The Journal of Emergency Medicine, Vol. ■, No. ■, pp. 1–9, 2017

0736-4679/$ - see front matter

https://doi.org/10.1016/j.jemermed.2017.09.001

Original Contributions

CLINICAL FACTORS AND OUTCOMES OF DIALYSIS-DEPENDENT END-STAGE RENAL DISEASE PATIENTS WITH EMERGENCY DEPARTMENT SEPTIC SHOCK

Kevin M. Lowe, MSN, ACNP-BC, CNN-NP,* Alan C. Heffner, MD, FCCM,†‡ and Colleen H. Karvetski, PHD§

*Center for Advanced Practice, Medical Critical Care Fellowship, Carolinas Healthcare System, Charlotte, North Carolina, †Department of Emergency Medicine, ‡Department of Internal Medicine, Division of Critical Care, Carolinas Medical Center, Charlotte, North Carolina, and §Information and Analytics Services, Carolinas Healthcare System, Charlotte, North Carolina

Reprint Address: Alan C. Heffner, MD, FCCM, Department of Internal Medicine and Department of Emergency Medicine, Carolinas Medical Center, 1000 Blythe Blvd., MEB 5, Charlotte, NC 28203

☐ **Abstract—Background: Infection is the second leading cause of death in end-stage renal disease (ESRD) patients. Prior investigations of acute septic shock in this specific population are limited. Objective: We aimed to evaluate the clinical presentation and factors associated with outcome among ESRD patients with acute septic shock. Methods: We reviewed patients prospectively enrolled in an emergency department (ED) septic shock treatment pathway registry between January 2014 and May 2016. Clinical and treatment variables for ESRD patients were compared with non-ESRD patients. A second analysis focused on ESRD septic shock survivors and nonsurvivors. Results: Among 4126 registry enrollees, 3564 (86.4%) met inclusion for the study. End-stage renal disease was present in 3.8% (n = 137) of ED septic shock patients. Hospital mortality was 20.4% and 17.1% for the ESRD and non-ESRD septic shock patient groups ($p = 0.31$). Septic shock patients with ESRD had a higher burden of chronic illness, but similar admission clinical profiles to non-ESRD patients. End-stage renal disease status was independently associated with lower fluid resuscitation dose, even when controlling for severity of illness. Age and admission lactate were independently associated with mortality in ESRD septic shock patients. Conclusion: ESRD patients comprise a small but important portion of patients with ED septic shock. Although presentation clinical profiles are similar to patients without ESRD, ESRD status is independently associated with lower fluid dose and compliance with the 30-mL/kg fluid goal. Hyperlactatemia is a marker of mortality in ESRD septic shock.** © 2017 Elsevier Inc. All rights reserved.

☐ **Keywords—end-stage renal disease (ESRD); fluid resuscitation; septic shock; sepsis**

INTRODUCTION

Severe sepsis is a leading cause of death in the United States, with an incidence of approximately 300 cases per 100,000 (1). Similarly, infection is the second leading cause of death in patients with end-stage renal disease (ESRD) (2). Infections remain a common admission diagnosis for hemodialysis-dependent patients presenting to the emergency department (ED) (3). Despite this information, prior investigations of acute septic shock in the ESRD population are limited. We aimed to evaluate the clinical presentation, infection source, treatments, and outcomes of ESRD patients with acute septic shock and compare them with septic shock patients without ESRD.

METHODS

Design and Setting

Our health care system has a "Code Sepsis" clinical pathway for the management of adult patients with acute septic shock. Enrollment criteria are suspected infection plus persistent hypotension, defined as systolic blood pressure (SBP) < 90 mm Hg or mean arterial pressure

RECEIVED: 8 May 2017; FINAL SUBMISSION RECEIVED: 19 August 2017;
ACCEPTED: 14 September 2017

(MAP) < 65 mm Hg after 20 mL/kg intravenous fluid bolus or serum lactate ≥ 4 mmol/L. The clinical pathway provides standardized management orders, fluid and hemodynamic resuscitation, clinical decision support for infection control measures, and serial monitoring to gauge response to resuscitation.

Enrolled patients are prospectively entered into a master quality improvement registry. Patients enrolled through the ED of one of 13 facilities in the Carolinas HealthCare System within metropolitan Charlotte, North Carolina served as the data source for this investigation. The Institutional Review Board and Privacy Board of Carolinas HealthCare System approved this study under waiver of informed consent.

Identification of Subjects

Clinical pathway enrollees registered between January 1, 2014 and May 31, 2016 served as the initial sample for this investigation. Subjects were divided into two groups based on the presence of ESRD on admission, as determined by International Classification of Diseases (ICD)-9 code 585.6 and ICD-10 code N18.6. We performed dedicated chart review on ESRD subjects to confirm chronic renal failure requiring renal replacement therapy as present on admission. Recognizing provider subjectivity in the clinical diagnosis of early infection, we then excluded patients without a final discharge diagnosis consistent with infection, sepsis, severe sepsis, or septic shock.

Data Collection and Analysis

We utilized a secure online Web application, Research Electronic Data Capture (REDCap) database, for data collection and organization. A single author performed chart reviews of the 219 ESRD patients using a standardized abstraction tool for additional data elements not included in the registry collection. Septic shock patients with ESRD were compared with septic shock patients without ESRD. A second analysis focused on clinical factors associated with hospital death in the ESRD septic shock group.

Continuous data are presented as means ± standard deviation using *t*-test for statistical differences. Categorical data presented as percentages and tested for significance using chi-squared tests of proportions. We considered $p \leq 0.05$ to be significant. In an attempt to identify factors independently associated with resuscitation, we used multiple variable linear regression modeling with fluid volume at 3 h as the dependent variable. A hierarchical logistic regression model was used to determine factors associated with ESRD septic shock death, where comorbidities, demographics, triage clinical markers, sepsis treatment variables, and treatment intensity models were generated. Variables from these models with $p \leq 0.15$ were included in the final model. The reduced final model includes variables significant at $p \leq 0.05$ level.

RESULTS

During the study period, 4126 patients were enrolled in our ED septic shock pathway (Figure 1). Of this group, 219 were coded with ESRD at admission, and 58 were excluded based on chart review that failed to confirm ESRD. We next excluded 504 (12.2% of total; 95% confidence interval [CI] 1.2–13.3) patients based on the absence of confirmed infection. This left a total cohort of 3564 study subjects for analysis. Overall, ESRD was a comorbid factor in 137 (3.8%; 95% CI 3.2–4.5) acute ED septic shock patients.

Comparison of ED Septic Shock with and without ESRD

Demographic and comorbid factors of the two groups are presented in Table 1. Compared with patients without ESRD, ESRD septic shock patients were younger ($p \leq 0.001$), more often female ($p = 0.01$), and more likely to have comorbid factors of diabetes, chronic obstructive pulmonary disease, and heart failure. ESRD patients were more likely to carry a "do not resuscitate" advanced directive status at admission ($p < 0.01$). There was no difference in hospital admission Premier CareScience® (Premier Inc., Charlotte, NC) Mortality Risk Model score or Acute Physiology and Chronic Health Evaluation (APACHE) IV score. ED presentation variables are reported in Table 1. ESRD patients had lower heart rates (96 vs. 106, $p < 0.001$) and triage shock index (0.9 vs. 1.0, $p = 0.01$). There was no significant difference in initial blood lactate between the two groups.

Table 2 demonstrates patient group treatment variables. ESRD patients were less likely to meet 3-h sepsis bundle treatment goals (35.0% vs. 56.3%, $p < 0.001$). Specifically, ESRD patients received less fluid at the 3- and 6-h treatment points ($p < 0.001$) and were less likely to meet the ≥ 30-mL/kg intravenous fluid (IVF) resuscitation goal within 3 h of ED arrival ($p < 0.001$). There was no difference in timeliness of initial antibiotic therapy. ESRD patients had higher rates of central venous catheter placement ($p = 0.001$), but no difference in vasopressor or mechanical ventilation requirements.

Hospital mortality for the entire cohort (n = 3564) was 17.3%. Mortality for septic shock patients with and without ESRD was 20.4% and 17.1%, respectively ($p = 0.31$; absolute difference: 3.3%; 95% CI of mortality difference: −10.2–3.6%). There was no difference in intensive care unit (ICU) length of stay (LOS) (3.3 ± 4.0 vs. 3.0 ± 3.5 days; $p = 0.58$) or hospital LOS (7.3 ± 7.7 vs. 7.6 ± 6.6 days; $p = 0.61$) between the groups.