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## EMS Patients and Walk-In Patients Presenting With Severe Sepsis: Differences in Management and Outcome

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### Abstract

**Objectives:** Sepsis is a significant problem. The differences between patients with sepsis who walk into the emergency department (ED) and those who are transported via emergency medical services (EMS) have not been clarified. The aim of the study was to determine whether there was a difference in outcome between patients arriving by EMS and those presenting directly to the ED.

**Methods:** We prospectively collected and reviewed a cohort of all cases of severe sepsis and septic shock admitted to the medical intensive care unit from the ED from November 2009 to March 2012. Extracted data were basic demographic information (including mode of ED arrival), clinical data, and treatments. We calculated Systemic Inflammatory Response Syndrome criteria, Acute Physiology and Chronic Health Evaluation II scores, and Sequential Organ Failure Assessment (SOFA) scores. The primary outcome was mortality in severely ill patients with sepsis.

**Results:** A total of 378 subjects (78%) presented by EMS and 107 subjects were walk-in patients (22%). Patients transported via EMS were older ( $P < 0.01$ ), had fewer lactates  $>4$  ( $P < 0.02$ ), a more altered mental status ( $P < 0.01$ ), and higher respiratory rates ( $P < 0.05$ ) than did walk-in patients. Patients transported by EMS had worse disease severity when measured by an Acute Physiology and Chronic Health Evaluation II score ( $P < 0.01$ ) but not by SOFA score. EMS patients had a shorter time to receiving antibiotics ( $P = 0.02$ ) and central line placement ( $P < 0.01$ ) than did walk-in patients. In a logistic model, mortality was associated with increasing age (adjusted odds ratio 1.3; 95% confidence interval [CI] 1.2–1.4), higher first-measured ED lactates (1.2; 95% CI 1.1–1.2), and increased initial SOFA score (adjusted odds ratio 1.2; 95% CI 1.1–1.3) but not EMS arrival or prehospital fluids.

**Conclusions:** Neither arrival by EMS nor fluid administration by EMS is associated with decreased mortality in severe sepsis.

### Keywords

critical care; prehospital care; sepsis

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Sepsis remains one of the leading causes of morbidity and mortality worldwide, despite the implementation of specific care pathways known as early goal-directed therapy (EGDT).<sup>1</sup> Many emergency department (ED) factors have been studied for means of improving survival from sepsis, including administering antibiotics more quickly, bundling care, and improving early diagnosis.<sup>2-4</sup> The use of lactates has been suggested as a marker to improve early sepsis diagnosis in the ED by considering both the lactates level and its rate of clearance.<sup>5-8</sup>

More attention has been paid to prehospital efforts to improve sepsis mortality.<sup>9-16</sup> Because prehospital interventions have affected both stroke and myocardial infarction mortality, the same principles could be applied to prehospital sepsis management.<sup>17-19</sup> To date, studies have focused on early diagnosis, including point-of-care lactates and aggressive fluid therapy.<sup>14</sup>

Management of sepsis and septic patients by emergency medical services (EMS) has been the subject of a number of studies. Seymour et al noted that fewer than one-third of patients with severe sepsis received fluids in the prehospital setting, which suggests room for improvement.<sup>11</sup> Other studies have looked at differences in the characteristics of transports compared with walk-in patients. These characteristics include Systemic Inflammatory Response Syndrome (SIRS) criteria, Sequential Organ Failure Assessment (SOFA) scores, and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores.<sup>9-12,15</sup> The outcome variable has been different among the studies. Some found no overall mortality differences or improvement in mean arterial pressure.<sup>9</sup> Others showed shorter times to antibiotics, earlier initiation of EGDT, or mortality differences.<sup>10</sup> For example, Wang et al showed an almost twofold increase in mortality when patients with severe sepsis were transported by EMS.<sup>13</sup>

Beginning in November 2009, our hospital began formal participation in a quality improvement project developed through an Institute for Healthcare Improvement initiative.<sup>20</sup> This initiative led to our prospective collection and review of all cases of severe sepsis and septic shock admitted to the medical intensive care unit (MICU) from the ED since November 21, 2009.

The aims of our study were to determine in severely ill patients with sepsis whether there is a difference between arriving via EMS and arriving directly to the ED in terms of presenting characteristics, speed of management, or outcome, and whether there is an association between prehospital volume resuscitation and mortality in severely ill patients with sepsis.

## Methods

This study was a retrospective review of the prospectively gathered quality improvement data, which were collected for all consecutive septic patients presenting to our inner-city tertiary care major trauma center and admitted to the MICU from November 2009 to March 2012. The study was approved by the University of New Mexico institutional human research review committee.

Inclusion was based on admission to the MICU with an admission diagnosis of sepsis or severe sepsis. Our ED sees approximately 80,000 patients per year and is the only level I trauma center in New Mexico. One private EMS provider transports >95% of all emergency patients to one of seven hospitals in the Albuquerque metropolitan area, with a total of >60,000 patient transports per year. All patients admitted to our MICU with a diagnosis of sepsis were included in the database. Only patients with adequate arrival information in the electronic medical record were analyzed.

Data were entered into the database by one individual based on sepsis admission to the ICU. APACHE II and SOFA scores were added to the database based on review of the chart, and each score was entered by a single reviewer. The database was divided into patients who arrived via EMS and patients who arrived directly at the ED. Independent variables included demographic data (age, sex, race), clinical data (mental status, vital signs, laboratory values), treatment data (time to antibiotics, initial care location, time to central venous catheter), and outcome data (hospital length of stay, mortality). We also reviewed validated scoring systems to determine differences between the two groups. The hospital data collected for this study are listed below:

1. Whether the patient died in the hospital or was discharged from the hospital
2. Whether the patient was initially taken to the resuscitation room or to a regular room
3. The patient's hospital length of stay until discharge or death
4. Dataset needed for SIRS criteria (first ED heart rate, respiratory rate, white blood cell count, and temperature)
5. Presence/absence of altered mental status on ED presentation
6. First ED blood glucose
7. Whether there was a positive blood culture during the hospital stay
8. First ED lactate
9. Dataset needed to calculate APACHE II scores
10. Dataset needed to calculate SOFA scores

Data collected from EMS run sheets included all of the following:

1. First EMS vital sign measurements, including heart rate, respiratory rate, and temperature
2. Presence/absence of altered mental status
3. Prehospital finger stick glucose measurement
4. EMS fluid amounts

The primary outcome measure was mortality. All of the variables were considered by bivariate analysis for inclusion in the model predicting the outcome of mortality. Variables were entered into a logistic model if they were significant in bivariate analysis. Before

inclusion, variables were evaluated for covariance and removed if they were highly correlated with other included variables.

Three scoring systems were used based on previous validation studies for the comparisons between groups in this study. These systems were SIRS criteria,<sup>1</sup> APACHE II scores,<sup>21</sup> and SOFA scores.<sup>22</sup> SIRS criteria were based on white blood count, initial heart rate, initial temperature, and initial respiratory rate.<sup>23</sup> APACHE II scores were determined by normal calculations based on the literature.<sup>21,24</sup> SOFA scores were based on six organ systems that were evaluated, including respiratory, circulatory, hepatic, cardiovascular, central nervous, and renal systems.<sup>22,25</sup>

## Statistical Analysis

Comparisons were made using nonparametric methods, unless the datasets were proven to be parametric by the Shapiro-Wilk test. The Mann-Whitney *U* test was used for nonparametric datasets with one-way analysis of variance used for parametric data. The Fisher exact test or  $\chi^2$  analysis was used for the binomial variables such as the comparison of mode of arrival and mortality during hospitalization and 95% confidence intervals (CIs) or interquartile ranges (IQRs) were used to describe the variability of the results between the groups. None of the variables extracted were missing from the database.

Two logistic models were compiled to evaluate variables associated with presentation by EMS and in-hospital mortality. A variable inflation factor was used to assess the need to manage collinearity. Variables were compared and any with correlations of  $r > 0.3$  were considered for removal from the model. The variable chosen for removal was based on developing the regression equation that explained the most variance. The Hosmer-Lemsho statistic was used for goodness of fit. The statistical analysis was performed using SPSS version 21 (IBM, Armonk, NY) and SAS version 9.3 (SAS Institute, Cary, NC).

We calculated our power based on previous estimates that 30%<sup>13</sup> to 50%<sup>10</sup> of patients with sepsis arrive by EMS. Assuming an equal number of walk-in patients to patients transported by EMS, we would require 120 per group to demonstrate a mortality difference of 20% with a power of 80%.

## Results

### Patient Characteristics

Of the 500 patients meeting inclusion criteria to the sepsis database, 485 patients had all of their information documented in the electronic medical record. Of the 485 patients analyzed, 378 (78%) arrived via EMS and 107 (22%) were walk-in patients. Patients arriving by EMS were older (59, IQR 57–60) than walk-in patients (52, IQR 49–55;  $P < 0.01$ ; Table 1), had a more altered mental status (57% vs 32%;  $P < 0.01$ ), and were more likely to be initially triaged to our highest level-of-care area (78% vs 64%;  $P < 0.01$ ; Table 1). There was no significant sex difference noted.

### Clinical Characteristics

Table 1 shows that patients presenting by EMS had higher respiratory rates ( $P < 0.05$ ), lower initial lactates ( $P < 0.01$ ), and met more SIRS criteria upon arrival ( $P = 0.01$ ) than patients arriving at the ED. Patients presenting via EMS also had a higher modified APACHE II score ( $P < 0.01$ ); however, SOFA scores were equivalent between the two groups. Patients arriving by EMS and walk-in patients were equally likely to present in shock.

### Treatments and Outcomes

Table 1 presents ED treatment times for the two patient sets and reveals that patients arriving via EMS received faster responses as measured by time to receiving antibiotics and time to central line placement. Despite differences in vital signs, laboratory values, and treatment times, both groups had equal mortality and hospital lengths of stay. EMS patients who received large-volume prehospital resuscitation had no mortality improvement but did have a shorter hospital stay if they survived (5 days, 95% CI 4–11 vs 10 days, 95% CI 5–19).

### Differences Based on Mortality

Table 2 shows the bivariate comparison of patients who died versus patients who left the hospital alive. There was a slight difference in age and initial temperature. Lactates, SIRS criteria, and APACHE II and SOFA scores all were higher in the group that died. No EMS variables were related to this outcome nor were there any differences in time to central lines or receiving of antibiotics.

### Logistic Models

The first logistic model was performed using EMS versus walk-in as the dependent variable. All of the variables from Table 1 that were significant were considered for entry in the model. Variables were checked for collinearity and the variables that were removed for high collinearity were “direct to resuscitation room,” “APACHE II score,” and “shock.” Table 3 shows that the variables most associated with EMS arrival in the ED were age, lactates  $>4$ , and altered mental status. We repeated the procedure using the bivariate analysis shown in Table 2 with mortality as the dependent variable and found that the variables most associated with mortality were age, lactates  $>4$ , SOFA score, and SIRS criteria. Both logistic models met criteria for goodness of fit based on a nonsignificant Hosmer-Lemshow statistic related to mortality in the logistic regression.

### Discussion

We found multiple significant differences in vital signs, time to treatment, and laboratory values results between EMS and walk-in patients diagnosed as having severe sepsis. Of note, neither length of stay nor mortality was associated with mode of arrival. Overall, patients arriving via EMS were older, more likely to have an altered mental state, and had more SIRS criteria and higher APACHE II scores. Because they arrived by ambulance, they were more likely to be sent to our resuscitation room where they received antibiotics earlier and a central line more quickly. Overall, this suggests that the EMS patients appeared sicker, were taken more seriously, and received more rapid management. It is interesting that these differences did not translate into comparatively different outcomes for either of our outcome

measures. We could interpret these results either as an increase in attention led to improvement in outcomes in a cohort of patients (EMS transports) who appeared sicker or that the inattention to the walk-in patients led to worsened outcome because those who presented directly to the ED appeared less ill.

The differences between studies are explored in Table 4. Our findings that there were no differences in either mortality or length of hospital stay were in agreement with some authors<sup>9</sup> and in disagreement with others.<sup>13</sup> Patients arriving by EMS transport were recognized as sicker upon presentation and were attended to more quickly. There are numerous factors that could affect these differences between studies. We had a higher percentage of patients with severe sepsis arriving by EMS than any other study. EMS patients had already received fluids in many cases, which may have led to an improved outcome for that group, equalizing the results. We are unable to explain the threefold increase in mortality noted by Wang et al,<sup>13</sup> but that result is not in agreement with either the results of Band et al<sup>9</sup> or our present study.

In our cohort of patients with severe sepsis who arrived by EMS, prehospital fluids, whether patients were transported by EMS, or the speed with which patients received central lines or antibiotics did not alter the outcome. Accounting for all variables, only age, initial lactates, and SOFA score were related to mortality.

Our study did not contain enough patients receiving large-volume prehospital resuscitation to evaluate them separately. Seymour et al<sup>12</sup> evaluated only those patients brought in by EMS and dichotomized them into patients receiving EGDT (in this case, early fluids), but they did not discuss the amount of fluids provided. We found that even if the intention was to give prehospital large-volume resuscitation, patients with short transport times may have only received small boluses before arriving at the hospital. Seymour et al do not take this into account; however, they were unable to find a significant improvement even when using a goal mean arterial pressure as the outcome variable. We found that the hospital length of stay was greatly shortened in patients who received >1 L of fluid in the prehospital setting; however, this was a small percentage of the patients transported.

Our study also showed that walk-in patients require some additional method of evaluation to ensure they are being treated in the most timely manner. Our data suggest that they may be sicker than they appear and therefore have a mortality estimate equivalent to EMS patients who appear sick. Either slow recognition of these walk-in patients with sepsis or slow management led to their having outcomes similar to the patients brought by EMS who appeared sicker on presentation. One such possible management improvement would be to check point-of-care lactates for walk-in patients, perhaps those who have positive SIRS criteria, to improve the speed of diagnosis.

### Limitations and Future Directions

The first limitation of our study is that >70% of the admitted patients with severe sepsis were brought to the ED by EMS. Although this was not surprising to us, it does conflict with other studies that found that only 30% to 50% of their patients with severe sepsis were transported by EMS. This conflicted with our a priori sample size calculation and may have

affected our primary outcome. It also may reflect that we are a level I inner-city hospital for which EMS transports a great percentage of the most ill patients. To make up for the discrepancy, we had more than 300 EMS transports in the database to obtain 100 walk-in patients. In recalculating the power based on these numbers, we had the power to find a difference of 16% in mortality, which was still fairly close to the original calculation.

This study is a database review and can only help us to find significant correlations among variables. To prove causality, we need to follow up with a study in which we evaluate the differences in outcome with randomly determined fluid amounts.

As suggested earlier, the walk-in patients appeared to be more sick than originally suspected. Another avenue of investigation is the use of lactates determination at triage to expedite the care of walk-in patients who had more occult presentations.

## Conclusions

Patients with severe sepsis arriving via EMS are older and have lower lactates, more altered mental status, and higher respiratory rates than do walk-in patients. They also are more likely to be sent to the resuscitation room for management and receive a central line and antibiotics in significantly less time. Mortality in severe sepsis is associated with age, first ED lactates, and SOFA score but not with arrival by EMS or the amount of prehospital fluids given. These results would pertain to any inner-city major trauma center.

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### Key Points

- Patients with sepsis who were transported by emergency medical services (EMS) were older, sicker, and had a more altered mental status. Overall, mortality was related to a patient's condition upon arrival at the emergency department, regardless of the method of presentation.
- Mortality was not affected by EMS arrival or prehospital fluid administration, which may mean that clinicians are not being aggressive enough in treating these patients in the prehospital environment.
- Although EMS patients were considerably sicker than those who walked directly into the emergency department, they did not have a higher mortality than walk-in patients, suggesting that clinicians need to place stronger emphasis on recognition of patients who arrive on their own and who do not appear as sick as EMS patients.

Comparison of data collected on all patients presenting by EMS with all septic patients who were walk-ins to the University of New Mexico ED

**Table 1.**

	EMS	Walk-in	Difference (95% CI)	P
N (%)	378 (78%)	107 (28%)	—	
<b>Patient characteristics</b>				
Age, y (IQR)	59 (57–60)	52 (49–55)	7 (6–7)	<0.01
Male sex (%)	195 (54)	60 (60)	6%	NS
AMS (%)	216 (57)	34 (32)	26%	<0.01
Direct to resuscitation room (%)	282 (78)	64 (64)	14%	<0.01
<b>SIRS criteria</b>				
Temperature (IQR)	36.8 (36.5–37.1)	36.9 (36.6–37.1)	0.1	NS
Heart rate (IQR)	110 (107–113)	112 (107–117)	2	NS
Respiratory rate (IQR)	25 (24–26)	23 (22–24)	2	0.047
WBC (IQR)	15.3 (14.4–16.3)	15.7 (13.5–18.0)	0.4	NS
<b>Illness severity</b>				
Lactates (IQR)	5.0 (4.6–5.3)	5.8 (5.1–6.4)	0.8	<0.01
Lactates >4.0 (%)	70 (65)	199 (53)	12%	0.02
SIRS criteria (IQR)	2.7 (2.6–2.8)	2.5 (2.3–2.7)	0.2	0.01
Patients in shock (%)	326 (76)	89 (79)	3%	NS
APACHE II score (IQR)	16 (16–17)	14 (13–15)	2	<0.01
SOFA score (IQR)	5 (3–7)	5 (2–7)	0	NS
<b>Outcomes</b>				
Time to antibiotics, median minutes (IQR)	87 (44–157)	120 (141–271)	33	0.02
Time to central line, median minutes (IQR)	200 (89–368)	275 (122–470)	75	<0.01
Length of stay if discharged alive, median days (IQR)	15 (13–17)	14 (10–17)	2	NS
Mortality (%)	113 (30)	34 (31)	1%	NS

AMS, altered mental status; APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; ED, emergency department; EMS, emergency medical services; IQR, interquartile range; NS, not significant; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell count.

Table 2.

Comparison of ED data collected on all living and dead sepsis patients

	N (%)	Died	Alive at discharge	Difference (95% CI)	P
	112 (30%)		266 (70%)	—	
Patient characteristics					
Age, y (IQR)	60 (49–70)	57 (45–66)	7 (6–7)		0.02
Male sex (%)	57 (51)	148 (56)	5%		NS
AMS (%)	85 (58)	151 (57)	1%		NS
Direct to resuscitation room (%)	92 (82)	202 (76)	6%		NS
SIRS criteria					
Temperature (IQR)	36.2 (5.6–37.0)	36.6 (36.1–37.9)	0.4		<0.01
Heart rate (IQR)	109 (89–129)	112(92–126)	3		NS
Respiratory rate (IQR)	24 (20–28)	23 (18–29)	1		NS
WBC (IQR)	15.2 (7.9–21.7)	13.3 (8.9–19.0)	1.9		NS
Illness severity					
Lactates (IQR)	5.6 (3.1–8.3)	4.0 (2.3–5.9)	0.8		<0.01
Lactates >4.0 (%)	72 (64)	127 (48)	16%		<0.01
SIRS criteria (IQR)	3 (2.0–3.0)	3 (2.0–3.0)	0.2		0.02
Patients in shock (%)	93 (83)	195 (74)	9%		0.048
APACHE II score (IQR)	17 (14–21.5)	14 (10–19)	3		<0.01
SOFA score (IQR)	6 (5–9)	4 (2.5–7)	0		<0.01
EMS variables					
Transported by EMS	112 (77)	266 (78)	1%		NS
Total fluid given by EMS (EMS cases only, cm <sup>3</sup> )	197 ± 376	175 ± 327	22		NS
Received >1 L fluid by EMS	8 (7)	11 (4)	3%		NS
Outcomes					
Time to antibiotics, median minutes (IQR)	94 (41–162)	92 (44.5–108)	2		NS
Time to central line, median minutes (IQR)	204 (102–371)	223 (102–412)	19		NS

AMS, altered mental status; APACHE II, Acute Physiology and Chronic Health Evaluation II; ED, emergency department; EMS, emergency medical services; IQR, interquartile range; NS, not significant; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell count.

**Table 3.**

Logistic regression of odds of EMS arrival (regression 1) and mortality (regression 2)<sup>a</sup>

<b>Variable in the equation</b>			
<b>AOR</b>	<b>95% CI</b>	<b>P</b>	
Regression 1: EMS vs walk-in			
Age	1.02	1.0–1.04	0.02
AMS	2.5	1.5–4.2	<0.01
Lactates >4	2.2	1.3–3.7	<0.01
Regression 2: dead vs alive			
Age	1.03	1.01–1.04	<0.01
Lactates >4	1.9	1.3–2.9	<0.01
SOFA score	1.3	1.2–1.3	<0.01
SIRS criteria	1.3	1.1–1.7	0.02

AMS, altered mental status; AOR, adjusted odds ratio; CI, confidence interval; EMS, emergency medical services; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>Based on predictor variables from Tables 1 and 2, respectively. Variables were entered into the model if bivariate significance was <0.05. Variables that correlated with other variables at  $r > 0.3$  were considered collinear, and the least significant variable was removed from the analysis.

Table 4.

## Comparison of articles related to sepsis management in EMS

	Setting	Outcome	Numbers	Results
Seymour et al <sup>11</sup>	EMS only	SOFA scores	216	Hypotension, lower GCS, including respiratory rate, were associated with higher SOFA score
Studnek et al <sup>10</sup>	ED sepsis patients; EMS vs walk-in	ED antibiotics initiation	311	Shorter time to antibiotics and EGD, higher SOFA score
Wang et al <sup>13</sup>	All ED infected patients; EMS vs walk-in	Mortality	4613	Higher mortality in EMS (OR 1.8); EMS more likely severe sepsis or shock
Band et al <sup>9</sup>	All ED; EMS vs walk-in; severe sepsis only	ED antibiotics time, ED IVF and mortality	983	No mortality benefit
Seymour et al <sup>12</sup>	EMS patients: receiving IVF vs no fluids	Resuscitation endpoints (CVP, MAP, SCvO <sub>2</sub> )	52	Did not achieve any endpoint differences
Seymour et al <sup>15</sup>	EMS severe sepsis vs AMI and stroke	Incidence rates	>400,000	3.3% for severe sepsis vs 2.3% for AMI and 2.2% for stroke; of EMS severe sepsis, 50% were admitted to ICU; 19% died
Femling et al (present study)	EMS vs walk-in and EMS patients with fluids (<1 L) vs >1 L fluids	ED time to antibiotics, time to central line placement, and mortality	485	Decreased time to antibiotics and time to central line placement, but no mortality difference in EMS; decrease in length of stay in EMS patients receiving > 1 L fluids

AMI, acute myocardial infarction; CVP central venous pressure; ED, emergency department; EGD, early goal-directed therapy; EMS, emergency medical services; GCS, Glasgow Coma Scale; ICU, intensive care unit; IVF, intravenous fluids; MAP, mean arterial pressure; OR, odds ratio; SCvO<sub>2</sub>, superior vena cava oxygen saturation; SOFA, Sequential Organ Failure Assessment.