THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 12 Issue 7

RESEARCH ARTICLE

Evolution of severe obesity and associated comorbidities in persons living with HIV with and without bariatric surgery at short and long term follow up

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OPEN ACCESS

PUBLISHED
31 July 2024

CITATION
De Wit, V., Delforge, M., et al., 2024. Evolution of severe obesity and associated comorbidities in persons living with HIV with and without bariatric surgery at short and long term follow up. Medical Research Archives, [online] 12(7). https://doi.org/10.18103/mra.v12i7.5540

DOI
https://doi.org/10.18103/mra.v12i7.5540

ISSN
2375-1924

ABSTRACT

Objectives: Obesity and related comorbidities are increasing among people living with HIV (PLWH). This study compared the evolution of severe obesity and related comorbidities in PLWH with (cases) or without (controls) bariatric surgery (BS).

Methods: Monocentric retrospective comparison of PLWH with severe obesity (body mass index (BMI) ≥40 kg/m^2 or BMI ≥ 35 together with ≥ 1 comorbidity (diabetes, dyslipidemia, arterial hypertension, sleep apnea, cardiovascular events)) between cases at baseline, 1, 2, 5 and 10 years after BS or as controls matched (1:3) on age, gender, ethnicity and severe obesity criteria.

Results: Between 2006 and 2019, we included 27 cases and 73 controls: 84% female, median age 43 years, 78% originated from sub-Saharan Africa; median time with HIVRNA <50 cp/ml 6 years in both groups. BMI decreased from 41 (baseline) to 29 kg/m^2 at 2 years after BS (p=0.002) while controls remained at 37 kg/m^2 both at baseline and 2 years. At 5 and 10 years, BMI was ≤31 in cases while controls remained ≥ 35 kg/m^2. Comorbidities favorable evolution at 2 years occurred in 50% of cases versus 12.5% in controls for diabetes, 44% versus 0 (p=0.006) for hypertension and 90% versus 0 (p<0.0001) for sleep apnea. Post-operative complications rate was 11% and HIV infection remained under control after BS.

Conclusion: Bariatric surgery is a safe and efficient treatment of severe obesity and its related comorbidities among patients with well-controlled HIV at short, middle and long terms with no impact on control of HIV disease.

Keywords: Bariatric surgery; severe obesity; HIV; comorbidity

Introduction

In countries with access to antiretroviral therapy (ART), HIV infection is now considered as a chronic disease[1] and the main causes of death among person living with HIV (PLWH) are metabolic and cardiovascular diseases[2,3], which are more prevalent in this population. Obesity and its related-comorbidities rise in people with HIV[4].

The worldwide prevalence of obesity, which has more than doubled since 1990 in adults, is estimated around 890 million in 2022 (about 16% of the adult population)[5]. The same rise has been observed in Belgium with a 16% prevalence of obesity[6].

In the Swiss HIV cohort, the prevalence of persons with body mass index (BMI) ≥ 25kg/m² increased from 13% (1990) to 38% (2012)[7]. These rates of overweight and obesity in PLWH tend to be similar to the general population although some ART drugs might cause weight gain[8].

The consequences of obesity are numerous: increase risk of diabetes, hyperlipidemia, obstructive sleep apnea (OSA), osteoarthritis, non-alcoholic fatty liver disease, gallbladder pathology, cancers, neurocognitive impairments and cardiovascular diseases (CVD)[5,9]. More recently, obesity was also associated with more severe covid-19 infection[10].

There are currently different weight loss strategies for persons with obesity: non-surgical treatments such as lifestyle modifications with dietary measures and increasing sport practice is the first step recommended by guidelines but leads to a 3-5% reduction in weight[11] . Studies on pharmacotherapy with GLP-1 receptor agonists have recently showed promising results with substantial weight loss (WL) at 72 weeks in persons with obesity but these treatments are costly and not always accessible to patients[12]. A third option is bariatric surgery (BS) which is indicated for patients with severe obesity defined as BMI ≥40 or ≥35 together with at least one associated comorbidity[9]. In a recent meta-analysis in the general population including adults with obesity, BS was associated with significantly lower mortality and longer life expectancy than usual obesity management strategies[13].

Although BS has proved to be the most effective weight loss option in the general population with severe obesity, it may lead to post-operative complications: systemic disorders, surgical complications, nutritional and behavioral consequences.

A large retrospective review compared the in-hospitalization mortality after BS in 346 persons with HIV to 266,000 HIV-negative patients from 2004 to 2014 and found no major differences[14].

Previous literature showing BS efficacy among HIV-patients include small cases-series with follow up inferior to 24 months in most cases[15].

The objective of this retrospective study is to compare the evolution of persons with HIV and severe obesity who underwent or not BS and to look at outcomes on both obesity and its related comorbidities at 1-, 2-, 5- and 10-years follow-up (FU).

Materials and methods

Retrospective monocentric analysis of epidemiological, clinical and biological data at baseline, 1, 2, 5 and 10 years. PLWH with severe obesity and BS (cases) or without BS (controls) were compared. After the Ethics committee agreement, we identified 37 persons followed in our HIV reference center who had BS between 1994 and 2019. Inclusion criteria were having undergone BS (gastric bypass (GB) or sleeve gastrectomy (SG) or adjustable gastric banding (AGB)) after a previous HIV diagnosis and FU of at least one-year after BS. Exclusion criteria were having BS before the diagnosis of HIV, FU in another institution or <1 year after BS.

Each case was matched with 2 to 3 controls based on gender, ethnicity, age and severe obesity criteria at baseline, set as the date of BS for cases and for controls at the closest date of FU to the surgery of their case with a maximum interval of 3 years +/- the surgery.

Primary outcome was WL at 2 years. Secondary outcomes were WL at 1, 5 and 10 years and evolution of comorbidities at FU. Excess WL (EWL) was defined as WL above BMI of 25 kg/m².

We reviewed all electronic medical files. Surrogate markers of HIV infection, BMI, comorbidities (defined and treated according to the EACS guidelines[16]) and their medications were retrieved from the Saint-Pierre HIV Cohort database, which prospectively collects these data at each consultation. All patients included in Saint-Pierre cohort have signed an informed consent allowing access to these data.

To define the evolution of comorbidities, we used these terms: appearance (new onset), increase (increased dosing of medication or adding new medication), decrease (decreased dosing or stopping medication), stability (no change), “unfavorable outcome” (appearance and/or increase) or “favorable outcome” (disappearance and/or decrease).

We used descriptive statistics for characteristics of patients using median and interquartile (IQRs) ranges for quantitative data, frequencies and percentages for qualitative data and conditional logistic regression in matched case-control analyses (SAS statistical softwarev version 9.4; SAS Institute,Cary,North Carolina,USA). All reported p-values are two-sided.

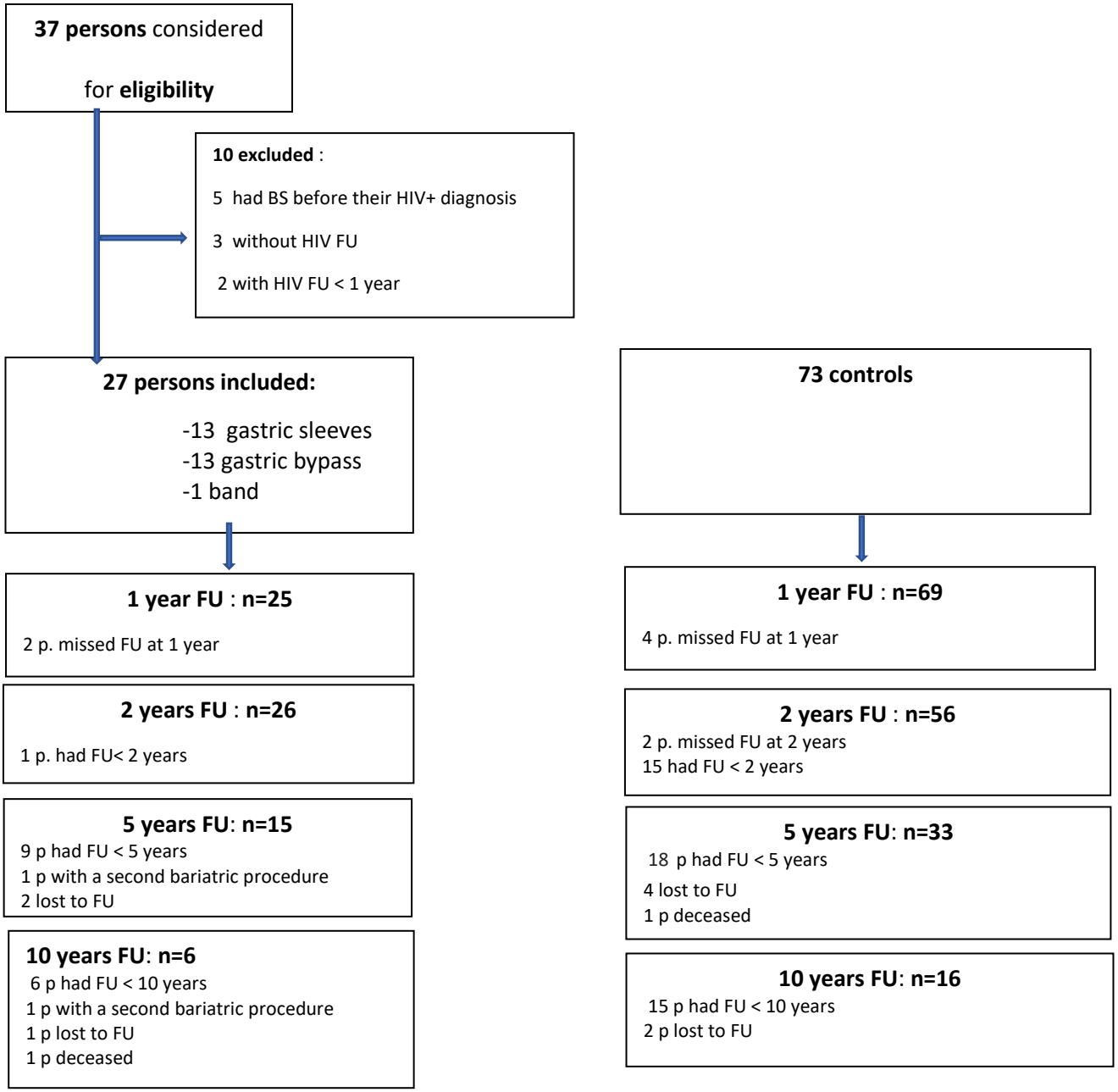
Results

Among 37 PLWH with BS, ten were excluded (Figure 1) leading to 27 cases (13 SG, 13 GB and 1 AGB) and 73 matched controls. Table 1 details patients’ baseline characteristics: 84% were female, median age was 43 years, median time with undetectable HIVRNA was 6 years in both groups. At baseline, cases had higher BMI than controls (41 vs 37.3 kg/m²), were younger at time of HIV diagnosis with longer durations of HIV diagnosis and treatment. Comorbidities, in particular diabetes and OSA, were more prevalent among cases but not statically significant with the exception of previous hypothyroidism (37% in cases vs 4% in controls, p=0.0009).

Table 1 Patients' characteristics at Baseline		Cases (n=27)	Controls (n=73)	*p*
Median age	(years) [IQR]	42 [33.4 ; 51.6]	44 [38.5 ; 50.4]	0.51
Gender n (%)	Female	23 (85.19%)	61 (83.56%)	
	Male	4 (14.81%)	12 (16.44%)	NA*
Ethnicity n (%)	Sub saharan African	21 (77.78%)	57 (78.08%)	
	Other	6 (22.22%)	16 (21.92%)	NA*
HIV acquisition n (%)	Heterosexual	21 (77.78%)	62 (84.93%)	
	Other	6 (22.22%)	11 (15.07%)	0.19
Smoking n (%)	Former/Never	25 (92.59%)	64 (87.67%)	
	Active	2 (7.41%)	9 (12.33%)	0.43
Death during FU n (%)		1 (3.7%)	1 (1.37%)	0.99
Weight and BMI				
Weight	Median [IQR] (kg)	112 [100 ; 135]	100 [96 ; 114]	**0.004**
BMI	Median [IQR] (kg/m²)	41.1 [37.8 ; 45.4]	37.3 [36.4 ; 39.1]	**0.002**
Obesity n (%)	35 -39 kg/m²	10 (37.04%)	59 (80.82%)	
	≥ 40 kg/m²	17 (62.96%)	14 (19.18%)	**0.0004**
HIV				
Age at diagnosis	Median [IQR] (years)	29 [23.3 ; 36.9]	33 [27.6 ; 39.7]	**0.047**
Duration of infection	Median [IQR] (years)	12.1 [7.1 ; 16.9]	10.4 [5.5 ; 15.2]	0.09
HIV follow-up	Median [IQR] (years)	5.1 [2.1 ; 9.8]	4.1 [2 ; 7.9]	0.32
on ARV treatment	Yes	25 (92.59%)	66 (90.91%)	
	No	2 (7.41%)	7 (9.59%)	0.56
DURATION OF :				
ARV treatment	Median [IQR] (years)	11.3 [6.6 ; 16.1]	7.7 [4.3 ; 13.2]	0.02
INSTI**	Median [IQR] (years)	0 [0 ; 2]	0 [0 ; 0.1]	0.19
Tenofovir disproxil	Median [IQR] (years)	3.6 [2.2 ; 9.5]	4.1 [2.6 ; 8.1]	0.66
Tenofovir alafelanide	Median [IQR] (years)	1.6 [0.8 ;2.2]	0.8 [0.5;1.6]	0.49
Rilpivirine	Median [IQR] (years)	2.1 [0.5;3.6]	0.7 [0.4;1.3]	0.69
Median CD4 lymphocytes	Current [IQR] (CD4/mm³)	646 [455 ; 862]	704 [460.5 ; 900.5]	0.91
cell count	Nadir [IQR] (CD4/mm³)	231 [135 ; 312]	253 [125 ; 403]	0.39
CD4/CD8 ratio	Median [IQR] (no unit)	0.7 [0.5 ; 1.1]	0.8 [0.5 ; 1]	0.63
Undetectable HIVRNA	Yes	18*** (72%)	47****(74.6%)	
(≤ 50 copies/ml)	No	7*** (28%)	16**** (25.4%)	0.72
Cumulative time with undetectable viral load	Median [IQR] (ans)	6.7 [3.8 ; 11.1]	5.7 [2.7 ; 10.3]	0.93
HIVRNA	Median [IQR] (copies/ml)	<50 [20 ; 67]	<50 [20 ; 77]	0.63
Comorbidities				
High blood pressure	**n (%)**	9 (33.33%)	17 (24.29%)	0.20
Diabetes	**n (%)**	6 (23.08%)	8 (11.27%)	0.08
HbA1c	Median [IRQ] (%)	5.8 [5.3 ; 7.7]	6 [5.7 ; 7.1]	0.98
OSA	**n (%)**	10 (37.04 %)	1 (1.41%)	0.99
Previous hypothyroidism	**n (%)**	10 (37.04%)	3 (4.11%)	**0.0009**
Previous CV event	**n (%)**	0	3 (4.23%)	0.99
LDL-cholesterol	Median [IQR] (mg/dL)	104.5 [82 ; 134]	105.5 [92 ; 127]	0.34
HDL-cholesterol	Median [IQR] (mg/dL)	50.1 [43.3 ; 59.9]	52.6 [43.6 ; 61.3]	0.09
Total cholesterol	Median [IQR] (mg/dL)	177.5 [150 ; 212]	188.5 [169 ; 214]	0.19
Triglycerides	Median [IQR] (mg/dL)	122 [84 ; 152]	96.5 [66.5 ; 124]	0.58
Framingham score	Median [IQR] (%)	4.1 [1.7 ; 9.2]	3.8 [2.1 ; 10.8]	0.65
Vitamine and minerals deficiencies				
Iron	< 30 µg/L	2/21 (9.52%)	1/17 (5.88%)	0.99
Folate	< 4.6 µg/L	2/14 (14.29%)	3/10 (30%)	0.99
Vitamine B12	< 197 ng/L	0/21	0/11	NA*
Vitamine D	< 30 µg/L	22/24 (91.67%)	42/48 (87.5%)	0.92

FU (follow-up), BMI (body mass index), ARV (antiretroviral), INSTI (integrase inhibitors), OSA (obstructive sleep apnea), CV (cardio-vascular)
*no application **Integrase inhibitors ***total cases =25 **** total controls = 63
Framingham score :% of risk for cardiovascular (CV) event at 10 years

Figure 1: Inclusion and follow up



Free consultations with a dietician specialized for comorbidities linked to HIV are proposed within our HIV clinic to all patients with weight problems. We could retrieve that 24 (89%) cases and 41 (56%) controls had attended at least one of these consultations (p=ns) before baseline, and 24 (89%) cases and 40 (55%) controls after baseline (p=ns). We could not retrieve the exact number of dietician consultations given outside the infectious diseases department.

Table 2 shows the evolution of weights. At 2 years, median BMI decreases from 41 to 29kg/m^2 (p=0.002) in cases but remains at 37kg/m^2 for controls (Figure 2).

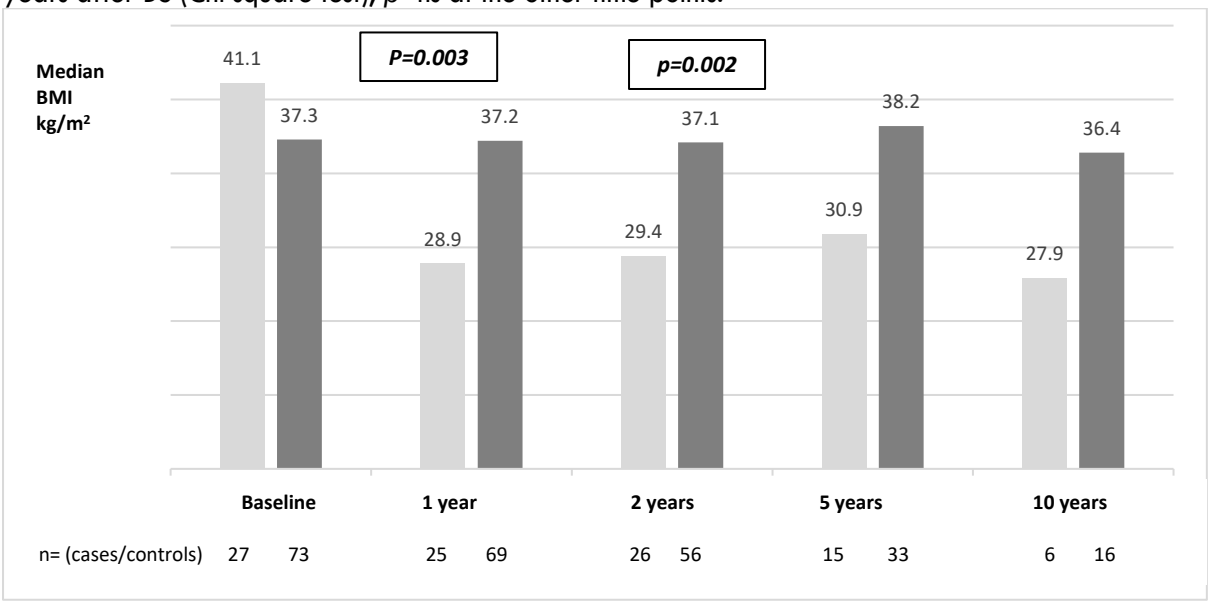
Table 2: Weight evolution

Median [IRQ]	Baseline			1 year			2 years			5 years			10 years		
	Cases : n=27	Controls n=73	P	Cases : n=20/25	Controls n=58/69	P	Cases n=21/26	Controls n=44/56	P	Cases : n=13/15	Controls n=28/33	P	Cases : n=6:6	Controls n=13/16	P
BMI (kg/m²)	41.1 [37.8 -45.4]	37.3 [36.4 -39.1]	0.02	28.9 [25.8 - 35.6]	37.2 [35.4 - 39.6]	0.003	29.4 [26.4 - 35.9]	37.1 [35.6 -39.4]	0.002	30.9 [28.7 - 35]	38.2 [35.9 - 40.4]	0.08	27.9 [26.1 - 29.7]	36.4 [34.2 - 40.8]	0.25
Change in BMI (kg/m²)	NA	NA	NA	-10.8 [-12.6 -9.3]	0 [-1.3 - 0.6]	0.21	-11.3 [-14.6 -9.3]	0 [-1.3 - 1.4]	0.99	- 6.9 [-12 - -6]	0 [-1.1 - 1.8]	0.02	-12 [-14.6 -9.3]	0.4 [-3.6 - 2.3]	0.19
Weight (kg)	112 [96 - 114]	100 [96 - 116.5]	0.004	80 [71.5 - 104]	100.5 [94 - 115]	0.009	77 [70 - 95]	101 [93.5-111.5]	0.005	84 [77 - 111]	100 [94.5 - 110]	0.13	76 [65 - 80]	98 [90 - 111]	0.16
Change in Weight (kg)	NA	NA	NA	-28 [-36.5 -25]	0 [-3 -2]	0.29	-29 [-39 -25]	0 [-3.5 - 4]	0.99	-18 [-36 -15]	0 [-3 - 5]	0.02	-31 [-38 -22]	1 [-10 - 5]	0.99
Total weight loss (%)	NA	NA	NA	-25.4 [-32.2 -23.4]	0 [-3.3 -1.4]	0.26	-27.4 [-32.4 -22.6]	0 [-3.5 - 3.8]	0.99	-17.9 [-29.3-12.5]	0 [-3.2 - 4.9]	0.03	-29.9 [-35.8 -23.8]	1 [-10 - 6.1]	0.17
Excess weight loss* (%)	NA	NA	NA	70.8 [48.9 - 94.9]	0 [-3.8 -10]	0.22	75.8 [47.7- 89.5]	0 [-11.4 - 10.6]	0.28	52.9 [38.5- 76.6]	0 [-15.1 -10.7]	0.03	81.4 [65.8 - 93.6]	-3.4 [-19.2 - 26.3]	0.17

BMI (body mass index), * Excess weight loss defined as weight above a BMI of 25kg/m; NA= not applicable

Figure 2: Median BMI evolution according to time points

cases in light grey, controls in dark grey; *p* between cases and controls =0.003 at 1 year after BS and =0.002 at 2 years after BS (Chi square test), *p*=ns at the other time points.



At 5 and 10 years, median BMI was ≤31kg/m² in cases versus ≥ 35kg/m²in controls. Nadir median BMI was 28 kg/m² in cases and 36.5 in controls (*p*<.001) (Tables A-B). GB led to greater EWL than SG, with a maximum at 2 years (89.3% versus 60.8% *p*=0.041).

Table A: Weight nadir during evolution

Variable		Cases=25/27	Controls=68/73	P value
Minimum BMI	Median[IRQ] (kg/m²)	28 [25.6- 34.7]	36.5 [33.7-38.8]	<0.001
Delta minimum BMI	Median[IRQ] (kg/m²)	11.9 [9.7-16]	2.9 [0.7-4.2]	<0.001
Minimum weight	Median[IRQ] (kg)	78 [68- 98]	97 [87-108]	0.0065
Delta minimum weight	Median[IRQ] (kg)	32 [26- 45]	7.5 [2 -12]	<0.001
Maximum total weight loss	Median[IRQ] (%)	-28.5 [-35.5 ; -24.5]	-1.5 [-6.5 - 0]	0.0026
Maximum excess weight loss	Median[IRQ] (%)	53 [42.9 - 87.2]	-4.7 [-14 ; 2.7]	0.0017
Minimum obesity category	<30	14 (56%)	2 (2.94%)	
	<35	5 (20%)	16 (23.53%)	
	<40	3 (12%)	37 (54.41%)	
	>=40	3 (12%)	13 (19.12%)	0.0051
Delta days at minimum weight	Median [IRQ] (days)	717 [460 - 1283]	431.5 [207 - 974]	0.1664

BMI (body mass index), IQR (interquartile range)

Table B: Weight evolution according to the different surgeries (Delta is the difference between baseline and the value at a certain time point)

	1 year			2 years			5 years		
Median [IRQ]	Sleeve : n=13	Bypass n=13	p	Sleeve : n=10	Bypass n=11	p	Sleeve : n=7	Bypass n=6	p
BMI (kg/m²)		26 [25.4 - 35.4]	0.1944	34.7 [29.4 - 40]	26.6 [25.7 - 30.8]	0.0542	32.8 [30.8 - 36.2]	29 [27.9 - 30.9]	0.2007
Delta BMI (kg/m²)	-10.1 [-11.3 - -9.3]	-11.6 [-14.8 - -9.7]	0.3208	-10.1 [-12.6 - -10.1]	-11.5 [-14.8 - -9.7]	0.3540	-6.7 [-11.1 - -6]	-11 [-12.6 - -6.2]	0.4862
Weight (kg)	100 [78 - 111]	74 [65 - 85]	0.2075	95 [82 - 113]	71 [64 - 77]	0.0399	98.5 [78 - 112]	80.5 [63 - 84]	0.1558
Delta (kg)	-26 [-35 - -25]	-30.5 [-39 - -27]	0.4711	-29 [-34 - -22]	-29 [-45 - -26]	0.4128	-17.5 [-36 - -17]	-27.5 [-36 - -15]	0.8136
Total weight loss(%)	-23.8 [-25 - -22.9]	-30.9 [-32.9 - -25.7]	0.1033	-23.4 [-28.5 - -21.2]	-30.4 [-35.5 - -27.1]	0.0467	-17.6 [-24.5 - -11.6]	-27.8 [-30 - -15.2]	0.3203
Excess weight loss (%)	53 [46.7 - 75.8]	93 [64.9 - 97.4]	0.1702	60.9 [44 - 64.7]	89.3 [81.1 - 93.5]	0.0401	52.2 [25.5 - 54.5]	75.8 [42.9 - 78.6]	0.3203

BMI (body mass index), IQR (interquartile range)

Two cases (7.4%) underwent a second bariatric surgery due to late weight regain at 5 and 10 years (SG to GB and AGB to SG).

Post-operative complications within 30 days occurred in 3 persons (11%): one perioperative bleeding leading to splenectomy, one fistula and one occlusion with hospital readmission and second surgery; their outcomes were favorable. One person had prolonged nausea that improved progressively and another developed acute intestine incarceration two years after BS with favorable outcome after surgery.

HIVRNA suppression was maintained in all but one case with transient dysphagia after SG; HIVRNA became undetectable again after 3 months. Table C shows the evolution of HIV markers and no difference between cases and controls in terms of exposure to ART that might affect weight (Tenofovir disoproxil or alafenamide/ Integrase Inhibitors/Rilpivirine).

Table C : Evolution of HIV Infection surrogate markers and of exposure to different antiretroviral drugs that might impact weight gain or loss

Median [IRQ]	Baseline			1 year			2 years			5 years			10 years		
	Cases n=25/27	Controls n=63/73	p	Case 23/25	Controls n=64/69	p	Cases n=22/26	Controls n=55/56	p	Cases n=13/15	Controls n=32/33	p	Cases n=4/6	Controls n=11/16	p
Median HIVRNA (copies/ml)	<20 [<20 - 67]	<20 [<20 - 77]	0.6268	<20 [20 - 50]	<20 [20 - 36]	0.4913	<20 [<20 - 50]	<20 [<20 - 47]	0.5780	<20 [<20 - 28]	<20 [<20 - <20]	0.5645	<20 [20 - 87]	<20 [20 - 20]	0.3476
Time with HIVRNA <50 cp/ml (years)	6.7 [3.8 - 11.1]	5.7 [2.7 - 10.3]	0.9316	7 [4.5 - 11]	5.9 [2.5 - 9.7]	0.5445	7.8 [5.3 - 12]	6.6 [3.4 - 10.1]	0.2936	10.2 [3 - 13.3]	8.3 [4.4 - 11.8]	0.5472	9.4 [4.8 - 15.9]	13.8 [7.8 - 16.7]	0.7935
CD4 median count (years)	646 [455 - 862]	704 [460.5 - 900.9]	0.9125	720 [474 - 915]	710 [476 - 898]	0.9139	692 [468 - 929]	798 [553 - 927]	0.5637	637 [378 - 853]	743 [411 - 1081]	0.8849	925.5 [534.5 - 1207]	780 [638 - 997]	0.8286
CD4/CD8 ratio	0.7 [0.5 - 1.1]	0.8 [0.5 - 1]	0.6394	0.9 [0.5 - 1.2]	0.9 [0.6 - 1.2]	0.4001	1.1 [0.5 - 1.3]	1 [0.6 - 1.3]	0.5377	0.9 [0.5 - 1.3]	1 [0.6 - 1.4]	0.9389	1 [0.9 - 1.3]	1.4 [0.8 - 1.6]	0.4548
Time under INSTI* (years)	0 [0 - 2]	0 [0 - 0.1]	0.1937	0 [0 - 3.2]	0 [0 - 0.9]	0.1811	0 [0 - 3.1]	0 [0 - 0.6]	0.1240	0 [0 - 1.4]	0 [0 - 0]	0.1801	0.5 [0 - 2.1]	0 [0 - 4.3]	0.9497
Time under TDF** (years)	3.6 [2.2 - 9.5]	4.1 [2.6 - 8.1]	0.6627	4 [2.2 - 9.7]	4.9 [3.2 - 8.9]	0.4992	4.3 [2.7 - 9.7]	5.7 [4.4 - 8.6]	0.6854	5.7 [3.7 - 11.5]	8 [2.7 - 10.7]	2023	10 [7.8 - 12.6]	10 [5.4 - 10.8]	0.2445
Time under TAF*** (years)	1.6 [0.8 - 2.2]	0.8 [0.5 - 1.6]	0.4890	1.7 [0.3 - 3]	1.7 [1.1 - 2.3]	0.4767	1.9 [1.2 - 4]	2.5 [0.7 - 2.9]	0.7607	3.1 [2 - 4.2]	2.1 [1 - 3.2]	NA	ND	3.1 [2.2 - 4]	NA
Time under RPV**** (years)	2.1 [0.5 - 3.6]	0.7 [0.4 - 1.3]	0.6952	3.1 [1.5 - 4.6]	1.1 [0.5 - 2]	0.5592	4.1 [2.5 - 5.6]	1.8 [0.7 - 2.8]	0.4709	2 [2 - 2]	3.1 [2.5 - 4.3]	NA	ND	2.4 [2 - 3.1]	NA
Treatment modification	NA	NA	NA	0 [0 - 1]	0 [0 - 0]	0.2196	0 [0 - 1]	0 [0 - 1]	0.6059	1 [0 - 2]	1 [1 - 1]	0.7366	2 [1 - 3]	1.5 [1 - 2]	0.5245

*INSTI : Integrase inhibitors **TDF : Tenofovir disproxil ***TAF : Tenofovir alafenamide ****RPV : Rilpivirine

Table D: Vitamins and minerals levels

Variable	Group	baseline	1 year	2 years	5 years	10 years
Iron < 30 µg/L	**Population Cases = Controls =**	**21/27 17/73**	**17/25 15/69**	**16/26 11/56**	**6/15 7/33**	**3/6 2/16**
	Cases	2 (9.52%)	1 (5.88%)	0	1 (16.67%)	0%
	Controls	1 (5.88%)	0	1 (9.09%)	1 (14.29%)	50%
	p	0.9961	0.9963	0.9975	0.9984	0.9990
Folate < 4.6µg/L	**Population Cases = Controls =**	**14/27 10/73**	**10/25 9/69**	**11/26 6/56**	**5/15 5/33**	**3/6 1/16**
	Cases	2 (14.29%)	1 (10%)	1 (9.09%)	2 (40%)	0
	Controls	3 (30%)	2 (22.22%)	2 (33.33%)	0	0
	p	0.9975	0.9984	0.9985	0.9990	NA
Vitamine B12 < 197 ng/L	**Population Cases = Controls =**	**21/27 11/73**	**18/25 10/69**	**16/26 7/56**	**6/15 6/33**	**3/6 2/16**
	Cases	0	0	2 (12.5%)	0	1 (33.33%)
	Controls	0	0	0	0	0
	p	NA	NA	NA	NA	NA
Vitamine D < 30 µg/L	**Population Cases = Controls =**	**24/27 48/73**	**20/25 52/69**	**19/26 39/56**	**10/15 27/33**	**4/6 10/16**
	Cases	22 (91.67%)	14 (70%)	13 (68.42%)	6 (60%)	2 (50%)
	Controls	42 (87.5%)	45 (86.54%)	28 7 (1.79%)	20 (74.07%)	2 (20%)
	p	0.9166	0.0582	0.5111	0.5057	0.4482

Vitamins and mineral deficiencies were similar between cases and controls at baseline and during FU (Table 1, Table D). During FU, lipid profile and Framingham score improved in cases but worsened in controls (Table E).

Comorbidities favorable evolution at 2 years was 50% in cases versus 12.5% in controls for diabetes, 44% versus 0 (p=0.006) for high blood pressure and 90% versus 0 (p<.0001) for OSA (Figure 3. Table F). Increase or new comorbidities were more frequent in controls than in cases. None of the cases developed CVD whereas one control had acute stroke.

Table E: Evolution of lipid and diabetes laboratory values

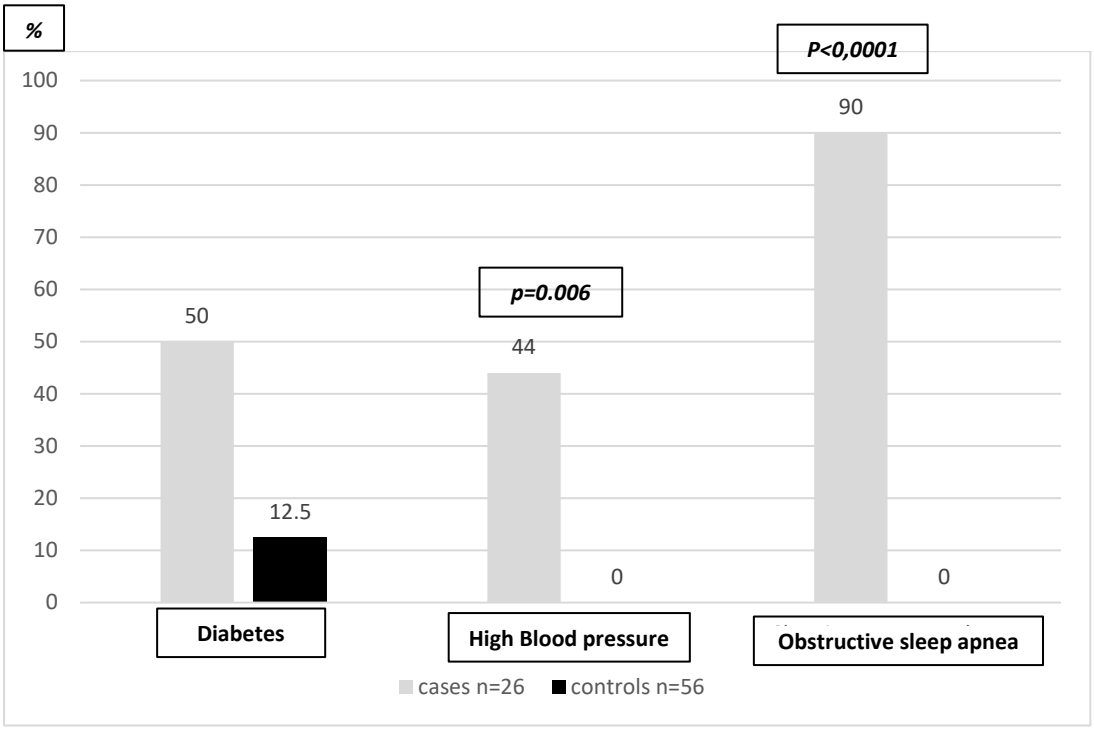
Median [IQR]	Baseline			1 year			2 years			5 years			10 years		
	Cases : n=27	**Controls n=73**	**p**	**Cases : n=25**	**Controls n=69**	**p**	**Cases : n=26**	**Controls n=56**	**p**	**Cases : n=15**	**Controls n=33**	**p**	**Cases : n=6**	**Controls n=16**	**p**
HbA1c %	5.8 [5.3 - 7.7]	6 [5.7 - 7.1]	0.9781	5.5 [5.1 - 6.4]	5.9 [5.5 - 6.4]	ND	5.4 [5 - 5.7]	6.4 [5.9 - 7]	0.2069	5.9 [5.1 - 6.8]	5.3 [5.5 - 6.9]	0.4078	6.8 [5.7 - 7.9]	6 [5.4 - 6.2]	NA
Delta HbA1c %	NA	NA	NA	-0.1 [-0.3 - 0]	-0.2 [-1 - 0.1]	0.5911	-0.2 [-0.3 - 0.2]	-0.4 [-0.7 - 0.2]	0.4131	-0.4 [-0.4 - 0]	0.1 [-0.4 - 0.5]	0.7042	-1 [-2.2 - 0.3]	NA	NA
LDL-cholesterol mg/dL	104.5 [82 - 134]	105.5 [92 - 127]	0.3357	93 [64 - 117]	103 [89 - 124]	0.0620	86 [67 - 114]	102.5 [86 - 129]	0.2251	108 [64 - 122]	106 [83 - 118]	0.8118	85 [68 - 93]	92.5 [75.5 - 116]	0.5439
Delta LDL-cholesterol mg/dL	NA	NA	NA	-20 [-25 - -2]	-3 [-15 - 14]	0.2598	-10.5 [-23 - -3]	-3 [-13 - 13]	0.2593	-12 [-27 - 3]	-2 [-17 - 4]	0.3863	-28 [-30 - -27]	-23 [-50 - -3]	0.7699
HDL-cholesterol mg/dL	50.1 [43.3 - 59.9]	52.6 [43.6 - 61.3]	0.0961	66.8 [57.6 - 81]	53.4 [44.5 - 64.5]	**0.0304**	69.1 [57.9 - 83.1]	53.2 [45.7 - 67.4]	**0.0322**	71.7 [54.7 - 84.3]	60.6 [42 - 70.8]	0.2694	81.3 [76.3 - 113.8]	71.5 [57.6 - 80.4]	0.2794
Delta HDL-cholesterol mg/dL	NA	NA	NA	13.9 [3.8 - 23.5]	0.3 [-3.3 - 5.4]	**0.0044**	15.2 [8.1 - 25.7]	1.6 [-4.2 - 10]	**0.0050**	9.9 [2.5 - 20.4]	1.2 [-5.2 - 8.2]	0.0882	32.4 [9 - 75.5]	8.9 [-8.9 - 19.1]	0.2799
Triglycerides mg/dL	122 [84 - 152]	96.5 [66.5 - 124]	0.5854	81 [51 - 104]	92 [67 - 128]	0.0993	74 [54 - 111]	87 [58 - 149]	0.1667	99 [80 - 130]	78 [58 - 142]	0.4568	91 [89 - 92]	72 [62.5 - 109.5]	0.5243
Delta triglycerides mg/dL	NA	NA	NA	-35 [-56 - -5]	-1 [-20 - 21]	0.1509	-39.5 [-70 - -4]	0 [-20 - 32]	0.2235	-10 [-44 - 11]	1.5 [-24.5 - 19]	0.3083	-61 [-64 - -50]	-5 [-26 - 20]	0.2101
Total cholesterol mg/dL	177.5 [150 - 212]	188.5 [169 - 214]	0.1977	178 [142 - 203]	186 [158 - 205]	0.2413	167 [150 - 204]	184 [154 - 220]	0.7476	180 [159 - 215]	186 [155 - 205]	0.3916	197 [179 - 200]	179 [148 - 210]	0.6597
Delta total cholesterol mg/dL	NA	NA	NA	-9 [-19 - 7]	0 [-19 - 12]	0.7366	-4.5 [-16 - 14]	-2 [-13 - 14]	0.6369	2 [-19 - 28]	-2.5 [-13.5 - 10]	0.4170	-2 [-33 - 32]	-20 [-57 - 19]	0.4836
Framingham score %)	4.1 [1.7 - 9.2]	3.8 [2.1 - 10.8]	0.6515	3.91 [2.4 - 2.9]	4.7 [2.1 - 13.8]	0.336	2.9 [1.8 - 7]	3.6 [1.7 - 8.5]	0.1765	3 [2.4 - 7.7]	4.5 [1.8 - 7.8]	0.4365	3.3 [2 - 11.9]	7.2 [4.1 - 9.4]	NA

HbA1c (glycosylated hemoglobin)

Table F: Co-morbidities evolution

Median [IQR]		Baseline			1 year			2 years			5 years			10 years		
		Cases : n=27	**Controls n=73**	**p**	**Cases n=25**	**Controls n=69**	**p**	**Cases n=26**	**Controls n=56**	**p**	**Cases n=15**	**Controls n=33**	**p**	**Cases n=6**	**Controls n=16**	**p**
High Blood pressure	Presence	9/27 (33.33%)	17/73 (24.29%)	0.2041	9/25 (36%)	18/69 (26.09%)	0.3470	8/26 (30.77%)	18/56 (32.14%)	0.7224	5/15 (33.33%)	15/33 (32.14%)	0.4171	2/6 (33.33%)	11/16 (68.75%)	0.3929
	Emergence	NA	NA	NA	0	1/18 (5.56%)	1.000	0	2/18 (11.11%)	1.000	1 (20%)	7/15 (46.67%)	0.9978	1/2 (50%)	7/11 (63.64%)	1.000
	Increase	NA	NA	NA	0	4/18 (22.22%)		0	6/18 (33.33%)		0	3/15 (20%)		1/2 (50%)	3/11 (27.27%)	
	Stablitily	NA	NA	NA	6/9 (66.67%)	13/18 (72.22%)		5/8 (62.5%)	10/18 (55.56%)		3/5 (60%)	4/15 (26.67%)		0	1/11 (9.09%)	
	Decrease	NA	NA	NA	3/9 (33.33%)	0		3/8 (37.5%)	0		1/5 (20%)	1/15 (6.67%)		0	0	
Diabètes	Presence	6/27 (23.08%)	8/73 (11.27%)	0.0842	4/25 (16%)	9/25 (13.04%)	0.6130	4/26 (15.38%)	11/56 (19.64%)	1.000	3/15 (20%)	5/33 (15.15%)	0.6088	1/6 (16.16%)	3/16 (18.75%)	0.9975
	Emergence	NA	NA	NA	0	1/9 (11.11%)	ND	0	3/11 (27.27%)	ND	0	1/5 (20%)	ND	0	2/3 (66.67%)	ND
	Increase	NA	NA		1/4 (25%)	2/9 (22.22%)		1/4 (25%)	5/11 (45.45%)		1/3 (33.33%)	3/5 (60%)		1/1 (100%)	0	
	Stablitily	NA	NA		1/4 (25%)	5/9 (55.56%)		1/4 (25%)	2/11 (18.18%)		1/3 (33.33%)	0		1/5 (20%)	1/3 (33.33%)	
	Decrease	NA	NA		2/4 (50%)	1/9 (11.11%)		2/4 (50%)	1/11 (9.09%)		1/3 (33.33%)	0		0	0	
Obstructive sleep Apnea	Presence	10/27 (37.04%)	1/73 (1.41%)	0.9934	2/25 (8%)	3/69 (4.35%)	0.4167	1/26 (3.85%)	2/56 (3.57%)	0.8092	0	1/33 (3.03%)	0.9952	0	1/16 (6.25%)	0.9969
	Emergence	NA	NA	NA	0	2/3 (66.67%)	ND	0	1/2 (50%)	ND	0	1/1 (100%)	ND	0	1/1 (100%)	ND
	Increase	NA	NA		0	0		0	0		0	0		0	0	
	Stablitily	NA	NA		1/2 (50%)	1/3 (33.33%)		1 /1 (100%)	1/2 (50%)		0	0		0	0	
	Decrease	NA	NA		1/2 (50%)	0		0	0		0	0		0	0	
Cardio-vascular event	Presence	0	3/73 (4.23%)	0.9944	0	0	NA	0	1/56 (1.8%)	0.9952	0	0	NA	0	0	NA

Figure 3: Percentage of patients with favorable outcome (= disappearance or decrease in medication) at 2 years of follow-up among patients with comorbidities (case n=26, controls n=56)
***p* between cases and controls (Chi square test)**



Discussion:

In this retrospective study among PLWH with severe obesity, bariatric surgery was a safe and effective treatment leading to a significant weight loss that persisted at mid and long term.

Although controls had lower baseline BMI and both cases and controls received the same dietary support, weight loss was statistically significantly greater in cases who all reached BMI ≤31 at all follow up times (including long term FU at 10 years) while all controls remained >35 kg/m².

After 1 and 10 years, respectively 55% and 83% of cases were not obese anymore (with a maximal EBW loss of 53% at 2 years), versus 2% and 8% of controls. These findings are similar to previous studies both in HIV-positive[15,17,18] and negative populations [19,20].
In this study, EBW loss after GB was greater than previously reported: 75.8% at 5 years and 84.1% at 10 years, compared to 60% at 5 and 10 years in HIV-negative patients[9,20]. This is consistent with a recent meta-analysis, which showed that EBW loss is generally higher in females, which indeed represent the majority of our cases[9].

Of note, a randomized trial performed in HIV-negative patients found a greater weight loss for GB at 5-7 years [18,20,21,22]. In the HIV population, two small cases series (n=3 and 5)[19,23] could not find difference in WL between procedures while a larger study (n=24) showed greater efficacy of GB[24].

In previous studies, bariatric surgery led to a significant reduction in obesity-associated comorbidities such as high blood pressure, diabetes, hyperlipemia or OSA among either HIV-negative patients or in PLWH, however none of the studies on PLWH included a comparator arm with severely obese PLWH without BS[15,19,25,26,27]. Our study shows that among PLWH with severe obesity, bariatric surgery significantly decreases comorbidities while patients without bariatric surgery had an increase in their comorbidities overtime.

Major complications of bariatric surgery was lower in our study than in the general population (11% versus 17% but 2 cases (7.41%) needed a second BS because of weight regain, similarly to the literature[21].

Although there are potential mechanisms that might change the ARV absorption after bariatric surgery, HIVRNA suppression was maintained in all but one patient with a transient rebound. Clinicians should discuss with their patients if their ARV therapy is still appropriate after BS, in particular checking for pill size, tolerance or drug-drug interaction with proton pump inhibitors, which are often prescribed after surgery[15,28].

When looking at other potential factors that could have also influenced the weight among our patients, we found that dietary advices or exposure to specific ARV that could have impact on weight were similar in cases and controls both at baseline and during follow up[29,30]. Intriguingly, we found that at baseline, there was significantly more cases with previous hypothyroidism than controls. Indeed, there are complex and mutual relationships between the thyroid axis and adiposity: for example, obesity and accumulation of adipocytes might lead to thyroid dysfunction[31]. In our study, the higher median BMI found at baseline in our cases could account for these results.

Our study has several limitations such as its monocentric and retrospective design and the limited number of cases in particular on the long term FU. Some of our results, although impressive (delta BMI at 2 years was -12 kg/m² in cases versus 0 in controls), were not statistically significant probably because of the small number of

patients. Another weakness of our study is the lack of precision regarding the total number of dietician consultations received by the cases and the controls due to the retrospective design of the study. Regarding the number of dietician consultations given in the HIV out-consultation, cases seem to have more consultations than controls although it was not statistically significant. These numbers are probably underestimating the reality in both cases and controls as patients have also consulted dieticians in other consultations such as bariatric surgery consultation or in private practice. On the other hand, although dietician advices are keys in the general management of weight problems, they have been shown to lead only to a 3-5% weight loss in obesity[11].

Our study has also strengths: it includes one of the largest HIV populations studied in a single center who underwent BS, with detailed data on biological and clinical markers (including the weight), ARV and comorbidities, collected prospectively.

It is also the first study matching PLWH with bariatric surgery with a control group including PLWH with severe obesity who did not undergo bariatric surgery, matched on age, sex, ethnicity and BMI while previous publications compared HIV-positive to HIV-negative patients, all with bariatric surgery. This allows avoiding potential biases such as the effect of HIV infection it-self or the effects of some specific ARV drug on weight or on comorbidities.

Conclusion

In conclusion, bariatric surgery is an efficient and safe treatment of severe obesity and its related comorbidities among persons living with well-controlled HIV at short, middle and long terms, with no deleterious impact on control of HIV disease.

Conflict of Interest statement:

We certify that none of the authors has commercial or other associations that might pose a conflict of interest for the performance or analysis of the study.

Data availability statement: data are available on request

Ethics approval statement: the Ethics committee of Saint-Pierre University hospital (CE / 20-10-10) approved this study on October 20th 2020.

Informed consent: all the patients included in the study have signed an informed consent statement

Funding: None

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