regarding the overall therapeutic plans and subtype of shock. Intensivists were encouraged to estimate their patient’s ventricular function based on vital signs, physical examination findings, hemodynamic, laboratory, and radiographic data, along with previous echocardiography findings if they are available in the patient’s medical records. Confidence levels were evaluated using a 10-point Likert scale, with 10 indicating the greatest confidence. Upon survey completion, FCU information was handed to the intensivists, and they were asked to resubmit

the same survey and answer an additional question rating the usefulness of FCU for patient management. The FCU examinations and physician surveys were conducted within 6 h after sepsis time 0.

Treating intensivists were allowed to integrate the ultrasonographic information with existing clinical information and to make any type of therapeutic decision for the patient. Apart from this FCU intervention, the patient received usual care, including the EGDT. Enrolled patients were followed after the survey to determine whether therapeutic changes mentioned in the surveys were actually performed.

If the patient remained critically ill, a repeat FCU was conducted within 8 h after sepsis time 0 if the patient met the following criteria: (1) initiation or addition of a new vasoactive or inotropic agent, or dose increment of >50% of a current vasoactive or inotropic agent; or (2) *ScVO₂* level of <70% or no available *ScVO₂* measurement. Treating intensivists again completed the surveys before and after the FCU.

Data collection and statistical analysis

In addition to FCU findings and intensivist survey results, patient characteristics and clinical information, such as *ScVO₂*, mechanical ventilation status, and sequential organ failure assessment [17], were prospectively collected.

For the primary outcome, we considered a change in intensivists’ therapeutic intention and in subjective confidence levels on their overall care plan of >17% as being clinically significant. With a sample size of 30, and assuming a 17% change in survey response after FCU evaluations, a 95% confidence interval (CI) was estimated to range from 7.3 to 34%. Considering the width of the 95% CI for sample sizes of 40 and the nature of this prospective

pilot study, we believed that reasonable precision would be achieved with a sample size of 30. The resulting test was calculated to have >90% power to detect a 17% change in survey answers. Descriptive statistical terms, such as proportion, median, and interquartile range (IQR), were used to summarize the data. JMP 10.0 software (SAS Institute Inc., Cary, NC) was used for the statistical analysis.

Results

During the study period, 631 patients were screened and 30 patients were eventually enrolled in the study (Fig. 2). Patient characteristics are shown in Table 1.

The results of the initial FCU conducted during the first 6 h of sepsis onset are summarized in Table 2. Data on wall motion abnormalities were not assessable for two patients and the IVC was not well visualized for one patient. Dynamic left ventricular outflow tract obstruction and cavitory obstruction were seen in one patient each. Twenty patients (67%) had at least one suboptimal ultrasonographic window in their FCU examinations.

During the 8-h study window, five patients met the criteria for a repeat FCU; however, for four patients, it could not be completed within the 8-h study period because of interference with other elements of care (e.g., procedures, radiology tests outside of the ICU, and care discussion at the bedside). The patient who had the repeat FCU showed improvement in biventricular function and a larger IVC with less collapsibility.

Seventeen intensivists participated in the study and reported diagnostic impression and therapeutic intention. Among the four subtypes of shock (distributive, hypovolemic, obstructive, and cardiogenic), distributive shock was considered to be the most common [$n = 21$ (70%)], followed by hypovolemic shock [$n = 7$ (23%)]. Intensivists believed that 15 patients had multiple subtypes of shock, most commonly a combination of distributive and hypovolemic shock ($n = 13$). Although the intensivists' diagnostic impression of the primary subtype of shock did not change after the FCU results became available, their impression of secondary or tertiary subtypes of shock did change for six patients (20%; 95% CI 9.5–37%). Diagnoses of obstructive and cardiogenic shocks were each added to two patients, and a diagnosis of hypovolemic shock was removed as a secondary subtype in two patients. The median physician confidence level regarding the initial diagnostic impression of shock subtype was 8 (IQR 7–9). Improvement in this score was seen in nine patients (30%; 95% CI 17–48%) after the FCU, whereas no score change was observed in 20 patients (67%, 95% CI 49–81%).

The intensivists' clinical impressions regarding ventricular function before the FCU results were available

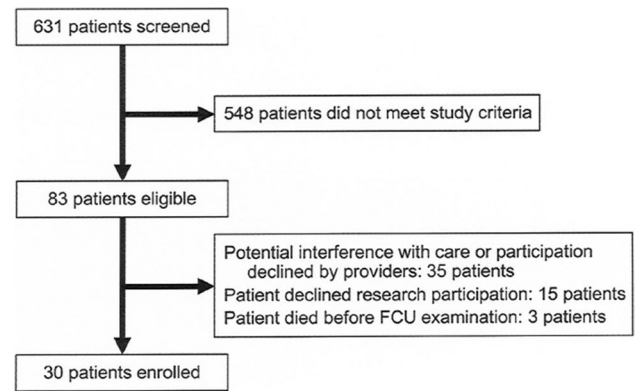


Fig. 2 Patient enrollment diagram. FCU Focused cardiac ultrasound

were compared with the actual FCU findings. Intensivists failed to correctly estimate left ventricular function in 12 patients (40%; 95% CI 25–58%), with overestimation and underestimation occurring in seven (23%) and five (17%) patients, respectively. Right ventricular function was estimated incorrectly in 15 patients (50%; 95% CI 33–67%), with overestimation and underestimation occurring in five (17%) and ten (33%) patients, respectively.

Based on the FCU findings, intensivists made changes to the therapeutic plans of eight patients (27%; 95% CI 14–44%), with three patients receiving more than one change to the care plan. Details of care modification are shown in Table 3. The actual interventions occurred within 1 h after the FCU findings were known for four patients. Subjective confidence levels for the therapeutic plans improved post-FCU for 11 patients (37%; 95% CI 22–55%). Overall, intensivists considered FCU beneficial for patient care in 14 patients (47%; 95% CI 30–64%).

Discussion

We evaluated the role of point-of-care cardiac ultrasonography using an ICU-based portable machine during the critical 6 h of early sepsis resuscitation. The study was designed to minimize potential biases and concerns regarding image acquisition and interpretation that are often raised when inadequately trained providers use a portable ultrasound machine. In this study protocol, FCU was conducted by sonographers trained to use an ICU-based portable ultrasound machine, and images were immediately interpreted by cardiologists. Patients undergoing early sepsis resuscitation were eligible for the study when echocardiography was not included in the care plan. Intensivists' therapeutic plans changed for eight patients (27%) during the first 6 h of sepsis resuscitation, and their confidence in the therapeutic plan improved for 11 patients

Table 1 Patient characteristics (*N* = 30)

Characteristics	Values
Age (years)	61 (50–71)
Male sex	18 (60)
SOFA score	9 (5–11)
Mechanical ventilation	8 (27)
Noninvasive positive-pressure ventilation	3 (10)
Use of vasoactive or inotropic agents	9 (30)
Lactate level (mmol/L)	2.7 (1.2–4.1)
ScVO ₂ (%) ^a	59.6 (53.1–66.2)
Time between sepsis time 0 and FCU (h)	3.3 (1.8–4.1)

Values in table are given as the median with the interquartile range (IQR) in parenthesis or as a number with the percentage in parenthesis, as appropriate

FCU Focused cardiac ultrasound, ScVO₂ central venous oxygen saturation, SOFA sequential organ failure assessment

^a Nine patients (30%) had documented low ScVO₂ level (<70%)

Table 2 Focused cardiac ultrasound findings (*N* = 30)

Characteristic	Values
Left ventricular function, <i>n</i> (%)	
Hyperdynamic	3 (10.0)
Normal	21 (70.0)
Mild dysfunction	3 (10.0)
Moderate dysfunction	1 (3.3)
Severe dysfunction	2 (6.7)
Left ventricular wall motion abnormality, <i>n</i> (%)	4 (13.3)
Right ventricular size	
Normal	14 (46.7)
Mild enlargement	10 (33.3)
Moderate enlargement	5 (16.7)
Severe enlargement	1 (3.3)
Right ventricular function, <i>n</i> (%)	
Hyperdynamic	2 (6.7)
Normal	20 (66.7)
Mild dysfunction	5 (16.7)
Moderate dysfunction	3 (10.0)
Severe dysfunction	0 (0)
McConnell sign	1 (3.3)
Severe valvular abnormality	3 (10.0)
IVC assessment, median (IQR)	
Maximal diameter (mm)	22 (19–26)
Minimal diameter (mm)	18.5 (10.5–20.5)
Collapsibility [(max – min)/max], in %	21 (8.9–38.8)
Collapsibility index [(max – min)/mean], in %	24 (10–48.1)
Cardiac tamponade, <i>N</i> (%)	0 (0)

Values in table are given as the median with the IQR in parenthesis or as a number with the percentage in parenthesis, as appropriate

IVC inferior vena cava, *max* maximal diameter, *min* minimal diameter, *mean* mean diameter

(37%). Approximately one-half of the intensivists believed that FCU improved patient care. Notably, intensivists’ initial estimation of ventricular function was limited by the absence of ultrasound information.

Previous studies reported that transesophageal or transthoracic echocardiography (or both) influenced therapeutic plans in approximately 25–50% of ICU cases [18–22]. However, inferences from those studies were limited by the lack of timeliness of echocardiography (examinations were conducted after the first 6 h of resuscitation). Our results compare favorably to these reports targeting a general ICU population, although the percentage change in therapeutic plans was near the lower end of the anticipated range. In our study, patients were not enrolled when the care providers had scheduled or ordered an echocardiographic evaluation as part of their medical care. Our results suggest that FCU provides clinically relevant information, even for settings in which providers have conventionally thought echocardiography was less helpful for decision-making.

This study has several unique elements in its design. First, treating intensivists were able to make any therapeutic changes after considering the ultrasound information. Before the study, we anticipated that common clinical decisions during the active resuscitation stage would include adjusting fluid infusion and selecting vasoactive and inotropic agents. In fact, these were among the most commonly observed therapeutic changes. As previously described, an advantage of FCU is its ability to assess fluid responsiveness in mechanically ventilated patients via IVC measurements and to identify cardiac dysfunction that often coexists in septic shock [15, 23]. The results of this study suggest that FCU in the early resuscitation phase potentially helps avoid insufficient or excessive fluid administration, both of which are associated with adverse patient outcomes [24, 25]. FCU also can feasibly guide selection of vasoactive or inotropic agents and help avoid hemodynamically deleterious situations (e.g., vasoconstrictive agent in severe septic cardiomyopathy or inotropic agent in the hyperdynamic heart).

Another unique aspect of the study was the criterion that the FCU examination could not exceed 10 min and was conducted using an ICU-based portable ultrasound machine. The examination was goal oriented and limited to basic echocardiographic elements that could be assessed visually, in a qualitative manner. With the development of compact, high-resolution ultrasound machines, providers are increasingly trained in ultrasonography [9, 11]. Our study not only showed the utility of FCU in sepsis resuscitation but also supports ongoing efforts to educate providers in ultrasonography. A previous report showed that the basic elements of FCU could be taught efficiently in a short, organized workshop [26]. We believe that intensivists who are capable of point-of-care ultrasonography should

Table 3 Changes in therapeutic plans

Measure	Values
Total number of patients with therapeutic plan changes	8 (27)
Two or more therapeutic plan changes per patient	3 (10)
Components of plan that changed	
Fluid administration	4
Imaging tests	4
Vasoactive or inotropic agents	2
Procedures	1
Transfusion	1
Corticosteroid administration	1

Values in table are given as a number with, as appropriate, the percentage in parenthesis

consider performing the examination during the active resuscitation of patients presenting with severe sepsis or septic shock. Alternatively, point-of-care sonographers and cardiologists should be included in the ICU resuscitation team, if intensivists are not yet skilled with point-of-care ultrasonography or if they are attending to other patients and not readily available.

Our study has several limitations. First, this was a pilot study of 30 patients to examine the utility of FCU-guided sepsis resuscitation. The number of enrolled patients was small, and there was no control group. Intensivists were allowed to participate in the study more than once because of the limited number of providers ($n = 17$) working in the ICU during the study period; this may have biased the survey results. Second, only intensivist-oriented outcomes were collected and analyzed in the study. This study lays the groundwork for a future study powered to detect differences in patient-oriented clinical outcomes between those who receive FCU-guided early sepsis resuscitation and those who received usual care. Third, because of the limited availability of sonographers, the study enrolled only those patients who presented during business hours, which may have created selection bias. However, we believe that patient and intensivist characteristics were unlikely to vary markedly between regular business hours versus other times. Fourth, evaluation of diastolic function was not included in the 10-min FCU examination, although diastolic dysfunction is common in patients with severe sepsis and septic shock [23, 27–29]. There have been conflicting reports on the relationship between diastolic dysfunction and patient prognosis [23, 27–29], and it is deemed technically impossible to accurately obtain diastolic parameters within 10 min of using an ICU-based ultrasound device. The value of diastolic evaluation in the early phase of sepsis resuscitation remains to be further investigated. Fifth, the study design may have increased the tendency for intensivists to change their survey answers after being provided the additional

information. Thus, the rate of therapeutic changes may be overestimated, although if intensivists did not incorporate ultrasonographic information appropriately in the care plan, its impact also may be underestimated. For a diagnostic modality such as FCU to be beneficial in clinical decision-making, it has to be interpreted correctly and integrated into a clinical scenario appropriately.

In summary, FCU using a portable ultrasound machine is a valuable examination tool during the early resuscitation of severe sepsis and septic shock. It guides intensivists in their initial assessment and treatment of critically ill patients with sepsis. A subsequent trial targeting clinical outcomes is warranted to investigate the role of FCU or critical care echocardiography, performed and interpreted by intensivists, in sepsis resuscitation. In the meantime, intensivists who can perform and interpret point-of-care ultrasonography could reasonably consider doing so during the early phase of sepsis resuscitation.

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Compliance with ethical standards

Conflict of interest None.

References

- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R, Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013;41(2):580–637.
- Zimmerman JE, Kramer AA, Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. *Crit Care.* 2013;17(2):R81.
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M, Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001;345(19):1368–77.
- Funk D, Sebat F, Kumar A. A systems approach to the early recognition and rapid administration of best practice therapy in sepsis and septic shock. *Curr Opin Crit Care.* 2009;15(4):301–7.
- Lin SM, Huang CD, Lin HC, Liu CY, Wang CH, Kuo HP. A modified goal-directed protocol improves clinical outcomes in intensive care unit patients with septic shock: a randomized controlled trial. *Shock.* 2006;26(6):551–7.
- Yealy DM, Kellum JA, Huang DT, Barnato AE, Weissfeld LA, Pike F, Terndrup T, Wang HE, Hou PC, LoVecchio F, Filbin MR, Shapiro NI, Angus DC, ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. *N Engl J Med.* 2014;370(18):1683–93.

7. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E; Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med.* 1999;340(6):409–17 [erratum in: *N Engl J Med* 1999;340(13):1056].
8. Petrucci N, Iacovelli W. Ventilation with lower tidal volumes versus traditional tidal volumes in adults for acute lung injury and acute respiratory distress syndrome. *Cochrane Database Syst Rev.* 2004;(2):CD003844 [update in: *Cochrane Database Syst Rev.* 2007;(3):CD003844].
9. Vieillard-Baron A, Mayo PH, Vignon P, Cholley B, Slama M, Pinsky MR, McLean A, Choi G, Beaulieu Y, Arntfield R, Koenig S, Colreavy F, Canivet JL, De Backer D. Expert round table on echocardiography in ICU. International consensus statement on training standards for advanced critical care echocardiography. *Intensive Care Med.* 2014;40(5):654–66.
10. Spencer KT, Kimura BJ, Korcarz CE, Pellikka PA, Rahko PS, Siegel RJ. Focused cardiac ultrasound: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2013;26(6):567–81.
11. Cholley BP, Mayo PH, Poelaert J, Vieillard-Baron A, Vignon P, Alhamid S, Balik M, Beaulieu Y, Breitzkreutz R, Canivet JL, Doelken P, Flaatten H, Frankel H, Haney M, Hilton A, Maury E, McDermid RC, McLean AS, Mendes C, Pinsky MR, Price S, Schmidlin D, Slama M, Talmor D, Teles JM, Via G, Voga G, Wouters P, Yamamoto T, Expert Round Table on Ultrasound in ICU. International expert statement on training standards for critical care ultrasonography. *Intensive Care Med.* 2011;37(7):1077–83.
12. Mayo PH, Beaulieu Y, Doelken P, Feller-Kopman D, Harrod C, Kaplan A, Oropello J, Vieillard-Baron A, Axler O, Lichtenstein D, Maury E, Slama M, Vignon P. American College of Chest Physicians/La Société de Réanimation de Langue Française statement on competence in critical care ultrasonography. *Chest.* 2009;135(4):1050–60.
13. Labovitz AJ, Noble VE, Bierig M, Goldstein SA, Jones R, Kort S, Porter TR, Spencer KT, Tayal VS, Wei K. Focused cardiac ultrasound in the emergent setting: a consensus statement of the American Society of Echocardiography and American College of Emergency Physicians. *J Am Soc Echocardiogr.* 2010;23(12):1225–30.
14. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent J-L, Ramsay G. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Crit Care Med.* 2003;31(4):1250–6.
15. Feissel M, Michard F, Faller JP, Teboul JL. The respiratory variation in inferior vena cava diameter as a guide to fluid therapy. *Intensive Care Med.* 2004;30(9):1834–7.
16. McConnell MV, Solomon SD, Rayan ME, Come PC, Goldhaber SZ, Lee RT. Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism. *Am J Cardiol.* 1996;78(4):469–73.
17. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG, On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med.* 1996;22(7):707–10.
18. Colreavy FB, Donovan K, Lee KY, Weekes J. Transesophageal echocardiography in critically ill patients. *Crit Care Med.* 2002;30(5):989–96.
19. Kanji HD, McCallum J, Sirounis D, MacRedmond R, Moss R, Boyd JH. Limited echocardiography-guided therapy in subacute shock is associated with change in management and improved outcomes. *J Crit Care.* 2014;29(5):700–5.
20. Orme RM, Oram MP, McKinstry CE. Impact of echocardiography on patient management in the intensive care unit: an audit of district general hospital practice. *Br J Anaesth.* 2009;102(3):340–4.
21. Stanko LK, Jacobsohn E, Tam JW, De Wet CJ, Avidan M. Transthoracic echocardiography: impact on diagnosis and management in tertiary care intensive care units. *Anaesth Intensive Care.* 2005;33(4):492–6.
22. Vignon P, Mentec H, Terre S, Gastinne H, Gueret P, Lemaire F. Diagnostic accuracy and therapeutic impact of transthoracic and transesophageal echocardiography in mechanically ventilated patients in the ICU. *Chest.* 1994;106(6):1829–34.
23. Pulido JN, Afessa B, Masaki M, Yuasa T, Gillespie S, Herasevich V, Brown DR, Oh JK. Clinical spectrum, frequency, and significance of myocardial dysfunction in severe sepsis and septic shock. *Mayo Clin Proc.* 2012;87(7):620–8.
24. Alsous F, Khamiees M, DeGirolamo A, Amoateng-Adjepong Y, Manthous CA. Negative fluid balance predicts survival in patients with septic shock: a retrospective pilot study. *Chest.* 2000;117(6):1749–54.
25. Durairaj L, Schmidt GA. Fluid therapy in resuscitated sepsis: less is more. *Chest.* 2008;133(1):252–63.
26. Sekiguchi H, Suzuki J, Gharacholou SM, Fine NM, Mankad SV, Daniels CE, Gajic O, Kashani KB. A novel multimedia workshop on portable cardiac critical care ultrasonography: a practical option for the busy intensivist. *Anaesth Intensive Care.* 2012;40(5):838–43.
27. Sturgess DJ, Marwick TH, Joyce C, Jenkins C, Jones M, Masci P, Stewart D, Venkatesh B. Prediction of hospital outcome in septic shock: a prospective comparison of tissue Doppler and cardiac biomarkers. *Crit Care.* 2010;14(2):R44.
28. Landesberg G, Gilon D, Meroz Y, Georgieva M, Levin PD, Goodman S, Avidan A, Beeri R, Weissman C, Jaffe AS, Sprung CL. Diastolic dysfunction and mortality in severe sepsis and septic shock. *Eur Heart J.* 2012;33(7):895–903.
29. Brown SM, Pittman JE, Hirshberg EL, Jones JP, Lanspa MJ, Kuttler KG, Litwin SE, Grissom CK. Diastolic dysfunction and mortality in early severe sepsis and septic shock: a prospective, observational echocardiography study. *Crit Ultrasound J.* 2012;4(1):8.