Original Research Article

A clinical analysis of Phlebolymphedema and its relationship with physical activity and disability

Abstract:

BACKGROUND: The clinical features and epidemiological data about patients with phebolymphedema or lymphedema related to Chronic Venous Disease in Mexico is limited and has been understudied, at the same time the relationships between its clinical features, physical activity level and disability remained unknown at all.

METHODS: This is a longitudinal cohort study based on the analysis of clinical data of 90 patients gathered between 2021 and 2022. The statistical analysis was carried out using the SPSS version 25 software and GrandhPad Prism 8; a descriptive analysis was carried out using measures of central tendency for the variables of a quantitative nature and frequency distribution for those categorical variables. The behavior of the variables was revealed through the Shapiro-Wilk statistic. The mean difference analysis was carried out with the Student's T for independent samples. To identify the effect of gender, age, and severity of the disease on the study variables, a three-way analysis of variance was obtained with a Sidak comparison analysis. For association between qualitative and dichotomous nature variables, the Chi-square statistic was obtained together with the Odds Ratio to determine the intensity of the associations found.

RESULTS: A total of 90 patients were included in the analysis; 71% (64) were female and 29% (26) were male; with a mean age of 62.7 years old (± 30.5). A mean BMI of 33.2, a distribution of 79.9% (77) of patients ranged in overweight and obesity ranges. 50% (45) of patients reported disability to perform one or more daily life activities related to the disease's condition (signs, symptoms, volume). Only 12% (10) of all patients performed at or above the minimum physical activity recommended for their population group, 88% (80) of patients had no physical activity or performed under the proper population group's recommendation of minimal physical activity. It was found that the practice of physical activity, the number of compromised segments, the stage of the pathology, and the presence of cardiological and metabolic antecedents presents a statistically significant association with disability. It was not found a significative statistical difference among sex as risk factor. Regarding the BMI, only differences were observed in the level of severity of the disease regardless of the presence of disability ($p=0.006$); evidencing that the greater the severity, the higher the BMI in both men and women. Regarding physical activity, it is observed that inactivity or minimal non-practice of physical activity is a risk factor with the referred disability ($p<0.05$), since it is prolonged that the non-practice of physical activity has 230% more risk of presenting disability compared to those people who referred to practice minimal or above minimal physical activity. In this same line, the presence of a cardiological and/or metabolic history is related to an approximate risk of 150% and 180% times of presenting disability compared to patients who do not have these pathologies.

CONCLUSION: This study reports clinical and epidemiological features of phlebolymphedema and its relationship with physical activity level and reported disability of 90 patients. Further studies are needed to improve and broaden the understanding of the clinical characteristics of phlebolymphedema and its correlations.

Keywords: lymphedema, phlebolymphedema, chronic venous disease, disability, physical activity

Introduction

Chronic venous disease (CVD) is a multifactorial, persistent, progressive condition that includes a broad spectrum of venous abnormalities that compromise venous blood return **(1)** and may lead to progress to clinical manifestations of chronic venous insufficiency as venous ulcers **(2,3)** and specially the under-considered phlebolymphedema **(4, 5)** which not only require extensive treatment and hospitalization in many times but also negatively impact patient quality of life and its complications represent substantial burdens on healthcare resources. **(6)**

Lymphedema is a chronic-progressive disease that produces rich protein edema, caused by the obstruction of lymph vessels, lymph nodes, or by lymphatic function disorders **(7)**. It may occur due to congenital malformations of the lymphatic and venous system, or secondary to different agents that damage lymphatic structures which is included the pathophysiology of advanced CVD and Chronic Venous Insufficiency (CVI), well known as phlebolymphedema or lymphedema related to CVD. (**8-11**)

Background

The clinical and epidemiological data about patients with chronic venous disease and phebolymphedema in Mexico is limited. A recent study reporting the clinical characteristics of 446 patients with lymphedema in Mexico found that 19.4% of them suffer phlebolymphedema or lymphedema related to CVD. **(12)** In the United States it was reported a prevalence of 41% of phlebolymphedema among 440 patients' population with lymphedema. **(13)** which is a considerable number of patients and makes visible a problem to put attention to.

Clinical guidelines of Mexican public health services barely suggest lymphedema management but is only mentioned in the context of breast cancer processes **(14)** while CVD Mexican guidelines only consider lymphedema as a contraindication against surgery in CVI without addressing any possible treatment or even mentioning any consideration about phlebolymphedema. **(15)** A similar absence of reports and consideration about lymphedema related to CVD or phlebolymphedema was identified in other recent studies in México or Latin America, lymphedema related to CVD processes or phlebolymphedema remains neglected. **(14-16)**

Thus, it was decided to explore the epidemiological and clinical features of this population.

Objective

The purpose of this study is to report epidemiological and clinical features of patients with phlebolymphedema or CVD related lymphedema and its relationship with physical activity and disability.

Materials and methods

This study aims to obtain epidemiological and clinical information about Mexican lymphedema patients and its relationship with physical activity and referred disability, employing information collected via direct clinical interview and physical examinations with previous written and verbal informed consent signed by patients or primary caregivers who agreed to share and use the data in the study while keeping their privacy.

Between January 2021 and May 2022, 90 Mexican patients went to rehabilitation services due to phlebolymphedema. Each patient was assessed in the first instance by an angiologist that confirmed diagnosis of CVD clinically and with duplex ultrasound. The patients were clinically assessed and interviewed in Fi Fisioterapia Integral S.C., a private physiotherapy clinic that specializes in rehabilitation services for patients with lymphedema and vascular peripheral disorders.

The data were collected during clinical assessment appointments conducted by lymphedema specialized clinicians employing a clinical datasheet file tool which included complete clinical history, clinical and physical characteristics, socio-demographic data, and physical functional status. A digital spreadsheet matrix was created employing all data and set to order to classify, and organize all the diverse items and information gathered, to be later analyzed it statistically.

For the selection of study participants, the inclusion criteria were that patients presented a confirmed diagnosis of CVD at any stage with clinically stablished phlebolymphedema, patients with a previous diagnosis of non-cancer related lymphedema with confirmed late diagnosis of CVD, patients with previous initial diagnosis of phlebolymphedema.

The exclusion criteria were those patients with any acute edema (less than 12 weeks), that which its primary cause was cardiac, hepatic, nephrotic, pharmacological, orthostatic, and/or hormonal; lymphedema related to cancer treatment or tumor compression, primary lymphedema, syndromic lymphedema, complex vascular malformations or those with

undetermined causes of lymphedema, and finally patients with any neurological and/or cognitive affectation that did not allow the collection of information.

The following items were included in the clinical file datasheet and spreadsheet: Gender, age, height, corporal weight measured at the clinic, body mass index, and its clinical stage based on the American Venous Forum (C1-C6) (**3,9**) and International Society of Lymphology lymphedema staging **(7)**; affected segments, circumferential measures of segments, comorbidities history, surgery history, previous and ongoing treatments, and their characteristics, pain (analogous visual scale employed), infection history, physical activity level based on total minutes per week and sessions per week and classified according to American College of Sport Medicine guidelines' recommendation for each age group **(17,18)**, self-reported disability for daily living activities caused by the clinical condition, occupation, among others for further studies. Concrete questions for each item were made when the patient did not mention explicitly the information.

Statistical analysis

The statistical analysis was carried out using the SPSS version 25 software and GrandhPad Prism 8, a descriptive analysis was carried out using measures of central tendency for the variables of a quantitative nature and frequency distribution for those categorical variables.

The behavior of the variables was revealed through the Shapiro-Wilk statistic, which was used due to the statistical power that this type of analysis has shown with large samples. Considering this, to determine the differences between the numerical variables with the categorical variables of study (referred disability), a mean difference analysis was carried out with a Student's T test for independent samples. Subsequently, to identify the effect of the gender, age, and severity of the disease on the study variable, a three-way analysis of variance was obtained with a Sidak comparison analysis.

Finally, to determine the association between the different study variables of a qualitative and dichotomous nature, the Chi-square statistic was obtained along with the Odds Ratio to determine the intensity of the associations found. The statistical significance threshold for all statistical tests was set at $p < 0.05$. and a confidence of 95%.

Results

A total of 90 of 112 patients were included in the analysis, who fully met the established inclusion criteria; 71% (64) were female and 29% (26) were male; with a mean age of 62.7 years old (± 30.5). According to the age distribution, 56% (50) of patients were elderly adults, while 44% (40) were under 65 years old.

As for their occupations, there is the following information: 46% (42) of patients only performed home chores, 12% (11) did office work, 6% (5) are health care professionals, 12% (11) are retired, 11% (10) merchants, 10% (9) tasks that require physical effort and 2% (2) did not answer. 21% (19) reported a family background of CVD in 1st grade relatives. Several patients, represented by 18% (16) were active alcohol consumers and 15% (13) were active smokers.

Table 1.– Patient's BMI distribution

BMI	**% Patients**
Low weight (-18.5)	1.1% (1)
Normal (18.5-24.9)	21.1% (10)
Overweight (25-29.9)	26.6% (24)
Obesity (30)	48% (48)
Not Reported	7.7% (7)
Number of comorbidities	**% Patients**
without comorbidities	27% (25)
between 1 and 2 comorbidities	38% (34)
between 3 and 4 comorbidities	28% (25)
more than 4 comorbidities	7% (6)

Anatomical distribution was 32% (29) for a unilateral presentation of CVD, among these patients 51% (15) for the left leg and 49% (14) for the right leg. Even 68% (61) presented a bilateral pathology this was asymmetrical, with a mild tendency for the left leg 52% (32) to be in a more advanced stage than the right leg.

Anthropomorphic data were a mean of a 162cm height and 88.5kg weight. It was found a mean BMI of 33.2, being a distribution of 79.9% (77) of patients ranged in overweight and obesity

range. The following distribution of BMI was found: 1.1% (1) in <18.5 BMI or low weight; 21.1% (10) 18.5–24.9 BMI in normal weight
range; 26.6% (24) 25-29.9 in overweight range; 53.3% (48) >30 BMI in obesity range; 7.7% (7) were unable to evaluate due to clinical difficulties during assessments such as extreme mobility limitation to measure weight and/or height.

The general distribution of phlebolymphedema clinical staging is as follows: 8% (7) of patients in stage I; 79% (1) in stage II; 13% (12) in stage III; while CVD staging is as follows: for C1 was 1% (1), C2 1% (1), 70% (63) of the patients in C3, C4 9% (8), C5 7% (6), C6 12% 11. 27% (25) of the patients did not present comorbidities and 38% (34) presented between one and two comorbidities; 35% (31) of patients have at least three or more comorbidities. **Table 1**

Comorbidities distribution is as follows: a 66% (60) with cardiac disease, 13% (12) nephrotic disease, 9% (8) hepatic disease, 9% (8) autoimmune disease, 11% gastric disease, 7% (6) neurologic disease, 11% (10) psychiatric disease, 13% (12) lung disease, 3% (3) hematological disease, 24% (22) diabetes, 47% (42) arterial hypertension. 19% (17) of patients had an active ulcer or an antecedent in the affected limb.

Previous events of regional or local infection such a bacterial cellulitis, lymphangitis and/or dermatolymphangioadenitis in the affected limb was reported by 30% (27) of patients. A 29% (26) of patients had a record of previous thrombotic events in any of the affected limbs. 30% (27) suffered a history of trauma in the limb such as: traumatological injury, vascular surgery, or trauma surgery. Among the participants, 50% (45) reported pain experience in the affected limbs, all patients referred that the pain was causally related to the evolution of their leg's clinical condition.

The 50% (45) of patients reported disability to perform one or more daily life activities related to the disease's condition (signs, symptoms, volume). Difficulties to perform daily tasks and chores were referred: some of them like moving the limb, wearing clothes, independent personal care, walking, climbing stairs, working, getting up from a chair or a bed, changing position, participating in social and family activities, lifting objects, exercising.

Concerning physical activity, patients' activity level and exercise habits were classified into 3 groups, these are: below minimum, minimum physical activity, and above the minimum physical activity recommended for their age group.

The recommendations were taken from American College of Sports Medicine (ACSM): 150 min/week of moderate-intensity or 75 min/week of vigorous-intensity activity, or an equivalent combination, and muscle-strengthening activities at least 2 days/week for each major muscle group. **[17,18]**

Only 12% (10) of all patients performed at or above the minimum physical activity recommended for their population group, 88% (80) of patients had no physical activity or performed under the proper population group's recommendation. The rest was unable to be classified or did not answer. The distribution of activity level by stage is seen in **Table 2.**

Clinical Stage	Above recommended	Recommended	Below recommended or no physical activity
C1			
C2		100% (1)	
C3	3.1% (2)	9.5% (6)	85.7% (54)
C4		12.5% (1)	84.5% (7)
C5			100% (6)
C6			100% (1)

Table 2. *Activity level distribution by clinical stage.*

Table 3 shows the behavior between different analysis variables with the disability reported by the subjects evaluated in the study. Regarding sex, even though 55.6% of the people who reported having a disability are women, this variable does not present any type of relationship or risk factor for the study variable. However, it is evidenced that the practice of physical activity, the number of compromised segments Constrasted statistics: Chi square, *p value<0,05, the state of the pathology, and the presence of cardiological and metabolic antecedents if it presents a statistically significant association with disability.

		Referred disability		
		Yes	No	P (OR)
		%	%	
Sex	Male	38,5	61,5	0,142
	Female	55,6	44,4	

Physical activity	Inactive	57,1	42,9	0,000*
	Active	0	100	(2,33)
Afected segment	Bilateral	86,4	52,2	0,000*
	Unilateral	13,6	47,8	(5,80)
Clinical Stage	Stage I	42,9	57,1	0,029*
	Stage II	44,9	55,1	(16,0)
	Stage III	84,6	15,4	
Cardiac disease	Si	66,7	33,3	0,045*
	No	43,5	56,5	(1,53)
Diabetes	Si	72,7	27,3	0,017*
	No	43,3	56,7	(1,68)

Table 3.- *Association with referred disability*

Regarding physical activity, it is observed that inactivity or minimal non-practice of physical activity is a risk factor with the referred disability ($p<0.05$), since it is prolonged that the non-practice of physical activity has a probability of 2.3 times more risk of presenting disability compared to those people who refer to physical activity. In this same line, the presence of a cardiological and/or metabolic history is related to an approximate risk of 1.5 and 1.8 times of presenting disability compared to users who do not have this type of history.

Table 4 shows the behavior of age, height, weight, and BMI between patients with and without disabilities; it is possible to show that there is a high prevalence of obesity in the entire participating population evaluated from the BMI, however, both the BMI, weight and height did not show differences between subjects with and without disabilities. In contrast to the above, the only variable that presents marginally statistically significant evidence is age ($p=0.047$), highlighting that people who report disability are older on average compared to those who do not report disability.

	Referred disability		P value
	Yes	No	
	Mean (SD)	Mean (SD)	
Age (years)	66,8 (15,3)	58,6 (18,5)	0,047*
Height (cm)	161,7 (9,5)	162,5 (10,08)	0,584
Weight (kg)	89,69 (31,02)	87,5 (23,3)	0,925
BMI	33,6 (10,04)	32,85 (8,25)	0,845

cm: centimeters, kg: Kilograms, BMI: Body Mass Index; SD: Standard Deviation

Table 4.- *Student's T independent samples*

It was found in the analysis of proportions that there is a statistically significant difference related to the proportion of physical activity. The performance of physical activity translates into a lower score in CEAP.

Considering the previous analysis and with the aim of identifying whether age, sex, and the presence or absence of disability influenced the severity of the disease (CEAP), a three-way analysis of variance was performed, which was related in **Figure 1.**

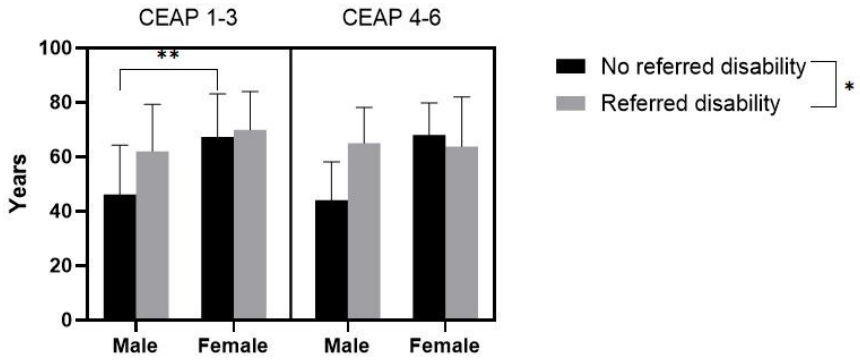

Fig.1.- Three-way analysis of variance

In general, a higher proportion of older women is observed, compared to men in the two categories of analysis (CEAP 1 - 3 and CEAP 4 - 6), these differences being statistically significant (p=0.02), equally, a greater age is observed regardless of the level of qualification on the CEAP scale in people with disabilities compared to those who do not report disability.

Regarding the BMI, only differences were observed in the level of severity of the disease regardless of the presence of disability (p=0.006); evidencing that the greater the severity, the higher the BMI in both men and women.

It was found a set of 5 relevant risk factors (p <0,05) with 95% odds ratio among all the items in relation to referred disability, in which being inactive have 233% more risk to develop disability in this patient's population; 580% for those with bilateral presentation of phlebolymphedema; 160% those with lymphedema (ISL classification system) late-stage clinical stages, 153% for those with cardiac disease, and 168% those with a diagnostic of diabetes. It was not found a significative statistical difference among sex as risk factor.

		Referred disability			
		Yes	No	P value	Odds Ratio (CI 95%)
		%	%		
Sex	Male	38,5	61,5	0,142	0,68 (0,275 – 1,72)
	Female	55,6	44,4		
Physical activity	Inactive	57,1	42,9	0,000* (2,33)	2,33 (1,22 – 4,64)
	Active	0	100		

Afected segment	Bilateral	86,4	52,2	0,000* (5,80)	5,80 (2,05 – 16,38)
	Unilateral	13,6	47,8		
Clinical Stage	Stage I	42,9	57,1	0,029* (16,0)	16,0 (1,97 – 129,90)
	Stage II	44,9	55,1		
	Stage III	84,6	15,4		
Cardiac disease	Si	66,7	33,3	0,045* (1,53)	1,53 (0,95 – 3,01)
	No	43,5	56,5		
Diabetes	Si	72,7	27,3	0,017* (1,68)	1,68 (1,15 – 2,44)
	No	43,3	56,7		

Table 5.- Odds ratio for referred disability in relation to risk factors,

Discussion

This data allows a preliminary better understanding of CVD and phlebolymphedema's clinical features and particularly its relations with disability and physical activity level, in a context of absence of this kind of analysis within the literature; it is to be noted that during the research we were unable to find information related to broad clinical analysis of phlebolymphedema and its relation to variables analyzed in this study. This information may guide not only a better integral understanding of the disease but also extract key points to determine aiming for better treatments, clinical approaching or clinical guidelines development.

The fact that CVD and its presentation as phlebolymphedema is a highly prevalent disease bigger samples are possible to be analyzed, unfortunately it is suspected a difficulty to do so in relation to do it when it comes to identify and diagnose phlebolymphedema as a concrete clinical entity.

The female-male distribution (71%-29%) is something to put attention to, as well as looking at the fact that around 90% live a life of low physical demand; as well as the fact that this pathology affects and cause disability to adults that still in a productive stage of their life (almost a half), but in conditions that might makes us ask which quality of life they are living considering that the mean BMI was in the range of established obesity and more than 50% had 2 or more comorbidities, being sedentary and as well as the half referring disability for daily life activities. Therefore, sociodemographical factors must be deeply investigated, especially those that determine lifestyle of this population and that seem to determine the risk and prognosis of the disease, as well as the associated quality of life once the pathology is established. Simultaneously, it should be considered to assess the socioeconomic level that could be conditioning these variables to develop integral healthcare practices. **[19, 20]**

This study brings out relevant information not only about phlebolymphedema but also critical points when it comes to possible treatments that require not only treatment of the disease locally but globally in its complexity, especially considering the axis of relations of BMI, physical activity level, disability, number of comorbidities, and clinical stage where can be found and intimate relation to worsening of the problem with solid statistical conclusions.
A set of questions arise, what in this axis came first? And what is conditioning each other? What is the priority to solve to succeed in the management of this disease? We hypothesize that factors like physical activity level, disability and BMI are both: risk factors that detonate the worsening or development of phlebolymphedema but also possible consequence of CVD given the two-way relationship among this axis.

Conclusion

This study reports clinical features of phlebolymphedema and its relationship with physical activity and disability of 90 Mexican patients. Further studies are needed to improve and broaden the understanding of the clinical characteristics of phlebolymphedema and its correlations to improve understanding of the disease and its possible treatment.

Consent

As per international standards or university standards, patients' written consent has been collected and preserved by the author(s).

Ethical approval

As per international standards, written ethical approval has been collected and preserved by the author(s).

Data access.

Data is available under reasonable request

References

1 Ortega MA, Fraile-Martínez O, García-Montero C, Álvarez-Mon MA, Chaowen C, Ruiz-Grande F, Pekarek L, Monserrat J, Asúnsolo A, García-Honduvilla N, Álvarez-Mon M, Bujan J. Understanding Chronic Venous Disease: A Critical Overview of Its Pathophysiology and Medical Management. J Clin Med. 2021 Jul 22;10(15):3239. doi: 10.3390/jcm10153239. PMID: 34362022; PMCID: PMC8348673.

2 Davies AH. The Seriousness of Chronic Venous Disease: A Review of Real-World Evidence. Adv Ther. 2019 Mar;36(Suppl 1):5-12. doi: 10.1007/s12325-019-0881-7. Epub 2019 Feb 13. PMID: 30758738; PMCID: PMC6824448.

3 Eklof B, Perrin M, Delis KT, Rutherford RB, Gloviczki P; American Venous Forum; European Venous Forum; International Union of Phlebology; American College of Phlebology; International Union of Angiology. Updated terminology of chronic venous disorders: the VEIN-TERM transatlantic interdisciplinary consensus document. J Vasc Surg. 2009 Feb;49(2):498-501. doi: 10.1016/j.jvs.2008.09.014. PMID: 19216970.

4 Farrow W. Phlebolymphedema-a common underdiagnosed and undertreated problem in the wound care clinic. J Am Col Certif Wound Spec. 2010 Apr 22;2(1):14-23. doi: 10.1016/j.jcws.2010.04.004. PMID: 24527138; PMCID: PMC3601853.

5 Lee BBB. Phlebolymphedema is the ultimate comorbidity/outcome of lymphedema. J Vasc Surg Venous Lymphat Disord. 2019 Sep;7(5):731. doi: 10.1016/j.jvsv.2019.03.001. PMID: 31421840.

6 Nicolaides AN, Labropoulos N. Burden and Suffering in Chronic Venous Disease. Adv Ther. 2019 Mar;36(Suppl 1):1-4. doi: 10.1007/s12325-019-0882-6. Epub 2019 Feb 13. PMID: 30758739; PMCID: PMC6824337.

7 Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology. 2020; 53 (1): 9. PMID: 32521126.

8 Lee BB. Phlebolymphedema: Neglected Outcome of Combined Venous and Lymphatic Insufficiency. Vasc Specialist Int. 2020 Mar 31;36(1):1-3. doi: 10.5758/vsi.2020.36.1.1. PMID: 32274370; PMCID: PMC7119152.

9 Lurie F, Malgor RD, Carman T, Dean SM, Iafrati MD, Khilnani NM, Labropoulos N, Maldonado TS, Mortimer P, O'Donnell TF Jr, Raffetto JD, Rockson SG, Gasparis AP. The American Venous Forum, American Vein and Lymphatic Society and the Society for Vascular Medicine expert opinion consensus on lymphedema diagnosis and treatment. Phlebology. 2022 May;37(4):252-266. doi: 10.1177/02683555211053532. Epub 2022 Mar 8. PMID: 35258350; PMCID: PMC9069652.

10 Ulloa H, Cifuentes S, Figueroa V, Uden VE, Bravo JA MD, Amore M, Ramirez J. Phlebolymphedema: an up to date review. Phlebolymphology. 2021; 104(28) 2: 49-58 ISSN 1286 0107 Retrieved:https://www.phlebolymphology.org/phlebolymphedema-an-up-to-date-review/#:~:text=Phlebolymphedema%20is%20a%20pathology%20with,it%20cannot%20be%20cleared%20away.

11 Endicott, K., Laredo, J., Lee, BB. Diagnosis and Management of Primary Phlebolymphedema. In: Lee, BB., Rockson, S., Bergan, J. (eds) Lymphedema. 2018 Springer, Cham. doi: 10.1007/978-3-319-52423-8_72

10 Montoya LL, Cabanillas YL, Aguirre JS, Luna C, Alcaraz I, Lopez AD. Lymphedema in Mexico: A Clinical and Epidemiological Overview. *Cardiology and Angiology: An International Journal* 2022, *11*(1), 21-31. https://doi.org/10.9734/ca/2022/v11i130186

11 Dean SM, Valenti E, Hock K, Leffler J, Compston A, Abraham WT. The clinical characteristics of lower extremity lymphedema in 440 patients. J Vasc Surg Venous Lymphat Disord. 2020 Sep;8(5):851-859. doi: 10.1016/j.jvsv.2019.11.014. Epub 2020 Jan 25. PMID: 31992537.

12 . Secretaría de Salud. "Guía de práctica clínica. Tratamiento del cáncer de mama en segundo y tercer nivel de atención" Evidencias y Recomendaciones Catálogo Maestro de Guías de Práctica Clínica: IMSS-232-09 Ciudad de México. Marzo 2017; ISBN: 978-607-8270-69-9. Disponible en: http://www.cenetec.salud.gob.mx/contenidos/gpc/catalogoMaestroGPC.html

13 Secretaría de Salud. "Guía de práctica clínica. Prevención, Diagnóstico y Tratamiento de la Insuficiencia Venosa Crónica" Evidencias y Recomendaciones Catálogo Maestro de Guías de Práctica Clínica: IMSS-232-09 Ciudad de México. 2009; ISBN 978-607-8270-47-7 Disponible en: http://www.imss.gob.mx/sites/all/statics/guiasclinicas/175GER.pdf

14 Espejel-Blancas JA, Chinchilla-Hernández RAJ, Garcés-Martínez MAG, et al. Insuficiencia venosa crónica y enfermedad hemorroidal en México: Opinión de expertos. Rev Mex Angiol. 2018;46(4):204-212.

15 Sánchez-Nicolat NE, Guardado-Bermúdez F, Arriaga-Caballero JE, et al. Revisión en úlceras venosas: Epidemiología, fisiopatología, diagnóstico y tratamiento actual. Rev Mex Angiol. 2019;47(1):26-38.

16 Nettal, Franciso, Rodríguez Neftali, Nigro Juan, et.al. Trabajo original Primer consenso latinoamericano de úlceras venosas. Revista Mexicana de Angiología 2013;41(3):95-126.

17 Bushman, Barbara A. Ph.D., FACSM, ACSM-CEP, ACSM-EP, ACSM-CPT. Exercise for Prevention of Chronic Diseases. ACSM's Health & Fitness Journal: 1/2 2020 - Volume 24 - Issue 1 - p 5-10 doi: 10.1249/FIT.0000000000000533

18 American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 10th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2017. 472 p.

19 Soydan E, Yılmaz E, Baydur H. Effect of socio-demographic characteristics and clinical findings on the quality of life of patients with chronic venous insufficiency. Vascular. 2017;25(4):382-389. doi:10.1177/1708538116685945

20 Natour AK, Rteil A, Corcoran P, Weaver M, Ahsan S, Kabbani L. Socioeconomic Status and Clinical Stage of Patients Presenting for Treatment of Chronic Venous Disease. Ann Vasc Surg. 2022;83:305-312. doi:10.1016/j.avsg.2021.12.010