OBSERVATIONAL STUDY

OPEN

Focused Cardiac Ultrasound Findings of Fluid Tolerance and Fluid Resuscitation in Septic Shock

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OBJECTIVES: Compliance with the fluid bonus component of the SEP-1 (severe sepsis and septic shock management) bundle remains poor due to concerns for iatrogenic harm from fluid overload. We sought to assess whether patients who received focused cardiac ultrasound (FCU) and were found to be fluid tolerant (FT) were more likely to receive the recommended 30 mL/kg fluid bolus within 3 hours of sepsis identification.

DESIGN: Retrospective, observational cohort study.

SETTING: University-affiliated, tertiary-care hospital in the United States.

PATIENTS: Emergency department patients presenting with septic shock from 2018 to 2021. The primary exposure was receipt of FCU with identification of fluid tolerance 3 hours from onset of septic shock.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Two hundred ninety-two of 1,024 patients with septic shock received FCU within 3 hours of sepsis onset. One hundred seventy-seven were determined to be FT. One hundred fifteen patients were determined to have poor fluid tolerance (pFT). FT patients were more likely to reach the recommended 30 mL/kg fluid bolus amount compared with pFT (FT 52.0% vs. pFT 31.3%, risk difference: 20.7%, [95% CI, 9.4–31.9]). Patients who did not receive FCU met the bolus requirement 34.3% of the time. FT patients received more fluid within 3 hours (FT 2,271 mL vs. pFT 1,646 mL, mean difference 625 mL [95% CI, 330–919]). Multivariable logistic regression was used to estimate the association between fluid tolerance FCU findings and compliance with 30 mL/kg bolus after adjustment for patient characteristics and markers of hemodynamic instability. FT with associated with a higher likelihood of meeting bolus requirement (odds ratio 2.17 [1.52–3.12]).

CONCLUSIONS: Patients found to be FT by FCU were more likely to receive the recommended 30 mL/kg bolus in the SEP-1 bundle when compared with patients found with pFT or those that did not receive FCU. There was no difference between groups in 28-day mortality, vasopressor requirement, or need for mechanical ventilation.

KEY WORDS: cardiac; echocardiography; fluid; resuscitation; sepsis; septic; shock; ultrasound

Sepsis is a highly morbid condition with a global pooled mortality of 26.7% (1) and annual incidence in hospitalized patients of 6% (2). Cornerstones of early sepsis management include utilization of screening tools, rapid antibiotic administration, and IV fluid bolus resuscitation (3).

Early versions of Surviving Sepsis Campaign (SSC) guidelines and Centers for Medicare and Medicaid Services (CMS) SEP-1 (severe sepsis and septic shock management bundle) measures mandated strict adherence to a 30-mL/

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KEY POINTS

Question: Is early focused cardiac ultrasound associated with improved compliance with fluid bolus requirement in patients with septic shock?

Findings: In this retrospective observational cohort study, 292 of 1,024 patients with septic shock received focused cardiac ultrasound within 3 hours of sepsis onset. Patients with focused cardiac ultrasound findings of fluid tolerance were more likely to meet the 30-mL/kg fluid bolus requirement at 3 hours even in the subgroup of patients with congestive heart failure or chronic kidney disease.

Meaning: Compliance with the fluid bolus requirements for high-quality sepsis care can be improved by early assessment of fluid tolerance.

kg fluid bolus within the first hours of resuscitation (3, 4). This requirement has come under increased scrutiny due to concerns about volume overload-associated harms (5, 6). To reflect this, the SSC changed their recommendation on the standard 30 mL/kg IV fluid bolus from strong to weak, based on low-quality evidence (3). Similarly, SEP-1 now accepts clinician documentation of potential fluid overload harms in lieu of the full 30 mL/kg bolus, reflecting growing trends toward individualized critical care (4).

The SSC recommends using dynamic markers of fluid status during resuscitation, which include focused cardiac ultrasound (FCU) (3). Typical FCU assessment includes right and left ventricular function as well as inferior vena cava (IVC) diameter and variability (7–10). To date, studies on using FCU to guide fluid resuscitation in ICU (10, 11) and emergency department (ED) settings (7, 12) have shown mixed results.

Unlike fluid responsiveness, defined as improved cardiac output in response to volume loading (13), fluid tolerance seeks to identify patients at risk of end-organ dysfunction and venous congestion from over-resuscitation (14). Although there is no universally agreed-upon definition of sonographic findings for fluid tolerance, prior studies have suggested systolic and diastolic dysfunction (14) and IVC dilation with lack of respiratory variation as resuscitation endpoints (7).

We sought to determine the association between FCU and volume of fluid administered early in the resuscitation of patients with septic shock. We hypothesized that patients who underwent FCU and were found to be fluid tolerant (FT) would be more likely to reach the recommended fluid target of 30 mL/kg of IV fluid bolus within the first 3 hours of sepsis identification.

MATERIALS AND METHODS

Study Design, Setting, and Selection of Patients With Septic Shock

We performed a retrospective, observational cohort study at a university-based, urban tertiary-care hospital with approximately 80,000 yearly adult ED visits. The study was approved by the University of Michigan institutional review board on April 19, 2022 (study number HUM00215603) as a secondary data use, exempt study. Informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki. The primary exposure under study was receipt of FCU within 3 hours of sepsis identification which resulted in three possibilities: no FCU performed, FCU without findings of poor fluid tolerance (pFT), and FCU with findings of pFT. The primary outcome was receipt of 30 mL/kg IV fluid bolus at 3 hours from sepsis identification. Adult (older than 18 yr) patients discharged between January 1, 2018, and December 31, 2021, were selected from our sepsis quality assurance database, using both *International Classification of Diseases* (ICD)-10 codes and previous definitions from Rhee et al (2). Patients were determined to have sepsis if they had a presumed serious infection (blood cultures being obtained and greater than or equal to 4 qualifying antimicrobial days within ± 2 d of blood cultures) plus acute organ dysfunction (2). From this group, septic shock was selected using the R65.21 code as a method of identifying sepsis severity. Patients who were transferred from an outside hospital's ED or who developed sepsis after admission to an inpatient service were excluded. Patients with COVID-19 were not excluded. An a priori sample size estimate was not conducted. The dates of the study were chosen based on stable clinical practice in our ED with implementation of standardized FCU reporting with image storage, and before an update to SEP-1 that allowed exceptions to the 30-mL/kg bolus requirement (7).

Performance of Focused Cardiac Ultrasound During Resuscitation

Clinical actions including fluid resuscitation and FCU were performed at the discretion of the treating team of clinicians. FCUs were performed by attending emergency physicians (EPs) or by house officers and physician assistants under their direct supervision. Image acquisition and interpretation were at the discretion of the treating team. FCU at our institution typically evaluates left ventricular ejection fraction (LVEF), right ventricular function, IVC diameter, and IVC respiratory variability. All assessments are described qualitatively. Left LVEF can be described as hyperdynamic, normal, mildly, moderately, or severely reduced. IVC characteristics are described as either normal, dilated, or collapsed with respiratory variation that is either increased, normal, or decreased when viewed in (long axis via the subxiphoid plane. This is similar to other previously published FCU assessments (15). Documentation of FCU is performed via a structured template for reporting point-of-care ultrasound findings. Treatment decisions in response to FCU findings were neither protocolized nor mandated. Images were not reviewed by the study team for correctness of findings. However, our institution has an established quality assurance process where images are reviewed shortly after capture by separate EPs with ultrasound expertise.

Data Collection From the Electronic Health Record

All data were extracted from the EHR using datasets maintained by our institution to provide operational and quality analytics reporting. All encounters during the study period and meeting the eligibility criteria above were included. Semistructured text of FCU imaging reports was extracted from the EHR. These reports were parsed to produce FCU variables of interest with clinician review to ensure accuracy. Time of FCU performance was extracted from the image archiving system. Patients were considered to have received FCU if performed before 3 hours from the onset of sepsis. Within the study dates, a single patient may have had multiple encounters. Each encounter was considered an individual observation.

Definition of Fluid Tolerance, Assessment of Outcomes, and Other Variables

All exposure, outcome, and other variables with definitions and data sources are detailed in **Supplemental Table S1** (http://links.lww.com/CCX/B280). No universally accepted definition for echocardiographic markers of fluid tolerance exists. We used a definition to maximize sensitivity for intolerance to fluid based on prior definitions (14). Patients were considered FT when all of the following were absent on FCU: 1) decreased left LVEF, 2) dilated IVC, and 3) decreased IVC respiratory variation. If any one of these findings were present, they were considered to have pFT even without other findings of pFT. A summary of FCU findings is detailed in **Supplemental Table S2** (http://links.lww.com/CCX/B280). Patients were considered to have met the 30-mL/kg fluid bolus requirement if, within 6 hours before and 3 hours after sepsis time zero, the total volume in milliliters of crystalloid fluid boluses administered or ordered exceeded 30 times the first measured weight in kilograms of the patient. As markers of shock severity and instability, we included systolic shock index and elevated lactate. Systolic shock index was chosen as it is a readily available and easy-to-calculate predictive marker for shock severity (16). Lactate values were categorized into three groups—normal (< 2), elevated (2–4), and significantly elevated (> 4) as this most typically reflects clinical practice and previous definitions of septic shock (17–19).

Statistical Analysis

Standard descriptive statistics were performed on all exposure and outcome variables. Continuous variables were evaluated for skew and normality. All differences in baseline characteristics between exposure groups were expressed as standardized mean differences (SMDs). Bivariate associations between secondary outcomes and FCU or fluid tolerance were assessed with standard statistical tests for continuous (two-sample *t* test or Wilcoxon rank sum test) and categorical data (Fisher exact test or expressed as risk difference [RD] if binary) as appropriate based on their distributions. A p value of less than 0.05 was considered statistically significant. Multivariable logistic regression was used to estimate the association between FCU fluid tolerance findings and the primary outcome. The selected model was evaluated for fit, multicollinearity, and outliers. A subgroup analysis

was planned for patients with heart failure and chronic kidney disease (CKD). Additionally, several sensitivity analyses were performed including an earlier cutoff for performance of FCU at 2 hours after onset of sepsis and an inverse probability weighted (IPW) analysis. The rationale and methods for these analyses are further detailed in the methods supplement. Initial data cleaning was performed using Tableau Prep Builder (Tableau Software, Seattle, WA, USA) and text of FCU reports was converted to structured variables using standard text parsing and regular expressions. There was no missing data for any exposure or outcome variables except lactate. Missing values for lactate (10 observations total and all in the no FCU group) were categorized into the normal group; a common practice in other observational sepsis studies (20). Final data cleaning and all statistical analyses were performed using R (v4.2.1) in R Studio (v2022.2.3, Posit, Boston, MA).

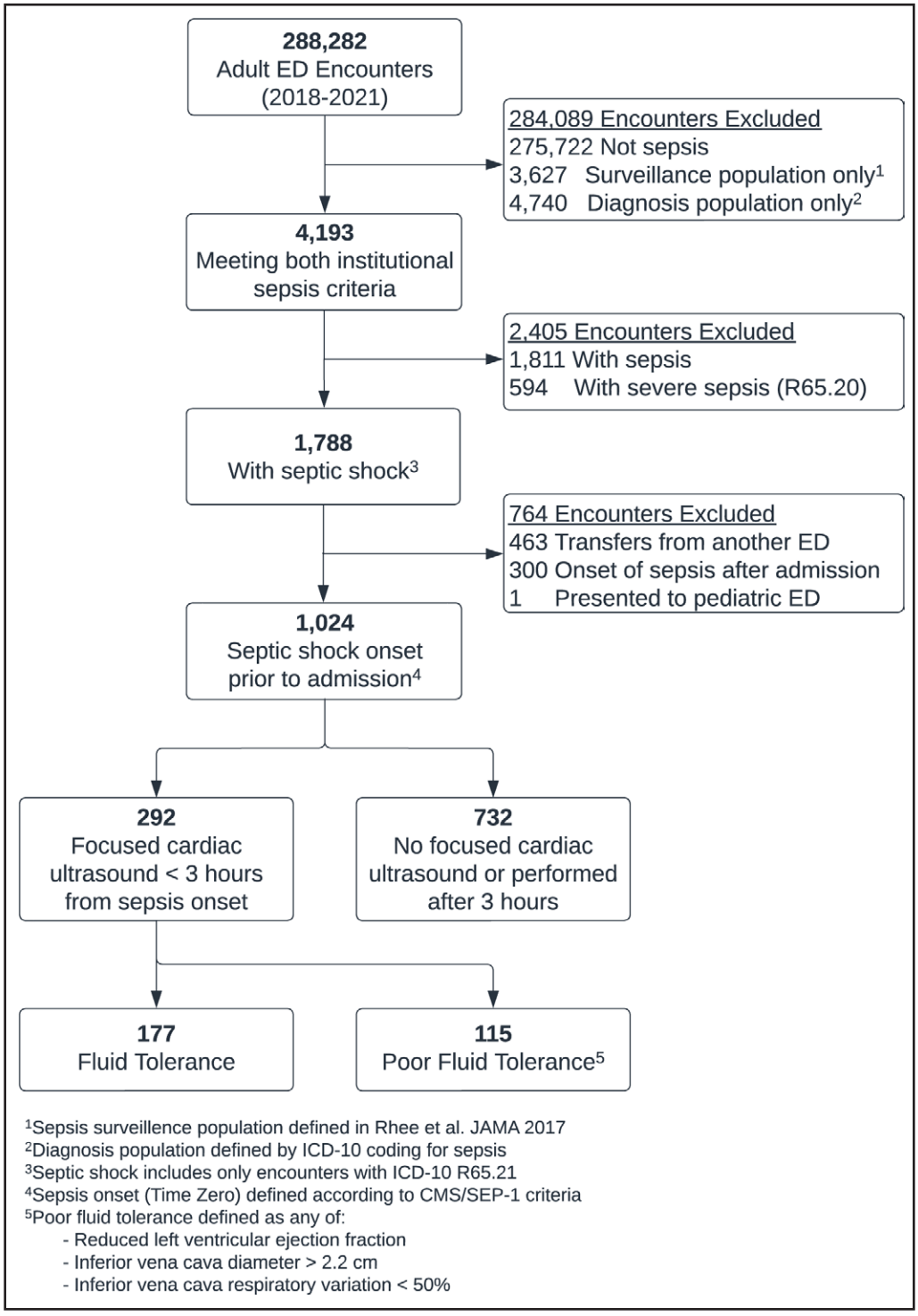

Figure 1. Flow diagram for patients with septic shock identification. Patients were required to meet both diagnosis code and organ dysfunction criteria (Rhee et al [2]). Focused cardiac ultrasound was identified by clinical documentation. ED = emergency department, CMS = Centers for Medicare and Medicaid Services, ICD-10 = *International Classification of Diseases*, 10th Edition, SEP-1 = severe sepsis and septic shock management bundle.

RESULTS

Patient and Encounter Characteristics

A total of 1,024 patient encounters were determined to have septic shock whose onset was in the ED before admission. FCU was performed within 3 hours of sepsis onset in 292 patients, whereas 732 patients either had FCU after 3 hours or not at all. Within the FCU group, 177 patients were determined to be FT, and 115 were found to have at least one finding of pFT. A cohort flow diagram is presented

in **Figure 1** and the characteristics of patients included in the cohort are detailed in **Table 1**. Patients who received FCU were older. Patient in the pFT group were more likely to have congestive heart failure (CHF) and CKD. There was no significant difference in weight, gender, and markers of hemodynamic instability or shock severity at presentation amongst all three groups. There was no significant difference in time to sepsis identification (time zero) between groups. The distribution of infection sources amongst FCU groups is detailed in **Supplemental Table S3** (http://links.lww.com/CCX/B280). Patients in the pFT group were more likely to have pneumonia (58.3% for pFT, 46.9% for FT, 42.2% for no FCU, $p = 0.005$).

Association Between Focused Cardiac Ultrasound and Fluid Resuscitation

Patients found to be FT were more likely to receive the 30-mL/kg fluid bolus within the first 3 hours in comparison to patients found to have pFT (52.0% vs. 31.3%, RD 20.7% with 95% CI, 9.4–31.9%). There was a significant difference in fluid given between groups at three hours (FT 2,271 mL vs. pFT 1646 mL) with a mean difference of 625 mL (95% CI, 330–919). Patients who did not receive FCU are provided for comparison in **Table 2** but only the difference between FT and pFT patients was assessed in bivariate comparisons. Multivariable logistic regression was used to estimate the odds of meeting the 30-mL/kg fluid target after adjustment for patient characteristics and initial markers of hemodynamic instability (**Fig. 2**). Fluid tolerance was associated with increased odds of achieving the fluid bolus target (odds ratio [OR] 2.17; 95% CI, 1.52–3.12). In this model, lactate greater than 4 mmol/L (OR 1.67; 95% CI, 1.15–2.45), higher shock index (OR 3.04; 95% CI, 2.14–4.37), and female gender (OR 2.00; 95% CI, 1.51–2.65) were also associated with increased odds of reaching the fluid target. CHF (OR 0.47; 95% CI, 0.34–0.64) and CKD (OR 0.47; 95% CI, 0.34–0.68) were associated with lower odds of meeting the fluid target.

Association Between Focused Cardiac Ultrasound and Resuscitation Outcomes

Resuscitation outcomes are detailed in Table 2. There was no difference in the percentage of patients requiring initiation of vasopressors on day 1 between FT and pFT patients (RD −9.8%; 95% CI, −20.3 to 0.1). There

TABLE 1.
Characteristics of Patients With Septic Shock

	No Focused Cardiac Ultrasound (n = 732)	Fluid Tolerant (n = 177)	Poor Fluid Tolerance (n = 115)	Standardized Mean Difference
Age, mean, yr (SD)	61.7 (15.1)	64.1 (13.9)	68.2 (15.6)	0.289
Female, *n* (%)	329 (44.9)	76 (42.9)	52 (45.2)	0.031
Weight, mean, kg (SD)	82.7 (28.3)	80.9 (27.6)	77.9 (21.0)	0.127
Charlson Comorbidity Index, points (SD)	6.55 (3.70)	6.54 (4.02)	7.57 (3.73)	0.182
Congestive heart failure, *n* (%)	225 (30.7)	54 (30.5)	64 (55.7)	0.35
Chronic kidney disease, *n* (%)	255 (34.8)	59 (33.3)	54 (47.0)	0.187
First lactate[a], mean, mmol/L (IQR)	2.9 (2.0, 4.4)	3.1 (2.2–5.3)	2.9 (1.95–5.25)	0.107
Systolic shock index, mean (SD)	1.29 (0.41)	1.36 (0.42)	1.32 (0.38)	0.113
Sepsis onset from emergency department arrival, median, min (IQR)	71 (29–162)	56 (23–123)	56 (27.5–155)	0.08

IQR = interquartile range.

[a]Lactate was not recorded for 10 patients in the no-focused cardiac ultrasound group and was categorized as normal, less than 2 mmol/L.

TABLE 2.
Resuscitation Outcomes

Resuscitation Outcome	No Focused Cardiac Ultrasound (n = 732)	Fluid Tolerant (n = 177)	Poor Fluid Tolerance (n = 115)	Difference[a] (95% CI)
Fluids administered at 3 hr, mean mL (SD)	1,780 (1,310)	2,271 (1,222)	1,646 (1,289)	625 (330 to 919)
Met 30 mL/kg fluid target at 3 hr, *n* (%)	251 (34.3)	92 (52.0)	36 (31.3)	20.7% (9.4% to 31.9%)
Mechanical ventilation on day 1, *n* (%)	228 (31.1)	58 (32.8)	42 (36.5)	–3.7% (–14.9% to 7.4%)
28-d ventilator-free days, mean (SD)	19.4 (11.5)	18.9 (11.9)	18.1 (12.1)	0.8 (–1.9 to 3.7)
Vasopressors on day 1, *n* (%)	423 (57.8)	118 (66.7)	88 (76.5)	–9.8% (–20.3% to 0.1%)
28-d vasopressor-free days, mean (SD)	20.0 (10.8)	19.4 (11.4)	18.2 (11.7)	1.2 (–1.6 to 3.8)
Deceased at 28 d, *n* (%)	151 (20.6)	44 (24.9)	32 (27.8)	–3.0% (–13.3% to 7.4%)

FCU = focused cardiac ultrasound.
[a]Comparison between fluid tolerant and poor fluid tolerance groups where risk or mean difference is presented with 95% CI. No focused cardiac ultrasound group is provided for reference only.

was also no difference in need for mechanical ventilation on day 1 (RD –3.7%; 95% CI, –14.9 to 7.4) despite the difference in amount of fluid administered. There was also no difference in either 28-day ventilator-free or 28-day vasopressor-free days between the FT and pFT groups. The daily status of each patient for the first 28 days from ED arrival is summarized in **Figure 3**. There was no difference in 28-day mortality (RD –3.0%; 95% CI, –13.3 to 7.4).

Fluid Resuscitation in Subgroup of Patients With CHF or CKD

To examine the effect of FCU in only those patients with preexisting CHF or CKD, we performed the multivariable analysis in this subgroup of patients. In this analysis (**Fig. 4**), FCU findings of fluid tolerance were the strongest predictor of meeting the fluid target (OR 3.32; 95% CI, 2.01–5.49). Female gender (1.58; 95% CI, 1.04–2.41) and shock index (2.72; 95% CI, 1.64–4.57) remained associated with meeting the fluid target. Bivariate analysis of resuscitation outcomes in this subgroup is detailed in **Supplemental Table S4** (http://links.lww.com/CCX/B280). Both fluid administered and proportion of patients meeting the fluid bolus target were significantly higher in the FT group.

Sensitivity Analyses

We also performed a sensitivity analysis where FCU performed after 2 hours from sepsis onset was considered as part of the "No FCU" group. In this analysis, 57 fewer patients received FCU, but fluid tolerance remained associated with receipt of 30 mL/kg bolus (**Supplemental Fig. S1**, http://links.lww.com/CCX/B280, OR 1.84; 95% CI, 1.25–2.71). Additionally, to improve covariate balance between FCU groups, IPW analyses were performed. A propensity score model using logic regression was created to estimate the probability of receiving FCU and used to create a weighted pseudo-cohort for subsequent analyses. SMDs were used to assess covariate balance after weighting by inverse propensity score (**Supplemental Table S5**, http://links.lww.com/CCX/B280). Weighted analyses were performed treating FCU exposure as either a binary (FCU or no FCU) or a three-level categorical (no FCU, FT, pFT). When FCU was considered a binary variable, FCU remained associated with receipt of 30 mL/kg within 3 hours of sepsis onset (**Supplemental Fig. S2**, http://links.lww.com/CCX/B280, OR 1.59; 95% CI, 1.18–2.15). When the FCU exposure was subdivided into fluid tolerance and pFT, fluid tolerance was associated with receipt of 30 mL/kg

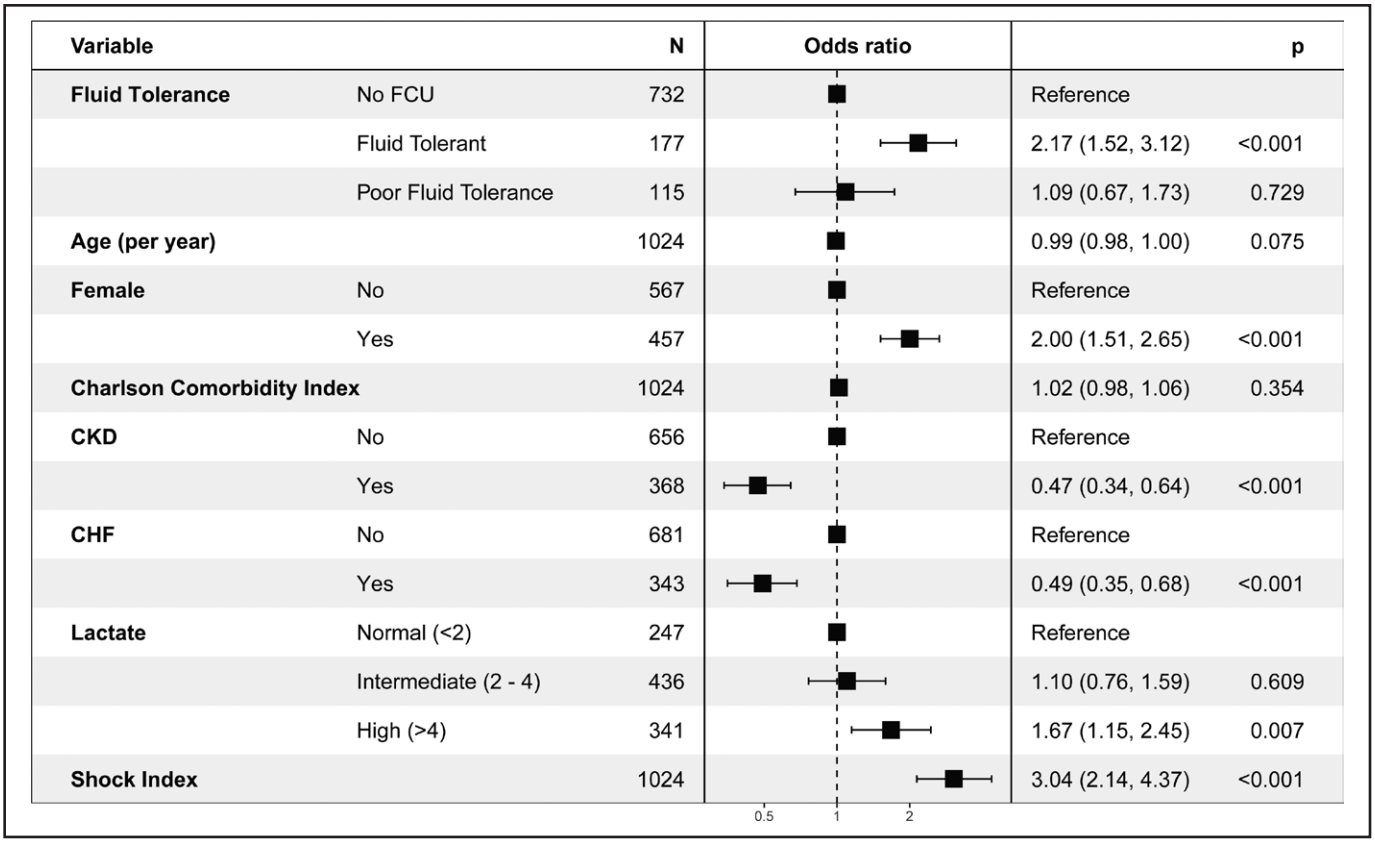

Figure 2. Forest plot for multivariable logistic regression model estimating the odds of compliance with 30 mL/kg IV fluid bolus within first 3 hours of sepsis onset. Fluid tolerance assessed by focused cardiac ultrasound, hemodynamic instability, and female gender were associated with higher odds of compliance with fluid bolus. Lactate was considered normal if greater than 2 mmol/L, intermediate if 2–4 mmol/L, and high if less than 4 mmol/L. Shock index here refers to the highest value of systolic shock index, calculated as heart rate/systolic blood pressure, in a single observation before 3 hours from sepsis onset. Shock index was the strongest predictor of fluid bolus compliance. Congestive heart failure (CHF) and chronic kidney disease (CKD) diagnoses were based on *International Classification of Diseases* (10th Edition) coding and were both associated with lower odds of compliance with fluid bolus.

bolus (**Supplemental Fig. S3**, http://links.lww.com/CCX/B280, 1.90; 95% CI, 1.34–2.70).

DISCUSSION

In our study, FCU findings of fluid tolerance were associated with a greater likelihood of meeting the SEP-1 recommended 30 mL/kg fluid target. Secondary outcomes including mechanical ventilation, vasopressor utilization, and 28-day mortality were not modified by FCU findings. Identifying the optimal fluid resuscitation strategy in critically ill patients with septic shock remains a major critical care research goal (21). Two large, multicenter randomized controlled trials to date have shown no mortality difference between restrictive and liberal fluid strategies (22, 23). However, these trials randomized patients after they were in the ICU (22) or more than 3 hours after sepsis identification (23), limiting their applicability to the early stages of resuscitation. Furthermore, cardiac ultrasound was not routinely used. Studies have shown an association between sepsis bundle compliance and improved mortality (24–27). There is some evidence that meeting the fluid metric alone (28, 29) is associated with improved mortality; however, these studies are at odds with those citing harm from positive fluid balance (5, 6), making this recommendation controversial. It is plausible that the same fluid administration strategy may have differing outcomes based on individual fluid tolerance states on presentation.

FCU may empower EPs to provide greater amounts of resuscitative fluid. This is especially true for patients who are assumed to be volume intolerant based on a history of CHF or CKD, which have been identified as risk factors for failure to provide the recommended fluid boluses (29, 30). In our analysis, CHF and CKD

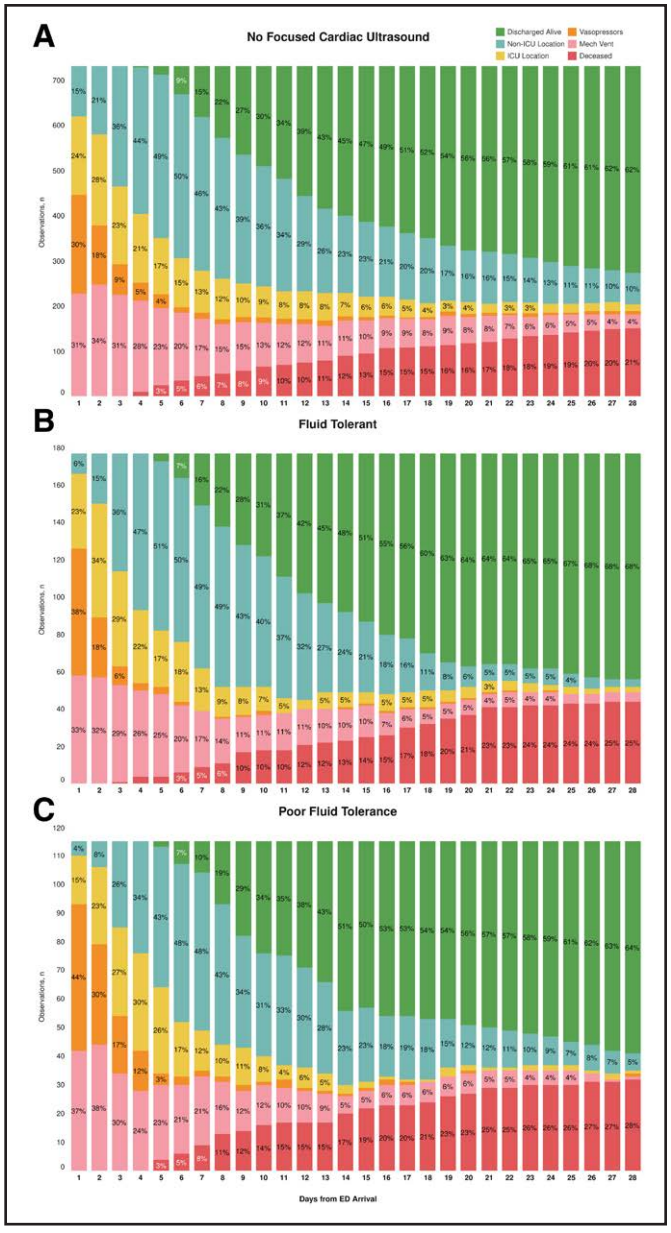

Figure 3. Twenty-eight-day ordinal status outcomes for: **A**, patients who did not receive focused cardiac ultrasound; **B**, patients who were found to be fluid tolerant; and **C**, patients who were found to have poor fluid tolerance. The *colored bars* represent the proportion of patients with each of six statuses in each 24-hour period (d) beginning at arrival to the emergency department. The worst status on each day is counted (deceased > mechanical ventilation > vasopressors only > ICU location > non-ICU location > discharged alive). Discharged alive include discharges to home, another facility, or hospice. Non-ICU location is any location other than an ICU including step-down, telemetry, and general care. Mechanical ventilation may include patients who are also on vasopressors.

history were associated with lower odds of meeting the fluid bolus target, which is similar to prior studies evaluating predictors of meeting the fluid bolus target (29). In the subgroup of patients with CHF and CKD, FCU findings of fluid tolerance were the strongest predictor of reaching the fluid bolus target. Additionally, ED-performed FCU may allow for earlier detection of sepsis-induced cardiac dysfunction (31). FCU may be one method to individualize care based on presenting volume status rather than underlying comorbidities and, given the increasing prevalence of ultrasound in emergency and critical care medicine, future prospective studies could mandate FCU in all patients with septic shock.

Although not the primary exposure of interest, female gender was associated with higher odds of reaching the recommended fluid amount. Similar patterns of increased fluid administration in female-identifying patients have been previously reported (29, 32), which may be due to females having lower weights, thus requiring a smaller absolute volume of fluid to reach the recommended weight-based amount. Our findings should be interpreted with caution given their nature as covariates in the model rather than the primary relationship being studied. Similar to other studies demonstrating poor fluid bolus compliance (33), in our cohort of patients with septic shock, about one-third of patients received the fluid bolus amount 3 hours from sepsis onset. Likewise, about one-third of our patients underwent FCU within the first few hours of their shock resuscitation. This raises the question of whether there would have been further FT patients identified in the no FCU group.

Our study may inform future prospective studies on protocolization of point-of-care ultrasound evaluation during the early resuscitation period for septic shock. Although we did not assess serial ultrasound, there is also likely a role for serial FCU considering the dynamic nature of fluid status. Lastly, FCU may also serve a role in justifying fluid management decision-making given recent changes to SEP-1 allowing documentation of the reason for giving less than the required 30 mL/kg in lieu of giving the full amount (4). Overall, given the recent proposal to add SEP-1 bundle compliance to CMS' value-based purchasing program (34), FCU could play an increasingly important role in sepsis quality programs by: 1) increasing documentation of volume associated harm or 2) empowering clinicians to give the full recommended fluid bolus in

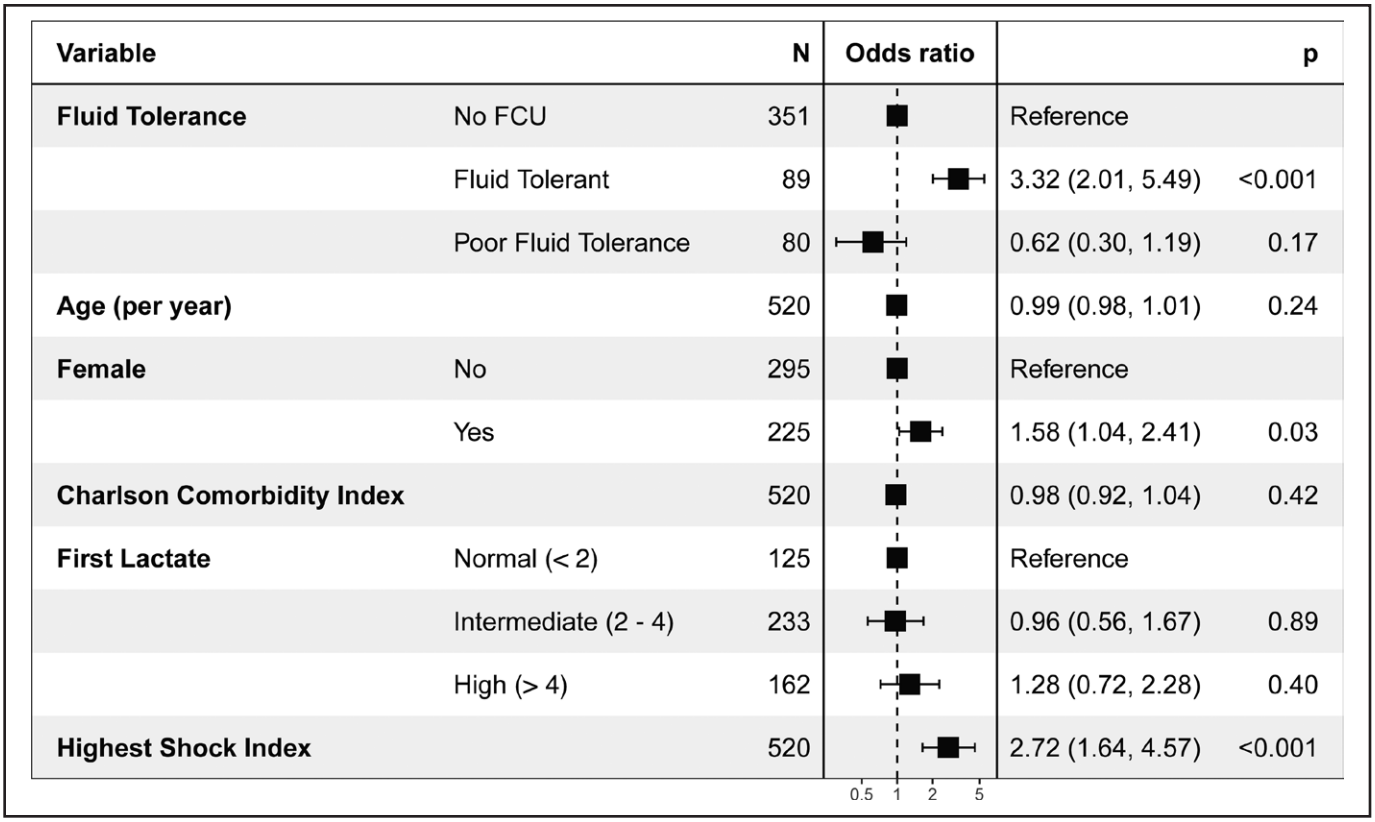

Figure 4. Forest plot for multivariable logistic regression model estimating the odds of meeting the 30-mL/kg fluid bolus goal in the subgroup of patients with previously diagnosed congestive heart failure and chronic kidney disease. Fluid tolerance, female gender, and systolic shock index are associated with a higher likelihood of meeting the fluid bolus goal. FCU = focused cardiac ultrasound.

patients who would otherwise be considered fluid intolerant using comorbidities alone.

LIMITATIONS

Our study was limited by factors common to retrospective studies. First, a major limitation is the selection bias regarding which patients receive FCU during the early resuscitation period. Notably, patients who did not receive FCU in our study were on average younger and less likely to have CHF or CKD. Tendencies of individual providers to perform or use FCU in their medical decision-making are also unmeasured in our data. To improve covariate balance between patients who received and those who did not receive FCU, we performed an IPW analysis, which produced similar results to our main finding. However, confounding from individual provider's practice habits remain. Finally, other clinical variables such as physical examination may have contributed to the selection of patients that received FCU or did not receive FCU but this also remains an unmeasured limitation. Future studies would benefit from individual clinician-level data to better understand factors that influence the use of FCU.

FCU findings of fluid tolerance were also determined by the treating team but not independently verified by the research team, thus either the interpretation or corresponding clinical actions may not have occurred as expected. However, EPs have been shown to accurately perform and interpret FCU in a myriad of conditions, including septic shock (31, 35–37). Before this study, there was an established quality assurance process at our institution, which may also mitigate the effect of FCU misinterpretation. In our cohort, we opted to include incomplete or conflicting studies to maximize specificity for any finding of pFT. For example, if a patient was found to have a decreased LVEF but IVC with increased or missing respiratory variability this patient was still classified as pFT. This may have the effect of misclassifying some FT patients as pFT.

Because we examined only imaging reports for FCU, there may also be a reporting bias in the FCU

group favoring studies that resulted in a change in clinical management. Conversely, some patients who were identified as having septic shock may have received FCU without proper documentation and may have been incorrectly included in the no FCU group. Although discouraged at our institution, failure to document bedside ultrasound findings is common in real-world clinical practice and may occur more frequently in critically ill patients (38).

We did not assess for recent or previous cardiology-based echocardiograms, which may have contributed to resuscitation decision-making. Findings of these studies were likely partially captured; however, by using ICD-10 codes for CHF whose diagnosis is predicated upon prior echocardiograms. FCU assessments in sepsis are not mandated at our institution and thus its use may be enriched in certain patients or providers. The directionality of these biases is uncertain although our study suggests that FCU is likely performed in sicker patients.

Lastly, our center uses a stand-alone ED-ICU (39) for critically ill patients before admission which may limit the generalizability of our findings. Patients typically are not transferred to this unit until several hours into their resuscitation and initial care is performed by ED clinicians. This is similar to the typical model of ED-to-ICU transfer and is unlikely to influence the early resuscitation period. Whether this unit influences longer-term secondary outcomes is unable to be assessed in this study. As a tertiary-care center, our patient population may also be enriched for patients with significant comorbid conditions including renal and cardiac disease that may further limit generalizability. Finally, we did not observe a difference in mortality or other secondary outcomes by FCU findings of fluid tolerance despite a significant increase in the fluid bolus amount given in this group of patients (Table 2). Thus, the addition of FCU to treatment algorithms may not ultimately lead to improvement inpatient outcomes beyond meeting an arbitrarily set government guideline.

CONCLUSIONS

Patients with septic shock who received FCU and had echocardiographic findings of fluid tolerance were more likely to receive the 30 mL/kg initial fluid bolus within 3 hours of sepsis onset. When restricting our analysis to only patients with CHF or CKD, FCU findings of fluid tolerance were the strongest predictor of receiving the required fluid bolus. Early FCU may be a strategy to increase compliance with the SEP-1 fluid requirements, either by identifying patients who could benefit despite historical risk factors for volume overload or by providing justification for giving less fluid.

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