# Systematic review of short-term prognostic factors of HIV patients admitted to an intensive care unit

## *Revisão sistemática de fatores prognósticos a curto prazo de pacientes HIV internados em uma unidade de cuidados intensivos*

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**ABSTRACT**

**Introduction:** Knowing the short-term prognostic factors of critically ill HIV patients admitted to intensive care units (ICUs) in the era of combination antiretroviral therapy (cART) is important for the adoption of preventive measures and more effective treatment. To identify the most significant and common factors that determine short-term mortality, a systematic review of the relevant literature was carried out. **Method:** An internet search was conducted in three databases indexing scientific articles (PubMed, Scopus, and Web of Science) for studies investigating the prognostic factors of mortality or short-term survival (in ICUs and elsewhere in hospitals following ICU admission) of critically ill HIV-infected patients. The articles were selected according to pre-established criteria and evaluated independently by two researchers. The variables collected were author, year, study location, study type, number of patients with HIV, mortality, significant factors in simple logistic regression and multiple regression, main causes of admission, and inclusion criteria. **Results:** Twenty-six articles were selected for systematic review. Fifteen dealt with factors that determine mortality in the ICU, nine with hospital mortality following ICU admission, and two with both. **Conclusions:** Factors associated with the severity of acute disease, such as prognostic scores, albumin, and organ failure (shock and respiratory failure), seem to be more important as determinants of short-term mortality than those associated with HIV.

**Keywords:** HIV; AIDS; intensive care; prognostic factors; mortality.

**RESUMO**

**Introdução:** Conhecer os fatores prognósticos de curto prazo de pacientes HIV, criticamente doentes, na era de terapia antirretroviral combinada, é importante para adoção de medidas preventivas e mais efetivas de tratamento. Para identificar os fatores mais significativos e comuns que determinam a mortalidade a curto prazo, uma revisão sistemática da literatura mais relevante foi conduzida. **Método:** Uma busca na internet foi conduzida em 3 bases de dados de artigos científicos indexados (PubMed, Scopus e *Web of Science*) para estudos que investigaram fatores prognósticos de mortalidade ou sobrevivência a curto prazo (em UTIs, ou em outros setores do hospital, seguindo a internação na UTI) de pacientes HIV criticamente enfermos. Os artigos foram selecionados de acordo com critérios pré-estabelecidos e avaliados independentemente por 2 pesquisadores. As variáveis coletadas foram autor, ano, local e tipo do estudo, número de pacientes com HIV, mortalidade, fatores significativos em regressão logística simples e múltipla, principais causas de admissão e critérios de inclusão. **Resultados:** Vinte e seis artigos foram selecionados para revisão sistemática. Quinze lidaram com fatores que determinavam mortalidade na UTI, 9 com mortalidade hospitalar após internação em UTI, e 2 com ambos. **Conclusões:** Fatores associados à gravidade de doença aguda, como escores prognósticos, albumina e disfunção orgânica (choque e insuficiência respiratória) parecem ser mais importantes como determinantes da mortalidade a curto prazo que aqueles associados ao HIV.

**Palavras-chave:** HIV; AIDS; cuidados críticos; prognóstico; mortalidade.

## INTRODUCTION

The introduction, in 1996, of combined antiretroviral therapy (cART) in the treatment of acquired immunodeficiency syndrome (AIDS) decisively improved the mid- and long-term prognoses of patients with human immunodeficiency virus (HIV)[1-4]. The introduction of cART led to the chronicity of HIV infection and decreased mortality. The mortality of HIV patients with CD4+ T-lymphocyte counts greater than 500 cells/mm$^3$ and under cART for more than six months is similar to that of the general population[5].

Despite therapeutic advances, the current challenges in the healthcare of patients with HIV/AIDS include late diagnosis, insufficient adherence to antiretroviral treatment, and increased complications related to the chronic use of these drugs[6], such as immune senescence[7] and cardiovascular, metabolic, and neoplastic complications[8].

Consequently, not only is there high demand for intensive care unit (ICU) beds[9] but also the mortality of critically ill HIV patients remains high in Brazil and throughout the world[4,10,11]. The management of these patients remains challenging once it is a field still full of uncertainties regarding treatment procedures[12,13].

Knowing the short-term prognostic factors of critically ill HIV patients admitted to ICUs in the cART era is important for the adoption of preventive measures and more effective treatment. Understanding the set of individuals who use the resources of this hospital sector, including their main sociodemographic and clinical characteristics, is necessary for the health system to meet the needs of the population and for the formulation of public policies[14].

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## OBJECTIVE

To review the determinants of short-term mortality (in the ICU and elsewhere in the hospital following ICU admission) of HIV patients admitted to ICUs through a systematic literature review focusing on articles from the cART era.

## METHODS

On February 10 2016, an internet search was performed in three databases indexing scientific articles (PubMed, Scopus, and Web of Science) for studies investigating the prognostic factors of mortality or short-term survival for critically ill HIV-infected patients admitted to ICUs after the introduction of cART in 1996.

The following search terms were used in PubMed and Web of Science: ("HIV" OR "Acquired Immunodeficiency Syndrome Virus" OR "AIDS Virus" OR "AIDS Viruses" OR "Virus, AIDS" OR "Viruses, AIDS" OR "Acquired Immunodeficiency Syndrome" OR "Immunologic Deficiency Syndrome, Acquired" OR "Acquired Immune Deficiency Syndrome" OR "Acquired Immuno-Deficiency Syndrome") AND ("Critical Care"[Mesh] OR "Intensive Care" OR "Critical Illness" OR "Critically Ill" OR "Intensive Care Units").

For Scopus, other terms were used because of the structure of the search engine: search - TITLE-ABS-KEY (hiv) OR TITLE-ABS-KEY (aids) AND TITLE-ABS-KEY (critical care) OR TITLE-ABS-KEY (intensive care) OR TITLE-ABS-KEY (critically ill) OR TITLE-ABS-KEY (critical illness) AND SUBJAREA (mult OR bioc OR immu OR neur orphar OR mult OR medi OR nurs OR heal) AND PUBYEAR > 1995 .

The articles identified were then selected in stages, through the following procedures:

1. The titles (*i.e.*, 745 PubMed, 484 Scopus, and 772 Web of Science results) were screened by the author, whereupon non-relevant publications — reviews, letters to the editor, opinions, pediatric and obstetric articles, and articles without information about HIV/AIDS or ICUs or without outcome evaluation — were eliminated. This procedure reduced the number of articles to 72 from PubMed, 18 from Scopus, and 49 from Web of Science.
2. After excluding duplicate articles, 76 abstracts were read by the author and one reviewer (Cássia R.S.) to assess their eligibility. The criteria were as follows: publication after January 1$^{st}$, 1996, subjects aged over 18 years old, information collected from cohorts after the onset of the cART era, and clear information available about the outcome of interest and its risk factors. In this manner, 36 articles were chosen to be read in full, whereas 40 ones were excluded due to their lack of data on prognostic factors or mortality/survival.
3. Upon reading, another 10 articles were removed, leaving 26 ones. Any disagreement between the author and reviewer was resolved by a third party (André M.J.).
4. Among the articles selected, 15 of them dealt with determinants of mortality in the ICU[4,15-28], 9 with hospital mortality[10,29-36], and 2 with both ICU and hospital mortality[37,38].

The following information was collected from each article: author, year, study location and type, number of patients with HIV, mortality, significant factors in simple logistic regression and multiple regression, main causes of admission, and general observations about each study, including the inclusion criteria. Figure 1 presents the review flowchart.

## RESULTS AND DISCUSSION

**Table 1** shows the main risk factors associated with ICU mortality in the reviewed articles. **Table 2** shows the factors associated with hospital mortality following ICU admission. The complete data tables are found in the **Appendix (Tables A and B)**.

### Main diagnoses upon admission

The 26 articles were published from 2001 to 2014 in several countries and included a total of 10,195 HIV patients, with ICU mortality of 35.1% and hospital mortality of 39.8%. Upon ICU admission, 48.5% presented with respiratory failure, 25.2% with shock, 17.1% with coma/changes in consciousness, and 9.2% with other diagnoses. The articles reported additional causes for the eventual hospitalization of patients with organ dysfunction: liver failure, renal failure, heart failure, postoperative hospitalization following major surgeries, and polytrauma[39].

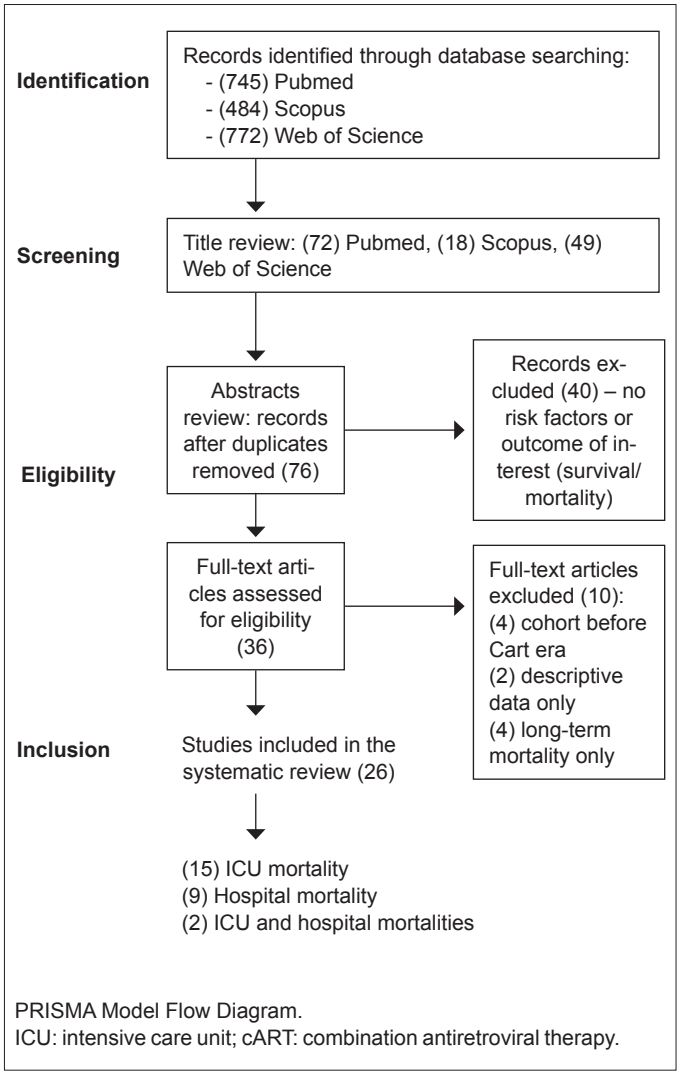


**Figure 1 –** Flow chart of the systematic review of the short-term prognostic factors of critically ill HIV patients (mortality in the intensive care unit and elsewhere in the hospital following intensive care unit admission).

All of the studies used single-center retrospective cohorts, except Japiassú et al.[33], which used a prospective cohort, and Barbier et al.[30], that used a multicenter retrospective cohort.

## Demographic factors

In studies evaluating the mortality of the general population of critically ill patients, age and gender are commonly associated with prognosis. Extreme age and male gender are generally related to higher short- and mid-term mortality[39]. However, because critically ill HIV patients are generally young, they do not clearly demonstrate this association; in 23 of the 26 studies[22,27,37], age was not independently related to ICU or hospital mortality, and none of the articles found gender to be an independent factor[4,16,21,22,24,31,38].

## Factors associated with the severity of acute disease

The factors most frequently associated with short-term mortality (ICU and hospital) are those that reflect the severity of the acute illness. Since disease severity is a subjective and complex concept, various predictive scoring systems have been developed in order to measure the severity of acute disease and predict the prognosis of ICU patients, including the Acute Physiologic and Chronic Health Evaluation (APACHE), the Simplified Acute Physiologic Score (SAPS), and the Sequential Organ Failure Assessment Score (SOFA)[40].

Of the 17 articles that studied ICU mortality, 6[15,18,25,27,37,38] reported a significant relationship between APACHE scores and outcomes in multivariate analyses, whereas 4[19,22,24,28]reported this relationship in univariate analyses.

Of the 11 articles that studied hospital mortality, 4[10,32,37,38]reported a significant relationship between APACHE scores and outcomes in multivariate analyses, whereas 2[35,36] reported this relationship in univariate analyses.

All five articles that related SAPS to ICU mortality[4,16,21,23,26] found a significant relationship in their multivariate analyses, as did the one article that related SAPS to hospital mortality[30].

One study[30] found a relationship between SOFA scores and hospital mortality in a multivariate analysis.

Serum albumin concentration is a significant laboratory parameter that mirrors the severity of acute diseases[41]. In the critically ill HIV patient population, albumin was an important prognostic factor; five articles[10,15,24,36,37] independently related albumin concentration to short-term mortality.

Four articles[20,26,29,37] reported a relationship between respiratory failure and ICU mortality in univariate analyses, and four[29,32,33,37] noted a relationship between respiratory failure and hospital mortality in univariate analyses. Only one study[29] reported an independent relationship between respiratory failure and hospital mortality.

In 9[4,16,18,20,22,23,27,37,38] of 13 articles[19,21,26,28], mechanical ventilation was significantly related to ICU mortality in multivariate analyses. Hospital mortality was independently associated with mechanical ventilation in 7 articles[10,29,30,34-37] and dependently associated in 3[31,32,38].

Respiratory failure and mechanical ventilation are confounding factors, once the latter is a treatment for the former. The two of them should not be analyzed together. It is important to differentiate, in conceptual and prognostic terms, between patients admitted to intensive care due to respiratory insufficiency and those who progress to mechanical ventilation during their stay in the unit[39,42]. The use of ventilation during a patient's stay is itself an obvious marker of mortality, once that most patients who die are on mechanical ventilation.

Shock is defined as a state of circulatory failure or insufficient tissue perfusion (cellular and tissue hypoxia) due to reduced oxygen supply and/or increased consumption or inefficient use of oxygen. Several authors[15,16,33,43-45] have shown that septic shock represents up

**Table 1 –** Risk factors most commonly associated with intensive care unit (ICU) mortality of critically ill patients with HIV - 17 articles.

| Risk factors | Number of articles that studied the factor | Number of articles with significance only in univariate analysis | Number of articles with significance in multivariate analysis |
|---|---|---|---|
| Demographic factors | | | |
| Age | 10 | 7 | 3 |
| Gender | 5 | 5 | 0 |
| Severity of acute disease | | | |
| APACHE | 10 | 4 | 6 |
| SAPS | 5 | 0 | 5 |
| SOFA | 0 | 0 | 0 |
| Admission causes | | | |
| Sepsis/septic shock | 5 | 1 | 4 |
| Respiratory failure | 4 | 4 | 0 |
| Coma | 3 | 2 | 1 |
| Evolution during ICU stay | | | |
| Albumin | 6 | 3 | 3 |
| Vasoactive drugs | 6 | 1 | 5 |
| Mechanical ventilation | 13 | 4 | 9 |
| HIV infection/AIDS | | | |
| Duration | 0 | 0 | 0 |
| CDC stage | 3 | 3 | 0 |
| CD4 | 8 | 6 | 2 |
| Viral load | 1 | 1 | 0 |
| cART before | 6 | 5 | 1 |
| cART ICU | 7 | 3 | 4 |
| Opportunistic infections | 4 | 0 | 4 |
| Infections by non- opportunistic agents | 3 | 1 | 2 |

APACHE: Acute Physiologic and Chronic Health Evaluation score; SAPS: Simplified Acute Physiologic Score; SOFA: Sequential Organ Failure Assessment score; Duration: duration of HIV infection; CDC stage: HIV staging system by the Centers for Disease Control and Prevention; CD4: CD4 count in peripheral blood; Viral load: viral load of HIV in peripheral blood; cART before: use of combination antiretroviral therapy prior to admission to the ICU; cART ICU: onset or maintenance of combination antiretroviral drugs during the ICU stay.

to 90% or more of shock cases in HIV/AIDS patients, and the terms sepsis and septic shock were used synonymously in the reviewed articles, as described in the tables in the Appendix.

Five studies[17,18,24,26,28] analyzed the relationship between sepsis/septic shock upon ICU admission and subsequent mortality. Only one of them[24] found an association in a univariate analysis, whereas[31,33] two of them established an independent relationship with hospital mortality.

**Table 2 –** Risk factors most commonly associated with hospital mortality, following ICU admission, of critically ill patients with HIV - 11 articles.

| Risk factors | Number of articles that studied the factor | Number of articles with significance only in univariate analysis | Number of articles with significance in multivariate analysis |
|---|---|---|---|
| Demographic factors | | | |
| Age | 4 | 3 | 1 |
| Gender | 3 | 3 | 0 |
| Severity of acute disease | | | |
| APACHE | 6 | 2 | 4 |
| SAPS | 1 | 0 | 1 |
| SOFA | 1 | 0 | 1 |
| Admission causes | | | |
| Sepsis/septic shock | 2 | 0 | 2 |
| Respiratory failure | 4 | 3 | 1 |
| Coma | 0 | 0 | 0 |
| Evolution during ICU stay | | | |
| Albumin | 5 | 2 | 3 |
| Vasoactive drugs | 4 | 1 | 3 |
| Mechanical ventilation | 10 | 3 | 7 |
| HIV infection/AIDS | | | |
| Duration | 1 | 1 | 0 |
| CDC stage | 0 | 0 | 0 |
| CD4 | 4 | 3 | 1 |
| Viral load | 2 | 2 | 0 |
| cART before | 3 | 3 | 0 |
| cART ICU | 7 | 2 | 1 |
| Opportunistic infections | 6 | 1 | 5 |
| Infections by non-opportunistic agents | 1 | 1 | 0 |

APACHE: Acute Physiologic and Chronic Health Evaluation score; SAPS: Simplified Acute Physiologic Score; SOFA: Sequential Organ Failure Assessment score; Duration: duration of HIV infection; CDC stage: HIV staging system by the Centers for Disease Control and Prevention; CD4: CD4 count in peripheral blood; Viral load: viral load of HIV in peripheral blood; cART before: use of combination antiretroviral therapy prior to admission to the ICU; cART ICU: onset or maintenance of combination antiretroviral drugs during the ICU stay.

The relationship between ICU mortality and the use of vasoactive amines in the unit was studied by six articles[4,20,21,23,24,38], only one of which[21] did not find this to be an independent factor in the outcome. The relationship between vasoactive amine use and hospital mortality was examined by three articles[29,30,32,38]; only one of them[32] found no relationship in a multivariate analysis.

Just as it is necessary to differentiate respiratory failure at admission from progression to mechanical ventilation following ICU admission, it is important to differentiate between patients who enter the ICU experiencing shock from those who develop complications from circulatory insufficiency and the consequent use of vasoactive drugs following admission.

The use of vasoactive drugs during a patient's stay is also an obvious marker of mortality, once that most patients who die are in shock and being treated with amines[39,46].

The third most frequent cause of ICU admission is coma, which is an altered level of consciousness in which the patient is difficult or impossible to be awaken in response to external stimuli. Coma can be both a cause and a consequence of shock and respiratory failure[47]. One[17] of three articles[17,21,26] found coma to be independently associated with death in the ICU.

Coma can be preceded by delirium or by metabolic or toxic encephalopathy. Delirium is also common in patients admitted to the ICU and reflects a central nervous system dysfunction[48]. The Glasgow Coma Scale is an objective way to standardize the description and severity of altered consciousness through a prognostic score[49]. Scores below 12 on a scale from 3 to 15 indicate torpor/coma, whereas scores below or equal to 8 indicate severe lesioning of the central nervous system, with a high risk of progression to respiratory failure. The frequent association of altered consciousness with shock and respiratory failure, as well as the sedation universally used in ICUs, may influence the interpretation of coma as an independent prognostic factor. Of the three most frequently occurring organ failures, altered consciousness was the least studied one, with only one article[17] establishing it as an independent relationship with short-term mortality.

## Factors associated with HIV/AIDS infection

Time of HIV diagnosis, disease classification according to CDC criteria, and viral load were not independently associated with short-term mortality.

Although the CD4+ lymphocyte count reflects the patient's immune status and, thus, the likelihood of their developing opportunistic diseases and, eventually, significant clinical severity, only three articles[4,18,31] found an independent association between CD4+ count and mortality.

Little information is available on the impact of cART on the mortality of HIV patients admitted to the ICU. The effect of pre-admission antiretroviral therapy on ICU mortality was studied by six articles[4,16,17,25,27,37], one of which[37] found this factor to be significant in a multivariate analysis. Five authors[23,28,35,37,38] found antiretroviral use during an ICU stay to have an independent effect on short-term mortality. The administration of cART is controversial; some groups recommend its initiation or maintenance during ICU stays[23,50], whereas others prefer to suspend cART until the ICU

patient improves or is discharged. Therefore, it is difficult to reach a conclusion without a clinical intervention study, preferably randomized, to test the influence of cART on the prognosis of this population.

Four studies identified two opportunistic infections — *Pneumocystis jiroveci* pneumonia (PCP)[4,15,22] and tuberculosis[38] — as factors independently associated with ICU mortality. Another six articles[10,29,30,34,35,38] found PCP, cytomegalovirus, cryptococcosis, aspergillosis, and invasive candidiasis to be independently associated with hospital mortality. PCP was the most prevalent one and the leading cause of respiratory failure upon admission in all 26 articles.

Two articles[24,25] observed that non-opportunistic bacterial infections were independently associated with death in the ICU, while a third[4] one noted the same association, only in a univariate analysis. Finally, one author[29] found an association in a univariate regression between *Pseudomonas* sp. pneumonia and hospital mortality.

Infectious agents commonly found in immunocompetent individuals, such as community- or hospital-acquired pyogenic bacteria (*Streptococcus pneumoniae, Staphylococcus aureus*, and gram-negative bacilli), are more frequently seen and severe in critically ill HIV patients and play important roles in morbidity and mortality[12,33,51-53]. In this review, one article[25] reported admission due to pneumonia or a bacterial infection as a factor independently associated with ICU mortality, while another[24] defined pneumonia associated with mechanical ventilation as an additional independent factor related to ICU mortality.

Importantly, the clinical severity of the infection may be more significant as a prognostic factor than its etiology (whether opportunistic or pathogenic in immunocompetent patients).

## CONCLUSIONS

This systematic literature review investigated the factors that determine the short-term prognosis (ICU and hospital mortality) of critically ill HIV patients. Factors associated with the severity of acute disease, such as prognostic scores, albumin, and organ failure (*i.e.*, shock and respiratory failure), seem to be more important determinants of short-term mortality than those associated with HIV (*i.e.*, time of HIV diagnosis, CD4+ lymphocyte count, viral load, pre-admission cART treatment history, or opportunistic infections). The use of cART during ICU hospitalization is controversial, and clinical intervention studies should be performed to clarify its usefulness in reducing short-term mortality.

### Conflict of interests

The authors declare no conflict of interests.

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# APPENDIX

**Table A –** Risk factors associated with intensive care unit mortality of critically ill patients with HIV.

| Author/ year | Location and type of study | nHIV | M% | Regression analysis (p<0.05) | Main causes of admission | Remarks |
|---|---|---|---|---|---|---|
| Adlakha et al.[37] | London, UK, 1999-2009, retrospective cohort | 192 | 22.39 | Multiple: Age, APACHE II, MV, albumin, cART before, cART ICU. Simple: CD4, hemoglobin, PaO2/FiO2 (respiratory failure on admission), hemodialysis | PCP (50%), sepsis (11.45%) | All patients with HIV |
| Alves et al.[15] | Barcelona, Spain, 1993-1998, prospective cohort | 57 | 40 | Multiple: APACHE II, albumin, PCP Simple: Age, CD4, CDC, LDH, cholesterol, acidosis | Pneumonia (52.6%), PCP (36.8%) | All patients with HIV and respiratory failure |
| Amâncio et al.[38] | Belo Horizonte, Brazil, Jan-Dec 2006, retrospective cohort | 125 | 46.4 | Multiple: APACHE II, MV, cART ICU, septic shock during ICU stay (use of amines), TB. Simple: Albumin, gender (male), opportunistic disease other than TB | Respiratory failure (43.2%), shock (20%), coma (24.8%), other causes (12%) | All patients with HIV |
| Casalino et al.[16] | Paris, France, 1995-1999, retrospective cohort | 230 | 23 | Multiple: SAPS II, MV, Omega score Simple: Age, gender (male), heart failure, respiratory failure, cART before | Respiratory failure (31.7%), sepsis/shock (22.6%), coma (23.9%), other causes (19.1%) | All patients with HIV |
| Coquet et al.[17] | Paris, France, 1996-2005, retrospective cohort | 284 | 13.73 | Multiple: Sepsis on admission, time until ICU admission, kidney failure, coma, cirrhosis Simple: cART before, year of ICU admission. | Respiratory failure (58.8)%, shock (20.77%), coma (32.04%) | All patients with HIV |
| Croda et al.[18] | São Paulo, Brazil,1996-2006, retrospective cohort | 278 | 26 | Multiple: Sepsis on admission, CD4 <50, APACHE II, MV, Simple: cART ICU, LDH, albumin, intravenous drug use, year of ICU admission. | Respiratory failure (33.1)%, shock (31.3%) | All patients with HIV with admission > 24h |
| Dickson et al.[19] | London, UK, 1999-2005, retrospective cohort | 102 | 23 | Simple: CD4, APACHE II, MV, anemia | Respiratory infection (48%)%, sepsis (9%), neurological disease (14%) | All patients with HIV, only univariate analysis |
| Ferrà et al.[20] | Barcelona, Spain, 2000-2010, retrospective cohort | 12 | 83 | Multiple: Septic shock during ICU stay (use of amines), MV Simple: Respiratory failure, liver disease | Respiratory failure (33.33%), shock (58.33%), coma (8.3%) | Subgroup of lymphoma patients with positive serology for HIV |
| Meybeck et al.[21] | Tourcoing, France, 2000-2009, retrospective cohort | 85 | 19 | Multiple: SAPS Simple: Age, gender (male), CDC, CD4, Glasgow scale, MV, MV duration, septic shock during ICU stay (use of amines), cART ICU | Respiratory failure (51%), shock (11%), coma (27%), other causes (11%) | All patients with HIV |
| Miller et al.[22] | London, UK, 1990-2005 retrospective cohort. | 59 | 34 | Multiple: Age, MV, pneumothorax, year of diagnosis of PCP (before 1996) Simple: Gender (male), albumin, APACHE II, MV duration | MV (57%) | HIV patients with microbiological diagnosis of PCP |
| Morquin et al.[23] | Montpellier, France,1997-2008, retrospective cohort | 98 | 36.7 | Multiple: Septic shock during ICU stay (use of amines), SAPS, MV, cART ICU Simple: No data | Respiratory failure (38.8%), sepsis (11.2%), coma (25.5%), other causes (24.4%) | All patients with HIV |
| Pathak et al.[24] | Chapel Hill, NC, USA, Jan-Dec 2009, retrospective case-control | 55 | 44 | Multiple: Shock during ICU stay (use of amines), fever, albumin, VAP Simple: Age, gender (male), CD4, CDC, APACHE II, heart failure, sepsis on admission, pneumonia | Acute infection (45.45%), sepsis (16:36%), coma (23.66%), other causes (23.66%) | All patients with HIV and respiratory failure on mechanical ventilation |
| Rosenberg et al.[25] | Washington DC, USA, 1993-1996, retrospective cohort | (1996) 129 | 41 | Multiple: APACHE II, bacterial infection, pneumonia Simple: cART before, number of granulocytes, bacteremia | Sepsis / shock (75.96%),pneumonia (24%) | All patients with HIV and infectious complications |
| Sonneville et al.[26] | Paris, France, 2001-2008, retrospective cohort | 210 | 29.5 | Multiple: Septic shock on admission, SAPS II, intracranial hypertension Simple: Age, CD4, viral load, respiratory failure, MV, kidney failure, encephalopathy, Glasgow and Knaus scales | Respiratory failure (39%), shock (29%), coma/delirium (84%) | HIV patients with neurological complications |
| van Lelyveld et al.[27] | Utrecht, Netherland, 2006-2008, retrospective cohort | 80 | 31 | Multiple: Age, APACHE II, MV Simple: cART before, cART ICU | Respiratory failure (59%), sepsis/shock (23%), neurological disease (16%) | All patients with HIV, excluding postoperative ones |
| Vargas-Infante et al.[28] | Mexico City, Mexico,1985-2006, retrospective cohort | 90 | 58.4 | Multiple: cART ICU, septic shock on admission Simple: Steroid use, MV, APACHE II | Respiratory failure/MV (83%), shock (26%), neurological disease (15%) | All patients with HIV. Pre-cART era group compared to cART era one. |
| Vincent et al.[4] | Paris, France, 1995-2000, retrospective cohort | 236 | 25 | Multiple: Shock during ICU stay (use of amines), SAPS II, CD4 (<50), MV, PCP with pneumothorax, Kaposi Simple: Age, gender, performance status, cART ICU, tumors related to HIV, bacterial infection | Respiratory failure/MV (38.6%), shock (38.6%), toxo (14%) | All patients with HIV. Pre-cART era group compared to cART era one. |

ICU: intensive care unit; nHIV: number of HIV patients; M%: mortality; APACHE: Acute Physiology and Chronic Health Evaluation score; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment score; MV: mechanical ventilation; PaO2/FiO2: ratio of arterial oxygen partial pressure to fractional inspired oxygen; CDC: HIV/AIDS staging system by the Centers for Disease Control and Prevention; CD4: CD4 cell count in peripheral blood; Viral load: HIV viral load in peripheral blood; cART: combination antiretroviral therapy; cART before: use of cART prior to admission to the ICU; cART ICU: onset or maintenance of cART during the ICU stay; PCP:*Pneumocystis jirovecii* pneumonia; TB: tuberculosis; Kaposi: Kaposi sarcoma; VAP: ventilator associated pneumonia.

**Table B –** Risk factors associated with hospital mortality, following intensive care unit admission, of critically ill patients with HIV.

| Author / Year | Location and type of study | nHIV | M% | Regression analysis (p <0.05) | Main causes of admission | Remarks |
|---|---|---|---|---|---|---|
| Adlakha et al.[37] | London, UK, 1999-2009, retrospective cohort | 192 | 30 | Multiple: Age, APACHE II, MV, albumin<br>Simple: CD4, hemoglobin, PaO2/ FiO2 (respiratory failure on admission), hemodialysis | PCP (50%), Sepsis (11.45%) | All patients with HIV |
| Amâncio et al.[38] | Belo Horizonte, Brazil, Jan-Dec06, retrospective cohort | 125 | 68 | Multiple: APACHE II, time until ICU admission, opportunistic infection, shock during ICU stay (use of amines)<br>Simple: Albumin, gender (male), age, MV, HIV duration | Respiratory failure (43.2%), shock (20%), coma (24.8%) | All patients with HIV |
| Barbier et al.[29] | Paris, France,1996-2006, retrospective cohort | 192 | 19.7 | Multiple: Shock during ICU stay (use of amines), invasive MV, number of causes of respiratory failure, time until ICU admission<br>Simple: SOFA, ARDS, hemodialysis, Pseudomonas pneumonia, CMV pneumonia, duration of noninvasive MV, time until intubation | Respiratory failure (100%), shock (26.5%), coma (-) | All HIV patients with respiratory insufficiency |
| Barbier et al.[30] | France, various ICU, 1999-2010, multicenter retrospective cohort | 6373 | 26.9 | Multiple: Shock during ICU stay (use of amines), MV, hemodialysis, SAPS II, aspergillosis, cryptococcosis, invasive candidiasis, CMV, heart failure, cancer, liver disease, surgical cause of admission, time until admission (> 24 h)<br>Simple: No data | Respiratory failure (39.8%), sepsis / shock (27.4%), coma (22.7%) | All patients with HIV. The only multicenter study. |
| Chiang et al.[31] | Taipei, Taiwan, 2001-2010, retrospective cohort | 135 | 48.9 | Multiple: Sepsis on admission, CD4<br>Simple: Age, gender, viral load, MV, time until ICU admission, albumin, cART ICU | Respiratory failure (44.48%), sepsis (33.3%), neurological disease (11.9%) | All patients with HIV |
| Greenberg et al.[32] | Atlanta, USA, 2006-2009, retrospective cohort | 125 | 42 | Multiple: APACHE II, ICU cART<br>Simple: Shock during ICU stay (use of amines), respiratory failure, MV, age, CD4, viral load | MV (80%), sepsis (100%) | All HIV patients with severe sepsis |
| Japiassú et al.[33] | Rio de Janeiro, Brazil, 2006-2008, prospective cohort | 88 | 49 | Multiple: Severe sepsis / septic shock on admission<br>Simple: Nosocomial infection, cardiovascular dysfunction, respiratory dysfunction, cART before | Respiratory failure (29%), shock (20%), coma / torpor (23%) | All patients with HIV. Cox hazard regression - 28 days. |
| Khouli et al.[34] | New York, USA, 1997-1999, retrospective cohort | 242 | 39 | Multiple: MV, AIDS-defining illness during ICU stay (other than PCP)<br>Simple: CD4, PCP, cART before | Respiratory failure (45%), shock (11%), coma (27%), other causes (11%) | All patients with HIV |
| Morris et al.[10] | San Francisco, USA, 1996-1999, retrospective cohort | 354 | 29 | Multiple: albumin, opportunistic disease, APACHE II, PCP, MV<br>Simple: LDH, cART before | Respiratory failure (40.7%)<br>sepsis (12%), neurological disease (12.14%) | All patients with HIV |
| Morris et al.[35] | San Francisco, USA,1996-2001, retrospective cohort | 58 | 55 | Multiple: MV, PCP with pneumothorax, cART ICU, time until ICU admission<br>Simple: APACHE II, albumin | Respiratory failure (100%) | All patients with HIV and microbiological diagnosis of PCP |
| Powell et al.[36] | San Francisco, USA,2000-2004, retrospective cohort | 306 | 30.7 | Multiple: MV, albumin<br>Simple: APACHE II, sepsis x respiratory failure, neurological disease x respiratory failure, PCP x other infections | Respiratory failure (40.3%),sepsis (20.3%), neurological disease (16.3%) | All patients with HIV |

ICU: intensive care unit; nHIV: number of HIV patients; M%: mortality; APACHE: Acute Physiology and Chronic Health Evaluation score; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment score; MV: mechanical ventilation; PaO2/FiO2: ratio of arterial oxygen partial pressure to fractional inspired oxygen; CDC: HIV/AIDS staging system by the Centers for Disease Control and Prevention; CD4: CD4 cell count in peripheral blood; Viral load: HIV viral load in peripheral blood; cART: combination antiretroviral therapy; cART before: use of cART prior to admission to the ICU; cART ICU: onset or maintenance of cART during the ICU stay; PCP: *Pneumocystis jirovecii* pneumonia; TB: tuberculosis; Kaposi: Kaposi sarcoma; VAP: ventilator associated pneumonia.