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Outcomes of Patients With Sepsis and Septic Shock Requiring Source Control: A Prospective Observational Single-Center Study

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OBJECTIVES: Source control is important in management of septic shock. We studied differences in outcomes of patients with sepsis and septic shock who required source control intervention compared with those who did not need such intervention and the effect of the timing of source control on various clinical outcomes.

DESIGN: Prospective observational study from February 28, 2020, to March 31, 2021.

SETTING: Medical ICU of academic quaternary medical center.

PATIENTS: Two hundred five adult (≥18 yr) ICU patients.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Patients were divided into a medical treatment group and a source control group. Patients requiring source control were further divided into early (intervention performed < 24 hr) and late (≥ 24 hr) source control groups. The primary outcomes were 30-day and ICU mortality. Secondary outcomes were ICU and hospital length of stay (LOS), days on mechanical ventilation, and need for renal replacement therapy. A total of 45.9% patients underwent source control. Of these, early source control was performed in 44.7% and late source control in 55.3% of patients. There was no significant difference in 30-day mortality or ICU mortality in the medical versus source control groups or in early versus late source control groups. Compared with the medical group, mean hospital LOS (11.5 vs 17.4 d; $p < 0.01$) and ICU LOS (5.2 vs 7.7 d; $p < 0.01$) were longer in the source control group. The hospital LOS (12.5 vs 21.4 d; $p < 0.01$) and ICU LOS (5.2 vs 9.7 d; $p < 0.01$) were also longer in patients who had delayed source control than in patients who had early source control. There were no significant differences in other outcomes.

CONCLUSIONS: Although mortality was similar, patients who had delayed source control had a longer ICU and hospital LOS. Early source control may improve health care utilization in septic shock patients.

KEY WORDS: intensive care unit and hospital length of stay; mortality; sepsis; septic shock; source control

Septic shock is a medical emergency with a mortality rate as high as 30% (1). Patients with sepsis often require ICU care for close monitoring, hemodynamic support, mechanical ventilation (MV), and renal replacement therapy (RRT). High resource utilization and prolonged hospital stays result in increased cost of care (2, 3). Optimal outcomes in sepsis require early recognition, administration of fluids, collection of blood cultures and lactate, appropriate antibiotics, and adequate source control (4).

Antibiotics alone are sometimes not sufficient for control of sepsis and septic shock. Some patients require source control interventions such as

DOI: 10.1097/CCE.0000000000000807

KEY POINTS

Question: What are the differences in outcomes of patients with septic shock who required source control compared with those who did not need such interventions. Is there an effect of the timing of source control?

Findings: In this prospective observational study, there was no significant difference in 30-day or ICU mortality in the medical versus source control group or in early versus late source control groups. Mean hospital LOS and ICU LOS were longer in the source control group and in those patients who had delayed source control.

Meanings: Early source control may improve health care utilization in septic shock patients.

abscess drainage and infected soft-tissue debridement to achieve more rapid clearance of systemic infection (5). Autopsy studies show a high prevalence of inadequate source control in patients who succumb to septic shock (6). Although the need for effective source control in certain patients is universally accepted, the optimal timing of intervention following this recognition remains debated. Although early source control led to better outcomes in intra-abdominal sepsis (7), ascending cholangitis (8), and necrotizing fasciitis (9, 10), studies that included patients with broad underlying causes of sepsis have reached conflicting results. Some studies seem to suggest a better outcome with source control within 6–12 hours (11), whereas others have found no effect of source control timing on mortality (12, 13). Similarly, the effect of timing of source control on resource utilization such as length of hospital stay remains poorly defined in patients with sepsis and septic shock (14, 15).

In this study, we compare the differences in outcomes and resource utilization of patients with sepsis and septic shock requiring source control versus those who did not require source control. We further studied the impact of timing of source control on clinical outcomes and resource utilization in patients who required a source control intervention in management of sepsis and septic shock.

MATERIALS AND METHODS

Design and Protocol

This prospective single-center observational study was performed in an academic quaternary medical center and included patients who were 18 years and older admitted to the ICU with sepsis and septic shock between February 2020 and March 2021. The majority included in the study came from the rural Appalachia. West Virginia University Institutional Review Board (IRB) approved the study (Protocol no. 200289266, Protocol title: Impact of early versus late source control on mortality in patients presenting with septic shock) under the West Virginia University Flexibility Review Model, with waiver of informed consent (Approval date February 17, 2020, to February 16, 2025). All procedures were followed in accordance with the ethical standards of the responsible IRB committee on human experimentation and with the Helsinki Declaration of 1975. Data were collected prospectively from the electronic medical record.

Population and Data Collection

All consecutive adult patients admitted to the ICU from the hospital's emergency department or transferred from the medical or surgical floor with a diagnosis of sepsis or septic shock were screened for inclusion in the study. Patients who were transferred from an outside ICU for septic shock were excluded from the study. Pregnant patients and prisoners were also excluded. For patients who required multiple admissions to the ICU within the same hospital stay, only the index admission to the ICU was included.

Patients admitted to the ICU were screened daily and included in the study if they met criteria for a diagnosis of sepsis or septic shock. Sepsis was defined as life-threatening organ dysfunction secondary to infection. Organ dysfunction was identified as an acute increase in total Sequential Organ Failure Assessment score greater than or equal to 2 points above baseline. Septic shock was defined as persistent hypotension requiring vasopressor support to maintain mean arterial pressure greater than or equal to 65 and blood lactate greater than 2 mmol/L despite adequate volume resuscitation.

The onset of sepsis (time zero) was defined as time of nursing triage in patients admitted to ICU from the

emergency department. For patients transferred to the ICU from nonemergency department units, time zero was the time at which a diagnosis of sepsis was initially suspected by the health care provider. This included, for example, a physician's note, timed and dated orders, a timed and dated note of a nurse's discussion of sepsis with a physician, or timed records initiating referral to the ICU for sepsis.

We collected data on demographic, clinical, and laboratory variables including preexisting comorbid conditions and organ dysfunction at presentation. Acute Physiology and Chronic Health Evaluation II (APACHE II) and Charlson Comorbidity Index (CCI) were calculated at time of patient presentation. Patients were prospectively followed from the time of admission. Timing of blood culture draws, administration of antibiotics, initiation of fluid resuscitation, and lactate measurement from time zero were recorded. In addition, information on microbiological results and inflammatory markers (C-reactive protein [CRP] and procalcitonin) performed within in the first 24 hours of sepsis diagnosis were obtained.

Patients were divided into a medical group when they were treated only with antimicrobial agents and supportive therapy and into a source control group when they additionally required a procedural intervention to control sepsis. Patients who required source control were further divided into an early source control group when intervention was performed within 24 hours of time zero and a delayed source control group when this period was greater than or equal to 24 hours.

Patients were followed until death or 30 days after hospital discharge. The primary outcomes studied were differences in overall 30-day mortality and ICU mortality between patients treated medically versus those requiring source control, and between those with early versus late source control. Secondary outcomes included ICU and hospital length of stay (LOS), days on MV, and need for RRT.

Data were aggregated using the HIPAA-compliant Research Electronic Data Capture electronic data capture tool (16, 17).

Statistical Analysis

Statistical Analysis System Version 9.4 was used for all statistical analysis. Mean and standard deviations were calculated for continuous variables. Proportions and percentages were calculated for categorical variables. Differences in outcomes by groups were presented as independent sample *t* tests for continuous variables. A chi-square test of independence was used to determine whether there was a significant association between two categorical variables, and Fisher exact test was used when one or more of the cells counts was less than five. The magnitude of the difference between groups was quantified using simple and multiple linear regression and logistic regression analysis for continuous and categorical outcomes, respectively. Factors that were not statistically significant (alpha = 0.01) in the adjusted models were deleted from the model in a stepwise manner. All statistical tests were 2-sided, and a p value of 0.05 was used to determine statistical significance. Post hoc analysis using multiple logistic regression was done to examine factors associated with 30-day mortality in the study population.

Data Collection and Quality Control

To ensure data quality, a fellow and staff physician with experience in sepsis and septic shock reviewed data entry.

RESULTS

A total of 205 patients were included in the study. Mean age of the total cohort was 59.7 ± 17.0 years, and 101 patients (49.3%) were female. Patients were predominantly of Caucasian ethnicity (99%). APACHE II score at admission was 52.5 ± 29.3. Comorbid conditions are listed in **Table 1**. CCI was 5.1 ± 3.0 for the entire study cohort. A microbial isolate was identified in 91 patients (44.6%), of which 63 (30.7%) were Gram-positive organisms. Respiratory infection was the most common source of sepsis (n = 81; 39.5%), followed by urological source (n = 57; 27.8%), and skin or soft-tissue infection (n = 40; 19.5%). Of the total cohort, 153 patients (74.6%) required vasopressor use, 102 (49.8%) patients required MV, and 40 (19.5%) patients received RRT.

A total of 94 patients (45.9%; 95% CI, 39.2–52.7) required source control intervention. Baseline characteristics of medical and source control groups are shown in Table 1. Although most baseline characteristics were similar, some differences were noted. CCI was higher in the medical group compared with the source control group (5.5 ± 2.9 vs 4.6 ± 3.2; p = 0.04). The CRP level was significantly higher in source control group than

TABLE 1.
Baseline Patient Characteristics

Variable, Mean ± SD or *n* (%)	Total Cohort (*n* = 205)	Medical Group (*n* = 111)	Source Control Group (*n* = 94)	*p*
Female (*n* [%])	101 (49.3)	52 (46.9)	49 (52.1)	0.45
Body mass index (mean ± SD)	30.8 (11.0)	31.0 (11.5)	30.5 (10.5)	0.78
Ethnicity–Caucasian (*n* [%])	203 (99.0)	109 (98.2)	94 (100)	0.19
Acute Physiology and Chronic Health Evaluation II (mean ± SD)	52.5 (29.3)	54.7 (30.0)	50.0 (28.4)	0.25
Hypertension (*n* [%])	108 (52.7)	60 (54.1)	48 (51.1)	0.67
Diabetes mellitus (*n* [%])	76 (37.1)	41 (36.9)	35 (37.2)	0.97
Coronary artery disease (*n* [%])	28 (13.7)	15 (13.5)	13 (13.8)	0.95
Cerebral vascular accident (*n* [%])	21 (10.2)	15 (13.5)	6 (6.4)	0.09
Congestive heart failure (*n* [%])	66 (32.2)	35 (31.5)	31 (33.0)	0.83
Chronic lung disease (*n* [%])	82 (40.0)	47 (42.3)	35 (37.2)	0.46
Liver disease (*n* [%])	39 (19.0)	22 (19.8)	17 (18.1)	0.75
Immunosuppression (*n* [%])	23 (11.2)	19 (17.1)	4 (4.3)	0.004
Cancer (*n* [%])	43 (21.0)	24 (21.6)	19 (20.2)	0.81
Charlson Comorbidity Index (mean ± SD)	5.1 (3.0)	5.5 (2.9)	4.6 (3.2)	0.04
Microbial isolate (*n* [%])	91 (44.61)	45 (40.9)	46 (48.9)	0.25
Gram-negative	17 (8.3)	7 (6.3)	10 (10.6)	0.26
Gram-positive	63 (30.7)	30 (27.0)	33 (35.1)	0.21
Source of sepsis (*n* [%])				
Pulmonary	81 (39.5)	62 (55.9)	19 (20.2)	< 0.01
Urological	57 (27.8)	24 (21.6)	33 (35.1)	< 0.01
Skin/soft tissue	40 (19.5)	13 (11.7)	27 (28.7)	0.03
Abdomen	37 (18.1)	13 (11.7)	24 (25.5)	0.01
CNS	4 (2.0)	1 (0.9)	3 (3.2)	0.24
Other	64 (31.2)	34 (30.6)	30 (31.9)	0.84
Vasopressor use (*n* [%])	153 (74.6)	80 (72.1)	73 (77.7)	0.36
Mechanical ventilation (*n* [%])	102 (49.8)	56 (50.5)	46 (48.9)	0.83
Need for renal replacement therapy (*n* [%])	40 (19.5)	22 (19.8)	18 (19.2)	0.90
Organ dysfunction at presentation (*n* [%])				
Respiratory	146 (71.2)	80 (72.1)	66 (70.2)	0.77
Renal	141 (68.8)	65 (58.6)	76 (80.9)	< 0.01
Cardiovascular	52 (25.4)	25 (22.5)	27 (28.7)	0.31
Thrombocytopenia	40 (19.5)	18 (16.2)	22 (23.4)	0.20
Coagulation dysfunction	34 (16.6)	14 (12.6)	20 (21.3)	0.10
Hyperbilirubinemia	29 (14.2)	11 (9.9)	18 (19.2)	0.06
C reactive protein within 24 hr (mean ± SD)	184.2 (123.3)	146.8 (130.0)	216.3 (108.4)	0.001
Procalcitonin at 24 hr (mean ± SD)	28.3 (73.9)	24.9 (69.0)	32.8 (80.5)	0.57

in medical group (p = 0.001). A higher proportion of patients in the medical group received immunosuppressive medications compared with the source control group (19 [17.1%] vs 4 [4.3%]; p = 0.004). A pulmonary source of infection was more common in the medical group (62 [55.9%] vs 19 [20.2%]; $p < 0.01$), whereas urological (24 [21.6%] vs 33 [35.1%]; p = 0.03), skin and soft-tissue (13 [11.7%] vs 24 [25.5%]; $p < 0.01$), and abdominal sources of infection (13 [11.7%] vs 27 [28.7%]; p = 0.01) were more common in the source control group (Table 1).

Early source control was performed in 44.7% (95% CI, 35–54.7) and late source control in 55.3% (95% CI, 45.3–65) of patients. Of those who required source control, 34 of 94 patients (36.2%; 95% CI, 27.2–46.3) had a surgical procedure, whereas the rest underwent percutaneous intervention. With the exception of diabetes mellitus, which was more common in the early source control group, the baseline demographic features, comorbid conditions, APACHE II score, CCI, and CRP levels were similar in two groups (Supplementary, http://links.lww.com/CCX/B97). Surgical drainage or debridement for skin and soft-tissue infection was the most common surgical procedure (n = 16; 17.0%), whereas nephrostomy and abdominal abscess drainage were the most common percutaneous procedures performed in 16 patients (17.0%) each (**Table 2**).

Primary Outcomes

There was no difference in 30-day mortality (39 [35.1%] vs 30 [31.9%]; p = 0.63) in the medical and source control groups. ICU mortality (26 [23.9%] vs 17 [18.1]; p value: 0.32) was also similar in the two groups (**Table 3**). Similarly, there were no significant differences in 30-day mortality and ICU mortality between the early versus late source control groups ($p > 0.05$ for both) (**Table 4**).

Secondary Outcomes

Hospital LOS (11.5 ± 10.2 vs 17.4 ± 15.2 d; $p < 0.01$) and ICU LOS (5.2 ± 5.6 vs 7.7 ± 6.9 d; $p < 0.01$) were significantly shorter in the medical group than that in the source control group. There was no significant difference in other outcomes including days on MV and RRT (all p values >0.05) (Table 3).

Hospital LOS (12.5 ± 10.9 vs 21.4 ± 16.9 d; $p < 0.01$) and ICU LOS (5.2 ± 5.6 vs 9.7 ± 7.4 d $p < 0.01$) were also significantly shorter for the early source control group than that in late source control group. There

TABLE 2.
Type of Intervention in the Source Control Group

Type of Intervention	Total (n = 94) (n [%])	< 24 hr (n = 42) (n [%])	≥ 24 hr (n = 52) (n [%])	p
Surgical[a]	34 (36.2)	8 (19.1)	26 (50.0)	< 0.01
Skin/soft-tissue abscess	16 (17.0)	4 (9.5)	12 (23.1)	0.08
Abdominal	9 (9.6)	3 (7.1)	6 (11.5)	0.47
Orthopedic	8 (8.5)	2 (4.8)	6 (11.5)	0.24
Cardiac	6 (6.4)	0 (0.0)	6 (11.5)	0.02
Nephrectomy	1 (1.1)	0 (0.0)	1 (1.9)	0.37
Percutaneous[b]	60 (63.8)	34 (56.7)	26 (43.3)	< 0.01
Abdominal abscess drainage	16 (17.0)	12 (28.6)	4 (7.7)	< 0.01
Nephrostomy	16 (17.0)	14 (14.9)	2 (3.9)	< 0.01
Chest tube	12 (12.8)	6 (14.3)	6 (11.5)	0.69
ERCP	4 (4.3)	2 (4.8)	2 (3.9)	0.83
Cholecystostomy	1 (1.1)	1 (2.4)	0 (0.0)	0.26
Skin/soft-tissue abscess drainage	10 (10.6)	1 (2.4)	9 (17.31)	0.02
Bone/joint abscess drainage	3 (3.2)	1 (2.4)	2 (3.9)	0.69

[a]Five patient had more than one procedure performed.
[b]Three patients had more than one procedure performed.

TABLE 3.
Differences in Outcome for Medical and Source Control Groups

Outcome Measures	Total Cohort ($n = 205$)	Medical Group ($n = 111$)	Source Control Group ($n = 94$)	p
30-d mortality (n [%]), mean (SD)	69 (33.7)	39 (35.14)	30 (31.9)	0.63
ICU mortality (n %), mean (SD)	45 (21.0)	26 (23.4)	17 (18.1)	0.32
Hospital LOS (mean ± SD)[a]	14.2 (13.0)	11.5 (10.2)	17.4 (15.2)	< 0.01
ICU LOS (mean ± SD)[b]	6.4 (6.4)	5.2 (5.6)	7.7 (6.9)	< 0.01
Days on mechanical ventilation (mean ± SD)	5.8 (6.1)	5.0 (4.5)	6.8 (7.5)	0.13
Acute kidney injury needing renal replacement therapy (n [%])	40 (19.5)	22 (19.8)	18 (19.2)	0.90

LOS = length of stay.
[a]Hospital LOS for the intervention group vs medical group remained statistically significant in the model (parameter estimate = 5.04 d [SE = 1.68]; $p = 0.0031$) adjusting for age and body mass index (BMI).
[b]ICU LOS for the intervention group vs medical group remained statistically significant in the model (parameter estimate = 2.25 d [SE = 0.85], $p = 0.0088$) adjusting for age and BMI.

TABLE 4.
Differences in Outcomes in the Early and Late Interventions in Source Control Group

Outcome Measures	Intervention Group (n = 94)	Intervention Group: Time < 24 hr (n = 42)	Intervention Group: Time ≥ 24 hr (n = 52)	p
30-d mortality (n [%])	30 (31.9)	10 (23.8)	20 (38.5)	0.13
ICU mortality (n [%])	17 (18.1)	7 (16.7)	10 (19.2)	0.75
Hospital LOS (mean ± SD)[1]	17.4 (15.2)	12.5 (10.9)	21.4 (16.9)	< 0.01
ICU LOS (mean ± SD)[2]	7.7 (6.9)	5.2 (5.5)	9.7 (7.4)	< 0.01
Days on mechanical ventilation (mean ± SD)	6.8 (7.5)	6.3 (7.9)	7.2 (7.3)	0.70
Acute kidney injury needing renal replacement therapy (n [%])	18 (19.2)	5 (11.9)	13 (25.0)	0.11

LOS = length of stay.
[1]Hospital LOS for the intervention group ≥24 hr vs <24 hr remained statistically significant in the model (parameter estimate = 9.27 d [SE = 2.83]; $p = 0.0015$) adjusting for age.
[2]ICU LOS for the intervention group ≥24 hr vs <24 hr remained statistically significant in the model (parameter estimate = 4.52 d [SE = 1.36]; $p = 0.0013$) adjusting for age.

was no significant difference in other outcomes (all p values >0.05). Hospital LOS ($p = 0.569$) and ICU LOS ($p = 0.868$) were similar in the medical group when compared with the early source control group.

No differences in primary or secondary outcomes were found when source control was performed less than 6 or less than 12 hours after onset of sepsis compared with greater than 6 or greater than 12 hours, respectively (**Supplementary File**, http://links.lww.com/CCX/B97).

Time taken for lactate measurement, obtaining blood cultures, administering antibiotics, and fluid resuscitation was similar in all study groups (p values >0.05). In the total cohort, 23.2% patients received antibiotics in less than or equal to 1 hour. Blood cultures were drawn, and lactate was measured in less than or equal to 1 hour in 33.3% and 50.7% of the patients, respectively; 49.1% of patients received intravenous fluids in less than or equal to 1 hour (**Table 5**).

TABLE 5.
Management of Sepsis (Sepsis Resuscitation Bundle)

Sepsis Resuscitation Bundle	Medical Group ($n = 111$),Median (IQR)	Intervention group ($n = 94$),Median (IQR)	p
Time taken for lactate measurement (hr)	0.87 (0.27–2.75)	1.12 (0.33–3.70)	0.21
Time taken for blood cultures (hr)	1.74 (0.67–3.33)	1.98 (0.95–5.33)	0.06
Time taken for antibiotic administration (hr)	2 (1.05–4.0)	2.65 (1.25–4.67)	0.21
Time taken for starting fluid administration (hr)	1.07 (0.64–2.0)	1 (0.33–3.0)	0.95

IQR = interquartile range.

In 97% of entire cohort, initial empiric antibiotics were appropriate for the final diagnosis according to established Infectious Disease Society of America guidelines, modified by local antibiogram. Furthermore, all organisms isolated in blood or other appropriate culture specimens were adequately covered by initially chosen antibiotics. Antimicrobial therapy was modified in 3.6% of patients in medical group and 2% in source control group to cover the fungal or other unusual organism. Drug dosage and levels were strictly monitored by clinical pharmacist as a part of local institutional practice to ensure appropriate blood level.

CCI at presentation was significantly associated with an increased hospital LOS for the overall cohort as well as the source control group (p value <0.01). CCI did not have a significant impact on ICU LOS for the overall cohort, medical, or source control groups. Use of immunosuppressive medications was not associated with increased hospital or ICU LOS. Respiratory source of infection was associated with increased LOS in both medical and source control group.

Factors associated with 30-day mortality for entire patient population are shown in **Table 6**. The risk of mortality was increased with higher APACHE II score, higher CCI, and respiratory, skin and soft-tissue, and abdominal sources of sepsis.

DISCUSSION

The main results of our study are as follows. Nearly one-half of our study patients with sepsis and septic shock required a source control intervention. Medical and source control groups had similar 30-day mortality. The lengths of hospital and ICU stay were longer in patients who needed source control intervention. Finally, source control intervention performed after 24 hours was not associated with a higher 30-day mortality but was associated with longer hospital and ICU LOS.

TABLE 6.
Multiple Logistic Regression Model for Risk Factors for 30-d Mortality in the Total Sample of Patients ($n = 205$)

Factors	OR (95% CI)	p
Age (yr)	1.02 (1–1.05)	0.0669
Charlson comorbidity	1.14 (1.01–1.3)	0.0402
Acute Physiology and Chronic Health Evaluation II score	1.02 (1.01–1.03)	0.0006
Respiratory source	2.44 (1.16–5.16)	0.0193
Skin/soft-tissue source	4.73 (1.91–11.72)	0.0008
Abdominal source	2.84 (1.18–6.81)	0.0197

OR = odds ratio.

Adjusted odds ratios and 95% CIs for 30-d mortality in total patients. Factors that were not significant in the model were deleted on at a time. Alpha was set to 0.01.

Continuous covariates: age, Charlton comorbidity index, Acute Physiology and Chronic Health Evaluation score.

A dysregulated host response to infection is the hallmark of sepsis and septic shock (18). With an aging population, sepsis has become a major public health concern resulting in high cost to the health care system (2, 19, 20). More than 50% of hospital deaths are attributable to sepsis (21). Source control is a key factor in management of sepsis (22). Our study provides useful insight on the need and timing of source control on mortality and health care utilization by in sepsis and septic shock. In general, the results are similar to those reported by others, but several differences in baseline characteristics of our patient population compared with other studies are noteworthy. Our patients were almost exclusively Caucasian and had a greater burden of chronic medical conditions, and had a higher APACHE II score at presentation compared with those in other studies (11, 12). Still, overall 30-day mortality in our study population was 31.9%, which is comparable to 20.1–35% mortality reported in other studies (11–13). Variation in 30-day mortality in different studies is likely to be due to differences in the baseline patient characteristics. In addition, underlying etiologies of sepsis were different in some of these studies compared with our study. For example, in some studies, intra-abdominal infection was the leading cause of sepsis (12, 13). In other studies (11) including ours, respiratory tract infection was the most common cause of sepsis. Almost half of our study population (45.9%) admitted to the ICU with sepsis and septic shock underwent source control. Other studies have reported need for source control in 32–42% of patients (12, 23). It is also important to note that indications and timing of source control and the type of procedures (surgical vs interventional radiology) were different in different studies. Source control was achieved with a surgical procedure in 19.7–84.8% of patients in prior studies (11, 13), whereas it was needed in 36.2% of our patients.

As observed in a prior study (3), patients in our study requiring source control had significantly higher CRP levels than those treated medically, indicating a more profound inflammatory state attributable to a higher bacterial load (6). Still, mortality was similar in both groups. Some investigators have reported lower mortality among patients who required source control compared with those who did not (11, 12). This could be explained by differences in patient population, underlying diagnosis, illness severity, and types of interventions in various studies.

Delay in source control is common (24). Although it is reasonable to assume that rapid source control would lead to a better survival, there is scant evidence to support actual outcome benefits with early source control. The definition of early versus delayed source control has varied between 2 and 24 hours in different studies (9, 10, 25). We found no effect of timing of source control on 28-day mortality in our patients. Prior studies have reached conflicting results in this regard. In one study, 28-day mortality was 26.7% and 42.9% when source control intervention was performed in less than 6 or greater than 6 hours, respectively. In contrast, other studies have found no effect of timing of source control intervention on mortality (12, 13). Although baseline patient characteristics were similar, percutaneous interventions were more commonly performed within 24 hours while surgical interventions were more commonly performed greater than 24 hours after identification of need for source control in our study. A longer wait time for surgical intervention for source control compared with percutaneous intervention in our study was most likely related to multiple factors such as a need for improved hemodynamic stability before anesthesia, further imaging, surgical planning, and availability of operating room. We did not include COVID-19 patients in this study. The required intervention may have been delayed due to mandatory testing requirements, long turnaround time for COVID test before surgery, diversion of health care work force, and lack of resources at least in early months of COVID-19 pandemic.

Patients admitted with sepsis have a longer LOS compared with most other conditions (4) with an increasing LOS as severity of sepsis increases (5). Our study demonstrates an increase in ICU and hospital LOS in patients undergoing source control compared with those who did not require source control. There is limited literature in this area, but similar to our findings, another prospective study has also shown an increase in hospital LOS in those patients undergoing source control (12). Longer hospital and ICU LOS may be related to a longer recovery time among patients who require source control interventions. We also found longer hospital and ICU LOS among patients who had delayed source control. Interestingly, hospital and ICU LOS were similar among those treated medically and those receiving early source control. This raises the

possibility that delayed source control is a primary culprit in increased LOS among those requiring procedural intervention for sepsis management. Further studies are needed to determine whether reducing delay in source control would decrease hospital and ICU LOS. Timing of source control was not associated with differences in duration of MV or need for RRT in our study.

Overall compliance with sepsis bundle recommendations in our study was suboptimal, but similar among patients stratified according to need for source control and timing of intervention if needed. Initial antibiotics chosen were equally adequate in both groups. Our data underscore a need for careful institutional review of current policies and procedures related to sepsis management to improve compliance with recommendations outlined in the sepsis bundle including timing of source control. Such audits have led to a better compliance with sepsis bundle (26) but have not always improved outcomes (27).

The strengths of our study are its prospective design, which allowed an accurate collection of data pertaining to the timing and type of source control intervention, resource utilization, and 30-day mortality. Variables were predefined to minimize the difference of judgment among individual investigators. There were multiple limitations to our study. This was a single-center study with a small sample size. Our study patients were predominantly Caucasian, limiting the external validity of the results to a more diverse population. Further studies are needed with greater representation of racial and ethnic minorities. We did not address the adequacy of source control, which has an important effect on patient outcomes and resource utilization (28, 29). Further, we did not study the timeliness of intervention for source control required over the weekends as opposed to the weekdays when specialized services are more readily available. Future studies and quality improvement initiatives should address this important issue.

CONCLUSIONS

Approximately half of our patients with sepsis admitted to the ICU needed source control. An early source control intervention was associated with shorter hospital and ICU LOS without a benefit in mortality. Our data indicate a considerable potential to improve compliance with sepsis bundle recommendations by initiating quality improvement in individual health care settings. Such initiatives should not only address compliance with the 1-hour bundle but also focus on timely recognition and adequate treatment of the source of infections causing sepsis and septic shock.

ACKNOWLEDGMENTS

We thank Dr. Prasoon Jain.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Dr. Hadique takes the responsibility of the content of the article, including the data and analysis. Drs. Naqvi, Umer, Rana, and Hadique had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed substantially to the study design and contributed toward the writing of article. All authors have read and approved the article.

The authors have disclosed that they do not have any potential conflicts of interest.

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The study protocol was approved by the institutional board review of West Virginia University.

All data generated or analyzed during this study are included in this published article.

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