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Improved Outcomes in Critically Ill Patients With AIDS: How Does This Trend Continue?*

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“Success needs no explanation. Failure does not have one that matters.”

—Jesse Jackson

In this issue of *Critical Care Medicine*, Huson et al (1) thoughtfully describe the clinical characteristics and outcomes of patients with AIDS admitted to Dutch ICUs during the era of combination antiretroviral therapy (cART) from 1997 to 2014. Their findings show that major progress has been made during this time period such that patients with AIDS being treated in ICUs now have mortality rates approaching that of patients without AIDS.

Although it could be argued that this success story needs no explanation, the true impact of this study may lie with the questions it raises. This study challenges care providers to search for the treatment modifications that may explain this trend so as to promote further improvement in the care of critically ill patients with AIDS.

Huson et al (1) performed a retrospective analysis of 1,127 AIDS patients and 4,479 controls (non-AIDS patients matched for age, sex, and admission type [medical or surgical and planned or unplanned]) treated in Dutch ICUs from 1997 to 2014. In general, AIDS patients had significantly more comorbidities, were more acutely ill based on Acute Physiology and Chronic Health Evaluation (APACHE) II scores, and were more likely to be admitted with another infection—typically a respiratory infection or sepsis. Not surprisingly, AIDS

*See also p. 291.

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patients experienced a higher overall mortality rate than controls (28.2% vs 17.8%; $p < 0.0001$).

More interesting and encouraging than these data are the favorable trends that were identified in critically ill AIDS patients from 1999 to 2014. Although the mortality rate for both AIDS and non-AIDS patients declined over the study period (39–16% and 22–14%, respectively), the average annual percentage change was greater for patients with AIDS than controls (-6.0 [-8.0 to -3.9] vs -2.1 [-4.1 to -0.1]; $p = 0.02$). This greater decline in mortality among AIDS patients coincided with a downward trend in the proportion of AIDS patients being admitted with a respiratory infection. Further analyses suggest that decline in mortality was largely a function of the improved outcome in the subset of AIDS patients admitted with an infectious diagnosis. Using standardized mortality rates to control for baseline differences in severity of illness, the authors showed that AIDS patients admitted with an infectious diagnosis had a greater decline in annual standardized mortality rate than non-AIDS patients (-4.7 [-7.3 to -2.1] vs -0.4 [-3.5 to 2.8]; $p = 0.026$).

Differences in the use of mechanical ventilation between AIDS and non-AIDS patients were also intriguing. Overall, mechanical ventilation use was similar in the AIDS and non-AIDS patients, despite the fact that a greater proportion of AIDS patients had chronic obstructive pulmonary disease at baseline and were more likely to be admitted with a respiratory infection. Furthermore, the use of mechanical ventilation in the first 24 hours of admission declined significantly in patients with AIDS, whereas its use in non-AIDS patients fluctuated without a significant downward trend.

This study is significant both for its findings and for the questions that it raises. Although previous investigators have described declining mortality rates in HIV patients admitted to the ICU, this study is unique in that it specifically focuses on the ICU course of AIDS patients (2–5). Most importantly, it reveals that the mortality improvement of critically ill AIDS patients has outpaced that of non-AIDS patients such that AIDS and non-AIDS patients have similar outcomes in the ICU. How this trend is explained is not entirely clear. The fact that fewer AIDS patients were admitted with an infectious diagnosis undoubtedly improved mortality over the study time period, as described in prior studies involving HIV patients (3–5). It is also likely that declining *Pneumocystis jirovecii* pneumonia rates and improved management of this infection as seen in other studies were a contributing factor (6). But how does one explain the greater improvement in mortality from 1999 to 2014 among AIDS patients admitted with a secondary infection compared with non-AIDS patients? Obviously the introduction of cART has been life changing for patients infected with HIV; however, the role of these medications in the ICU is controversial (6). Although some studies would suggest that cART should be continued or even started in the ICU in certain situations, this decision is complicated by concerns for variable ART absorption in critically ill patients, life-threatening drug side effects, drug-drug interactions, and the risk of immune reconstitution syndrome (7–9). A descriptive study of cART practice patterns and how these patterns may have changed over time possibly could explain the trend in improved mortality, particularly with the development of new cART agents and formulations. Concurrent with the increasing availability of cART, the development of point-of-care testing for HIV may have resulted in a more timely diagnosis and led to more appropriate

empiric antimicrobial therapy early in the hospital course (10). One also has to wonder whether noninvasive ventilation played a pivotal role in improving the mortality rate for critically ill AIDS patients. Noninvasive ventilation use in the ICU became more commonplace over the course of this study (11, 12). The declining rate of mechanical ventilation in the cohort of AIDS patients and the similar rates of intubation between the two groups, despite the higher rate of chronic obstructive pulmonary disease and infection as an admitting diagnosis in patients with AIDS, raises the possibility that noninvasive ventilation was increasingly used to avoid intubation of HIV patients. Also, changes in “do-not-resuscitate” orders may also have influenced the results of this study as seen in prior critical care trials (13). Appropriately changing patient and physician perceptions regarding the survivability of AIDS may have led more patients to choose “full-code” status over the course of the study. Finally, it should also be noted that APACHE II scores for AIDS patients remained stable over the course of this study, despite the decline in mortality, once again raising concerns regarding this scoring system and its usefulness in predicting mortality in patients with AIDS (14).

The over-riding message of this well-crafted and well-written study is uplifting: the care that is delivered to critically ill AIDS patients continues to improve, and the expectations for a favorable outcome now approaches that of the general ICU patient population. Nonetheless, this study challenges both clinicians and researchers to take the next step and explore the reasons for this success so that this trend of improved care for critically ill AIDS patients continues for the benefit of future patients.

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References

1. Huson MA, Bakhshi-Raiez F, Grobusch MP, et al. Characteristics and Outcome of Patients With AIDS in Dutch ICUs Between 1997 and 2014. *Crit Care Med*. 2016; 44:291–299. [PubMed: 26474113]
2. Akgün KM, Huang L, Morris A, et al. Critical illness in HIV-infected patients in the era of combination antiretroviral therapy. *Proc Am Thorac Soc*. 2011; 8:301–307. [PubMed: 21653532]
3. Akgün KM, Tate JP, Pisani M, et al. Medical ICU admission diagnoses and outcomes in human immunodeficiency virus-infected and virus-uninfected veterans in the combination antiretroviral era. *Crit Care Med*. 2013; 41:1458–1467. [PubMed: 23507717]
4. Casalino E, Wolff M, Ravaud P, et al. Impact of HAART advent on admission patterns and survival in HIV-infected patients admitted to an intensive care unit. *AIDS*. 2004; 18:1429–1433. [PubMed: 15199319]
5. Vincent B, Timsit JF, Auburtin M, et al. Characteristics and outcomes of HIV-infected patients in the ICU: Impact of the highly active antiretroviral treatment era. *Intensive Care Med*. 2004; 30:859–866. [PubMed: 14767592]
6. Powell K, Huang L. The ART of caring for patients with HIV infection in the ICU. *Intensive Care Med*. 2009; 35:1659–1661. [PubMed: 19636534]
7. Croda J, Croda MG, Neves A, et al. Benefit of antiretroviral therapy on survival of human immunodeficiency virus-infected patients admitted to an intensive care unit. *Crit Care Med*. 2009; 37:1605–1611. [PubMed: 19325488]

8. Ganesan A, Masur H. Critical care of persons infected with the human immunodeficiency virus. *Clin Chest Med.* 2013; 34:307–323. [PubMed: 23702179]
9. Meybeck A, Lecomte L, Valette M, et al. Should highly active antiretroviral therapy be prescribed in critically ill HIV-infected patients during the ICU stay? A retrospective cohort study. *AIDS Res Ther.* 2012; 9:27. [PubMed: 23020962]
10. Lubelchek R, Kroc K, Hota B, et al. The role of rapid vs conventional human immunodeficiency virus testing for inpatients: Effects on quality of care. *Arch Intern Med.* 2005; 165:1956–1960. [PubMed: 16186464]
11. Confalonieri M, Calderini E, Terraciano S, et al. Noninvasive ventilation for treating acute respiratory failure in AIDS patients with *Pneumocystis carinii* pneumonia. *Intensive Care Med.* 2002; 28:1233–1238. [PubMed: 12209270]
12. Anjos CF, Schettino GP, Park M, et al. A randomized trial of noninvasive positive end expiratory pressure in patients with acquired immune deficiency syndrome and hypoxemic respiratory failure. *Respir Care.* 2012; 57:211–220. [PubMed: 21762561]
13. Bradford MA, Lindenauer PK, Wiener RS, et al. Do-not-resuscitate status and observational comparative effectiveness research in patients with septic shock*. *Crit Care Med.* 2014; 42:2042–2047. [PubMed: 24810532]
14. Brown MC, Crede WB. Predictive ability of acute physiology and chronic health evaluation II scoring applied to human immunodeficiency virus-positive patients. *Crit Care Med.* 1995; 23:848–853. [PubMed: 7736742]