Clinical Study

Intensive Care Usage by HIV-Positive Patients in the HAART Era

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1. Introduction

In the 1980s, the outlook for patients with the acquired immunodeficiency syndrome (AIDS) and critical illness was poor [1, 2], and intensive care for these patients was felt inappropriate [3, 4]. Most studies showed the worse survival the lower the CD4 count [5–10]. The prognosis of HIV-infection has improved dramatically with highly active antiretroviral therapy (HAART) [11–13]. Survival of HIV+ individuals admitted to intensive care has now improved, the case mix has changed and CD4 count at admission relates less to outcome [14–21]. The prognosis of HIV-infection has improved dramatically with highly active antiretroviral therapy (HAART) [11–13]. Survival of HIV+ individuals admitted to intensive care has now improved, the case mix has changed and CD4 count at admission relates less to outcome [14–21]. We, in combination with others, have previously published our intensive care experience with HIV infected patients from the mid 1990s [7]. Survival was shorter with CD4 count <100 cells/mL. Few of the published studies, however, have followed up patients long term [16, 22], and these only recruited up until 1999.

In recent years, the long-term prognosis of HIV+ individuals has continued to improve. With longer survival and more patients on treatment, the cohort of HIV+ patients has increased in size. In the UK, still one-third of patients are diagnosed with advanced HIV disease (CD4 count <200 cells/mm3). Therefore, we undertook a service review to examine usage of the ICU facility in our hospital by HIV+ patients. We have investigated the numbers of admissions, case mix, and long-term survival following intensive care unit (ICU) admission during recent years in a large London unit.

2. Methods

The Chelsea and Westminster Hospital in South West London provides care for over 5000 HIV-infected individuals, one of the largest cohorts in the UK. We conducted a retrospective review of electronic ICU records of known HIV+ patients of our hospital who were admitted to the ICU between April 1st, 2001 and April 1st, 2006. All of the patients included in this study were already under the care of the HIV/GUM department for their HIV disease. The hospital ethics committee was consulted and deemed formal ethical review unnecessary. Data collected were age at admission, sex, race, risk factor for HIV acquisition, receipt of antiretroviral therapy, admission diagnosis, reason for ICU...
Table 1: Characteristics of the 43 patients included in this study. The second column is percentage, unless stated otherwise. IQR: interquartile range; ART: antiretroviral therapy; MSM: men who have sex with men.

| Characteristic                                     | Absolute numbers | Percentage (%) or IQR |
|---------------------------------------------------|------------------|-----------------------|
| Median age (IQR)                                  | 44 (40–60)       |                       |
| Male                                              | 32 (73%)         |                       |
| Race                                              |                  |                       |
| White                                             | 23 (53.5%)       |                       |
| Black                                             | 10 (23.6%)       |                       |
| Asian                                             | 4 (9.3%)         |                       |
| Other                                             | 2 (4.7%)         |                       |
| Unknown                                           | 4 (9.3%)         |                       |
| HIV risk factor                                   |                  |                       |
| Heterosexual                                      | 15 (34.9%)       |                       |
| MSM                                               | 23 (53.5%)       |                       |
| Injection drug use                                | 3 (7%)           |                       |
| Unknown                                           | 2 (4.7%)         |                       |
| On ART                                            |                  |                       |
| Yes                                               | 24 (55.8%)       |                       |
| No                                                | 13 (30.2%)       |                       |
| Unknown                                           | 6 (14%)          |                       |
| Median CD4 (IQR)                                  | 128 (9–627)      |                       |
| Median APACHE II (IQR)                            | 21 (10–38)       |                       |
| AIDS-defining diagnosis at time of ICU admission   | 19 (44%)         |                       |

admission, CD4 count, HIV viral load, acute physiology and chronic health evaluation II (APACHE II) score, length of stay, organs systems supported, and outcome. Admissions were defined as AIDS-related if prompted by an AIDS defining illness [23]. Standard definitions were used for sepsis and septic shock [24]. Followup lasted until April 1st, 2007, a minimum followup period of one year for all patients.

2.1. Data Analysis. Cox regression was used to correlate variables of interest with outcome. Kaplan-Meier analysis and log rank test were used to examine long-term survival. The Wilcoxon rank sum test was used to compare CD4 counts between groups. Stata 10 and r software were used for analysis. A significance level of 0.05 was used throughout.

3. Results

3.1. Descriptive Analysis. During the study period, 43 patients were admitted to the ICU, each on one occasion. All patients were known to be HIV+ at the time of ICU admission, there were no diagnoses made on the ICU during the study period. Characteristics of the patients in this study are shown in Table 1.

3.2. Reason for Admission to ICU and Usage. The reasons for admission to ICU by category and subsequent outcome are shown in Table 2. All of the patients in this study had only one admission to ICU. The mean length of ICU stay was 10 days (median 6 days; range 1 to 47).

Thirty-three patients (78.7%) had respiratory support, 26 (62%) underwent tracheal intubation and mechanical ventilation, and seven (16.7%) had noninvasive ventilation. Twenty-three patients (56%) had cardiovascular support with inotropes (data missing for two patients). Eleven patients (26.8%) had renal replacement therapy (data missing for two patients).

3.3. Diagnosis. A wide variety of diagnoses were made (Table 3). Seven patients had more than one diagnosis made (not including patients with organ failure as part of a sepsis syndrome or neutropaenic sepsis occurring on the background of chemotherapy for malignancy). These were Castleman’s disease/PCP (at presentation), Burkitt’s lymphoma/pneumonia (at presentation), PCP/pulmonary oedema, pneumonia/pontine haemorrhage, tuberculous arthritis/renal failure (unexplained), anal carcinoma/renal failure (drug related), and multiple myeloma/non-Hodgkin’s lymphoma.

Nineteen admissions (44%) were for AIDS-related diagnoses (according to 1993 CDC criteria). However, 31 admissions (72%) in total were for HIV-related diagnoses, this includes the 19 AIDS-related admissions plus further 12 patients with serious infections but CD4 counts greater than 200. Twelve patients were admitted to ICU for reasons not directly related to HIV infection. These were pneumothorax/threatened airway, pancreatitis (2 patients), GI bleed (2 patients), liver failure, renal failure (2 patients), status epilepticus, deliberate drug overdose, adhesional bowel obstruction on a background of ulcerative colitis, and neutropaenic sepsis related to chemotherapy for anal carcinoma (considered not related to HIV).
two patients (51%) died in hospital. Median time to death ICU admission (mean 37.1 days; range 3 to 77). Twenty-survived after ICU admission but died in hospital; median days, IQR 2 to 16 days; range 1 to 23 days). Eight patients the median time to death on ICU was 8.5 days (mean 9.8 HIV infection (100 versus 242 cells/mL, compared with patients admitted for reasons unrelated to mortality among patients requiring invasive ventilation was slightly, though not significantly, higher than total mortality (P = 0.108).

We did not observe any association between CD4 count and survival in this population (P = 0.77). Figure 1 shows Kaplan-Meier analysis of survival for patients with a CD4 count greater than or less than 100. There was no difference in long-term survival between patients with CD4 counts above or below 100 cells/mL (log rank test, P = 0.56). Analysis using CD4 count cut-offs of 50 and 200 cells/mL gave similar results.

There was a nonsignificant trend to increasing mortality with increasing APACHE II score, hazard ratio 1.04 per point increase in APACHE II score, P = 0.056 (a doubling of mortality with 17 point increase in APACHE II score). No other variables were significantly associated with mortality; therefore, multivariate analysis was not performed.

The median followup for the study was 1008 days (range 1–2015 days). Overall, 29 (67.4%) patients died during the study period. Median survival in those who died was 20 days after ICU admission (range 1–565). Median time to death from ICU admission for nonsurvivors was 20 days (mean 86.3 days).

Mortality was higher than average in patients with a respiratory diagnosis (Table 2) although the median APACHE II score was lower in the respiratory group (17 versus 26). Adjustment for this, however, showed no significant difference in mortality between the two groups. Mortality among patients requiring invasive ventilation was slightly, though not significantly, higher than total mortality (P = 0.108).

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The median followup for the study was 1008 days (range 1–2015 days). Overall, 29 (67.4%) patients died during the study period. Median survival in those who died was 20 days after ICU admission (range 1–565 days). Twenty-six of the 29 patients who died had died by one year of followup. Although early mortality was high, all patients that survived to hospital discharge but died during followup (seven patients) was 352 days from ICU admission (mean 295.7 days; range 81 to 565). Median time to death from ICU admission for nonsurvivors was 20 days (mean 86.3 days).

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4. Discussion

It is striking that, despite coming from a large unit, the number of patients admitted to ICU during a five-year period was low, only 43. Because of this small number, it is difficult to make generalisations to a larger population, however it is clear that the burden placed on the ICU facility by our large HIV+ population is not great. Our unit took part in an earlier study on ICU usage by HIV+ patients in the same region [7]. Whilst it may be difficult to make direct comparisons between the studies, ICU mortality was 33% in each study.
Using a CD4 cut-off P category greater or less than 100.

18 and ICU mortality 23% [14]. The fact that mortality re-involved in the original study; median APACHE II score was published the recent experience of another ONE of the ICUs by Gill et al., 15 versus 21 in this study. Dickson et al. have 1: Survival of HIV+ patients admitted to ICU by CD4 count Figure 4 Interdisciplinary Perspectives on Infectious Diseases

1.5% of patients in the 1993–1997 period to 26.8% of pa-

in this study period. Despite the small population size, this is

likely to represent an increase from 10.5% in 1993–1997 [7].

This study compared with the pre-HAART era. Two patients

who assisted with statistical advice.

had complications of liver disease, variceal haemorrhage, and liver failure. Although conclusions cannot be drawn from

such small numbers, our only patient with liver failure died on ICU, consistent with the findings of Dickson et al. where

liver failure in the context of HIV had a poor ICU prognosis

[14]. Liver disease is making an increasing contribution to mortality in HIV+ patients [25].

There were a large number (28%) of admissions for sepsis in this study period. Despite the small population size, this is

likely to represent an increase from 10.5% in 1993–1997 [7].

This is consistent with trends in US death certificate report-
ed in the late 1990s showing an increase in deaths from septic aemia in HIV+ patients [26]. ICU mortality from sepsis was

25% in this study, lower than in 1993–1997 (50%).

The use of renal replacement therapy increased from 1.5% of patients in the 1993–1997 period to 26.8% of pa-
tients in this cohort, partially (though not fully) accounted for by the increased number of patients with sepsis who had
renal replacement therapy. Renal failure is more common in HIV+ patients than other groups and it is associated with an
increase in mortality [27]. The increase in use of renal re-
placement therapy perhaps reflects an underlying trend to treat these patients more aggressively in the light of their im-
proved long-term prognosis.

Interestingly the majority of patients who were admitted to ICU were admitted for reasons directly related to HIV in-
fection (72%). Of those who were not, at least five had med-
cal conditions caused or exacerbated by drug or alcohol mis-
use (liver failure, two GI bleeds, one case of pancreatitis and deliberate drug overdose). Although not directly HIV relat-
ed these admissions (12% of all admissions) underline the significant burden of psychiatric co-morbidity occurring in
the context of HIV infection.

In our study, HAART use and CD4 count at ITU ad-
mission were not related to long-term survival. However, our
population is too small to adequately interrogate this differ-
ence. There may be other reasons for changes in CD4 count
and/or survival over time, such as improvements in nutrition,
prophylaxis or other aspects of care. Two larger studies with
long followup did detect an influence of HAART on sur-

dival [16, 22]. Four of our patients appeared to be failing
HAART; a shortcoming of this study is that we did not collect the reasons for this. Median long-term survival in this
study was 1008 days, and no patient who survived for more than 2 years after ICU admission died during the study
period. Two recent studies have also reported encouraging
long-term survival [16, 22].

This study has significant shortcomings. The population
is small making it difficult to generalise to larger populations.
Data on antiretroviral therapy are incomplete, and duration
and type of regime were not collected. Nevertheless, the small
size of the population in this study drawn from such a large
unit (5000 patients) is indicative of the improved health of
HIV+ patients in the era of HAART. Despite its size and ret-

spective nature, our study adds to the growing body of evi-
dence that ICU care is not futile even in the setting of advanc-
ed HIV disease.

Authors’ Contributions

LT: data collection, data analysis/interpretation, drafting ar-

ticle. All authors approved submission of the article.

Conflict of Interests

The authors declare there is no conflict of interests.

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