




Venous thromboembolic outcomes in patients with lymphedema and lipedema: An analysis from the National Inpatient Sample

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Abstract

Background: Patients with lymphedema and lipedema share physical exam findings that may lead to misdiagnosis. Poor mobility is common in patients with obesity and patients with lymphedema and lipedema. This may constitute a risk factor for venous thromboembolism (VTE). Our objective was to evaluate the association of VTE in obese patients with lymphedema and lipedema. **Methods:** The National Inpatient Sample (NIS) was searched from 2016 to 2020 to identify hospital admissions of obese female patients with lymphedema and lipedema. Patients were analyzed in the context of presence or absence of VTE while adjusting for complex cluster sampling techniques. Predictors of VTE were accessed by multivariable regression. **Results:** Lymphedema was identified in 189,985 patients and lipedema in 50,645 patients. VTE was observed in 3.12% ($n = 374,210$) of patients with obesity. In patients with obesity, VTE was more common in patients with lymphedema than without (2.6% vs 1.6%; $p < 0.01$). Similarly, VTE was more common in patients with lipedema than without (0.6% vs 0.4%; $p < 0.01$). After multivariable logistic regression, VTE events in obese patients with lymphedema were higher versus without (OR 1.6; CI 1.08–2.43; $p = 0.02$). Similarly, VTE events were more common in obese patients with lipedema versus obese patients without lipedema (OR 1.20; CI 1.03–1.41; $p = 0.02$). **Conclusions:** In this hypothesis-generating study, lymphedema and lipedema show a positive association with VTE after adjusting for baseline patient characteristics such as obesity, which is a known independent risk factor for VTE. Mechanisms whereby lymphedema and lipedema are associated with VTE should be investigated.

Keywords

deep vein thrombosis (DVT), leg swelling, lipedema, lymphedema, venous thromboembolism (VTE)

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Background

Venous thromboembolism (VTE) is a driver of morbidity and mortality.¹ VTE has an estimated annual global incidence of one to two per 1000 persons with incremental direct medical costs reaching \$12,000 to \$15,000 per patient in the first year following diagnosis.^{2,3} Deep vein thrombosis (DVT) alone is observed in up to two-thirds of this population.⁴ Signs and symptoms at presentation, although not diagnostic, play an important role in the suspicion and risk stratification of patients with VTE. Lower-extremity swelling and edema are common DVT symptoms in the acute medical setting. These physical exam findings also occur in a myriad of other conditions, including: heart failure, nephrotic syndrome, infections, lymphedema, chronic venous insufficiency, and lipedema.⁵

In patients with lymphedema and lipedema, lower-extremity edema and a suboptimal quality of life are common

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findings.^{6,7} Limited mobility, common in lymphedema and lipedema, is also a risk factor for VTE. Elevated body mass index (BMI) is not only an independent predictor of VTE events in the general population but associated with increased risk of developing lymphedema.^{8,9} Clinical exam findings of lymphedema are commonly missed, even by trained medical professionals.¹⁰ Distinguishing lymphedema from lipedema is even more challenging when both conditions co-exist in the same patient (lipo-lymphedema).¹¹ A consequence of a missed diagnosis of lipedema or lymphedema may be the impact on subsequent VTE events. Limited data exist for lymphedema as a potential risk factor for VTE in patients with obesity.

Lipedema is an orphan disease, frequently overlooked by medical professionals due to deficiencies in general medical education as well as a lack of understanding about its underlying etiology. As a progressive condition involving abnormal limb distribution of adipose tissue and increased capillary permeability leading to fluid accumulation, outcomes in patients with lipedema deserve careful attention.¹² Though not fully understood, microvasculature dysfunction in addition to tissue inflammation were proposed as underlying mechanisms for asymmetric adipocyte deposition in the limbs of patients with lipedema.^{13–15} The afore-mentioned data place the vascular internist in a strong position to further evaluate patients with lipedema for the purpose of risk factor modification, especially for VTE. As such, the primary goal of this investigation was to capitalize on a large clinical dataset to investigate independent predictors of VTE and adverse outcomes in lipedema and lymphedema in the context of BMI, comparing this to other independent predictors of VTE. We also explored clinical co-morbidities common to lipedema and lymphedema to provide more insight into these disorders.

Methods

Data for this study were obtained from the Agency for Healthcare Research in Quality (AHRQ) Nationwide Inpatient Sample (NIS) from January 2016 to December 2020.¹⁶ Because AHRQ and NIS collect de-identified data, institutional review board approval was waived at the time of study design. IRB approvals there therefore not required. The NIS is an all-payer, administrative claims-based database containing information about patient discharges linked with unique nonfederal hospitals in the United States of America. The NIS approximates a 20% stratified sample of all discharges from US community hospitals, excluding rehabilitation and long-term acute care hospitals according to hospital types, patient volume, teaching status, location, and geographical region. NIS contains clinical and resource utilization information with safeguards to protect privacy and identity of the patients. Each author is responsible for study design, analysis of the data, and accuracy of the analysis presented.

Study population

Patients carrying a discharge diagnosis of obesity and BMI \geq 30 kg/m² were identified using the International Classification of Disease (ICD) 10th revision, Clinical Modification (CM)

(ICD-10-CM) coding in the NIS database for the years 2016, 2017, 2018, 2019, and 2020. ICD-10-CM codes utilized for Lymphedema (I89.0 or I89.9) and Lipedema (E88.2 or R60.9) were selected based on previously published studies and billing recommendations and specifically proposed by the Lipedema Foundation, an acknowledged group of experts in the care of patients with lipedema.^{17,18} The study population was identified by the presence of either one or both of the above-mentioned ICD codes in their categories. Patients were further stratified by the presence or absence of obesity with the help of ICD-10-CM codes (Supplemental Table 1, available online). A comparison among patients with obesity was based on the presence of VTE. Because lipedema is a medical condition identified almost exclusively in women, our investigation of large datasets in the NIS focused on female sex, given a secondary goal was to compare VTE outcomes directly with lymphedema. Patients under the age of 18 were excluded from the study as lipedema is more common in middle-aged women.¹⁹

Statistical analysis

All analyses were conducted using complex survey analyses which account for hospital stratification, clustering, and discharge weights in the NIS domain. Independent sample *t*-tests were used to evaluate the continuous variables, which are expressed as means \pm SD. Pearson's chi-squared test was used to evaluate categorical variables, which are expressed as absolute values and their percentage of the study population. Patient groups were compared by baseline characteristics displayed in Table 1. Univariate logistic regression identified the potential predictor co-variables of VTE in lymphedema and lipedema patients with and without concomitant obesity. Statistically significant variables with a *p*-value less than 0.05 after univariate regression were finally included in the multivariate logistical regression model to evaluate lymphedema and lipedema as potential predictors of VTE. All statistical analyses were performed using a standard software package (Stata, version 17.0; StataCorp, College Station, TX, USA).

Results

A total of 11,976,992 hospital admissions with obesity were identified and included in the analysis. Lymphedema was observed in 1.6% ($n = 189,985$) of the population. Patients with lymphedema had a higher prevalence of congestive heart failure (3.2% vs 1.2%; $p < 0.01$), hypertension (79.7% vs 62%; $p < 0.01$), chronic kidney disease (CKD) (37.9% vs 30.6%; $p < 0.01$), dyslipidemia (40.7% vs 37%; $p < 0.01$), and hypothyroidism (27.5% vs 18%; $p < 0.01$). CKD occurred twice as frequently in patients with lymphedema with obesity (30.8% vs 17.1%; $p < 0.01$).

Lipedema was diagnosed in 0.4% ($n = 50,645$) of the patient population. CKD (20.29% vs 17.32%; $p < 0.01$), cancer (67.4% vs 68.5%; $p = 0.02$), hypothyroidism (23.3% vs 19%; $p < 0.01$), and rheumatoid disease (35.5% vs 36.7%; $p = 0.02$) were more common in patients with lipedema at baseline.

Overall, VTE was observed in 3.12% ($n = 374,210$) of patients with obesity. Patients with VTE had a higher

Table 1. Baseline characteristics of the female population with obesity (weighted sample) based on the presence or absence of venous thromboembolism (VTE).

Baseline variable	No VTE (N = 11,602,782)		VTE (N = 374,210)		p-value
	n	%	n	%	
Age, y, mean ± SD	55.4 ± 17.66		59.6 ± 15.7		< 0.01
Acute myocardial infarction	8,037,143	69.34	259,145	69.23	0.47
Congestive heart failure	2,321,430	20.01	90,080	24.07	< 0.01
Peripheral vascular disease	7,362,973	63.41	237,390	63.35	0.76
Cerebrovascular disease	7,209,233	62.13	231,410	61.91	0.08
Dementia	6,822,868	58.78	219,705	58.57	0.21
COPD	10,931,022	94.19	352,090	94.09	0.01
Rheumatoid disease	4,115,009	35.47	134,675	35.99	0.07
Peptic ulcer disease	2,367,444	20.38	78,055	20.81	< 0.01
Liver disease (mild)	6,033,688	51.87	193,175	51.38	< 0.01
Liver disease (mod-severe)	2,496,524	21.49	82,910	22.21	< 0.01
Diabetes	10,587,067	91.21	340,780	90.93	< 0.01
Diabetes with complications	9,234,507	79.63	297,775	79.43	0.15
Hemiplegia/paraplegia	3,368,999	29.09	108,960	29.12	0.48
Chronic kidney disease	1,997,485	17.83	78,550	21.33	< 0.01
Cancer	7,809,332	67.19	260,540	69.43	< 0.01
Metastatic disease	4,443,643	38.21	154,025	40.97	< 0.01
Hypertension	7,200,754	62.06	260,270	69.54	< 0.01
Chronic pulmonary disease	3,568,084	30.75	115,270	30.80	0.76
Dyslipidemia	4,295,295	37.02	138,265	36.95	0.69
Carotid artery disease	107,235	0.92	2455	0.66	< 0.01
Anemia	3,265,030	28.14	153,355	40.98	< 0.01
Dialysis	264,905	2.28	11,340	3.03	< 0.01
Atrial fibrillation/flutter	1,522,275	13.12	52,680	14.08	< 0.01
Hypothyroidism	2,208,324	19.03	73,305	19.59	< 0.01
Valvular heart disease	477,840	4.12	19,385	5.18	< 0.01
Smoking	3,761,409	32.42	118,350	31.63	< 0.01
Drug abuse	447,930	3.86	15,055	4.02	0.02
Alcohol abuse	226,410	1.95	6245	1.67	< 0.01
Cerebrovascular accident	808,875	6.97	27,830	7.44	< 0.01
Black population	2,302,560	19.84	89,660	23.96	< 0.01
Hispanic population	1,352,049	11.65	31,810	8.50	< 0.01
White population	7,131,393	61.46	231,010	61.73	< 0.01
Native American population	74,105	0.64	1930	0.52	< 0.01
Asian population	140,975	1.22	2445	0.65	< 0.01
Teaching hospitals	8,070,013	69.55	268,915	71.86	< 0.01
Urban hospitals	10,655,584	91.84	348,605	93.16	< 0.01
QTR1	3,786,824	32.64	121,765	32.54	0.57
QTR2	3,085,364	26.59	96,805	25.87	< 0.01
QTR3	2,732,709	23.55	88,315	23.60	0.76
QTR4	1,842,730	15.88	61,925	16.55	< 0.01
Lymphedema	180,290	1.55	9695	2.59	< 0.01
Lipedema	48,605	0.42	2040	0.55	< 0.01

COPD, chronic obstructive pulmonary disease; QTR1, median household income quartile 1; QTR2, median household income quartile 2; QTR3, median household income quartile 3; QTR4, median household income quartile 4.

prevalence of CKD, CHF, cancer, metastatic disease, and hypertension compared with obese patients without VTE. Lymphedema was nearly twice as prevalent in patients with VTE (2.6% vs 1.6%; $p < 0.01$). Similarly, lipedema was observed in 0.6% of the patients with VTE compared to only 0.4% in patients without VTE ($p < 0.01$) (Table 1).

By multivariable logistic regression analysis, the odds of VTE events in obese patients with lymphedema were 1.5-fold higher than in patients without lymphedema (OR 1.5; CI 1.4–1.6; $p < 0.01$). Similarly, patients with lipedema

also had greater odds of VTE events (OR 1.2; CI 1.1–1.3; $p < 0.01$) (Table 2).

Patients with obesity > 65 years of age more commonly had VTE events (OR 1.26; CI 1.2–1.3; $p < 0.01$). Among other co-variables, hypertension (OR 1.22; CI 1.2–1.3; $p < 0.01$), iron deficiency anemia (OR 1.27; CI 1.2–1.3; $p < 0.01$), and drug abuse (OR 1.13; CI 1.1–1.2; $p < 0.01$) were independent predictors of VTE events. Black women also had higher odds of developing VTE (OR 1.17; CI 1.15–1.19; $p < 0.01$) (Table 2 and Figure 1).

Table 2. Univariate and multivariate logistic regression for predictors of venous thromboembolism.

	Univariate Regression			Multivariate Regression		
	Odds ratio	p-value	95% CI	Odds ratio	p-value	95% CI
Age > 65 years	1.37	< 0.01	1.35–1.39	1.26	< 0.01	1.24–1.28
Diabetes	0.97	0.09	0.95–1.00			
Hypertension	1.40	< 0.01	1.37–1.42	1.22	< 0.01	1.20–1.25
Alcoholism	0.85	< 0.01	0.81–0.90	0.85	< 0.01	0.81–0.91
Liver disease (mild)	0.98	0.04	0.97–0.99	0.99	0.17	0.97–1.00
Liver disease (mod-severe)	1.04	< 0.01	1.02–1.06	1.06	< 0.01	1.04–1.08
Congestive heart failure	1.27	< 0.01	1.25–1.29	1.05	< 0.01	1.03–1.07
Acute myocardial infarction	0.99	0.92	0.98–1.02			
Cerebrovascular disease	0.98	0.10	0.97–1.00			
Chronic kidney disease	1.27	< 0.01	1.25–1.30	0.95	< 0.01	0.93–0.97
COPD	0.98	0.16	0.95–1.01			
Peripheral vascular disease	1.00	0.91	0.98–1.01			
Iron deficiency anemia	1.82	< 0.01	1.78–1.87	1.27	< 0.01	1.24–1.30
Chronic pulmonary disease	1.00	0.76	0.99–1.02			
Lymphedema	1.68	< 0.01	1.61–1.76	1.48	< 0.01	1.41–1.55
Lipedema	1.30	< 0.01	1.18–1.44	1.22	< 0.01	1.1–1.34
Dyslipidemia	1.00	0.69	0.98–1.01			
Carotid artery disease	0.71	< 0.01	0.65–0.77	0.62	< 0.01	0.57–0.69
Chronic anemia	1.77	< 0.01	1.75–1.80	1.61	< 0.01	1.58–1.63
Dialysis	1.34	< 0.01	1.28–1.40	1.03	0.27	0.98–1.07
Atrial fibrillation/flutter	1.08	< 0.01	1.06–1.11	0.88	< 0.01	0.86–0.90
Hypothyroidism	1.04	< 0.01	1.02–1.05	0.96	< 0.01	0.95–0.98
Valvular heart disease	1.27	< 0.01	1.23–1.31	1.09	< 0.01	1.05–1.13
Smoking	0.96	< 0.01	0.95–0.98	0.96	< 0.01	0.94–0.97
Drug abuse	1.04	0.02	1.01–1.08	1.13	< 0.01	1.09–1.18
Cerebrovascular accident	1.07	< 0.01	1.04–1.10	0.95	< 0.01	0.92–0.97
Black population	1.27	< 0.01	1.25–1.29	1.17	< 0.01	1.15–1.19
White population	1.01	0.14	1.0–1.03			
Hispanic population	0.70	< 0.01	0.69–0.72	0.76	< 0.01	0.74–0.78
Asian population	0.53	< 0.01	0.49–0.58	0.55	< 0.01	0.50–0.60
Native American population	0.81	< 0.01	0.73–0.89	0.84	< 0.01	0.76–0.93

COPD, chronic obstructive pulmonary disease.

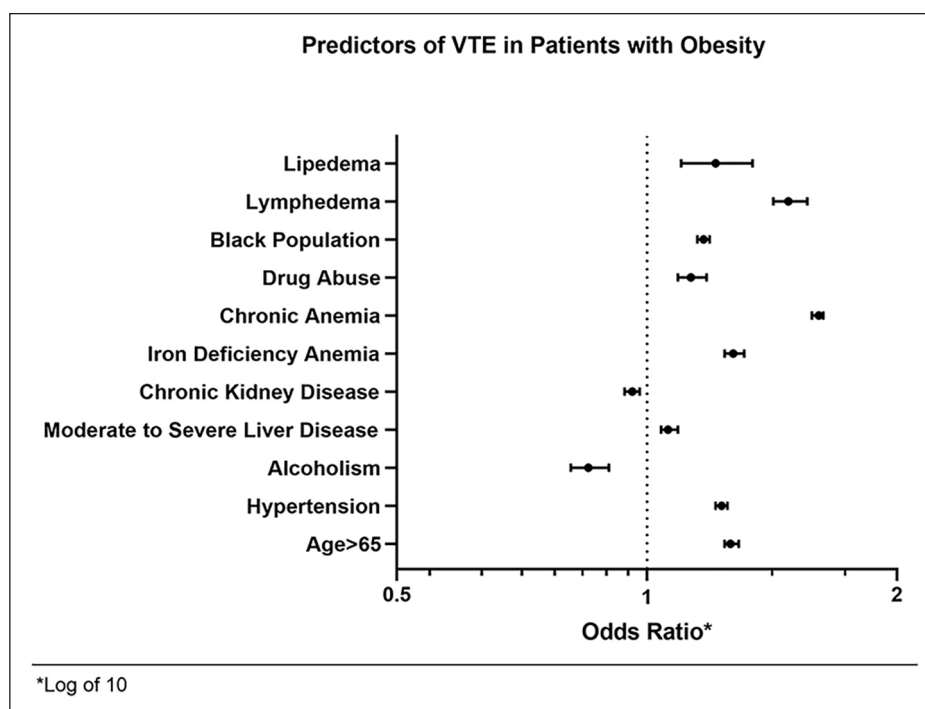


Figure 1. Independent predictors of venous thromboembolism in patients with obesity.

Discussion

This investigation revealed that lymphedema and lipedema are associated with a higher risk for VTE in the obese patient population. Limited mobility is common in the elderly and obese population and is therefore associated with an increased VTE risk.^{20–24} Similarly, in patients with lymphedema, limb volume reduction has demonstrated improvement in the mobility of patients with obesity.²⁵ This suggests the risk of VTE is higher in the elderly individuals with lymphedema and may also be observed in lipedema. Because limited mobility is common to lymphedema and lipedema and is more frequent in patients with obesity, this may potentiate the over-all combined risk of VTE.

Among other predictors of VTE, disorders associated with persistent inflammatory conditions including CKD, rheumatoid disease, and hypothyroidism increased the risk of VTE events. At baseline, female patients above 65 years old were at a higher risk of developing VTE. This finding was in concordance with other large studies suggesting a temporal relationship between advancing age and increased frequency of VTE events.^{26–28} An increased incidence of VTE in the elderly is also attributed to increased fibrinogen, factors VIII and IX, and other proteins of the coagulation cascade, without a proportional increase in circulating antithrombotic proteins.^{29–31} In addition, elevated interleukin 6 (IL-6) and C-reactive protein (CRP) in the elderly population may portend an imbalance toward a pro-inflammatory state, which contributes to thrombosis risk.^{32–34}

Chronic vascular inflammation as a consequence of lymphatic dysfunction is common in lymphedema.^{35,36} Increased inflammatory markers including leukotriene B4 (LTB4) were reported in lymphedema, suggesting a mechanistic role in its pathogenesis.³⁷ Lipedema is regarded as a disorder with altered adipogenesis, microangiopathy, and dysregulated lymphatic function. Studies suggest an imbalance between pro-inflammatory and anti-inflammatory cytokines in adipose tissue that may increase VTE risk.^{38–40} Lipedema and lymphedema are associated with substantial morbidity and decreased quality of life. All these factors can increase the risk of VTE, as noted in our analysis.

Study limitations

This is a retrospective analysis using an administrative claims-based database which raises multiple limitations. Being retrospective in nature, merely an association instead of a causal relationship between lymphedema or lipedema and VTE events can be established by our study. Furthermore, this database consists of estimates from the US population which is not representative of the global population. Hence, inferences cannot be generalized to other demographics and populations.

Identification of diseases in our study was based on ICD-10 codes. Lipedema, being an under-appreciated disease, is not well-characterized in the administrative coding system by a unique identifier. For the purposes of our study, surrogate diagnoses codes for lipedema were used based on recommendations from the Lipedema Foundation to identify the population of interest. Obesity is historically seen in

up to 40% of the US population; however, our estimates suggest ~30% the population had either elevated BMI or obesity. Similarly, our study population underestimates the presence of lipedema as compared to previously published studies. This is due to a lack of disease-specific ICD-10-CM codes, underdiagnosis given that lipedema is under-recognized by clinicians, and loss of sample volume as a consequence of inadequate ICD coding during hospital encounters.^{41,42} Under-coding or mis-coding may have also led to decreased sample size in our study. The study population was selected based on ICD-10 codes for lymphedema, including 'I89.0' which includes patients with lymphedema not classified elsewhere. Inclusion of these patients may have also included patients with secondary upper-extremity lymphedema after mastectomy despite a dedicated code of 'I97.2'. This could have led to underestimation of VTE risk in our patient population. Lastly, absence of data on the timing of these events makes it impossible to establish a tangential relationship between risk factors and subsequent VTE events.

Conclusion

Our observation that VTE remains prevalent in patients with lymphedema and lipedema even after adjusting for baseline characteristics, including obesity, suggests lymphedema and lipedema constitute a residual risk for VTE, and these patients should be carefully targeted for thrombotic risk factor reduction.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplementary material

The supplementary material is available online with the article.

References

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: A report from the American Heart Association. *Circulation* 2019; 139: e56–e528.
2. Wendelboe AM, Raskob GE. Global burden of thrombosis. *Circ Res* 2016; 118: 1340–1347.
3. Grosse SD, Nelson RE, Nyarko KA, et al. The economic burden of incident venous thromboembolism in the United States: A review of estimated attributable healthcare costs. *Thromb Res* 2016; 137: 3–10.
4. Cushman M. Epidemiology and risk factors for venous thrombosis. *Semin Hematol* 2007; 44: 62–69.

5. Gasparis AP, Kim PS, Dean SM, et al. Diagnostic approach to lower limb edema. *Phlebology* 2020; 35: 650–655.
6. Romeijn JRM, de Rooij MJM, Janssen L, Martens H. Exploration of patient characteristics and quality of life in patients with lipoedema using a survey. *Dermatol Ther (Heidelb)* 2018; 8: 303–311.
7. Morgan PA, Franks PJ, Moffatt CJ. Health-related quality of life with lymphoedema: A review of the literature. *Int Wound J* 2005; 2: 47–62.
8. Eichinger S, Hron G, Bialonczyk C, et al. Overweight, obesity, and the risk of recurrent venous thromboembolism. *Arch Intern Med* 2008; 168: 1678–1683.
9. Savetsky IL, Torrisi JS, Cuzzone DA, et al. Obesity increases inflammation and impairs lymphatic function in a mouse model of lymphedema. *Am J Physiol Heart Circ Physiol* 2014; 307: H165–H172.
10. Kamran H, Hornacek D, Mix D, et al. A survey of commonly misunderstood vascular medicine physical exam findings among medical trainees. *Vasc Med* 2020; 25: 351–353.
11. Herbst KL, Kahn LA, Iker E, et al. Standard of care for lipedema in the United States. *Phlebology* 2021; 36: 779–796.
12. Crescenzi R, Donahue PMC, Weakley S, et al. Lipedema and Dercum's disease: A new application of bioimpedance. *Lymphat Res Biol* 2019; 17: 671–679.
13. Herpertz U. [Lipedema]. *Z Lymphol* 1995; 19: 1–11.
14. Gould DJ, El-Sabawi B, Goel P, et al. Uncovering lymphatic transport abnormalities in patients with primary lipedema. *J Reconstr Microsurg* 2020; 36: 136–141.
15. Van Geest AJ, Esten SCAM, Cambier JPRA, et al. Lymphatic disturbances in lipedema. *Phlebologie* 2003; 32: 138–142.
16. Elixhauser A, McCarthy E. *Clinical classifications for health policy research, Version 2: Hospital inpatient statistics*. Healthcare Cost and Utilization Project (HCUP-3) Research Note 1, AHCPR Publication No. 96-0017, Feb 1996. Agency for Health Care Policy and Research.
17. Herbst KL. Subcutaneous adipose tissue diseases: Dercum disease, lipedema, familial multiple lipomatosis, and Madelung disease. In: Feingold KR, Anawalt B, Blackman MR, et al. (eds) *Endotext*; 2019.
18. Lipedema Foundation. About lipedema, <https://www.lipedema.org/about-lipedema> (2023, accessed 1 Nov 2023).
19. Falck J, Rolander B, Nygårdh A, et al. Women with lipedema: A national survey on their health, health-related quality of life, and sense of coherence. *BMC Womens Health* 2022; 22: 457.
20. Weill-Engerer S, Meaume S, Lahlou A, et al. Risk factors for deep vein thrombosis in inpatients aged 65 and older: A case-control multicenter study. *J Am Geriatr Soc* 2004; 52: 1299–1304.
21. Hull RD, Schellong SM, Tapson VF, et al. Extended-duration venous thromboembolism prophylaxis in acutely ill medical patients with recently reduced mobility: A randomized trial. *Ann Intern Med* 2010; 153: 8–18.
22. Vincent HK, Vincent KR, Lamb KM. Obesity and mobility disability in the older adult. *Obes Rev* 2010; 11: 568–579.
23. Anton SD, Manini TM, Milsom VA, et al. Effects of a weight loss plus exercise program on physical function in overweight, older women: A randomized controlled trial. *Clin Interv Aging* 2011; 6: 141–149.
24. DiPietro L, Jin Y, Talegawkar S, Matthews CE. The joint associations of weight status and physical activity with mobility disability: The NIH-AARP Diet and Health Study. *Int J Obes* 2019; 43: 1830–1838.
25. Şahinoğlu E, Ergin G, Karadibak D. The efficacy of change in limb volume on functional mobility, health-related quality of life, social appearance anxiety, and depression in patients with lower extremity lymphedema. *Phlebology* 2022; 37: 200–205.
26. Geerts WH, Heit JA, Clagett GP, et al. Prevention of venous thromboembolism. *Chest* 2001; 119(1 suppl): 132s–175s.
27. Bizien N, Noel-Savina E, Tromeur C, et al. Age is a major risk factor of venous thromboembolism (VTE). *Eur Respir J* 2011; 38(Suppl 55): p3936.
28. Stein PD, Hull RD, Kayali F, et al. Venous thromboembolism according to age: The impact of an aging population. *Arch Intern Med* 2004; 164: 2260–2265.
29. Mari D, Coppola R, Provenzano R. Hemostasis factors and aging. *Exp Gerontol* 2008; 43: 66–73.
30. Ershler WB. Interleukin-6: A cytokine for gerontologists. *J Am Geriatr Soc* 1993; 41: 176–181.
31. Meade TW, North WR, Chakrabarti R, et al. Population-based distributions of haemostatic variables. *Br Med Bull* 1977; 33: 283–288.
32. Galeano-Valle F, Ordieres-Ortega L, Oblitas CM, et al. Inflammatory biomarkers in the short-term prognosis of venous thromboembolism: A narrative review. *Int J Mol Sci* 2021; 22: 2627.
33. Puzianowska-Kuźnicka M, Owczarż M, Wieczorowska-Tobis K, et al. Interleukin-6 and C-reactive protein, successful aging, and mortality: The PolSenior study. *Immun Ageing* 2016; 13: 21.
34. Harris TB, Ferrucci L, Tracy RP, et al. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. *Am J Med* 1999; 106: 506–512.
35. Avraham T, Zampell JC, Yan A, et al. Th2 differentiation is necessary for soft tissue fibrosis and lymphatic dysfunction resulting from lymphedema. *FASEB J* 2013; 27: 1114–1126.
36. Rockson SG. The lymphatics and the inflammatory response: Lessons learned from human lymphedema. *Lymphat Res Biol* 2013; 11: 117–120.
37. Jiang X, Nicolls MR, Tian W, Rockson SG. Lymphatic dysfunction, leukotrienes, and lymphedema. *Annu Rev Physiol* 2018; 80: 49–70.
38. Rasmussen JC, Aldrich MB, Fife CE, et al. Lymphatic function and anatomy in early stages of lipedema. *Obesity (Silver Spring)* 2022; 30: 1391–1400.
39. Szuba A, Rockson SG. Lymphedema: Classification, diagnosis and therapy. *Vasc Med* 1998; 3: 145–156.
40. Chachaj A, Dudka I, Jeziorek M, et al. Lymphoscintigraphic alterations in lower limbs in women with lipedema in comparison to women with overweight/obesity. *Front Physiol* 2023; 14: 1099555.
41. Kruppa P, Georgiou I, Biermann N, et al. Lipedema—Pathogenesis, diagnosis, and treatment options. *Dtsch Arztebl Int* 2020; 117: 396–403.
42. Buck DW 2nd, Herbst KL. Lipedema: A relatively common disease with extremely common misconceptions. *Plast Reconstr Surg Glob Open* 2016; 4: e1043.