Critical Illness in HIV-Infected Patients in the Era of Combination Antiretroviral Therapy

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As HIV-infected persons on combination antiretroviral therapy (ART) are living longer and rates of opportunistic infections have declined, serious non–AIDS-related diseases account for an increasing proportion of deaths. Consistent with these changes, non–AIDS-related illnesses account for the majority of ICU admissions in more recent studies, in contrast to earlier eras of the AIDS epidemic. Although mortality after ICU admission has improved significantly since the earliest HIV era, it remains substantial. In this article, we discuss the current state of knowledge regarding the impact of ART on incidence, etiology, and outcomes of critical illness among HIV-infected patients. In addition, we consider issues related to administration of ART in the ICU and identify important areas of future research.

Keywords: MeSH; intensive care unit; critical illness, human immunodeficiency virus; antiretroviral therapy; aging, quality of life

Life expectancy for HIV-infected patients on effective antiretroviral therapy (ART) has improved considerably since the earliest periods of the HIV epidemic. As HIV-infected people are living longer, noninfectious complications and comorbid diseases have increased in frequency (1, 2). The spectrum of critical illness among HIV-infected patients also reflects these changes. This review describes the current state of knowledge regarding the impact of ART on the incidence and spectrum of critical illness in HIV-infected patients. We also address survival and quality of life (QOL) for HIV-infected patients with critical illness and review issues related to ART use in the ICU.

IMPACT OF ART ON THE INCIDENCE OF CRITICAL ILLNESS AMONG HIV-INFECTED PATIENTS

Many HIV-infected patients develop critical illness. Although overall hospitalization rates have decreased in regions with access to ART, rates of ICU admission have remained constant or in some series have even increased since 1996, the beginning of the combination ART era (3–7). In epidemiologic studies from the pre-combination ART to the current combination ART era, 3 to 12% of all hospitalized HIV-infected patients required ICU admission (4–14). Many HIV-infected patients may be admitted to the ICU before having been diagnosed with HIV infection. Approximately 25 to 40% of critically ill HIV-infected patients were not known to be HIV-infected at the time of ICU admission in recent studies from the combination ART era (4, 7, 15). This proportion may be increasing over time, particularly in those who present with opportunistic infections, and likely depends upon the patient population in the region (16). Also, many HIV-infected patients (up to 50%) are not on ART at the time of ICU admission (Table 1) (4, 7, 12, 15). Thus, previously undiagnosed HIV infection and lack of ART may be possible contributing factors to the steady rate of ICU admissions. The stability of ICU admission rates in HIV-infected patients may also be influenced by increasingly optimistic attitudes among ICU providers (17, 18). At the start of the HIV epidemic, providers were discouraged by poor ICU outcomes for HIV-infected patients and did not see a role for ICU care (17, 18). Since that time and with the introduction of combination ART, ICU and hospital survival has improved significantly and approaches survival among HIV-uninfected ICU populations (4, 5, 14, 19, 20).

Data on the impact of ART on the incidence of critical illness among HIV-infected persons in medical care are limited. ART leads to decreased opportunistic infections that collectively could contribute to lower risk of ICU admission. Because HIV-infected patients are living longer, however, they are at increasing risk of developing comorbid illnesses not previously thought to be HIV-related, and these "non-AIDS" conditions account proportionally for the majority of deaths in recent studies (1, 2, 21–23). Thus, these chronic medical diseases may contribute overall to an increased risk for ICU admission, particularly among older HIV-infected patients. Further research is needed to describe the incidence of critical illness among HIV-infected persons in care in the current era (Table 2).

IMPACT OF ART ON THE ETIOLOGY OF CRITICAL ILLNESS AMONG HIV-INFECTED PATIENTS

The spectrum of critical illness in HIV-infected patients has changed over the course of the HIV epidemic, particularly since the introduction of combination ART. During the earliest HIV era, HIV-infected patients admitted to the ICU were mostly young men presenting with advanced AIDS and opportunistic infections. The most common ICU admitting diagnosis was acute respiratory failure from *Pneumocystis jirovecii* pneumonia (PCP) (18). Since the onset of the HIV epidemic, however, there has been a significant shift away from AIDS-defining diagnoses as indications for ICU admission. In recent studies from the combination ART era, more than half of ICU admissions in HIV-infected patients were for non–HIV-related critical illness (5, 8–11). Although the most common ICU admission

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TABLE 1. COMBINATION ANTIRETROVIRAL USE, INDICATIONS AND OUTCOMES AMONG CRITICALLY ILL HIV-INFECTED PATIENTS

Study	Years of Study	Number of Patients	Mean/Median Age in Years (± SD/IQR)	ART Prescribed Before ICU (%)	Non-AIDS Admissions (%)	ICU/Hospital Survival Among Those Not on ART (%)	ICU/Hospital Survival Among Those on ART (%)
Casalino (7)	1997–1999	230	389 ± 9	28	63	73*	80* (NS)
Morris (6)	1996–1999	295	42 (23–67)	25	63	69	80 ($P = 0.04$)
Morris (35)†	1996–2001	58	37–42 (24–61)	21	0	37	75 ($P = 0.03$)
Vargas-Infante (39)	1996–2006	53	38 ± 10	28	23	22‡	57‡ ($P = 0.003$)
Khouli (12)	1997–1999	259	43 (24–82)	48	40	49	51 (NS)
Nuesch (72)	1997–1999	170	N/A	43	52	87§	94§ ($P < 0.001$)
Palacios (13)	1997–2003	49	40 (33–48)	31	39	33‖	43‖ (NS; $P = 0.37$)
Vincent (4)	1998–2000	236	40 ± 9	50	50	77¶	75¶ (NS; $P = 0.71$)
Narasimhan (5)	2001	53	42	52	67	49**	71** ($P < 0.01$)
Dickson (19)	1999–2005	102	39 (32–44)	37	33	66	67 (NS)
Powell (14)	2000–2004	311	44 (24–72)	33	79	70	67 ($P = 0.70$)
Barbier (20)††	1996–2006	147	43 (37–51)	29	50	85	70 ($P = 0.07$)
Mendez-Tellez (43)‡‡	2004–2007	66	43 (38–49)	38	N/A	54	60

Definition of abbreviations: ART, antiretroviral therapy; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; N/A, not applicable; NS, nonsignificant; SD, standard deviation.

Data from studies cited in the table are restricted to the populations enrolled during the combination ART era (1996 onward) with exceptions as noted.

* ICU survival by pre-combination ART vs. combination ART era

† Study investigated all HIV-infected patients admitted to the ICU with PCP and compared patients on combination ART prior to or during ICU admission compared with patients who received no combination ART.

‡ Comparison made by precombination ART vs. combination ART era: 1986–1996 vs. 1996–2006

§ Comparison made by precombination ART vs. combination ART era: 1994–1996 vs. 1997–1999, respectively.

‖ Comparison made by precombination ART vs. combination ART era: 1990–1996 vs. 1997–2003, respectively.

¶ Comparison made by precombination ART vs. combination ART era: 1995–1996 vs. 1998–2000, respectively.

** Comparison made by precombination ART vs. combination ART era: 1991–1992 vs. 2000, respectively.

†† Study investigated all HIV-infected patients admitted to the ICU with respiratory failure.

‡‡ Study investigated all patients admitted to the ICU with acute lung injury and compared patients by HIV status.

diagnosis for HIV-infected patients remains acute respiratory failure from pneumonia, the pathogens have changed (6, 12, 14, 19). Bacterial infections rather than *Pneumocystis* now account for most causes of pneumonia in HIV-infected critically ill patients (4–6, 12, 14). Opportunistic infections and AIDS-related illness are responsible for a smaller proportion of ICU admissions and are most commonly seen in patients with a new HIV diagnosis (4–6, 10, 12, 14). HIV-infected patients on ART who are admitted to the ICU in the current era may develop critical illnesses more traditionally encountered among older HIV-uninfected patients. Ongoing alcohol use, substance use, and cigarette smoking, which are prevalent among many HIV-infected populations, may further contribute to the risk for comorbidities and development of critical illness.

IMPACT OF ART ON OUTCOMES OF CRITICAL ILLNESS

Short-term Survival after Critical Illness

Survival rates after critical illness among HIV-infected patients have undergone significant improvement from the earliest era to the more recent era (Table 1). Uncontrolled HIV disease,

TABLE 2. EXAMPLES OF FUTURE AREAS OF RESEARCH FOR CRITICALLY ILL HIV-INFECTED PATIENTS

Predisposing risk factors for ICU admission
- How does ART use affect risk for ICU admission due to comorbid medical disease?
- How do health insurance status and health-care use affect risk for ICU admission?

Use and delivery of ICU care
- Are there disparities in ICU admission patterns and delivery of ICU interventions for critically ill HIV-infected patients compared with HIV-uninfected patients?
- Do clinical tools that assess severity of illness for HIV-infected patients, incorporating AIDS-related disease and measures of multimorbidity, identify HIV-infected patients at greatest risk of ICU-related morbidity and mortality?
- Are medical provider attitudes toward care of critically ill HIV-infected patients different from attitudes toward non–HIV-infected patients?
- How and when should palliative care for critically ill HIV-infected patients be provided? (This may be particularly challenging with regard to how ART may affect long-term survival in ART-naive patients.)

ART in the ICU
- When should ART be initiated in the ICU? Should this be based on stability of presenting critical illness or failure of response to initial treatment of presenting critical illness?
- Are there specific AIDS-related diseases where ART initiation in the ICU is warranted (i.e., ART use in refractory respiratory failure from PCP)?
- When is it safe to continue ART in the ICU? Which regimens of ART are safe to use with specific organ failure (acute kidney injury vs. decompensated cirrhosis)?
- What are the risk factors for development of IRIS in critically ill HIV-infected patients?

Outcomes after ICU admission
- How do long-term outcomes differ by ICU admission diagnosis (i.e., AIDS-related disease vs. decompensated comorbid disease)?
- Are there outcome differences between patients who do and do not receive ART in the ICU?
- Is there a difference in 90-d or 1-yr mortality between patients who initiate ART in the ICU compared with those who do not?
- Is there a difference in mortality between patients who continue ART in the ICU compared with those who do not?
- What are the functional status, exercise capacity, cognitive function, and health-related quality of life in HIV-infected survivors of critical illness, and how do these vary by indications for ICU admission, ART use, and delivery of ICU care?
- Do outcomes after critical illness differ in older vs. younger HIV-infected patients?

Definition of abbreviations: ART = antiretroviral therapy; ICU = intensive care unit; IRIS = immune reconstitution inflammatory syndrome; PCP = *Pneumocystis jirovecii* pneumonia.

advanced opportunistic infections, and limited therapeutic options contributed to poor ICU outcomes in the early days of the AIDS epidemic (18). The first study of six that comprise a consecutive series from San Francisco General Hospital reported hospital survival for HIV-infected patients who required ICU admission of only 31% from 1981 through 1985; for patients who required mechanical ventilation because of PCP and respiratory failure, survival was only 13% (18). Other studies reported a similarly poor survival of only 9% among HIV-infected patients admitted to the ICU with respiratory failure (17).

In the current ART era, hospital survival for HIV-infected patients admitted to the ICU has increased to between 61 and 80% (4–6, 12, 19, 20). Although this improved survival coincides with more widespread use of combination ART in 1996, other factors are likely to contribute to better outcomes, including low tidal volume ventilation for acute lung injury, early goal-directed therapy for sepsis, and other improvements in delivery of care (24, 25) as well as improvements in care of HIV-associated conditions. Although long-term mortality remains significantly higher for HIV-infected persons compared with HIV-uninfected persons, it is unclear if survival to ICU or hospital discharge is different depending upon HIV status because studies have had conflicting results (19, 26–28).

Access to medical care and health insurance may play an important role in disparities in ICU use and outcomes between HIV-infected and uninfected persons in some studies. Among critically ill populations in general, uninsured patients may be less likely to be hospitalized but more likely to be admitted to an ICU once hospitalized; these patients may also be more likely to die in the ICU than patients with insurance (29). Multiple studies have shown that delays in ICU admission portend worse outcomes in non-HIV populations (30). In a recent meta-analysis of ICU use by the American Thoracic Society, uninsured patients were less likely to receive ICU care, and, once admitted to the ICU, uninsured patients received fewer ICU interventions and had higher mortality (31). Another study investigating risk factors for ICU admission within 3 days of an emergency department visit showed that Medicaid patients were more likely to be admitted to the ICU (32). However, among HIV-infected patients, patients with PCP who had Medicaid insurance were less likely to receive ICU care (33). Further studies are necessary to evaluate the impact of insurance status on disparities in ICU use and outcomes among HIV-infected patients.

A number of risk factors for decreased short-term survival to ICU or hospital discharge have been identified and are similar to risk factors for poor outcomes in HIV-uninfected patients. These include poor baseline health as reflected by poor performance status or greater burden of comorbid illnesses, higher severity of acute illness, and delayed delivery of critical care. For example, low serum albumin, hepatic cirrhosis, and history of opportunistic infections have been identified as risk factors for higher mortality after ICU admission (14, 15, 26).

In the acute setting, higher severity of illness scores (e.g., the Acute Physiology and Chronic Health Evaluation [APACHE II]), requirement for vasopressor medications, need for mechanical ventilation, PCP diagnosis, and other AIDS-related illnesses responsible for ICU admission have been associated with worse outcomes (6, 9, 10, 12, 14, 19, 20). Additional ICU diagnoses associated with worse outcomes include acute renal failure, severe sepsis, and admission for coma (15, 34). Several studies have identified delayed admission to the ICU as an independent risk factor for worse survival (15, 35). In general, CD4 cell count and HIV viral load have not been predictive of ICU survival (14, 15).

The impact of ART on ICU or short-term survival in HIV-infected patients is conflicting (5, 12–14, 19). In non-ICU settings, early initiation and continued administration of combination ART is clearly associated with improved outcomes (36–38). Unfortunately, most studies examining ART use in the ICU are retrospective. These studies are generally limited to assessing whether patients were prescribed ART before or during ICU admission and cannot accurately evaluate viral resistance patterns and medication adherence among patients before ICU admission. In addition, these studies cannot fully assess changes in ICU practices that also affect the outcomes of HIV-infected patients admitted to the ICU. Most studies evaluating the effects of ART on ICU outcomes for critically ill HIV-infected patients were also not adequately powered to detect outcome differences by ART use.

With these limitations in mind, some studies suggest that patients who are already on combination ART or who are started on combination ART during their ICU hospitalization may have a survival benefit (6, 35, 39). In HIV-infected patients admitted to the ICU with severe PCP, Morris and colleagues showed that mortality was 25% in patients who had been or were started on ART, compared with 63% in patients who were not on ART ($P = 0.03$) (35). In another study, patients whose ART was discontinued at ICU admission had worse 6-month survival than patients who remained on ART during their ICU stay (34). Although ART use was not associated with improved survival in the two most recent reports from San Francisco General Hospital (6, 14), in the study by Powell and colleagues, ART use was associated with factors that were predictive of improved survival, namely higher serum albumin and decreased PCP admissions.

Other studies have not demonstrated an ICU survival benefit associated with combination ART use. In one study from New York City, ICU mortality was not different in patients admitted between 1997 and 1999 when comparing patients receiving and not receiving ART (12). Furthermore, the prior use of ART was not associated with differences in overall hospital mortality or length of ICU or hospital stay (12). Two additional studies likewise failed to show survival differences between patients on ART and patients not on ART (19, 40).

Although ART use may not be associated with short-term ICU survival in some studies, longer-term survival may be improved in the group of ICU survivors who received ART (4, 7, 34). For example, patients started on ART while they were in the ICU had improved 6-month survival, even though ART use did not affect ICU mortality (34). Additional research is needed to address the long-term impact of ART on survival after ICU and hospital discharge and on the optimal timing for ART initiation in these critically ill HIV-infected patients (Table 2).

Long-Term Outcomes among HIV-Infected Survivors of Critical Illness

As more HIV-infected patients experience and survive critical illness, ICU clinicians will increasingly need to consider disposition after hospital discharge, functional status, health-related QOL, and long-term survival in HIV-infected survivors of critical illness. Before the introduction of combination ART, long-term survival after ICU admission was poor; although more than half of ICU survivors were alive at 6 months in one study (41), only about 18% were alive at 2 years (9, 41). Predictors associated with poor long-term survival included specific ICU admission diagnosis, low $CD4^+$ T-cell count, advanced stage of HIV disease, increased duration of AIDS, low serum albumin, weight loss, poor functional status, need for and duration of mechanical ventilation, and higher severity of illness scores (9, 41). After the introduction of ART, 70% of patients in another study who survived their ICU admission were alive after 2 years (7). In this population, advanced stage of HIV disease, $CD4^+$

T-cell count less than 50 cells/μl, presence of AIDS-related malignancy, poor functional status, higher severity of illness scores, and use of mechanical ventilation were predictors of worse long-term (3–24 months) survival (4, 7).

Little has been reported on discharge location, functional status, or QOL in HIV-infected ICU survivors. In studies of HIV-uninfected patients, those with the greatest burden of chronic diseases before ICU admission have the greatest decline in QOL and mortality after ICU discharge (42, 43). Studies have shown that up to 27% of HIV-uninfected patients surviving the ICU have major impairments in QOL up to 24 months after ICU discharge (44–46). In HIV-uninfected sepsis survivors, physical and social functions were impaired compared with the general population more than 1 year after discharge (47).

Given their burden of comorbid disease, HIV-infected individuals may be a particularly vulnerable population at increased risk for significantly impaired QOL after ICU discharge. Change in functional status after ICU discharge has not been examined in HIV-infected patients. As HIV-infected patients age, QOL will be an important consideration for ICU outcomes research.

COMPLICATIONS AND CONTROVERSIES SURROUNDING ART ADMINISTRATION IN THE ICU

There are no prospective studies evaluating the safety, efficacy, and timing of ART administration in the ICU. This lack of data poses significant challenges to ICU clinicians, who are left with mostly expert opinions to guide their decision-making. During the earlier ART era, ART was frequently stopped or held, or initiation was delayed, in HIV-infected patients admitted to the ICU. Valid concerns persist regarding administration of ART in critically ill HIV-infected patients, such as the possibility of unpredictable medication absorption, variable drug levels, and the potential for medication toxicities and drug–drug interactions (3). In addition, critically ill HIV-infected patients may have limited reserve to tolerate further organ injury from drug hypersensitivity reactions or immune reconstitution inflammatory syndrome (IRIS).

On the other hand, initiation of ART in critically ill patients may have benefits that outweigh the risks. ART improves immune function and reduces the risk of opportunistic infections and HIV-associated neoplasms. Furthermore, some patients may require ART despite the potential complications if they have conditions for which other effective therapy is lacking and for which ART alone has been shown to be useful, such as Kaposi sarcoma or progressive multifocal leukoencephalopathy (49–51). Particularly for patients who have not been on ART, initiation of therapy could contribute to reductions in morbidity and mortality in critically ill HIV-infected patients by decreasing the risk of subsequent HIV-associated opportunistic infections. Thus, ICU clinicians must weigh the pros and cons of ART initiation, continuation, or interruption on a case-by-case basis in addition to managing critical illnesses. In these complex cases, consultation with an HIV/AIDS expert is generally recommended.

ART Interruption in the ICU

For patients who are on ART at the time of ICU admission, clinicians must decide whether to continue or discontinue therapy. Treatment interruptions of ART can have significant deleterious consequences in HIV-infected patients. ART resistance mutations may be seen up to 3 months after interruption of ART (52). Data suggest that treatment interruption of ART is also deleterious in terms of non–AIDS-related events: In the Strategies for Management of Antiretroviral Therapy study, participants who had planned treatment interruptions based on $CD4^+$ T-cell count had higher HIV-specific and non–HIV-specific (e.g., cardiovascular, renal, or liver) disease progression and mortality (37, 53). If treatment interruption routinely accompanies ICU admission, resistant viral mutations may develop during an average ICU admission. Before resuming ART, patients may require HIV genotyping that could further delay reinstitution of ART. In addition, patients who survive ICU hospitalization are frequently frail, and ART interruption may be particularly harmful in these patients. The impact of treatment interruption on viral resistance and long-term care of HIV-infected patients must be considered when ICU clinicians hold ART. As the harm of treatment interruptions is understood in non–critically ill HIV-infected patients, the impact on outcomes for vulnerable HIV-infected patients admitted to the ICU requires further study.

ART Initiation in the ICU: IRIS

Among patients who are newly initiated on ART in the ICU, IRIS may complicate care (54, 55). Despite the risks of developing IRIS, evidence in non–critically ill HIV-infected patients now favors the early initiation of ART among most patients with acute opportunistic infections. In a randomized, controlled trial of patients admitted with nontuberculosis opportunistic infections (63% due to PCP), Zolopa and colleagues showed that early initiation of ART within 14 days of beginning treatment for the opportunistic infection lessened AIDS progression or death without an associated increase in adverse events when compared with delayed initiation of ART a median of 45 days after completing treatment for the opportunistic infection (48). In a study of HIV-infected patients with tuberculosis, mortality was also significantly lower among those started on ART during treatment for tuberculosis rather than delaying ART until treatment was complete (56). However, these studies did not include patients who were critically ill, on mechanical ventilation, or with multiorgan failure.

Manifestations of IRIS that can result in critical illness include pneumonitis, meningitis, hepatitis, and pericarditis. Respiratory failure secondary to IRIS is most often associated with tuberculosis and PCP (57, 58). IRIS associated with PCP can mimic acute respiratory distress syndrome, with fever, worsening hypoxia, and alveolar opacities on chest radiograph. Central nervous system involvement from tuberculosis and cryptococcus may also complicate IRIS and can be associated with significant morbidity and mortality (54, 59). Risk factors for IRIS include starting ART in close proximity to treatment for an acute opportunistic infection (60, 61), lower CD4 cell counts at the time of ART initiation (61, 62), rapid decline in HIV RNA after initiation of ART, and the use of boosted protease inhibitors (these inhibit intestinal and hepatic metabolism of other protease inhibitors, thus increasing drug exposure, plasma concentration, and drug half-life) (63). The pathogenesis of IRIS remains incompletely understood. In general, ART can be continued, although a careful review on a case-by-case basis is required. In patients who have potentially life-threatening manifestations of IRIS due to severity or location of the inflammatory response, it may be prudent to interrupt ART. Nonsteroidal anti-inflammatory agents and corticosteroids can be used to decrease inflammation, particularly in more severe cases.

ART Administration in the ICU: Toxicities, Drug Interactions, and Side Effects

If ART is continued or initiated in the ICU, numerous drug toxicities, drug–drug interactions, and concerns regarding absorption and metabolism of specific medications can complicate care. Between polypharmacy and organ dysfunction, which are com-

mon in patients admitted to the ICU, and the fact that nearly all antiretrovirals are administered enterally, altered drug levels may result and lead to impaired efficacy of ART or to drug toxicities (55). Except for abacavir, all nucleoside reverse transcriptase inhibitors require dose adjustment with renal insufficiency (55). Protease inhibitors and nonnucleoside reverse transcriptase inhibitors are cleared via the hepatic cytochrome p-450 system and need dose adjustment with hepatic insufficiency. With organ function recovery, dosages of these drugs need to be readjusted.

Medication toxicities may also be seen in HIV-infected patients admitted to the ICU due to altered absorption and metabolism of ART. In addition, certain antiretroviral medications are associated with a number of specific toxicities and complications, including lactic acidosis (64, 65), pancreatitis (66, 67), liver failure (68, 69), cardiovascular disease (70), and hypersensitivity reactions (71). These side effects may result in ICU admission or may occur with administration of ART while the patient is in the ICU for other reasons.

RECOMMENDATIONS

Early and continuous administration of combination ART has continued to show benefit in non-ICU settings and may be particularly helpful for critically ill HIV-infected patients (37, 48). ART should be continued in the ICU for critically ill HIV-infected patients already on ART who have achieved viral suppression if ART can be safely administered with minimal drug–drug interactions or risk of toxicities while receiving ICU medications (55). For patients admitted to the ICU for AIDS-related diseases, initiation of ART should be strongly considered in consultation with an infectious disease specialist, although data to support early initiation of ART are largely in noncritically ill and nonmechanically ventilated patients. HIV-infected patients admitted for non–AIDS-related conditions but with prolonged ICU hospitalizations or $CD4^+$ T-cell count less than 200 cells/μl should also be considered for ART initiation (55). These recommendations are based on expert opinion because no randomized clinical trials have been completed on the safety and efficacy of ART in critically ill HIV-infected patients. Further research is needed to determine which critically ill HIV-infected patients benefit most from ART initiation, and whether initiation of ART in all or only in certain critically ill patients is safe (Table 2).

CONCLUSIONS

As HIV-infected patients on combination ART are living longer, they are developing more non–HIV-related chronic diseases. This change in the epidemic may contribute to an increased proportion of ICU admissions for non-AIDS associated causes. ICU survival for HIV-infected patients has improved dramatically since the start of the epidemic. HIV-infected patients often benefit from aggressive ICU care, with survival approaching that of HIV-uninfected ICU patients. The impact of ART on the indications and outcome of ICU admission remains controversial. Numerous drug interactions and toxicities of ART can occur in critically ill patients, and ICU clinicians need to be familiar with ART use in the ICU. Consultation with an HIV/AIDS expert and experienced clinical pharmacist is also advised when initiating or continuing ART in critically ill patients. Finally, ICU research must evolve beyond mortality outcomes alone. Additional research is needed on patient-centered outcomes including QOL and functional capacity among HIV-infected ICU survivors.

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