**Supplementary Appendix.**

**Contents: Page number**

Supplementary Materials 2

* Acknowledgement

Supplementary Methods 4

* Propensity score matching

Supplementary Tables cited in main text 5

* Supplemental Table 1: Extended baseline characteristics
* Supplemental Table 2: Fluid and vasopressor use in 24 hours after shock
* Supplemental Table 3: Multivariate association model for PA and fluid
* Supplemental Table 4: Multivariate association model for PA and vasopressor use
* Supplemental Table 5: Multivariate association model for PA and vasopressor dose
* Supplemental Table 6: Predictors of in-hospital mortality
* Supplemental Table 7: Sensitivity analysis of association of different PA and fluid and vasopressor
* Supplemental Table 8: Sensitivity analysis of association of different PA and in-hospital mortality

Supplemental Figure cited in the main text 15

* Supplemental Figure 1
* Supplemental Figure 2

|  |  |
| --- | --- |
| **Supplemental material: Acknowledgement**  VOLUME-CHASERS Study Group acknowledges the following sites and individuals for their efforts on the project. Sites are organized alphabetically. | |
| **Hospital Sites** | **Individuals by site** |
| **Bridgeport Hospital** | Tina McCurry |
| **Brigham and Women's Hospital** | Jeremy R. DeGrado, PharmD Kevin M. Dube, PharmD Kenneth E. Lupi, PharmD |
| **Cleveland Clinic Foundation** | Andrei Hastings, MD  Omar Mehkri, MD |
| **Duke University School of Medicine** | Raquel R. Bartz, MD, MMCi  Angela L. Pollak, MD  Sarah Kendall Smith, MD, PhD |
| **Emory University Hospital/Grady Hospital** | Marguerite Stewart  Leona Wells |
| **Geisinger Wyoming Valley Medical Center** | Jamie Kerestes, PharmD  Kayla Kotch Sarah Miller |
| **Intermountain Healthcare** | Brent Armbruster  Valerie Aston  Katie Brown Mardee Merrill |
| **King Hussein Cancer Center** | Nadeen Anabtawi, PharmD |
| **Lahey Hospital** |  |
| **Lake Region Medical Center** | Kerri L. Federico, PharmD, BCPS  Peter-John Trapp, PharmD |
| **Mayo Clinic** | Joseph C. Farmer, MD  Pablo Moreno Franco, MD  Shurong Gong  Rahul Kashyap, MBBS Sidhant Singh |
| **University of Texas MD Anderson Cancer Center** | Reagan D. Collins PharmD, BCCCP |
| **Massachusetts General Hospital** | Natasha Lopez, PharmD, BCCCP, BCPS  Kristy Phillips, PharmD, BCCCP, BCPS |
| **Montefiore Medical Center, Albert Einstein College of Medicine** | Jorge Ataucuri-Vargas, MD  Vladyslav Dieiev, MD  Ashley Kang, MD  Ann Wang, MD |
| **Mt Sinai Health System** | Neha N. Goel, MD, MSCR |
| **New York University** | Oscar Mitchell, MD |
| **Ohio Health/Riverside Methodist Hospital** | Jordan DeWitt, PharmD, BCPS, BCCCP Alex Heine, PharmD, BCCCP Abby Tyson, PharmD, BCPS |
| **Oregon Health and Science University** | Parshwan Lahiji  Dubier Matos  Ebaad Haq |
| **Rush University Medical Center** | Katie Dalton, PharmD Drayton Hammond, PharmD, MBA, MSc  Gourang Patel, PharmD, MSc |
| **St Agnes Hospital** | Valentina Amaral, MD Jasmine Aulakh, MD Nauman Farooq, MD |
| **Truman Medical Center** | Kerra Cissne, PharmD, BCPS |
| **University of Arizona** | Jose Camarena  Kristen Deupree Alexia Demitsas  Karen Lutrick, PhD |
| **University of Cincinnati** | Nora Elson, MS  Dina Gomaa John Shinn III Anthony Spuzzillo Devin Wakefield |
| **University of Maryland** | Mehrnaz Pajoumand, PharmD  Sharon Wilson, PharmD  Siu Yan Amy Yeung, PharmD |
| **University of Michigan** | Tina Chen  Sinan Hanna |
| **University of Oklahoma Health Sciences Center** | Lauren Sinko  Kassidy Malone  Deamber Piel |
| **University of Utah** | Chloe Skidmore |
| **University California Los Angeles** | Ji Yeon Seo, MD Matt Flynn, MD |
| **University of Rochester Medical Center** | Nicole M. Acquisto, PharmD  Kathryn Connor​, PharmD  Samantha Delibert, PharmD  Christine Groth, PharmD  Jeff Huntress, PharmD  Gregory Kelly, PharmD  Therese Makhoul, PharmD  Hannah Mierzwa, PharmD  Stephen Rappaport, PharmD |
| **University of Southern California** | Daisy Rios |
| **Vidant Medical Center** | Bethany Crouse, PharmD |
| **Wake Forest Baptist Health** |  |
| **Yale-New Haven Health** | Abdalla A. Ammar, PharmD, BCPS, BCCCP Shamsuddin Akhtar, MD |

Supplemental Methods:

**Propensity score matching**

We generated propensity scores by including covariates that were associated with in-hospital mortality and covariates that confound the relationship between PA and in-hospital mortality. Patients were matched 1 to 1 using naïve matching at a caliper of 0.20 to further assess the association between PA and in-hospital mortality.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Supplemental Table 1: Extended baseline characteristics the VOLUME-CHASERS cohort by the use of physiologic assessment | | | | |
| **Variables** | **All, N = 1639** | **Empiric management,**  **n = 993** | **physiologic assessment*a*,**  **n = 646** | **P- value*b*** | |
| Secondary Contributors of Shock, n(%) |  |  |  |  | |
| Hypovolemia | 293 (17.9) | 170 (17.1) | 123 (19) | 0.323 | |
| **Cardiac dysfunction** | **275 (16.8)** | **129 (13)** | **146 (22.6)** | **<0.001** | |
| Neurologic | 87 (5.3) | 57 (5.7) | 30 (4.6) | 0.368 | |
| **Trauma** | **42 (2.6)** | **18 (1.8)** | **24 (3.7)** | **0.024** | |
| Intoxication | 60 (3.7) | 35 (3.5) | 25 (3.9) | 0.788 | |
| Metabolic | 146 (8.9) | 78 (7.9) | 68 (10.5) | 0.076 | |
| Past Medical History |  |  |  |  | |
| AIDS | 23 (1.4) | 10 (1) | 13 (2) | 0.131 | |
| Metastatic cancer | 179 (10.9) | 108 (10.9) | 71 (11) | 0.936 | |
| Lymphoma | 189 (11.5) | 115 (11.6) | 74 (11.5) | 1 | |
| **Leukemia** | **56 (3.4)** | **43 (4.3)** | **13 (2)** | **0.012** | |
| Immune Suppression | 318 (19.4) | 196 (19.7) | 122 (18.9) | 0.702 | |
| Hepatic Failure | 81 (4.9) | 48 (4.8) | 33 (5.1) | 0.816 | |
| **Cirrhosis without Failure** | **87 (5.3)** | **101 (10.2)** | **33 (5.1)** | **0.008** | |
| **CKD, not on HD** | **195 (11.9)** | **101 (10.2)** | **94 (14.6)** | **0.008** | |
| ESRD on HD | 129 (7.9) | 77 (7.8) | 52 (8) | 0.851 | |
| **CHF** | **232 (14.2)** | **117 (11.8)** | **115 (17.8)** | **0.001** | |
| Quartiles of Hours in the Hospital before Shock Onset,  n (%) |  |  |  | **< 0.001** | |
| 0 to 1.5 hour | 422 (25.7) | 230 (23.2) | 192 (29.7) |  | |
| > 1.5 to 10 hours | 388 (23.7) | 221 (22.3) | 167 (25.9) |  | |
| > 10 to 48 hours | 419 (25.6) | 282 (28.4) | 137 (21.2) |  | |
| > 48 hours | 410 (25.0) | 260 (26.2) | 150 (23.2) |  | |

*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’s exact test for categorical variables.

AIDS = acquired immunodeficiency syndrome; CKD = chronic kidney disease; HD = hemodialysis; ESRD = end stage renal disease; CHF = congestive heart failure;

Supplemental Table 2: Fluid administration and vasopressor use in the 24 hours following shock onset

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Time from shock** |  | **Hour 0-3** | |  | |  | | **Hour 3-6** | |  | |  | | **Hour 6-12** | |  |  | **Hour 12-24** |  |
| **Fluid** | **n (%)** | **Volume, mL, median (IQR)** | | **P*a*** | | **n (%)** | | **Volume, mL, median (IQR)** | | **p** | | **n (%)** | | **Volume, mL, median (IQR)** | | **p** | **n (%)** | **Volume, mL, median (IQR)** | **p** |
| **Cumulative fluid*b*** |  |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 1189 (72.5) | 1000 (284, 1859) | |  | | 1333 (81.3) | | 1135 (500, 2250) | |  | | 1444 (88.1) | | 1813 (751, 3092) | |  | 1487 (90.7) | 2529 (1217, 4500) |  |
| EM | 701 (70.6) | 953 (281, 1587) | | 0.228 | | 793 (79.9) | | 1106 (480, 2100) | | 0.202 | | **855 (86.1)** | | **1612 (750, 3000)** | | **0.033** | **882 (88.8)** | **2445 (1188, 4235)** | **0.010** |
| PA | 488 (75.5) | 1000 (296, 2000) | |  | | 541 (83.7) | | 1178 (500, 2296) | |  | | **589 (59.3)** | | **1934 (825, 3500)** | |  | **605 (93.7)** | **2806 (1268, 4926)** |  |
| **Total fluid at each time period** | | |  | |  | |  | |  | |  | |  | |  | |  |  |  |
| Total cohort | 1189 (72.5) | 1000 (284, 1850) | |  | | 1069 (65.2) | | 400 (170, 1000) | |  | | 1200 (73.21) | | 631 (275.5, 0.011117) | |  | 1221 (74.5) | 992 (420, 1702) |  |
| EM | 701 (70.6) | 953 (281, 1587) | | 0.228 | | 631 (63.5) | | 380 (160, 1000) | | 0.986 | | 687 (69.2) | | 600 (290, 1027) | | 0.052 | 706 (71.1) | 977 (410, 1700) | 0.406 |
| PA | 488 (75.5) | 1000 (296, 2000) | |  | | 438 (67.8) | | 430.5 (170, 1000) | |  | | 513 (79.4) | | 700 (251, 1285) | |  | 515 (79.7) | 1000 (450, 1736) |  |
| **Crystalloid received** |  |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 1120 (68.3) | 1000 (250, 1800) | |  | | 973 (59.4) | | 350 (140, 1000) | |  | | 1119 (68.3) | | 591 (234, 1050) | |  | 1149 (70.1) | 940 (410, 1542) |  |
| EM | 658 (66.3) | 923 (250, 1500) | | 0.22 | | 574 (57.8) | | 334 (132, 1000) | | 0.746 | | 635 (63.9) | | 565 (250, 1000) | | 0.243 | 662 (66.7) | 963 (400, 1535) | 0.717 |
| PA | 462 (71.5) | 1000 (250, 2000) | |  | | 399 (61.8) | | 380 (150, 1000) | |  | | 484 (74.9) | | 636.5 (209, 1144) | |  | 487 (75.4) | 923 (425, 1550) |  |
| **Colloid** |  |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 123 (7.5) | 250 (112, 500) | |  | | 112 (6.8) | | 250 (100, 500) | |  | | 151 (9.2) | | 250 (100, 500) | |  | 162 (9.9) | 250 (170, 500) |  |
| EM | 68 (6.8) | 258 (120, 500) | | 0.788 | | 54 (5.4) | | 250 (76, 500) | | 0.195 | | 73 (7.4) | | 250 (100, 500) | | 0.186 | 88 (8.9) | 250 (122.5, 525) | 0.523 |
| PA | 56 (8.7) | 250 (108, 500) | |  | | 58 (9) | | 266.5 (200, 500) | |  | | 78 (12.1) | | 250 (125, 538) | |  | 74 (11.5) | 330 (195, 500) |  |
| **Blood*c*** |  |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 134 (8.18) | 500 (300, 900) | |  | | 143 (9.7) | | 347 (300, 670) | |  | | 179 (10.9) | | 350 (296, 610) | |  | 117 (7.1) | 400 (300, 741) |  |
| EM | 83 (8.4) | 445 (300, 800) | | 0.233 | | 89 (9) | | 352 (300, 650) | | 0.171 | | 99 (10) | | 367 (282, 642) | | 0.71 | 106 (10.7) | 415 (310, 700) | 0.154 |
| PA | 51 (7.9) | 542 (310, 932) | |  | | 54 (8.4) | | 330 (275, 670) | |  | | 80 (12.4) | | 350 (300, 600) | |  | 82 (12.7) | 350 (280, 600) |  |
| **Packed red blood cell** | |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 117 (7.14) | 400 (300, 741) | |  | | 122 (7.4) | | 340 (300, 600 | |  | | 133 (8.1) | | 350 (300, 600) | |  | 142 (8.7) | 350 (300, 645) |  |
| EM | 72 (7.3) | 387 (300, 700) | | 0.343 | | 79 (8) | | 350 (300, 600) | | 0.396 | | 75 (7.6) | | 350 (300, 600) | | 0.958 | 87 (8.8) | 357 (300, 700) | 0.605 |
| PA | 45 (7) | 433 (330, 852) | |  | | 43 (6.7) | | 330 (300, 600) | |  | | 58 (9) | | 343 (300, 600) | |  | 55 (8.5) | 350 (300, 600) |  |
| **Platelet** |  |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 26 (1.59) | 247 (198, 346) | |  | | 32 (1.6) | | 237 (200, 301) | |  | | 38 (2.3) | | 282 (200, 400) | |  | 41 (2.5) | 218 (200, 289) |  |
| EM | 15 (1.5) | 243 (198, 350) | | 0.876 | | 22 (2.2) | | 245 (200, 293) | | 0.919 | | 19 (1.9) | | 282 (204, 400) | | 0.599 | 20 (2) | 202 (200, 288) | 0.917 |
| PA | 11 (1.7) | 299 (180, 346) | |  | | 10 (1.5) | | 218.5 (192, 350) | |  | | 19 (2.9) | | 282 (170, 336) | |  | 21 (3.3) | 219 (191, 300) |  |
| **Fresh frozen plasma** | |  | |  | |  | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 33 ( 2.01) | 500 (275, 608) | |  | | 27 (1.6) | | 440 (327, 926) | |  | | 40 (2.4) | | 443 (251, 575) | |  | 45 (2.7) | 447 (250, 625) |  |
| EM | 19 (1.9) | 449 (250, 608) | | 0.585 | | 15 (1.5) | | 440 (346, 1396) | | 0.283 | | 25 (2.5) | | 416 (252, 530) | | 0.548 | 24 (2.4) | 525 (352, 724) | 0.072 |
| PA | 14 (2.2) | 552.5 (275, 700) | |  | | 12 (1.9) | | 443 (313.5, 710) | |  | | 15 (2.3) | | 500 (250, 590) | |  | 21 (3.3) | 342 (211, 532) |  |
| **Cumulative vasopressor (mg NEQ)** | | | | | | | |  | |  | |  | |  | |  |  |  |  |
| Total cohort | 622 (37.9) | 1.5 (0.8, 3.1) | |  | | 751 (45.8) | | 2.8 (1.4, 5.9) | |  | | 858 (52.3) | | 5.8 (2.6, 11.7) | |  | 935 (57.0) |  |  |
| EM | 310 (31.2) | 1.6 (0.8, 3.1) | | 0.949 | | **386 (38.9)** | | **2.6 (1.2, 5.3)** | | **0.015** | | **442 (44.5)** | | **5.0 (2.4, 10.5)** | | **0.002** | **481 (48.4)** | **9.4 (3.8, 20.9)** | **0.0005** |
| PA | 312 (48.3) | 1.5 (0.8, 3.2) | |  | | **365 (56.5)** | | **2.9 (1.6, 6.8)** | |  | | **416 (64.4)** | | **6.5 (2.9, 13.2)** | |  | **454 (70.3)** | **12.6 (5.3, 26.9)** |  |
| **Maximum vasopressor rate at each period from shock (mcg/min NEQ)** | | | | | | | | | |  | |  | |  | |  |  |  |  |
| Total cohort | 622 (37.9) | 10 (5, 20) | |  | | 676 (41.2) | | 5 (10, 21.5) | |  | | 740 (45.1) | | 12 (6, 28) | |  | 752 (45.9) | 12.7 (6, 28) |  |
| EM | 310 (18.9) | 10.00 (5, 20) | | 0.949 | | **347 (21.2)** | | **10.00 (5, 20)** | | **0.002** | | **375 (22.9)** | | **11.34 (5, 24)** | | **0.007** | 369 (22.5) | 12.00 (5.00, 24.00) | 0.072 |
| PA | 312 (19.0) | 10.00 (5, 20) | |  | | **329 (20.1)** | | **11.20 (6, 25)** | |  | | **365 (22.3)** | | **15.00 (7.5, 3)** | |  | 382 (23.4) | 14.04 (6.23, 29.56) |  |

*a* Mann-Whitney rank sum test used to compare the volume of fluid or dosage of vasopressor use at each time point

*b* Crystalloid plus colloid fluid plus blood product fluid volume

*c* Blood product fluid volume consists of packed red blood cells, platelets, and fresh frozen plasma

EM = empiric management, PA = physiologic assessment, NEQ = norepinephrine equivalents,

Supplemental Table 3: The association between the log-transformed cumulative fluid received in the 24 hours from shock with the use of physiologic assessment during the 24 hours following shock onset in patients who received any fluid. n = 1260

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Unadjusted beta coefficient (95% CI)*a*** | **Unadjusted p-value** | **Adjusted beta coefficient (95% CI)*b*** | **Adjusted p-value** |
| Physiologic Assessment | 0.14 (0.03, 0.26) | 0.013 | 0.04 (-0.07, 0.15) | 0.516 |
| Age | 0.00 (-0.01, 0.00) | 0.044 | 0.00 (0.00, 0.00) | 0.660 |
| Race (vs. White) |  |  |  |  |
| Black | 0.21 (0.05, 0.36) | 0.008 | 0.14 (-0.02, 0.30) | 0.085 |
| Other | 0.06 (-0.07, 0.20) | 0.368 | 0.04 (-0.10, 0.18) | 0.585 |
| Female (vs. Male) | 0.01 (-0.11, 0.12) | 0.919 | 0.06 (-0.04, 0.17) | 0.247 |
| **APACHE III Score** | 0.01 (0.00, 0.01) | < 0.001 | **0.003 (0.0001, 0.01)** | **0.04** |
| Baseline SOFA Score | 0.05 (0.03, 0.06) | < 0.001 | -0.01 (-0.03, 0.01) | 0.365 |
| **Highest lactate in 12 hours before and 12 hours from shock** | 0.07 (0.05, 0.08) | < 0.001 | 0.04 (0.02, 0.05) | < 0.001 |
| Fluid received in the 12 hours before shock (vs. no fluid) |  |  |  |  |
| **≤ 1000mL** | -0.58 (-0.71, -0.44) | < 0.001 | -0.21 (-0.36, -0.06) | 0.006 |
| >1000mL | -0.26 (-0.39, -0.13) | < 0.001 | -0.05 (-0.20, 0.10) | 0.517 |
| Location of Shock (vs. ICU) |  |  |  |  |
| **ED** | 0.68 (0.56, 0.80) | < 0.001 | **0.44 (0.28, 0.59)** | **<0.001** |
| **Ward of hospital, non-ICU** | 0.44 (0.27, 0.60) | < 0.001 | **0.30 (0.13, 0.46)** | **<0.001** |
| PACU | 0.12 (-0.31, 0.56) | 0.578 | 0.42 (-0.04, 0.87) | 0.07 |
| Other location | 0.48 (0.06, 0.90) | 0.026 | 0.19 (-0.25, -.63) | 0.41 |
| Type of ICU the patient was admitted to (vs. Medical ICU) |  |  |  |  |
| **Surgical** | **0.20 (0.04, 0.37)** | **0.016** | **0.25 (0.08, 0.42)** | **0.003** |
| **Mixed Medical/Surgical** | **0.41 (0.25, 0.57)** | **< 0.001** | **0.27 (0.10, 0.44)** | **0.002** |
| CTICU | -0.31 (-0.54, -0.08) | 0.010 | -0.02 (-0.26, 0.21) | 0.843 |
| Other ICU | -0.09 (-0.27, 0.09) | 0.308 | 0.03 (-0.16, 0.23) | 0.733 |
| Primary Etiology of Shock (vs. Septic shock) |  |  |  |  |
| Hypovolemic shock | -0.02 (-0.16, 0.12) | 0.818 | 0.12 (-0.03, 0.26) | 0.120 |
| **Cardiogenic shock** | **-0.86 (-1.04, -0.67)** | **< 0.001** | **-0.69 (-0.88, -0.50)** | **< 0.001** |
| **Other shock** | **-0.53 (-0.72, -0.33)** | **< 0.001** | **-0.32 (-0.53, -0.11)** | **0.003** |
| Secondary contributors of shock |  |  |  |  |
| **Cardiac dysfunction** | **-0.14 (-0.29, 0.00)** | **0.058** | **-0.17 (-0.31, -0.02)** | **0.022** |
| Neurogenic | 0.01 (-0.24, 0.25) | 0.949 | -0.11 (-0.33, 0.12) | 0.354 |
| Trauma | 0.38 (0.03, 0.72) | 0.032 | 0.33 (-0.02, 0.69) | 0.066 |
| Intoxication | 0.08 (-0.21, 0.37) | 0.596 | -0.05 (-0.31, 0.22) | 0.734 |
| Metabolic | 0.36 (0.17, 0.55) | < 0.001 | 0.11 (-0.07, 0.29) | 0.221 |
| Hypovolemia | 0.22 (0.08, 0.36) | 0.002 | 0.10 (-0.04, 0.23) | 0.156 |
| **Use of vasopressor in the 24 hours from shock** | **0.62 (0.51, 0.73)** | **< 0.001** | **0.35 (0.22, 0.48)** | **< 0.001** |
| **Mechanically vented during 24 hours from shock** | **0.34 (0.23, 0.45)** | **< 0.001** | **0.17 (0.04, 0.30)** | **0.009** |
| Past medical history |  |  |  |  |
| AIDS | 0.03 (-0.45, 0.50) | 0.911 | -0.04 (-0.46, 0.38) | 0.843 |
| Cancer*c* | 0.20 (0.06, 0.34) | 0.005 | 0.00 (-0.15, 0.15) | 0.994 |
| Immune suppression | 0.12 (-0.05, 0.30) | 0.171 | -0.04 (-0.21, 0.13) | 0.658 |
| Hepatic failure | 0.17 (-0.08, 0.42) | 0.188 | -0.06 (-0.30, 0.18) | 0.621 |
| Cirrhosis without failure | 0.08 (-0.17, 0.32) | 0.542 | -0.02 (-0.25, 0.22) | 0.873 |
| **CKD, not HD** | **-0.24 (-0.41, -0.07)** | **0.006** | **-0.24 (-0.40, -0.07)** | **0.005** |
| **ESRD** | **-0.48 (-0.69, -0.27)** | **< 0.001** | **-0.40 (-0.61, -0.20)** | **< 0.001** |
| **CHF** | **-0.39 (-0.55, -0.23)** | **< 0.001** | **-0.16 (-0.33, 0.00)** | **0.052** |

*a* Univariate unadjusted association between log-transformed cumulative fluid received in 24 hours following shock and individual independent variables.

*b* Multivariate mixed effect linear regression for the association between log-transformed cumulative fluid received in 24 hours following shock and all adjusted independent variables. Hospital site was used as a random intercept in the random effect model.

*c* Cancer includes metastatic cancer, lymphoma, and leukemia

CI = confidence interval; APACHE = acute physiology and chronic health evaluation; SOFA = sequential organ failure assessment; IQR = interquartile range ; ED = emergency department; ICU = intensive care unit; PACU = post-anesthesia care unit; CTICU = cardiothoracic intensive care unit; AIDS = acquired immunodeficiency syndrome; CKD = chronic kidney disease; HD = hemodialysis; ESRD = end stage renal disease; CHF= congestive heart failure

Supplemental Table 4: The association between the use of vasopressor with physiologic assessment in the 24 hours following shock onset. n = 1347

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Odds Ratio (95% CI)*a*** | **Unadjusted p-value** | **Adjusted odds ratio (95% CI)*b*** | **Adjusted p-value** |
| **Physiologic Assessment** | 2.38 (1.93, 2.94) | **<0.01** | **1.98 (1.45, 2.71)** | **<0.001** |
| **Age** | 1.01 (1.00, 1.01) | 0.01 | **1.01 (1.00, 1.02)** | **0.013** |
| Race (vs. White) |  |  |  |  |
| **Black** | 0.96 (0.73, 1.26) | 0.763 | **0.52 (0.33, 0.83)** | **0.006** |
| Other | 0.99 (0.78, 1.25) | 0.907 | 0.73 (0.49, 1.10) | 0.131 |
| Female (vs. Male) | 0.98 (0.80, 1.19) | 0.84 | 1.22 (0.91, 1.64) | 0.189 |
| APACHE III Score | 1.03 (1.03, 1.04) | <0.01 | 1.00 (1.00, 1.01) | 0.326 |
| **Baseline SOFA Score** | 1.38 (1.33, 1.44) | **<0.01** | **1.32 (1.24, 1.41)** | **<0.001** |
| Highest lactate in 12 hours before and 12 hours from shock | 1.12 (1.07, 1.16) | <0.01 | 0.99 (0.94, 1.04) | 0.654 |
| Fluid received in the 12 hours before shock (vs. no fluid) |  |  |  |  |
| ≤ 1000mL | 0.54 (0.42, 0.69) | <0.01 | 1.21 (0.79, 1.85) | 0.390 |
| > 1000mL | 0.63 (0.50, 0.80) | <0.01 | **1.54 (1.01, 2.35)** | **0.046** |
| Location of Shock (vs. ICU) |  |  |  |  |
| ED | 0.97 (0.74, 1.20) | <0.01 | **2.47 (1.61, 3.79)** | **<0.001** |
| **Ward of hospital, non-ICU** | 0.93 (0.62, 1.25) | **<0.01** | **3.23 (1.96, 5.32)** | **<0.001** |
| PACU | -0.45 (-1.28, 0.38) | 0.286 | 0.70 (0.20, 2.52) | 0.59 |
| Other location | 0.82 (0.05, 1.59) | 0.038 | 1.51 (0.40, 5.71) | 0.54 |
| Type of ICU the patient was admitted to (vs. Medical ICU) |  |  |  |  |
| Surgical | 0.82 (0.61, 1.11) | 0.201 | 1.23 (0.77, 1.97) | 0.392 |
| Mixed Medical/Surgical | 1.80 (1.33, 2.45) | <0.01 | 1.46 (0.88, 2.42) | 0.145 |
| **CTICU** | 1.01 (0.68, 1.49) | 0.961 | **2.17 (1.09, 4.32)** | **0.027** |
| **Other** | 0.94 (0.69, 1.30) | 0.726 | **1.75 (1.02, 2.98)** | **0.041** |
| Primary Etiology of Shock (vs. Septic shock) |  |  |  |  |
| **Hypovolemic shock** | 0.32 (0.25, 0.42) | **<0.01** | **0.34 (0.23, 0.51)** | **<0.001** |
| **Cardiogenic shock** | 0.46 (0.34, 0.63) | **<0.01** | **0.58 (0.35, 0.98)** | **0.043** |
| **Other shock** | 0.29 (0.20, 0.41) | **<0.01** | **0.49 (0.28, 0.85)** | **0.012** |
| Secondary contributors of shock |  |  | 0.86 (0.58, 1.27) | 0.446 |
| Cardiac dysfunction | 1.33 (1.02, 1.74) | 0.036 | 0.89 (0.59, 1.34) | 0.571 |
| Neurogenic | 1.14 (0.73, 1.77) | 0.561 | 0.66 (0.34, 1.26) | 0.206 |
| Trauma | 0.72 (0.39, 1.33) | 0.294 | 0.66 (0.24, 1.77) | 0.407 |
| Intoxication | 1.18 (0.69, 2.00) | 0.55 | 1.28 (0.58, 2.81) | 0.541 |
| Metabolic | 1.39 (0.98, 1.99) | 0.068 | 0.72 (0.42, 1.23) | 0.228 |
| Hypovolemia | 1.17 (0.91, 1.52) | 0.225 | 0.86 (0.58, 1.27) | 0.446 |
| **Cumulative fluid in 24 hours (1000mL)** | 1.32 (1.26, 1.39) | **<0.01** | **1.21 (1.13, 1.3)** | **<0.001** |
| **Mechanically vented during 24 hours from shock onset** | 4.97 (4.00, 6.17) | **<0.01** | **2.53 (1.79, 3.58)** | **<0.001** |
| Past medical history |  |  |  |  |
| AIDS | 1.67 (0.68, 4.09) | 0.26 | 0.99 (0.30, 3.27) | 0.983 |
| Cancer*c* | 1.08 (0.84, 1.39) | 0.543 | 0.65 (0.42, 1.01) | 0.056 |
| Immune suppression | 1.68 (1.21, 2.35) | 0.002 | 1.16 (0.70, 1.92) | 0.567 |
| Hepatic failure | 1.77 (1.09, 2.88) | 0.021 | 0.62 (0.31, 1.27) | 0.192 |
| Cirrhosis without failure | 0.98 (0.63, 1.52) | 0.93 | 0.67 (0.35, 1.30) | 0.236 |
| CKD, not on HD | 1.05 (0.78, 1.42) | 0.751 | 0.77 (0.48, 1.24) | 0.279 |
| ESRD | 1.08 (0.75, 1.56) | 0.672 | 0.77 (0.44, 1.34) | 0.355 |
| CHF | 1.25 (0.94, 1.66) | 0.128 | 1.39 (0.87, 2.22) | 0.164 |

*a* Univariate association between the use of vasopressor and individual independent variables.

*b* Multivariate mixed effect logistic regression for the association between log-transformed cumulative fluid received in 24 hours following shock and all adjusted independent variables. Hospital site was used as a random intercept in the random effect model.

*c* Cancer includes metastatic cancer, lymphoma, and leukemia

CI = confidence interval; APACHE = acute physiology and chronic health evaluation; SOFA = sequential organ failure assessment; IQR = interquartile range ; ED = emergency department; ICU = intensive care unit; PACU = post-anesthesia care unit; CTICU = cardiothoracic intensive care unit; AIDS = acquired immunodeficiency syndrome; CKD = chronic kidney disease; HD = hemodialysis; ESRD = end stage renal disease; CHF= congestive heart failure

Supplemental Table 5: The association between cumulative vasopressor dose (in norepinephrine equivalent) with the use of physiologic assessment in those who received vasopressor in the 24 hours follow shock onset. N = 799

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variables** | **Unadjusted beta coefficient (95% CI)*a*** | **Unadjusted p-value** | | **Adjusted beta coefficient (95% CI)*b*** | **Adjusted**  **p-value** |
| **Physiologic Assessment** | **0.33 (0.13, 0.52)** | **0.001** | | **0.37 (0.19, 0.55)** | **<0.001** |
| **Age** | **-0.01 (-0.01, 0.00)** | **0.108** | | **-0.01 (-0.01, -0.00)** | **0.031** |
| Race (vs. White) |  |  | |  |  |
| Black | 0.71 (0.44, 0.98) | <0.001 | | 0.18 (-0.08, 0.44) | 0.185 |
| Other | 0.35 (0.11, 0.58) | 0.004 | | 0.01 (-0.22, 0.24) | 0.923 |
| Female (vs. Male) | -0.17 (-0.37, 0.03) | 0.093 | | -0.06 (-0.23, 0.11) | 0.468 |
| **APACHE III Score** | **0.02 (0.02, 0.02)** | **<0.001** | | **0.01 (0.01, 0.02)** | **<0.001** |
| Baseline SOFA Score | 0.12 (0.10, 0.15) | <0.01 | | -0.00 (-0.04, 0.03) | 0.798 |
| **Highest lactate in 12 hours before and 12 hours from shock** | **0.13 (0.10, 0.15)** | **<0.001** | | **0.06 (0.03, 0.08)** | **<0.001** |
| Fluid received in the 12 hours before shock (vs. to no fluid) |  |  | |  |  |
| ≤ 1000mL | -0.10 (-0.35, 0.14) | 0.403 | | 0.20 (-0.04, 0.45) | 0.101 |
| >1000mL | -0.37 (-0.60, -0.14) | 0.002 | | 0.03 (-0.21, 0.27) | 0.809 |
| Location of Shock (vs. ICU) |  |  | |  |  |
| ED | 0.41 (0.19, 0.63) | <0.001 | | 0.05 (-0.20, 0.30) | 0.272 |
| Ward of hospital, non-ICU | 0.53 (0.25, 0.82) | <0.001 | | 0.20 (-0.06, 0.46) | 0.692 |
| PACU | -0.09 (-1.16, 0.97) | 0.862 | | -0.53 (-1.50, 0.45) | 0.252 |
| Other location | 0.74 (0.06, 1.42) | 0.033 | | 0.40 (-0.25, 1.05) | 0.282 |
| Type of ICU the patient was admitted to (vs. Medical ICU) |  |  | |  |  |
| **Surgical ICU** | **-0.58 (-0.89, -0.27)** | **<0.001** | | **-0.68 (-0.96, -0.39)** | **<0.001** |
| Mixed Medical/Surgical ICU | 0.43 (0.16, 0.69) | 0.001 | | -0.01 (-0.28, 0.26) | 0.951 |
| Cardiothoracic ICU | 0.19 (-0.20, 0.58) | 0.342 | | 0.21 (-0.17, 0.58) | 0.279 |
| Other ICU | -0.12 (-0.44, 0.21) | 0.479 | | -0.02 (-0.35, 0.31) | 0.904 |
| Primary Etiology of Shock (vs. Septic shock) |  |  | |  |  |
| **Hypovolemic shock** | **-0.54 (-0.83, -0.25)** | **<0.001** | | **-0.35 (-0.61, -0.08)** | **0.010** |
| **Cardiogenic shock** | **-0.55 (-0.88, -0.22)** | **0.001** | | **-0.37 (-0.68, -0.05)** | **0.023** |
| Other shock | -0.37 (-0.79, 0.04) | 0.076 | | -0.37 (-0.77, 0.02) | 0.064 |
| Secondary contributors of shock |  |  | |  |  |
| Cardiac dysfunction | 0.01 (-0.24, 0.26) | 0.923 | | -0.07 (-0.30, 0.16) | 0.548 |
| Neurogenic | 0.19 (-0.23, 0.62) | 0.375 | | 0.16 (-0.21, 0.52) | 0.399 |
| Trauma | 0.13 (-0.53, 0.79) | 0.696 | | 0.10 (-0.49, 0.70) | 0.731 |
| Intoxication | 0.29 (-0.21, 0.79) | 0.258 | | 0.04 (-0.38, 0.47) | 0.839 |
| Metabolic | 0.26 (-0.07, 0.59) | 0.117 | | -0.23 (-0.51, 0.06) | 0.123 |
| Hypovolemia | 0.03 (-0.22, 0.28) | 0.831 | | -0.11 (-0.33, 0.10) | 0.304 |
| **Cumulative fluid in 24 hours (log transformed)** | **0.38 (0.28, 0.48)** | **< 0.001** | | **0.25 (0.15, 0.35)** | **<0.001** |
| **Mechanically vented during 24 hours from shock onset** | **0.93 (0.73, 1.12)** | **< 0.001** | | **0.49 (0.27, 0.70)** | **<0.001** |
| Past medical history |  |  | |  |  |
| **AIDS** | **0.02 (-0.74, 0.78)** | **0.959** | | **-0.76 (-1.45, -0.08)** | **0.028** |
| Cancer*c* | 0.31 (0.06, 0.55) | 0.014 | | 0.08 (-0.17, 0.32) | 0.533 |
| **Immune suppression** | **0.07 (-0.22, 0.36)** | **0.624** | | **-0.27 (-0.53, -0.01)** | **0.045** |
| Hepatic failure | 0.65 (0.24, 1.07) | 0.002 | | -0.10 (-0.48, 0.29) | 0.623 |
| Cirrhosis without failure | 0.25 (-0.20, 0.69) | 0.274 | | 0.26 (-0.13, 0.65) | 0.183 |
| CKD, not on HD | 0.33 (0.13, 0.52) | 0.001 | | 0.03 (-0.24, 0.30) | 0.848 |
| ESRD | -0.01 (-0.01, 0.00) | 0.108 | | 0.13 (-0.21, 0.47) | 0.447 |
| CHF | 0.35 (0.11, 0.58) | 0.004 | 0.08 (-0.18, 0.34) | | 0.539 |

*a* Univariate association between cumulative vasopressor dose in the 24 hours following shock and individual independent variables.

*b* Multivariate mixed effect linear regression for the association cumulative vasopressor dose in 24 hours following shock and all adjusted independent variables. Hospital site was used as a random intercept in the random effect model.

*c* Cancer includes metastatic cancer, lymphoma, and leukemia

CI = confidence interval; APACHE = acute physiology and chronic health evaluation; SOFA = sequential organ failure assessment; IQR = interquartile range ; ED = emergency department; ICU = intensive care unit; PACU = post-anesthesia care unit; CTICU = cardiothoracic intensive care unit; AIDS = acquired immunodeficiency syndrome; CKD = chronic kidney disease; HD = hemodialysis; ESRD = end stage renal disease; CHF= congestive heart failure

Supplemental Table 6: Predictors of in-hospital mortality. n = 1292

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Unadjusted odds ratio (95% CI)*a*** | **Unadjusted p-value** | **Adjusted odds ratio (95% CI)*b*** | **Adjusted p-value** |
| Physiologic assessment | 1.22 (0.97, 1.53) | 0.089 | 0.86, (0.63, 1.18) | 0.268 |
| **APACHE III score** | **1.03 (1.03, 1.04)** | **<0.001** | **1.02 (1.01, 1.03)** | **<0.001** |
| **Highest lactate in 12 hours before and 12 hours from shock onset** | **1.16 (1.12, 1.20)** | **<0.001** | **1.10 (1.05, 1.15)** | **<0.001** |
| Hours in the hospital before shock onset (compare to < 1.5 hours) |  |  |  |  |
| >1.5-10 hour | 0.63 (0.45, 0.89) | 0.01 | 0.74 (0.48, 1.14) | 0.166 |
| >10-48 hour | 0.62 (0.44, 0.87) | 0.01 | 0.77 (0.46, 1.31) | 0.344 |
| >48 hour | 2.03 (1.51, 2.73) | <0.001 | 1.64 (0.95, 2.81) | 0.075 |
| **Surgical ICU (vs Medical ICU)** | **0.40 (0.26, 0.60)** | **<0.001** | **0.39 (0.23, 0.66)** | **<0.001** |
| Cumulative fluid in 24 hours from shock onset (1000mL) | 1.05 (1.01, 1.08) | 0.025 | 0.95 (0.90, 1.00) | 0.074 |
| **Use of vasopressor in the 24 hour from shock onset** | **3.68 (2.83, 4.79)** | **<0.001** | **1.88 (1.27, 2.78)** | **0.001** |
| **Mechanically vented during 24 hours from shock onset** | **3.51 (2.77, 4.46)** | **<0.001** | **1.95 (1.36, 2.78)** | **<0.001** |
| **Require renal replacement therapy during hospitalization** | **2.74 (2.11, 3.56)** | **<0.001** | **1.66 (1.17, 2.34)** | **0.004** |
| **Cancer** | **2.83 (2.18, 3.66)** | **<0.001** | **2.33 (1.60, 3.39)** | **<0.001** |
| **Trauma as a secondary contributor of shock** | **0.93 (0.45, 1.91)** | **0.841** | **3.11 (1.16, 8.32)** | **0.024** |

*a* Univariate association between in-hospital mortality and individual independent variables.

*b* Multivariable model for in-hospital mortality adjusting for 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, mechanical ventilation in the 24 hours following shock and renal replacement therapy. Hospital site was used as a random intercept in the random effect model.

CI = Confidence interval

|  |  |  |
| --- | --- | --- |
| Supplemental Table 8: Sensitivity analysisa of the association between different PA and in-hospital mortality | | |
| **PA methods** | **Mortality aOR (95% CI)** | **n** |
| All PA vs EM | 0.84 (0.62, 1.14) | 1327 |
| CCUS only vs EM | 0.94 (0.69, 1.30) | 1324 |
| Non-CCUS PA vs EM | 0.66 (0.38, 1.14) | 886 |
| CCUS vs non-CCUS PA | 1.31 (0.68, 2.52) | 475 |
| a Multivariate mixed effect models adjusted for age, sex, race, past medical history (cancer), APACHE III score, SOFA score, maximum lactate, hours in hospital before shock, shock onset location, ICU location, primary contributors of shock, secondary contributors of shock (trauma), cumulative fluid, any vasopressor, and mechanical ventilation in the 24 hours following shock onset. Site was used as a random intercept.  aOR = adjusted odds ratio; CI = confidence interval; APACHE = acute physiology and chronic health evaluation; SOFA = sequential organ failure assessment | | |

|  |  |  |  |
| --- | --- | --- | --- |
| Supplemental Table 7: Sensitivity analysisa of different types of PA and association with cumulative fluid or any vasopressor use | | | |
| **PA methods** | **Cumulative fluid aOR (95% CI)** | **Any vasopressor use aOR (95% CI)** | **n** |
| All PA vs EM | 1.00 (1.00, 1.00) | 2.01 (1.47, 2.74) | 1347 |
| CCUS only vs EM | 1.00 (1.00, 1.00) | 1.48 (1.03, 2.11) | 1141 |
| Non-CCUS PA vs EM | 1.00 (1.00, 1.00) | 3.70 (1.93, 7.09) | 904 |
| CCUS vs non-CCUS PA | 1.00 (1.00, 1.00) | 0.26 (0.11, 0.62) | 479 |
| a Multivariate mixed effect models adjusted for age, sex, race, past medical history (chronic kidney disease, congestive heart failure, cancer), APACHE III score, SOFA score, maximum lactate, hours in the hospital before shock, shock onset location, ICU location, primary contributor of shock, secondary contributors of shock (cardiac dysfunction, trauma, neurogenic shock), and the use of mechanical ventilation. Site was used as a random intercept. | | | |

aOR = adjusted odds ratio; CI = confidence interval; APACHE = acute physiology and chronic health evaluation; SOFA = sequential organ failure assessment

**Supplemental figures captions and legends:**

Supplemental Figure 1: Critical care ultrasound body sites.

CCUS = critical care ultrasound; IVC = inferior vena cava



Supplemental Figure 2: Propensity Score Matching

