European Review for Medical and Pharmacological Sciences 2023; 27: 2899-2907

The association between chronic venous disease and knee osteoarthritis

T.-N. CAO[1,2], C.-T. NGUYEN[2], M.-D. NGUYEN[3]

[1]Department of Geriatrics and Gerontology, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[2]Department of Rheumatology, University Medical Center HCMC, Ho Chi Minh City, Vietnam
[3]Department of Radiology, Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam

Cao Thanh Ngoc and Nguyen Minh Duc contributed equally to this article as co-first authors

Abstract. – OBJECTIVE: Chronic venous disease (CVD) and knee osteoarthritis (KOA) are two common diseases in the elderly. Both share common risk factors, such as age, sex, and obesity, and are believed to be associated with inflammatory conditions and venous stasis. However, studies of the association between CVD and KOA are limited, especially in the elderly. To investigate the association between CVD and KOA and their effects on pain and functional status in the elderly at the Rheumatology Clinic of University Medical Center Ho Chi Minh City (HCMC).

PATIENTS AND METHODS: This cross-sectional study included 222 elderly patients (aged ≥60 years) at the Rheumatology Clinic of University Medical Center HCMC from December 2019 to June 2020, including 167 with and 55 without KOA. Patient data were collected for both groups, including demographics, symptoms, clinical signs, and diagnostic tests for KOA and CVD, including knee radiographs and duplex scanning of the lower extremity veins.

RESULTS: CVD was a common comorbidity among elderly patients with KOA (73.65% *vs.* 58.18%; $p = 0.030$). CVD symptoms did not differ significantly between patients with and without KOA. After adjusting for age, sex, body mass index, and some comorbid conditions, the differences in CVD incidence between the groups remained significant (odds ratio = 2.46, 95% confidence interval: 1.20-5.06; $p = 0.014$). Visual Analog Scale and Western Ontario and McMaster Universities Osteoarthritis Index pain scores were higher in elderly patients with KOA and CVD.

CONCLUSIONS: CVD is common in elderly patients with KOA. While age, sex, and weight are risk factors for both conditions, there is an independent association between them. Patients comorbid with KOA and CVD have more pain and limited functional status.

Key Words:
Knee osteoarthritis, Chronic venous disease, Elderly.

Introduction

Knee osteoarthritis (KOA) is one of the most common diseases in the elderly, resulting in pain, loss of function and disability. Eventually, KOA reduces the quality of life[1]. It affects approximately one-third of people aged >60 years[2]. In Vietnam, >85% of elderly individuals have knee pain due to osteoarthritis[3]. Its pathophysiology is believed to affect the entire joint, mainly in its subchondral areas[4].

Chronic venous diseases (CVDs) are also a relevant problem in the aging population and have various manifestations such as telangiectasia, varicose veins, and venous ulcers[5]. KOA and CVD share common risk factors, such as aging, obesity, and prolonged standing. Elderly individuals are more likely to have symptoms and progress to severe CVD manifestations[6]. Some studies found that the venous stasis and inflammation mechanism in CVD can damage the subchondral areas, leading to cartilage loss and osteoarthritis[7-9]. Data on the relationship between CVD and KOA is limited, especially in the elderly. With the rapidly aging population in Vietnam, the incidence of individuals comorbid with KOA and CVD is increasing, requiring a comprehensive assessment and treatment. This study aimed to investigate the relationship between KOA and CVD and their effects on pain and functional disability in the elderly.

Patients and Methods

Study Location

This is a prospective cross-sectional study. Our study selected participants among the elderly who attended the Rheumatology Clinic at the

Corresponding Author: Nguyen Minh Duc, MD; e-mail: bsnguyenminhduc@pnt.edu.vn

University Medical Center Ho Chi Minh City between October 2019 and June 2020. All participants signed informed consent. The patients with a history of knee trauma, previous knee surgery, peripheral neuropathy, heart failure, cirrhosis, nephrotic syndrome, hypothyroidism, and mental health were excluded. This study was approved by the Institution Review Board of the University of Medicine and Pharmacy at Ho Chi Minh City (approval number: 574/ĐHYD-HĐĐĐ).

Data Collection

Participants were interviewed to collect relevant information using a structured questionnaire. The questionnaire and objective assessment recorded their symptoms and CVD and KOA signs (Figure 1). We also evaluated their weight, height, and frailty condition. Their knee radiographic and lower limbs Doppler ultrasound results were obtained from their medical records.

Measurements

KOA

All participants were evaluated for KOA signs and symptoms. The diagnosis was made according to the 1986 clinical and imaging criteria of the American College of Rheumatology (ACR)[10]. Patients were diagnosed with KOA if they described knee pain, osteophytes were visible in X-ray images (Figure 2), and they had at least one of the following criteria: aged >50 years, morning stiffness of <30 minutes, and crepitus. Pain severity and functional disability were assessed using the Visual Analog Scale (VAS)[11] and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[12].

CVD

CVD symptom characteristics and duration were collected by subjective patient assessment. A clinician performed an objective examination to record the different clinical CVD manifestations. They were classified according to the clinical, etiological, anatomical, and pathological classification (CEAP) system, including telangiectasias, varicose veins, edemas, hyperpigmentation/skin changes, healed venous ulcers, and active venous ulcers (Table I)[5]. Lower extremity venous Doppler ultrasonography was performed by a specialist using a 7-12 MHz linear probe (LOGIQ P5, GE HealthCare, Chicago, Illinois, USA) to assess reflux time in the venous system (Figure 3). A diagnosis was made based on the combination of clinical signs and the Doppler ultrasound result.

Covariates

Participants' demographic characteristics were collected, including age, sex, body mass index (BMI), previous occupational activities, comorbidities (e.g., hypertension and type 2 diabetes), mediation number, daily living activities (ADL) according to the Katz index[13], the instrumental daily living activities (IADL) according to the Lawton index[14], and

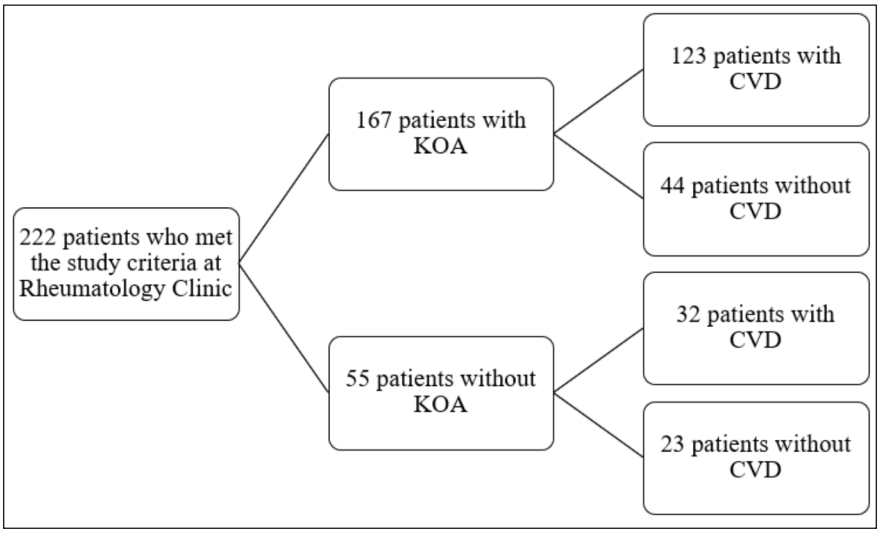

Figure 1. The flow diagram of the study. KOA: Knee osteoarthritis; CVD: Chronic venous diseases.

frailty classification according to the Clinical Frailty Scale[15].

Statistical Analysis

Data were analyzed using the software STATA/MP 14.0 for Windows (StataCorp LLC, College Station, Texas, USA). Binary and categorical variables are presented as percentages and numbers. Continuous variables are presented as mean ± standard deviation or median and interquartile range. Univariable and multivariable logistic regression analyses were performed to determine the relationship between KOA and CVD. The odds ratio (OR) and 95% confidence interval (CI) were calculated. Proportions were compared with Chi-square or Fisher's exact tests, and means and medians were compared using *t*-tests or Mann-Whitney U tests. All results with $p < 0.05$ were considered statistically significant.

Results

This study included 222 elderly patients who met the study criteria, of which 167 had KOA according to ACR criteria. Their mean age was 70.85 ± 7.45 years, and most were female (85.59%), classified as non-frail (63.97%), and had multimorbidity and polypharmacy conditions. Complete participant characteristics are listed in Table II. Demographic characteristics did not differ significantly between groups.

Table I. CEAP classification[5].

Clinical manifestation
C0: No visible or palpable signs of venous disease
C1: Telangiectasis or reticular veins
C2: Varicose veins
C3: Edema
C4: Changes in skin and subcutaneous tissue secondary to CVD
C4a: Pigmentation or eczema
C4b: Lipodermatosclerosis or atrophie blanche
C5: Healed venous ulcer
C6: Active venous ulcer
Etiologic classification
Ec: Congenital
Ep: Primary
Es: Secondary (post-thrombotic)
En: No venous cause identified
Anatomic classification
As: Superficial veins
Ap: Perforator veins
Ad: Deep veins
An: No venous location identified
Pathophysiologic classification
Pr: Reflux
Po: Obstruction
Pr,o: Reflux and obstruction
Pn: No venous pathophysiologic identifiable

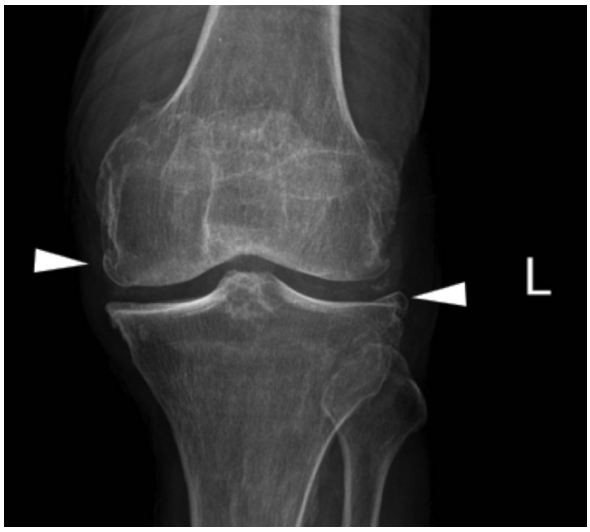

Figure 2. Representative X-ray image showing osteophytes (white arrowheads).

As shown in Table III, CVD frequency was significantly higher in the KOA group (73.65%) than in the control group (58.15%; $p = 0.030$). According to the CEAP classification, telangiectasia and varicose vein were the study population's two most common clinical manifestations. The prevalence of varicose veins was significantly higher in the KOA group (70.06%) than in the control group (47.27%). However, the prevalence of other manifestations did not differ significantly. Furthermore, the mean CVD duration was longer in the KOA group than in the control group.

The prevalence of CVD symptoms in both groups is shown in Table IV. Over half of the participants had pain and heaviness in their legs, the most common CVD symptom. Furthermore, we found no differences in reported symptoms between groups. The number of CVD symptoms was higher in the KOA group, with 31.74% of participants reporting >2 symptoms.

A sex-based subgroup analysis showed that CVD prevalence was significantly higher in females with than without KOA. However, this relationship was not observed in males (Table V).

As shown in Table VI, the association between CVD and KOA remained after adjusting for related factors in a multivariate logistic analysis.

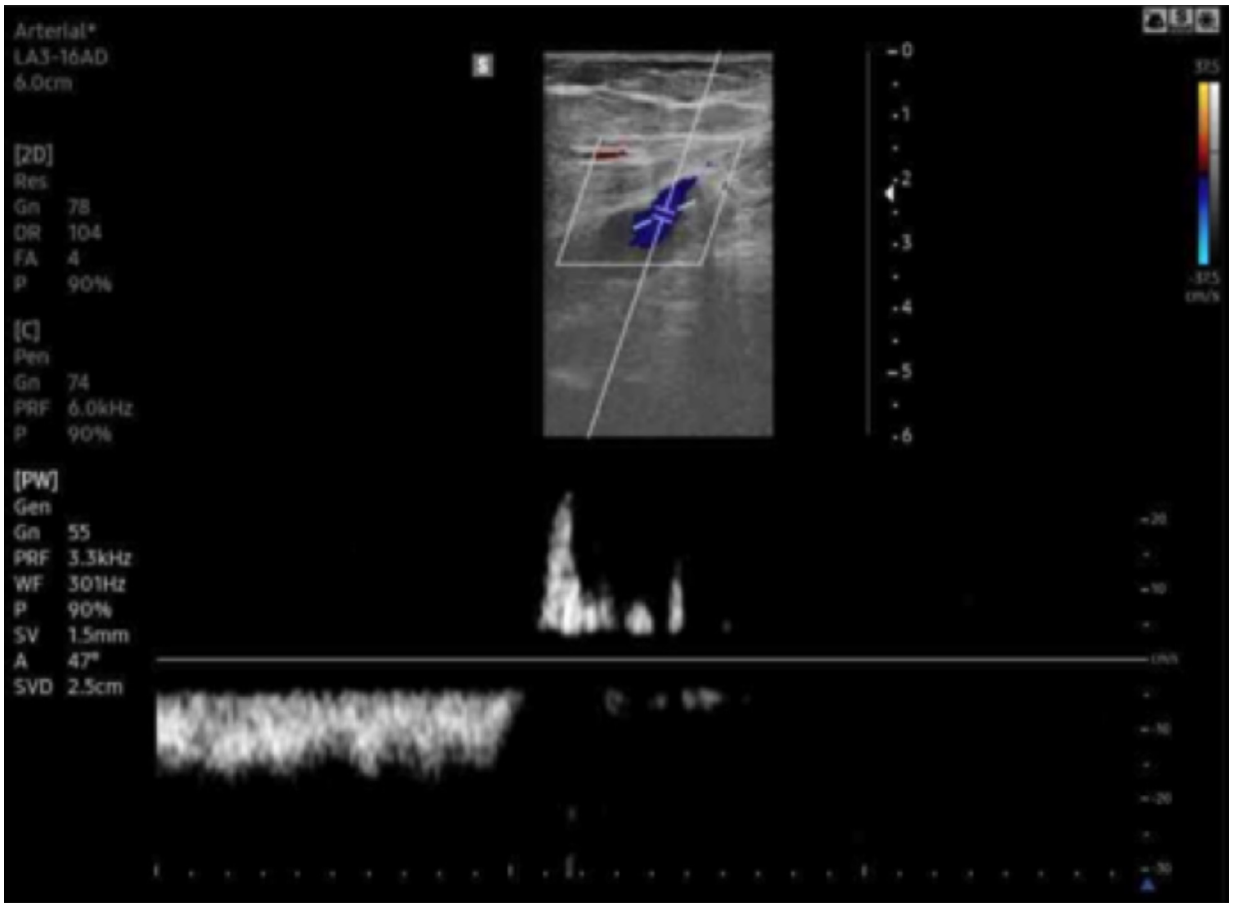

Figure 3. Reflux flow in lower extremity venous on Doppler ultrasonography.

Participants with CVD were more likely to have KOA (OR = 2.46, 95% CI: 1.20-5.06; $p = 0.014$).

Table VII compares the WOMAC and VAS pain scores between KOA patients with and without CVD. WOMAC pain (10.28 ± 2.80 *vs.* 9.04 ± 4.14; $p = 0.030$) and function (28.73 ± 8.05 *vs.* 24.38 ± 10.86; $p = 0.006$) scores were significantly higher in elderly participants with KOA and CVD than KOA only. A similar significant difference was found with VAS scores (6.49 ± 1.50 *vs.* 5.79 ± 1.57; $p = 0.009$).

Total WOMAC scores did not differ significantly among clinical CVD manifestations (Figure 4).

Discussion

This study investigated the relationship between KOA and CVD in the elderly. Table III showed a significant association between CVD and KOA in elderly patients ($p = 0.030$), which remained significant after adjusting for some related factors. Participants with CVD were more likely to have KOA than those without CVD (OR = 2.46, 95% CI: 1.20-5.06; $p = 0.014$).

Two theoretical mechanisms potentially explain this relationship: venous stasis and pre-inflammatory condition[7]. Vascular pathology plays an important role in osteoarthritis initiation and progression. Venous stasis in the subchondral bone can reduce blood flow, leading to subchondral ischemia. Therefore, these factors can compromise nutrient and oxygen-carbon dioxide exchange in the articular cartilage, a potential osteoarthritis initiator[7]. In addition, CVD is thought to be associated with the inflammation process. In CVD patients, neutrophils increase superoxide production and the expression of several adhesion molecules, including interleukin-8 and cluster of differentiation 35. A white cell trapping study showed that activated leukocytes are trapped in the lower limb's microcirculation in CVD, inducing the release of inflammatory chemicals and damage to the articular cartilage[9]. The degeneration process

Table II. Baseline demographic characteristics of the study population.

	KOA group (n = 167)	Control group (n = 55)	Total (n = 222)	p
Sex				
Male	26 (15.57%)	6 (10.91%)	32 (14.41%)	0.393
Female	141 (84.43%)	49 (89.09%)	190 (85.59%)	
Age (year)	71.08 ± 7.59	70.16 ± 7.01	70.85 ± 7.45	0.431
Age group (years)				
60-69	85 (50.90%)	29 (52.73%)	114 (51.35%)	0.257
70-79 52 (31.14%)	21 (38.18%)	73 (32.88%)		
≥80	30 (17.96%)	5 (9.09%)	35 (15.77%)	
BMI group				
Underweight	7 (4.19%)	3 (5.45%)	10 (4.50%)	0.054
Normal	65 (38.92%)	31 (56.36%)	96(43.24%)	
Overweight-obese	95 (56.89%)	21 (38.18%)	116 (52.25%)	
Prolonged (≥5 hours) standing at work				
Upright posture	15 (8.98%)	4 (7.27%)	19 (8.56%)	0.918
With substantial movement	64 (38.32%)	22 (40.00%)	86 (38.74%)	
No	88 (52.69%)	29 (52.73%)	117 (52.70%)	
ADL dependent	20 (11.98%)	8 (14.55%)	28 (12.61%)	0.619
IADL dependent	57 (34.13%)	23 (41.82%)	80 (36.03%)	0.303
Frailty classification				
Non-frail	110 (65.87%)	32 (58.18%)	142 (63.97%)	0.588
Mild frailty	37 (22.16%)	15 (27.27%)	52 (23.42%)	
Moderate-severe frailty	20 (11.98%)	8 (14.55%)	28 (12.61%)	
Number of comorbidities	4.73 ± 2.09	5.23 ± 2.22	4.85 ± 2.13	0.127*
Number of medications	6.68 ± 3.48	6.8 ± 2.64	6.71 ± 3.28	0.819*
Hypertension	100 (59.88%)	27 (49.09%)	127 (57.21%)	0.161
Type 2 diabetes	67 (40.12%)	18 (32.73%)	85 (38.29%)	0.328

*, compared using a *t*-test; KOA, knee osteoarthritis; BMI, body mass index; ADL, daily living activities; IADL, instrumental daily living activities.

Table III. The relationship between clinical CVD and KOA manifestations in the elderly.

	KOA group (n = 167)	Control group (n = 55)	p
CVD	123 (73.65%)	32 (58.18%)	0.030
C1 – Telangectasia	91 (54.49%)	25 (45.45%)	0.245
C2 – Varicose vein	117 (70.06%)	26 (47.27%)	0.002
C3 – Venous edema	36 (19.37%)	7 (12.73%)	0.151
C4 – Pigmentation/skin changes	2 (1.20%)	0	0.415
C5 – Healed venous ulcer	0	0	
C6 – Active venous ulcer	0	0	
CVD duration	6.54 ± 5.33	5.12 ± 3.75	0.150*
KOA duration	4.62 ± 3.66		

*, compared using *t*-test; KOA, knee osteoarthritis; CVD, chronic venous disease.

Table IV. The relationship between CVD and KOA symptoms in the elderly.

	KOA group (n = 167)	Control group (n = 55)	p
Pain and heaviness in legs	107 (64.07%)	28 (50.91%)	0.083
Ankle edema	61 (36.53%)	14 (25.45%)	0.132
Leg cramps at night	66 (39.52%)	22 (40.00%)	0.950
Itching of the legs	12 (7.19%)	3 (5.45%)	0.657
Tinglings/numbness	44 (26.35%)	16 (29.09%)	0.691
Number of symptoms			
0	49 (29.34%)	23 (41.82%)	0.229
1-2	65 (38.92%)	18 (32.73%)	
>2	53 (31.74%)	14 (25.45%)	

KOA, knee osteoarthritis.

Table V. Sex-based subgroup analysis comparing CVD signs in patients with and without KOA.

	Females With (n = 141)	Without (n = 49)	p	Males With (n = 26)	Without (n = 6)	p
CVD (C1-C6)	115 (81.56%)	29 (59.18%)	0.002	8 (30.77%)	3 (50.00%)	0.638*
Telangiectasias	86 (60.99%)	23 (46.94%)	0.087	5 (20.00%)	2 (33.33%)	0.596*
Varicose veins	107 (75.89%)	24 (48.98%)	<0.001	10 (38.46%)	2 (33.33%)	0.815*
Other manifestations (C3-C6)	33 (23.40%)	5 (10.20%)	0.049	3 (11.54%)	2 (33.33%)	0.241*

*, compared using Fisher's exact test; KOA, knee osteoarthritis; CVD: chronic venous disease.

Table VI. Multivariate logistic analysis of the relationship between CVD and KOA in the elderly.

	OR	95% CI	p
CVD	2.46	1.20-5.06	0.014
Sex	0.37	0.12-1.15	0.087
Age group (years)			
60-69	1		
70-79	1.44	0.62-3.35	0.392
≥80	4.89	1.16-20.47	0.030
BMI group			
Underweight	1		
Normal	1.04	0.22-4.81	0.956
Overweight-obese	2.59	0.54-12.33	0.229
Prolonged (≥5 hours) standing at work			
Upright posture	1		
With substantial movement	0.82	0.23-2.94	0.766
No	0.92	0.26-3.24	0.904
Frailty classification			
Non-frail	1		
Mild frailty	0.47	0.19-1.15	0.102
Moderate-severe frailty	0.24	0.06-0.92	0.038
Hypertension	1.34	0.67-2.68	0.998
Type 2 diabetes	1.22	0.59-2.54	0.396

KOA, knee osteoarthritis; BMI, body mass index; OR, odds ratio; CI, confidence interval.

Table VII. The relationship of CVD with pain and functional status in the KOA group.

	KOA and CVD (n = 123)	KOA only (n = 44)	p
WOMAC 1 (pain)	10.28 ± 2.80	9.04 ± 4.14	0.030*
WOMAC 2 (stiffness)	2.03 ± 1.22	1.77 ± 1.36	0.240*
WOMAC 3 (function)	28.73 ± 8.05	24.38 ± 10.86	0.006*
WOMAC total	40.90 ± 11.00	35.27 ± 15.56	0.010*
VAS	6.49 ± 1.50	5.79 ± 1.57	0.009*

*, compared using *t*-tests; KOA, knee osteoarthritis; CVD: chronic venous disease; VAS: Visual Analog Scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

is initiated from the subchondral bone, forming osteophytes and decreasing joint cartilage thickness[8].

Our results showed a significant relationship between varicose veins and KOA but not between telangiectasia and KOA. These findings are similar to Lesnyak et al[9], potentially reflecting differences in the severity of clinical venous disease signs. Specifically, varicose veins are a more severe telangiectasia form. Since venous stasis is higher in the varicose vein than in telangiectasia, it can have greater effects on the subchondral bone. Since venous pressure has not yet increased as high in telangiectasia as in varicose veins, it affects the knee joint's subchondral bone layer less, leading to an unclear clinical relationship with KOA.

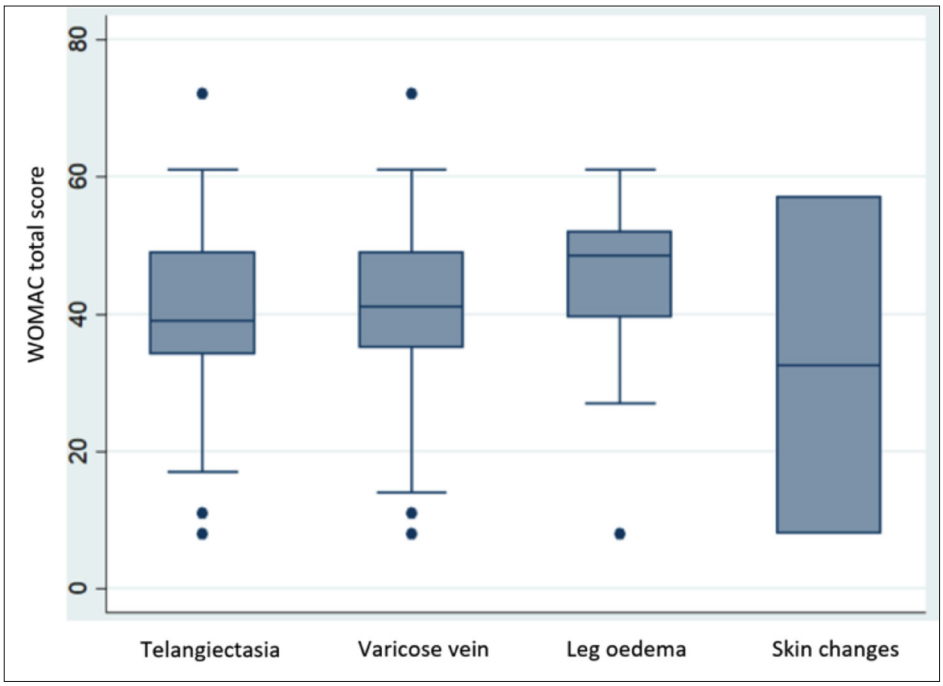

Figure 4. Boxplot showing total WOMAC scores for different clinical CVD manifestations in KOA patients.

Similar to other studies, individuals with more severe CVD manifestations were uncommon. Our study only included two patients with a C4 classification (pigmentation/lipodermatosclerosis) in its KOA group (1.2%). In addition, we did not find a significant relationship between this classification and KOA. In contrast, Lesnyak et al[9] reported an association between KOA and this CVD classification ($p = 0.046$). However, because the number of patients with this classification remains limited, it is difficult to conclude whether there is a relationship between severe CVD manifestations and KOA. Therefore, more studies focusing on these particular patients are needed.

Our study found no significant differences in CVD symptoms between participants with and without KOA. These results show that CVD symptoms are not highly specific and can be found in both patient populations. Nonetheless, CVD symptoms were more common in participants with KOA than those without. In addition, the number of symptoms was greater in participants with than without KOA. Specifically, 31.74% of participants with KOA had ≥ 2 CVD symptoms compared to 25.45% without KOA. However, this difference was not statistically significant. This result may suggest a pathophysiological relationship between KOA and CVD. In addition, patient complaints associated with their symptoms may overlap since both present in the lower extremities. Nevertheless, symptom duration was longer with CVD than with KOA[9], potentially supporting the hypothesis that venous stasis causes articular cartilage damage[7]. Oga et al[16] found that after endovascular treatment, KOA patients with varicose veins often experienced improved knee joint symptoms. This observation suggests that clinicians should assess both KOA and CVD. Furthermore, treating CVD can improve knee symptoms by reducing muscle loads in the lower legs[16].

Our study found that pain severity in KOA patients differed between those with and without CVD (Table VI). Specifically, participants comorbid with KOA and CVD had significantly higher WOMAC and VAS pain scores than those with only KOA. Bagis et al[17] also reported that patients with KOA and varicose veins suffered more pain according to WOMAC and VAS scales. Güneş et al[8] noted that increased intraosseous venous pressure led to increased substance P, which plays an important role in pain response and increased pain perception. In addition, increased pressure in lower limb veins was found to cause resting pain in osteoarthritis[8]. Therefore, both KOA and CVD can cause pain, leading to higher pain sensations in patients comorbid with KOA and CVD than with KOA only. Our population study included few patients with severe CVD forms. That was the

reason why we could not find any significant differences in WOMAC scores among KOA patients with different clinical CVD manifestations. Pain due to musculoskeletal diseases is one of the main causes of chronic pain in the elderly[18]. Therefore, pain in the elderly is a matter of great concern since it affects their quality of life and daily activities. Consequently, when examining patients with KOA, assessing, and treating their pain is essential, especially for those with CVD.

Limitations

Our study had several limitations. First, its cross-sectional study design could not determine the cause-effect relationship between CVD and KOA. Second, its data was not nationally representative since it was conducted in a specialist clinic. Further studies are needed to determine CVD's role in KOA pathogenesis. However, to our knowledge, this is the first study addressing the association between CVD and KOA in elderly Vietnamese men and women, providing some guidance for evaluating and managing these two diseases. Furthermore, it emphasizes the effect of CVD and KOA comorbidity in the elderly. Thus, healthcare system should focus on to improve their symptoms and quality of life.

Conclusions

CVD and KOA are two common conditions in the elderly. There is an association between CVD and KOA through venous stasis and the inflammatory mechanism. Therefore, it is necessary to assess KOA and CVD comorbidity in elderly adults to provide comprehensive treatment. However, their coexistence could cause more pain and limit functional status. Evaluating and managing pain and CVD symptoms are needed in elderly patients with KOA.

Acknowledgements

The authors are grateful to the study participants and the medical staff for their assistance.

Ethics Approval

The study was approved by the Institution Review Board of the University of Medicine and Pharmacy at Ho Chi Minh City (approval number: 574/ĐHYD-HĐĐĐ). Our study was performed in compliance with the principles outlined in the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from all individual patients included in the study.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to privacy concerns, but are available from the corresponding author on reasonable request..

Authors' Contributions

Cao TN and Nguyen MD contributed equally to this article as co-first authors. Cao TN, Nguyen CT, and Nguyen MD gave a substantial contribution in acquisition, analysis, and data interpretation. Cao TN and Nguyen MD prepared, drafted, and revised manuscript critically for important intellectual content. Each author gave the final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Funding

This research received no external funding.

ORCID ID

Cao Thanh Ngoc: 0000-0002-9812-4276; Nguyen Minh Duc: 0000-0001-5411-1492.

References

1) Martel-Pelletier J, Barr AJ, Cicuttini FM, Conaghan PG, Cooper C, Goldring MB, Goldring SR, Jones G, Teichtahl AJ, Pelletier JP. Osteoarthritis. Nature Reviews Disease Primers 2016; 2: 16072.
2) Palazzo C, Nguyen C, Lefevre-Colau MM, Rannou F, Poiraudeau S. Risk factors and burden of osteoarthritis. Ann Phys Rehabil Med 2016; 59: 134-138.
3) Ho-Pham LT, Lai TQ, Mai LD, Doan MC, Pham HN, Nguyen TV. Prevalence of radiographic osteoarthritis of the knee and its relationship to self-reported pain. PLoS One 2014; 9: e94563.
4) Primorac D, Molnar V, Rod E, Jeleč Ž, Čukelj F, Matišić V, Vrdoljak T, Hudetz D, Hajsok H, Borić I. Knee Osteoarthritis: A Review of Pathogenesis

and State-Of-The-Art Non-Operative Therapeutic Considerations. Genes (Basel) 2020; 11: 854.

5) Eberhardt RT, Raffetto JD. Chronic venous insufficiency. Circulation 2014; 130: 333-346.
6) Molnár AÁ, Nádasy GL, Dörnyei G, Patai BB, Delfavero J, Fülöp GÁ, Kirkpatrick AC, Ungvári Z, Merkely B. The aging venous system: from varicosities to vascular cognitive impairment. GeroScience 2021; 43: 2761-2784.
7) Findlay DM. Vascular pathology and osteoarthritis. Rheumatology (Oxford) 2007; 46: 1763-1768.
8) Güneş S, Şehim K, Cüneyt K, Gökmen D, Küçükdeveci AA. Is there a relationship between venous insufficiency and knee osteoarthritis? Turk J Phys Med Rehabil 2020; 66: 40-46.
9) Lesnyak OM, Zubareva EV, Goncharova MG, Maksimov DM. [Lower extremity venous diseases in primary knee osteoarthritis]. Ter Arkh 2017; 89: 53-59.
10) Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M, Howell D, Kaplan D, Koopman W, Longley SIII, Mankin H, McShane DJ, Medsger T Jr, Meenan R, Mikkelsen W, Moskowitz R, Murphy W, Rothschild B, Segal M, Sokoloff L, Wolfe F. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986; 29: 1039-1049.
11) Klimek L, Bergmann KC, Biedermann T, Bousquet J, Hellings P, Jung K, Merk H, Olze H, Schlenter W, Stock P, Ring J, Wagenmann M, Wehrmann W, Mösges R, Pfaar O. Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care: Position Paper of the German Society of Allergology (AeDA) and the German Society of Allergy and Clinical Immunology (DGAKI), ENT Section, in collaboration with the working group on Clinical Immunology, Allergology and Environmental Medicine of the German Society of Otorhinolaryngology, Head and Neck Surgery (DGHNOKHC). Allergo J Int 2017; 26: 16-24.
12) McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Rheum 2001; 45: 453-461.
13) Shelkey M, Wallace M. Katz Index of Independence in Activities of Daily Living (ADL). Director 2000; 8: 72-73.
14) Graf C. The Lawton instrumental activities of daily living scale. Am J Nurs 2008; 108: 52-62.
15) Sternberg SA, Wershof Schwartz A, Karunananthan S, Bergman H, Mark Clarfield A. The identification of frailty: a systematic literature review. J Am Geriatr Soc 2011; 59: 2129-2138.
16) Oga Y, Sugiyama S, Matsubara S, Inaki Y, Matsunaga M, Shindo A. The Effectiveness of Endovenous Thermal Ablation for the Knee Symptoms of the Osteoarthritis with Varicose Veins. Ann Vasc Dis 2021; 14: 108-111.
17) Bagis S, Duche M, Sahin G, Ozer C, Karabiber M, Erdogan C. Coexistence of venous insufficiency and knee osteoarthritis in postmenopausal women and its effect on pain and function. The Pain Clinic 2005; 17: 101-105.
18) Ali A, Arif AW, Bhan C, Kumar D, Malik MB, Sayyed Z, Akhtar KH, Ahmad MQ. Managing Chronic Pain in the Elderly: An Overview of the Recent Therapeutic Advancements. Cureus 2018; 10: e3293.