

Aetiology and prognostic factors of patients with AIDS presenting life-threatening acute respiratory failure

A. Torres, M. El-Ebiary, R. Marrades, J-M. Miró, J-M. Gatell, J.M. Sanchez-Nieto, A. Xaubet, C. Agustí, R. Rodriguez-Roisin

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ABSTRACT: Respiratory failure is a significant contributor to morbidity and mortality in patients with the acquired immune deficiency syndrome (AIDS). We performed a study to investigate the aetiology, prognostic factors, and short- and long-term outcome of AIDS patients with life-threatening respiratory failure and pulmonary infiltrates.

Forty-two AIDS patients (29 of whom required mechanical ventilation), admitted to a Respiratory Intensive Care Unit (ICU) from 1985 to 1992 because of severe respiratory failure (arterial oxygen tension/fractional inspiratory oxygen ($P_{a,O_2}/F_{I,O_2}$) ratio at hospital admission 19 ± 14 kPa (mean \pm SD)) and diffuse pulmonary infiltrates, were studied for evaluation of the aetiology and outcome. Necropsy studies were performed in 14 out of 23 (61%) patients who died.

Pneumocystis carinii was the most common aetiology of pulmonary infiltrates (28 patients (67%)). Overall, 19 patients survived (45%) and 23 (55%) died. A multivariate analysis of prognostic factors influencing the outcome of the whole population showed that the presence of *P. carinii* pneumonia and the requirement for mechanical ventilation (MV) were the major determinants of outcome for this type of patient. The median survival time after ICU discharge for *P. carinii* pneumonia patients was lower (49 days) when compared to that of the remaining patients (154 days). Median survival time after ICU discharge for patients needing MV (112 days) did not differ from that observed in patients not requiring artificial ventilatory support (154 days).

Although the ICU survival rate in this study was reasonable, 55% for the whole population, and 36% for *P. carinii* pneumonia patients, the poor outcome after ICU discharge, in particular for *P. carinii* pneumonia patients, deserves the reassessment of ICU admission criteria for this type of AIDS population.

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Acute respiratory failure is a frequent complication during the evolution of acquired immune deficiency syndrome (AIDS) patients [1]. For this reason, they may require intensive care unit (ICU) admission. *Pneumocystis carinii* pneumonia (PCP) is the most frequent aetiology of respiratory failure that develops in approximately 60–80% of patients with AIDS [1, 2]. Although respiratory failure due to PCP has decreased because of prophylactic measures, other infectious aetiologies, such as tuberculosis, cytomegalovirus, bacteria and fungi, represent an increasing cause of severe acute respiratory failure [2].

Data regarding mortality of AIDS patients with severe respiratory failure are only known when considering PCP. Mortality of severe PCP is around 60% [3, 4]. Prognostic factors of outcome for this subset of the population have been investigated in some clinical studies [5–8]. Established predictors of acute and long-term

Serveis de Pneumologia i Al·lèrgia Respiratòria and Malalties Infeccioses, Hospital Clínic, Departament de Medicina, Universitat de Barcelona, Spain.

Correspondence: A. Torres
Servei de Pneumologia
Hospital Clínic
Villarroel 170
08036 Barcelona
Spain

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survival of patients with AIDS and PCP have been based on information obtained at the initial clinical presentation [7]. Among these predictors are alveolar-arterial oxygen tension gradient ($A-aPO_2$), Acute Physiology and Chronic Health Evaluation (APACHE) score, severity of chest radiographic abnormalities, and lactate dehydrogenase (LDH) serum levels [5–8]. A recent study by Wächter *et al.* [9] using stepwise logistic regression demonstrated that ICU admission era (after 1985) and albumin levels were the only variables associated with survival of AIDS patients with PCP admitted to an ICU.

We performed this study to investigate the aetiology and prognostic factors of outcome of AIDS patients with severe respiratory failure admitted to a respiratory ICU. Specifically, we compared PCP with other infectious aetiologies. Necropsy studies were performed in 14 out of 23 (61%) of the nonsurvivors.

Material and methods

Patients

Forty two AIDS patients with bilateral pulmonary infiltrates and severe acute respiratory failure were admitted to the Respiratory Intensive Care Unit of the Hospital Clínic of Barcelona between 1985 and 1992. All patients accomplished all of the following criteria of admission to the ICU: 1) presence of severe acute respiratory failure (arterial oxygen tension (P_{a,O_2}) <7 kPa breathing room air or P_{a,O_2} /inspiratory oxygen fraction (F_{I,O_2}) ratio <33 kPa); 2) respiratory rate higher than 30 breaths·min⁻¹; and 3) bilateral pulmonary infiltrates. AIDS patients were diagnosed based on the Centers for Disease Control (CDC) criteria. All patients met Class IV criteria of the CDC [10]. Infectious diseases indicative of AIDS prior to ICU admission included: oropharyngeal candidiasis in eight cases; oesophageal candidiasis in one case; cerebral toxoplasmosis in one case; pulmonary tuberculosis in two cases; cutaneous Herpes simplex in two cases; and diarrhoea due to Cryptosporidia in one case. No patient with PCP had received prophylaxis against it. Patients admitted to our unit after 1988, and previously controlled in the Infectious Disease Unit, received antiretroviral drugs. Patients were divided into two groups depending on whether they were survivors or not.

Antibiotic therapy against *Pneumocystis carinii* included *i.v.* trimethoprim/sulphamethoxazole (TMP/SMZ), the maximal dosage for TMP was 20 mg·kg⁻¹ *q.d.*, and for SMZ dosage 100 mg·kg⁻¹ *q.d.*, in divided doses; or, *i.v.* pentamidine (4 mg·kg⁻¹ *q.d.*) according to the decision of the attending physician. After 1987, corticosteroids were routinely administered at the dosage of 1 mg·kg⁻¹ *q.d.* of methylprednisolone for 3 days. The dosage was later gradually reduced.

Study variables

The following variables were recorded: age; gender; AIDS risk factors; time course from hospital to ICU admission; and years since diagnosis of human immunodeficiency virus (HIV) antibodies. Leucocyte, lymphocyte and CD4+ counts, serum LDH, cholesterol, total proteins, albumin, creatinine and Simplified Acute Physiology Score (SAPS) were recorded upon ICU admission. The standardized and validated technique for CD4+ counting was not introduced in our Institution until 1988, since before that date antiretroviral treatment was not authorized in Spain. Therefore, we only report values from 18 patients belonging to the period after 1988 (n=18).

Time course from ICU admission to mechanical ventilation (MV) was assessed. The era of admission (before or after 1987) and the presence or absence of corticosteroid therapy were registered. All the following variables were registered before admission to ICU, at admission to ICU, after MV institution, with maximal F_{I,O_2} and with maximal positive end-expiratory pressure (PEEP), and before death: pH; P_{a,O_2} ; arterial carbon dioxide tension

(P_{a,CO_2}); $P_{a,O_2}/F_{I,O_2}$ ratio, alveolar to arterial difference in oxygen tension ($A-aPO_2$) (calculated according to a standard formula [11]); PEEP; duration (hours) of maximal F_{I,O_2} ; duration (hours) of maximal PEEP; P_{a,O_2} /alveolar oxygen tension (PA_{a,O_2}) ratio; base deficit and/or base excess. The presence or absence of adult respiratory distress syndrome (ARDS) during ICU stay was also registered [12]. Diagnosis of ARDS was established by using the score described by MURRAY *et al.* [12] (>2.5). Since this definition of ARDS was not published until 1988, this variable was retrospectively recorded. Survivors were followed until death or last hospital control.

Microbiological methods

Bronchoalveolar lavage (BAL) was performed in 30 (71%) cases, autopsy in 14 (33%) and BAL together with protected specimen brush (PSB) (BFW 1.0/70/90; Mediatech Inc., Water-town, MA, USA) in 24 (57%). All these samples were retrieved by means of a fiberoptic bronchoscope (Olympus BFT3R, New Hyde Park, NY, USA) exclusively used for HIV-infected patients. Invasive techniques were carried out based on the decision of the attending clinician not involved in the study. BAL was performed using three aliquots of sterile 0.9% sodium chloride solution (50 mL each) instilled and subsequently aspirated. The lavage was performed in the middle lobe or lingula. The fluid obtained was pooled and divided into two: half of it was for microbiological cultures, and the other half was centrifuged (500×g, 10 min) and the cell pellet was resuspended in phosphate-buffer solution. Smears were obtained by cytocentrifugation (500 rpm, 10 min) (Cytospin, Shandon), stained by the Papanicolaou, Ziehl-Neelsen, Giemsa, periodic acid-Schiff (PAS), haematoxylin and eosin, Perls' and Grocott methenamine-silver methods, and examined for the presence of fungal hyphae and yeasts, as well as for *Pneumocystis carinii*, viral inclusion bodies, malignant cells and haemosiderin-laden macrophages.

The diagnosis of cytomegalovirus was only considered if cytopathic changes were found in BAL samples or on histopathological examination at autopsy. PSB samples were retrieved following methods described previously [13]. Serial dilutions of BAL and PSB samples were prepared to obtain final concentrations of 1/10, 1/100 and 1/1000. Diluted and undiluted specimens were inoculated into the next media: blood-agar, Wilkins-Chalgren, chocolate-agar, BCYE- α , and fungal media. Staining for *Legionella pneumophila* using the direct fluorescent antibody technique was performed. All cultures were incubated at 37°C under aerobic and anaerobic conditions and in a CO₂-enriched atmosphere. If negative, they were discarded after 5 days for bacteria, and after 4 weeks for fungi. In each case, blood cultures were prepared for bacteria and fungi. Serological tests for respiratory virus (influenza, parainfluenza, adenovirus, respiratory syncytial virus), *Mycoplasma pneumoniae*, and *Legionella pneumophila* were also performed. For serological studies, one blood specimen was obtained at the time of the diagnosis and, when possible, another specimen was taken 2 weeks later.

Statistical analysis

For comparison between survivors and nonsurvivors, we used the unpaired t-test and the Mann-Whitney test for continuous variables and the chi-squared test (Fisher's exact test when needed) for discrete data. The Mantel-Haenzel statistics, the levels of significance, the relative risks and their confidence intervals were calculated using the EPIinfo software [14].

For multivariate analysis, a stepwise logistic regression technique was applied, as described by COX [15]. Pitfalls associated with this analysis were avoided as described by CONCATO *et al.* [16]; special care was taken to avoid overfitting: a model estimating the relative risk of death (yes/no) adjusted for the presence of PCP (yes/no); MV (yes/no); interval between hospital to ICU admission (≥ 3 or < 3 days); $P_{a,O_2}/F_{I,O_2}$ at hospital admission (≤ 20 or > 20 kPa); and corticosteroid therapy (yes/no) was fit. Each variable included in the multivariate analysis was coded "0" for absence of the event and "1" for presence. These variables were selected because there was imbalance in the univariate analysis or they were considered clinically relevant (*e.g.*: corticosteroid therapy). Interactions were tested in the model; variables with association between each other were not included in the analysis. Colinearity was assessed by means of a correlation matrix. No factors in the model correlated. As for influential observations, no patients with outlier values in any variable were detected. A stepforward approach was used, with 0.05 as a limit for entering or removing new terms.

The survival probability curves were calculated according to standard methods. Variable related to the time interval from ICU discharge to death was analysed by survival methods, including Kaplan-Meier estimate and log-rank test [15]. The "0" time interval was considered as the time of discharge from the ICU. Data were censored at 400 days. All p-values reported are two-tailed.

Results

Forty two AIDS patients were enrolled into the study. Nineteen (45%) were survivors and 23 (55%) were non-survivors. Mean SAPS at admission to ICU was 6.9 ± 4.4 (SD). All patients were admitted because of acute respiratory failure ($P_{a,O_2}/F_{I,O_2}$ ratio at hospital admission 19 ± 14 kPa) and diffuse pulmonary infiltrates. Twenty nine (69%) patients required MV. Twenty eight (67%) patients had PCP, which was the first episode. The main characteristics of the population are summarized in table 1. Mean CD4+ counts for the survivors (n=11) was $0.11 \pm 0.13 \times 10^9$ cells·L⁻¹ (reference values of our laboratory 0.8–1.2 $\times 10^9$ cells·L⁻¹), and $0.08 \pm 0.11 \times 10^9$ cells·L⁻¹ for the non-survivors (n=7) (NS).

Microbiology

The microorganisms isolated are shown in table 2. Diagnosis of *Pneumocystis carinii* was achieved via microscopic examination of BAL fluid in 28 cases and

Table 1. – Main characteristics of the study population at ICCU admission (n=42)

Age yrs		37±12
Gender (M/F)		35/7
Risk factors		
<i>i.v.</i> drug abusers	n (%)	14 (33)
Homosexuals	n (%)	16 (38)
Others	n (%)	12 (28)
Interval from hospital to ICU admission days		
		4.3±5.2
Time since diagnosis of HIV antibodies yrs		
		1.1±2
MV requirement n (%)		
		29 (69)
Interval from ICU admission to MV days		
		2.9±4.2
<i>Pneumocystis carinii</i> pneumonia n (%)		
		28 (67)
$P_{a,O_2}/F_{I,O_2}$ at hospital admission kPa		
		19±14
P_{A-a,O_2} kPa		
		43±22
SAPS		
		6.9±4.4
Leucocytes $\times 10^9 \cdot L^{-1}$		
		6.3±3.9
Lymphocytes $\times 10^9 \cdot L^{-1}$		
		0.6±0.5
CD4+ $\times 10^9 \cdot L^{-1}$ (n=18)		
		0.10±0.11
LDH $\mu\text{kat} \cdot L^{-1}$		
		21.6±9.2
Cholesterol $\text{mol} \cdot L^{-1}$		
		3.4±1.3
$\text{mg} \cdot dL^{-1}$		
		132±50
Proteins $\text{g} \cdot L^{-1}$		
		58±7
Albumin $\text{g} \cdot L^{-1}$		
		24±6
Creatinine $\text{mmol} \cdot L^{-1}$		
		103±60

Values are presented as mean±SD. ICU: Intensive Care Unit; HIV: human immunodeficiency virus; SAPS: Simplified Acute Physiology Score; MV: mechanical ventilation; M: male; F: female; LDH: lactate dehydrogenase; P_{a,O_2} : arterial oxygen tension; F_{I,O_2} : inspiratory oxygen fraction; P_{A-a,O_2} : alveolar to arterial difference in oxygen tension.

confirmed by autopsy in 10 cases. Cytomegalovirus pneumonia was diagnosed in five cases (12%). The comparison of *in vivo* diagnoses versus necropsy diagnoses is shown in table 3. Five cases infected with cytomegalovirus (three pulmonary infections, one renal and one adrenal) and one with *Pneumocystis carinii* were diagnosed based on postmortem findings only. Thirteen (31%) patients had polymicrobial aetiologies of their pulmonary infiltrates. Seven out of 28 cases (25%) of PCP had other concomitant pulmonary infections. Blood cultures and serologies were always negative.

Table 2. – Microorganisms isolated from the 42 patients

Microorganism isolated	Cases		Diagnostic method*
	n	%	
<i>P. carinii</i> alone	21	(50)	BAL (except 1 case)
<i>P. carinii</i> + <i>M. tuberculosis</i>	1	(2)	BAL
<i>P. carinii</i> + Cytomegalovirus	5	(12)	BAL and necropsy
<i>P. carinii</i> + <i>P. aeruginosa</i>	1	(2)	BAL
<i>Haemophilus influenzae</i>	1	(2)	BAL
<i>Mycobacterium kansasii</i>	1	(2)	BAL
<i>Streptococcus pneumoniae</i>	1	(2)	BAL + PSB
Negative cultures	11	(26)	-

*: one case was only diagnosed by autopsy findings, in addition autopsy findings confirmed the diagnosis achieved by BAL in 10 of the cases previously diagnosed by BAL. *P. carinii*: *Pneumocystis carinii*; *M. tuberculosis*: *Mycobacterium tuberculosis*; *P. aeruginosa*: *Pseudomonas aeruginosa*. BAL: bronchoalveolar lavage; PSB: protected specimen brush.

Table 3. – Comparison of *in vivo* diagnosis versus necropsy studies

Pt	<i>In vivo</i>	Necropsy
1	PCP	PCP
2	PCP	PCP, pulmonary cytomegalovirus
3	Bacterial pneumonia	Acute lung injury
4	Bacterial pneumonia	PCP, liver cirrhosis, diffuse alveolar damage
5	PCP	PCP, cutaneous Kaposi's sarcoma
6	PCP	Pulmonary condensation, cerebral oedema
7	PCP	Bacteria pneumonia
8	PCP	PCP, pulmonary cytomegalovirus, diffuse alveolar damage
9	PCP, cytomegalovirus	Pulmonary infarction, pulmonary thromboembolism, alcoholic hepatitis
10	PCP	PCP, cutaneous Kaposi's sarcoma, suprarenal cytomegalovirus, pleural effusion
11	PCP, pulmonary TB	PCP, diffuse alveolar damage, hepatic cirrhosis
12	PCP	PCP, diffuse alveolar damage, cytomegalovirus, adrenalitis, steatosis, Kaposi's sarcoma
13	PCP	PCP, diffuse alveolar damage, bilateral bacterial bronchopneumonia
14	PCP	PCP, pulmonary cytomegalovirus

PCP: *Pneumocystis carinii* pneumonia; TB: tuberculosis; Pt: patient.

Prognostic factors influencing the outcome

Univariate analysis. Table 4 shows the relative risks of death among survivors and nonsurvivors using the univariate analysis. The following variables proved to be statistically significant: requirement of MV; MV period (>6 h) while breathing 100% O₂; presence or absence of ARDS; pH before death (≤7.35); and, interval between hospital to ICU admission (<3 days). The following variables proved to be statistically nonsignificant: *P*_aO₂/*F*_IO₂ ratio at hospital admission; presence or absence of PCP; corticosteroid therapy (yes/no); era of admission (before/after 1987); polymicrobial aetiology (yes/no); interval since diagnosis of HIV antibodies; age; serum cholesterol; LDH; creatinine at ICU admission; SAPS at ICU admission; interval between ICU admission to initiation of MV; serum albumin; leucocyte count at ICU admission; and A-a*P*O₂ at admission to ICU.

Twenty nine patients (69%) needed MV versus 13 (31%) who required other types of ventilatory support and oxygen delivery, such as continuous positive airway pressure (CPAP), Venturi masks, or masks with reservoirs. There were more nonsurvivors among patients needing MV (21 out of 29, (72%)) versus those who did not require it (2 out of 13 (15%); *p*=0.0019). Patients with MV periods >6 h while breathing 100% O₂ had a three times greater risk of not surviving (16 out of 18 (89%) versus 4 out of 13 (31%)). Likewise, nonsurvivors were more frequent among patients with ARDS (13 out of 15 (87%)) versus patients without ARDS (6 out of 20 (30%); *p*=0.0028). Patients with arterial pH <7.35 had twice the risk of dying (8 out of 9 (89%) versus 9 out of 20 (45%)).

Although not statistically significant, the risk of death was 2.2 times greater in patients in whom the *P*_aO₂/*F*_IO₂ ratio was <20 kPa at admission to ICU (15 out of 22 (68%) versus 4 out of 13 (31%); *p*=0.07). Also, the risk

Table 4. – Relative risks of death among survivors and nonsurvivors in descending order

	Nonsurvivors		Survivors*		RR	(95% CI)	p-value
	n	(%)	n	(%)			
Mechanical ventilation	21	(72)	8	(28)	4.7	(1.3–17.2)	0.0019
MV period (>6 h) with <i>F</i> _I O ₂ =1.0	16	(89)	2	(11)	2.9	(1.3–6.6)	0.002
Adult respiratory distress syndrome	13	(87)	2	(13)	2.9	(1.4–5.8)	0.0028
<i>P</i> _a O ₂ / <i>F</i> _I O ₂ ratio (≤20 kPa) on admission	15	(68)	7	(32)	2.2	(0.9–5.2)	0.07
Arterial blood pH (≤7.35)	8	(89)	1	(11)	1.9	(1.1–3.3)	0.04
Interval between hospital to ICU admission (<3 days)	10	(45)	12	(55)	1.8	(0.8–4.53)	0.0539
<i>Pneumocystis carinii</i> pneumonia	18	(64)	10	(36)	1.8	(0.85–3.8)	0.08
Corticosteroid therapy	11	(73)	4	(27)	1.65	(0.98–2.78)	0.13
Era of admission (before 1987)	11	(73)	4	(27)	1.65	(0.98–2.78)	0.13
Polymicrobial aetiology	10	(77)	3	(23)	1.26	(0.78–2.02)	0.45
Months since diagnosis of HIV (≤6 months)	16	(64)	9	(36)	1.4	(0.7–2.6)	0.29
Age (≥35 yrs)	14	(58)	10	(42)	1.17	(0.66–2.07)	0.59
Cholesterol ≥5 mmol·L ⁻¹ (≥200 mg·dL ⁻¹)	21	(55)	17	(45)	1.1	(0.4–3.06)	0.9
Lactate dehydrogenase (≥24 μkat·L ⁻¹)	12	(52)	11	(48)	0.9	(0.4–1.6)	0.7
Creatinine (≥88 mmol·L ⁻¹)	13	(54)	11	(46)	0.9	(0.5–1.5)	0.76
SAPS (≥12)	10	(45)	12	(55)	0.72	(0.41–1.28)	0.41
Interval ICU admission to MV (≥4 days)	5	(83)	1	(17)	0.69	(0.41–1.15)	0.36
Serum albumin (<25 g·L ⁻¹)	11	(85)	2	(15)	0.69	(0.3–1.51)	0.4
Leucocyte count (≤4.0×10 ⁹ cells·L ⁻¹)	5	(38)	8	(62)	0.62	(0.29–1.3)	0.2
<i>P</i> A-aO ₂ on admission to ICU (≥40 kPa)	6	(37)	10	(63)	0.5	(0.2–1.1)	0.1

Patients were classified into "high" or "low" risk based upon an arbitrary cut-off value for quantitative variables. RR: relative risk; 95% CI: 95% confidence interval. For further abbreviations see legend to table 1.

of death was 1.8 times higher when the interval between hospital to ICU admission was greater than 3 days (13 out of 17 (76%) *versus* 10 out of 22 (45%); $p=0.0539$). There was a trend for a worse outcome for patients having PCP (18 out of 28 (64%) *versus* 5 out of 14 (36%); $p=0.08$) compared to the remaining aetiologies (including patients without aetiological diagnosis).

Multivariate analysis

The multivariate analysis (stepwise logistic regression) after adjusting for the presence of PCP, the requirement of MV, interval between hospital and ICU admission, $P_{a,O_2}/F_{I,O_2}$ ratio at hospital admission, and treatment with corticosteroids, demonstrated that the presence of PCP (relative risk (RR): 3.2; 95% confidence interval (95%

CI): 2.4–26; $p=0.005$), and the requirement for MV (RR 2.6; 95% CI: 1.3–14.5; $p=0.018$) were independent factors significantly related with death.

Follow-up of survivors

Nineteen (45%) patients were discharged alive from the ICU. When analysing patients who had PCP *versus* those who had other infectious or unknown aetiologies of respiratory failure, initial differences ($p=0.014$) were shown in the probability to survive among both populations (median survival times were 49 days for PCP population *versus* 154 days for other aetiologies). These probabilities lost their significance after the 170 day survival time ($p=0.25$). Again survival plots were compared for patients with and without MV. No differences were shown when comparing both survival curves. Median survival times were 112 days for patients with MV and 154 days for those without MV (fig. 1).

Discussion

The main findings of the present study show that AIDS patients presenting with pulmonary infiltrates and severe acute respiratory failure have a high mortality rate (23 out of 42 (55%)). This mortality rate increased markedly (72%) when MV was required. The presence of PCP and the requirement of MV were the main factors related to prognosis. Patients with PCP showed a poor outcome after ICU discharge, with a median survival period of 49 days. In our series, we found that Cytomegalovirus pneumonia is not an uncommon aetiological agent, causing severe respiratory failure in AIDS and being under-diagnosed during life.

Whilst respiratory failure is the most common cause of ICU admission for AIDS patients [17], the admission to ICU of these patients has been a controversial issue. The first reports indicated that this population had a very low ICU survival rate; suggesting, therefore, the avoidance of ICU admission for this type of patient [18]. However, these opinions have recently been challenged when confirming better survival rates of 40–50% [3, 8, 9, 18]. Most of these views were based upon patients presenting with the first episode of PCP. In our study, we obtained a survival rate of around 45% for the whole population and 36% for patients with PCP. When examining outcomes before and after 1987, we found a trend towards a better short-term ICU outcome after 1987 (56%) *versus* (27%) before 1987. Thus, our results agree with those reported in the literature [18, 19]. We think that the short-term prognosis of AIDS patients with acute severe respiratory failure is not so poor as originally expected and is much better when compared to other immunosuppressed populations, such as bone marrow transplant patients with acute respiratory failure [20].

The better prognosis of AIDS patients with acute respiratory failure in the recent era seems to be related to several factors, such as: the use of corticosteroids for PCP [21]; an improvement in the learning process of the disease and its complications; a better nutritional status

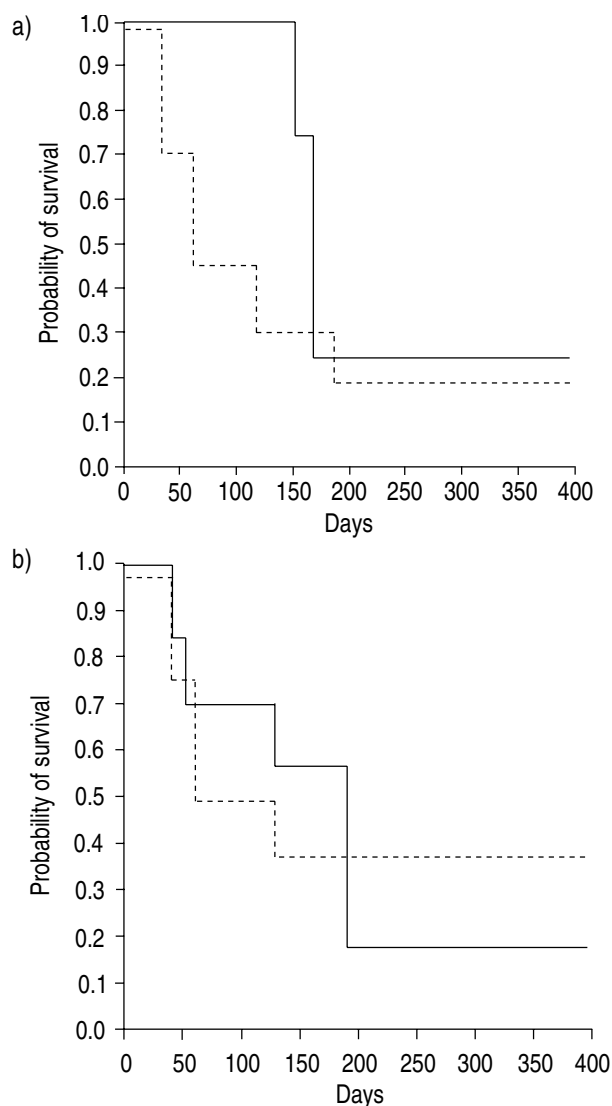


Fig. 1. — Kaplan-Meier estimates of probability to survive: a) in patients with (-----) and without (——) *Pneumocystis carinii* pneumonia (PCP); and, b) in patients with (-----) and without (——) mechanical ventilation (MV), $p=0.25$ for both plots. a) Median survival time for PCP and non-PCP was 49 and 154 days, respectively ($p=0.014$). b) Median survival time for mechanically ventilated and non-mechanically-ventilated was 112 and 154 days, respectively (NS).

of these patients; better critical care management [9]; and perhaps an adequate prophylaxis against PCP, although none of our patients had received it. Despite the improvement of short-term prognosis of these patients, the survival curves after ICU discharge in our study are quite disappointing - in terms of long-term outcome - for patients with PCP (median survival time 49 days). These results suggest, therefore, that the admission of patients with PCP to ICU needs to be seriously reconsidered in terms of life-expectancy.

The presence of PCP was an independent prognostic factor for mortality in this study. These results may be partially biased by the cases in which cytomegalovirus was concomitantly isolated and all died; although, polymicrobial associations proved to be nonsignificant in the univariate analysis of prognosis. However, a recent article from BOZZETTE *et al.* [22] demonstrated that neither cytomegalovirus nor PCP were predictors of mortality in a multivariate analysis. The discrepancies with our study may be explained by differences in populations studied.

Several prognostic factors have been detected in AIDS patients admitted to ICU because of respiratory failure. In particular, these have been studied in patients with PCP [3, 9, 19, 23, 24]. Some studies showing an improved outcome [23] were unable to find predictors. Others have found that prognosis is directly related to the severity of acute respiratory failure. In the present study, we found that the major determinant of prognosis in AIDS patients admitted to ICU with acute respiratory failure was the requirement of MV. Other related factors, such as the presence of ARDS, and breathing 100% oxygen for more than 6 h proved to be significant in the univariate analysis.

By contrast, we have recently shown that the outcome of general ICU admitted populations is not related to the severity of the respiratory failure within the first 48 h of ICU admission [25]. Conceivably, this finding denotes that the pathophysiology of acute respiratory failure in AIDS patients, particularly when caused by *Pneumocystis carinii*, needs to be regarded as a "unique" situation. There is evidence that PCP by itself limits the alveolar endocapillary diffusion for O₂, possibly related to a large reduction in the membrane diffusing capacity of the alveoli [26]. Direct evidence confirming our hypothesis comes from one study that found a correlation between the severity of interstitial oedema and the prognosis of the patients with PCP [7].

Other factors related to a better outcome referred to in the literature are: treatment with corticosteroids; decrease in serum lactate; high serum albumin and cholesterol levels; shorter duration of symptoms before admission to ICU; absence of metabolic acidemia; duration of known seropositivity for HIV antigen; the interval between the onset of medical treatment and that of MV; and the immunological status of patients as measured by the CD4+ levels [3, 19, 23]. Some of these factors were not specifically examined in this study, and others were not significant except for the presence of metabolic acidosis, found to be significant in univariate analysis. As regards CD4+ counts, we did not find differences when comparing survivors and nonsurvivors, although these counts

were available in only 18 patients. This finding has also recently been reported in a series of PCP patients requiring ICU treatment [27].

A possible pitfall of this study is the lack of information regarding the prior management of the patients before ICU admission, depending mainly on out-patient care physicians. However, we could evaluate the interval between hospital to ICU admission. In the univariate analysis, patients in whom this period was higher than 3 days had a poorer prognosis compared to those admitted to the ICU before this period.

Another finding in our study was the relatively high prevalence of cytomegalovirus infection in patients who died (22%). In the present study, the diagnosis of cytomegalovirus during life was infrequent. This may be due to the poor sensitivity of the diagnostic method used (detection of cytopathic effect in cells retrieved from BAL fluid). Other methods, such as immunocytochemical staining and viral culture, appear to be more sensitive [28]. Although cytomegalovirus pneumonia was recognized early as a true pathogen for AIDS patients [29], the finding of this microorganism in the absence of histological evidence of cytopathic abnormalities in the lung is common and has caused great confusion between the concepts of infection and disease. For instance, at least two studies have suggested that the detection of cytomegalovirus does not imply an indication for antiviral treatment in noncritically ill patients, particularly when *Pneumocystis carinii* is concomitantly isolated [22, 30]. In our series, cytomegalovirus infection has been demonstrated at autopsy, but not *in vivo*, on five occasions (three lung infections, one renal, and one adrenal) indicating that this viral infectious complication has to be taken into account in severely critically-ill AIDS patients.

The relatively low incidence of bacterial pneumonia (16%) in our population could be explained by the selective features of the study population, that mainly comprised AIDS patients with diffuse pulmonary infiltrates and severe respiratory failure, in whom opportunistic infections are much more common. However, prior information from our group [31] demonstrated that the overall incidence of bacterial pneumonia in HIV patients with pulmonary infiltrates is 21%.

In summary, although the ICU survival rate in this study was reasonable (55% for the whole population and 36% for *P. carinii* pneumonia patients) the poor outcome after ICU discharge, in particular for *P. carinii* pneumonia patients, deserves the reassessment of ICU admission criteria for this type of AIDS population.

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