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A View of the Literature

The most influential articles in critical care medicine☆

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Keywords:
Critical care;
ICU;
Citation classics;
Landmark articles

Abstract

Purpose: The study aimed to examine query strategies that would provide an exhaustive search method to retrieve the most referenced articles within specific categories of critical care.

Material and Methods: A comprehensive list of the most cited critical care medicine articles was generated by searching the Science Citation Index Expanded data set using general critical care terms such as “critical care,” critical care journal titles, and keywords for subsubjects of critical care.

Results: The final database included 1187 articles published between 1905 and 2006. The most cited article was referenced 4909 times. The most productive search term was intensive care. However, this term only retrieved 25% of the top 100 articles. Furthermore, 662 of the top 1000 articles could not be found using any of the basic critical care search terms. Sepsis, acute lung injury, and mechanical ventilation were the most common areas of focus for the articles retrieved.

Conclusion: Retrieving frequently cited, influential articles in critical care requires using multiple search terms and manuscript sources. Periodic compilations of most cited articles may be useful for critical care practitioners and researchers to keep abreast of important information.

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1. Introduction

Modern methods to search for important medical literature have recently flourished with the dissemination and near ubiquity of Internet-based search engines (eg, PubMed, MEDLINE, OVID). Articles that have been cited most often, referred to as “citation classics,” are frequently important sources of both detailed information that has changed clinical/research practices as well as of useful connectors to other relevant literature that cites these articles. Finding landmarks or classic articles still requires an understanding of the literature and how articles are referenced. Different databases may categorize disciplines and journals from the same clinical areas under different terms and yield different results when using the same search term.

These referencing differences as well as other conceptual arguments have led to some debate regarding attributing the number of times an article is cited to its quality [1-4] However, there is general agreement that the number of times an article is cited does reflect the “impact of that article on the scientific market” [5].

Garfield [6] first published citation classics of the Journal of the American Medical Association in 1987. Similar studies (citations classic or impact factors) have been published with respect to various clinical specialties [7-15]. In 2004, Baltussen and Kindler [16] published citation classics of the critical care literature and enumerated the 71 top-cited articles in critical care journals and the 45 top-cited critical care articles in non–critical care journals. This article was somewhat limited by the number of citations referenced as

☆ This study was funded entirely by the Department of Anesthesiology, University of Michigan, Ann Arbor, Mich.
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0883-9441/$ – see front matter © 2010 Published by Elsevier Inc.
doi:10.1016/j.jcrc.2008.12.010
well as the absence of specific critical care topic citations groups. The first and primary aim of this study was to expand on Baltussen’s earlier work and provide an updated and more comprehensive catalogue of the most influential articles pertaining to critical care medicine and within specific categories of critical care, something not done in previous studies of this type. We also examined the methods used to retrieve articles to provide an exhaustive search method that future researchers may use in modern electronic databases to find frequently cited critical care articles.

2. Methods

2.1. Creation of master comprehensive list

To develop the most comprehensive master list of most often cited critical care medicine–related articles, we first focused on querying the ISI Web of Knowledge (2008 Thompson Corporation) using the Science Citation Index Expanded (SCI Expanded) data set. The SCI Expanded is a database that provides bibliographic information, abstracts, references, and citations counts for more than 6650 scholarly science and technology journals. The SCI Expanded search was limited to articles published from 1900 to December 31, 2007. To find any article among the broadest selection of scientific journals related to critical care, we searched for any article that contained the keywords “critical-care,” “intensive-care,” “ICU,” or “critically-ill OR critical-illness” and that had been cited more than 100 times. A total of 472 articles were retrieved with this technique after duplicates were removed (see Fig. 1A).

Because many critical care articles found in the SCI Expanded were not tagged by the general keywords noted above, we also searched within critical care journals. To do this, we used the Journal Citation Report (JCR) 2006 to identify journals specializing in critical care medicine from more than 7500 scholarly journals. We first reduced the target list to 16 English-language journals of 18 critical care journals identified by the JCR. We reviewed any article that had been cited more than 100 times and saved articles pertaining to critical care medicine (Fig. 1B). This search resulted in 470 hits; however, we removed 159 duplicate articles that were already found by keyword searches to bring the total database to 783 articles (Fig. 1).

2.2. Creation of disease/condition-specific lists

A representative list of most cited articles for each of the specific critical care topics was created from the existing database and by searching each topic individually using the terms in Table 1. Using these search terms, articles pertinent to
critical care and referenced more than 100 times were added to the database. These searches by specific disease or conditions added 404 articles to the master database as 194 articles were already in the database from either the initial search or from the journal search. From this master database of 1187 articles, we then generated a list of all articles cited more than 150 times (Table 2). We organized this table by topics particularly relevant to critical care. Within each category we listed both the most cited articles within that topic as well as that article’s ranking within the top 200 most cited articles. Finally, we also listed the absolute number of citations for each article.

3. Results

The final database included 1187 articles (Fig. 1). The articles collated in this study came from almost 100 different journals with publication years ranging from 1905 (#149) to 2006 (average publication year = 1991). Surprisingly, of the top 100 most cited critical care articles, 662 were not found using any of the basic critical care search terms—critical care, intensive care, ICU, or critically ill/critical illness. These articles were discovered only after searching within a specific critical care journal (n = 227) or by specific critical care topics (Table 1) (n = 373). In fact, only 4 of the top 1000 articles could be found using any 1 of the 4 basic critical care terms listed above. Of these search terms, the most productive was “intensive care” (25 of top 100 articles), then “critically ill” or “critical illness” (19/100), “ICU” (11/100), and finally “critical care” (5/100). Sepsis/systemic inflammatory response syndrome was the most common topic (193 articles), followed by acute lung injury and mechanical ventilation (177 articles). Overall, 41% of the most cited articles came from critical care journals as designated by the JCR. The most articles were from Critical Care Medicine (23%) followed by American Journal of Respiratory and Critical Care (7%), Journal of Trauma (5%), Intensive Care Medicine (4%), and Shock (1%). Among the non–critical care journals, the New England Journal of Medicine (11%) followed by JAMA (9%) provided the most articles.

4. Discussion

One method to quickly retrieve scholarly articles related to critical care medicine is by using readily available, Internet-based, bibliographic database search tools supported by most medical libraries. We have found, however, that commonly used basic search terms retrieve under only 50% of the most cited and therefore arguably most influential articles in critical care. Therefore, although searches may have become much faster and easier, they may not be sufficient to retrieve a comprehensive list of articles.

We found that there is no single term that exhaustively retrieves all critical care medicine articles. The best generic search term, “intensive care,” only retrieved 25% of what one would consider the 100 of the most influential articles in critical care. Furthermore, the search term “critical care” was linked to only 5 of the top 100 articles, although it is a common keyword used by many search engines. Not to mention the fact that it is in the title of 8 of the 18 “critical care” journals.

One goal of this study was to determine the most efficient search terms for future literature searches. The capriciousness of how efficient a search term is perhaps no better illustrated than with our experience retrieving articles on ICU mortality prediction models. That not one of the basic critical care search terms in the Science Citation Index was tagged to these most influential articles highlights some of the difficulties in finding the most cited studies in critical care. It is clear that even for other types of articles, the best yield of

| Table 1 Specific critical care subjects | Search terms |
|----------------------------------------|--------------|
| Subject area                           | Search terms |
| Sepsis and infectious disease          | “sepsis” “septic” “nosocomial” |
| Mechanical ventilation and lung injury | “ventilation” “respiratory failure” |
| Monitors                               | “hemodynamic-monitor” “CVC” |
| Mental status                          | “coma” “brain-damage” “brain-injury” |
| Physiologic predictors                 | “physiology score” “severity of illness” |
| Organ dysfunction                      | “organ-failure” “organ-dysfunction” |
| Resource utilization                   | “intensivist” “leap frog” “ICU-administration” “critical care management” “ICU management” |
| Kidney injury                          | “kidney-injury” “renal-failure” |
| Resuscitation                          | “life-support” “cardiac-arrest” “cpr” |
| Shock (excluding infectious causes)    | “shock” “hypoperfusion” “CHF” |
| Transfusions                           | “transfusion” “fluid-therapy” |

*Denotes any form of the word preceding the symbol, i.e., septic shock, septic.
## Table 2  Most cited articles in critical care medicine by subject

| Overall Citation Rank | A. Sepsis/systemic inflammatory response syndrome (no. of times cited) |
|-----------------------|-----------------------------------------------------------------------|
| 1. (#6) Tracey, KJ et al. Anti-cachectin TNF monoclonal-antibodies prevent septic shock during lethal bacteremia. Nature 1987. (1983) |
| 2. (#7) Bone, RC et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest 1992. (1389) |
| 3. (#8) Bernard, GR et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 2001. (1827) |
| 4. (#10) Bone, RC et al. American-College of Chest Physicians Society of Critical Care Medicine Consensus Conference—definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992. (1724) |
| 5. (#12) Van den Berghe, G et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001. (1608) |
| 6. (#19) Ziegler, EJ et al. Treatment of gram-negative bacteremia and septic shock with HA-1a human monoclonal-antibody against endotoxin—a randomized, double-blind, placebo-controlled trial. N Engl J Med 1991. (1072) |
| 7. (#22) Angus, DC et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001. (1016) |
| 8. (#25) Bone, RC. The pathogenesis of sepsis. Ann Intern Med 1991. (982) |
| 9. (#28) Waage, A et al. The complex pattern of cytokines in serum from patients with meningococcal septic shock—association between interleukin-6, interleukin-1, and fatal outcome. J Exp Med 1989. (892) |
| 10. (#31) Wichterman, KA et al. Sepsis and septic shock—a review of laboratory models and a proposal. J Surg Res 1980. (846) |
| 11. (#34) Bone, RC et al. A controlled clinical-trial of high-dose methylprednisolone in the treatment of severe sepsis and septic shock. N Engl J Med 1987. (791) |
| 12. (#37) Parrillo, JE. Mechanisms of disease—pathogenetic mechanisms of septic shock. N Engl J Med 1993. (756) |
| 13. (#41) Aneman, D et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002. (712) |
| 14. (#43) Petros, A et al. Effect of nitric-oxide synthase inhibitors on hypotension in patients with septic shock. Lancet 1991. (705) |
| 15. (#52) Cannon, JG et al. Circulating interleukin-1 and tumor necrosis factor in septic shock and experimental endotoxin fever. J Infect Dis 1990. (642) |
| 16. (#55) Casey, LC et al. Plasma cytokine and endotoxin levels correlate with survival in patients with the sepsis syndrome. Ann Intern Med 1993. (624) |
| 17. (#56) Vanzee, KJ et al. Tumor-necrosis-factor soluble receptors circulate during experimental and clinical inflammation and can protect against excessive tumor-necrosis-factor–alpha in vitro and in vivo. Proc Nat Acad Sci USA 1992. (600) |

## Table 2 (continued)  Overall Citation Rank

| A. Sepsis/systemic inflammatory response syndrome (no. of times cited) |
|-----------------------|-----------------------------------------------------------------------|
| 18. (#59) Hack, CE et al. Increased plasma-levels of interleukin-6 in sepsis. Blood 1989. (589) |
| 19. (#62) Moore, FA et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications—the results of a metaanalysis. Ann Surg 1992. (578) |
| 20. (#64) Lowenstein, CJ et al. Nitric-oxide—a physiological messenger. Ann Intern Med 1994. (574) |
| 21. (#69) Fry, DE et al. Multiple system organ failure—role of uncontrolled infection. Arch Surg 1980. (549) |
| 22. (#70) Parker, MM et al. Profound but reversible myocardial depression in patients with septic shock. Ann Intern Med 1984. (548) |
| 23. (#72) Kudsk, KA et al. Enteral versus parenteral-feeding—effects on septic morbidity after blunt and penetrating abdominal-trauma. Ann Surg 1992. (543) |
| 24. (#75) Fisher, CJ et al. Treatment of septic shock with the tumor necrosis factor receptor:Fc fusion protein. N Engl J Med 1996. (540) |
| 25. (#77) Hotchkiss, RS et al. Medical progress: the pathophysiology and treatment of sepsis. N Engl J Med 2003. (538) |
| 26. (#78) Greenman, RL et al. A controlled clinical-trial of E5 murine monoclonal IgM antibody to endotoxin in the treatment of gram-negative sepsis. JAMA 1991. (536) |
| 27. (#81) Martin, GS et al. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med 2003. (529) |
| 28. (#83) Glauser, MP et al. Septic shock—pathogenesis. Lancet 1991. (522) |
| 29. (#89) Dellinger, RP et al. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004. (513) |
| 30. (#94) Bone, RC et al. Sepsis syndrome—a valid clinical entity. Crit Care Med 1989. (506) |
| 31. (#96) Fisher, CJ et al. Recombinant human interleukin-1 receptor antagonist in the treatment of patients with sepsis syndrome—results of a randomized, double-blind, placebo-controlled trial. JAMA 1994. (499) |
| 32. (#97) Parrillo, JE et al. Septic shock in humans—advances in the understanding of pathogenesis, cardiovascular dysfunction, and therapy. Ann Intern Med 1990. (499) |
| 33. (#105) Assicot, M et al. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993. (481) |
| 34. (#109) Ochoa, JB et al. Nitrogen-oxide levels in patients after trauma and during sepsis. Ann Surg 1991. (464) |
| 35. (#114) Moore, FA et al. TEN versus TPN following major abdominal-trauma—reduced septic morbidity. J Trauma 1997. (435) |
| 36. (#120) Abraham, E et al. Efficacy and safety of monoclonal-antibody to human tumor necrosis-factor–alpha in patients with sepsis syndrome—a randomized, controlled, double-blind, multicenter clinical-trial. JAMA 1995. (425) |
Table 2 (continued)

Overall Citation Rank

| A. Sepsis/systemic inflammatory response syndrome (no. of times cited) |
|---|
| 37. (#121) Meakins, JL et al. Delayed-hypersensitivity—indicator of acquired failure of host defenses in sepsis and trauma. *Ann Surg* 1977. (425) |
| 38. (#122) Pinsky, MR et al. Serum cytokine levels in human septic shock—relation to multiple system organ failure and mortality. *Chest* 1993. (422) |
| 39. (#131) Danner, RL et al. Endotoxemia in human septic shock. *Chest* 1991. (409) |
| 40. (#132) Eickhoff, TC et al. Neonatal sepsis + other infections due to group b beta-hemolytic streptococci. *N Engl J Med* 1964. (408) |
| 41. (#134) Wheeler, AP et al. Treating patients with severe sepsis. *N Engl J Med* 1999. (405) |
| 42. (#151) Sprung, CL et al. The effects of high-dose corticosteroids in patients with septic shock—a prospective, controlled-study. *N Engl J Med* 1984. (386) |
| 43. (#153) Damas, P et al. Cytokine serum level during severe sepsis in human il-6 as a marker of severity. *Ann Surg* 1992. (382) |
| 44. (#157) Askhani, J et al. Influence of total parenteral-nutrition on fuel utilization in injury and sepsis. *Ann Surg* 1980. (377) |
| 45. (#162) Docke, WD et al. Monocyte deactivation in septic patients: restoration by IFN-gamma treatment. *Nature Med* 1997. (372) |
| 46. (#168) Petros, A et al. Effects of a nitric-oxide synthase inhibitor in humans with septic shock. *Cardiovasc Res* 1994. (366) |
| 47. (#173) BrunBuisson, C et al. Incidence, risk-factors, and outcome of severe sepsis and septic shock in adults—a multicenter prospective-study in intensive-care units. *JAMA* 1995. (361) |
| 48. (#174) Nava, E et al. Inhibition of nitric-oxide synthesis in septic shock—how much is beneficial. *Lancet* 1991. (361) |
| 49. (#178) Szabo, C. The pathophysiological role of peroxyxinitrite in shock, inflammation, and ischemia-reperfusion injury. *Shock* 1996. (350) |
| 50. (#180) Warren, BL et al. High-dose a randomized antithrombin III in severe sepsis—a randomized controlled trial. *JAMA* 2001. (348) |
| 51. (#181) Bone, RC. Sir Isaac Newton, Sepsis, SIRS, and cars. *Crit Care Med* 1996. (348) |
| 52. (#182) Schumer, W. Steroids in treatment of clinical septic shock. *Ann Surg* 1976. (348) |
| 53. (#183) Damas, P et al. Tumor necrosis factor and interleukin-1 serum levels during severe sepsis in humans. *Crit Care Med* 1989. (346) |
| 54. (#185) Cohen, J et al. The immunopathogenesis of sepsis. *Nature* 2002. (345) |
| 55. (#187) Rush, BF et al. Endotoxemia and bacteremia during hemorrhagic-shock—the link between trauma and sepsis. *Ann Surg* 1988. (341) |
| 56. (#190) Fourrier, F et al. Septic shock, multiple organ failure, and disseminated intravascular coagulation—compared |

Table 2 (continued)

Overall Citation Rank

| A. Sepsis/systemic inflammatory response syndrome (no. of times cited) |
|---|
| 57. (#192) Munoz, C et al. Dysregulation of in vitro cytokine production by monocytes during sepsis. *J Clin Invest* 1991. (336) |

B. Outcome/benchmarking/prediction model articles (no. of times cited)

| 1. (#1) Knaus, WA et al. APACHE-II—a severity of disease classification-system. *Crit Care Med* 1985. (4909) |
| 2. (#4) Baker, SP et al. Injury severity score—method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974. (2637) |
| 3. (#13) Legall, JR et al. A new simplified acute physiology score (SAPS-II) based on a European North-American multicenter study. *JAMA* 1993. (1402) |
| 4. (#14) Knaus, WA et al. The APACHE-III prognostic system—risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991. (1357) |
| 5. (#21) Knaus, WA et al. A controlled trial to improve care for seriously ill hospitalized-patients—the study to understand prognoses and preferences for outcomes and risks of treatments (support). *JAMA* 1995. (1056) |
| 6. (#26) Fine, MJ et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997. (965) |
| 7. (#33) Deitch, EA. Multiple organ failure—pathophysiology and potential future therapy. *Ann Surg* 1992. (793) |
| 8. (#36) Knaus, WA et al. APACHE-acute physiology and chronic health evaluation—a physiologically based classification-system. *Crit Care Med* 1981. (758) |
| 9. (#38) Vincent, JL et al. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intens Care Med* 1996. (735) |
| 10. (#40) Knaus, WA et al. An evaluation of outcome from intensive-care in major medical centers. *Ann Intern Med* 1986. (715) |
| 11. (#47) Legall, JR et al. A simplified acute physiology score for ICU patients. *Crit Care Med* 1984. (667) |
| 12. (#49) Boyd, CR et al. Evaluating trauma care—the TRISS method. *J Trauma* 2001. (658) |
| 13. (#58) Marshall, JC et al. Multiple organ dysfunction score—a reliable descriptor of a complex clinical outcome. *Crit Care Med* 1995. (592) |
| 14. (#63) Carrico, CJ et al. Multiple-organ-failure syndrome. *Arch Surg* 1986. (575) |
| 15. (#80) Baker, SP et al. Injury severity score—update. *J Trauma* 1997. (532) |
| 16. (#87) Champion, HR et al. A revision of the trauma score. *J Trauma* 1997. (516) |
| 17. (#98) Pollock, MM et al. Pediatric risk of mortality (prism) score. *Crit Care Med* 1988. (498) |

(continued on next page)
Table 2 (continued)

B. Outcome/benchmarking/prediction model articles (no. of times cited)

18. (#103) Champion, HR et al. Trauma score. Crit Care Med 1981. (486)
19. (#112) Keene, AR et al. Therapeutic intervention scoring system—update 1983. Crit Care Med 1983. (444)
20. (#115) Higgins, TL et al. Stratification of morbidity and mortality outcome by preoperative risk-factors in coronary-artery bypass patients—a clinical severity score. JAMA 1992. (435)
21. (#149) Lemeshow, S et al. Mortality probability-models (MPM-II) based on an international cohort of intensive-care unit patients. JAMA 1993. (388)
22. (#150) Champion, HR et al. The major trauma outcome study—establishing national norms for trauma care. J Trauma 1996. (386)
23. (#169) Takala, J et al. Increased mortality associated with growth hormone treatment in critically ill adults. N Engl J Med 1999. (365)
24. (#184) Vincent, JL et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Crit Care Med 1998. (346)
25. (#197) Faist, E et al. Multiple organ failure in polytrauma patients. J Trauma 1995. (332)
26. Moore, EE et al. Organ injury scaling—spleen, liver, and kidney. J Trauma 1995. (317)
27. Cockburn, F et al. The CRIB (clinical risk index for babies) score—a tool for assessing initial neonatal risk and comparing performance of neonatal intensive-care units. Lancet 1993. (273)
28. Greenspan, L et al. Abbreviated injury scale and injury severity score—a scoring chart. J Trauma 1993. (267)
29. Ware, JE et al. Comparison of methods for the scoring and statistical-analysis of SF-36 health profile and summary measures—summary of results from the medical outcomes study. Med Care 1995. (259)
30. Richardson, DK et al. Score for neonatal acute physiology—a physiological severity index for neonatal intensive-care. Pediatrics 1993. (252)
31. Moore, EE et al. Organ injury scaling—spleen and liver [1994 revision]. J Trauma 1993. (233)
32. Copes, WS et al. The injury severity score revisited. J Trauma 1988. (217)
33. Pollack, MM et al. PRISM III: an updated pediatric risk of mortality score. Crit Care Med 1996. (212)

C. Mechanical and positive pressure ventilation/airway articles (no. of times cited)

1. (#9) Brower, RG et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000. (1750)
2. (#27) Amato, MBP et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998. (911)
3. (#42) Gregory, GA et al. Treatment of idiopathic respiratory-distress syndrome with continuous positive airway pressure. N Engl J Med 1971. (708)

4. (#44) Suter, PM et al. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. N Engl J Med 1975. (698)
5. (#53) Dreyfuss, D et al. Ventilator-induced lung injury—lessons from experimental studies. Am J Resp Crit Care 1992. (641)
6. (#65) Brochard, L et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary-disease. N Engl J Med 1995. (561)
7. (#85) Staufer, JL et al. Complications and consequences of endotracheal intubation and tracheotomy—a prospective-study of 150 critically ill adult patients. Am J Med 1981. (517)
8. (#93) Ranieri, VM et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome—a randomized controlled trial. JAMA 1999. (508)
9. (#106) Nash, G et al. Pulmonary lesions associated with oxygen therapy and artificial ventilation. N Engl J Med 1967. (478)
10. (#108) Bendixen, HH et al. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation—a concept of atelectasis. N Engl J Med 1963. (465)
11. (#111) Webb, HH et al. Experimental pulmonary-edema due to intermittent positive pressure ventilation with high inflation pressures, protection by positive end-expiratory pressure. Amer Rev Resp Dis 1974. (445)
12. (#113) Boyd, O et al. A randomized clinical-trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. JAMA 1993. (439)
13. (#129) Muscedere, JG et al. Tidal ventilation at low airway pressures can augment lung injury. Am J Resp Crit Care 1994. (412)
14. (#135) Kumar, A et al. Continuous positive-pressure ventilation in acute respiratory failure—effects on hemodynamics and lung function. N Engl J Med 1970. (403)
15. (#138) Hickling, KG et al. Low mortality associated with low-volume pressure limited ventilation with permissive hypercapnia in severe adult respiratory-distress syndrome. Intens Care Med 1990. (402)
16. (#139) Arorosa, NS et al. Respiratory muscle strength and maximal voluntary ventilation in undernourished patients. Amer Rev Resp Dis 1982. (402)
17. (#142) Kolobow, T et al. Severe impairment in lung-function induced by high peak airway pressure during mechanical ventilation—an experimental-study. Amer Rev Resp Dis 1987. (398)
18. (#147) Haldine, JS et al. The regulation of the lung-ventilation. J Physiol-London 1905. (390)
19. (#154) Ashbaugh, DG et al. Continuous positive-pressure breathing (CPPB) in adult respiratory distress syndrome. J Thorac Cardiov Surg 1969. (382)
20. (#196) Bott, J et al. Randomized controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. Lancet 1993. (333)
21. Falke, KJ et al. Ventilation with end-expiratory pressure in acute lung-disease. J Clin Invest 1972. (325)
Table 2 (continued)

C. Mechanical and positive pressure ventilation/airway articles (no. of times cited)

22. Kramer, N et al. Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory-failure. *Am J Resp Crit Care* 1995. (323)
23. Stewart, TE et al. Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. *N Engl J Med* 1998. (322)
24. Yang, KL et al. A prospective-study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med* 1991. (322)
25.Gattinoni, L et al. Low-frequency positive-pressure ventilation with extracorporeal CO2 removal in severe acute respiratory-failure. *JAMA* 1986. (321)

D. Acute lung injury/adult respiratory distress syndrome articles (no. of times cited)

1. (#11) Bernard, GR et al. The American-European Consensus Conference on ARDS—definitions, mechanisms, relevant outcomes, and clinical-trial coordination. *Am J Resp Crit Care* 1994. (1627)
2. (#16) Ashbaugh, DG et al. Acute respiratory distress in adults. *Lancet* 1967. (1283)
3. (#17) Murray, JF et al. An expanded definition of the adult respiratory-distress syndrome. *Amer Rev Resp Dis* 1988. (1133)
4. (#18) Rossaint, R et al. Inhaled nitric-oxide for the adult respiratory distress syndrome. *N Engl J Med* 1993. (1083)
5. (#32) Ware, LB et al. Medical progress—the acute respiratory distress syndrome. *N Engl J Med* 2000. (794)
6. (#46) Tate, RM et al. Neutrophils and the adult respiratory-distress syndrome. *Amer Rev Resp Dis* 1983. (668)
7. (#48) Montgomery, AB et al. Causes of mortality in patients with the adult respiratory-distress syndrome. *Amer Rev Resp Dis* 1985. (663)
8. (#51) Brigham, KL et al. Endotoxin and lung injury. *Amer Rev Resp Dis* 1986. (650)
9. (#57) Rinaldo, JE et al. Adult respiratory-distress syndrome—changing concepts of lung injury and repair. *N Engl J Med* 1982. (599)
10. (#68) Weiland, JE et al. Lung neutrophils in the adult respiratory-distress syndrome—clinical and pathophysiologic significance. *Amer Rev Resp Dis* 1986. (551)
11. (#77) Fowler, AA et al. Adult respiratory-distress syndrome—risk with common predispositions. *Ann Intern Med* 1983. (540)
12. (#88) Hammerschmidt, DE et al. Association of complement activation and elevated plasma-C5a with adult respiratory-distress syndrome—pathophysiological relevance and possible prognostic value. *Lancet* 1980. (515)
13. (#99) Lee, CT et al. Elastolytic activity in pulmonary lavage fluid from patients with adult respiratory-distress syndrome. *N Engl J Med* 1981. (497)
14. (#100) Bell, RC et al. Multiple organ system failure and infection in adult respiratory-distress syndrome. *Ann Intern Med* 1983. (495)
15. (#107) Poutanen, SM et al. Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003. (468)

Table 2 (continued)

D. Acute lung injury/adult respiratory distress syndrome articles (no. of times cited)

16. (#116) Pepe, PE et al. Clinical predictors of the adult respiratory-distress syndrome. *Am J Surg* 1982. (432)
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1. (#30) Hebert, PC et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999. (867)
2. (#54) Besarab, A et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med 1998. (637)
3. (#163) Samama, MM et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. N Engl J Med 1998. (372)
4. (#166) Hastings, SPR et al. Antacid titration in prevention of acute gastrointestinal bleeding-controlled randomized trial in 100 critically ill patients. N Engl J Med 1978. (369)
5. (#172) Pribe, JH et al. Antacid versus cinetidine in preventing acute gastrointestinal-bleeding-randomized trial in 75 critically ill patients. N Engl J Med 1980. (364)
6. Marik, PE et al. Effect of stored-blood transfusion on oxygen delivery in patients with sepsis. JAMA 1993. (302)
7. Vincent, JL et al. Anemia and blood transfusion in critically ill patients. JAMA 2002. (245)
8. Wu, WC, et al. Blood transfusion in elderly patients with acute myocardial infarction. N Engl J Med 2001. (235)
9. van de Watering, LMG. Beneficial effects of leukocyte depletion of transfused blood on postoperative complications in patients undergoing cardiac surgery—a randomized clinical trial. Circulation 1998. (234)
10. Rohrer, MJ et al. Effect of hypothermia on the coagulation cascade. Crit Care Med 1992. (213)
11. Horwich, TB et al. Anemia is associated with worse symptoms, greater impairment in functional capacity and a significant increase in mortality in patients with advanced heart failure. J Amer Coll Cardiol 2002. (206)
Table 2 (continued)

| L. Transfusion medicine/hematology/bleeding articles (no. of times cited) |
|---|
| 12. Hebert, PC et al. Is a low transfusion threshold safe in critically ill patients with cardiovascular diseases? Crit Care Med 2001. (161) |
| 13. Moore, FA et al. Blood transfusion—an independent risk factor for postinjury multiple organ failure. Arch Surg 1997. (158) |
| 14. Corwin, HL et al. The CRIT study: anemia and blood transfusion in the critically ill—current clinical practice in the United States. Crit Care Med 2004. (150) |
| 15. Corwin, HL et al. Efficacy of recombinant human erythropoietin in critically ill patients—a randomized controlled trial. JAMA 2002. (147) |
| 16. Ferrara, A et al. Hypothermia and acidosis worsen coagulopathy in the patient requiring massive transfusion. Am J Surg 1990. (144) |
| 17. Rao, SV et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA 2004. (139) |
| 18. Corwin, HL et al. Efficacy of recombinant human erythropoietin in the critically ill patient: a randomized, double-blind, placebo-controlled trial. Crit Care Med 1999. (137) |
| 19. Boiffard, KD et al. Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: two parallel randomized, placebo-controlled, double-blind clinical trials. J Trauma 1984. (129) |
| 20. Hebert, PC et al. Does transfusion practice affect mortality in critically ill patients? Am J Resp Crit Care 1997. (125) |
| 21. Cosgroff, N et al. Predicting life-threatening coagulopathy in the massively transfused trauma patient: hypothermia and acidoses revisited. J Trauma 1997. (118) |
| 22. Corwin, HL et al. RBC transfusion in the ICU—is there a reason. Chest 1995. (118) |
| 23. Fitzgerald, RD et al. Transfusing red blood cells stored in citrate phosphate dextrose adenine-1 for 28 days fails to improve tissue oxygenation in rats. Crit Care Med 1997. (100) |

Article’s rankings listed by subgroup then by its position within the overall top 200 citations.

Only 25% indicates the need for a comprehensive search strategy such as the one used in this study.

Although this is a problem for those looking for research articles, it can also be an issue for the way published research becomes cited by others. For example, articles without abstracts or very brief abstracts were often found only after using exact topic words found in the article’s title or by starting a search from within a specific critical care journal itself. Our experience has been previously demonstrated where the choice of keywords and abstract construction significantly impacts the likelihood that an article will be found using modern electronic searches [17].

This study does highlight the importance of sepsis and infectious disease as well as respiratory physiology in critical care with more than half the articles falling into 1 of these 2 broad categories. On the other hand, the most cited article was related to physiologic predictors of morbidity and mortality and the next 3 articles were related to mental status.

4.1. Limitations

This study, like previous ones focusing on citations, has several limitations. Perhaps the most relevant is the debate as to what constitutes the most influential articles within a professional discipline [1,4,8,18]. Citation data found in all bibliographic databases rely not only on correctly acquiring cited references but also on the assumption that a primary study cites other references that are most relevant to the published article. It is likely that this study captured many of the classic articles in critical care as each article in our list of the top 200 articles was cited at least 300 times. Considering that 46% of articles published in medicine are never even cited, this is a remarkable observation [19]. Certainly, these articles deserve attention and must have made an indelible impact. However, this is not always the case. Authors may preferentially cite their or their colleagues’ previous works both because of familiarity or to increase the citation of that article. Recent scholarship on social networks, especially in the age of accelerated knowledge transmission, suggests that there may be an enhanced level of “connectedness” related to these networks [20,21]. It is not known whether, or how, this connectedness may be influencing the dissemination and therefore the pattern of references within the critical care community or among specific critical care topics. However, it is possible that the pattern of some citations may reflect the influence of an individual, as some have referred to as the “ceremonial citation,” rather than the specific findings within an article [16,22,23]. In addition, authors are more likely to cite articles of their own language [8,24] or articles that come from a highly cited journal. Not surprisingly, Baltussen found that among the most cited 45 articles, most of them came from non–critical care-focused journals [16]. Nevertheless, using citations as a proxy for influence and importance has both face validity and is supported by empiric data demonstrating that citation analyses correlate with articles with the highest quality hierarchies of evidence and research design [25].

Most importantly, the use of citations is also confounded by the effect of time from the year of publication [26] with peak of citations differing for different journals and areas of research. Once citations do peak, they eventually become part of common knowledge and are no longer cited. Previous studies suggest that articles peak 7 to 10 years after publication [15,26]. It has been suggested that “classic” articles are relevant to only a few decades and many important articles are lost to the passage of time [15]. These findings may be supported by the fact that among the top 200 articles in this study, 158 were published during or after 2000. It is probably too early to tell how electronic databases...
will change the epidemiology of citation classics because it is easier to retrieve and perhaps cite influential articles than before the age of the Internet.

In conclusion, although Web-based search engines can produce lists of references within seconds to minutes, the utility of these searches can be quite limited as a complete end effective literature search remains an art. Periodic reviews of the literature may prove helpful to trainees mastering the most influential literature of our field as well as more established professionals searching for starting points for new investigations.

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