Intensive Care of Human Immunodeficiency Virus–infected Patients during the Era of Highly Active Antiretroviral Therapy

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Highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection has produced significant declines in morbidity and mortality from acquired immunodeficiency syndrome (AIDS). Whether this therapy has resulted in changes in epidemiology and outcomes of intensive care among HIV-infected patients is unknown. We performed chart review of all intensive care unit admissions for HIV-infected patients at San Francisco General Hospital from 1996 through 1999. There were an average of 88.5 admissions per year with 71% survival to hospital discharge. Univariate analysis demonstrated that prior highly active antiretroviral therapy (odds ratio [OR] = 1.8, p = 0.04), a non–AIDS-associated admission diagnosis (OR = 3.7, p = 0.001), a lower Acute Physiology and Chronic Health Evaluation II score (OR = 5.4, p = 0.001), and higher serum albumin (OR = 4.4, p = 0.001) predicted improved survival. *Pneumocystis carinii* pneumonia (OR = 0.24, p = 0.001), mechanical ventilation (OR = 0.19, p = 0.001), or a pneumothorax (OR = 0.08, p = 0.001) were associated with worse survival. In multivariate logistic regression, all variables except prior use of highly active antiretroviral therapy and pneumothorax were significant independent predictors of outcome. At our institution, overall survival for HIV-infected intensive care unit patients has improved, especially among patients receiving highly active antiretroviral therapy. These patients may have an improved survival because of effects of therapy on variables such as likelihood of non–AIDS-associated admission diagnoses and serum albumin levels.

Keywords: mechanical ventilation; acquired immunodeficiency syndrome; protease inhibitors

Both admission and survival rates for human immunodeficiency virus (HIV)-infected patients in the intensive care unit (ICU) have fluctuated since the first reports of acquired immunodeficiency syndrome (AIDS) in the 1980s. Patterns of ICU use and outcomes have been documented at San Francisco General Hospital during several "eras" of the AIDS epidemic (1–4). After peaking in 1984, the number of HIV-infected patients admitted to intensive care, particularly those with *Pneumocystis carinii* pneumonia (PCP), decreased significantly despite rising hospital admissions for AIDS patients during the mid and late 1980s (1). Overall hospital mortality for those admitted to an ICU during Era I (1981–1985) was 69%, and the median survival after discharge was only 7 months. Decreased ICU admissions during this time were attributed to the perceived poor outcome of ICU care by both health care providers and patients. During Era II (1986–1988), there was a threefold improvement in mortality among PCP patients admitted to the ICU, attributed in large measure to the use of adjunctive corticosteroids (2). Era III (1989–1991) patients with PCP had a somewhat worse survival with an increased length of ICU stay, possibly reflecting a bias away from withholding or withdrawing support in these patients (3). The most recent series, Era IV (1992–1995), documented stable rates of ICU admissions for HIV-infected patients with overall hospital mortality rates of 37% (4). During this era, respiratory failure was still the most common admission diagnosis (40.4%) and still carried a poor prognosis (45.8% hospital mortality).

The advent of highly active antiretroviral therapy (HAART) has ushered in a new era in the AIDS epidemic. Studies have shown that the mortality rate and the incidence of opportunistic infections decreased dramatically in HIV-infected patients receiving HAART (5, 6). Whether the use of HAART has changed the demographics or outcomes of HIV-infected patients in the ICU is unknown. Although three studies have reported on ICU admissions in the late 1990s, the studies either did not comment on subjects' HAART use or had only 6% of subjects on HAART (7–9). We performed a retrospective study of all HIV-infected ICU patients at San Francisco General Hospital from 1996 to 1999 and documented outcomes and use of HAART.

METHODS

Subjects

Subjects were HIV-infected patients admitted to any ICU at San Francisco General Hospital from 1996 through 1999. The University of California, San Francisco Institutional Review Board approved the study protocol. Patient names were obtained from computerized medical records search and were confirmed by review of ICU admission logs. If patients were admitted to the ICU more than one time during any hospitalization, only data from their first ICU admission were analyzed. Repeat ICU admissions that occurred during subsequent hospitalizations were considered as separate events. To assess for possible effects of repeated measures, analyses were also performed using only first hospital admission, and results were not significantly different from those including all admissions.

Data Collection

Data were collected by standardized chart review using predetermined definitions. The use of specific antiretroviral medications and PCP prophylaxis at time of ICU admission was recorded. HAART was defined as use of at least three antiretroviral drugs of at least two classes (i.e., nucleoside reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors, or protease inhibitors) at the time of hospital admission (10). The primary diagnosis leading to admission was recorded from a standardized list of ICU diagnoses (4). Diagnoses were also classified as AIDS associated (i.e., PCP, tuberculosis) or non-AIDS associated (i.e., trauma, myocardial ischemia, gastrointestinal bleed) from a predetermined list (*see* online data supplement). Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were calculated for each admission (11).

(*Received in original form November 13, 2001; accepted in final form March 14, 2002*)

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This article has an online data supplement, which is accessible from this issue's table of contents online at www.atsjournals.org

Am J Respir Crit Care Med Vol 166. pp 262–267, 2002
DOI: 10.1164/rccm.2111025
Internet address: www.atsjournals.org

We noted the date of death while in the ICU or hospital. For those patients who survived the hospitalization, we obtained a date of death from the hospital chart whenever possible. For all patients who did not have a date of death recorded, we used information from the San Francisco AIDS registry to acquire survival information. This registry follows all HIV-infected patients in the county of San Francisco until death. Dates of death are obtained from city and county registries as well as from national death registries. The date last known alive was sought from records of a hospital admission, clinic visit, or laboratory test.

Statistical Analysis

Data were double entered to ensure accuracy. Statistical analysis was performed with SAS (SAS Institute, Cary, NC). The number of ICU admissions, survival rates, and percentage of patients on HAART were computed by year. Demographic and clinical characteristics of the cohort were described. For continuous variables, either Wilcoxon rank sum or Student's *t* test was used to compare groups. The presence of a non–AIDS-associated admission diagnosis, a diagnosis of PCP, or use of mechanical ventilation were also examined. Univariate analysis was performed using chi-square or Fisher's exact test to determine variables that were predictive of survival until hospital discharge. Mean or median of CD4 cell count, APACHE II, albumin, and lactate dehydrogenase (LDH) were used to create dichotomous variables for analysis. Variables that were associated with survival at a level of $p = 0.1$ were included in multivariate analyses using stepwise backward and forward logistic regression (*see* online data supplement) (12). Significance for the multivariate model was determined at $p < 0.05$.

Kaplan-Meier survival curves were computed for the cohort stratified by use or nonuse of HAART and the presence or absence of an AIDS-associated admission diagnosis. Log-rank testing was performed to determine differences in survival among the four groups.

RESULTS

Subjects

During the study period, there were 354 ICU admissions for 295 HIV-infected patients. Most patients (83.3%) were admitted to the ICU only once. The maximum number of admissions for a single patient was six (n = 1). The number of ICU admissions remained consistent each year of the study (1996 through 1999), averaging 88.5 patients per year (Table 1). Overall survival rates were also consistent, with an average survival to hospital discharge of 71%. The use of HAART was much more common from 1997–1999 (30–35%) than in 1996 (4%, p = 0.001). The majority of the ICU cohort were men (80.5%) and were more likely to be African American (44.6%) and intravenous drug users (49.7%) (Table 2). Approximately 25% of patients were receiving HAART at the time of ICU admission. Most ICU patients (63.3%) were admitted because of a non–AIDS-associated diagnosis.

Predictors of Survival

The characteristics of patients who survived until hospital discharge were compared with those who died while hospitalized. There were no differences in age, sex, race/ethnicity, or HIV risk factors between survivors and nonsurvivors. In univariate analysis, patients on HAART at the time of ICU admission were more likely to survive to hospital discharge than patients not on HAART (odds ratio [OR] = 1.8, 95% confidence interval [CI] = 1.02–3.2, p = 0.04) (Table 3). Survival was not predicted by CD4 cell count (p = 0.53) or log HIV viral RNA level (p = 0.27). Admission with a non–AIDS-associated diagnosis was highly predictive of an improved hospital survival (OR = 3.7, 95% CI = 2.3–5.9, p = 0.001). A low APACHE II score (OR = 5.4, 95% CI = 3.2–9.2, p = 0.001) and high albumin (OR = 4.4, 95% CI = 2.6–7.3, p = 0.001) were also associated with an increased odds of survival. Those admitted with PCP (OR = 0.24, 95% CI = 0.13–0.43, p = 0.001) or an elevated LDH (OR = 0.53, 95% CI = 0.26–1.1, p = 0.08), however, had a worse prognosis. Mechanical ventilation (OR =

TABLE 1. NUMBER OF ADMISSIONS OF HIV-INFECTED PATIENTS TO THE ICU AND SURVIVAL RATES PER YEAR

	1996	1997	1998	1999	Total
ICU admissions	96	79	88	91	354
Survived, %	67, 70	57, 72	56, 64	72, 79	252, 71
ICU admissions on HAART, %	4, 4*	27, 34	26, 30	32, 35	89, 25

Definition of abbreviations: HAART = highly active antiretroviral therapy; HIV = human immunodeficiency virus; ICU = intensive care unit.

* p = 0.001 compared with all other years.

TABLE 2. CHARACTERISTICS OF ICU ADMISSIONS OF HIV-INFECTED PATIENTS FROM 1996 THROUGH 1999

Characteristic	Number of Patients (%)
Age, years, mean (range)	41.7 (23–67)
Male sex	285 (80.5)
Race/ethnicity	
White	140 (39.6)
African American	158 (44.6)
Other/unknown	56 (15.8)
HIV risk factor	
Men who have sex with men	119 (33.7)
Intravenous drug use	176 (49.7)
Other/unknown	59 (16.6)
Medical history	
Initial HIV diagnosis	20 (5.6)
History of PCP	66 (18.6)
Use of PCP prophylaxis	192 (54.2)
Use of HAART	89 (25.1)
Admission diagnosis	
Non–AIDS-associated*	224 (63.3)
PCP	38 (10.7)
Clinical characteristics	
CD4, cells/μl, median (range)	64 (2–596)
HIV viral load, copies/ml, mean log (SD)	9.8 (2.7)
APACHE II score, median (range)	13 (2–44)
Albumin, g/dl, median (range)	2.6 (1.3–4.5)
LDH, U/L, mean (SD)	537 (534)
Complications	
Mechanical ventilation	191 (54.0)
PCP-related pneumothorax	6 (1.7)

Definition of abbreviations: AIDS = acquired immunodeficiency syndrome; APACHE = Acute Physiology and Chronic Health Evaluation; HAART = highly active antiretroviral therapy; HIV = human immunodeficiency virus; ICU = intensive care unit; LDH = lactate dehydrogenase; PCP = *Pneumocystis carinii* pneumonia.

* Non–AIDS-associated diagnoses: trauma, myocardial infarction/unstable angina, gastrointestinal hemorrhage (not caused by Kaposi's sarcoma or cytomegalovirus), drug overdose, pulmonary edema (not caused by HIV-associated cardiomyopathy), cardiac arrhythmia, aspiration pneumonia, and obstructive airways disease. AIDS-associated diagnoses: PCP, mycobacterial disease, bacterial pneumonia, Kaposi's sarcoma, fungal infections, lymphoma, and toxoplasmosis.

TABLE 3. UNIVARIATE PREDICTORS OF HOSPITAL SURVIVAL FOR HIV-INFECTED ICU PATIENTS

Characteristic	Odds Ratio (*95% CI*)	p Value
Use of HAART	1.8 (1.02–3.2)	0.04
Non–AIDS-associated admission diagnosis	3.7 (2.3–5.9)	0.001
PCP	0.24 (0.13–0.43)	0.001
APACHE II score of less than 13	5.4 (3.2–9.2)	0.001
Albumin of more than 2.6 g/dl	4.4 (2.6–7.3)	0.001
Lactate dehydrogenase of more than 537 U/L	0.53 (0.26–1.1)	0.08
Mechanical ventilation	0.19 (0.11–0.31)	0.001
Pneumothorax	0.08 (0.01–0.66)	0.001

Definition of abbreviations: AIDS = acquired immunodeficiency syndrome; APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; HAART = highly active antiretroviral therapy; HIV = human immunodeficiency virus; ICU = intensive care unit; PCP = *Pneumocystis carinii* pneumonia.

0.19, 95% CI = 0.11–0.31, p = 0.001) or the development of a PCP-related pneumothorax (OR = 0.08, 95% CI = 0.01–0.66, p = 0.001) also portended a poor outcome.

Several multivariate models were examined and all produced similar results (i.e., contained the same predictors of survival with ORs of similar magnitudes). Although use of HAART at the time of ICU admission was associated with an improved survival in the univariate analysis, this association was not detected in multivariate analyses. Predictors of survival in stepwise backward and forward logistic regression were a non–AIDS-associated admission diagnosis (OR = 2.9, 95% CI = 1.5–5.8, p = 0.002), high albumin (OR = 3.5, 95% CI = 1.8–6.6, p = 0.001), and a low APACHE II score (OR = 6.1, 95% CI = 3.0–12.4, p = 0.001) (Table 4). A diagnosis of PCP (OR = 0.30, 95% CI = 0.11–0.82, p = 0.02) or the need for mechanical ventilation (OR = 0.22, 95% CI = 0.11–0.44, p = 0.001) predicted worse survival. The numbers of PCP-related pneumothoraces were too low to reach statistical significance in the multivariate model; however, all patients with a PCP-related pneumothorax died (n = 6). Although LDH met our criteria for inclusion in the multivariate model (p = 0.08), over 20% of subjects did not have a value recorded. Deleting these patients from the model would have significantly biased the results, particularly because most missing values for LDH were among those patients who did not have PCP. Thus, it was thought that LDH served as a marker for PCP, and therefore, it was not included in the multivariate model.

Use of HAART

For the total cohort, there were 89 patients who were receiving HAART at the time of ICU admission. Characteristics of patients receiving HAART were compared with those not receiving HAART (all p values nominal uncorrected). HAART patients were mostly male (93%) and white (49%). They were equally likely to be men who had sex with men or intravenous drug users (47% for both). Survival to hospital discharge for patients receiving HAART was higher than for those not on HAART (80.0% versus 68.6%, p = 0.04). Patients receiving HAART were less likely to present with an AIDS-associated diagnosis (OR = 0.54, 95% CI = 0.32–0.91, p = 0.02). Similarly, they were less likely to have PCP, although this finding was not statistically significant (p = 0.07). The median CD4 cell count for those on HAART was 120 cells/μl, significantly higher than the median of 64 cells/μl in the group not receiving HAART (p = 0.02). The mean log HIV RNA level was lower among those on HAART (8.8 log copies/ml [81,967 copies/ml] versus 10.4 log copies/ml [147,204 copies/ml], p = 0.001). LDH and APACHE II scores did not differ significantly depending on HAART use (LDH for HAART = 515 U/L versus for no HAART = 549 U/L, p = 0.73; APACHE II = 13 for both, p = 0.22). HAART use did predict a higher level of albumin (2.8 versus 2.6 g/dl, p = 0.02).

To clarify further the effects of HAART and AIDS-associated admission diagnosis on survival, we plotted Kaplan-Meier survival curves for patients stratified by use of HAART and admission diagnosis (Figure 1). Median survival for all subjects was 324 days. The median survival time for patients on HAART at the time of admission who were admitted with a non–AIDS-associated diagnosis was 971 days. Those patients not on HAART but with a non–AIDS-associated diagnosis also had a long median survival time (728 days). Median survival was poor for patients with an AIDS-associated diagnosis regardless of HAART status (30 days for HAART and 26 days for no HAART). Log-rank testing showed that there was a significant survival difference between the four groups (p = 0.001). This survival difference was between the groups with a non–AIDS-associated diagnosis and those patients who were admitted with an AIDS-associated diagnosis (p < 0.05). Differences between the groups based on use of HAART were not significant.

TABLE 4. MULTIVARIATE MODEL OF PREDICTORS OF IN-HOSPITAL SURVIVAL FOR HIV-INFECTED PATIENTS

Characteristic	Odds Ratio (*95% CI*)	p Value
Non–AIDS-associated admission diagnosis	2.9 (1.5–5.8)	0.002
Albumin of more than 2.6 g/dl	3.5 (1.8–6.6)	0.001
APACHE II score of less than 13	6.1 (3.0–12.4)	0.001
PCP	0.30 (0.11–0.82)	0.02
Mechanical ventilation	0.22 (0.11–0.44)	0.001

Definition of abbreviations: AIDS = acquired immunodeficiency syndrome; APACHE II = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; HIV = human immunodeficiency virus; PCP = *Pneumocystis carinii* pneumonia.

ICU Diagnoses

To describe the epidemiology of intensive care during the HAART era, frequencies of specific admitting diagnoses were calculated (Table 5). Overall, respiratory failure was the most common admitting diagnosis (n = 144, 40.7% of diagnoses). Its cause was most likely to be PCP (n = 38, 26.4% of cases of respiratory failure). Bacterial pneumonia was the second most common cause of respiratory failure in the population (n = 31, 21.5% of cases of respiratory failure). Respiratory failure was also the most common admission diagnosis among those on HAART, although PCP was uncommon in this group (n = 38 for respiratory failure, 42.7% of diagnoses; n = 6 for PCP, 15.8% of cases of respiratory failure with HAART). Among those on HAART, noninfectious indications, such as need for airway protection, were more common reasons for mechanical ventilation (n = 7, 18.4%) than was PCP. Overall, patients with PCP had the worst survival rate for the cohort (44.7%). Respiratory failure from any cause also had a poor survival (61.5%) and was not significantly better for patients on HAART (65.7%, data not shown).

DISCUSSION

This study is the fifth in a continuous series reporting ICU outcomes of HIV-infected patients at San Francisco General Hospital and differs importantly from previous eras in that it

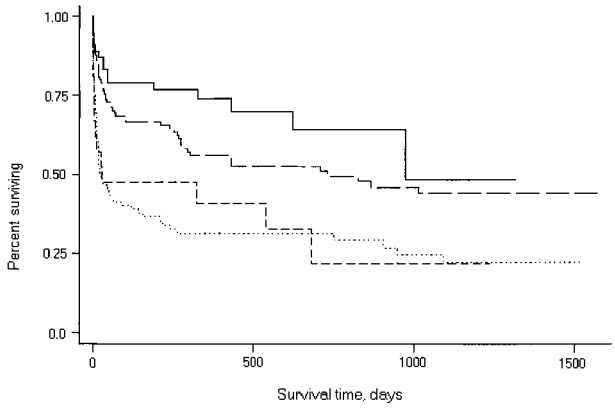

Figure 1. Kaplan-Meier survival curves for all ICU patients stratified by use of HAART and presence of an AIDS-associated diagnosis at ICU admission. Survival for groups on HAART or not on HAART with a non–AIDS-associated diagnosis is significantly different from survival for groups with HAART or no HAART and an AIDS-associated diagnosis (p < 0.05). (*Solid line*) HAART and non–AIDS-associated diagnosis, n = 65. (*Long-dashed line*) No HAART and non–AIDS-associated diagnosis, n = 155. (*Short-dashed line*) HAART and AIDS-associated diagnosis, n = 24. (*Dotted line*) No HAART and AIDS-associated diagnosis, n = 106.

TABLE 5. SUMMARY OF FREQUENCY OF ICU ADMISSION DIAGNOSES AND USE OF HAART

Diagnosis	On HAART (%)* (*n = 89*)	Not on HAART (%)* (*n = 261*)	Total (%)† (*n = 354*)	Survival (%)
Respiratory failure	38 (42.7)	106 (40.6)	144 (40.7)	61.5
PCP	6 (6.7)	32 (12.3)	38 (10.7)	44.7
Sepsis	7 (7.9)	34 (13.0)	42 (11.9)	65.1
Neurologic	9 (10.1)	35 (13.4)	44 (12.4)	75.6
Cardiac	13 (14.6)	22 (8.4)	35 (9.9)	91.4
GI bleed	4 (4.5)	20 (7.7)	26 (7.3)	79.2
Postoperative	5 (5.6)	10 (3.8)	15 (4.2)	100.0
Trauma	2 (2.2)	10 (3.8)	13 (3.7)	76.9
Metabolic	1 (1.1)	5 (1.9)	6 (1.7)	50.0
Overdose	2 (2.2)	2 (0.8)	4 (1.1)	100.0
Miscellaneous	8 (9.0)	17 (6.5)	25 (7.1)	76.0

Definition of abbreviations: GI = gastrointestinal; HAART = highly active antiretroviral therapy; ICU = intensive care unit; PCP = *Pneumocystis carinii* pneumonia.

* Percentage according to HAART use.

† Percentage of total ICU cohort.

coincides with the first use of HAART (1–4). The study includes a substantial number of patients who were receiving HAART at the time of admission, allowing us to begin to examine the potential impact of HAART on ICU-related mortality. Our study had several important findings. First, survival of HIV-infected patients admitted to our ICU has significantly improved in the HAART era compared with the immediately preceding era. Second, the demographics of HIV-infected patients admitted to the ICU have changed. Third, the use of HAART was associated with improved survival in univariate analysis and was likely important in multivariate modeling through its impact on ICU admission diagnosis (i.e., AIDS- or non–AIDS-associated diagnosis, diagnosis of PCP) and serum albumin level.

In concert with the well-documented declines in morbidity and mortality associated with the use of HAART (5, 6), survival of HIV-infected patients admitted to an ICU at our institution has improved significantly in the HAART era compared with previous eras. In this study, overall survival to hospital discharge was 71%. This rate may be somewhat higher than rates reported at other institutions (44–61%), but important potential differences, including variations in patient populations, differing ICU admission standards, and variable clinical practices, limit the conclusions that can be drawn by comparing results across different institutions (7, 8, 13, 14). We were able to lessen these potential differences by examining continuous data from a single institution, although changing thresholds for ICU admissions and changes in withholding of ICU care may still influence these survival rates. Survival of HIV-infected patients admitted to an ICU at San Francisco General Hospital has improved since the beginning of the AIDS epidemic. During Era I (1981–1985), survival was only 31%. Our current survival rate of 71% is a dramatic improvement from that time, and it is also a significant improvement from the survival rate of 63% during Era IV (1992–1995) ($p = 0.03$). Long-term survival after ICU admission has also improved compared with previous eras. Our overall median survival was almost 11 months, with survival in some subgroups as high as 2.5 years. Earlier series have reported median survival ranging from 3 to 7 months (1, 15, 16). However, in our cohort, most survival gains were realized in the groups admitted with a non–AIDS-associated diagnosis, as those with AIDS-associated diagnoses survived, on average, less than 1 month.

The causes of ICU admissions have not shifted significantly, although some changes were seen (*see* Table E1 in the online data supplement). Between Era IV and Era V, the total number of ICU admissions declined from an average of 110.8 admissions per year to 88.5 admissions per year. Respiratory failure is still the most common reason for admission, and PCP is still the most common cause of respiratory failure. Series from the early 1990s reported higher rates of PCP, however, with up to 87% of admissions for respiratory failure resulting from PCP (15, 17, 18). During the first era documented at San Francisco General Hospital, 62% of all ICU admissions were due to PCP (1). This number had fallen to 17.6% in Era IV (4) and has continued to fall to 10.7% currently, representing a significant decrease ($p = 0.001$). Other series have reported similar declining rates of ICU admissions for PCP (8, 13, 19).

Other characteristics of the ICU population have changed in the current era. The ICU population at San Francisco General Hospital in the previous era was mostly white men whose HIV risk factor was sex with men (4). Although the majority of the patients are still male, they are now more commonly African American and intravenous drug users and include a higher number of women (Table E1 in the online data suppplement). These changes reflect the overall shift in the face of the epidemic with minorities and women now at increased risk of HIV and AIDS.

Our study is unique in that it explicitly examined the relationship of HAART to ICU outcome and found that use of HAART at the time of ICU admission may be associated with survival in several ways. In univariate analysis, HAART was associated with improved survival, and patients who were using HAART at the time of ICU admission were 1.8 times more likely to survive than patients not receiving HAART. The effect of HAART on survival is intriguing. Although the effect was diminished in multivariate modeling, we believe that this occurred because HAART acted by influencing other variables in the model that have a strong relationship to survival. HAART may exert an effect on several key variables. For example, HAART patients had a significantly higher serum albumin level compared with patients not on HAART. Others have also shown that HAART increases serum albumin (20, 21), and higher albumin levels are one of the most powerful and consistent predictors of ICU survival (2, 4, 8, 16, 22). Also, CD4 cell counts were higher and HIV viral RNA levels were lower in HAART patients than in patients not on HAART. Although in our study and others, CD4 cell count and HIV viral RNA levels are not consistent predictors of ICU mortality, they do clearly affect many outcomes and aspects of HIV infection (23, 24). The fact that the subjects had improved CD4 counts and viral levels may indicate an improved overall physiologic status. Furthermore, the higher CD4 cell counts and lower HIV viral RNA levels that resulted from use of HAART may in turn have influenced the risk of developing an AIDS-associated opportunistic infection. In our cohort, admission for an AIDS-associated diagnosis, espe-

cially PCP, dramatically increased the risk of mortality. Throughout the course of the AIDS epidemic, our institution and others have shown that PCP and other AIDS-associated illnesses portend a poor outcome in the ICU (1, 3, 7, 13). Any shift due to HAART in the spectrum of intensive care diagnoses from AIDS-associated conditions to non–AIDS-associated ones would be predicted to impact ICU survival. In addition, failure to use HAART may be associated with failure to use other opportunistic infection prophylaxis, therefore altering the admission diagnoses among patients not on HAART. The impact of diagnosis on survival is further supported by our Kaplan-Meier analysis demonstrating that patients with a non–AIDS-associated diagnosis had a dramatically improved median survival compared with those with an AIDS-associated diagnosis.

The study has several limitations in interpretation and the ability to generalize from its results. Because of the study's retrospective nature, we were unable to obtain reliable information on HAART adherence. There may actually have been a stronger effect of HAART on survival than we were able to demonstrate because we may have included patients who were prescribed HAART but who were nonadherent. Some of the HAART group may also have been failing therapy, as many had low CD4 cell counts and high HIV viral RNA levels. We were also unable to obtain reliable information indicating why patients were not taking HAART, making it impossible to characterize survival in this group according to characteristics such as nonadherence, HAART failure, or lack of medical care.

Another difficulty with a retrospective study is the inability to analyze subtle differences between treatment groups. It is possible that patients receiving HAART differ in some systematic way beyond the direct effects of the medications. These differences may impact survival. For example, HAART patients may be more health conscious or have better social support than patients not offered or interested in HAART. The nature of our study precludes controlling for these potential confounders.

Also problematic with any study of ICU outcomes in HIV are the changing attitudes toward aggressive care for patients with AIDS and the variation in levels of care in different institutions. Attitudes about withholding ICU care for patients with HIV infection have shifted with different stages of the AIDS epidemic (1–4). We do not know how many patients were admitted to the hospital but chose either because of patient preference or physician advice to forgo ICU admission. The sense at our institution is that attitudes toward ICU care for HIV-infected patients have not changed significantly compared with the early 1990s. If attitudes have changed, it is likely toward more aggressive care, as both patients and physicians view HIV as a more treatable disease than previously. However, we lack exact numbers of HIV-infected patients who were not transferred to the ICU, and the effect of these patients on our reported survival rates is unknown. Also, the ability to generalize our results to other institutions may be limited. Thresholds for ICU admissions and survival rates of HIV-infected patients have been shown to differ according to geographic location as well as by type of institution (25).

With the exception of HAART use, predictors of survival in our study were similar to those found previously. Low APACHE II score, high serum albumin, and no mechanical ventilation predicted improved survival. All of these factors have been consistently shown to be associated with ICU outcome. Nickas and Wachter reported that serum albumin, acute physiology score, mechanical ventilation, and a diagnosis of PCP were all predictors of mortality in an earlier series at San Francisco General Hospital (4). Several series at other institutions have also reported that APACHE II, serum albumin, and a need for mechanical ventilation predict survival (8, 14, 22, 26, 27). CD4 cell count, although a marker for disease stage, did not predict mortality in our cohort. Although this finding has been reported by other investigators, some have found that a CD4 cell count close to the time of ICU admission did predict survival (4, 8, 19, 28). A diagnosis of PCP was also significantly related to outcome. PCP is a well-known risk factor for mortality, particularly in the setting of mechanical ventilation or pneumothorax (4, 22).

In summary, an HIV-infected patient admitted to the ICU in the HAART era has an improved chance of survival. Intravenous drug users and African American men are now the most common demographic groups admitted to the ICU. Patients are still most likely to be admitted to the ICU for respiratory failure but are less likely to have PCP. Traditional prognostic indicators such as serum albumin, APACHE II score, need for intubation, and a diagnosis of PCP remain significant predictors of survival. Patients taking HAART have an improved survival compared with those who are not, and this observation is most likely accounted for by improvement in baseline characteristics such as serum albumin and by a changing spectrum of admission diagnoses among those on HAART. Future prospective studies should be designed to validate our observations as well as to address the important question of whether the initiation of HAART in a critically ill patient improves survival.

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