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EDITORIAL

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# The ART of caring for patients with HIV infection in the ICU

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William Osler once wrote, "The practice of medicine is an art, based on science." Never is this statement truer than in the care of patients with HIV infection in the intensive care unit (ICU) in the current era of combination antiretroviral therapy (ART). In this issue of *Intensive Care Medicine*, Barbier and colleagues describe the etiologies and outcomes of acute respiratory failure in patients with HIV infection over the first decade of ART (1996–2000) [1]. Remarkably, the etiology of respiratory failure was identified in >98% of the 145 patients in the retrospective study. Bacterial pneumonia was the most common cause, followed by *Pneumocystis* pneumonia (PCP). Notably, non-invasive ventilation averted the need for endotracheal intubation and mechanical ventilation in 19 of 22 patients. To differentiate between patients taking ART and patients only reporting receipt of ART, the authors considered patients with evidence of poor adherence (i.e., patients for whom medical chart review indicated non-adherence with prescription of ART, patients with stationary viral loads and no evidence of viral resistance, or patients who had not received therapy for >6 months) in the non-treatment group. Almost one-third of patients were considered in the ART treatment group at the time of ICU admission. Although not a statistically significant difference, patients receiving ART actually had higher mortality (30%) compared to those not receiving ART (15%) ($p = 0.07$), despite having higher CD4 lymphocyte counts, lower HIV viral loads, and fewer opportunistic infections. Overall hospital survival was 80%, was stable across the study period, and was not statistically different across different etiologic groups.

The current study adds to the growing number of studies of the critical care of patients with HIV infection in the ART era. Following the introduction of HIV protease inhibitors and their use in combination with HIV reverse transcriptase inhibitors in 1996, improved outcomes were documented with ART among outpatients [2]. A study from San Francisco General Hospital in the early years of the ART era (1996–1999) provided encouraging evidence that the protective influence of ART might be extended to critically ill patients with HIV infection [3]. The potential lifesaving role of ART led to the consideration of its use during the period of acute illness in the ICU, though this practice has remained controversial [4]. At least one retrospective study investigated the effect of continuation of ART during ICU stay and the effect of initiation of ART on ICU and 6-month outcome; the authors concluded that 6-month survival was associated with ART [5]. In addition, a recent multicenter randomized controlled trial found that initiation of ART during an acute opportunistic infection, rather than deferring treatment, reduces progression of HIV disease and mortality, although the study was not designed specifically to study critical illness [6].

Despite the immunologic and virologic advantages conferred by ART, several recent studies have found no improvement in hospital or short-term survival between patients receiving or not receiving ART at the time of ICU admission [7–11]. Even when authors have not attempted to define treatment adherence as in the current study, investigators have noted higher CD4 lymphocyte counts and lower viral loads among ART recipients [11]. Nevertheless, the current study and these prior studies demonstrate the improved survival of critically ill patients with HIV infection in the ART era.

Although ART has not been associated consistently with this improved survival, one possible explanation is the decreased percentage of patients admitted to the ICU with PCP, a recognized risk factor for in-hospital mortality among critically ill patients with HIV infection, compared to the pre-ART era [12–14]. In the most recent studies in a continuing series out of San Francisco General Hospital, ongoing since 1981, respiratory failure has remained the most common indication for ICU admission, and PCP has remained the most frequent etiology of respiratory failure [3, 11]. However, the percentages have decreased throughout the study period, presumably in part due to prophylactic therapy and ART. In addition, several studies have found that patients on ART were more likely to have non-AIDS-related admissions, which has been associated with improved survival [3, 7, 10, 11].

Nonetheless, the changing etiology of respiratory failure fails to explain completely the improved survival. The current study and other ART era studies have demonstrated improved survival even among patients with PCP [9, 15–17]. Although infection with *Pneumocystis* was a risk factor for in-hospital mortality in the current study, survival exceeded 85%, similar to that in other recent studies, and a striking improvement compared with the earliest studies from the beginning of the HIV epidemic.

Advancements in ICU care that are unrelated to HIV care may also explain the survival gains in the care of critically ill patients with HIV infection, though studies designed to determine the individual effects of these interventions have been limited. For example, the current ART era has coincided with the adoption of low tidal volume ventilation [18], intensive insulin therapy [19], and early goal-directed therapy for sepsis [20]. In the current study, the authors hypothesized that early transfer of patients to the ICU, noninvasive ventilation for PCP, and aggressive management of sepsis contributed to the high in-hospital survival, independent of ART or its effects (i.e., ICU admission diagnosis or CD4 cell count). Therefore, improvements in ICU practice remain a plausible contributing factor.

Unfortunately, the current study and many of its contemporary comparisons have considered only hospital survival, not longer term survival. Therefore, the well-recognized benefits that ART exerts over periods longer than typical ICU stays cannot be excluded.

Regardless, in the absence of prospective, ICU-based randomized clinical trials, retrospective observational studies such as the current study can provide useful clinical information to inform clinicians. Despite the inconsistent findings of the influence of ART on the outcome of critically ill patients with HIV infection, this study and others reinforce key points. First, in-hospital survival for these critically ill patients has improved in the current ART era. Second, the etiologic spectrum of respiratory failure, as well as indication for ICU admission, has shifted. Therefore, clinicians should remain vigilant for both non-HIV-associated and HIV-associated conditions, including the side effects of ART (such as drug interactions or immune reconstitution syndrome) among critically ill patients with HIV infection.



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