

# Il carico delle comorbidità non infettive nei pazienti con infezione da HIV, oltre i 60 anni: uno studio cross-sectional.

The burden of non-infectious comorbidities in people living with HIV, older than 60 years: a cross-sectional study.

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## Riassunto

In seguito all'introduzione della terapia antiretrovirale di combinazione (cART), le persone con infezione da HIV stanno vivendo più a lungo. Per tali ragioni, lo specialista in malattie infettive dovrà essere capace di gestire i pazienti sia per gli aspetti immuno-virologici che per le molteplici comorbidità che i pazienti stanno sviluppando. Con il presente studio abbiamo voluto descrivere i pattern di comorbidità in pazienti con infezione da HIV con più di 60 anni seguiti presso l'Ambulatorio di Malattie Infettive della Azienda Ospedaliero Universitaria di Sassari. Per ogni paziente abbiamo raccolto i dati demografici, clinici e virologici. Abbiamo, inoltre, focalizzato l'attenzione sulle più importanti comorbidità a su come sono state gestite. I nostri risultati hanno confermato l'elevato impatto delle comorbidità già descritto in letteratura a hanno mostrato come l'approccio futuro ai pazienti con infezione da HIV più anziani dovrà necessariamente includere una gestione multidisciplinare di tali condizioni.

## Abstract

*Since the introduction of the combination antiretroviral therapy (cART), people living with HIV (PLWHIV) are living older with a progressive increase of older patients. For these reason, the infectious disease specialists should be able to manage the patients both for the immune-virological aspect and the many comorbidities that the patient are developing. With this study we wanted to describe the comorbidities patterns of the subject over 60 years old attending the Infectious Disease Outpatient Unit of the University Hospital of Sassari. In each patient we collected demographic, clinical and virological data. Furthermore, we have focused our attention to the most important comorbidities and how we have managed them. Our results confirmed the high burden of comorbidities already described in literature and showed how the future approach to older PLWHIV should necessarily include a multidisciplinary management of these conditions.*

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## Introduction

Since the introduction of the combination antiretroviral therapy (cART), the profile of HIV patients has changed. People living with HIV (PLWHIV) are getting older, indeed, a statistical model forecasts that in 2030 the average age will be 56.6 years and the PLWHIV older than 50 years old will be the 73%. [1]

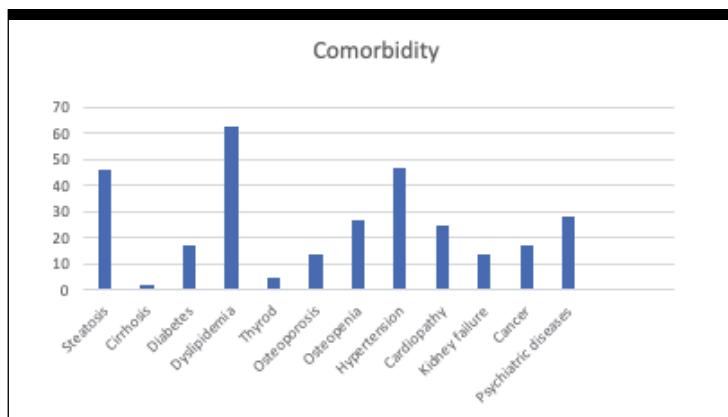
The number of elderly patients is growing year by year and they will increasingly develop age-related non-communicable diseases (NCDs) [2–8]. The causes of death are changing as well. Only a small percentage of these patients die cause an AIDS-defining diseases [9]. In the PLWHIV, the NCDs' prevalence is higher than in general population and at an earlier age [10]. For these reasons, it is important that the screening for these pathologies

starts at a substantially earlier age for PLWHIV.

In this study, we try to give an overview of the comorbidity pattern of the PLWHIV older than 60 years old followed in our center.

## Methods

Every patients of our center with 60 or more years have been included in this retrospective study. Demographic, clinical and virologic data have been collected for every individual. Furthermore, we have gathered data regarding the history of HIV infection, such as CDC classification, zenith HIV-RNA, nadir CD4, months of therapy or possible failure. Among comorbidities, we collected data about cardiovascular, liver, metabolic, bones, kidney, oncologic and psychiatric diseases.



**Figure 1.** Prevalence of comorbidities among patients older than 60 years old.

### Statistical analysis

We have evaluated all the descriptive statistics. Mean and standard deviation (SD) were used for normally distributed variables, and median and interquartile range (IQR) for non-normally distributed variables. Correlations between continuous variables were analyzed using Pearson correlation coefficient. A p-value < 0.05 was considered to indicate significance.

### Results

A total of 87 patients have been included in the study. The clinical characteristics of the patients are summarized in Table 1.

Patients were 85.1% males and median age was 65 (IQR 62 – 70) years. Most of them received a triple-antiretroviral therapy (ART). The most used backbone was TAF/FTC in 39 (66.1%) patients, followed by ABC/3TC with 18 (30.5%) patients. About the third drug, the most used class was represented by integrase inhibitors, which were prescribed to 33 (55.9%) patients, the second drug class was non-nucleoside reverse transcriptase inhibitors (NNRTI) with 17 (28.8%) patients followed by protease inhibitors (PI) prescribed in 9 (15.3%) patients.

Concerning the dual therapy strategy, the most used combination was 3TC/DTG in 10 patients.

We also collected information about past medical history and of the present illness for each patient. Furthermore, we performed a physical examination.

For what regards comorbidity, we have focused on cardiac, liver, metabolic, kidney, bone, lung,

oncologic and psychiatric diseases (**Figure 1**). The patients have then been divided into three groups if their comorbidities were  $\leq 3$ , between 4 e 5 or  $\geq 6$  (**Figure 1**). The first group was composed by 37 (41.4%) patients, the second by 42 (48.3%) patients and the third by 8 (9.2%) patients.

### Cardiovascular disease

Fifty-one patients suffered from a cardiovascular problem, in particular 25 (49%) patients had an isolated hypertension, 21 (41.2%) were both hypertensive and cardiopathic, and 4 (7.8%) had a cardiopathy. Among the 46 patients with hypertension, only 40 (87%) were taking a treatment for it and only 28 have reached a good therapeutic target (< 140/90 mm/Hg).

The cardiovascular risk has been calculated for all patients, using both Framingham score and the ASCVD. For the latter, the median of the risk was 17.9% (IQR 12.3 – 26.1).

### Liver disease

Among the 25 HCV positive patients 23 (92%) have been eradicated. In particular, 17 patients have been treated with DAA, 5 with interferon plus ribavirine and one patient cleared the virus naturally. Regarding HBV infection, the patients who had a positive HBsAg were 14. Furthermore, 6 patients had the triple coinfections HIV/HCV/HBV. Abdominal ultrasound examination was performed in 61 patients, 46 (75.4%) of these had steatosis, while 4 (6.6%) patients had cirrhosis.

### Metabolic disease

Dyslipidemia was the most common comorbidity in PLWHIV older than 60 years, indeed 63 (72.4%) patients suffered from this condition.

Diabetes was quite common, affecting 17 (19.5%) patients. Regarding the data on BMI, we have divided the patients in 4 groups (**Figure 2**). Only two patients were underweight. Most of the subject (44) had a normal constitution, having a BMI between 20 and 25, while 28 were overweight and 18 patients were obese.

### Bone disease

Unfortunately, only half of the subject have done a DEXA scan. Of these patients 13 had osteoporosis (T score < -2.5), 25 had osteopenia (T score between

-2.5 and -1) whereas a normal bone mineral density (BMD) was shown in 6 patients only.

### Kidney disease

We have collected blood tests including creatinine dosage for each patient and we have calculated the eGFR using the MDRD formula. Furthermore, in patients with a reduction of the eGFR we have performed an ultrasound examination. From these data, it emerged that 14 (16.1%) patients had a chronic kidney disease.

### Cancer

Fifteen (17.2%) patients had in the medical history a malignant cancer. 7 patients had an AIDS-defining cancer; indeed, we have registered 3 Kaposi's Sarcoma, 2 Cervical Cancer a 2 Non-Hodgkin Lymphoma. The other 8 patients had a non-AIDS-defining cancer.

### Psychiatric disease

Regarding psychiatric diseases, 30 (34.5%) patients had in their history a psychiatric comorbidity needing treatment. In particular 11 (30.7%) had a depression, 9 (30%) had an anxiety disorder and depression, 5 (16.7%) psychosis, 4 (13.3%) cases had only anxiety and 1 (1.1%) patient had a bipolar disorder.

### Correlations

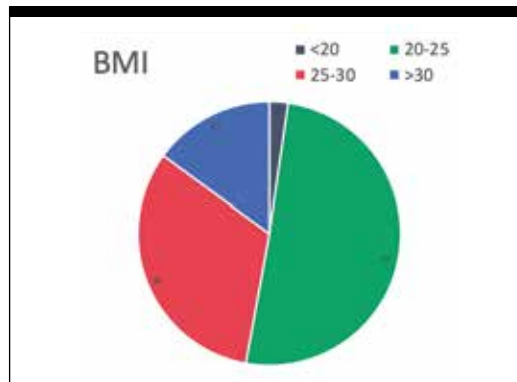
We studied the linear correlation of the variables considered. Surprisingly, there was no significant correlation between age and the number of comorbidities, ( $r=0.21$ ;  $p = 0.054$ ). Interestingly, a significant correlation between the number of comorbidity and the years of antiretroviral therapy ( $r=0.27$ ;  $p=0.015$ ).

When considering the immunologic profile, there was no correlation between comorbidity and CD4 nadir ( $r=0.04$ ;  $p=0.728$ ) and with the baseline CD4 and CD8 count.

On the contrary there was a correlation between age of the patients' and CD4 count ( $r=0.23$ ,  $p=0.34$ ) as shown in **Table 1**.

### Discussion

Our results show how PLWHIV aged 60 or older are susceptible to developing numerous comorbidities despite the achievement of viral suppression in more than 90% of the patients. However, the Swiss



**Figure 2.** Body Mass Index distribution in patients older than 60 years old.

	Patients (n°= 87)
<b>Male</b>	74 (85.1%)
<b>Female</b>	13 (14.9%)
<b>Age (year), median</b>	65 (IQR 62 – 70)
<b>Risk factors</b>	
Heterosexual	55 (63.2%)
MSM	15 (17.2%)
IVU	17 (19.6%)
<b>Smokers</b>	32 (36.8%)
<b>Previous smokers</b>	29 (33.3%)
<b>Alcohol &gt; 35 g/dL</b>	17 (19.5%)
<b>CD4 nadir (cells/<math>\mu</math>l), median</b>	225 (IQR 148.5 – 349.5)
<b>CD4 baseline (cells/<math>\mu</math>l), median</b>	788 (IQR 528 – 1094)
<b>CD8 baseline (cells/<math>\mu</math>l), median</b>	969 (IQR 602 – 1433.5)
<b>Undetectable HIVRNA</b>	79 (90.8%)
<b>CDC classification</b>	
CDC A	16 (18.4%)
CDC B	43 (49.4%)
CDC C	28 (32.2%)
<b>HCV coinfection</b>	25 (28.7%)
<b>HBV coinfection</b>	14 (16.1%)
<b>Years of treatment, median</b>	19 (IQR 13 – 22)
<b>Mono therapy</b>	2 (2.3%)
<b>Dual therapy</b>	26 (29.9%)
<b>Triple therapy</b>	59 (67.8%)

**Table 1.** Patients' demographical and clinical characteristics.

HIV Cohort Study (SHCS) showed how the majority of deaths between 2005 and 2010 were caused by a non-communicable disease [11]. Since a small percentage of deaths are due by an AIDS disease, we should reduce the impact of modifiable risk factors on the morbidity and mortality of elderly PLWHIV. Therefore, our future goal should be to improve management, which will need to be multidisciplinary to reach therapeutic targets. CDC studies show how only a 5% of patients between 50 and 64 years old are tested for HIV, and this percentage became smaller for patients with more than 65 years [9]. In these patients the delay in the beginning of therapy is due to the lack of early diagnosis [12]. In order to reduce transmission among older adults, we should

improve tailored prevention interventions. We should also increase testing rates in this populations to reach an earlier diagnosis and treatment.

In conclusion, the management of older patients is challenging beyond viral undetectability due to comorbidity burden and specific needs in this population. A comprehensive package of tailored interventions including preventive and management strategies is necessary in order to reduce transmission and reduce morbidity and mortality burden in this population.

### Conflict of interest

The authors declare that they have no conflict of interest regarding the present study. ■

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