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Outcomes of varicose vein surgery in patients with HIV/AIDS – a nested case-control study

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ABSTRACT

INTRODUCTION: Currently, people living with HIV/ AIDS (PLWHA) attain a life expectancy similar to a non-HIV population. However, these patients experience a status of chronic inflammation, which is a known cause of arteriopathy. Yet, literature is scarce regarding the potential venous inflammatory effect, especially after varicose vein surgery. The aim of this study was to perform a descriptive analysis alongside evaluating short and long-term outcomes after varicose vein surgery in PLWHA while comparing with a control group.

METHODS: A retrospective nested case-control study was performed resorting to codification. All PLWHA patients which had any hospital interaction with the Vascular Surgery Department (either outpatient clinic, emergency or surgery) due to venous disease between April 2006 and December 2019 were identified. PLWHA found to have undergone varicose vein surgery within the study inclusion period were included. The immediately consecutive varicose vein surgery in a patient with no-HIV infection was included in the control group in a 1:1 ratio. Comorbidities were collected at the time of index event.

RESULTS: The cohort included 118 patients (59 PLWHA and 59 control) and had a mean follow-up of 86 [Interquartile range (IQR) 25-75%, 43-111] months. At baseline, PLWHA were younger (45.2 ± 10.71 vs 49.9 ± 10.69 years, p=0.017) and had a male predominance (54% vs 27%, p=0.003). Furthermore, there were a higher prevalence of smokers (54% vs 17%, p<0.001) and history of drug abuse (34% vs 2%, p<0.001) in the study group. Although not statistically significant, PLWHA presented higher pre-operative CEAP classifications. Regarding post-operative outcomes, no differences were found for complications, reinterventions or overall-mortality.

CONCLUSION: To the authors knowledge, this is the first study addressing varicose vein treatment in PLWHA. In summary, PLWHA undergoing varicose vein surgery seem to be younger and have higher CEAP classifications. Nonetheless, short and long-term outcomes seem to be good and similar to a control population. Further studies with larger populations and disease specific outcomes are necessary to confirm such findings.

Keywords: HIV/AIDS care; chronic venous disease; varicose veins; venous surgery

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INTRODUCTION

The Human Immunodeficiency Virus remains a global epidemic with increasing prevalence[1]. Moreover, due to the advent of combination of antiretroviral therapy (ART), people living with HIV/ AIDS (PLWHA) attain a similar life expectancy to a non-HIV population[2,3]. Given this, PLWHA are also susceptible to develop chronic non-communicable diseases. In fact, they seem prone to higher incidences of cardiovascular diseases mediated by atherosclerosis, especially coronary and cerebrovascular events, and at a younger age [1,4,5]. Although not completely elucidated yet, the pathogenesis of this excess risk, seems to be linked to chronic inflammation mediated by both the HIV infection itself and ART besides other hypothesized mechanisms[1,4,6]. This chronic inflammation is described to affect arteries in different territories such as the carotid artery and femoral artery with progression of intima-media thickness[5,7]. Yet, literature is scarce regarding the potential venous inflammatory effect, especially after varicose vein surgery. The aim of this study was to perform a descriptive analysis alongside evaluating short and long-term outcomes after varicose vein surgery in PLWHA while comparing with a control group.

METHODS

Design and population

A retrospective nested case-control study was performed based on a retrospective review, in a tertiary university hospital's database, resorting to ICD 9 codification. All PLWHA signalized trough codification and which simultaneously had any hospital interaction with the Vascular Surgery Department, either outpatient clinic, hospitalization, emergency or surgery, due to venous disease between April 2006 and December 2019, were identified. PLWHA found to have undergone varicose vein surgery within the study inclusion period were included. The immediately consecutive patient submitted to varicose vein surgery with no-HIV infection was included in the control group in a 1:1 ratio.

Data Management

Comorbidities were collected at the time of index event resorting to electronic records which were further used for the collection of outcomes also through retrospective analyzed of clinical records. The study protocol (number 361-20) was approved by the local Ethics Committee and respected the Helsinki Declaration.

Definitions

Chronic kidney disease (CKD) was defined as a glomerular filtration rate (GFR) <60mL/min Cockcroft-Gault. Clavien-Dindo classification was adopted for surgical complications.

Endpoints

Primary endpoints were postoperative complications and recurrence with surgery. Secondary outcomes were long-term mortality.

Statistical analysis

A descriptive statistical analysis was performed resorting to SPSS (IBM Corp., released 2019. IBM SPSS Statistics for Windows, version 26.0, Armonk, NY, USA). Categorical variables are presented as count and percentage, and compared using the Pearson´s $\chi 2$ test. Continuous variables are presented as mean and standard deviation or as median and interquartile range (IQR).

RESULTS

The cohort included 118 patients (59 PLWHA and 59 control) and had a mean follow-up of 86 [Interquartile range (IQR) 25-75%, 43-111] months. At baseline, PLWHA were younger (45.2 ± 10.71 vs 49.9 ± 10.69 years, p=0.017) and had a male predominance (54% vs 27%, p=0.003). Furthermore, the study group showed a higher prevalence of smokers (54% vs 17%, p<0.001) as well as patients with a history of drug abuse (34% vs 2%, p<0.001).

With regard to venous characteristics, there were no statistically significant differences at baseline, including previous varicose vein surgery, history of deep vein thrombosis and deep vein pathology. Moreover, although not statistically significant, PLWHA presented a tendency towards higher pre-operative CEAP classifications. (Table 1)

Table 1. Demographics

Demographics	HIV + n=59(%)	HIV - n=59(%)	P - value
Age (years)	45.2 ± 10.71	49.9 ± 10.69	0.017
Male Gender	32 (54)	16 (27)	0.003
Dylipidemia	24 (41)	18 (31)	NS
Hypertension	11 (19)	18 (31)	NS
Diabetes	4 (7)	9 (15)	NS
Smoker	32 (54)	10 (17)	<0.001
CAD	5 (8)	4 (7)	NS
CKD*	6 (10)	2 (3)	NS
BMI >30	9 (15)	8 (14)	NS
History of Drug Abuse	20 (34)	1 (2)	<0.001
Previous Surgery	6 (10)	11 (19)	NS
History of DVT	1 (2)	1 (2)	NS
Deep Vein Pathology	0 (0)	1 (2)	NS
CEAP Classification			
C2			
C3	34 (58)	39 (66)	
C4	9 (15)	12 (20)	
C5	1 (2)	1 (2)	NS
C6	2 (3)	0 (0)	
	3 (5)	0 (0)	

G*GFR <60mL/min Cockcroft-Gault

BMI – body mass index; **CAD** – coronary artery disease; **CKD** – chronic kidney disease; **DVT** – deep vein thrombosis; **NS** – Non-significant

Technical surgical data, including bilaterality, type of surgery (endovascular vs direct surgery) and number of saphenous trunks treated did not differed significantly among groups. (Table 2)

Table 2. Technical surgical data

Technical Surgical data	HIV + n=59(%)	HIV - n=59(%)	P - value
Ambulatory	23 (39)	25 (42)	NS
Endovascular Intervention	1 (2)	1 (2)	NS
Bilateral Surgery	54 (92)	54 (92)	NS
Saphenous Trunks			
0	16 (32)	9 (15)	NS
1	23 (39)	24 (41)	
2	17 (29)	22 (37)	
3	3 (5)	2 (3)	

NS - Non-significant

Regarding post-operative outcomes, no statistically significant differences were found for complications, reinterventions or overall-mortality during follow-up. There was one death per group, none of each related to chronic venous disease.

All complications were inserted in the category of Clavien-Dindo 1, except a distal deep vein thrombosis in the negative-HIV group (which inserts as a complication Clavien-Dindo 2). Furthermore, the authors analyzed a composite outcome of recurrence of varicose veins (previous surgery + PREVAIT with re-intervention) which equals to more than one surgery for each patient, which did also not showed to be statistically different between study groups.

Table 3. Outcomes

Outcomes	HIV + n=59(%)	HIV - n=59(%)	P - value
30-day Urgency Department Visit	3 (5)	5 (8)	NS
Complications*	4 (7)	7 (12)	NS
PREVAIT with Re-operation	5 (8)	8 (14)	NS
Mortality	1 (2)	1 (2)	NS

* Clavien-Dindo ≥1

NS - Non-significant; **PREVAIT** - PREsence of Varices (residual or recurrent) after InTervention

DISCUSSION

To the best of our knowledge, this is the first study addressing varicose vein post-operative outcomes in PLWHA. Similar outcomes were seen either in short or long-term, despite a non-significant higher CEAP score at baseline.

HIV infection became more prevalent with the increase of life expectancy and so, chronic diseases in PLWHA became also a major concern among these patients. Arterial complications have a higher incidence with a multi factorial pathophysiology including traditional risk factors, HIV-specific factors, behavioral factors, exposure to ART and other therapies, co-infections and comorbidities[8,9]. For instance, a retrospective study in Netherlands including 14 389 PLWHA and 99 762 person-years of follow-up, with median follow-up of 7.2 years (IQR 3.3-11.1), reported a crude incidence of 2.23 events per 1000 person-years (95% CI 2.04-2.64) and an incidence standardized for age and sex of 2.5 events per 1000 (2.18-2.82). Furthermore, lower CD4 counts, higher viral loads and current or recent opportunistic infections as independently associated with higher risk of venous thrombotic event. On the other hand, no specific ART showed to be a risk factor[10]. The increased risk of VTE can be explained by the presence of hypercoagulable state, with increased procoagulant factors such as endothelial TF expression, associated with a decrease in anticoagulant factors, including AT III, HC II and the protein C pathway[11].

On the other hand, literature on chronic venous disease or varicose vein surgery outcomes is almost absent. In this regard, our study revealed a male predominance among the HIV group compared to a control group (54% vs 27%, p=0.003). This is probably related to the significantly higher proportion of male patients with HIV infection which is reported in at least some regions[12,13] as in opposite to a female predominance in varicose vein surgery as reported observed in the control group[14]. Moreover, in our study PLWHA were younger (45.2 ± 10.71 vs 49.9 ± 10.69 years, p=0.017) and had higher level of clinical CEAP C classifications. The authors acknowledge the latter may reflect an unconscious selection bias, even though this last point was not statistically significant. The study group also revealed a higher smoking rate and history of drug abuse which goes in line with previous findings[6,13].

Limitations

Limitations of this study arise from the retrospective nature of the investigation which brings its inherent limitations and the small number of patients. Moreover, those who were unaware of their HIV infection were also not identified. Incapacity to evaluate the incidence and prevalence of Chronic Venous Disease in PLWHA due to the nature of the study also poses an important limitation. Furthermore, recurrence was defined as more than one varicose vein surgery identified however, clinical or Doppler ultrasound identified recurrence was not evaluated.

Lastly, due to limited number of patients, authors cannot eliminate the chance of type 2 error, limiting the hypothesis of unveil subtle differences among groups throughout the follow-up period. Yet, the authors highlight the importance of treatment of these patients, that now face a similar life expectancy to the general population, not only with the best medical treatment both to their HIV infection and remaining chronic comorbidities but also to those pathologies that can impact negatively their quality of life such as chronic venous disease.

CONCLUSION

To the authors knowledge, this is the first study addressing varicose vein treatment in PLWHA. In summary, PLWHA undergoing varicose vein surgery seem to be younger and have higher CEAP classifications. Nonetheless, short and long-term outcomes seem to be good and similar to a control population. Further studies with larger populations and disease specific outcomes are necessary to confirm such findings.

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