

Effect of Meeting the 1-Hour Bundle Target on Outcomes in Septic Shock

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Abstract

This research explored whether completing the 1-hour resuscitation bundle influences clinical outcomes in patients suffering from septic shock. The analysis utilized prospectively gathered data from multiple centers involving individuals who received standardized bundle-based resuscitation in emergency departments. Using multivariable logistic regression, in-hospital mortality was assessed according to whether the 1-hour bundle was fulfilled. Participants were further classified into three subgroups based on completion time to evaluate temporal outcome differences: group 1 (≤ 1 hour, reference), group 2 (1–3 hours), and group 3 (3–6 hours). Among the 1,612 patients included, only 461 (28.6%) achieved bundle completion within the first hour. Statistical evaluation showed that completing the 1-hour bundle did not significantly reduce in-hospital mortality when compared to those exceeding one hour (odds ratio = 0.74, $p = 0.091$). Conversely, meeting the 3-hour and 6-hour bundle targets was linked to substantially lower mortality odds (<3 vs. >3 hours and <6 vs. >6 hours; odds ratio = 0.604 and 0.458, respectively). No significant mortality variation was observed between groups 2 and 3 compared with the reference group. The findings indicate that adherence to the 1-hour bundle alone may not yield better survival outcomes in septic shock, underscoring the necessity for additional studies to clarify its clinical importance.

Keywords: Emergency department, Sepsis, 1-h bundle, Septic shock, Mortality, Outcome

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Introduction

Sepsis remains one of the most critical global health issues, responsible for an estimated 48.9 million cases each year and nearly one-fifth of all recorded deaths worldwide [1, 2]. Its occurrence tends to rise among elderly populations, individuals with multiple comorbidities, and those with weakened immune systems [3, 4]. The observed increase in sepsis incidence may partly reflect enhanced clinical recognition due to improved awareness programs and educational initiatives. Despite notable advances in intensive care medicine,

sepsis continues to present high levels of mortality and long-term morbidity.

Early detection and prompt initiation of therapy are crucial for favorable outcomes in patients with sepsis. To streamline care, the Surviving Sepsis Campaign (SSC) introduced standardized “bundle” strategies in 2005 to ensure timely and consistent bedside interventions [5, 6]. These bundles were later refined—from a 6-hour format to a 3-hour version in 2015—and further condensed in 2018 into what became known as the 1-hour bundle [7]. The 2018 update required that resuscitation procedures begin within one hour of emergency department (ED)

triage or from the earliest recorded time of presentation if the patient arrived from another facility.

The 1-hour bundle includes five major interventions: (1) measurement of serum lactate, (2) obtaining blood cultures before antibiotic therapy, (3) immediate administration of broad-spectrum antibiotics, (4) rapid infusion of 30 mL/kg crystalloid fluid for patients with hypotension or lactate levels ≥ 4 mmol/L, and (5) use of vasopressors to maintain a mean arterial pressure (MAP) ≥ 65 mmHg if hypotension persists despite fluid resuscitation. In October 2019, “time zero” was redefined as the moment of shock recognition rather than initial triage [8]. This modification was influenced by prior research demonstrating that faster completion of the 3-hour bundle correlated with reduced mortality [9]. Although that study did not specifically evaluate the 1-hour bundle, its findings supported the rationale for earlier intervention. Nevertheless, the 1-hour target has been controversial because of limited evidence for the strict time threshold and the potential risks of rushed management decisions, such as excessive fluid delivery and unnecessary use of broad-spectrum antibiotics [10, 11]. The quality of supporting evidence for individual bundle components remains variable, ranging from low to moderate [7]. Notably, the prognostic relevance of full compliance with the 1-hour bundle in septic shock has not yet been comprehensively studied.

The present study aimed to determine whether adherence to the 1-hour bundle affects clinical outcomes in patients presenting to the ED with septic shock. We proposed that completion of the 1-hour bundle would not significantly improve outcomes compared to completion within 3 or 6 hours.

Materials and Methods

Study design

This investigation involved a secondary analysis of prospectively gathered data from the Korean Shock Society septic shock registry, which includes records from 10 university-affiliated emergency departments across Korea. Data were collected between October 2015 and December 2018. Adult patients (≥ 19 years old) with suspected or confirmed infection accompanied by refractory hypotension or hypoperfusion were considered eligible [12, 13].

Hypotension was defined as systolic blood pressure (SBP) < 90 mmHg, mean arterial pressure (MAP) < 70 mmHg, or a decline in SBP > 40 mmHg. Refractory hypotension referred to persistent hypotension despite receiving a 30 mL/kg crystalloid bolus or requiring vasopressors to maintain SBP ≥ 90 mmHg or MAP ≥ 70 mmHg. Hypoperfusion was identified by serum lactate levels ≥ 4 mmol/L.

Patients were excluded if they had “do not attempt resuscitation” directives, met inclusion criteria more than

6 hours after ED arrival, were transferred from another hospital but did not meet inclusion criteria upon arrival, or were directly transferred out of the ED to other institutions. The study was approved by the institutional review boards of all participating centers, and informed consent was obtained before data entry. The registry contained precise timestamps for lactate measurement, blood culture collection, antibiotic initiation, fluid therapy, and vasopressor use. Comprehensive methodological details of the registry have been described previously [14–16].

For this specific analysis, only direct ED admissions were included to ensure uniformity in time measurements. We further restricted inclusion to patients diagnosed based on refractory hypotension, as the registry did not record fluid administration details for those categorized solely under hypoperfusion. Participants missing any bundle component data or outcome information were excluded.

Definitions and outcomes

Participants were categorized by the time elapsed between recognition of septic shock and completion of bundle components into three groups:

- Group 1 (≤ 1 hour) – reference group
- Group 2 (1–3 hours)
- Group 3 (3–6 hours)

The onset of septic shock was marked by the recognition of refractory hypotension—defined as sustained low blood pressure following fluid challenge. Failure to complete any of the five bundle interventions within the designated time frame constituted bundle non-compliance. Although treatment decisions were made at the discretion of attending physicians, all centers adhered to SSC-based sepsis protocols.

The primary endpoint was in-hospital mortality, whereas 28-day and 90-day mortality served as secondary outcomes.

Statistical analyses

Continuous data were summarized as either mean $\pm$ standard deviation or median with interquartile range (IQR), depending on distribution type, while categorical data were expressed as counts and percentages. Median values with corresponding quartiles (Q1–Q3) were compared using the Kruskal–Wallis test. For categorical comparisons, either the chi-square test or Fisher’s exact test was employed as appropriate.

To evaluate the association between timely bundle completion and clinical outcomes, both univariate and multivariable logistic regression analyses were conducted for three time thresholds (< 1 h vs. > 1 h, < 3 h vs. > 3 h, and < 6 h vs. > 6 h). Multivariable models were adjusted for confounders that demonstrated potential relevance in univariate analysis ($p < 0.2$), which were then entered into the model using a backward elimination approach.

Participants were additionally categorized into three groups based on the duration to complete bundle interventions: Group 1 (≤ 1 h; reference), Group 2 (1–3 h), and Group 3 (3–6 h). The relationship between time to bundle achievement and patient outcomes was further analyzed using multivariable logistic regression, comparing each group to the reference category to identify any time-dependent trends in outcome.

A two-tailed p -value < 0.05 was interpreted as statistically significant. The Bonferroni correction was applied to adjust for multiple comparisons within each analytical category. All statistical computations were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results and Discussion

Participant characteristics

During the study period, 1777 patients presenting with refractory hypotension were directly admitted to the emergency departments. After excluding 165 patients with incomplete data regarding bundle implementation (**Figure 1**), a total of 1612 patients remained for analysis. Among these, 461 patients were classified into Group 1 (≤ 1 h), 637 into Group 2 (1–3 h), and 293 into Group 3 (3–6 h).

Baseline demographics and clinical characteristics are summarized in **Table 1**. The mean ages across the three groups were 68, 70, and 71 years, respectively, with no significant differences observed in either age or gender distribution. The median interval from ED arrival to shock recognition was 87 minutes (IQR 26–150 min). Achievement of the 1-hour bundle was documented in 28.6% ($n = 461$) of all cases.

Initial systolic blood pressure (SBP) values were comparable among groups ($p = 0.152$). In contrast, serum lactate concentrations showed significant variation: 2.5 mmol/L, 2.7 mmol/L, and 3.2 mmol/L for Groups one, two, and three, respectively ($p < 0.001$). In-hospital mortality rates were 13.8%, 16.9%, and 20.1% across the three groups, though this difference did not reach statistical significance ($p = 0.075$).

Univariate logistic regression analyses examining two-group comparisons for 1-, 3-, and 6-hour bundle completion are presented in **Table 2**. Completion of the 1-hour bundle was significantly linked with a reduction in in-hospital mortality ($p = 0.005$). Similarly, completion of the 3-hour and 6-hour bundles also demonstrated lower mortality risks, with odds ratios (ORs) of 0.603 and 0.511, respectively ($p < 0.001$ for both). Additional univariate findings indicated that advanced age, higher Sequential Organ Failure Assessment (SOFA) scores, and elevated Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) scores were each associated with increased risk of in-hospital mortality.

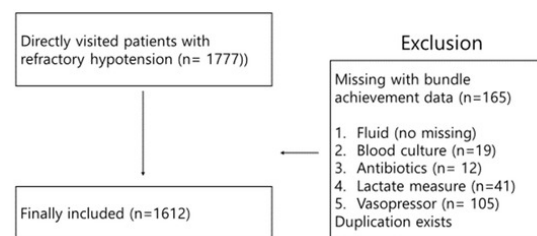


Figure 1. Flowchart illustrating the process of patient enrollment and selection

Table 1. Clinical Characteristics and Outcomes Across Three Bundle Groups

Variables	Group 1 (≤ 1 h) (n = 461)	Group 2 (1–3 h) (n = 637)	Group 3 (3–6 h) (n = 293)	p Value
Age, years	68 (60–76)	70 (59–78)	71 (60–78)	0.063
Male, n (%)	255 (55.3)	352 (55.2)	173 (59.0)	0.514
Initial Vital Signs				
SBP, mm Hg	91 (77–111)	89 (74–108)	88 (74–107)	0.152
DBP, mm Hg	56 (48–67)	54 (45–64)	54 (46–64)	0.057
Heart rate, beats/min	111 (94–128)	111 (93–127)	111 (94–130)	0.899
Respiratory rate, breaths/min	20 (18–24)	20 (18–22)	20 (18–23)	0.054
Body temperature, °C	38.1 (37.1–38.9)	38.0 (36.9–39.0)	38.0 (36.8–38.8)	0.256
Comorbidities, n (%)				
Hypertension	184 (39.9)	252 (39.5)	103 (35.1)	0.361
Diabetes mellitus	105 (22.7)	180 (28.2)	73 (24.9)	0.114
Cardiac disease	81 (17.5)	72 (11.3)	33 (11.2)	0.005
COPD	40 (8.6)	46 (7.2)	20 (6.8)	0.566
CKD	33 (7.1)	47 (7.3)	17 (5.8)	0.668
Chronic liver disease	57 (12.3)	68 (10.6)	25 (8.5)	0.253
Infection Site, n (%)				
Respiratory	123 (26.6)	128 (20.1)	66 (22.5)	0.036
Urinary tract	93 (20.1)	140 (21.9)	51 (17.4)	0.271
Gastrointestinal tract	48 (10.4)	104 (16.3)	37 (12.6)	0.016
Hepato-biliary and pancreas	85 (18.4)	96 (15.1)	57 (19.4)	0.167
Others*	20 (4.3)	32 (5.0)	18 (6.1)	0.543
Lactate, mmol/L	2.5 (1.7–3.5)	2.7 (1.6–4.8)	3.2 (1.9–5.0)	< 0.0001

SOFA	6 (4–8)	6 (4–8)	6 (4–8)	0.635
APACHE II	19 (13–25)	19 (13–25)	21 (15–27)	0.021
Positive blood culture, n (%)	208 (45.1)	289 (45.3)	135 (46.0)	0.966
Outcomes, n (%)				
In-hospital mortality	64 (13.8)	108 (16.9)	59 (20.1)	0.075
28-day mortality (n = 1292)	57 (13.2)	98 (16.4)	55 (20.6)	0.037
90-day mortality (n = 1148)	102 (26.1)	138 (26.4)	75 (31.7)	0.243

APACHE 2: Acute Physiology and Chronic Health Evaluation 2; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; SOFA: Sequential Organ Failure Assessment. Continuous variables are expressed as median (Q1–Q3) and compared using the Kruskal–Wallis test, while categorical variables are reported as n (%) and analyzed with the chi-squared test. * “Others” refers to infection sites including soft tissue, central nervous system, catheter-related infections, bloodstream infections, and endocarditis.

Table 2. Univariate and Multivariable Logistic Regression Analysis for In-Hospital Mortality

Variables	Unadjusted OR	95% CI of OR	p Value	Adjusted OR	95% CI of OR	p Value
Bundle Achievement (2-Group Comparison)						
1-h bundle (<1 h vs. >1 h)	0.649	0.481–0.877	0.005	0.740	0.522–1.049	0.091
3-h bundle (<3 h vs. >3 h)	0.603	0.465–0.783	<0.001	0.604	0.446–0.819	0.001
6-h bundle (<6 h vs. >6 h)	0.511	0.369–0.707	<0.001	0.458	0.312–0.672	<0.01

CI: Confidence Interval, OR: Odds Ratio

Multivariable logistic regression analysis of 1-, 3-, and 6-Hour bundle completion for in-hospital mortality (Two-group comparison)

In the multivariable logistic regression analysis, achieving the 1-hour bundle (<1 h vs. >1 h) was associated with an adjusted odds ratio (OR) of 0.74 for in-hospital mortality, but this did not reach statistical significance (95% confidence interval [CI]: 0.522–1.049, $p = 0.091$) (**Table 2**). By contrast, completion of the 3-hour bundle (<3 h vs. >3 h) was significantly linked to reduced in-hospital mortality (OR = 0.604, 95% CI: 0.446–0.819, $p = 0.001$). Similarly, patients who completed the 6-hour bundle showed a significant reduction in in-hospital mortality (OR = 0.458, 95% CI: 0.312–0.672, $p < 0.01$).

Time-dependent analysis across three groups: Group 1 (≤ 1 h; Reference), group 2 (1–3 h), and group 3 (3–6 h)

To explore whether the timing of bundle completion influenced outcomes, multivariable analyses were conducted using Group 1 (≤ 1 h) as the reference. The cohort included 461 patients in Group 1, 637 in Group 2, and 293 in Group 3. Comparison of in-hospital mortality across the three groups revealed no statistically significant differences or consistent temporal trend in risk for Groups 2 or 3 relative to the reference group.

Additional multivariable models were applied to evaluate 28-day mortality, again using Group 1 as the reference. No significant differences were observed for either Group 2 or Group 3 compared with Group 1. Similarly, analysis of 90-day mortality demonstrated no significant variation among the three groups.

In this research, achieving the 1-hour bundle did not independently correlate with improved outcomes among patients with septic shock presenting to the emergency department. Additionally, no consistent linear relationship

was observed between delays in bundle completion and patient outcomes. Conversely, completing the 3-hour and 6-hour bundles was associated with improved survival.

To our knowledge, this is the first investigation specifically evaluating the impact of full 1-hour bundle adherence on septic shock outcomes. While prior studies have examined individual components of sepsis bundles, few have assessed the prognostic significance of completing the entire bundle. Our analysis benefits from a prospectively collected, multicenter dataset with a large sample size, which included precise timing information for all bundle elements. Although the registry was not originally designed to assess 1-hour bundle efficacy, the availability of detailed temporal data allows meaningful insight into this question. Given ongoing debate surrounding the clinical value of the 1-hour bundle, these findings provide a foundation for further research and may guide clinicians in optimizing sepsis management.

The overall effectiveness of sepsis bundles remains controversial [11, 17–19]. For instance, a multicenter retrospective cohort evaluating compliance with the SEP-1 performance measure found higher crude mortality among patients who did not meet the bundle, yet no significant difference persisted after adjusting for disease severity and clinical variables [20]. SEP-1, like the 1-hour bundle, includes five key interventions, although its timing targets are set at 3 and 6 hours rather than 1 hour. Similarly, Baghdadi *et al.* reported that timely lactate measurement reduced mortality, but adherence to the complete SEP-1 bundle did not confer additional survival benefit in hospital- or community-onset sepsis [21]. A systematic review further concluded that there is no high- or moderate-quality evidence demonstrating that SEP-1 or its hemodynamic interventions improve adult sepsis survival [22].

In contrast, a study in New York analyzing the effect of 3-hour bundle completion among 49,311 patients across 149

hospitals found that faster bundle implementation was associated with lower in-hospital mortality [9]. Longer delays were linked with progressively higher risk-adjusted mortality. While our study also demonstrated better outcomes for patients achieving bundles versus those who did not in two-group comparisons, overall differences between groups defined by time to completion were not statistically significant. It is important to note that our bundle included five interventions, whereas the New York study evaluated only three (blood culture, lactate measurement, and antibiotic administration), making direct comparison challenging.

Several limitations of our study should be acknowledged. First, the registry was not explicitly designed to evaluate 1-hour bundle implementation, and our analysis is a secondary evaluation of prospectively collected data rather than a dedicated performance-improvement initiative. Second, patients presenting with hypoperfusion but without overt hypotension were excluded, limiting generalizability to cryptic shock populations. Third, defining the time of shock recognition as the onset of refractory hypotension raises uncertainty regarding whether the rapid 30 mL/kg crystalloid infusion was initiated within 1 hour. However, the median time from ED triage to fluid completion was 87 minutes, suggesting that fluid resuscitation was likely initiated promptly. Fourth, as with all registry-based observational studies, residual confounding by unmeasured variables cannot be excluded despite multivariable adjustment. Finally, inter-hospital differences in outcomes were not analyzed in this study.

Conclusion

In this cohort, 28.6 percent of septic shock patients achieved the 1-hour bundle in the emergency department. Completion of the 1-hour bundle was not independently associated with improved outcomes, and no linear relationship between delay in bundle implementation and patient outcomes was observed. In contrast, achievement of the 3-hour and 6-hour bundles was linked to better outcomes compared with patients who failed bundle completion in two-group comparisons. These findings highlight the need for further research to clarify the clinical significance and potential benefits of rapid 1-hour bundle implementation in septic shock management.

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References

1. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: Analysis for the Global Burden of Disease Study. *Lancet*. 2020;395:200–11.
2. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315:801–10.
3. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: Secondary analysis of the ICNARC Case Mix Programme Database. *Crit Care*. 2006;10:R42.
4. Kaukonen KM, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000–2012. *JAMA*. 2014;311:1308–16.
5. Rhee C, Gohil S, Klompas M. Regulatory mandates for sepsis care—reasons for caution. *N Engl J Med*. 2014;370:1673–6.
6. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock: 2016. *Intensive Care Med*. 2017;43:304–77.
7. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign bundle: 2018 update. *Intensive Care Med*. 2018;44:925–8.
8. Society of Critical Care Medicine (SCCM). Surviving Sepsis Campaign: Guidelines for adult patients [Internet]. Available from: <https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Adult-Patients> [Accessed 10 Oct 2019].
9. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, et al. Time to treatment and mortality during mandated emergency care for sepsis. *N Engl J Med*. 2017;376:2235–44.
10. Marik PE, Farkas JD, Spiegel R, Weingart S. Rebuttal from Drs. Marik, Farkas, Spiegel et al. *Chest*. 2019;155:17.
11. Marik PE, Farkas JD, Spiegel R, Weingart S, Abernethy S, Beck-Esmay J, et al. POINT: Should the Surviving Sepsis Campaign guidelines be retired? Yes. *Chest*. 2019;155:12–4.
12. Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med*. 2015;372:1301–11.
13. ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. *N Engl J Med*. 2014;370:1683–93.

14. Ko BS, Kim K, Choi SH, Kang GH, Shin TG, Jo YH, et al. Prognosis of patients excluded by the definition of septic shock based on their lactate levels after initial fluid resuscitation: A prospective multicenter observational study. *Crit Care*. 2018;22:47.
15. Jung SM, Kim YJ, Ryoo SM, Kim WY. Relationship between low hemoglobin levels and mortality in patients with septic shock. *Acute Crit Care*. 2019;34:141.
16. Ryoo SM, Han KS, Ahn S, Shin TG, Hwang SY, Chung SP, et al. Usefulness of C-reactive protein and procalcitonin to predict prognosis in septic shock patients: A multicenter prospective registry-based observational study. *Sci Rep*. 2019;9:1–8.
17. Levy MM, Rhodes A, Evans LE, Antonelli M, Bailey H, Kesecioglu J, et al. COUNTERPOINT: Should the Surviving Sepsis Campaign guidelines be retired? No. *Chest*. 2019;155:14–7.
18. Freund Y, Khoury A, Möckel M, Karamercan M, Dodt C, Leach R, et al. European Society of Emergency Medicine position paper on the 1-h sepsis bundle of the Surviving Sepsis Campaign: Expression of concern. *Eur J Emerg Med*. 2019;26:232–3.
19. Murri R, Taccari F, Palazzolo C, Fantoni M, Cauda R. IDSA did not endorse the Surviving Sepsis Campaign guidelines. *Clin Infect Dis*. 2018;66:1815–6.
20. Rhee C, Filbin M, Massaro AF, Bulger A, McEachern D, Tobin KA, et al. Compliance with the national SEP-1 quality measure and association with sepsis outcomes: A multicenter retrospective cohort study. *Crit Care Med*. 2018;46:1585.
21. Baghdadi JD, Brook RH, Uslan DZ, Needleman J, Bell DS, Cunningham WE, et al. Association of a care bundle for early sepsis management with mortality among patients with hospital-onset or community-onset sepsis. *JAMA Intern Med*. 2020;180:707–16.
22. Pepper DJ, Jaswal D, Sun J, Welsh J, Natanson C, Eichacker PQ. Evidence underpinning the CMS severe sepsis and septic shock management bundle (SEP-1): A systematic review. *Ann Intern Med*. 2018;168:558–68.