

# TARV en UCI. ¿Es posible?

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# Historia clínica UCI

36 años, sexo femenino, procedente de Rocha

AP: hipotiroidismo en tratamiento

colecistectomizada

pareja serodiscordante conocida(VIH +)

FI a UCI: 31/3/10

MI: Neumopatía bilateral con insuficiencia  
respiratoria severa



AEA:

- Un mes previo a ingresar : marcada repercusión general (astenia, adinamia, anorexia, adelgazamiento)
- Agrega 10 días antes de ingreso tos mucosa, fiebre diaria y disnea progresiva por lo que consulta en Rocha

**Se realiza DG de Neumonía bilateral  
1º Test de ELISA reactivo para VIH**

- En sala rápida peoria, instala insuficiencia respiratoria severa por lo cual se traslada a UCI



# Al ingreso:

- Paciente adelgazada, vigil , SCG 15, relleno capilar lento, saturación de pulso O2 82% con MBF/R
- Piel y mucosas: leucoplasia vellosa oral .
- Ex PP: estertores crepitantes bilaterales en tercios inferiores pulmonares



## De la paraclínica se destaca

|            |         |
|------------|---------|
| UREA       | 0.67    |
| CREA       | 0,66    |
| HB         | 10,4    |
| GB         | 2500    |
| LINF TOTAL | 500     |
| PTQ        | 210.000 |

|                                   |      |
|-----------------------------------|------|
| Na                                | 132  |
| K                                 | 3.4  |
| LDH                               | 1740 |
| Antígeno<br>Neumococo<br>en orina | (-)  |



**En Suma: 36 años**

**Elementos de inmunodepresión severa  
Neumopatía sub aguda grave  
Con insuficiencia respiratoria severa  
Elisa reactivo**

**PLANTEOS DE UCI:**

- **Debut de VIH en estadio SIDA**
- **Neumopatía con etiología:**
  - 1) **PCP**
  - 2) **NAC a inespecíficos**
  - 3) **Mas alejado TB**



# Tratamiento inicial:

- Sostén de funciones
- Antibioticoterapia empírica
- Ventilación no invasiva
  
- Se solicita:
  - Cultivo de secreciones, HC, UC
  - FBC con LBA
  - Estudios imagenológicos
  - Confirmatorio de VIH



VNI  
PAFI

185 200

Ingreso  
UCI

WB  
VIH  
reactivo

31/3

3/4

9/4

Inicia  
TMP/SMX  
Corticoides  
VNI

Se agrega  
Ampicilina  
Sulbactam  
Y  
Claritromicina



# EVOLUCIÓN I

- Tórpida con imposibilidad de destete de VNI
- Persiste febril
- No se realiza FBC por IR ni TC de tórax
- 15/04: instala diarrea sin elementos anormales, alta tasa, con repercusión (disonías)
- Agrega shock con requerimiento de inotrópicos
- **20/4: Hemorragia alveolar**

**Peoría de Insuficiencia respiratoria**

**IOT + ARM**



|      |     |     |     |     |     |
|------|-----|-----|-----|-----|-----|
| VNI  |     |     | IOT |     |     |
| PAFI | 185 | 200 | 100 | 300 | 450 |

Ingreso UCI

Planteos de:  
 Infección nosocomial (MOMR)  
 Otras EO: TB, hongos

31/3

Se amplía plan AT  
 MO INESPI  
 MICOBAC  
 HONGOS

*K. pneumoniae* en  
 AT 18/4

Inicia  
 TMP/SMX  
 Corticoides  
 VNI

Se agreg  
 Ampicili  
 Sulbacta  
 Y  
 Claritromi

Meropenem  
 Anti TB  
 Anti MAI  
 Anfotericina B



# Evolución II

- *K. pneumoniae* en AT
- FBC 22/4 : IFI negativa para PCP

## Baciloscopías negativas

- TC Tx : consolidaciones pulmonares extensas bilaterales.
- Mejoría del intercambio gaseoso y de estado hemodinámico, defervescencia de la fiebre.
- Persiste con diarrea con alta tasa



# Evolución III

6/5 (36 días en UCI):

Reitera hemorragia alveolar

Anemia aguda, nuevo deterioro del intercambio gaseoso    Shock

Inotrópicos, volumen, transfusión GR

Paciente extremadamente grave

**SE MANTIENE CONDUCTA**

**\_Sotén de funciones**

**\_Antimicrobianos con amplia cobertura**



# Evolución IV

- Mejoría del intercambio gaseoso, no reitera sangrados, se mantiene en apirexia, sin leucocitosis.
- Persiste con diarrea
- Coprocultivos y coproparasitarios negativos
- Toxina para *Clostridium difficile* negativas
- FCC y FGC: no lesiones macroscópicas



# INICIO TARV?

**Dado el gran deterioro inmunológico  
en una paciente VIH estadio SIDA, con al menos dos EO, que  
persiste con diarrea incontrolable con trastornos iónicos  
Se plantea inicio de TARV como la medida principal efectiva  
con impacto en sobrevida  
para control de eventuales EO actuales y futuras**

## PLANTEOS ?:

- \_CMV
- \_Parásitos intestinales
- \_LNH
- \_Mycobacterias
- \_Enteropatía por VIH

Se solicita: Fondo de ojo s/p  
Se reclama biopsia FGC y FCC

Biopsia duodeno  
*Microsporidium*  
y biopsia de  
Colon  
*Criptosporidium*  
*parvum*



# Evolución V

- 2/6
- 63 días en UCI
- Nuevamente deterioro oximétrico, polipnea de 38 pm.
- Ascenso de leucocitosis y fiebre.

**Planteos DG:**

¿NAV?

¿SIRI?

**Se inicia colistina  
+  
corticoterapia**

VNI  
PAFI

X  
350

44 días  
en UCI

Biopsia duodeno  
*Microsporidium*  
y biopsia de  
Colon  
*Cryptosporidium*  
*parvum*

SIRI?  
NAV?

14/5

20/5

2/6

Ronda  
bacteriológica  
negativas

Inicio TARV

Albendazol y  
azitromicina

Colistina i/v  
Y  
Nebulizada  
corticoterapia



# Evolución VI

- Mejoría
- En apirexia
- Se extuba con buena tolerancia
- Cumple 14 días de tratamiento para NAV
- Mejoría de diarrea.



- Egresada de UCI 30/6 a sala de medicina
- Ingresa SEIC 5/7/10
- Del ingreso paciente mal estado general desnutrición proteico calórico, hipocoloreada
- Úlcera por presión sacra
- **A dos meses de TARV**
- VHC, VHB Y VDRL negativo  
Carga viral 307 copias/ml  
CD4 362
- Se realiza rehabilitación motora con Fisioterapia
- Paciente con buena evolución se otorga alta a domicilio



# Control en policlínica

| Fecha    | Carga viral   | PL CD4 | TARV           |
|----------|---------------|--------|----------------|
| 12/5/10  | 500000 (5,79) |        | ABC/3TC<br>EFV |
| 7/7/10   | 307 (2,48)    | 362    | ''             |
| 13/10/10 | 1725 (3,23)   | 467    | ''             |
| 9/3/11   | 5423 (3,3)    | 355    | ''             |
| 9/6/11   | 5706 (3,75)   | 312    | ''             |

Test de Resistencia



Mutaciones de RT asociadas a resistencia: L74V, L100I, K103N, M184V\*

Inhibidores nucleosídicos y nucleotídicos de la RT

Interpretación de las resistencias

abacavir (ABC)  
 didanosina (ddI)  
 lamivudina (3TC)/emtricitabina (FTC)  
 estavudina (d4T)  
 tenofovir (TDF)  
 zidovudina (AZT)

Resistencia  
 Resistencia  
 Resistencia  
 No hay pruebas de resistencia  
 No hay pruebas de resistencia  
 No hay pruebas de resistencia

Inhibidores no nucleosídicos de la RT

Interpretación de las resistencias

efavirenz (EFV)  
 etravirina (ETR)  
 nevirapina (NVP)

Resistencia  
 Posible resistencia  
 Resistencia

Mutaciones de PR asociadas a resistencia: K20R, M36I

Inhibidores de la proteasa

Interpretación de las resistencias

atazanavir (ATV)  
 ATV/r \*\*  
 darunavir + ritonavir (DRV/r)  
 fosamprenavir (FPV)  
 FPV/r \*\*  
 indinavir (IDV)  
 IDV/r \*\*  
 lopinavir + ritonavir (LPV/r)  
 nelfinavir (NFV)  
 saquinavir + ritonavir (SQV/r)  
 tipranavir + ritonavir (TPV/r)

No hay pruebas de resistencia  
 No hay pruebas de resistencia

\*\* Inhibidores de la proteasa administrados con ritonavir en dosis bajas como refuerzo farmacológico.



# TEST RESISTENCIA

- Se cambia plan por test resistencia a

TNF / 3TC - LVP Rit

20/1/12 inicia nuevo plan TARV



| Fecha   | Carga viral | PL CD4     | TARV                   |
|---------|-------------|------------|------------------------|
| 20/1/12 |             |            | TNF / 3TC -<br>LVP Rit |
| 11/4/12 | <u>50</u>   | <u>466</u> | ''<br>''               |

inicio



# Conclusiones

- ✓ Paciente extremadamente grave.
- ✓ Internación prolongada en UCI (90 días )
- ✓ Debut de VIH con severa inmunodepresión y carga viral muy elevada.



# Conclusiones

- ✓ Que presentó varias infecciones oportunistas simultáneas o sucesivas (algunas confirmadas)

A Probable neumonía a *Pneumocistis*

Probable asociación lesional con micosis o micobacterias

Diarrea a *Microsporidium*  
*Criptosporidium parvum*



# Conclusiones

- B Probable SIRS que determinó evolución a la gravedad y re intubación orotraqueal
  
- C Dos infecciones nosocomiales  
Neumonía asociada a ventilador a *Klebsiella spp*  
Eventual neumonía a MO multiresistentes



D Resistencia primaria a AZT 3TC EFV

E Actualmente excelente evolución y del estado general, con carga viral indetectable y con CD4 en ascenso



# Benefit of antiretroviral therapy on survival of human immunodeficiency virus-infected patients admitted to an intensive care unit

Julio Croda, MD; Mariana Garcia Croda, MD; Alan Neves, MD; Sigrid De Sousa dos Santos, MD, PhD

**Objective:** To evaluate the impact of antiretroviral therapy (ART) and the prognostic factors for in-intensive care unit (ICU) and 6-month mortality in human immunodeficiency virus (HIV)-infected patients.

**Design:** A retrospective cohort study was conducted in patients admitted to the ICU from 1996 through 2006. The follow-up period extended for 6 months after ICU admission.

**Setting:** The ICU of a tertiary-care teaching hospital at the Universidade de São Paulo, Brazil.

**Participants:** A total of 278 HIV-infected patients admitted to the ICU were selected. We excluded ICU readmissions (37), ICU admissions who stayed less than 24 hours (44), and patients with unavailable medical charts (36).

**Outcome Measure:** In-ICU and 6-month mortality.

**Main Results:** Multivariate logistic regression analysis and Cox proportional hazards models demonstrated that the variables associated with in-ICU and 6-month mortality were sepsis as the cause of admission (odds ratio [OR] = 3.16 [95% confidence interval [CI] 1.65–6.06]); hazards ratio [HR] = 1.37 [95% CI 1.01–1.88]), an Acute Physiology and Chronic Health Evaluation II score >19 [OR = 2.81 (95% CI 1.57–5.04); HR = 2.18 (95% CI

1.62–2.94)], mechanical ventilation during the first 24 hours [OR = 3.92 (95% CI 2.20–6.96); HR = 2.25 (95% CI 1.65–3.07)], and year of ICU admission [OR = 0.90 (95% CI 0.81–0.99); HR = 0.92 (95% CI 0.87–0.97)]. CD4 T-cell count <50 cells/mm<sup>3</sup> was only associated with ICU mortality [OR = 2.10 (95% CI 1.17–3.76)]. The use of ART in the ICU was negatively predictive of 6-month mortality in the Cox model [HR = 0.50 (95% CI 0.35–0.71)], especially if this therapy was introduced during the first 4 days of admission to the ICU [HR = 0.58 (95% CI 0.41–0.83)]. Regarding HIV-infected patients admitted to ICU without using ART, those who have started this treatment during ICU stay presented a better prognosis when time and potential confounding factors were adjusted for [HR 0.55 (95% CI 0.31–0.98)].

**Conclusions:** The ICU outcome of HIV-infected patients seems to be dependent not only on acute illness severity, but also on the administration of antiretroviral treatment. (Crit Care Med 2009; 37: 1605–1611)

**KEY WORDS:** intensive care; human immunodeficiency virus; acquired immunodeficiency syndrome; antiretroviral therapy; prognostic factors; critical care; mortality



# Critical Illness in HIV-Infected Patients in the Era of Combination Antiretroviral Therapy

Kathleen M. Akgün<sup>1,2</sup>, Laurence Huang<sup>3</sup>, Alison Morris<sup>4</sup>, Amy C. Justice<sup>1,5</sup>, Margaret Pisani<sup>2</sup>, and Kristina Crothers<sup>6</sup>

Proc Am Thorac Soc Vol 8. pp 301–307, 2011

## ART Initiation in the ICU: IRIS

Among patients who are newly initiated on ART in the ICU, IRIS may complicate care (54, 55). Despite the risks of developing IRIS, evidence in non-critically ill HIV-infected patients now favors the early initiation of ART among most patients with acute opportunistic infections. In a randomized, controlled trial of patients admitted with nontuberculosis opportunistic infections (63% due to PCP), Zolopa and colleagues showed that early initiation of ART within 14 days of beginning treatment for the opportunistic infection lessened AIDS progression or death without an associated increase in adverse events when compared with delayed initiation of ART a median of 45 days after completing treatment for the opportunistic infection (48). In a study of HIV-infected patients with tuberculosis, mortality was also significantly lower among those started on ART during treatment for tuberculosis rather than delaying ART until treatment was complete (56). However, these studies did not include patients who were critically ill, on mechanical ventilation, or with multiorgan failure.



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Manifestations of IRIS that can result in critical illness include pneumonitis, meningitis, hepatitis, and pericarditis. Respiratory failure secondary to IRIS is most often associated with tuberculosis and PCP (57, 58). IRIS associated with PCP can mimic acute respiratory distress syndrome, with fever, worsening hypoxia, and alveolar opacities on chest radiograph. Central nervous system involvement from tuberculosis and cryptococcus may also complicate IRIS and can be associated with significant morbidity and mortality (54, 59). Risk factors for IRIS include starting ART in close proximity to treatment for an acute opportunistic infection (60, 61), lower CD4 cell counts at the time of ART initiation (61, 62), rapid decline in HIV RNA after initiation of ART, and the use of boosted protease inhibitors (these inhibit intestinal and hepatic metabolism of other protease inhibitors, thus increasing drug exposure, plasma concentration, and drug half-life) (63). The pathogenesis of IRIS remains incompletely understood. In general, ART can be continued, although a careful review on a case-by-case basis is required. In patients who have potentially life-threatening manifestations of IRIS due to severity or location of the inflammatory response, it may be prudent to interrupt ART. Non-steroidal anti-inflammatory agents and corticosteroids can be used to decrease inflammation, particularly in more severe cases.



# Short- and long-term outcomes of HIV-infected patients admitted to the intensive care unit: impact of antiretroviral therapy and immunovirological status

*Annals of Intensive Care* 2012, 2:25 doi:10.1186/2110-5820-2-25

## Abstract

### Background

The purpose of this study was to assess the short- and long-term outcomes of HIV-infected patients admitted to intensive care units (ICU) according to immunovirological status at admission and highly active antiretroviral therapy (HAART) use in ICU.

### Methods

Retrospective study of 98 HIV-infected patients hospitalized between 1997 and 2008 in two medical ICU in Montpellier, France. The primary outcome was mortality in ICU. The secondary end point was probability of survival in the year following ICU admission.



**Table 1. General characteristics of the 98 HIV-infected patients admitted to the ICU**

| <b>Variable (n, %)</b>                    | <b>Total<br/>(n = 98)</b>             | <b>Survived the ICU<br/>(n = 62)</b> | <b>Died in the ICU<br/>(n = 36)</b> | <b>p value</b> |       |
|---|---------------------------------------|--------------------------------------|-------------------------------------|----------------|-------|
| Age, yr (mean ± SD)                       | 43.1 ± 10.7                           | 43.2 ± 10.6                          | 42.9 ± 10.9                         | 0.815          |       |
| Males                                     | 69 (70.4)                             | 44 (71)                              | 25 (69.4)                           | 0.873          |       |
| <b>Comorbidities</b>                      |                                       |                                      |                                     |                |       |
| Diabetes                                  | 10 (10.2)                             | 8 (12.9)                             | 2 (5.6)                             | 0.316          |       |
| HBs Ag-positive                           | 14 (14.3)                             | 8 (12.9)                             | 6 (16.7)                            | 0.607          |       |
| Anti-hepatitis C virus positive           | 30 (30.6)                             | 16 (25.8)                            | 14 (38.9)                           | 0.175          |       |
| Alcohol abuse                             | 29 (29.9)                             | 18 (29.0)                            | 11 (31.4)                           | 0.804          |       |
| Smoking                                   | 30 (30.9)                             | 23 (37.1)                            | 11 (31.4)                           | 0.08           |       |
| <b>Main reason for ICU admission</b>      |                                       |                                      |                                     |                |       |
| Acute respiratory failure                 | 38 (38.8)                             | 24 (38.7)                            | 14 (38.9)                           | 0.888          |       |
| Sepsis                                    | 11 (11.2)                             | 6 (9.7)                              | 5 (13.9)                            | 0.57           |       |
| Severe neurologic disorders               | 25 (25.5)                             | 15 (24.9)                            | 10 (27.8)                           | 0.542          |       |
| Miscellaneous                             | 24 (24.4)                             | 17(27.4)                             | 7 (19.4)                            | -              |       |
| <b>Type of diagnosis at ICU admission</b> |                                       |                                      |                                     |                |       |
| Related to HIV                            | Opportunistic infection               | 25 (25.5)                            | 16 (25.3)                           | 9 (25.7)       | 0.975 |
|   | Severe bacterial infection            | 36 (36.7)                            | 22 (34.9)                           | 14 (40)        |       |
|   | HAART-induced complications           | 6 (6.1)                              | 5 (7.9)                             | 1 (2.8)        |       |
|   | Non infectious disease related to HIV | 15 (15.3)                            | 7 (11.1)                            | 8 (22.8)       |       |
|   | Total                                 | 82 (83)                              | 50 (79.3)                           | 32 (91.4)      |       |
| Unrelated to HIV                          | 16 (16.3)                             | 13 (20.7)                            | 3 (8.6)                             | 0.169          |       |



**Table 1. General characteristics of the 98 HIV-infected patients admitted to the ICU**

| Variable (n, %)  | Total<br>(n = 98) | Survived the ICU<br>(n = 62) | Died in the ICU<br>(n = 36) | p value |
|--|-------------------|------------------------------|-----------------------------|---------|
| <b>Details of opportunistic infection at the admission</b> |                   |                              |                             |         |
| <i>Pneumocystis jirovecii</i> pneumonia                    | 11 (11.2)         | 6 (9.7)                      | 5 (13.9)                    |         |
| Tuberculosis   | 1 (1)             | 0                            | 1 (2.8)                     |         |
| Cerebral toxoplasmosis                                     | 6 (6.1)           | 5 (8.1)                      | 1 (2.8)                     | -       |
| Cryptococcosis   | 3 (3.1)           | 2 (3.2)                      | 1 (2.8)                     |         |
| Others   | 4 (4)             | 3 (4.8)                      | 2 (5.6)                     |         |
| No opportunistic infection                                 | 73 (74.5)         | 46 (74.2)                    | 27 (75)                     | 0.621   |
| <b>Life-supporting procedures in ICU</b>                   |                   |                              |                             |         |
| Mechanical ventilation during the 24 first hours           | 59 (60.2)         | 28 (45.2)                    | 31 (86.1)                   | <0.001  |
| Duration of mechanical ventilation, days (mean ± SD)       | 9.59 ± 17.0       | 7.61 ± 15.4                  | 13 ± 19.4                   | 0.003   |
| Renal replacement therapy                                  | 15 (15.3)         | 7 (11.3)                     | 8 (22.2)                    | 0.147   |
| Duration of renal replacement therapy, days (mean ± SD)    | 1.7 ± 6.4         | 1.3 ± 5.3                    | 2.3 ± 8.1                   | 0.37    |
| Vasopressors   | 51 (52)           | 21 (33.9)                    | 30 (83.3)                   | <0.001  |
| Duration of vasopressors, days (mean ± SD)                 | 3.8 ± 6.6         | 2.6 ± 4.5                    | 5.9 ± 8.8                   | <0.001  |
| Length of stay in ICU, days (mean ± SD)                    | 14 ± 17.5         | 13.4 ± 16.1                  | 15.0 ± 19.9                 | 0.431   |
| <b>Severity score (at 24 h)</b>                            |                   |                              |                             |         |
| SAPS II (mean ± SD)  | 53.8 ± 20.7       | 46.5 ± 13.5                  | 66.2 ± 24.9                 | <0.001  |
| <b>Biological data at admission</b>                        |                   |                              |                             |         |
| Albumin, g/L (mean ± SD)                                   | 31.1 ± 14.2       | 32.8 ± 14.8                  | 27.6 ± 12.4                 | 0.125   |
| Lactic acid, mmol/l (mean ± SD)                            | 2.9 ± 2.9         | 2.1 ± 1.9                    | 4.4 ± 3.9                   | <.001   |
| Thrombin time, % (mean ± SD)                               | 68.4 ± 22.9       | 72.5 ± 22                    | 61.6 ± 23                   | 0.034   |



**Table 2. Demographic and baseline clinical characteristics of HIV-infected patients admitted to the ICU, stratified according to immunovirological statuses**

| Variable (n, %)  | Total<br>n = 98 | Patients with complete immunovirological status available |  |   |  | p value |
|--|-----------------|---|--|---|--|---------|
|  |                 | CD4 <sup>high</sup><br>VL <sup>high</sup><br>n = 14       | CD4 <sup>low</sup><br>VL <sup>high</sup><br>n = 40 | CD4 <sup>low</sup><br>VL <sup>low</sup><br>n = 10 | CD4 <sup>high</sup><br>VL <sup>low</sup><br>n = 12 |         |
| Males  | 69 (70.4)       | 8 (57.1)  | 28 (70)  | 8 (80)  | 10 (83.3)  | 0.496   |
| Age, yr (mean ± SD)                                    | 43.1 (10.7)     | 42.2 (8.5)  | 40.1 (8.7)   | 46.8 (16.7)                                       | 54.7 (10.5)  | <0.001  |
| <b>Time since HIV diagnosis</b>                        |                 |   |  |   |  |         |
| Less than 6 months                                     | 17 (17.3)       | 1 (7.1)   | 8 (20)   | 1 (10)  | 0 (0)  |         |
| Intermediate   | 14 (14.3)       | 4 (28.6)  | 6 (15)   | 2 (20)  | 2 (16.7)   | 0.62    |
| More than 5 years                                      | 67 (68.4)       | 9 (64.3)  | 26 (65)  | 7 (70)  | 10 (83.3)  |         |
| HIV diagnosis in ICU                                   | 8 (8.2)         | 0 (0)   | 6 (15)   | 0 (0)   | 0 (0)  | 0.217   |
| <b>Comorbidities</b>                                   |                 |   |  |   |  |         |
| HbsAg-positive.  | 14 (14.3)       | 3 (21.4)  | 6 (15)   | 0 (0)   | 1 (8.3)  | 0.532   |
| Anti-hepatitis C virus positive                        | 30 (30.6)       | 10 (71.4)   | 7 (17.5)   | 4 (40)  | 2 (16.7)   | 0.001   |
| HbsAg + antihepatitis C virus positive                 | 7 (7.1)         | 3 (21.4)  | 2 (5)  | 0 (0)   | 0 (0)  | 0.117   |
| Alcohol abuse  | 29 (30)         | 8 (57.1)  | 13 (32.5)  | 2 (20)  | 2 (16.7)   | 0.137   |
| Tobacco  | 30 (31)         | 8 (57.1)  | 15 (37.5)  | 1 (10)  | 3 (25)   | 0.099   |
| Past medical history of cancer                         | 13 (12.6)       | 0 (0)   | 3 (7.5)  | 4 (40)  | 2 (16.7)   | 0.016   |
| <b>Main reasons for ICU admission</b>                  |                 |   |  |   |  |         |
| Acute respiratory failure                              | 38 (38.8)       | 8 (57.1)  | 16 (40)  | 2 (20)  | 3 (25)   |         |
| Sepsis   | 11 (11.2)       | 1 (7.1)   | 3 (7.5)  | 1 (10)  | 2 (16.7)   | 0.749   |
| Severe neurologic disorders                            | 25 (25.5)       | 2 (14.3)  | 11 (27.5)  | 4 (40)  | 3 (25)   |         |
| Miscellaneous  | 24 (24.5)       | 3 (21.5)  | 10 (25)  | 3 (30)  | 6 (33.3)   |         |
| <b>Opportunistic infections</b>                        |                 |   |  |   |  |         |
| No opportunistic infection                             | 73              | 14 (100)  | 25 (62.5)  | 10 (100)  | 11 (91.7)  | 0.002   |
| <i>Pneumocystis jirovecii</i> pneumonia                | 11 (11.2)       | 0 (0)   | 5 (12.5)   | 0 (0)   | 1 (8.3)  |         |
| Tuberculosis   | 1 (1)           | 0 (0)   | 1 (1)  | 0 (0)   | 0 (0)  | -       |
| Toxoplasmosis  | 6 (6.1)         | 0 (0)   | 4 (10)   | 0 (0)   | 0 (0)  |         |
| Cryptococcosis   | 3 (3)           | 0 (0)   | 2 (5)  | 0 (0)   | 0 (0)  |         |
| Reactivation of cytomegalovirus (antigenemia positive) | 15 (15.3)       | 0 (0)   | 10 (25)  | 0 (0)   | 1 (8.3)  | 0.054   |
| <b>ICU data</b>  |                 |   |  |   |  |         |
| SAPS II score (median)                                 | 49.5            | 52  | 48.5   | 56  | 49.5   | 0.522   |



**Table 3. Specific characteristics of the 98 HIV-infected patients**

| Variables (%)   | Total<br>(n = 98)                        | Survived the<br>ICU<br>(n =62) | Died in the<br>ICU<br>(n =36) | p value            |       |
|---|--|--------------------------------|-------------------------------|--------------------|-------|
| <b>HAART</b>  |  |                                |                               |                    |       |
| No past history of HAART                                      | 24 (24.5)                                | 16 (25.8)                      | 8 (22.2)                      | 0.669              |       |
| No HAART at the admission + no introduction in ICU            | 45 (45.9)                                | 28 (45.2)                      | 17 (47.2)                     |                    |       |
| No HAART at the admission + introduction in ICU               | 9 (9.2)                                  | 7 (11.3)                       | 2 (5.6)                       | 0.106              |       |
| HAART active at the admission and pursued                     | 20 (20.4)                                | 16 (25.8)                      | 4 (11.1)                      |                    |       |
| HAART active at the admission and stopped                     | 24 (24.5)                                | 11 (17.7)                      | 13 (36.1)                     |                    |       |
| Introducing or pursuing HAART in ICU                          | 29 (29.6)                                | 23 (37.1)                      | 6 (16.7)                      | 0.032              |       |
| <b>Immunovirological data</b>                                 |  |                                |                               |                    |       |
| Mean ± SD CD4 (/mm <sup>3</sup> ) §                           | 173.5 ± 192                              | 176.3 ± 197.1                  | 168.7 ± 185.8                 | 0.701 <sup>¶</sup> |       |
| Mean ± SD HIV RNA VL (10 <sup>3</sup> copies/ml) <sup>¶</sup> | 274.8 ± 664.9                            | 282.6 ± 709.5                  | 261.1 ± 591                   | 0.975              |       |
| CD4 <sup>high</sup> (≥200/mm <sup>3</sup> )                   | 30 (32.3)                                | 20 (33.9)                      | 10 (29.4)                     | 0.656              |       |
| CD4 <sup>low</sup> (<200/mm <sup>3</sup> )                    | 63 (67.7)                                | 39 (66.1)                      | 24 (70.6)                     |                    |       |
| Combined<br>subgroups   | CD4 <sup>high</sup> + VL <sup>high</sup> | 14 (18.4)                      | 9 (18.4)                      | 5 (18.5)           |       |
|   | CD4 <sup>high</sup> + VL <sup>low</sup>  | 12 (15.8)                      | 10 (20.4)                     | 2 (7.4)            | 0.429 |
|   | CD4 <sup>low</sup> + VL <sup>high</sup>  | 40 (52.6)                      | 25 (51)                       | 15 (55.6)          |       |
|   | CD4 <sup>low</sup> + VL <sup>low</sup>   | 10 (13.2)                      | 5 (10.2)                      | 5 (18.6)           |       |

§93 patients; ¶77 patients

**Table 4. Evolution of ICU mortality, age, and SAPS II score of HIV-infected patients admitted to the ICU**

| Period                                | All period<br>n = 98 | 1997–2000<br>n = 29 | 2001–2004<br>n = 37 | 2005–2008<br>n = 32 | p value |
|---------------------------------------|----------------------|---------------------|---------------------|---------------------|---------|
| Died in ICU (n, %)                    | 36 (36.7)            | 13 (44.8)           | 13 (35.1)           | 10 (31.2)           | 0.529   |
| Died before hospital discharge (n, %) | 47 (52.8)            | 13 (44.8)           | 20 (54.0)           | 14 (43.7)           | 0.832   |
| Died at one year* (%)                 | 55                   | 50.4                | 59.6                | 52.7                | 0.843   |
| Age (means, SD)                       | 42.8 ± 10.6          | 36.1 ± 6.1          | 44.6 ± 10.1         | 47.6 ± 11.6         | <0.001  |
| SAPS II (means, SD)                   | 53.2 ± 20.3          | 52.9 ± 25.7         | 51.7 ± 15.0         | 56.9 ± 21.5         | 0.406   |



### *In-ICU mortality and 1-year mortality*

Thirty-six patients (36.7%) died in the ICU and 12 patients (12.2%) died in the hospital after ICU discharge (Figure 1). From 1997 to 2008, ICU mortality decreased, whereas severity score remained constant and patients were older, but those trends were not significant (Table 4). In univariate analysis, factors significantly associated with ICU mortality were the use of vasopressive agents or mechanical ventilation, the arterial lactic acid value, and the severity scores (SAPS II or APACHE II) at admission. In our study, neither CD4 T-cell count (even for patient with very low cell count as  $<50/\text{mm}^3$ ) nor anteriority of HIV diagnosis, viral load, HAART at admission, reason for admission, and immunovirological status were significantly associated with ICU mortality. Introducing or continuing HAART in ICU was significantly associated with a better outcome (Table 3).

After multivariate logistic regression analysis including the SAPS II score, the only independent predictors of ICU mortality were the use of vasopressive agents (OR, 3.78; 95% CI, 1.11-12.86,  $p = 0.03$ ) and the SAPS II score (OR, 1.04; 95% CI, 1.00-1.08;  $p = 0.03$ ), whereas introducing or continuing HAART in ICU was protective (OR, 0.28; 95% CI, 0.08-0.94;  $p = 0.04$ ; Table 5).



**Table 5. Univariate and multivariate analysis of variables associated with in-ICU and 1-year mortality**

| Variables                                      | ICU mortality                            |                               | One-year mortality         |                             |                            |
|--|--|-------------------------------|----------------------------|-----------------------------|----------------------------|
|  | Crude odds ratio                         | Adjusted odds ratio           | Crude hazard ratio         | Adjusted hazard ratio       |                            |
|  | OR [95% CI] <i>p</i>                     | OR [95% CI] <i>p</i>          | HR [95% CI] <i>p</i>       | HR [95% CI] <i>p</i>        |                            |
| <b>HAART</b>                                   |  |                               |                            |                             |                            |
| No HAART at admission + no introduction in ICU | 1.00 [-] -                               | -                             | 1.00 [-] -                 | 1.00 [-]                    |                            |
| No HAART at admission + introduction in ICU    | 0.471 [0.087-2.533]<br>0.380             | -                             | 0.807 [0.277-2.355] 0.695  | 0.166 [0.043-0.642] 0.009   |                            |
| HAART active at admission and pursued          | 0.412 [0.118-1.438]<br>0.164             | -                             | 0.948 [0.446-2.014] 0.889  | 1.519 [0.519-4.444] 0.446   |                            |
| HAART active at the admission and stopped      | 1.947 [0.713-5.312]<br>0.193             | -                             | 1.827 [0.963-3.466] 0.065  | 1.758 [0.633-4.887] 0.279   |                            |
| Introducing or pursuing HAART in ICU           | 0.339 [0.123-0.937]<br>0.037             | 0.278 [0.082-0.939]<br>0.039  | 0.72 [0.39-1.33]<br>0.294  | -                           |                            |
| <b>Immunovirological status</b>                |  |                               |                            |                             |                            |
| CD4 T-cell count <200 /mm <sup>3</sup>         | 1.332 [0.542-3.273]<br>0.532             | -                             | 1.348 [0.73-2.489]<br>0.34 | -                           |                            |
| HIV RNA load >1,000 copy/mL                    | 1.153 [0.503-2.645]-<br>0.737            | -                             | 0.935 [0.541-1.616] 0.809  | -                           |                            |
| Combination                                    | CD4 <sup>high</sup> + VL <sup>low</sup>  | 1.00 [-] -                    | 1.00 [-] -                 | 1.00 [-] -                  |                            |
|  | CD4 <sup>high</sup> + VL <sup>high</sup> | 2.778 [0.428-18.037]<br>0.857 | -                          | 2.736 [0.707-10.594] 0.145  | 2.344 [0.442-12.434] 0.317 |
|  | CD4 <sup>low</sup> + VL <sup>high</sup>  | 3.000 [0.578-15.583]<br>0.659 | -                          | 2.583 [0.77-8.670]<br>0.124 | 5.19 [1.328-20.279] 0.018  |
|  | CD4 <sup>low</sup> + VL <sup>low</sup>   | 5.000 [0.704-35.493]<br>0.208 | -                          | 7.411 [2.02-27.195] 0.002   | 4.714 [1.178-18.867] 0.028 |

**Table 5. Univariate and multivariate analysis of variables associated with in-ICU and 1-year mortality**

| Variables                     | ICU mortality                  |                               | One-year mortality           |                           |
|-------------------------------|--------------------------------|-------------------------------|------------------------------|---------------------------|
|                               | Crude odds ratio               | Adjusted odds ratio           | Crude hazard ratio           | Adjusted hazard ratio     |
|                               | OR [95% CI] <i>p</i>           | OR [95% CI] <i>p</i>          | HR [95% CI] <i>p</i>         | HR [95% CI] <i>p</i>      |
| <b>Comorbidity</b>            |                                |                               |                              |                           |
| Hepatitis C virus infection   | 1.83 [0.760-4.406]<br>0.178    | -                             | 1.469 [0.829-2.603] 0.1879   | 3.268 [1.29-8.278] 0.012  |
| <b>In-ICU data</b>            |                                |                               |                              |                           |
| Use of vasoactive drugs       | 9.762 [3.512-27.132]<br><0.001 | 3.779 [1.11-12.861]<br>0.033  | 4.2 [2.257-7.815]<br><0.001  | 3.68 [1.394-9.716] 0.008  |
| Mechanical ventilation        | 7.529 [2.585-21.923]<br><0.001 | 3.317 [0.955-11.521]<br>0.059 | 3.139 [1.64-6.007]<br><0.001 | -                         |
| Albumin                       | 0.97 [0.926-1.015]<br>0.19     | -                             | 0.968 [0.937-1.001] 0.058    | -                         |
| Acid lactic in the first 24 h | 1.326 [1.104-1.593]<br>0.002   | -                             | 1.205 [1.109-1.31]<br><0.001 | -                         |
| SAPS II                       | 1.06 [1.029-1.091]<br><0.001   | 1.04 [1.003-1.077]<br>0.032   | 1.065 [1.048-1.084] <0.001   | 1.09 [1.057-1.124] <0.001 |



In this study, we observed a high rate of mortality in ICU, a majority of admissions not primarily related to opportunistic infections and only a few discoveries of HIV infection after ICU admission. In this HIV-infected population, we showed that mortality in ICU and during the first year following admission were related to the acute illness severity and immunovirological statuses at ICU admission and that introduction or pursuit of HAART seemed to be associated with a better outcome. The 1-year mortality contrasted with the ICU

## Conclusions

In a population of HIV-infected patients admitted to ICU, short- and long-term outcomes are related to acute illness severity and immunovirological status at admission. Complementary studies are necessary to identify HIV-infected patients who benefit from HAART use in ICU according to immunovirological status and the reasons of ICU admission.



# La ausencia de evidencia no es evidencia de ausencia

- Evidencia aún no es suficiente
- Recomendaciones cambiantes
- Vinculado a nivel de inmunosupresión
- Vinculado a enfermedad oportunista (TB, PCP, Cryptococosis)
- Pero la evidencia actual apunta a inicio precoz.



Gracias

