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#### 9 Abstract

10 Objective: To determine the burden and impact of chronic venous insufficiency (CVI) of the lower limbs in

Severity Stages of Chronic Venous Insufficiency: A Study in Kinshasa, DR Congo

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- 11 Kinshasa, Democratic Republic of Congo (DRC).
- 12 Methods: We conducted a retrospective clinical study on a random sample of 393 patients diagnosed with
- 13 chronic venous disease (CVD) between 2019 and 2024 at an urban hospital in Kinshasa. These patients
- represented 81% of a larger cohort of 486 individuals who presented with dermatologic disorders of the lower 14
- 15 limbs during the period.
- 16 Results: Disease severity, per the CEAP clinical classification, indicated that 362 patients (92%) were
- 17 diagnosed with CVI (classes C3 through C6), most commonly presenting at stage C3 (26.5%, edema) or C6
- (44.5%, active venous ulcers). Limb-level disease patterns were as follows: (1) Symmetric Disease: 33% of 18
- 19 patients exhibited identical CEAP classes in both lower limbs; (2) Asymmetric Bilateral C6 Involvement: 14%
- had left-dominant and 10% had right-dominant presentation; (3) Unilateral Involvement: 17% of patients had 20
- disease confined to the left limb and 11% to the right limb. 21
- 22 **Conclusions**: Our observations confirm the significant role of venous pathology in lower limb dermatologic
- 23 disorders, establishing it as the primary cause of lower limb ulcers, consistent with findings from Western
- 24 populations. In Kinshasa, and likely in other megacities across sub-Saharan Africa, these data highlight an
- 25 evolving epidemiological landscape characterized by a dual burden of non-communicable and
- 26 communicable diseases. At the community level, the vernacular term "MBASU" is indiscriminately applied to
- a variety of dermatologic conditions, including erythema, papules, unsightly wounds, edema, fibrosis, and 27
- 28 both healed and active ulcers. To enhance clarity in clinical management and inform public health policy, we
- 29 propose the adoption of a locally rooted terminology that distinguishes "Non-infectious MBASU (NIM)" from
- 30 "Infectious MBASU (IM)", emphasizing a necessary semantic and conceptual shift.

#### 2 Introduction

- 32 Chronic venous insufficiency (CVI) constitutes a significant global health burden, affecting a substantial
- 33 proportion of the worldwide population. According to the Vein Consult Program, a study involving over 91,000
- 34 adults from 23 countries, the overall prevalence of chronic venous disease (CVD) was estimated at 83.6%.
- 35 Among these, 32.3% of patients exhibited signs consistent with CVI, defined as CEAP clinical classes C3
- through C6. (1) 36

- 37 In sub-Saharan Africa, and particularly within the Democratic Republic of Congo (DRC), the presentation of
- 38 CVI is characterized by unique social, epidemiological, and clinical specificities, distinguishing it from
- 39 manifestations observed in other global regions. Several contributing factors underpin these regional
- 40 distinctions.
- 41 Demographic Context
- 42 Sub-Saharan Africa's demographic landscape is undergoing profound transformation. With an estimated
- 43 population of 1.2 billion in 2022, projections indicate a rise to 2.7 billion within the next half-century, thereby
- surpassing the populations of both China and India. This trajectory positions the region as the sole global area
- experiencing sustained growth in its labor market. Over this horizon, the working-age population (15-64 years)
- in sub-Saharan Africa is projected to constitute a progressively dominant share of the global total, increasing
- 47 from 12% in 2022 to an estimated 22% by 2050 and 30% by 2075. (2)
- 48 Habitat
- 49 African megacities are currently undergoing explosive growth. For instance, Kinshasa's population tripled
- 50 between 2000 and 2024 to 20 million inhabitants, at an annual growth rate of 4.50%. (3) This urban
- 51 concentration shapes distinct epidemiological profiles related to etiologies s.a. veinous insufficiency,
- 52 arteriopathy and diabetes, distinct from those observed in rural areas with a focus on infectious pathologies.
- 53 Cultural Perception
- 54 Dermatological disorders are widely perceived, even among the intellectual elite, as having a mystical
- etiology. The vernacular term "MBASU," which translates to 'malevolent sorcery' in the Democratic Republic
- of Congo, exemplifies this. The management of these conditions frequently involves traditional healers,
- 57 Indigenous practitioners, or religious leaders, who employ traditional rituals and administer ineffective or
- 58 inappropriate esoteric remedies. In this context, patients grappling with disabling sequelae often experience
- 59 profound professional, familial, and psychological difficulties.
- 60 Infectious diseases
- 61 Traditionally, infectious diseases have been a significant health challenge in many parts of Sub-Saharan
- 62 Africa, particularly in rural areas. Infectious pathologies, such as Buruli ulcer, are still widely associated with
- 63 malevolent sorcery and popularization of the subject by modern media has created collective psychosis. (4)
- 64 (5) (6) Buruli ulcer affects the trunk and all four limbs, and is predominant in adolescents living in rural
- 65 marshy regions. It is the third mycobacterial disease affecting humans, after leprosy and tuberculosis. It
- 66 frequently manifests as an initially painless nodule that can evolve into a plaque or diffuse edema on the face,
- arms, and legs. The disease can progress without pain or fever. In the absence of treatment, or sometimes
- 68 even during antibiotic therapy, the nodule, plaque, or edema can ulcerate within four weeks. In some cases,
- 69 bone involvement may occur, resulting in deformities. (7) The number of cases remains however marginal in
- 70 comparison to other wound etiologies. According to the WHO, the confirmed cases for the DRC (2025
- 71 population: 111 million) were: 74 (2023), 84 (2022), 54 (2021), and 111 (2020). (8) (9) In Kinshasa
- 72 (population: 20 million), 13 positive cases were reported over three years of observation (2016–2018). (10)
- 73 (11)
- 74 Chronic venous insufficiency

Diagnosis is often significantly delayed due to a confluence of factors. The complex interplay between coexisting endemic infectious and emerging non-communicable diseases (NCDs), coupled with the aforementioned socio-demographic challenges, collectively impairs timely and accurate etiological diagnosis, frequently resulting in severe complications such as edema, fibrosis, and active or healed ulcers at advanced stages. Furthermore, effective CVI management necessitates substantial human and material resources, which are inaccessible in regions with limited healthcare infrastructure. This includes, but is not limited to, diagnostic tools like Doppler ultrasound, advanced wound care modalities (e.g., specialized dressings, high-quality compression stockings, pressotherapy, negative pressure therapy), interventional procedures (e.g., foam sclerotherapy, endovenous radiofrequency or glue ablation).

#### Objective 3

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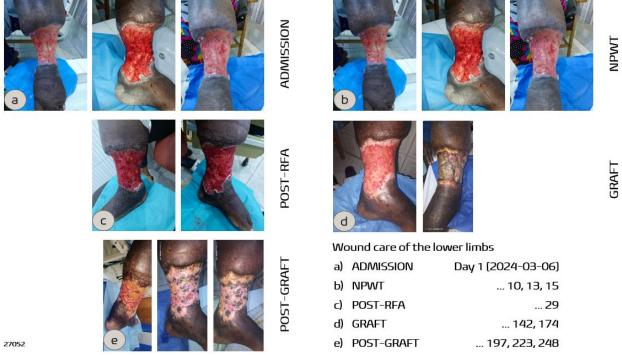
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This study addresses the well-established scarcity of clinical data and medical research on CVI in sub-Saharan Africa. (1) By providing clinical examination-based data and analysis, this research will help to objectify the necessary human, financial, and material resources and conditions required for the effective management of CVI.

#### 4 Context

This study was conducted at a hospital in Kinshasa (DRC), which provides a comprehensive care pathway for lower limb wounds. The accompanying images (Figure 1) illustrate the clinical case of a 57-year-old male with post-thrombotic syndrome and CEAP C3,6 CVI (indicating edema and active ulcer) secondary to left great and small saphenous vein incompetence. The key stages of this pathway demonstrate wound evolution and the impact of the interventions from admission through post-procedural care, including patient admission, debridement, negative pressure wound therapy (NPWT), minimally invasive radiofrequency ablation (RFA) surgery, grafting, and post-procedural care.



#### 99 5 Methods

### 100 5.1 Study Design

- 101 This retrospective observational study aims to analyze chronic venous insufficiency (CVI) in the lower limbs
- as observed in clinical practice. It is based on data collected between January 2019 and June 2024 from a
- larger cohort of patients evaluated for dermatologic conditions, locally referred to as "MBASU". Patients are
- from Kinshasa and were included in the study based on the following two criteria: (1) **Medical Criteria:**
- Patients exhibited signs and symptoms of varying severity related to diseases affecting the lower limbs. These
- 106 conditions included venous disorders, arterial diseases, diabetic complications, cancerous conditions, and
- infectious diseases. (2) **Financial Criteria:** Except for social cases, patients were financially responsible for
- the long-term costs associated with general and specialized medical consultations, as well as wound care
- tailored to their specific condition. For context, a general consultation was billed at 6 USD (2024), while
- specialized consultations ranged from 20 to 30 USD, depending on the specialty.
- 111 All patients were examined by the (lead) author using Doppler ultrasound over the specified period. Patients'
- 112 clinical severity was classified according to the Clinical, Etiological, Anatomical, Pathophysiological (CEAP)
- 113 classification system. (12) Briefly, the clinical (C) component grades severity from C0 (no visible or palpable
- signs of venous disease) to C6 (active venous ulcer). Specific clinical classes include C0: No visible or
- palpable signs of venous disease; C1: Telangiectasias or reticular veins; C2: Varicose veins; C3: Edema; C4:
- 116 Skin changes ascribed to venous disease (e.g., pigmentation, eczema, lipodermatosclerosis); C5: Healed
- venous ulcer; and C6: Active venous ulcer.
- 118 The distinction was made between CVD (chronic venous insufficiency; classes C0-C6) and CVI (chronic
- venous insufficiency; classes C3-C6). Disease severity was defined as either mild (C0 to C2: no visible signs
- to varicose veins) or severe (C3 to C6: edema to active venous ulceration), thus corresponding to CVI. The
- 121 CEAP class was assigned per patient based on the highest class of clinical signs identified in either of the
- lower limbs. For analyses of limb laterality, the highest CEAP value was determined for each limb, and these
- 123 paired values were compared within patients. To conduct a systematic bilateral limb assessment, we
- supplemented the CEAP classes with a 'Not Affected' (NA) grade for cases where only one limb was affected.

#### 125 5.2 Statistical Analysis

- 126 **1. Etiology:** Clinical data characterizing the etiology of dermatological conditions were retrospectively
- 127 collected from patient medical records over the period. Upon analysis, venous disease emerged as the most
- 128 prevalent cause, prompting a more detailed examination of the following variables: patient sex, age, disease
- severity. CEAP (Clinical, Etiological, Anatomical, Pathophysiological) classes were further regrouped by
- patient age, sex, and limb laterality (right vs. left).
- 131 **2. Patient sex**: The distribution was analyzed using the chisquare goodness of fit. Ratios and effect sizes were
- 132 computed.
- 133 **3,4,5. Patient age:** Descriptive statistics of age distribution, including the median, Median Absolute Deviation
- 134 (MAD), and Interquartile Range (IOR), were evaluated using bootstrap resampling methods. Normality of the
- distributions was assessed separately by sex, bilaterality, and laterality using the Shapiro-Wilk test.
- 136 Comparisons between groups were performed using non-parametric tests, including the Mann-Whitney U

- 137 test and the Kolmogorov-Smirnov test. The Fligner–Killeen test was used to assess differences in age
- dispersion. Normalized cumulative distribution functions were used to evaluate differences in age-related
- 139 consultation patterns between male and female patients.
- **6. Disease Severity**: The association between disease severity (C0–C2 vs. C3–C6) and sex was assessed
- using the Fisher's exact test. Additionally, the overall sex distribution (male vs. female) was evaluated against
- 142 a 50:50 ratio using the binomial test. Relative risks were calculated to quantify associations related to
- disease severity and sex.
- 7. CEAP classes by sex: Sex-related CEAP association analyses included a chi-square test of independence,
- identification of significant adjusted residuals, and quantification of associations using Cramér's V.
- 146 Considering the ordinal nature of CEAP stages, we compared sex distributions using the Mann-Whitney U
- 147 test. Additionally, we evaluated each CEAP class stratum using Chi-Squared or Fisher's exact tests ("in
- 148 class"/ "not in class" vs. sex), a two-proportion z-test to compare male and female frequencies across their
- respective distributions, and a binomial test for deviation from an equal split. We assessed risk ratios and
- their 95% confidence intervals. Finally, we used ordinal logistic regression to model CEAP class as a function
- 151 of sex.
- **8. CEAP classes by age**: The association between CEAP classes and age, treated as a continuous variable,
- 153 was evaluated using correlation analyses, including Spearman's rank correlation coefficient and Kendall's
- tau-b. Asymmetric association patterns were assessed using Goodman-Kruskal gamma and Somers' D.
- Additionally, Theil's uncertainty coefficients were used to quantify the predictive association between the
- variables. Finally, we used ordinal logistic regression to model CEAP class as a function of age.
- **9. CEAP classes by laterality**: Laterality-related CEAP evaluations utilized paired statistical methods,
- 158 including the Stuart-Maxwell and Bowker tests for assessing overall marginal homogeneity and symmetry, the
- 159 Wilcoxon signed-rank test, and the McNemar test for evaluating marginal homogeneity within CEAP
- 160 categories. Disease patterns were further characterized using cross-tabulations of paired limb-specific CEAP
- 161 classifications.
- 162 10. CEAP classes by sex, age, laterality as predictors (using CLMM, CLM, ordinal GEE, binary GEE): To
- 163 evaluate how age, sex, and limb side predict clinical signs, we fitted several ordinal logistic regression
- models: (1) A Cumulative Link Mixed Model (CLMM) with random intercepts for patient ID to account for
- within-subject correlation due to multiple limbs per patient; (2) A Cumulative Link Model (CLM) with fixed
- effects to simplify inference on covariates such as age, sex, and limb side; and (3) The ordinal variant of the
- 167 Generalized Estimating Equations (GEE) model for analyzing population-averaged effects while accounting
- 168 for within-cluster correlation. For a CEAP stratum-wise regression analysis, the binary GEE model variant was
- employed. To account for cases of unilateral limb disease, the CEAP classification was supplemented with
- the 'NA' (Not Affected) class.
- 171 **11. CEAP analysis subject to multiple testing adjustments**: These consisted of applying Bonferroni and
- 172 False Discovery Rate (FDR) corrections for statistical tests iterating through the 7 CEAP classes,
- 173 supplemented with the 'NA' value.
- 174 **12. Patient treatment**: A basic summary report was produced.

## 175 5.3 Tools

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All analyses were performed using statistical libraries either in Python 3.11 or R 4.5.1. Statistical significance was assessed at a threshold of p < .05, and confidence intervals (CIs) were calculated at the 95% level, using the Wilson method by default. Bootstrap resampling was conducted with a default of 10,000 iterations. For multiple testing correction in the context of iterative CEAP analyses, the nominal p-value of .05 was adjusted to a Bonferroni-corrected threshold of .00625 (.05/8), and to .01875 (.05/8 $^{*}$ 3) using the False Discovery Rate (FDR) method.

### 182 6 Results

#### 183 6.1 Tables

Table 1	Etiology of dermatologic disorder in lower limbs								
	Pathology	%	Patients						
	Venous	81%	393						
	Arterial	5%	26						
	Mixed	2%	8						
	Diabetic	9%	45						
	Cancerous	3%	14						
	Total		486						

Table 2	Age by sex	(patient-l	evel)								
		10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Tota
	M	3	7	12	27	43	39	31	6	0	168
	F	2	8	25	35	49	53	41	11	1	225
	Total	5	15	37	62	92	92	72	17	1	393
Table 3	Age by bila	aterality (p	atient-le	vel)							
		10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Tota
	U	3	6	8	25	24	18	18	8	0	110
	В	2	9	29	37	68	74	54	9	1	283
	Total	5	15	37	62	92	92	72	17	1	393
Table 4	Age by late	el)									
		10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Tota
	R	0	5	1	9	7	10	8	3	0	43
	L	3	1	7	16	17	8	10	5	0	67
	Total	3	6	8	25	24	18	18	8	0	110
Table 5	Disease S	everity (pa	tient-lev	el)							
	Sex	Severity									
		C0C2	C3C6	Total							
	M	12	156	168							
	F	19	206	225							
	Total	31	362	393							

Table	e 6.1	CEAP	clas	ses by	sex (p	atien	t-leve	l)								
		Sex	(	CEAP												
				C0	(	21	C2	С	3	C4	C5	5	C6	Total		
		М		0		3	9	3	5	20	13	3	88	168		
		F		1		3	15	6	9	31	19	)	87	225		
		Tota	ι	1		6	24	10		51	32		175	393		
				_												
Table	e 6.2	CEAP	class	es by s	ex, cu	mulat	ive pe	rcenta	ages (	patien	t-leve	l)				
		Sex		CEAP												
				C0	C	21	C2	С	3	C4	C5	5	C6			
		М		100.0	100	.0	98.2	92.	9	72.0	60.1	L 5	2.4			
		F		100.0	99	.6	98.2	91.	6 (	60.9	47.1	1 3	8.7			
		Tota	l	100.0	99	.7	98.2	92.	1 (	65.6	52.7	7 4	4.5			
Table 7	CEAP	classes b	y age (	patient-le	vel)											
Age	CEAP															
		C0		C1	C	2	C	3	C	4	C	5	(	6	Tot	al
	abs	pct	abs	pct	abs	pct	abs	pct	abs	pct	abs	pct	abs	pct	abs	pct
10-19	(	0.0	(	0.0	0	0.0	3	3.0	0	0.0	1	1.0	1	1.0	5	5.0
20-29	(	0.0	1	1.0	1	1.0	4	4.0	3	3.0	0	0.0	6	6.0	15	15.0
30-39		0.0	(	0.0	4	4.0	9	9.0	4	4.0	1	1.0	19	19.0	37	37.0
40-49		0.0	1	1.0	3	3.0	15	15.0	8	8.0	5	5.0	30	30.0	62	62.0
50-59	(	0.0	(	0.0	5	5.0	29	29.0	6	6.0	7	7.0	45	45.0	92	92.0
60-69	:	1 1.0	:	1.0	9	9.0	20	20.0	21	21.0	10	10.0	30	30.0	92	92.0
70-79		0.0	;	3.0	2	2.0	20	20.0	7	7.0	7	7.0	33	33.0	72	72.0
80-89		0.0	(	0.0	0	0.0	4	4.0	2	2.0	1	1.0	10	10.0	17	17.0
90-99		0.0	(	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	1.0	1	1.0
Total		1 0.3	(	3 1.5	24	6.1	104	26.5	51	13.0	32	8.1	175	44.5	393	100.0

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	Limb	CEAP								
		NA	C0	C1	C2	C3	C4	C5	C6	Total
	R	67	4	10	66	98	41	24	83	39
	L	43	3	9	48	101	47	29	113	39
	Total	110	7	19	114	199	88	53	196	78
Table 8.2	CEAP clas	sses by lat	erality, cı	umulative	e percent	tages (lin	nb-level)			
	Limb	CEAP								
		NA	C0	C1	C2	C3	C4	C5	C6	
	R	100.0	83.0	81.9	79.4	62.6	37.7	27.2	21.1	
	L	100.0	89.1	88.3	86.0	73.8	48.1	36.1	28.8	
	Total	100.0	86.0	85.1	82.7	68.2	42.9	31.7	24.9	
Table 9	CEAP cla	ass pairs l	oy latera							
	ceap_R	ceap_L								
		NA	C0	C1	C2	C3	C4	C5	C6	Tota
	C6	21	1	0	17	11	4	8	21	8
	C5	0	0	1	2	2	6	6	7	2
	C4	3	1	2	2	6	21	1	5	4
	C3	13	0	2	7	60	7	2	7	9
	C2	3	1	0	17	8	2	4	31	6
	C1	2	0	3	0	0	1	1	3	1
	C0	1	0	0	1	0	1	0	1	
	NA	0	0	1	2	14	5	7	38	6
	Total	43	3	9	48	101	47	29	113	39

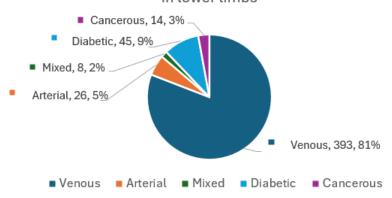
Table 10	CEAP class pairs b	v latarality	by say /li	mb level				
Table 10				mb-level,			_	
	Disease schema	Pattern	All		Males		Females	
	Bilateral symmetric	Diagonal	128	33%	42	25%	86	38%
	Bilateral C6 right	C6_right	41	10%	18	11%	23	10%
	Bilateral C6 left	C6_left	54	14%	26	15%	28	12%
	Unilateral left	NA_right	67	17%	34	20%	33	15%
	Unilateral right	NA_left	43	11%	21	13%	22	10%
	Remainder	Other	60	15%	27	16%	33	15%
		Total	393	100%	168	100%	225	100%

Table 11	CEAP clas	s by sex, age	, laterality								
	Logistic re	gression wi	thout limb clust	tering (CLM)							
	Variable	Estimate	Std. Error	zvalue	Pr(> z )	Estimate	OR	Lower 95%CI	Upper 95%CI		
	age	0.007	0.004	1.573	0.116	0.007	1.007	0.998	1.015		
	sexM	0.010	0.129	0.075	0.940	0.01	1.01	0.784	1.3		
	lateralityR	-0.452	0.127	-3.557	0.000	-0.452	0.637	0.496	0.816		
	NA C0	-1.688	0.269	-6.283	The right li	mb has 36.	3% lower odds o	of being in a hig	sher CEAP clas		
	C0 C1	-1.615	0.268	-6.035	compared	to the left l	imb (OR=0.637;	95% CI: 0.50-	0.82; p<0.001		
	C1 C2	-1.435	0.266	-5.404	This difference is statistically significant.						
	C2 C3	-0.623	0.260	-2.396							
	C3 C4	0.445	0.260	1.709							
	C4 C5	0.933	0.262	3.558							
	C5 C6	1.270	0.264	4.810							
	McFadden	pseudo R <sup>2</sup>	0.0055								

## 191 6.2 Figures

## 192 Figure 2

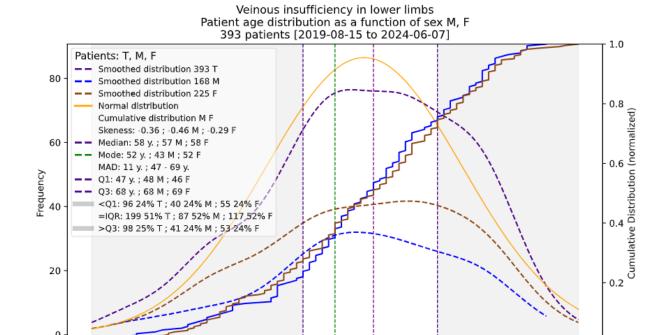
## Etiology of dermatologic disorder in lower limbs



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### 194 Figure 3



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Age

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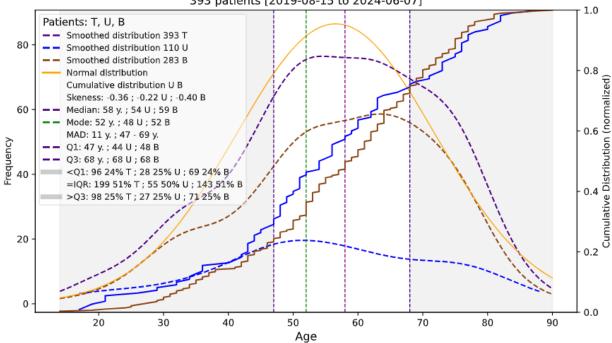
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196 Figure 4

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#### Veinous insufficiency in lower limbs Patient age distribution as a function of bilaterality U, B 393 patients [2019-08-15 to 2024-06-07]

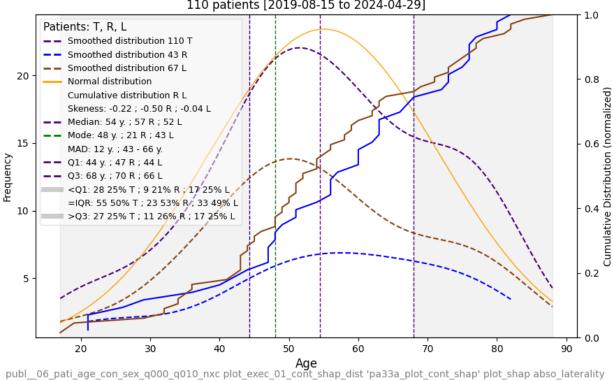


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#### 198 Figure 5

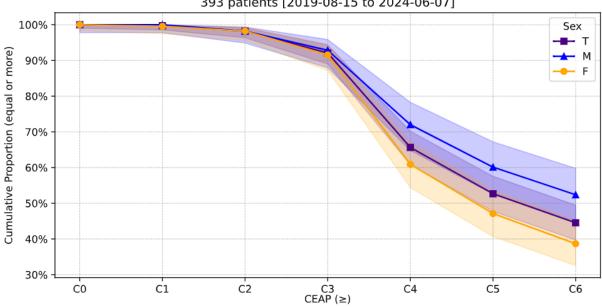
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#### Veinous insufficiency in lower limbs Patient age distribution as a function of laterality R, L 110 patients [2019-08-15 to 2024-04-29]



## 200 Figure 6

# Veinous insufficiency in lower limbs Patient CEAP by sex (with Wilson CI) [Cumulative distribution proportions] 393 patients [2019-08-15 to 2024-06-07]



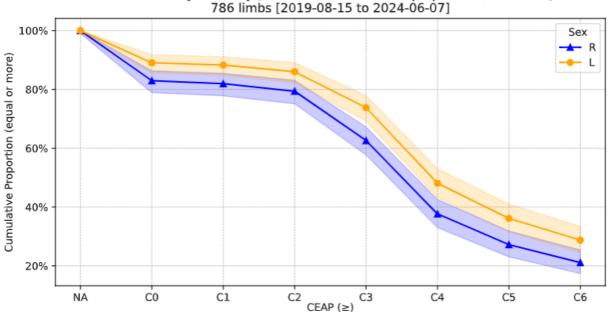
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## 202 Figure 7

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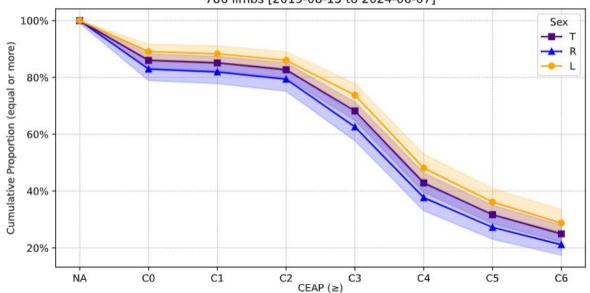
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# Veinous insufficiency in lower limbs Limb CEAP by laterality [Cumulative distribution proportions, Wilson CI] 786 limbs [2019-08-15 to 2024-06-07]



eap sex 99 age bin sex g000 g045 nx2 plot exec 02 dist cumu pa37a plot dist cumu plot limb more than abso R L

## Veinous insufficiency in lower limbs Limb CEAP by laterality [Cumulative distribution proportions, Wilson CI] 786 limbs [2019-08-15 to 2024-06-07]

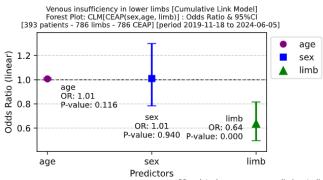


204 11 ceap sex 99 age bin sex g000 g045 nx2 plot exec 02 dist cumu 'pa37a plot dist cumu' plot limb more than abso

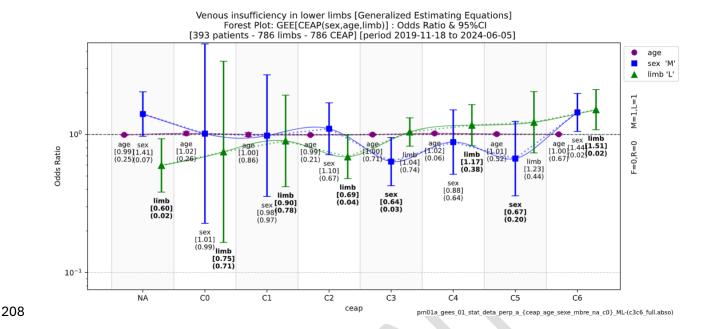
### 205 Figure 8

Figure 9

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Predictors
pa33a plot clm ceap age sex limb rstudio



#### 6.3 Presentation

#### 6.3.1 Etiology (table 1, figure 2)

The venous cohort, consisting of 393 patients, was drawn from a population of 486 patients who were examined for disorders in their lower limbs. **Pathologies of venous vascular (80%)**, arterial (6%), mixed (2%), as well as diabetic without venous involvement (10%), and cancerous (3%) origin were diagnosed. No infectious causes were identified.

#### 6.3.2 Patient sex (table 5)

The cohort comprised 168 men (42.7%) and 225 women (57.3%), resulting in a female-to-male ratio of 1.34:1. A chi-square goodness-of-fit test indicated a significant deviation from an equal distribution ( $\chi^2 = 8.27$ , p = .004). The effect size was small (Cohen's h = 0.146).

#### 6.3.3 Patient age by sex (table 2, figure 3)

The continuous age distributions of male and female patients were closely aligned. Both groups had nearly identical median ages, with men at 57 years and women at 58 years. Women showed only slightly greater variability in age (MAD = 12 years) compared to men (MAD = 10 years). The confidence intervals for the median, Median Absolute Deviation (MAD), and Interquartile Range (IQR) largely overlapped, indicating strong similarities between the two groups. Non-normal distributions were confirmed for both sexes using the Shapiro-Wilk test (p < 0.01). The Mann-Whitney U test (U = 18,729, p = .878, rank-biserial correlation = -0.005, 95% CI [-0.108, 0.124]) revealed no significant difference in the ranking of ages between the sexes, while the Kolmogorov-Smirnov test (D = 0.052, p = .938) found no significant difference in their overall age distributions. Fligner–Killeen test found no significant difference in age dispersion ( $\chi^2$  = 1.050, p = .305). Levene and Ansari–Bradley tests confirmed this result. **Beyond these similarities**, the absolute frequency of female patients exceeded that of male patients across all ages. More subtle, yet notable, differences existed between the age distributions. Regarding kurtosis, females exhibited a more pronounced platykurtic value (-

- 233 0.57 vs. -0.21), meaning their age distribution was more spread out and less peaked compared to that of
- males. In terms of skewness, males exhibited slightly higher negative skewness (-0.46 vs. -0.29), indicating a
- 235 greater relative concentration of older individuals among male patients. The normalized cumulative
- distribution functions revealed that women tended to consult at an earlier age compared to men, with
- notable peaks of divergence at 46 years for women and 64 years for men. The crossover point, where
- cumulative consultation rates between women and men equalize, occurred at 55 years.

#### 239 6.3.4 Patient age by bilaterality (table 3, figure 4)

- The continuous age distributions of patients with unilateral and bilateral disease were generally aligned.
- The median age was slightly lower in unilateral cases (54 years) compared to bilateral cases (59 years). Age
- variability was marginally greater in the unilateral group (MAD = 12 years) than in the bilateral group (MAD =
- 243 10 years). The confidence intervals for the median, Median Absolute Deviation (MAD), and Interquartile Range
- 244 (IOR) largely overlapped, indicating strong similarities between the two groups. The Shapiro-Wilk test
- confirmed a non-normal distribution for the bilateral group and marginally rejected the normality hypothesis
- for the unilateral group (p = 0.067). The Mann-Whitney U test (U = 14,337, p = .225, rank-biserial correlation =
- 247 –0.039, 95% CI [-0.050, 0.208]) revealed no significant difference and the Kolmogorov-Smirnov test (D =
- 248 0.127, p = .138) both supported the conclusion that unilateral and bilateral patients were age-matched.
- Fligner-Killeen test found no significant difference in age dispersion ( $\chi^2 = 2.123$ , p = .145). Levene and Ansari-
- 250 Bradley tests confirmed this result. **Beyond these similarities**, the absolute frequency of bilateral patients
- exceeded that of unilateral patients across all ages. Subtle, yet notable, differences existed between the age
- distributions. Regarding kurtosis, unilateral cases exhibited a more pronounced platykurtic value (-0.52)
- compared to bilateral cases (-0.42). In terms of skewness, bilateral cases showed a higher negative skewness
- 254 (-0.40) compared to unilateral cases (-0.22). The normalized cumulative distribution functions indicated that
- 255 patients tended to present with unilateral cases earlier than bilateral cases up to age 70, after which the
- trend reverses. There were notable peaks of divergence at 52 years for unilateral cases and at 75 years for
- 257 bilateral cases.

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#### 6.3.5 Patient age by laterality (table 4, figure 5)

- 259 The continuous age distributions of unilateral patients with either right- or left-sided disease were closely
- aligned. Median ages were 57 years for right-sided and 52 years for left-sided cases. Variability in age was
- comparable between groups, with a median absolute deviation (MAD) of 10 years in both. The confidence
- intervals for the median, MAD, and interquartile range (IQR) exhibited substantial overlap, suggesting
- 263 significant similarities between the two cohorts. The Shapiro-Wilk test indicated a non-normal distribution for
- the left-sided presentation and a near-normal one for the right-sided presentation (p = .053). The Mann-
- 265 Whitney U test (U = 1,578, p = .399, rank-biserial correlation = 0.048, 95% CI [-0.312, 0.130]) and the
- 266 Kolmogorov-Smirnov test (D = 0.149, p = .547) confirmed age distributions were not significantly different.
- Fligner-Killeen test found no significant difference in age dispersion ( $\chi^2 = 0.045$ , p = .832). Levene and Ansari-
- 268 Bradley tests confirmed this result. **Beyond these similarities**, the absolute frequency of left-sided cases
- 269 exceeded that of right-sided cases across all ages. Subtle yet notable differences were also observed in their
- age distributions. In terms of skewness, right-sided cases demonstrated a more pronounced age distribution
- skewed toward younger patients, with a higher degree of negative skewness (-0. 50) compared to left-sided
- 272 cases (-0.04). However, the overall shape of the distributions was similar, as reflected by comparable
- kurtosis values for the right (-0.48) and left limb sides (-0.46). Normalized cumulative distribution functions
- further revealed a consistently higher cumulative proportion of younger patients with left-sided disease
- between ages 29 and 75, with the greatest divergence occurring around age 56.

- 276 6.3.6 Disease severity (table 5)
- 277 Among the 393 patients assessed, the majority (n = 362; 92.1%) presented with severe disease (CVI, C3–C6),
- while only 31 patients had mild disease (C0–C2). Of those with CVI, 156 (43%) were male and 206 (57%) were
- 279 female. Within the mild disease group, 12 (39%) were male and 19 (61%) were female. There was **no**
- 280 statistically significant association between sex and disease severity (Fisher's exact test odds ratio =
- 281 0.834, p = .708). The risk of severe disease was slightly lower in males than females, with a risk ratio of 0.85
- 282 (95% CI [0.42, 1.69]). The magnitude of association was negligible (Cramer's V = 0.014), indicating no
- 283 meaningful sex-based difference in disease severity. Additionally, exact binomial tests performed separately
- 284 within severity groups revealed a statistically significant overrepresentation of females in the severe
- 285 **disease category** (statistic = 0.569, p = .010).
- 286 6.3.7 CEAP classes by sex (tables 6.1, 6.2, figure 6)
- A descriptive analysis revealed a bimodal distribution of CEAP stages, with peaks at C3 (edema; 104
- patients, 26.5%) and C6 (active ulcers; 175 patients, 44.5%). Together, these two stages accounted for 71%
- of the total study population.
- 290 Male patients presented with 20.8% of cases at the C3 stage and 52.4% at the C6 stage, whereas female
- patients presented with 30.7% of cases at C3 and 38.7% at C6. These findings were further supported by a
- 292 high median CEAP stage of C6 (MAD = 0.0) among males, indicating strong clustering at the most severe
- class. In contrast, females showed a lower median severity (C4) and slightly greater variability (MAD = 1.0),
- reflecting the combined weight of cases at both C3 and C6. Overall dispersion of CEAP stages was modest in
- both groups, with an interquartile range (IQR) of 3.0. The most frequent stage (mode) was C6 in both sexes.
- 296 A distribution-wide analysis revealed the following findings. A chi-square test of independence indicated no
- 297 statistically significant association between sex and CEAP classification when categories were treated
- nominally ( $\chi^2 = 9.042$ , p = .171). The effect size, measured by Cramér's V (0.152), suggests a small
- association. Examination of the adjusted residuals showed that females had a significantly higher-than-
- 300 expected frequency in CEAP class C3 (adjusted residual = 2.19), whereas males exhibited a notable excess in
- 301 C6 cases (adjusted residual = 2.71). However, since the overall chi-square test was not statistically
- 302 significant, these findings should be interpreted with caution.
- 303 A Mann–Whitney U test showed a statistically significant difference in CEAP grades favoring higher values
- among male patients (U = 21,696; p = .008), corresponding to a 14.79% shift from the median. The rank-
- 305 biserial correlation indicated a small effect size (r = 0.127). Furthermore, the common language effect size
- 306 (Vargha–Delaney A) revealed that a randomly selected male patient had a 57.4% probability (95% CI: 0.521–
- 307 0.627) of having a higher CEAP grade than a randomly selected female patient.
- 308 **Stratum-wise analysis** of the CEAP distributions reinforced the observations from the descriptive
- analysis. For CEAP categories C0, C1, C2, C4, and C5, no significant sex differences were identified across
- any of the statistical tests, indicating proportional sex representation within these categories and relative to
- 311 the overall population. However, significant differences emerged in the C3 and C6 strata.
- 312 In the C3 category, 69 of 225 females (30.7%) were affected, compared to 35 of 168 males (20.8%). This
- difference was statistically significant, as demonstrated by several tests: the chi-square test ( $\chi^2$  = 4.287, p =
- 314 .038; Cohen's w = 0.104, indicating a small effect size), the two-proportion z-test (z = -2.186, p = .029; 95%

- 315 CI: -0.180 to -0.010), and the binomial test (p = .001). The risk ratio for females compared to males was 1.47
- 316 (95% CI: 1.03–2.10), indicating a 47% higher likelihood of C3 classification among female patients.
- In the C6 category, 88 of 168 males (52.4%) were affected, compared to 87 of 225 females (38.7%). This
- 318 difference was statistically significant, as shown by the chi-square test ( $\chi^2 = 6.779$ , p = .009; Cohen's w =
- 319 0.131, small effect size) and the two-proportion z-test (z = 2.706, p = .007; 95% CI: 0.038 to 0.234). The risk
- ratio for males versus females was 1.36 (95% CI: 1.09–1.69), indicating a 36% higher likelihood of C6
- 321 **classification among males**. However, the absolute counts were nearly equal, and the binomial test was not
- 322 significant (p = 1.0).
- 323 Finally, **ordinal logistic regression** results by threshold were not retained due to violation of the proportional
- odds assumption, indicating that the effect of sex on CEAP severity differs across CEAP stages.
- 325 6.3.8 CEAP classes by age (table 7)
- 326 Descriptive analysis using 10-year age bins revealed that patients categorized in classes C3 through C6
- were predominantly concentrated within a narrow age range, specifically in their 50s and 60s. Among
- 328 these, male patients had a median age of 57 years (MAD = 10), while female patients had a slightly higher
- 329 median age of 58 years (MAD = 12), indicating similar central tendencies but modestly greater age variability
- among females. Within the 30 to 79-year age range, female C3 cases peaked in the 50–59 age bin, while their
- 331 C6 cases showed a steady increase across the age groups. Conversely, male C3 cases increased steadily
- with age, and their C6 cases peaked in the 50–59 age bin.
- 333 **CEAP and continuous age demonstrated a negligible association** across all analytical approaches. The
- absence of a **monotonic relationship** was confirmed by Spearman's rank correlation, which yielded a
- coefficient (p) of 0.011 (p = .835), and Kendall's tau, which produced a coefficient ( $\tau$ ) of 0.008 (p = .832).
- 336 **Asymmetric ordinal associations** were also absent: Somers' D for CEAP conditioned on age was 0.007 (p =
- .832), and in the reverse direction, 0.010 (p = .832). Goodman-Kruskal's gamma corroborated these findings,
- showing y = 0.010 (p = .992, SE = 1.000, Z = 0.010). **Information-theoretic association** measures based on
- Theil's entropy indicated that knowledge of age reduced uncertainty in CEAP classification by 9% (using
- continuous age, with a potential for overfitting) and by 7% (using optimally 15–20 age bins). Conversely,
- knowledge of the CEAP classification reduced uncertainty about age by 26% (continuous age) and by 4%
- 342 (binned age).
- 343 A sex-stratified analysis of CEAP-age associations yielded further nuanced insights. For females, the results
- 344 closely mirrored those of the overall cohort, showing no statistically significant relationship between age
- and CEAP classification. Spearman's p was 0.104 (p = 0.118), Kendall's  $\tau$  was 0.080 (p = 0.113), and Somers'
- D values were similarly low (CEAP | age = 0.069; age | CEAP = 0.093; both p = 0.111). Goodman-Kruskal's
- gamma was 0.094 (p = 0.924), and Theil's uncertainty coefficients were U(CEAP|age) = 0.410 and
- 348 U(age | CEAP) = 0.583, consistent with a weak, non-significant association.
- 349 By contrast, the **male subgroup** showed a slightly stronger but still non-significant negative
- association between CEAP stage and age. Spearman's  $\rho$  was -0.138 (p = 0.075), and Kendall's  $\tau$  was -0.109
- 351 (p = 0.066), suggesting a slight, non-significant trend toward lower age with increasing severity. Supporting
- this, Somers' D was negative in both directions (CEAP | age = -0.089; age | CEAP = -0.132; both p = 0.075), and
- 353 Theil's uncertainty coefficients were slightly higher (U(CEAP|age) = 0.419; U(age|CEAP) = 0.627). Goodman-
- Kruskal's gamma was –0.135 (p = 0.892), again indicating insufficient statistical evidence despite directional
- consistency. This mild inverse relationship in males was driven primarily by the disproportionately high

- frequency of C6 classification in younger male patients. Specifically, of the 168 male patients, 88 (52%) were
- 357 classified as C6, with a median age of just 54 years, which is notably younger than the median ages observed
- in males across other CEAP stages: C1 = 71 years, C2 = 57, C3 = 62, C4 = 62, and C5 = 64.
- 359 Finally, ordinal logistic regression analyses demonstrated consistent coefficient estimates for age across
- 360 CEAP categories, with no statistically significant differences at any threshold. Correspondingly, the ordinal
- 361 logistic regression model confirmed that age was not a significant predictor of disease severity (coefficient =
- 362 0.0032, p = .593), indicating no meaningful association between patient age and CEAP classification.
- 363 6.3.9 **CEAP classes by laterality** (tables 8, 9, 10, figure 7)
- 364 **Symmetry and Asymmetry Testing: (1) Contingency table analysis** of right-versus-left CEAP classes did not
- demonstrate significant overall asymmetry (Stuart-Maxwell test: p = 0.128; Bowker test: p = .226). (2)
- 366 Cumulative CEAP distributions by laterality revealed a consistent predominance of higher severity on the left
- side, with disjoint Wilson confidence intervals observed for all CEAP grades. (3) The Wilcoxon signed-rank
- 368 **test** further confirmed this lateralization (observed statistic = 28,486.5; p = .006). This is substantially lower
- than the expected value adjusted for ties (34,582.5) and the simulated mean under equilibrium (37,642.4; SD
- = 290.7; z-score = -31.5), indicating that when a difference exists, the left limb is more often and more
- 371 severely affected.
- 372 **Subgroup and Class-Based Asymmetry:** McNemar's test identified specific laterality asymmetries: NA class:
- 373 Right limb only = 67, Left limb only = 43 (p = .028)); C6 class: Right limb only = 62, Left limb only = 92 (p =
- 374 .019); C2 class: Right limb only = 49, Left limb only = 31 (p = .057; marginal significance); on sex stratification,
- 375 the C6 class among males showed significant asymmetry (right limb only = 30, left limb only = 49; p = .043).
- 376 A cross-tabulation of limb-related paired CEAP classifications was conducted to characterize the patterns
- of CVD among patients, comparing left and right lower limb findings per individual: (1) Symmetric Disease:
- 33% of patients exhibited identical CEAP classes in both lower limbs; (2) Asymmetric Bilateral C6
- 379 **Involvement**: C6 grade involvement was found asymmetrically, affecting 14% of patients on the left side and
- 380 10% on the right side; (3) Unilateral Involvement: 17% of patients demonstrated unilateral disease in the left
- 381 limb, while 11% were affected unilaterally on the right limb; (4) Other Patterns: The remaining 15% of
- 382 patients had CEAP pairings distributed across other combinations. Stratified by sex, females demonstrated a
- 383 higher rate of bilateral concordance (38%) compared to males (25%).
- 384 6.3.10 CEAP classes by sex, age, laterality as predictors (table 11, figures 8, 9)
- In our evaluation of the association between CEAP classes and patient characteristics a Cumulative Link
- 386 Mixed Model (CLMM) was applied using the formula ceap ~ sex + age + laterality + (1 | patient). This model
- revealed negligible variance for the random effect, resulting in numerical instability.
- 388 Subsequently, a Cumulative Link Model (CLM) was employed, yielding stable parameter estimates and
- 389 standard errors, particularly highlighting improved stability compared to the univariate test for sex. The
- analysis indicated that only laterality, and not age or sex, was a significant predictor for CEAP classes.
- 391 Specifically, patients with right limb involvement exhibited 36.3% lower odds of being classified into higher
- 392 CEAP class compared to those with left limb involvement (OR=0.637; 95% CI: 0.50–0.82; p<0.001). The
- overall model fit, as measured by McFadden's pseudo R<sup>2</sup>, was negligible at 0.55%. Furthermore, relaxing the
- 394 proportional odds assumption for each predictor did not improve the model fit, since the AIC value remained
- 395 stable.

- Finally, stratum-wise CEAP binary GEE analysis revealed the following predictor effects: (1) Age: is not
- significantly associated with any outcome of CEAP; (2) Sex: males have a 36% lower odds (OR = 0.636,
- 0.425-0.950, p = .027) of presenting with C3 disease than women as well as a 44% higher odds (OR = 1.443,
- 399 1.051–1.982, p = .023) of having CEAP class C6 compared to women (3) Laterality: left limb is associated with
- 400 a 40% reduction in odds of having venous disease (NA) compared to the right limb (OR = 0.596, 0.382–0.931,
- 401 p = .023), a 31% reduction in odds of having CEAP class C2 (OR = 0.689, 0.479–0.991, p = .045) and a 51%
- 402 increase in odds of having CEAP class C6 (OR = 1.511, 1.081–2.112, p = .016).
- 403 6.3.11 CEAP analysis subject to multiple testing adjustments
- 404 Across all iterative, stratum-based CEAP class analyses, we examined associations between clinical sign
- class and the variables sex, age, and laterality. After applying Bonferroni or False Discovery Rate (FDR)
- 406 corrections, no results remained statistically significant. The only borderline findings were observed for limb
- 407 laterality in the NA (p = .113), C2 (p = .153), and C6 (p = .113) classes, where p-values approached
- 408 significance using the FDR method.
- 409 6.3.12 Patient treatment
- 410 All patients benefited from nursing care, tailored to their follow-up compliance and financial capacity. Where
- 411 appropriate, our procedures included the use of compression stockings and advanced wound-healing
- 412 techniques, such as specialized dressings and negative pressure wound therapy. Radiofrequency ablation
- 413 (RFA) surgery was performed on 90 out of the 362 severely diseased patients (25%). Additionally, two patients
- 414 underwent further treatment for recurrence involving the small saphenous veins.
- 415 7 Key Findings
- **1. Etiology:** Our analysis of a cohort of 486 patients presenting with lower limb dermatologic disorders upon
- 417 clinical examination revealed a high prevalence (80%) of vascular venous etiology.
- 418 2. Patient sex: The cohort of 393 venous patients included 225 females and 168 males, resulting in a female-
- 419 to-male sex ratio of 1.34:1. This highlights a higher burden of chronic venous disease (CVD) among women in
- 420 this population, consistent with trends reported in other studies, such as the Bonn study. (13)
- 421 **3. Patient age by sex**: Although the overall age distribution was broadly similar between sexes, females
- 422 tended to present at younger ages (below 55 years, with the greatest divergence around 46 years), whereas
- 423 males predominated among older patients (above 55 years, with the greatest divergence around 64 years).
- 424 **4. Patient age by bilaterality**: Although bilateral involvement was more frequent overall, it became
- increasingly common after age 70. Notable peaks of divergence were observed around age 52 for unilateral
- 426 cases and around age 75 for bilateral cases.
- **5. Patient age by laterality**: Left-sided cases were consistently more frequent than right-sided cases across
- all ages and represented a higher proportion than unilateral cases up to age 70.
- 429 **6. Disease severity**: The findings underscored the high burden of CVI in this population, with patient-level
- 430 grades C3 to C6 accounting for 92% of cases. Females were significantly overrepresented in the severe
- 431 disease category.

- **7. CEAP classes by sex**: Although the overall distribution of CEAP classes was broadly similar between sexes,
- 433 males were more likely to present with advanced ulcerative disease (C6), whereas females were more evenly
- distributed between the C3 (edema) and C6 stages.
- 435 **8. CEAP classes by age:** This cohort exhibited a negligible association between CEAP class and patient age.
- Female age distribution closely mirrored that of the overall cohort. However, among males, a slight negative
- association between age and clinical severity was observed, driven by their overrepresentation in the C6
- 438 stage, which was associated with a younger median age (54 years) compared to males in other CEAP classes.
- 439 9. CEAP classes by laterality: Limb-level analysis of CEAP classes demonstrated a consistent predominance
- of higher disease severity on the left side. In addition, the study revealed streamlined disease patterns in 85%
- of cases. Symmetrical limb severity was observed in 33% of cases. Among patients exhibiting asymmetrical
- presentations (52% of cases), there was a marked predominance and greater severity of chronic venous
- disease in the left lower limb (31% versus 21% for the right). When stratified by sex, a higher proportion of
- females exhibited bilateral concordance (38%) compared to males (25%).
- 10. CEAP classes by sex, age, laterality as predictors: Logistic regression methods contextualized the
  - individual results produced by classical analysis using univariate assessments. Age showed no significant
- 447 association with CEAP disease severity in this cohort. The effect of sex varied by CEAP grade: males were
- overrepresented in unilateral cases (NA), underrepresented in moderate disease (C3), and overrepresented
- in severe disease (C6). Laterality emerged as a consistent predictor of CEAP severity, with a shift in
- 450 preponderance from the right limb in unilateral cases toward the left limb in severe cases (C6). Although
- 451 statistically significant associations exist, the models explained only a small proportion of the variance in
- 452 disease severity.

- 453 **11. CEAP analysis subject to multiple testing adjustments**: Stratified analyses examining the associations
- between individual CEAP classes and the variables age, sex, and laterality did not retain statistical
- significance after applying False Discovery Rate (FDR) correction for multiple comparisons. However, in the
- 456 McNemar test evaluating paired limb laterality, the associations for the NA, C2, and C6 classes approached
- 457 significance under the FDR-adjusted threshold.
- 458 **12. Patient treatment:** Only 25% patient underwent radiofrequency ablation (RFA).
- 459 8 Discussion
- 460 8.1 Etiology
- In the original cohort of 486 patients presenting with chronic lower limb ulcers or other severe dermatologic
- 462 conditions, no infectious etiology was formally identified through laboratory testing. While this represents a
- 463 potential limitation, several consistent clinical and contextual factors strongly support the non-infectious
- 464 nature of these conditions:
- Anatomical and Clinical Schemas: All patients exhibit dermatologic manifestations confined to the
- 466 lower limbs. This distribution aligns with chronic vascular or diabetic pathologies, differing markedly from
- the more disseminated or anatomically distinct presentations typically observed in infectious diseases
- 468 such as Buruli ulcer.

- Clinical Diagnosis: Each patient has been examined by the author, enabling an evidence-based clinical diagnosis supported by duplex Doppler ultrasonography to evaluate chronic venous insufficiency.
- **Socioeconomic Constraints:** Laboratory investigations require out-of-pocket payment by patients, limiting access to outsourced and costly complementary testing.
- **Demographic Characteristics:** Patients range from 20 to 80 years old, with a median age skewed toward older adults, an age profile inconsistent with infectious diseases like Buruli ulcer, which predominantly affect adolescents. Additionally, all participants are residents of Kinshasa, an urban area where infectious dermatoses, particularly mycobacterial infections, are rare. For example, reported Buruli ulcer cases in Kinshasa number 13 from 2016 to 2018, compared to 74 cases across the entire DRC in 2023. (9) (10)
- Taken together, these clinical, demographic, and contextual factors substantially reduce the likelihood—and arguably exclude—the presence of underlying infectious causes in the studied population. In this context, a preliminary analysis of this cohort leads to two primary conclusions.
- First, vascular etiology predominates (393 patients, 81% of cases) over other causes of lower limb
  dermatologic disorders in this cohort of patients. Consequently, the idea that infectious causes are a
  significant or prevalent source of skin wounds, particularly in tropical megacities, appears questionable and
  is challenged by our findings. It actually highlights the dual burden of non-communicable and infectious
  diseases that challenges healthcare systems in sub-Saharan African countries. (14) (15) Our observations
  confirm the significant role of venous pathology in lower limb dermatologic disorders, establishing it as the
  primary cause of lower limb ulcers, consistent with findings from Western populations. (16)
- Second, advanced venous disease levels within our cohort are overwhelming, with **362 patients (92% of**cases) classified in CEAP C3-C6 severity categories. These results contrast with large-scale global
  epidemiological studies, most notably the Vein Consult Program, which in 2012 reported that 24% of 70,000
  screened patients across 13 countries had progressed to CVI (CEAP stages C3–C6), with a prevalence of
  venous ulcers (healed and active) of 2.1% (1) (17)
- 494 The above observations are commonly reported in many low-income settings, where dermatological 495 conditions are often misunderstood by the general population, including educated individuals. These 496 conditions are attributed to mystical or spiritual causes, such as ancestral or familial transgressions, and 497 patients frequently consult traditional healers, spiritual leaders, or religious practitioners before seeking 498 formal medical care. These culturally embedded health-seeking behaviors, combined with a shortage of 499 trained medical personnel and limited access to affordable healthcare, contribute to delayed medical 500 consultations and, consequently, to the high prevalence of advanced CVI stages observed in this study. This 501 stands in stark contrast to trends in high-income countries, where early detection and the broad availability of 502 minimally invasive interventions have significantly slowed disease progression. (18) (19) (20)

#### 8.2 CEAP, age, sex, laterality

- Our cohort exhibits a female-to-male ratio of 1.34, which is not statistically different from the ratio of 1.28 observed in the Bonn study. (13)
- Patient age and the maximum CEAP classification in the lower limbs shows a negligible association. This finding diverges from the well-established positive correlation between age and CEAP clinical classification. It

likely reflects the specific socioeconomic context of Kinshasa, where financial constraints delay healthcare-

seeking behavior and alter the natural history of disease presentation. Our results corroborate similar

510 observations reported from other low-income settings. (21) (22) (23)

511 The tendency for women to present with venous disease at an earlier age than men with the most pronounced

512 divergence observed around age 46 can be attributed to a combination of sociocultural and biological

factors. Women are often more health-aware and place greater emphasis on body aesthetics, both of which

may lead to increased vigilance and earlier medical consultation. Additionally, well-established risk factors

for venous disease, such as hormonal fluctuations related to the menstrual cycle, pregnancy, and

516 menopause, may accelerate disease progression and prompt timelier medical evaluation. Women also tend

to present with a broader age range (from their 40s through their 70s) and exhibit a balanced distribution of

518 clinical signs (C3 to C6).

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Among men, the highest incidence occurs in those in their 50s, with the greatest age divergence compared to

women observed at age 64. Clinical sign C6 peaks at these ages, with a frequency double that seen in other

age ranges between 40 and 80. Occupational factors, such as prolonged standing or heavy lifting, may

522 accelerate progression to advanced stages. Men also traditionally bear the primary financial responsibility for

523 their families, which may motivate timely health-seeking behavior when severe disease threatens their

524 capacity to work.

525 Bilateral limb-level CEAP disease schemas explain 85% of all combination pairs, further refining our findings

by demonstrating that females are more frequently affected by symmetrical patterns, whereas males exhibit

a higher prevalence of unilateral left-sided disease. Regarding asymmetry, left-sided involvement may be

528 partly attributed to anatomical factors such as compression of the left common iliac vein (May-Thurner

529 syndrome) (24) (25). However, other contributors, such as occupational asymmetry, repetitive strain, or limb

530 dominance, may also play a role...

In summary, our cohort likely represents a delayed, cross-sectional snapshot across the age spectrum,

where the disease burden is disproportionately concentrated in severe cases. Significant trends, associated

with small effect sizes and negligible model fits, predominantly follow sex and limb-side specific patterns.

#### 9 Conclusions

With respect to Chronic Venous Insufficiency (CVI), our findings highlight a crucial opportunity to strengthen

536 health systems in the rapidly urbanizing Democratic Republic of Congo (DRC). While the rural population is

projected to grow from 50 million to 70 million, the urban population is expected to surge dramatically from

538 30 million in 2025 to 200 million by 2050. When not effectively prevented or treated, severe forms of CVI can

result in debilitating physical outcomes such as amputation, as well as profound psychological

consequences including social isolation. Although current public health frameworks, including the "WHO

Cooperation Strategy with the Democratic People's Republic of Congo 2024–2029," acknowledge the dual

burden of communicable and non-communicable diseases, there remains significant potential to enhance

these initiatives by explicitly integrating CVD (Chronic Venous Disease) prevention and CVI management in

these policies. Proactively addressing this silent epidemic, a cause of severe dermatologic complications,

would directly align with the priorities of the 78th World Health Assembly (Geneva, 2025). Its resolution, 'Skin

diseases as a global public health priority,' calls for prevention, early detection, treatment, burden reduction,

and increased awareness of skin diseases and related conditions. (26) (27) (28)

548	10 Recommendations
549 550 551 552 553 554 555 556	At the community level in Kinshasa, the term "MBASU" encompasses diverse dermatological signs, including simple erythema or papules, unsightly wounds, edema or fibrosis, and healed or active ulcers. By echoing late 20th-century views, this usage perpetuates misconceptions in public health policy, as it has traditionally been narrowly associated with infectious causes such as Buruli ulcer. Therefore, to promote clarity in language, we propose adopting the terms "Non-infectious MBASU (NIM)" and "Infectious MBASU (IM)," emphasizing a necessary semantic and conceptual shift. It is vital that vernacular terminology reflects the scientific evidence provided by this study, ensuring that collective understanding incorporates this crucial distinction.
557 558	Strategically, the importance of CVI, an eminently manageable condition with timely intervention, underscores significant opportunities for targeted healthcare investment and policy development, including:
559 560 561	<b>Funding prioritization:</b> Private and public funding should be primarily directed towards managing vascular-related conditions (direct costs) and implementing measures to alleviate the economic burden (indirect costs) of this scourge.
562 563	<b>Public Awareness Campaigns:</b> Information, awareness, screening, and prevention campaigns should be conducted, emphasizing the benefits of early detection and the treatable nature of vascular diseases.
564 565 566	<b>Hospital Assessment:</b> At initial presentation, hospitals should consider the possibility of "Non-infectious MBASU (NIM)", thereby prioritizing Chronic Venous Disease (CVD) or, in advanced stages, Chronic Venous Insufficiency (CVI) when managing lower limb ulcer wounds.
567 568	<b>Medical Education Reform:</b> Higher education curricula for medical and nursing students should incorporate the significant importance of therapies related to vascular conditions. (29)
569 570	<b>Collaborative Expertise:</b> We propose to establish shared expertise between vascular and infectious disease specialists to optimize available resources for the benefit of patient health.
571	11 Funding
572	This study is self-funded.
573	12 Conflict of interest
574	None.
575	13 Keywords
576	chronic venous insufficiency, clinical epidemiology, CEAP clinical signs, patient demography

#### 14 References 577

- 578 1. An Epidemiological Survey of Venous Disease Among General Practitioner Attendees in Different
- Geographical Regions on the Globe: The Final Results of the Vein Consult Program. Marc E. 579
- Vuylsteke, Roos Colman, Sarah Thomis, Geneviève Guillaume, Damien Van Quickenborne, Ivan 580
- **Staelens.** 9, s.l.: SAGE Journals, Angiology, Vol. 69, pp. 779-785. 581

- 582 2. Worldbank. Afrique Capital Humain Sommets des chefs d'Etat Juillet 2023. [Online]
- 583 https://thedocs.worldbank.org/en/doc/a328ed9a49f4b7fbf56d4d91093d53ac-
- 584 0010012023/original/le-temps-de-l-afrique-tirer-parti-du-dividende-d-mographique-fr.pdf.
- 585 3. World Population review. Kinshasa, DR Congo Population 2024.
- 586 https://worldpopulationreview.com/. [Online] https://worldpopulationreview.com/cities/dr-
- 587 congo/kinshasa.
- 588 4. Etude des appellations et des représentations attachées à l'infection à Mycobacterium ulcerans
- dans différents pays endémiques d'Afrique. **Kibadi, K., et al.** 3, 2007, Medecine Tropicale, Vol. 67, pp.
- 590 241-248.
- 591 5. Committee A, first report WHA 57.1 Surveillance and control of Mycobacterium ulcerans disease
- 592 (Buruli ulcer). World Health Organization. 21 May 2004. 57th plenary meeting Geneva 17-22 May
- 593 2004. p. 1.
- 6. World Health Organization. Cotonou Declaration on Buruli Ulcer 2009. [Online] 30 March 2009.
- 595 https://www.who.int/publications/i/item/WHO-HTM-NTD-GBUI-2009.1.
- 596 7. —. En République démocratique du Congo, un hôpital traque l'ulcère de Buruli. World Health
- 597 Organization Organisation Mondiale de la Santé. [Online]
- 598 https://www.afro.who.int/fr/countries/democratic-republic-of-congo/news/en-republique-
- 599 democratique-du-congo-un-hopital-traque-lulcere-de-buruli.
- 8. Worldometer, RDC. DR Congo Demographics. [Online]
- 601 https://www.worldometers.info/demographics/democratic-republic-of-the-congo-demographics.
- 602 9. World Health Organization. Number of confirmed cases of Buruli Ulcer reported. World Health
- 603 Organisation. [Online] 2024. https://www.who.int/data/gho/data/indicators/indicator-
- details/GHO/number-of-confirmed-cases-of-buruli-ulcer-reported.
- 10. Surveillance of the Buruli Ulcer in The Democratic Republic of Congo (Drc): Preliminary Results
- 606 (2016-2018). Bajani, Marie José Kabedi. 5, 2019, Am J Biomed Sci & Res., Vol. 6.
- 607 AJBSR.MS.ID.001062.
- 11. Phénomène 'mbasu' ou ulcère de Buruli à Kinshasa: mythe ou réalité! Résultats préliminaires.
- 609 **Kibadi, K., et al.** 11, s.l.: Congo Médical, 2007, Vol. 4, pp. 1000-1005.
- 12. **Eklöf Bo, et al.** *Revision of the CEAP classification for chronic.* American Venous Forum. 2004.
- 611 13. What have we learned from the Bonn Vein Study? Rabe Eberhard, Pannier Felizitas. 4, 2006,
- 612 Phlebolymphology, Vol. 13.
- 613 14. Leg ulcers: uncommon presentations Clinics in Dermatology. Finn Gottrup MD, Tonny
- 614 **Karlsmark MD.** 6, 2005, Vol. 23, pp. 601-611.
- 15. Skin Disease in the Tropics and the Lessons that can be Learned from Leprosy and Other
- 616 Neglected Diseases. Hay, Roderick J. 9, 2020, Acta Derm Venereol., Vol. 100.
- 16. *Ulcères de jambe*. **Bureau, J.-M & Debure, C.** 2006, EMC Angéiologie, Vol. 1, pp. 1-12.

- 17. VEIN CONSULT Program: interim results. Françoise, Pitsch. 3, s.l.: Les Laboratoires Servier,
- 619 2012, Phlebolymphology, Vol. 19, pp. 132-137.
- 18. Long-term Clinical and Cost-effectiveness of Early Endovenous Ablation in Venous Ulceration: A
- Randomized Clinical Trial. Manjit S Gohel, Jocelyn Mora MSc, Matyas Szigeti, David M Epstein,
- 622 Francine Heatley, Andrew Bradbury, Richard Bulbulia, Nicky Cullum, Isaac Nyamekye, Keith R
- 623 **Poskitt, Sophie Renton, Jane Warwick, Alun H Davies.** [ed.] Early Venous Reflux Ablation Trial
- 624 Group. 12, 2020, JAMA Surg, Vol. 155, pp. 1113-1121.
- 625 19. Epidemiology of chronic venous disorders in geographically diverse populations: results from the
- 626 Vein Consult Program. Rabe E, Guex JJ, Puskas A, Scuderi A, Fernandez Quesada F, VCP
- 627 **Coordinators and Collaborators.** 2, 2012, International Angiology: a Journal of the International
- 628 Union of Angiology, Vol. 31, pp. 105-115.
- 629 20. The burden and treatment of non-communicable diseases among healthcare workers in sub-
- 630 Saharan Africa: a multi-country cross-sectional study. Müller Sophie Alice, et al. 12, May 13, 2024,
- 631 Frontiers in Public Health.
- 632 21. Pattern of Chronic Venous Insufficiency among Patients Presenting to a Vascular Surgery Clinic in
- 633 Low- to Middle-Income Countries (LMIC): A Cross-Sectional Study. Rehman, Zia Ur. 2, s.l.: J-Stage,
- 634 2021, Annals of Vascular Diseases, Vol. 14, pp. 118-121.
- 22. Race, sex, and socioeconomic disparities affect the clinical stage of patients presenting for
- treatment of superficial venous disease. **Misaki M. Kiguchi, et al.** 5, s.l.: Elsevier, 2023, Journal of
- 637 Vascular Surgery: Venous and Lymphatic Disorders, Vol. 11, pp. 897-903.
- 638 23. The prevalence, disease characteristics and treatment of chronic venous disease: an
- 639 international web-based survey. Eberhard Rabe, Catherine Régnier, Fabienne Goron, Ghislaine
- 640 Salmat, Felizitas Pannier. 17, Journal of Comparative Effectiveness Research, Vol. 9.
- 24. Evaluation of clinical and ultrasonographic prognostic factors for detection of iliac venous
- obstructions in patients with advanced chronic venous insufficiency. Viviane Chaib Gomes Stegun,
- Patrick Bastos Metzger, Ana Amélia Carvalho Melo Cavalcante, Thaís Lye Okamoto Yamakami,
- 644 **Fabio Henrique Rossi.** 3 17, 2025, Phlebology.
- 645 25. The clinical characteristics of lower extremity lymphedema in 440 patients. **Steven M. Dean,**
- 646 Elizabeth Valenti, Karen Hock, Julie Leffler, Amy Compston, William T. Abraham. 5, 9 2020, JVS-
- 647 VL, Vol. 8, pp. 851-859.
- 648 26. UN Department of Economic and Scial Affairs. Country Profiles Democratic Republic of the
- 649 Congo. [Online]
- 650 https://population.un.org/wup/countryprofiles?country=Democratic%20Republic%20of%20the%20
- 651 Congo.
- 652 27. World Health Organization. Stratégie de coopération de l'OMS avec la République démocratique
- du Congo 2024-2029. https://www.afro.who.int. [Online]
- 654 https://www.afro.who.int/fr/countries/democratic-republic-of-congo/publication/strategie-de-
- 655 cooperation-de-loms-avec-la-republique-democratique-du-congo-2024-2029.

	On the discourse of the bold with the state of the FOoding I May 07, 0005
	28. —. Skin diseases as a global public health priority. [Online] May 27, 2025. https://apps.who.int/gb/ebwha/pdf_files/WHA78/A78_R15-en.pdf.
	29. <b>National Institute for Health and Care Excellence.</b> Varicose veins: diagnosis and management. <i>NICE</i> . [Online] 7 2013. https://www.nice.org.uk/guidance/cg168/chapter/recommendations.
	30. Skin diseases as a global public health priority. <b>Organization, World Health.</b> Geneva: s.n., 2025. Executive Board.
662	
663	0-0-0