

## ORIGINAL RESEARCH

## Does Sepsis Treatment Differ Between Primary and Overflow Intensive Care Units?

Kittane Vishnupriya, MBBS,\* Olufunmilayo Falade, MD, Addisu Workneh, MD, MSc, Satish Chandolu, MBBS, Regina Landis, BA, Kaweesa Elizabeth, Reethi Iyengar, PhD, Scott Wright, MD, Jonathan Sevransky, MD, MHS

Department of Medicine, Johns Hopkins University School of Medicine and Johns Hopkins Bayview Medical Center, Baltimore, Maryland.

**BACKGROUND:** Sepsis is a major cause of death in hospitalized patients. Early goal-directed therapy is the standard of care. When primary intensive care units (ICUs) are full, sepsis patients are cared for in overflow ICUs.

**OBJECTIVE:** To determine if process-of-care measures in the care of sepsis patients differed between primary and overflow ICUs at our institution.

**DESIGN:** We conducted a retrospective study of all adult patients admitted with sepsis between July 2009 and February 2010 to either the primary ICU or the overflow ICU.

**MEASUREMENTS:** Baseline patient characteristics and multiple process-of-care measures, including diagnostic and therapeutic interventions.

**RESULTS:** There were 141 patients admitted with sepsis to our hospital; 100 were cared for in the primary ICU and 41 in the overflow ICU. Baseline acute physiology and chronic

health evaluation (APACHE II) scores were similar. Patients received similar processes-of-care in the primary ICU and overflow ICU with the exception of deep vein thrombosis (DVT) and gastrointestinal (GI) prophylaxis within 24 hours of admission, which were better adhered to in the primary ICU (74% vs 49%,  $P = 0.004$ , and 68% vs 44%,  $P = 0.012$ , respectively). There were no significant differences in hospital and ICU length of stay between the 2 units (9.68 days vs 9.73 days,  $P = 0.98$ , and 4.78 days vs 4.92 days,  $P = 0.97$ , respectively).

**CONCLUSIONS:** Patients with sepsis admitted to the primary ICU and overflow ICU at our institution were managed similarly. Overflowing sepsis patients to non-primary intensive care units may not affect guideline-concordant care delivery or length of stay. *Journal of Hospital Medicine* 2012;7:600–605. © 2012 Society of Hospital Medicine

Sepsis is a major cause of death in hospitalized patients.<sup>1–3</sup> It is recommended that patients with sepsis be treated with early appropriate antibiotics, as well as early goal-directed therapy including fluid and vasopressor support according to evidence-based guidelines.<sup>4–6</sup> Following such evidence-based protocols and process-of-care interventions has been shown to be associated with better patient outcomes, including decreased mortality.<sup>7,8</sup>

Most patients with severe sepsis are cared for in intensive care units (ICUs). At times, there are no beds available in the primary ICU and patients presenting to the hospital with sepsis are cared for in other units. Patients admitted to a non-preferred clinical inpatient setting are sometimes referred to as “overflow.”<sup>9</sup> ICUs can differ significantly in staffing patterns, equipment, and training.<sup>10</sup> It is not known if overflow sepsis patients receive similar care when admitted to non-primary ICUs.

At our hospital, we have an active bed management system led by the hospitalist division.<sup>11</sup> This system includes protocols to place sepsis patients in the overflow ICU if the primary ICU is full. We hypothesized that process-of-care interventions would be more strictly adhered to when sepsis patients were in the primary ICU rather than in the overflow unit at our institution.

### METHODS

#### Design

This was a retrospective cohort study of all patients with sepsis admitted to either the primary medical intensive care unit (MICU) or the overflow cardiac intensive care unit (CICU) at our hospital between July 2009 and February 2010. We reviewed the admission database starting with the month of February 2010 and proceeded backwards, month by month, until we reached the target number of patients.

#### Setting

The study was conducted at our 320-bed, university-affiliated academic medical center in Baltimore, MD. The MICU and the CICU are closed units that are located adjacent to each other and have 12 beds each. They are staffed by separate pools of attending physicians trained in pulmonary/critical care medicine and cardiovascular diseases, respectively, and no attending physician attends in both units. During the study period, there were 10 unique MICU and 14 unique

\*Address for correspondence and reprint requests: Kittane Vishnupriya, MBBS, Johns Hopkins Bayview Medical Center, 5200 Eastern Ave, Baltimore, MD 21224; Telephone: 410-550-5018; Fax: 410-550-2972; E-mail: kvishnu1@jhmi.edu

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CICU attending physicians; while most attending physicians covered the unit for 14 days, none of the physicians were on service more than 2 of the 2-week blocks (28 days). Each unit is additionally staffed by fellows of the respective specialties, and internal medicine residents and interns belonging to the same residency program (who rotate through both ICUs). Residents and fellows are generally assigned to these ICUs for 4 continuous weeks. The assignment of specific attendings, fellows, and residents to either ICU is performed by individual division administrators on a rotational basis based on residency, fellowship, and faculty service requirements. The teams in each ICU function independently of each other. Clinical care of patients requiring the assistance of the other specialty (pulmonary medicine or cardiology) have guidance conferred via an official consultation. Orders on patients in both ICUs are written by the residents using the same computerized order entry system (CPOE) under the supervision of their attending physicians. The nursing staff is exclusive to each ICU. The respiratory therapists spend time in both units. The nursing and respiratory therapy staff in both ICUs are similarly trained and certified, and have the same patient-to-nursing ratios.

## Subjects

All patients admitted with a possible diagnosis of sepsis to either the MICU or CICU were identified by querying the hospital electronic triage database called “etriage.” This Web-based application is used to admit patients to all the Medicine services at our hospital. We employed a wide case-finding net using keywords that included pneumonia, sepsis, hypotension, high lactate, hypoxia, UTI (urinary tract infection)/urosepsis, SIRS (systemic inflammatory response syndrome), hypothermia, and respiratory failure. A total of 197 adult patients were identified. The charts and the electronic medical record (EMR) of these patients were then reviewed to determine the presence of a sepsis diagnosis using standard consensus criteria.<sup>12</sup> Severe sepsis was defined by sepsis associated with organ dysfunction, hypoperfusion, or hypotension using criteria described by Bone et al.<sup>12</sup>

Fifty-six did not meet the criteria for sepsis and were excluded from the analysis. A total of 141 patients were included in the study. This being a pilot study, we did not have any preliminary data regarding adherence to sepsis guidelines in overflow ICUs to calculate appropriate sample size. However, in 2 recent studies of dedicated ICUs (Ferrer et al<sup>13</sup> and Castellanos-Ortega et al<sup>14</sup>), the averaged adherence to a single measure like checking of lactate level was 27% pre-intervention and 62% post-intervention. With alpha level 0.05 and 80% power, one would need 31 patients in each unit to detect such differences with respect to this intervention. Although this data does not necessarily apply to overflow ICUs or for combi-

nation of processes, we used a goal of having at least 31 patients in each ICU.

The study was approved by the Johns Hopkins Institutional Review Board. The need for informed consent was waived given the retrospective nature of the study.

## Data Extraction Process and Procedures

The clinical data was extracted from the EMR and patient charts using a standardized data extraction instrument, modified from a case report form (CRF) used and validated in previous studies.<sup>15,16</sup> The following procedures were used for the data extraction:

1. The data extractors included 4 physicians and 1 research assistant and were trained and tested by a single expert in data review and extraction.
2. Lab data was transcribed directly from the EMR. Calculation of acute physiology and chronic health evaluation (APACHE II) scores were done using the website <http://www.sfar.org/scores2/apache22.html> (Société Française d'Anesthésie et de Réanimation). Sepsis-related organ failure assessment (SOFA) scores were calculated using usual criteria.<sup>17</sup>
3. Delivery of specific treatments and interventions, including their timing, was extracted from the EMR.
4. The attending physicians' notes were used as the final source to assign diagnoses such as presence of acute lung injury, site of infection, and record interventions.

## Data Analysis

Analyses focused primarily on assessing whether patients were treated differently between the MICU and CICU. The primary exposure variables were the process-of-care measures. We specifically used measurement of central venous saturation, checking of lactate level, and administration of antibiotics within 60 minutes in patients with severe sepsis as our “primary” process-of-care measures.<sup>13</sup> Continuous variables were reported as mean  $\pm$  standard deviation, and Student's *t* tests were used to compare the 2 groups. Categorical data were expressed as frequency distributions, and chi-square tests were used to identify differences between the 2 groups. All tests were 2-tailed with statistical significance set at 0.05. Statistical analysis was performed using SPSS version 19.0. (IBM, Armonk, NY).

To overcome data constraints, we created a dichotomous variable for each of the 3 primary processes-of-care (indicating receipt of process or not) and then combined them into 1 dichotomous variable indicating whether or not the patients with severe sepsis received all 3 primary processes-of-care. The combined variable was the key independent variable in the model.

We performed logistic regression analysis on patients with severe sepsis. The equation  $\text{Logit [P(ICU Type = CICU)]} = \alpha + \beta_1\text{Combined} + \beta_2\text{Age}$

describes the framework of the model, with ICU type being the dependent variable, and the combined variable of patients receiving all primary measures being the independent variable and controlled for age. Logistic regression was performed using JMP (SAS Institute, Inc, Cary, NC).

We additionally performed a secondary analysis to explore possible predictors of mortality using a logistic regression model, with the event of death as the dependent variable, and age, APACHE II scores, combined processes-of-care, and ICU type included as independent variables.

## RESULTS

There were 100 patients admitted to the MICU and 41 patients admitted to the CICU during the study period (Table 1). The majority of the patients were admitted to the ICUs directly from the emergency department (ED) ( $n = 129$ ), with a small number of patients who were transferred from the Medicine floors ( $n = 12$ ).

There were no significant differences between the 2 study groups in terms of age, sex, primary site of

infection, mean APACHE II score, SOFA scores on day 1, chronic organ insufficiency, immune suppression, or need for mechanical ventilation (Table 1). The most common site of infection was lung. There were significantly more patients with severe sepsis in the MICU (88% vs 51%,  $P < 0.001$ ).

### Sepsis Process-of-Care Measures

There were no significant differences in the proportion of severe sepsis patients who had central venous saturation checked (MICU: 46% vs CICU: 41%,  $P = 0.67$ ), lactate level checked (95% vs 100%,  $P = 0.37$ ), or received antibiotics within 60 minutes of presentation (75% vs 69%,  $P = 0.59$ ) (Table 2). Multiple other processes and treatments were delivered similarly, as shown in Table 2.

Logistic regression analysis examining the receipt of all 3 primary processes-of-care while controlling for age revealed that the odds of the being in one of the ICUs was not significantly different ( $P = 0.85$ ). The secondary analysis regression models revealed that only the APACHE II score (odds ratio [OR] = 1.21; confidence interval [CI], 1.12–1.31) was significantly associated with higher odds of mortality. ICU-type [MICU vs CICU] (OR = 1.85; CI, 0.42–8.20), age (OR = 1.01; CI, 0.97–1.06), and combined processes of care (OR = 0.26; CI, 0.07–1.01) did not have significant associations with odds of mortality.

A review of microbiologic sensitivities revealed a trend towards significance that the cultured microorganism(s) was likely to be resistant to the initial antibiotics administered in MICU vs CICU (15% vs 5%, respectively,  $P = 0.09$ ).

### Mechanical Ventilation Parameters

The majority of the ventilated patients were admitted to each ICU in “assist control” (AC) mode. There were no significant differences in categories of mean

**TABLE 1.** Baseline Patient Characteristics for the 141 Patients Admitted to Intensive Care Units With Sepsis During the Study Period

	MICU (N=100)	CICU (N=41)	P Value
Age in years, mean $\pm$ SD	67 $\pm$ 14.8	72 $\pm$ 15.1	0.11
Female, n (%)	57 (57)	27 (66)	0.33
Patients with chronic organ insufficiency, n (%)	59 (59)	22 (54)	0.56
Patients with severe sepsis, n (%)	88 (88)	21 (51)	<0.001
Patients needing mechanical ventilation, n (%)	43 (43)	14 (34)	0.33
APACHE II score, mean $\pm$ SD	25.53 $\pm$ 9.11	24.37 $\pm$ 9.53	0.50
SOFA score on day 1, mean $\pm$ SD	7.09 $\pm$ 3.55	6.71 $\pm$ 4.57	0.60
Patients with acute lung injury on presentation, n (%)	8 (8)	2 (5)	0.50

Abbreviations: CICU, cardiac intensive care unit; MICU, medical intensive care unit; APACHE II, acute physiology and chronic health evaluation; SOFA, sepsis-related organ failure assessment.

**TABLE 2.** ICU Treatments and Processes-of-Care for Patients With Sepsis During the Study Period

Primary Process-of-Care Measures (Severe Sepsis Patients)	MICU (N = 88)	CICU (N = 21)	P Value
Patients with central venous oxygen saturation checked, n (%)*	31 (46)	7 (41)	0.67
Patients with lactate level checked, n (%)*	58 (95)	16 (100)	0.37
Received antibiotics within 60 min, n (%)*	46 (75)	11 (69)	0.59
Patients who had all 3 above processes and treatments, n (%)	19 (22)	4 (19)	0.79
Received vasopressor, n (%)	25 (28)	8 (38)	0.55
ICU Treatments and Processes (All Sepsis Patients)	(N = 100)	(N = 41)	
Fluid balance 24 h after admission in liters, mean $\pm$ SD	1.96 $\pm$ 2.42	1.42 $\pm$ 2.63	0.24
Patients who received stress dose steroids, n (%)	11 (11)	4 (10)	0.83
Patients who received Drotrecogin alfa, n (%)	0 (0)	0 (0)	
Morning glucose 24 h after admission in mg/dL, mean $\pm$ SD	161 $\pm$ 111	144 $\pm$ 80	0.38
Received DVT prophylaxis within 24 h of admission, n (%)	74 (74)	20 (49)	0.004
Received GI prophylaxis within 24 h of admission, n (%)	68 (68)	18 (44)	0.012
Received RBC transfusion within 24 h of admission, n (%)	8 (8)	7 (17)	0.11
Received renal replacement therapy, n (%)	13 (13)	3 (7)	0.33
Received a spontaneous breathing trial within 24 h of admission, n (%)*	4 (11)	4 (33)	0.07

Abbreviations: CICU, cardiac intensive care unit; DVT, deep vein thrombosis; GI, gastrointestinal; ICU, intensive care unit; MICU, medical intensive care unit; RBC, red blood cell; SD, standard deviation. \* Missing data causes percentages to be other than what might be suspected if it were available for all patients.

**TABLE 3.** Patient Outcomes for the 141 Patients Admitted to the Intensive Care Units With Sepsis During the Study Period

Patient Outcomes	MICU (N = 100)	CICU (N = 41)	P Value
ICU mortality, n (%)	19 (19)	4 (10)	0.18
Hospital mortality, n (%)	21 (21)	6 (15)	0.38
Discharged home with unassisted breathing, n (%)	33 (33)	19 (46)	0.14
ICU length of stay in days, mean $\pm$ SD	4.78 $\pm$ 6.24	4.92 $\pm$ 6.32	0.97
Hospital length of stay in days, mean $\pm$ SD	9.68 $\pm$ 9.22	9.73 $\pm$ 9.33	0.98

Abbreviations: CICU, cardiac intensive care unit; ICU, intensive care unit; MICU, medical intensive care unit; SD, standard deviation.

tidal volume (TV) ( $P = 0.3$ ), mean plateau pressures ( $P = 0.12$ ), mean fraction of inspired oxygen (FiO<sub>2</sub>) ( $P = 0.95$ ), and mean positive end-expiratory pressures (PEEP) ( $P = 0.98$ ) noted across the 2 units at the time of ICU admission, and also 24 hours after ICU admission. Further comparison of measurements of tidal volumes and plateau pressures over 7 days of ICU stay revealed no significant differences in the 2 ICUs ( $P = 0.40$  and  $0.57$ , respectively, on day 7 of ICU admission). There was a trend towards significance in fewer patients in the MICU receiving spontaneous breathing trial within 24 hours of ICU admission (11% vs 33%,  $P = 0.07$ ) (Table 2).

### Patient Outcomes

There were no significant differences in ICU mortality (MICU 19% vs CICU 10%,  $P = 0.18$ ), or hospital mortality (21% vs 15%,  $P = 0.38$ ) across the units (Table 3). Mean ICU and hospital length of stay (LOS) and proportion of patients discharged home with unassisted breathing were similar (Table 3).

### DISCUSSION

Since sepsis is more commonly treated in the medical ICU and some data suggests that specialty ICUs may be better at providing desired care,<sup>18,19</sup> we believed that patients treated in the MICU would be more likely to receive guideline-concordant care. The study refutes our a priori hypothesis and reveals that evidence-based processes-of-care associated with improved outcomes for sepsis are similarly implemented at our institution in the primary and overflow ICU. These findings are important, as ICU bed availability is a frequent problem and many hospitals overflow patients to non-primary ICUs.<sup>9,20</sup>

The observed equivalence in the care delivered may be a function of the relatively high number of patients with sepsis treated in the overflow unit, thereby giving the delivery teams enough experience to provide the desired care. An alternative explanation could be that the residents in CICU brought with them the experience from having previously trained in the MICU. Although, some of the care processes for sepsis patients are influenced by the CPOE (with embedded

order sets and protocols), it is unlikely that CPOE can fully account for similarity in care because many processes and therapies (like use of steroids, amount of fluid delivered in first 24 hours, packed red blood cells [PRBC] transfusion, and spontaneous breathing trials) are not embedded within order sets.

The significant difference noted in the areas of deep vein thrombosis (DVT) and gastrointestinal (GI) prophylaxis within 24 hours of ICU admission was unexpected. These preventive therapies are included in initial order sets in the CPOE, which prompt physicians to order them as standard-of-care. With respect to DVT prophylaxis, we suspect that some of the difference might be attributable to specific contraindications to its use, which could have been more common in one of the units. There were more patients in MICU on mechanical ventilation (although not statistically significant) and with severe sepsis (statistically significant) at time of admission, which might have contributed to the difference noted in use of GI prophylaxis. It is also plausible that these differences might have disappeared if they were reassessed beyond 24 hours into the ICU admission. We cannot rule out the presence of unit- and physician-level differences that contributed to this. Likewise, there was an unexpected trend towards significance, wherein more patients in CICU had spontaneous breathing trials within 24 hours of admission. This might also be explained by the higher number of patients with severe sepsis in the MICU (preempting any weaning attempts). These caveats aside, it is reassuring that, at our institution, admitting septic patients to the first available ICU bed does not adversely affect important processes-of-care.

One might ask whether this study's data should reassure other sites who are boarding septic patients in non-primary ICUs. Irrespective of the number of patients studied or the degree of statistical significance of the associations, an observational study design cannot prove that boarding septic patients in non-primary ICUs is either safe or unsafe. However, we hope that readers reflect on, and take inventory of, systems issues that may be different between units—with an eye towards eliminating variation such that all units managing septic patients are primed to deliver guideline-concordant care. Other hospitals that use CPOE with sepsis order sets, have protocols for sepsis care, and who train nursing and respiratory therapists to meet high standards might be pleased to see that the patients in our study received comparable, high-quality care across the 2 units. While our data suggests that boarding patients in overflow units may be safe, these findings would need to be replicated at other sites using prospective designs to prove safety.

Length of emergency room stay prior to admission is associated with higher mortality rates.<sup>21–23</sup> At many hospitals, critical care beds are a scarce resource such that most hospitals have a policy for the “triage” of patients to critical care beds.<sup>24,25</sup> Lundberg and



colleagues' study demonstrated that patients who developed septic shock on the medical wards experienced delays in receipt of intravenous fluids, inotropic agents and transfer to a critical care setting.<sup>26</sup> Thus, rather than waiting in the ED or on the medical service for an MICU bed to become available, it may be most wise to admit a critically sick septic patient to the first available ICU bed, even to an overflow ICU. In a recent study by Sidlow and Aggarwal, 1104 patients discharged from the coronary care unit (CCU) with a non-cardiac primary diagnosis were compared to patients admitted to the MICU in the same hospital.<sup>27</sup> The study found no differences in patient mortality, 30-day readmission rate, hospital LOS, ICU LOS, and safety outcomes of ventilator-associated pneumonia and catheter-associated bloodstream infections between ICUs. However, their study did not examine processes-of-care delivered between the primary ICU and the overflow unit, and did not validate the primary diagnoses of patients admitted to the ICU.

Several limitations of this study should be considered. First, this study was conducted at a single center. Second, we used a retrospective study design; however, a prospective study randomizing patients to 1 of the 2 units would likely never be possible. Third, the relatively small number of patients limited the power of the study to detect mortality differences between the units. However, this was a pilot study focused on processes of care as opposed to clinical outcomes. Fourth, it is possible that we did not capture every single patient with sepsis with our keyword search. Our use of a previously validated screening process should have limited the number of missed cases.<sup>15,16</sup> Fifth, although the 2 ICUs have exclusive nursing staff and attending physicians, the housestaff and respiratory therapists do rotate between the 2 ICUs and place orders in the common CPOE. The rotating housestaff may certainly represent a source for confounding, but the large numbers (>30) of evenly spread housestaff over the study period minimizes the potential for any trainee to be responsible for a large proportion of observed practice. Sixth, ICU attendings are the physicians of record and could influence the results. Because no attending physician was on service for more than 4 weeks during the study period, and patients were equally spread over this same time, concerns about clustering and biases this may have created should be minimal but cannot be ruled out. Seventh, some interventions and processes, such as antibiotic administration and measurement of lactate, may have been initiated in the ED, thereby decreasing the potential for differences between the groups. Additionally, we cannot rule out the possibility that factors other than bed availability drove the admission process (we found that the relative proportion of patients admitted to overflow ICU during hours of ambulance diversion was

similar to the overflow ICU admissions during non-ambulance diversion hours). It is possible that some selection bias by the hospitalist assigning patients to specific ICUs influenced their triage decisions—although all triaging doctors go through the same process of training in active bed management.<sup>11</sup> While more patients admitted to the MICU had severe sepsis, there were no differences between groups in APACHE II or SOFA scores. However, we cannot rule out that there were other residual confounders. Finally, in a small number of cases (4/41, 10%), the CICU team consulted the MICU attending for assistance. This input had the potential to reduce disparities in care between the units.

Overflowing patients to non-primary ICUs occurs in many hospitals. Our study demonstrates that sepsis treatment for overflow patients may be similar to that received in the primary ICU. While a large multicentered and randomized trial could determine whether significant management and outcome differences exist between primary and overflow ICUs, feasibility concerns make it unlikely that such a study will ever be conducted.

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