Contents lists available at ScienceDirect

# Turkish Journal of Emergency Medicine

journal homepage: http://www.elsevier.com/locate/TJEM

**Original Article** 

# Placement of central venous lines for sepsis in the elderly has markedly increased—Evidence from a cohort of New Jersey (USA) emergency departments



Turkish Journal of

## Brandon Close <sup>a</sup>, Peter Richman <sup>a, \*</sup>, Barnet Eskin <sup>b</sup>, John R. Allegra <sup>b</sup>

<sup>a</sup> Christus Spohn/Texas A&M School of Medicine, Corpus Christi, TX, USA

<sup>b</sup> Morristown Medical Center, Morristown NJ and Emergency Medical Associates Research Foundation, Parsippany, NJ, USA

#### ARTICLE INFO

Article history: Received 3 June 2017 Received in revised form 26 October 2017 Accepted 12 November 2017 Available online 27 November 2017

*Keywords:* Central line Sepsis

## ABSTRACT

*Background:* Early goal directed therapy for sepsis patients requires placement of central lines (CVPL) to measure central pressure.

*Objective:* We hypothesized that the percentage of CVPL placed for sepsis has increased over time, whereas the frequency of lines placed for other conditions has not changed.

*Methods:* This was a retrospective cohort study. Investigators analyzed records from consecutive ED patients in nine hospitals over a 10-year period. Patients >65 years identified with CVPL by CPT codes and diagnoses established by ICD-9 codes.

We computed the annual number of patients that had a CVPL placed for sepsis and other conditions. We calculated the change from 2005 and 2014 in the normalized number of patients >65 with sepsis and other conditions and the 95% confidence intervals (CIs).

We normalized the annual number of CVPLs by the average number of total annual visits for those >65 years as the annual visits in the >65 years cohort increased by > 25% over the course of the study. We then plotted the annual number of normalized CVPLs for sepsis and other conditions placed versus year and computed the linear regression coefficients ( $R^2$ ). Alpha was set at 0.05.

*Results:* Of the 3,772520 visits in the data base there were 711,435 visits by patients >65 years; 3184 (0.45%) had CVPL placed and 784 of those patients were treated for sepsis. The percent of patients with CVPL for sepsis increased 212% (95% CI: 115% to 356%) from 2005 to 2014, but there was no statistically significant annual change in percent of CVPL placed for other conditions (10% decrease, 95% CI: -26% to 9%). The linear regression coefficient for the plot of annual normalized number of CVPLs vs. year (See table and plot) was statistically significant for sepsis ( $R^2 = 0.94$ , p < 0.001) but not for other conditions ( $R^2 = 0.09$ , p = 0.80).

*Conclusion:* We found that CVPL placed for sepsis tripled from 2004 to 2011, whereas CVPL placed for other conditions did not change significantly.

Copyright © 2017 The Emergency Medicine Association of Turkey. Production and hosting by Elsevier B.V. on behalf of the Owner. This is an open access article under the CC BY-NC-ND license (http:// creativecommons.org/licenses/by-nc-nd/4.0/).

## 1. Introduction

Sepsis is a common and costly condition in the United States that places patients at significant risk of morbidity and mortality.

\* Corresponding author. Department of Emergency Medicine, Christus Spohn/ Texas A&M School of Medicine, Corpus Christi, TX 78405, USA.

E-mail address: PRichmanMDMBA@gmail.com (P. Richman).

Around 751,000 cases of severe sepsis occur annually with half of these patients admitted to ICUs and 17% requiring mechanical ventilation at some point in their hospital stay.<sup>1</sup> Overall mortality rates from sepsis are from 20–50%.<sup>1–3</sup> The average cost is \$22,000 per case and the U.S. spends nearly \$17 billion per year on this condition alone.<sup>1</sup>

The incidence of sepsis, rates of hospitalization, and mortality increase with age.<sup>1–3</sup> Patients ages 80 years and older are at particular risk, with mortality rates that approach 10%.<sup>1</sup> Concomitant conditions, including, malignancy, chronic kidney disease, congestive heart failure and diabetes, increase risk of morbidity and

https://doi.org/10.1016/j.tjem.2017.11.002

Peer review under responsibility of The Emergency Medicine Association of Turkey.

<sup>2452-2473/</sup>Copyright © 2017 The Emergency Medicine Association of Turkey. Production and hosting by Elsevier B.V. on behalf of the Owner. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

readmission rate.<sup>4</sup> Over the past several years, CMS has tied hospital reimbursement to quality care measures and use of care bundles.<sup>5</sup> To date, there is a relative paucity of research to evaluate how such measures have influenced physician practices, utilization of resources, and the cost to care for elderly sepsis patients.

Undoubtedly, CMS was influenced to establish sepsis care bundles by research published in 2001 that showed the positive benefits of early goal directed therapy (EGDT)<sup>6</sup> Rivers et al. reported a significant decrease in mortality and less severe organ dysfunction when they utilized a specific EGDT protocol that required placement of a CVPL to guide the efficacy of resuscitation for severe sepsis and septic shock.<sup>6</sup> Subsequently, the Surviving Sepsis Campaign guidelines recommend EGDT in the treatment of sepsis.<sup>7,8</sup> This was an international effort intended to improve sepsis care by directing physicians to focus on EGDT in the first 6 h of sepsis care.<sup>8</sup>

With emergency physicians directly in the line of fire for meeting this new early sepsis standard, researchers asked whether less invasive methods of early intervention would be equally efficacious. Several investigators found that resuscitation adequacy could be safely ascertained through less invasive means including lactate clearance and structured traditional therapy without the need for CVPL placement and ScV02 measurements.<sup>9–12</sup> Nonetheless, new findings take time to be accepted into practice, so we hypothesized that the Rivers et al. study and Surviving Sepsis Campaign would still have had a profound influence on the utilization of CVPL by ED clinicians following the publication of the Rivers study. In this study, we compared the frequency for which CVPL were placed for sepsis versus for other conditions in a multicenter cohort after the publication of the Rivers study.

## 2. Materials and methods

## 2.1. Study design

We performed a retrospective review of a multi-center database of ED patients to assess the frequency of CVPL placement for patients with sepsis versus other indications.

#### 2.2. Setting

Data was collated from EDs in nine New Jersey hospitals that shared a common EMR during the period from January 2005–Sept 2014. The study was approved by the Morristown Medical Center Institutional Review Board. Data was collected from nine New Jersey suburban and urban emergency departments with annual visits from 22,000 to 82,000. All of the hospitals used the same billing service. Coders in the ED physicians' billing department assign codes to each patient based on the clinicians' written diagnoses, using International Classification of Diseases, Ninth Revision, and Clinical Modification Codes (ICD9).

## 2.3. Population

Patients age >65 years who received a CVPL were identified by the Current Procedural Terminology (CPT) code (36556) and further stratified for diagnosis based on primary, secondary and tertiary ICD-9 code descriptors: sepsis, septic shock and septicemia.

## 2.4. Data analysis

We computed the annual number of patients that had a CVPL placed for sepsis and other conditions. We calculated the change from 2005 and 2014 in the percentage of patients >65 with sepsis and other conditions and the 95% confidence intervals (CIs). We

used the percent rather than actual numbers as the annual visits in the >65 years cohort increased by > 25% over the course of the study. We therefore also normalized the annual number of CVPLs by the average number of total visits for those >65 years as the annual visits increased over the course of the study. We then plotted the annual number of normalized CVPLs placed versus year and computed the linear regression coefficients ( $R^2$ ). T-tests were utilized to analyze continuous variables. Alpha was set at 0.05. We utilized EXCEL Version 14.0 (Redmond, Washington) for computations.

Results: Of the 3,772520 visits in the data base there were 711,435 visits by patients >65 years; 3184 (0.45%) had CVPL placed and 784 of those patients were treated for sepsis. The mean age, interquartile range and percent females were respectively: for sepsis [80.0 years, (73.1–86.4), 52.3\%] and for other conditions [79.4 years (72.3–85.4), 57.1\%].

The percent of patients with CVPL for sepsis increased 213% (95% CI: 115% to 356%) from 2005 to 2014, but there was no statistically significant annual change in percent of CVPL placed for other conditions (10% decrease, 95% CI: -26% to 9%). The linear regression coefficient for the plot of annual normalized number of CVPLs vs. year (See Table 1 and Fig. 1) was statistically significant for sepsis ( $R^2 = 0.94$ , p < 0.0001) but not for other conditions ( $R^2 = 0.09$ , p = 0.8).

#### 3. Discussion

At the turn of the century, Rivers et al. profoundly influenced the care of sepsis when their study showed the benefits of EGDT and invasive monitoring of sepsis patients.<sup>6</sup> The authors randomized patients with severe sepsis or septic shock into two treatment arms, one with standard therapy, and the other with 6 h emergency department goal-directed care prior to transfer to the intensive care unit. Rivers et al. reported higher mean central venous oxygen saturation levels in the EGDT group and markedly improved inhospital mortality for EGDT patients versus standard therapy (31% vs. 47%).

It would be nearly a decade before other investigators provided evidence that invasive monitoring might not lead to improved outcomes as compared with alternative markers of resuscitation efficacy. Jones et al. conducted a non-inferiority, multi-center randomized trial involving 300 patients to assess the safety of use lactate clearance as a surrogate for central venous oxygen saturation in EGDT.<sup>9</sup> During the first six hours of care, clinicians normalized central venous pressure and mean arterial pressure in both treatment arms. However, each group had an additional treatment endpoint with physicians seeking to maintain an ScV02 of at least 70% in the invasive monitoring group vs 10% lactate clearance for the non-invasively monitored group. The investigators found that mortality was 23% and 17%, in the ScvO2 and

Table 1

Number of patients >65 Years who had CVPs placed for sepsis and other conditions (Normalized by average annual visits for patients > 65 years).

Year	Sepsis	Other
2005	40	242
2006	54	259
2007	58	226
2008	69	243
2009	68	241
2010	81	232
2011	79	267
2012	103	224
2013	101	246
2014	125	218





lactate clearance groups respectively (95% CI for the difference = -3% to 15%). Furthermore, there were no significant change in treatment related adverse events. Subsequent studies evaluating the utility of lactate clearance in combination with other biomarkers and lung ultrasound appear to confirm the findings of Jones et al.<sup>13,14</sup>

The ProCESS study conducted at 31 centers represented a significant advance towards establishing the safety of non-invasive monitoring of sepsis resuscitation.<sup>10</sup> Over 1300 patients were randomized to one of three treatment arms, including protocol-based EGDT, protocol-based standard therapy, and usual care. Standard therapy did not require the use of central venous catheters, inotropes, and/or blood transfusions. The primary outcome measure was 60-day in-hospital mortality. The ProCess authors observed 21, 18, and 19% 60-day mortality in the EGDT, standard, and usual care groups, respectively<sup>10</sup>; these were not statistically significantly different. Other major outcome measures, such as 90-day mortality, 1-year mortality, and the need for organ support were also similar between treatment groups. The findings in the ProCess study mirrored those observed previously in the 1600 patient ARISE study in which septic patients without CVPL/invasive monitoring (usual care) had similar 90-day mortality rates as those observed within an EGDT group (18.6 vs. 18.8%; p = 0.90).

With these aforementioned studies suggesting similar efficacy, investigators in England have recently questioned the cost effectiveness of EGDT vs usual care.<sup>12</sup> Mouncey et al. (ProMISe trial) enrolled 1260 patients at 56 hospitals assigned to receive either EGDT or usual care. At the 90-day endpoint, 29.5% of patients in the EGDT group had died vs 29.2% in the usual care group (OR 1.01; 0.85–1.2). They concluded that "on average, EGDT increased costs, and the probability that it was cost-effective was below 20%." The increasing evidence in favor of less invasive management of sepsis has not gone unnoticed by organizations with the power to influence practice changes. The new Surviving Sepsis Campaign has recently removed CVPL placement and ScvO2 as components of their recommendations.<sup>15</sup>

Our results illustrate just how far the emergency medicine practice of sepsis will need to readjusted in order to return to a less invasive pattern of care. Over a period of 8 years (2004–2011), we observed a 3.4 fold increase in the number of central lines placed for sepsis within a large multi-center database of elderly patients. This increase occurred while the frequency of placement of CVPL was essentially constant for elderly patients with other diagnoses. Although we can only speculate as to the reasons behind this finding, in all likelihood, emergency physicians increased the use of

CVPL for sepsis because of the Rivers study and subsequent guidelines based on the Rivers study. In view of the soaring costs to government to insure the elderly, our results suggest an opportunity to reduce expenditures for Medicare-aged patients with sepsis by requiring less invasive resuscitation monitoring.

Our study has several limitations. First of all, the retrospective nature of our analysis does not provide full details of each patient encounter. Thus, we are unable to differentiate between CVPL that were placed due to difficult peripheral access versus those placed solely for monitoring purposes. Likewise, we identified the placement of CVPL for patients solely by CPT codes. While this likely led to some underreporting, we suspect that this would be occur similarly for septic patients and those with other diagnoses. In addition, our results may not be generalizable to other settings as our participating institutions were largely suburban, community EDs. However, it is likely that inner-city and academic centers would have also been equally influenced by the Rivers et al. and resultant quality measures that existed at that time.

The majority of studies that have shown safety for non-invasive methods to measure the adequacy of sepsis resuscitation largely were published toward the end or after our study period ended.<sup>9–12,14</sup> Thus, we do not know how these studies will have influenced practice at our study centers over the past 4 years. Our study illustrates the potential influence of a single study (Rivers et al.) to dramatically change practice and the frequency by which invasive procedures are performed on patients. Future investigators should evaluate how effectively more recent studies supporting non-invasive management of these patients have been promulgated into the practice of emergency medicine.

Finally, our study group only included elderly patients. Nonelderly adults comprise a large (need number) subset of septic patients. Future studies should evaluate whether similar patterns of increased use of CVPL has occurred in this group as well as whether the pattern has changed over the past several years.

## 4. Conclusions

We found that CVPL placed for sepsis tripled from 2004 to 2011, whereas CVPL placed for other conditions did not significantly change. Recent research suggests that invasive monitoring of central venous pressure may not be necessary to optimize care, and, therefore, our findings suggest an opportunity for future cost savings in the care of elderly septic patients.

## **Conflict of interest**

The authors do not have any conflicts/financial relationships to disclose.

#### References

- Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med.* 2001;29:1303–1329. https://doi.org/10.1097/00003246-200107000-00002, 1.
- Kumar G, Kumar N, Taneja A, et al. Milwaukee initiative in critical care outcomes research group of investigators. Nationwide trends of severe sepsis in the 21st century (2000-2007). *Chest.* 2011 Nov;140(5):1223–1231. https:// doi.org/10.1378/chest. 11-0352. Epub 2011 Aug 18.
- Dombrovskiy VY, Martin AA, Sunderram J, Paz HL. Rapid increase in hospitalization and mortality rates for severe sepsis in the United States: a trend analysis from 1993 to 2003. Crit Care Med. 2007;35:1244–1335. https:// doi.org/10.1097/01.CCM.0000261890.41311.E9, 1.
- Goodwin AJ, Rice DA, Simpson KN, Ford DW. Frequency, cost, and risk factors of readmissions among severe sepsis survivors. *Crit Care Med.* 2015 Apr;43(4): 738–746. https://doi.org/10.1097/CCM.00000000000859.
- Proposed Clinical Quality Measures for 2014 CMS EHR Incentive Programs for Eligible Hospitals and CAHs. CMS.gov.
- 6. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the

treatment of severe sepsis and septic shock. N Engl J Med. 2001;345: 1368–2345. https://doi.org/10.1056/NEJMoa010307.

- Zhang Ling, Zhu Guijun, Han Li, Fu Ping. Early goal-directed therapy in the management of severe sepsis or septic shock in adults: a meta-analysis of randomized controlled trials. *BMC Med.* 2015 Apr 3. https://doi.org/10.1186/ s12916-015-0312-9. Published online.
- Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41:580–641. https://doi.org/10.1097/CCM.0b013e31827e83af, 58.
- Jones AE, Shapiro NI, Trzeciak S, et al. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010;303. https://doi.org/10.1001/jama.2010.158, 739–303.
- Yealy DM, Kellum JA, Huang DT, et al. A randomized trial of protocol-based care for early septic shock. N Engl J Med. 2014;370:1683–2370. https://doi.org/ 10.1056/NEJMoa1401602.
- 11. Peake SL, Bailey M, Bellomo R, et al. ARISE Investigators, for the Australian and New Zealand Intensive Care Society Clinical Trials Group. Australasian

resuscitation of sepsis evaluation (ARISE): a multi-centre, prospective, inception cohort study. *Resuscitation*. 2009 Jul;80(7):811–818. https://doi.org/ 10.1016/j.resuscitation.2009.03.008. Epub 2009 May 20.

- Mouncey PR, Osborn TM, Power GS, et al. ProMISe Trial Investigators. Trial of early, goal-directed resuscitation for septic shock. N Engl J Med. 2015 Apr 2;372(14):1301–1311. https://doi.org/10.1056/NEJMoa1500896. Epub 2015 Mar 17.
- Nguyen HB, Loomba M, Yang JJ, et al. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. J Inflamm Lond. 2010 Jan 28;7:6. https://doi.org/10.1186/1476-9255-7-6.
- Coen D, Cortellaro F, Pasini S, et al. Towards a less invasive approach to the early goal-directed treatment of septic shock in the ED. *Am J Emerg Med.* 2014 Jun;32(6):563–568. https://doi.org/10.1016/j.ajem.2014.02.011. Epub 2014 Feb 17.
- 15. Surviving Sepsis Campaign. Updated Bundles in Response to New Evidence; Apr 2015. survivingsepsis.org.