CHEST™

The Volume-Outcome Relationship in Critical Care
A Systematic Review and Meta-analysis

Yên-Lan Nguyen, MD, MPH; David J. Wallace, MD, MPH; Youri Yordanov, MD; Ludovic Trinquart, PhD; Josefin Blomkvist, MSc; Derek C. Angus, MD, MPH, FCCP; Jeremy M. Kahn, MD; Philippe Ravaud, MD, PhD; and Bertrand Guidet, MD

OBJECTIVE: The purpose of this study was to systematically review the research on volume and outcome relationships in critical care.

METHODS: From January 1, 2001, to April 30, 2014, MEDLINE and EMBASE were searched for studies assessing the relationship between admission volume and clinical outcomes in critical illness. Bibliographies were reviewed to identify other articles of interest, and experts were contacted about missing or unpublished studies. Of 127 studies reviewed, 46 met inclusion criteria, covering seven clinical conditions. Two investigators independently reviewed each article using a standardized form to abstract information on key study characteristics and results.

RESULTS: Overall, 29 of the studies (63%) reported a statistically significant association between higher admission volume and improved outcomes. The magnitude of the association (mortality OR between the lowest vs highest stratum of volume centers), as well as the thresholds used to characterize high volume, varied across clinical conditions. Critically ill patients with cardiovascular (n = 7, OR = 1.49 [1.11-2.00]), respiratory (n = 12, OR = 1.20 [1.04-1.38]), severe sepsis (n = 4, OR = 1.17 [1.03-1.33]), hepato-GI (n = 3, OR = 1.30 [1.08-1.78]), neurologic (n = 3, OR = 1.38 [1.22-1.57]), and postoperative admission diagnoses (n = 3, OR = 2.95 [1.05-8.30]) were more likely to benefit from admission to higher-volume centers compared with lower-volume centers. Studies that controlled for ICU or hospital organizational factors were less likely to find a significant volume-outcome relationship than studies that did not control for these factors.

CONCLUSIONS: Critically ill patients generally benefit from care in high-volume centers, with more substantial benefits in selected high-risk conditions. This relationship may in part be mediated by specific ICU and hospital organizational factors. CHEST 2015; 148(1):79-92

Manuscript received September 5, 2014; revision accepted March 20, 2015; originally published Online First April 30, 2015.

AFFILIATIONS: From the Anesthesiology and Surgical Critical Care Department (Dr Nguyen), Cochin Hospital, Assistance Publique - Hôpitaux de Paris (APHP), Paris Descartes University, Paris, France; Clinical Epidemiology Center, Institut National de la Santé et de la Recherche Médicale (INSERM) U1153, (Drs Nguyen, Yordanov, Trinquart, and Ravaud and Ms Blomkvist), Hôtel-Dieu Hospital, APHP, Paris, France; Institut Pierre Louis d'Epidémiologie et de Santé Publique INSERM U1136 (Drs Nguyen and Guidet), UPMC Université Paris 06, Sorbonne Universités, Paris, France; CRISMA Center (Drs Wallace, Angus, and Kahn), Department of Critical Care Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA; Emergency Department (Dr Yordanov), Saint Antoine Hospital, APHP, Paris, France; French Cochrane Centre, The Cochrane Collaboration (Drs Trinquart and Ravaud and Ms Blomkvist), Paris, France; and Medical Intensive Care Unit (Dr Guidet), Saint Antoine Hospital, APHP, Paris, France.

FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

CORRESPONDENCE TO: Yên-Lan Nguyen, MD, MPH, Anesthesiology and Surgical Critical Care Department, CHU Cochin, Université Paris Descartes, 27 rue du Faubourg Saint Jacques, 75679 Paris Cedex 14, France; e-mail: yenlanc.nguyen@gmail.com

DOI: 10.1378/chest.14-2195

Volume-outcome relationships are well established in many surgical conditions and high-risk procedures in health care.[1] Under these relationships, higher numbers of procedures are thought to lead to better patient outcomes through the development of procedural skill.[2] Such observations lend conceptual support to the development of regionalized systems of surgical care, in which patients are selectively referred to high-volume providers.[3] Selective referral has substantially improved the quality of care for patients in need of these planned high-risk procedures, with improved outcomes over time due in large part to concentration of care.[2]

Given the current shortage of ICU physicians and the overall complexity of critical illness, critical care is also an attractive target for regionalization. However, unlike in many surgical conditions, the volume-outcome relationship in critical illness is still incompletely characterized.[4] In the absence of a well-defined volume-outcome relationship, regionalization of critical care may increase costs while delaying definitive therapy for extremely sick patients in need of rapid diagnosis and treatment. Moreover, regionalization is only one potential strategy for region-wide organization of critical care.[5] Without a greater understanding of the mechanism of the volume-outcome relationship, which may in part be determined by organizational factors that are correlated with volume, we may miss out on opportunities to improve outcomes for small-volume providers without large-scale reorganization of care.

The goal of this study was to perform a systematic review of literature to assess the volume-outcome relationship among critically ill adult patients. In addition to providing summary information, we sought to understand organizational factors that may be potential mechanisms for this effect by analyzing the differences between positive and negative studies.

Materials and Methods

We performed a systematic review of research studies examining the volume-outcome relationship in critical care. The complete review protocol was submitted to the PROSPERO registry of systematic reviews (CRD42011001265) prior to beginning the study search, study review, data extraction, and analyses.

Study Selection Criteria

Eligible studies were observational studies that assessed the association between critically ill admissions volume (at either the level of the hospital, ICU, ED, or physician) and patient mortality (within the ICU, hospital, or a fixed time period after admission). All observational studies including registries and retrospective observational analyses of existing clinical or administrative databases were eligible. We excluded studies on volume and outcome in trauma, neonatal critical care, and pediatric critical care as these service lines are already extensively regionalized. We also excluded studies when we either could not determine the proportion of patients who were admitted to an ICU or the proportion of patients in the ICU was $<50\%$.

Search Methods

To identify candidate studies we searched MEDLINE and EMBASE for English-language articles published between January 1, 2001, and April 30, 2014. Our search algorithm included medical subject heading terms and text words for both critical illness and clinical conditions that are likely to result in critical illness (e-Appendix 1, e-Table 1). All searches were combined in a reference manager database (Resyweb). When articles separately analyzed distinct clinical conditions, we analyzed the data of each condition separately, treating the data as separate studies. We excluded studies published before 2001 because the practice of critical care and critical care outcomes has changed considerably since that time.[6,7] We also searched several other sources: we reviewed the reference lists of selected studies, we contacted experts in the field to identify missed or unpublished studies, and we performed a manual examination of abstracts books from the main international meetings of critical care medicine (International Symposium on Intensive Care and Emergency Medicine, European Society Intensive Care Medicine Meeting, Society of Critical Care Medicine) between 2007 and 2014 to locate additional relevant titles. For studies published in abstract form, the primary author was contacted to identify manuscripts in progress.

Study Selection, Data Collection, and Analyses

Identifying Studies: All retrieved records and reports were assessed independently by two authors. First, titles and abstracts were screened to identify obvious exclusions (ie, records that were found by our electronic searches but were clearly irrelevant to this review). Second, full-text reports were retrieved to determine whether they met the selection criteria. Any disagreements were resolved through discussion.

Data Extraction: Data extraction was performed independently by two authors using a prespecified data extraction form. Information extracted included the following: study characteristics (study design, period, and setting); patient characteristics (inclusion and exclusion criteria); definition of volume (unit of measurement, continuous or categorical variable and, if categorical, thresholds); outcomes (mortality in the ED, ICU, hospital, or at a fixed time point, ICU, and hospital lengths of stay); statistical methods (multivariable modeling technique, adjustment for cluster effect, and list of adjustment variables); and structural characteristics of the ICU, hospital, and health system. We collected the effect size quantifying the strength of the association between volume and mortality. We collected all available estimates, regardless of the unit of measurement for volume, the method of operationalizing volume, the end point, and the type of statistical analysis, that is, according to the measurement unit of volume (at the hospital, unit, or care provider level), to the definition of the volume variable (continuous or categorical), to the end point (intensive care, in-hospital, or 30-day mortality), and according to the analysis (raw or adjusted estimates). For each study, two authors evaluated independently the risk of bias using a modification of a previously published approach to effectiveness reviews.[8] This scale included attributes of risk adjustment, adjustment for correlated data, and adjustment for temporal trends.

Data Analysis

First, among selected studies, we checked the data used to exclude in the final analysis results from subpopulation of studies already included. For the synthesis, we initially planned to primarily focus on the volume treated as a continuous variable. However, the most frequently reported measure of the volume-outcome effect was the OR of death in patients treated in a low-volume center compared with patients treated in a high-volume center, so that an $OR>1$ would indicate increased risk in low-volume compared with high-volume center. Because of considerable variability in the numbers of categories used (defined according