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# Variation in Fluid and Vasopressor Use in Shock With and Without Physiologic Assessment: A Multicenter Observational Study

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## Abstract

**Objectives:** To characterize the association between the use of physiologic assessment (central venous pressure, pulmonary artery occlusion pressure, stroke volume variation, pulse pressure variation, passive leg raise test, and critical care ultrasound) with fluid and vasopressor administration 24 hours after shock onset and with in-hospital mortality.

**Design:** Multicenter prospective cohort study between September 2017 and February 2018.

**Settings:** Thirty-four hospitals in the United States and Jordan.

**Patients:** Consecutive adult patients requiring admission to the ICU with systolic blood pressure less than or equal to 90 mm Hg, mean arterial blood pressure less than or equal to 65 mm Hg, or need for vasopressor.

**Interventions:** None.

**Measurement and Main Results:** Of 1,639 patients enrolled, 39% had physiologic assessments. Use of physiologic assessment was not associated with cumulative fluid administered within 24 hours of shock onset, after accounting for baseline characteristics, etiology and location of shock, ICU types, Acute Physiology and Chronic Health Evaluation III, and hospital (beta coefficient, 0.04; 95% CI, –0.07 to 0.15). In multivariate analysis, the use of physiologic assessment was associated with a higher likelihood of vasopressor use (adjusted odds ratio, 1.98; 95% CI, 1.45–2.71) and higher 24-hour cumulative vasopressor dosing as norepinephrine equivalent (beta coefficient, 0.37; 95% CI, 0.19–0.55). The use of vasopressor was associated with increased odds of in-hospital mortality (adjusted odds ratio, 1.88; 95% CI, 1.27–2.78). In-hospital mortality was not associated with the use of physiologic assessment (adjusted odds ratio, 0.86; 95% CI, 0.63–1.18).

**Conclusions:** The use of physiologic assessment in the 24 hours after shock onset is associated with increased use of vasopressor but not with fluid administration.

Fluid resuscitation is a mainstay of treatment for most patients with noncardiogenic circulatory shock, with vasopressors used as an adjunctive therapy (1, 2). For patients in septic shock, the Surviving Sepsis Campaign clinical guidelines recommend the administration of 30 mL/kg of fluid as initial resuscitation, but there is substantial variation in practice between clinicians and less guidance with regard to other types of shock (3–5). Although adequate fluid resuscitation is an important part of treatment to enhance preload and cardiac output, excessive fluid resuscitation appears to be associated with organ failure and worse clinical outcomes (2, 6). Thus, determining when and how much fluid to administer is an important clinical question. It is recommended to use dynamic physiologic assessment (PA) like passive leg raise (PLR) test to assess for fluid responsiveness in persistent shock and to guide fluid management (7). However, the use of PA varies, and its effect on clinical management in shock in the usual clinical setting is not well defined (5, 3, 8). The most common trigger for fluid bolus in managing shock is vital signs and physical examination (5), this is an empiric decision without assessment of physiologic responsiveness to fluid resuscitation.

Our primary aim was to describe the variation in fluid resuscitation and vasopressor use in the 24 hours after shock onset, with and without the use of PA. We defined PA as the documentation of static assessments such as central venous pressure (CVP) or pulmonary artery occlusion pressure, or dynamic assessments such as stroke volume variation, pulse pressure variation, PLR test, or critical care ultrasound (CCUS). Our secondary aim was to determine the association between the use of PA and clinical outcomes such as in-hospital mortality and change in Sequential Organ Failure Assessment (SOFA) score, compared with empiric management.

# MATERIALS AND METHODS

Observation of variation in fluids administered and characterization of vasopressor requirements in shock (VOLUME-CHASERS) is a multicenter prospective cohort study conducted through the Discovery Network, the Society of Critical Care Medicine's research network (ClinicalTrials.gov NCT03190408).

Each site screened adult patients (≥ 18 yr) intended for ICU admission with shock (systolic blood pressure < 90 mm Hg, mean arterial blood pressure < 65 mm Hg, or initiation of vasopressor). Patients were excluded for: 1) previous enrollment into this study, 2) shock occurring during surgery in the operating room, 3) cardiac surgery with primary cardiogenic shock, and 4) transfer from another hospital to the study hospital. Sites screened for all consecutive patients for a 2- to 4-week period between September 2017 and February 2018. This study was approved by the Institutional Review Board at all 34 participating hospitals. The requirement for informed consent was waived by all centers. No external funding was provided for this study.

## Data Collection

We collected baseline demographics, shock etiology, medication history, comorbidities, location of shock onset, and ICU type. Variables needed for the Acute Physiology and Chronic Health Evaluation (APACHE) III and SOFA scores were collected during the time period from 12 hours before to 12 hours after shock onset. During the 24-hour following shock, we collected data on fluid (crystalloid, colloid, packed RBC, fresh frozen plasma, and platelet) and vasopressor (dopamine, epinephrine, norepinephrine, phenylephrine, and vasopressin) administration and mechanical ventilation in four time periods (hours 0–3, 3–6, 6–12, and 12–24). We recorded the use of any PA documented in the chart, whether free text or structured data. Empiric treatment was defined as the absence of any of PA documented during resuscitation. Patients were followed until hospital discharge or death for hospital mortality, hospital and ICU lengths of stay, and the use of mechanical ventilation, and renal replacement therapy. De-identified site data were uploaded into a secure online form using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Montefiore Medical Center/ Albert Einstein College of Medicine (funded by National Institutes of Health UL1TR001073) (9). We held instructional webinars to standardize data collection across sites.

## Statistical Analysis

**Primary Aim.**—Describing the use of PA. Statistical analysis was done using STATA release 15.0 (StataCorp LLC, College Station, TX). Mean and median were used to describe normal continuous variables and nonnormal continuous variables, respectively. For bivariate association, we used the Student $t$ test for normally distributed variables and the Mann-Whitney rank-sum test for nonnormally distributed continuous variables, and Fisher exact test for categorical variables to determine bivariate associations with the use of PA versus empiric management. Age, sex, race, APACHE III and SOFA score, lactate level, shock onset location, ICU types, and amount of fluid received prior to shock were determined a priori as confounders and are adjusted in multivariate models. In addition, we included

past medical history and secondary contributors of shock in associative models between the cumulative fluid, vasopressor use, and cumulative vasopressor dose with the use of PA in the 24 hours following shock onset.

**Primary Aim.**—Determining the predictors of PA. We used hospital sites as a random intercept in random effect models to determine the association between the use of PA and patient factors. We derived the final parsimonious model by performing backward elimination at $p$ value of less than 0.20, keeping confounding variables defined by changing the beta coefficient by 10% or clinical considerations as determined above, were forced into the model. The model with the lowest Akaike information criterion was chosen.

**Association Between PA and Variations in Fluid or Vasopressor Use.**—We calculated the cumulative fluid (mL) and cumulative vasopressor doses, expressed in norepinephrine equivalent (NEQ, mg) (10–12), by summing the intake 24 hours after shock onset. We used random intercept mixed effects multivariable linear regression to determine the association between outcome (cumulative fluid received and cumulative vasopressor dose) with the use of PA. Intraclass correlation coefficients (ICCs) estimated between-site variability. Cumulative fluid and vasopressor doses were log transformed to satisfy the assumption of normality. Random effect logistic regression was used to determine the association between the use of vasopressor in the 24 hours after shock onset and the use of PA. Linear models were tested for normality and linearity visually. Interactions were not observed between covariates.

**Secondary Aim.**—We also examined the association between the use of PA with clinical outcomes, including in-hospital mortality, change in SOFA score from baseline to 24–48 hours after shock onset. A parsimonious random effect logistic regression was used to determine the predictors of in-hospital mortality and the relationship between in-hospital mortality and the use of PA. The association for change in SOFA score was assessed by using linear regression.

Propensity score analysis tested the association between in-hospital mortality and PA (Supplemental Methods, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). We used logistic regression to determine the association of the use of PA and in-hospital mortality in the matched cohort.

## RESULTS

### Baseline Characteristics

The VOLUME-CHASERS study enrolled 1,639 patients (Table 1; and Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). The primary etiology of shock in this cohort was septic shock (60%), hypovolemic shock (8.9%), cardiogenic shock (11.8%), and other shock (9.2%), which includes 63 patients with neurogenic shock and 87 with other distributive shock.

Patients were more often diagnosed with shock in the ICU followed by the emergency department (ED) and were most often admitted to a medical or surgical ICU.

**Use of PA**

PA was less commonly used (*n* = 639, 39.4%) than empiric management (*n* = 993, 60.6%) in the first 24 hours after shock onset (Fig. 1A). CCUS (*n* = 502, 78%) was the most frequently used type of PA (Supplemental Fig. 1, Supplemental Digital Content 1, http:// links.lww.com/CCM/F562). Patients with septic shock and cardiogenic shock were more likely to have PA in bivariate analysis (Table 1). Patients were more likely to receive PA when presented with cardiac dysfunction as a secondary contributor of shock (Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). Notably, both the mean baseline APACHE III and SOFA scores were higher in those who received PA than empiric management. The amount of fluid received in the 12 hours before the shock was not different between the two groups (Table 1).

In multivariate analysis, PA was more frequently used in patients with higher APACHE III scores, secondary contributors of shock from cardiac dysfunction or trauma, and vasopressor administration in the 24 hours after shock onset (aOR [adjusted odds ratio], 1.99; 95% CI, 1.46–2.71; *p* < 0.001; Table 2). Patients with neurogenic shock as a secondary contributor of shock were less likely to have PA. There was substantial hospital site variation in the use of PA, with the ICC for site estimated to be 0.25 (95% CI, 0.13–0.42; Fig. 2). In sensitivity analysis, various PA methods (CCUS only and non-CCUS PA) were not associated with cumulative fluid but were consistently associated with increased odds of any vasopressor use; but non-CCUS PA was associated with a higher likelihood of any vasopressor use than CCUS PA (Supplemental Table 7, Supplemental Digital Content 1, http://links.lww.com/CCM/F562).

**Fluid Administration in the First 24 Hours After Shock Onset**

The most common type of fluid used in the 24 hours after shock onset was crystalloid at every time period (Supplemental Table 2, Supplemental Digital Content 1, http:// links.lww.com/CCM/F562). On univariate analysis, patients with PA were more likely to receive any fluid at hour 0–3 (odds ratio [OR], 1.29; 95% CI, 1.03–1.61), hour 6–12 (OR, 1.72; 95% CI, 1.35–2.19), hour 12–24 (OR, 1.60; 95% CI, 1.26–2.04), and not at hour 3–6 (OR, 1.21; 95% CI, 0.97–1.50).

Of the patients who received fluid, the fluid received at each time period did not differ between the PA and empiric management groups (Fig. 1B). There was a nonsignificant variation in fluid received at each time period, which led to a small but significant difference in cumulative fluid after 12 hours and after 24 hours between the two groups; median difference between the PA and empiric groups was 159 mL (interquartile range [IQR], 4–327 mL) 12 hours after shock and 277 mL (IQR, 57–500 mL; *p* = 0.010) 24 hours after shock (Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/CCM/ F562; and Fig. 1C).

After multivariate analysis, adjusting for severity of illness and baseline characteristics, there was no association with the cumulative fluid administered in the 24 hours following shock onset between PA or empiric management (beta coefficient, 0.04; 95% CI, –0.07 to 0.15) (Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/CCM/F562).

We saw that higher APACHE III, having received less than 1,000 mL prior to the onset of shock, shock onset locations, ICU types, the use of vasopressor, and mechanical ventilation were all associated with higher cumulative fluid. On the other hand, past medical history of renal disease and congestive heart failure or cardiac dysfunction were associated with less cumulative fluid in the 24 hours following shock onset (Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). There was little site variation in the amount of fluid administered in the 24 hours after shock onset, with (ICC, 0.04; 95% CI, 0.02–0.12).

### Use of Vasopressor in the First 24 Hours Following Shock Onset

In the 24 hours following shock onset, vasopressors were used in 68.9% of all patients. Norepinephrine (54.3%) was the most commonly used vasopressor, followed by vasopressin (21%), phenylephrine (13%), epinephrine (7.2%), and dopamine (4.2%). At every time period in the 24 hours after shock onset, the PA group was more likely to receive vasopressor (Fig. 1D).

In multivariate analysis, PA was associated with 1.98 times increased likelihood of using any vasopressor during the 24-hour period after shock onset (95% CI, 1.45–2.71; Supplemental Table 4, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). Patients in the PA group received 45% higher cumulative vasopressor dose in the 24 hours after shock onset than those in the empiric management group (beta coefficient, 0.37; 95% CI, 0.19–0.55; Supplemental Table 5, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). The ICC for the use of vasopressor across hospital sites was 0.14 (95% CI, 0.06–0.30) and for the cumulative vasopressor dose in NEQ was 0.10 (95% CI, 0.05–0.19).

The use of vasopressor increased cumulative fluid received in 24 hours by 42% (beta coefficient, 0.35; 95% CI, 0.22–0.48). For every 1,000 mL of cumulative fluid received in the 24 hours after shock onset, patients were more likely to receive any vasopressor (aOR, 1.21; 95% CI, 1.13–1.3). Cumulative fluid in the 24 hours after shock onset was also associated with cumulative vasopressor dose (beta coefficient, 0.25; 95% CI, 0.15–0.35).

### Patient Outcomes

The overall in-hospital mortality was 25.1%. There was no difference in in-hospital mortality between the use of PA or empiric management in bivariate analysis (Table 3). The SOFA score in hour 24–48 after shock onset remained higher in the PA group. The change in SOFA was −1 (−3 to 1) in both groups, but the difference was statistically significant in bivariate analysis. The overall hospital length of stay was not different between the PA and empiric management groups. ICU length of stay was longer in the group receiving PA in bivariate analysis. The PA group was more likely to require mechanical ventilation and new renal replacement therapy during the hospitalization (Table 3).

### Change in SOFA

The use of PA was not associated with a change in SOFA score from shock onset and after 24 hours of shock onset (at hour 24–48), after adjusting for baseline characteristics and

severity of illness (adjusted beta coefficient, –0.075; 95% CI, –0.57 to 0.42). There was no significant site variation for change in SOFA (ICC, 0.006; 95% CI, 0.0004–0.082).

### Associations Between PA and In-Hospital Mortality

The use of PA during the first 24 hours after shock onset was not associated with in-hospital mortality in multivariate adjusted models (aOR, 0.86; 95% CI, 0.63–1.18; Supplemental Table 6, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). Similarly, in a sensitivity analysis after matching for propensity score for using PA, there was no association between the use of PA and in-hospital mortality (aOR, 0.85; 95% CI, 0.64–1.14; $p = 0.561$; Supplemental Fig. 2, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). The use of vasopressor was associated with increased odds of in-hospital mortality (aOR, 1.88; 95% CI, 1.27–2.78; Supplemental Table 6, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). There was no association between cumulative fluid and in-hospital mortality (aOR, 0.95; 95% CI, 0.90–1.00; Supplemental Table 6, Supplemental Digital Content 1, http://links.lww.com/CCM/F562). The ICC for the random effect of the hospital for in-hospital mortality was 0.02 (95% CI, 0.005–0.10; Fig. 2). Additional sensitivity analysis of different PA methods (CCUS only and non-CCUS PA) were not associated with in-hospital mortality (Supplemental Table 8, Supplemental Digital Content 1, http://links.lww.com/CCM/F562).

## DISCUSSION

We found that PA was not commonly practiced in the first 24 hours following shock onset. When performed, PA is more commonly used for sicker patients. The use of PA was associated with increased use of vasopressor but was not associated with the amount of fluid patients received in the 24 hours following shock onset. We did not find an association between the use of PA and of in-hospital mortality. Hospital site variation contributed significantly to the variation in the use of PA and the use of vasopressor, but we found less site contribution to the observed variation in fluid administration and in-hospital mortality.

The goal of this study was to capture contemporary usual practice of shock management in terms of fluid resuscitation and vasopressor administration. The distribution of shock etiology in this cohort is consistent with other observational cohorts of circulatory shock (13). Current literature advocates for the use of PA in the management of shock (4, 14, 15). However, previous studies have also found low rates of PA in patients with shock: rates of PA in our study (39.5%) were within the range of published literature, such as Boulain et al (5) (23.6%) and the Fluid Challenge in Intensive Care (FENICE) cohort (57.3%) (3, 5). Our study is different in that we included patients with shock in any location within the study hospital; we did not limit our observation to the ICU. In two largely European studies, CVP was the most commonly used method of assessing hemodynamic status (3, 5). In our mainly U.S. cohort, CCUS was the most common modality (78%), suggesting that the practice of PA is moving away from invasive hemodynamic and pressure monitors. CCUS is generally accessible, inexpensive, noninvasive, and usable in any hospital setting. However, CCUS interpretation may be subjective and dependent on operator experiences (16). This may impact clinical decision making and ultimately lead to variation in management.

PA is intended to assess hemodynamics and may help clinicians make decisions on fluid responsiveness in a shock patient, thus affecting fluid and vasopressor use. In our present study, we saw that fluid resuscitation was more often guided without PA, rather, relying on empiric determinations from vital signs, physical exams, or laboratory data. On the other hand, we also saw an association between the use of PA and vasopressor use in the 24 hours following shock onset, after adjusting for severity of illness. PA was employed to guide the use of vasopressor.

There is substantial variation in the current literature in terms of the impact of PA on fluid and vasopressor use in shock patients (17–22). Dynamic PA have been shown to predict fluid responsiveness (23), but randomized controlled studies comparing various modalities of PA do not find consistent associations between PA and fluid, vasopressor use, or in-hospital mortality (18–21, 24–26), despite having high protocol compliance. Although our study was similar to both FENICE and Boulain's (5) observational cohorts in finding no association between PA and fluid administration (3, 5), we did find associations between PA and vasopressor use, suggesting clinicians may rely on PA to initiate and titrate vasopressor use in shock patients, but not necessarily to limit fluid boluses. In addition, PA seems to be more commonly used in sicker patients requiring the use of vasopressors. It is possible that clinicians felt that the additional data afforded from PA is not needed or would not change their management if the patient is improving or not deteriorating. The clinical decision-making process with regards the choice of PA, fluid resuscitation, and vasopressor cannot be simply discerned by quantitative study. Further studies using qualitative think aloud study are being conducted to better understand the thinking process.

There was variation between hospital sites in the management of shock patients. However, after accounting for patient-level differences, the choice of whether to use PA or vasopressor remained consistent within individual institutions, suggesting local culture affects shock management. But even with such local practice patterns, the amount of fluid administered and in-hospital mortality were less dependent on individual site practices. This is consistent with previous European multicenter observational studies showing variability with PA use but not with fluid administration (3, 5, 8). We were able to expand on these previous studies by studying variability in vasopressor use between hospital sites. Although PA use is associated with more vasopressor use and sicker patients, we did not find an association between use of PA and outcomes in shock. Given the recommendations for PA use and its adoption at some sites, prospective randomized control trials are needed to better understand how PA use can improve outcomes.

There are a number of strengths to this study. We described usual care in 34 hospitals within the Discovery Research Network in the 24 hours following shock onset for a diverse range of shock types. Our cohort was not limited to the ICU, and we captured shock management as early as when the patients arrived in the ED or when shock first occurred on the wards. This is a significant strength to our study, as we were able to follow patients as they moved between different hospital settings. We obtained detailed fluid and vasopressor administration during the 24 hours following shock onset.

There are a few limitations to our study. We did not assess the quality of PA or how it impacted physician decision making. Furthermore, our study relies on what was documented by the treating clinician and would not have captured undocumented management of the patient. The lack of documentations may contribute to the low PA utility. However, our studies is consistent with previous European cohorts demonstrating rare and inconsistent use of PA in septic patients in the ICU (3, 5). We combined all modalities of hemodynamic assessments into one general catch-all category of "physiologic assessment" because the overall frequency of PA was very low. In addition, PA such as CCUS may be used as both statically and dynamically, making it difficult to categorize. Furthermore, in sensitivity analysis comparing different PA methods with empiric management, we found consistent relationship between PA, fluid, use of any vasopressor, and in-hospital mortality. As a cohort observation study, there would be possible unaccounted confounders in our adjustment. Nevertheless, this reflects realworld practice of hemodynamic assessment in shock management, as clinicians often rely on more than one modality. We do not have individual characteristics of each hospital sites, future study to determine specific site attribution to the use of PA is warranted.

## CONCLUSIONS

We found that the use and type of PA varies vary between hospital sites. PA was not associated with fluid administration but was associated with increased use of vasopressor. Ultimately, site-to-site variability in the use of PA did not impact in-hospital mortality. Further study in the direct relationship between PA and clinician response can shed light on the variation in fluid and vasopressor administered in shock.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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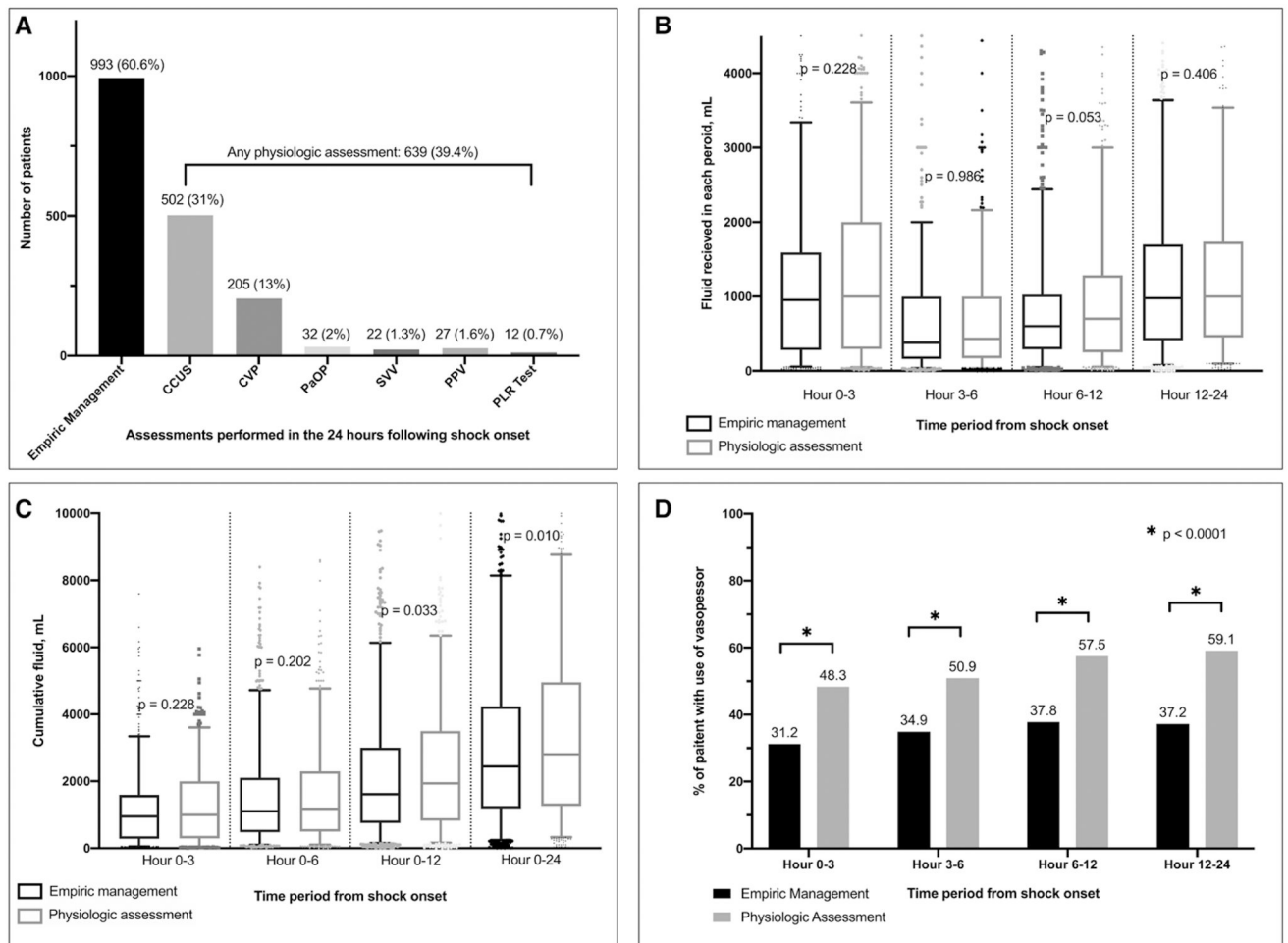
**Figure 1.**
The use of physiologic assessment, fluid, and vasopressor in the 24hr following shock onset.
**A**, the use of physiologic assessment and empiric management in the 24hr following shock
onset. **B**, Fluid received at each time period between hour 0–3, hour 3–6, hour 6–12, and
hour 12–24. **C**, Cumulative fluid received from hour 0 to 24. **D**, The percent of patients with
the use of vasopressor at each time period from hour 0–3, hour 3–6, hour 6–12, and hour 12–
24. The *black box* represents empiric management group and the *gray box* are physiologic
assessment group. CCUS = critical care ultrasound, CVP = central venous pressure, PaOP
= pulmonary artery occlusion pressure, PLR = passive leg raise, PPV = pulse pressure
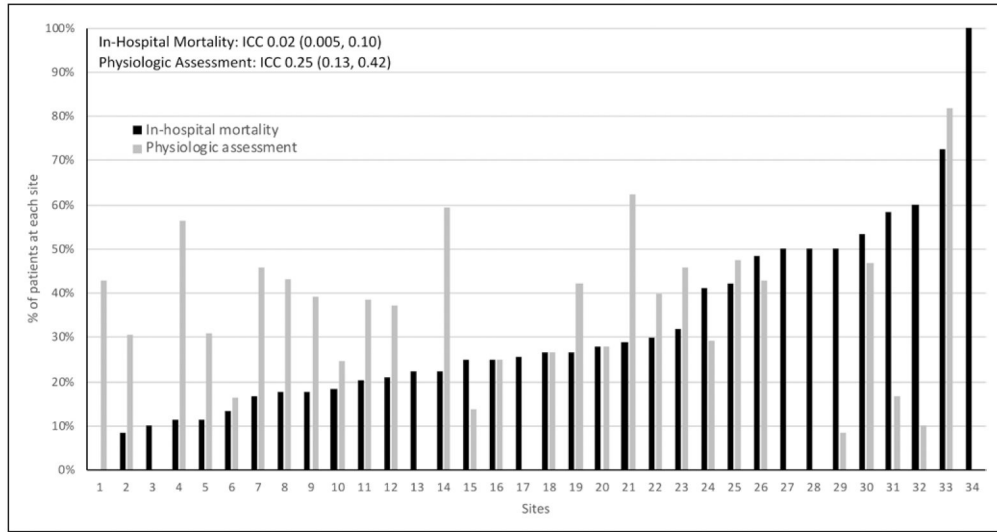variation, SVV = stroke volume variation.

**Figure 2.**
Percent of patients at each site with physiologic assessment and in-hospital mortality, in the order of in-hospital mortality by site. Physiologic assessment intraclass correlation coefficient (ICC) derived from using hospital site as random intercept in random effect model adjusting for age, race, sex, Acute Physiology and Chronic Health Evaluation (APACHE) score, Sequential Organ Failure Assessment (SOFA), maximum lactate level, shock onset location, ICU type, primary shock etiology, cardiac dysfunction, trauma, neurogenic shock as secondary contributor, and mechanical ventilation in the 24hr from shock onset. In-hospital mortality ICC derived from using hospital site as random intercept in random effect model adjusting, use of physiologic assessment, age, race, sex, APACHE score, SOFA, maximum lactate level, hours in hospital prior to shock onset, shock location, ICU types, past medical history of cancer, trauma as a secondary contributor of shock, fluid received, use of vasopressor, and mechanical ventilation in the 24hr following shock and renal replacement therapy.

**TABLE 1.**

Baseline and Severity of Illness Around Shock Onset of the VOLUME-CHASERS (Observation of Variation in Fluids Administered and Characterization of Vasopressor Requirements in Shock) Cohort by the Use of Physiologic Assessment

| Variables | All, $n = 1,639$ | Empiric Management, $n = 993$ | Physiologic Assessment[a], $n = 646$ | $p$[b] |
|---|---|---|---|---|
| Age[c], years, mean (SD) | **62.5 (16.4)** | **61.5 (16.9)** | **63.9 (5.4)** | **0.004** |
| Race, $n$ (%) | | | | 0.7 |
| White | 991 (60.5) | 605 (61.2) | 386 (59.8) | |
| Black | 266 (16.2) | 155 (15.7) | 111 (17.2) | |
| Other | 382 (23.3) | 233 (23.6) | 149 (23.1) | |
| Sex, $n$ (%) | | | | 0.14 |
| Male | 901 (55) | 530 (53.6) | 371 (57.4) | |
| Female | 733 (44.7) | 458 (46.4) | 275 (42.6) | |
| Primary etiology of shock, $n$ (%)[d] | | | | |
| Septic shock | **977 (60)** | **569 (57.9)** | **408 (63.3)** | **0.02** |
| Hypovolemic shock | 308 (18.9) | 206 (21) | 102 (15.8) | 0.14 |
| Cardiogenic shock | **192 (11.8)** | **99 (10.1)** | **93 (14.4)** | **0.007** |
| Other shock | **150 (9.2)** | **108 (11)** | **42 (6.5)** | **0.003** |
| Shock onset locations, $n$ (%)[e] | | | | |
| ICU | 806 (49.3) | 503 (50.9) | 303 (46.9) | 0.143 |
| Emergency department | **547 (33.5)** | **312 (31.6)** | **235 (36.4)** | **0.042** |
| Wards | 224 (13.7) | 139 (14.1) | 85 (13.2) | 0.659 |
| Postanesthesia care unit | 25 (1.5) | 19 (1.9) | 6 (0.9) | 0.148 |
| Other | 32 (2) | 15 (1.5) | 17 (2.6) | 0.143 |
| ICU types, $n$ (%)[f] | | | | |
| Medical | 858 (52.6) | 526 (53.3) | 332 (51.4) | 0.544 |
| Surgical | 222 (13.6) | 133 (13.5) | 89 (13.8) | 0.825 |
| Mixed medical/surgical | 245 (15) | 135 (13.7) | 110 (17) | 0.065 |
| Cardiothoracic ICU | 117 (7.2) | 70 (7.1) | 47 (7.3) | 0.922 |
| Other | 190 (11.6) | 122 (12.4) | 68 (10.5) | 0.305 |
| Severity of illness in the 24 hr around shock | | | | |

| Variables | All, n = 1,639 | Empiric Management, n = 993 | Physiologic Assessment[a], n = 646 | p[b] |
|---|---|---|---|---|
| Acute Physiology and Chronic Health Evaluation III, mean (SD) | 86.6 (28.2) | 83.6 (27.8) | 91.2 (28.6) | < 0.0001 |
| Sequential Organ Failure Assessment, median (IQR) | 7 (5–10) | 7 (5–10) | 8 (5–11) | 0.0001 |
| Lactate level,[g] mg/dL, median (IQR) | | | | |
| 12 hr before shock | 2.1 (1.40–3.74) | 2 (1.4–3.34) | 2.3 (1.4–4) | 0.071 |
| 12 hr after shock | 2.3 (1.40–4.3) | 2.4 (1.4–4.3) | 2.21 (1.4–4.4) | 0.869 |
| Baseline fluid in 12 hr prior to shock onset, mL, median (IQR)[h] | 1065 (500–2200) | 1070 (506–2060) | 1064 (500–2505) | 0.495 |

IQR = interquartile range.

[a] Physiologic assessment includes central venous pressure, pulmonary artery occlusion pressure, stroke volume variation, pulse pressure variation, critical care ultrasound, and/or passive leg raise test.

[b] Each independent variable was compared between the empiric management and the use of physiologic assessment. t test and Mann-Whitney rank-sum test were used for continuous variables, and Fisher exact test for categorical variables.

[c] Age data available in 1,634 participants.

[d] Primary etiology of shock was available in 1,627 participants.

[e] Shock location was available in 1,634 participants.

[f] ICU types was available in 1,632 patients.

[g] Lactate data available in 844 prior to shock and 1,105 12-hr following shock.

[h] Preshock fluid data available in 1,027.

Boldface values represent statistically significance difference detected in bivariate comparison between physiologic assessment and empiric management.

**TABLE 2.**

Predictors of the Use of Physiologic Assessment ($n = 1,346$)

| Variables | Adjusted OR (95% CI)[a] | p |
|---|---|---|
| Acute Physiology And Chronic Health Evaluation III score | 1.01 (1.00–1.02) | 0.001 |
| Secondary contributors of shock | | |
| Cardiac dysfunction | 1.45 (1.04–2.03) | 0.005 |
| Trauma | 3.04 (1.64–10.0) | 0.001 |
| Neurogenic | 0.52 (0.29–0.92) | 0.019 |
| Vasopressor use[b] | 1.99 (1.46–2.71) | < 0.001 |
| Cumulative fluid (1,000 mL) | 1.02 (0.97–1.07) | 0.348 |

OR = odds ratio.

[a] Multivariate model adjusted for age, race, Acute Physiology And Chronic Health Evaluation score, Sequential Organ Failure Assessment, maximum lactate level, shock onset location, ICU type, primary shock etiology, cardiac dysfunction, trauma, neurogenic shock as secondary contributor, and mechanical ventilation in the 24hr from shock onset.

[b] Within the first 24hr after shock onset.

**TABLE 3.**

Patient Outcomes: Clinical Outcomes and ICU Resources Utilization in the VOLUME-CHASERS Cohort by the Use of Physiologic Assessment

| Variables | Total, $n = 1,639$ | Empiric Management, $n = 993$ | Physiologic Assessment, $n = 646$ | $p$ [g] |
|---|---|---|---|---|
| In-hospital mortality, $n$ (%) | 412 (25.1) | 235 (23.7) | 177 (27.4) | 0.091 |
| Highest lactate in hour 24–48 from shock, mg/dL, median (IQR) [a] | 2 (1.3–3.5) | 1.9 (1.3–3.1) | 2 (1.2–3.8) | 0.294 |
| SOFA score in hour 24–48 from shock [b] | 6 (3–10) | 5 (3–9) | 7 (4–11) | < 0.001 |
| Change in SOFA at hour 24–48 from shock | −1 (−3–1) | −1 (−3–1) | −1 (−3–1) | 0.019 |
| Vasopressor-free days—7 d, median (IQR) [c] | 6 (3–7) | 6 (4–7) | 5 (2–7) | < 0.001 |
| Mechanical ventilation | | | | |
| Ever vented during hospitalization, $n$ (%) | 984 (60) | 544 (55.3) | 440 (68.1) | < 0.001 |
| Ventilator duration (of those vented) d, median (IQR) | 4 (2, 8) | 4 (2, 8.5) | 4 (2, 8) | 0.615 |
| Ventilator-free days—28 d (of those vented) d, median (IQR) [d] | 18 (0–25) | 16 (0–25) | 18 (0–25) | 0.866 |
| RRT, $n$ (%) | 305 (18.6) | 171 (17.2) | 134 (20.7) | 0.105 |
| Types of RRT (of those who required RRT), $n$ (%) | | | | |
| Intermittent hemodialysis, $n$ (%) | 178 (58.4) | 99 (55.6) | 79 (59) | 0.194 |
| Continuous renal replacement therapy/sustained low efficiency dialysis, $n$ (%) | 192 (63) | 105 (54.7) | 87 (45.3) | 0.084 |
| New RRT in all, $n$ (%) | 193 (11.8) | 103 (10.4) | 90 (13.9) | 0.034 |
| New RRT (of those who required HD), $n$ (%) | 193 (63.3) | 103 (53.4) | 90 (67.2) | 0.034 |
| RRT required at discharge, $n$ (%) | 107 (35.1) | 67 (62.6) | 40 (29.9) | 0.099 |
| Hospital length of stay, days, median (IQR) [e] | 11 (6, 20) | 11 (6, 20) | 12 (7, 21) | 0.108 |
| ICU length of stay, d, median (IQR) [f] | 5 (3–9) | 5 (3–9) | 5 (3–11) | 0.003 |

IQR = interquartile range, RRT = renal replacement therapy, SOFA = Sequential Organ Failure Assessment.

[a] Lactate data available in 789 patients.

[b] Postresuscitation SOFA calculated from 1,465 patients.

[c] Vasopressor-free days available in 1,568 patients.

[d] Ventilator-free days is available in 845 patients.

[e] Hospital length of stay available in 1,568 patients.

[f] ICU length of stay available in 1,489 patients.

[g] We compare each independent variable between the empiric management and the use of physiologic assessment. *t* test and Mann-Whitney rank-sum test were used for continuous variables and Fisher exact test for categorical variables.