Infectious Diseases Physicians' Approach to Antiretroviral Therapy in HIV/AIDS Patients Admitted to an Intensive Care Unit

An Emerging Infections Network Survey

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Purpose: Little is known regarding administration of antiretroviral therapy (ART) regimens in the setting of critical illness. We developed a survey to better understand how infectious disease experts use ART in critically ill HIV/AIDS patients admitted to an intensive care unit (ICU).

Methods: Web-based surveys were distributed in October 2010 to the 1080 adult infectious disease physician members of the Emerging Infections Network. Responses were stratified by region, practice type, years of HIV experience, and by a cumulative HIV medicine score developed to measure expertise in managing HIV.

Results: A total of 501 members (46%) responded. In both ART-naive and -experienced patients, respondents were more likely to initiate or continue ART during treatment of an opportunistic infection (OI) (69% and 87%, respectively) than for low CD4 count/high viral load (25% and 79%, respectively). The OI for which respondents would most likely start ART was *Pneumocystis jiroveci* pneumonia. Reported barriers for use of ART in the ICU included immune reconstitution syndrome (71%), drug interactions (72%), and variable drug absorption (65%).

Conclusions: There is a lack of consensus of how to manage ART in the critically ill HIV patient. Infectious disease specialists were most likely to initiate or continue ART in the setting of an OI. Among OIs, respondents would most likely initiate ART for *P. jiroveci* pneumonia. Immune reconstitution syndrome, drug interactions, and outpatient follow-up were the most common reported barriers to use of ART in the ICU. Further studies are needed to provide better guidance on ART use in critically ill patients.

Key Words: ART, critically ill, HIV/AIDS

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Since the advent of antiretroviral therapy (ART), the overall morbidity and mortality of HIV/AIDS patients admitted to the intensive care unit (ICU) have significantly declined.[1,2] Data suggest a survival benefit or a protective effect in critically ill patients when ART is initiated while in the intensive care setting. Of note, the end points differed among the studies and varied from short-term survival (overall hospital and in-ICU) to long-term survival (6 months and 1 year after ICU discharge).[3–7] Furthermore, the initiation of ART within the first 14 days in primarily ART-naive patients admitted with an acute opportunistic infection (OI) proved to have a significant survival benefit without an increased incidence in adverse effects within the first 6 months.[8] Although this trial did not report the percentage of patients admitted to the ICU, the median CD4 count (29 cells/μL) suggests a population comparable in disease severity to that in the ICU studies above. These studies have focused mainly on patients presenting with acute OIs. However, this may no longer be representative of all patients admitted to the ICU in the ART era. In the developed world with access to antiretroviral medications, the epidemiology of HIV-infected patients admitted to ICUs has evolved over the years, resultant of initiation of ART and timing of HIV diagnosis.[9,10] Although many patients still present with advanced disease and AIDS-associated OIs such as *Pneumocystis jiroveci* pneumonia (PJP), patients in some institutions are also presenting to ICUs with complications which include chronic comorbidities such as renal failure, cardiomyopathy, liver, and pulmonary diseases.[1,3,9]

Although the data for acute administration of ART are compelling, the management of critically ill patients with HIV/AIDS poses unique challenges. Potential limitations for the lack of a standardized approach could be due to several factors. Patients in the ICU unable to take antiretrovirals by mouth are often administered medications via enteral feeding tubes, for which there are limited safety and efficacy data. Most of what is published regarding feeding tube administration is in the pediatric literature, where the enteral tube was placed as a measure to ensure medication adherence and not in the setting of critical illness.[11] In addition, critical illness is associated with numerous physiologic changes, which could potentially alter the pharmacokinetic and pharmacodynamic parameters of ART. These alterations include decreased drug absorption due to gastrointestinal immobility and altered drug distribution secondary to changes in fluid status and pH, along with the potential for altered drug elimination due to decreases in renal and hepatic function. Other challenges include drug-drug interactions with medications frequently used in ICU patients such as proton pump inhibitors, H_2 receptor antagonists, and benzodiazepines, as well as overlapping toxicities. As a result of these potential limitations, a standardized, evidence-based approach has not been established for how antiretroviral regimens can be optimally selected and administered in the setting of critical illness. The antiretroviral guidelines for adults and adolescents developed by the Department of Health and Human Services

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Panel and commissioned by the National Institutes of Health as well as the International Aids Society comprehensively address many aspects of the use of ART.[12,13] Yet there is a paucity of information in the current Department of Health and Human Services and International Aids Society guidelines regarding the approach of ART in the critically ill.

The investigators of the current study found it prudent to survey US-based infectious disease (ID) physicians to better understand how ID experts across a range of practice settings approach the use of ART in critically ill HIV/AIDS patients admitted to an ICU. We developed a survey and queried ID physicians who are members of the Emerging Infections Network (EIN) and who follow adult patients with HIV/AIDS.

MATERIALS AND METHODS

Between September and October 2010, a Web-based survey was distributed to the 1080 members of the EIN who see adults ID patients. The network is funded by the Centers for Disease Control and Prevention and sponsored by the Infectious Diseases Society of America. It is a sentinel network of ID consultants who regularly engage in clinical activity and whose participation is voluntary. Data on geographic location and practice type are maintained for all members. The EIN provided demographic information on both responders and nonresponders. Staff at the coordinating center of the EIN (Iowa City, Iowa) sent the initial survey invitation by e-mail or facsimile, followed by 2 reminders to nonresponders at 1 and 2 weeks following the initial mailing.

An 11-question survey was developed to assess the decisions made by ID practitioners in the care of critically ill patients infected with HIV. Survey questions included amount of total and ICU HIV experience, use of routine HIV infection monitoring parameters, specific indications for ART initiation or continuation, and perceived barriers to use of ART therapy. A copy of the survey has been included as a supplemental attachment.

Based on the survey responses, a cumulative HIV medicine score was developed to measure expertise in managing HIV based on the number of HIV patients treated per month and the percentage of HIV in their practice, each of which were scored on a scale of 0 to 3 (Table 1). An HIV medicine score was determined by adding up the 2 individual scores; a total score of 0 to 1 was defined as little to no HIV practice; score of 2, 3, or 4 was defined as some HIV practice, and score of 5 or 6 was defined as considerable HIV practice.

TABLE 1. Development of HIV Medicine Score

No. HIV-infected patients treated in a usual month	
None	Add 0
1–20	Add 1
21–50	Add 2
>50	Add 3
Portion of practice that HIV medicine constitutes	
None to very little (0%–4%)	Add 0
Some (5%–25%)	Add 1
Moderate (26%–50%)	Add 2
Considerable (≥50%)	Add 3
Summary of HIV medicine score	
No HIV	Total score 0 or 1
Some HIV practice	Total score 2, 3, or 4
Considerable HIV practice	Total score 5 or 6

Data Analysis

Frequencies and descriptive statistics were used to define the demographic data of the respondents. Statistical tests were performed using Excel (Microsoft) and SPSS 17.0. Results were analyzed using the Mantel-Haenszel χ^2 test or a 2-tailed Fisher exact test where appropriate.

RESULTS

Demographics

Of 1080 adult ID physician members, a total of 501 (46%) responded. Response rates did not differ between region or practice type. Respondents were significantly more likely than nonrespondents to have at least 5 years of ID experience ($P < 0.0001$). Responses were stratified by region, practice type, and cumulative HIV medicine score. Summary data of geographic region, years since ID fellowship, and type of practice for respondents are shown in Table 2.

Eighty-five percent of respondents reported providing HIV care in both inpatient and outpatient settings; the remainder practice in only 1 setting. Academic physicians, defined as any practitioner with an academic appointment regardless of type of hospital in which he/she practices, were significantly more likely to report both considerable HIV practice experience (21%) and little HIV practice experience (40%) when compared with nonacademic physicians (10% considerable vs 32% with very little HIV practice experience, respectively) ($P < 0.0001$). Nonacademic physicians were most likely to have some HIV medicine practice (58%) when compared with academic physicians (39%). HIV practice experience did not vary by years of experience or by US Census Bureau Division.

HIV and ART in ICU

When asked which laboratory parameters (CD4 count and percentage, HIV viral load [VL], or HIV resistance genotype) should be routinely monitored while patients are in the ICU, the results varied greatly (Table 3). Forty-five percent of respondents believed CD4 count and percentage should be monitored, and 35% believed that VL should be monitored, whereas 43% reported none of these parameters should be monitored regularly. Sixteen percent responded that it would be dependent on the patient scenario; for example, one time only while in the ICU, or only if a recent CD4/VL was not available. These results did not vary by geographic region or hospital practice type. Based on HIV medicine score, practitioners with the least HIV experience (HIV medicine score 0–1) were somewhat more likely to monitor CD4 count and VL compared with those who had more experience (HIV medicine score of 2–5).

Respondents were asked when they would initiate or continue ART while a patient is in the ICU in 3 circumstances: for newly diagnosed patients, for ART-naive, and for ART-experienced patients. In all 3 cases, respondents were more likely to initiate or continue ART during treatment of an OI than for only low CD4 count/high VL. Practitioners with considerable HIV experience were more likely to continue ART for experienced patients compared with those with some to no HIV experience ($P = 0.03$). All practitioners, regardless of HIV medicine score, were more likely to continue than initiate ART for all HIV patients, irrespective of CD4 count or VL.

Respondents were asked to rank order OIs for which they would initiate ART in patients not already on therapy. The available options included *Pneumocystis jiroveci pneumonia* (PJP) , cryptococcal meningitis, cytomegalovirus, toxoplasmosis, *Mycobacterium avium* complex (MAC), and *Mycobacterium tuberculosis* (MTB). Respondents were most likely to start ART for PJP,

TABLE 2. Demographic Characteristics for 501 Respondents

Characteristic	n (%)
US Census Bureau Division	
Mid-Atlantic	31 (6)
New England	72 (14)
East North Central	75 (15)
West North Central	40 (8)
South Atlantic	96 (19)
East South Central	26 (5)
West South Central	33 (6)
Mountain	32 (6)
Pacific	91 (18)
Puerto Rico	1 (0.2)
Canada	4 (0.8)
Years of experience since ID fellowship	
<5 (includes fellows)	133 (27)
5–14	121 (24)
15–24	158 (31)
≥25	89 (18)
Type of practice	
Academic	203 (41)
Nonacademic	298 (59)
No. HIV-infected patients treated in a usual month	
None	135 (27)
1–20	192 (38)
21–50	115 (23)
>50	59 (12)
Portion of practice that HIV medicine constitutes	
None to very little (0%–4%)	52 (10)
Some (5%–25%)	82 (17)
Moderate (26%–50%)	190 (38)
Considerable (≥50%)	177 (35)
Summary HIV medicine score	
No HIV	177 (35)
Some HIV practice	253 (51)
Considerable HIV practice	71 (14)
Average no. HIV cases seen per month in institution's ICU(s)	
None	32 (9)
<5	216 (58)
5–10	58 (16)
11–20	19 (5)
>20	12 (3)
Do not know	34 (10)
Percentage of HIV-infected patients in ICU for whom ID is consulted for HIV medical management	
<25%	23 (6)
25%–50%	14 (4)
51%–75%	31 (8)
>75%	272 (73)
Do not know	30 (8)

with 50% ranking PJP as number 1. Figure 1 depicts the rankings 1 to 6 of the survey respondents. All other individual choices were ranked first by less than 20% of respondents. Practitioners were most likely to initiate ART in critically ill patients during the treatment of PJP compared with any other OI irrespective of region, hospital practice type, or HIV medicine score. Cytomegalovirus was the infection for which respondents were next most likely to start ART, with 40% of respondents ranking it as their first or second choice. Respondents were least likely to initiate ART for *M. tuberculosis* or cryptococcal meningitis, which were ranked lowest by 27% and 25% of those surveyed. However, each of these choices was ranked first by 16% of respondents, reflecting significant variability in opinions of the survey participants.

In addition to treatment-naive patients with OIs, most respondents also indicated they would initiate ART in naive patients for other specific HIV-associated complications including lymphoma, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenia purpura, and neurocognitive disorders (Table 3). The responses for all of these indications were similar across region and hospital practice type. However, a significant difference was seen when responses were stratified according to HIV medicine score, as practitioners with more HIV experience were more likely to initiate ART for HIV-associated ITP ($P = 0.0002$).

A variety of barriers to initiating ART while in the ICU were identified. Barriers were categorized as those related to drug concerns, host concerns, and long-term concerns (Table 3). Of the drug concerns, most respondents reported drug interactions (72%), drug absorption (65%), and drug adverse events (64%). The most commonly reported host concern was risk of developing immune reconstitution syndrome (IRIS; 71%), whereas patient follow-up was identified as the most common long-term concern (67%). Of note, respondents with the least HIV experience were more likely to be concerned about longer-term issues, including concern for potential development of resistance and uncertainty about outpatient follow-up.

DISCUSSION

This survey of ID specialists demonstrates a wide variability in self-reported practice patterns for administration of ART in the critically ill patient with HIV. Responses differed based on practice setting and amount of HIV experience. Some variability in approach was observed in almost every aspect of patient care. This variability in self-reported physician practice may reflect the lack of awareness of results from the multiple studies demonstrating mortality benefit in both hospitalized patients with acute OIs and critically ill patients with HIV/AIDS, but may also reflect the changing characteristics of HIV patients admitted to the ICU, unique challenges of administering ART in the ICU setting, and the unknown risk-benefit ratio with antiretroviral drugs in the critically ill.[1,4–8,14]

When asked what laboratory parameters should be routinely monitored, respondents were almost evenly split between those who felt that CD4 count and percentage should be monitored and those who responded that no laboratory parameters should be routinely monitored, irrespective of the patient presentation or prior ART history. When asked in which HIV patients ART should be considered while in the ICU, responses varied from none to all HIV patients. The initiation of ART in a patient not already on therapy elicited the greatest variability in responses. Although the majority of practitioners would most strongly consider initiating ART in a patient presenting with PJP, the responses for the remaining OIs were more strongly divided. Of note, this survey was conducted before the most recent data on the benefit of early ART in patients with HIV/tuberculosis coinfection and low CD4 counts and may explain the variability of this response.[15,16]

TABLE 3. Management of HIV Patient and Consideration of ART While in the ICU by Practice Type and HIV Medicine Score

	All Respondents	Practice Type		HIV Medicine Score		
		Academic	Nonacademic	0–1	2–4	5–6
Total no. possible respondents in each category	501	203	298	177	253	71
Which of the following laboratory parameters should be monitored during HIV/AIDS patients' ICU stay?	n = 333	n = 123	n = 210	n = 35	n = 229	n = 69
CD4 count and CD4 percentage	150 (45)	52 (42)	98 (47)	19 (54)	103 (45)	28 (41)
HIV VL	117 (35)	38 (31)	79 (38)	14 (40)	83 (36)	20 (29)
HIV resistance genotype	26 (8)	6 (5)	20 (9)	3 (8)	18 (8)	5 (7)
Not applicable; these parameters should not be routinely monitored	144 (43)	54 (44)	90 (43)	13 (37)	100 (44)	31 (45)
In which of these HIV patient populations would you consider ART while a patient is in the ICU?						
Newly diagnosed patients	n = 261	n = 98	n = 163	n = 24	n = 182	n = 55
With OI	177 (68)	70 (71)	107 (66)	15 (62)	122 (67)	40 (73)
With low CD4 count	107 (41)	32 (33)	75 (46)*	9 (37)	74 (41)	24 (44)
All	16 (6)	5 (5)	11 (7)	2 (8)	10 (5)	4 (7)
None	60 (23)	25 (25)	35 (21)	6 (25)	46 (25)	8 (14)
Treatment-naive patients	n = 254	n = 99	n = 155	n = 22	n = 180	n = 52
With OI	176 (69)	70 (71)	106 (68)	14 (64)	125 (69)	37 (71)
With low CD4 count	114 (45)	40 (40)	74 (48)	11 (50)	81 (45)	22 (42)
All	17 (4)	4 (4)	13 (8)	2 (9)	10 (5)	5 (10)
None	56 (12)	24 (24)	32 (21)	5 (23)	40 (22)	11 (21)
Continue therapy in treatment-experienced patients	n = 335	n = 126	n = 209	n = 34	n = 232	n = 69
With OI	290 (87)	105 (83)	185 (88)	25 (73)	204 (88)	61 (88)
Low CD4 count	265 (79)	96 (76)	169 (81)	21 (62)	187 (81)	57 (83)*
All	211 (63)	75 (59)	136 (65)	21 (62)	150 (65)	40 (58)
None	28 (8)	11 (9)	17 (8)	5 (15)	19 (8)	4 (6)
For which of the following would you likely start ART in an HIV patient not already on treatment?	n = 329	n = 124	n = 205	n = 31	n = 230	n = 68
Lymphoma or other malignancy	275 (84)	107 (86)	168 (82)	27 (87)	191 (83)	57 (84)
HIV-associated ITP	283 (86)	105 (85)	178 (87)	20 (64)	198 (86)	65 (95)†
HIV-associated thrombotic thrombocytopenic purpura	270 (82)	99 (80)	171 (83)	23 (74)	190 (83)	57 (84)
HIV-associated neurocognitive disorders	264 (80)	103 (83)	161 (78)	23 (74)	187 (81)	54 (79)
Which of the following do you view as barriers to starting ART in the ICU?	n = 340	n = 127	n = 213	n = 36	n = 235	n = 69
Drug concerns						
Adverse drug effects	217 (64)	79 (62)	138 (65)	26 (72)	142 (60)	49 (71)
Available dosage forms	210 (62)	78 (61)	132 (62)	18 (50)	150 (64)	42 (61)
Consistent medication administration	96 (28)	40 (31)	56 (26)	7 (19)	73 (31)	16 (23)
Drug interactions	245 (72)	91 (72)	154 (72)	27 (75)	165 (70)	53 (77)
Variable drug absorption	222 (65)	87 (68)	135 (63)	20 (55)	157 (67)	45 (65)
Unknown achievable ART blood levels	68 (20)	27 (21)	41 (19)	10 (28)	49 (21)	9 (13)
Lack of baseline resistance testing/genotype	193 (57)	66 (52)	127 (60)	25 (69)	128 (54)	40 (58)
Host concerns						
Immune reconstitution inflammatory syndrome	240 (71)	86 (68)	155 (73)	29 (80)	162 (69)	49 (71)
Organ failure	188 (55)	73 (60)	115 (54)	22 (61)	123 (52)	43 (62)
Long-term concerns						
Concern for potential development of resistance	83 (24)	27 (21)	56 (26)	13 (36)	56 (24)	14 (20)
Uncertainty about outpatient follow-up	227 (67)	85 (67)	142 (67)	26 (72)	158 (67)	43 (62)
Uncertainty about access to medications after hospital discharge	180 (53)	65 (51)	115 (54)	19 (53)	128 (54)	33 (48)

Data are reported as n (%). Instructions were to select all that apply, so numbers add to more than the total respondents; "n" represents the actual respondents to that question out of the total respondents.

*$P < 0.05$.

†$P = 0.0002$.

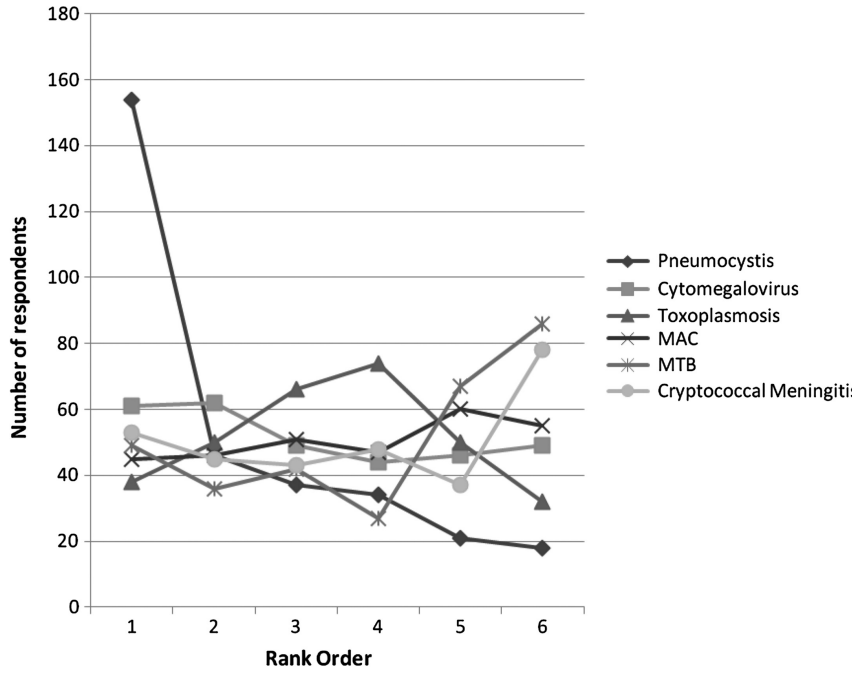

FIGURE 1. Rank order of the OIs for which respondents would likely start ART in an HIV patient not already on treatment. Rank 1 is the OI for which the physician would most likely start ART; rank 6 is the least likely.

Despite these large variations in response patterns, there were some consistencies observed across groups. The ID specialists responding to the survey were most likely to initiate or continue ART in the ICU setting when the patient is being treated for an OI, regardless of HIV experience. Furthermore, all practitioners irrespective of HIV practice experience responded they would continue ART in those already on therapy in any situation regardless of CD4 count or VL. Among OIs, respondents would most likely initiate ART for PJP. Most practitioners would also initiate ART for specific HIV-related non-OI complications such as lymphoma and ITP. Concerns about IRIS, drug interactions, variable drug absorption, and uncertainty of outpatient follow-up were the most common reported barriers to use of ART in the ICU.

Multiple studies have assessed the impact of early ART on the outcomes of HIV patients with acute OIs. The patient populations, study sites, end points, definition of early ART, and results varied between studies. Three studies of patients with TB showed reduced rates of death with early administration of ART, including those in the lowest CD4 count strata.[17–19] Zolopa et al[8] conducted a study of patients presenting with OIs, of which 63% of cases were attributed to PJP, and showed a decreased risk of progression to AIDS or death with early ART. Conversely, 1 study in cryptococcal meningitis showed an increased mortality rate in patients who received early ART.[20] Although these studies overall show that there may be benefit to early initiation of ART in many patients presenting with acute OIs, they did not specifically assess outcomes in the subset of critically ill patients admitted to the ICU who received early therapy. These studies also do not answer the question of initiation or continuation of ART in critically ill patients with HIV who are admitted with non–AIDS-related diagnoses.

In addition to treatment of OIs, survey respondents strongly favored the use of ART in critically ill patients with other specific HIV-related complications. In all of these processes, either uncontrolled HIV infection has been directly or indirectly implicated in disease pathogenesis, or control of HIV infection is associated with improved outcomes.[21–23] Initiation or continuation of ART in critically ill patients with immediately life-threatening complications such as ITP or thrombotic thrombocytopenic purpura may be a crucial component of disease management, but there is much less information on the short-term benefits of ART in critically ill patients with more chronic processes such as lymphoma or HIV-associated neurocognitive disorders.

There are relatively few studies that assess the impact of ART during acute hospitalization. With the exception of the study by Zolopa et al, which was a prospective, randomized, multicenter study, most available data come from retrospective studies in patients predominantly presenting with OIs.[8] Morris et al[24] reported the outcomes of 58 patients admitted to their ICU with severe PJP. They found ART started before or during hospitalization to be an independent predictor of decrease in ICU and overall mortality. Another more recent study assessed the outcomes of critically ill HIV patients with high rates of AIDS-defining illnesses (80.6%) and low CD4 counts (median, 39 cells/mL).[6] This study found antiretroviral administration during ICU admission to be an independent predictor of survival at 6 months. Of interest, they also found that discontinuation of ART during ICU admission was associated with a higher mortality risk compared with patients who continued therapy. Data such as these may have influenced the survey respondent's approaches to initiating or continuing ART in patients presenting with OIs.

Although OIs remain a major indication for ICU admission, there are increasing case series reported in which OIs are less common as the admitting diagnosis, presumably because of the introduction of ART. [9,10] Although published data provide some evidence supporting administration of ART to critically ill patients with OIs, such patients may not be entirely representative of the patients with HIV now most admitted to the ICU in developed countries.[1,24,25] Powell et al[3] reported a

decrease in PJP diagnosis (24% vs 9%, $P = 0.03$), AIDS-associated admission diagnoses (34% vs 19%, $P = 0.17$), and improved survival (58% vs 75%; $P = 0.001$) from 2000 to 2004. Antiretroviral therapy was not found to be an independent predictor of survival. However, prior ART administration was associated with lower rates of AIDS-associated ICU admission diagnosis (12% vs 25%; $P = 0.008$), lower rates of PJP (3% vs 19%, $P < 0.001$), and higher baseline albumins compared with patients not on ART before hospitalization. Despite that ART was not identified as an independent predictor of outcomes, it is likely that ART had some effect on patient admission characteristics and thus impacted hospital outcomes at least indirectly. A study by Casalino et al[1] showed a similar decrease in AIDS-related ICU admissions (57.7% vs 37%, $P = 0.00002$) and a decrease in ICU length of stay (13 vs 9 days, $P = 0.008$) from the pre-ART to ART eras.

Not all of the more recent ICU studies demonstrate differences in ICU admission characteristics compared with the pre-ART era. A study by Coquet et al[2] compared admission characteristics in 4 different time periods from 1996 to 2005. Although they did not demonstrate a difference in admission characteristics, this may have been influenced by the fact that the rates of prior ART administration were similar between all 4 time periods. Finally, a study comparing patients on ART before admission compared with no ART before admission found no difference in admission characteristics between the 2 groups. However, a significant portion of patients (40%) were admitted with non–HIV-related diagnoses.[3] There are minimal available data regarding the impact of ART initiation or continuation in critically ill patients without AIDS-defining illnesses. This may have contributed to our survey responses indicating that fewer respondents were comfortable with the administration of antiretrovirals in this patient population.

The most commonly reported barriers to initiation of ART included IRIS, drug interactions, and outpatient follow-up. Surprisingly, less than one-third of respondents indicated that uncertainty about consistent medication delivery in critically ill patients, lack of predictability of achievable ART blood levels, and concern for potential development of resistance were barriers to ART usage. Many of these barriers are theoretically important considerations in the use of ART in the ICU, but no studies to date have assessed the impact of these factors on the outcomes of critically ill patients. Specific information on these issues that can inform the debate on initiation or continuation of ART in critically ill patients is needed.

The results of our survey varied greatly, particularly when responses were stratified according to hospital practice type and HIV medicine score. One-third of the ID physician survey respondents saw very few HIV patients routinely, yet might still be required to consult on critically ill HIV infected patients in the ICU setting. This further increases the value of and need for specific guidelines. This also strongly indicates the need for well-designed observational studies to provide better guidance on ART use in critically ill patients.

REFERENCES

1. Casalino E, Wolff M, Ravaud P, et al. Impact of ART advent on admission patterns and survival in HIV-infected patients admitted to an intensive care unit. *AIDS*. 2004;18(10): 1429–1433.
2. Coquet I, Pavie J, Palmer P, et al. Survival trends in critically ill HIV-infected patients in the highly active antiretroviral therapy era. *Crit Care*. 2010;14(3):R107.
3. Powell K, Davis JL, Morris A, et al. Survival for patients with HIV admitted to the ICU continues to improve in the current era of combination antiretroviral therapy. *CHEST*. 2009;135:11–17.
4. Morris A, Wachter RM, Luce J, et al. Improved survival with highly active antiretroviral therapy in HIV-infected patients with severe *Pneumocystis carinii* pneumonia. *AIDS*. 2003;17(1):73–80.
5. Vargas-Infante Y, Guerrero M, Ruiz-Palacios M, et al. Improving outcomes of human immunodeficiency virus–infected patients in a Mexican intensive care unit. *Arch Med Res*. 2007;38:827–833.
6. 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.
7. 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.
8. Zolopa A, Andersen J, Powderly W, et al. Early antiretroviral therapy reduces AIDS progression/death in individuals with acute opportunistic infections: a multicenter randomized strategy trial. *PLoS One*. 2009;4(5):e5575.
9. Akgun KM, Pisani M, Crothers K. The changing epidemiology of HIV-infected patients in the intensive care unit. *J Intensive Care Med*. 2011;26(3):151–164.
10. Shosbree J, Campbell LJ, Ibrahim F, et al. Late HIV diagnosis is a major risk factor for intensive care unit admission in HIV-positive patients: a single centre observational cohort study. *BMS Infect Dis*. 2013;13:23.
11. Prohaska ES, King AR. Administration of antiretroviral medication via enteral tubes. *Am J Health Syst Pharm*. 2012;69:2140–2146.
12. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1–infected adults and adolescents. Department of Health and Human Services February 12, 2013; 1–267. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed March 2013s.
13. Thompson MA, Aberg JA, Cahn P et al. Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society USA Panel. *JAMA*. 2010;304(3):321–333.
14. Akgun 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.
15. Suthar A, Lawn SD, del Amo J, et al. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. *PLos Med*. 2012;9(7):1–15
16. Jonsson M, Fusco JS, Cole SR, et al. Timing of HAART initiation and clinical outcomes in human immunodeficiency virus type 1 seroconverters. *Arch Intern Med*. 2011;171(17):1560–1569.
17. Abdool Karim SS, Naidoo K, Grobler A, et al. Timing of initiation of antiretroviral drugs during tuberculosis therapy. *N Engl J Med*. 2010;362(8):697–706.
18. Blanc F-X, Sok T, Laureillard D, et al. Earlier versus later start of antiretroviral therapy in HIV-infected adults with tuberculosis. *NEJM*. 2011;365:1471–1481.
19. Havkir, DV, Kendall MA, Ive P et al. Timing of antiretroviral therapy for HIV-1 infection and tuberculosis. *N Engl J Med*. 2011;5:1482–1491.
20. Makadzange AT, Ndhlovu CE, Takarinda K, et al. Early versus delayed initiation of antiretroviral therapy for concurrent HIV infection and cryptococcal meningitis in sub-Saharan Africa. *Clin Infect Dis*. 2010;50(11):1532–1538.
21. Hart D, Sayer R, Miller R et al. Human immunodeficiency virus associated thrombotic thrombocytopenic purpura—favourable outcome

with plasma exchange and prompt initiation of highly active antiretroviral therapy. *Br J Haematol*. 2011;153:515–519.

22. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117:4190–4207.
23. Achenbach CJ, Cole SR, Kitahata MM et al. Mortality after cancer diagnosis in HIV-infected individuals treated with antiretroviral therapy. *AIDS*. 2011;25:691–700.
24. Morris A, Creasman J, Turner J, et al. Intensive care of human immunodeficiency virus-infected patients during the era of highly active antiretroviral therapy. *Am J Respir Crit Care Med*. 2002;166(3):262–267.
25. Khouli H, Afrasiabi A, Shibli M, et al. Outcome of critically ill human immunodeficiency virus-infected patients in the era of highly active antiretroviral therapy. *J Intensive Care Med*. 2005;20(6):327–333.