JK SCIENCE pISSN: 0972-1177

ORIGINAL ARTICLE

Histopathological Alterations in the Wall of Varicose Veins as compared to Normal Vessel

Megha Sharma, Subhash Bhardwaj

Abstract

Background: Varicosity is a complex venous pathology affecting the lower extremities.It affects 5 to 30% of adult population. Varicose veins arise due to incompetence in valves of deep, superficial and/or perforating veins . The exact etiology and pathophysiology of varicose vein disease remain,however unclear. This study aims to look at the histopathological changes in wall of varicose veins and to correlate the changes with normal vessels also. Material and Methods: A total of 120 vein specimens were collected from 42 patients (6 trauma cases and 36 varicose vein cases) at Govt Medical College& Hospital,Jammu for a period of 4 years June 2015 to May 2019. 108 vein specimens were collected from proximal thigh long saphenous vein (LSV) and distal calf varicosites in 36 primary varicose vein patients and 12 specimens from the normal , 6 vascular trauma patients which acted as normal controls while the primary varicose vein patients consisted of 12 females and 24 male patients. **Results:** In our study , varicose vein was more common in younger age group and in males(66.6%) as compared to females (33.3%).50% were in occupations involving prolonged standing.The family history of varicose veins was present in 2.7%. 30.5% patients had a history of smoking. Amongst female patients ,22.2% were multipare and 5.5% had a history of OC pills use. The most common complain was swelling of vein followed by pain and presentation was mainly of varicosity.In varicose vein patients , sections from proximal LSV and distal calf varicosities showed varying degrees of dilation of the lumen,irregular intimal surface and marked hypertrophy of the intima,which was thrown into folds. **Conclusion**:The present study suggests that the main abnormalities in the wall of varicose vein is intimal hypertrophy,thining of muscle layer.

Key Words

Varicose, Intimal media, Hypertrophy

Introduction

Varicosity is a complex venous pathology affecting the lower extremities.It affects 5 to 30% of adult population. [1] The prevalance of varicose veins varies widely from 2% to 56% in men and 1 to 73% in women. [2] In Western nations, varicose veins affect approximately one-third of the adult population. [3] Varicose veins arise due to incompetence in valves of deep, superficial and/or perforating veins. This incompetence leads to reflux of blood causing increase in venous pressure resulting in dilated, elongated or tortuous subcutaneous veins of lower leg. This condition is primarily considered to be a cosmetic problem and widely mistaken to be medically unimportant and given low priority for treatment. [4,5] However the

PG Department of Pathology, GMC, Jammu, Jammu and Kashmir, India

Correspondence to: Dr Megha Sharma. Medical officer, PG Department of Pathology, Government Medical College, Jammu- J&K- India

Manuscript Received: 22.7.2021; **Revision Accepted**: 29.11.2021;

Published Online First: 10 July 2022

Open Access at: https://journal.jkscience.org

Cite this article as: Sharma M, Bhardwaj S.. Histopathological Alterations in the Wall of Varicose Veins as compared to Normal Vessel . JK Science 2022; 24(3):183-87

fact is that the associated pain, swelling, open ulceration and other morbidities increase cost of its management. [3,4] It is not surprising that several studies have found that it affects the quality of life (QoL) of the individual .[5,6] As for socioeconomic impact,it occupies position among top 50 disease to cause leave from work in Brazilian social security system also.[7] Despite it being a common condition affecting adolescents to elderly, the etiological aspect of it is not completely understood . [2,4] Moreover the type of patients who tend to be more vulnerable to the severity or complications in this condition is also not known .

The exact etiology and pathophysiology of varicose vein disease remain,however unclear.Vein wall distensibility is controlled by collagen,elastin and smooth muscle.Loss of tone of varicose veins could be due to defects in these wall components. However,recent histological studies performed on varicose vein walls have lead to several hypothesis with contradicting evidence on connective tissue concentration.Several workers have found collagen decreases in varicose veins.Andreotti et al also found a significant decrease in elastin with an increase in total sugars and soluble,non scleroproteins.[8] In contrast ,Rose and Ahmed [9] and Maurel *et al* [10] have shown that varicose vein walls have a higher than normal collagen content .

Similar contradicting evidence also exists on the pathology of smooth muscle in varicose veins.Several studies have reported an increase in smooth muscle or its activity whereas others reported reduced amount of smooth muscle due to replacement by connective tissue. [11] Rose and Ahmed suggested that seperation of muscle cells by fibrous infiltration prevents them from acting as a unified whole with subsequent alterations in wall tone leading to pathological dilation.

Because of these conflicting reports on the structural abnormalities in the wall of varicose vein, this study aims to look at the histopathological changes in wall of varicose veins and to correlate the changes with normal vessels also.

Material and Methods

To study the pathological changes in the wall of varicose veins, a total of 120 vein specimens were collected from 42 patients (6 trauma cases and 36 varicose vein cases) at Govt Medical College& Hospital,Jammu for a period of 4 years June 2015 to May 2019. 108 vein specimens were collected from proximal thigh long saphenous vein (LSV) and distal calf varicosites in 36 primary varicose vein patients and 12 specimens from the normal , proximal thigh LSV from 6 vascular trauma patients.The trauma patients acted as normal controls ,included 4 males and 2 females with mean age of 28 years and with no clinical evidence of varicose veins.

The primary varicose vein patients consisted of 12 females and 24 male patients.

Inclusion criteria: Patients with lower limb venous disease(varicose vein) were included in the study.

Exclusion criteria: Patients of peripheral artery disease, malignancy, pregnancy,DVT were excluded from the study.

A detailed history related to symptoms and their duration, past history of DVT, family history and occupation were noted from record files. Personal history of smoking,oral contraceptive use in females were also recorded.

The samples of varicose veins collected from patients were routinely fixed in 10% formalin and grossed to obtain representative 3-4mm thick tissue sections, processed for embedding in paraffin wax.3 micron thin sections were cut from paraffin embedded blocks and placed on albumin coated glass slides for hematoxylin and eosin (H&E) staining.The H&E stained slides of normal veins from control subjects were also prepared.All the H&E stained slides of varicose veins were studied to see the changes and all the observed changes were compared with histology of control leg veins.This retrospective study was approved by institutional ethical committee under no IEC/GMC/2021/608 with registration no C-203.

Results

In our study , varicose vein was more common in younger age group(25-40 years) as shown in *table 1*

Varicose veins were more common in males(66.6%,24 cases) as compared to females (33.3%,12 cases). The trauma patients acted as normal controls ,included 4 males and 2 females with mean age 28 years and with no clinical

Table 1. Age wise distribution of cases

Age Group	No Of Cases
11-20 yrs	03
21-30 yrs	14
31-40 yrs	10
41-50 yrs	05
> 50 yrs	04
TOTAL	36

Table 2. Sex wise distribution of cases

Sex	Varicose Vein cases	Control cases
Males	24(66.6%)	4
Females	12(33.3%)	2
Total	36	6

Table 3. Risk Factors

Risk Factors	No Of Cases
Prolonged standing	18(50%)
Smoking	11(30.5%)
Pregnancy	8(22.2%)
Oral contraceptives	2(5.5%)
Family history of varicose veins	1(2.7%)
Trauma	2(5.5%)

Table 4. Clinical presentation

Swelling near ankles	63%
Pain in legs	49.2%
Swelling in entire lower legs	48%
Itching	20%
Cramps & heaviness	18.2%
Superficial thrombophlebitis	14%
Change in skin colour	9.4%
Ulceration & Bleeding	5.3%
Cellulitis	3%

Table5. Histopathological alterations seen in varicose vein(VV) in H&E stain

Pathological changes in V V wall	No of cases
Changes in tunica intima (Intimal hypertrophy, irregular intimal surface)	32
Changes in tunica media (layers of the media disorganized and loose increased amount of intervening fibrous tissue.	26
	30
Changes in tunica adventia (increasecollegen deposition)	19

evidence of varicose veins as shown in *Table 2.*

18 cases (50%) were in occupations involving prolonged standing.The family history of varicose veins was present in one patient (2.7%). 11(30.5%) patients had a history of smoking. Out of 12 female patients ,8 (22.2%) were multipare and 2 (5.5%) had a history of OC pills and 2 cases (5.5%) was associated with history of previous trauma. 15 (41.6 %) patients had received previous medical treatment for varicose vein.

The most common complain was swelling of vein followed by pain and presentation was mainly of varicosity rather than ulceration as illustrated in *table 4*

H&E sections of the normal LSV showed regular intimal surface ,regular circumferential sheets of the medial smooth muscle and a loose adventitial layer. The normal ratio of intima to media was 1:2. At higher magnification the endothelial layer appeared regular and smooth surfaced with a normal proportion of intimal smooth muscle.Both circular and longitudinal muscle layers of the media were tightly packed with a minimal amount of extracellular fibrous tissue.

In varicose vein patients , sections from proximal LSV and distal calf varicosities showed varying degrees of dilation of the lumen,irregular intimal surface and marked hypertrophy of the intima,which was thrown into folds.The ratio of intima to media was reversed at 2:1 in many areas of the wall. At higher magnification the endothelial layer was interupted in many places.The surface showed deep clefts in between thickened intimal folds. There was marked cellular infilteration of the intimal layer.Both the circular and longitudinal muscle layers of the media were loosely packed with increased amount of intervening fibrous tissue.

Discussion

Our study shows that majority of the VV were seen in the young age group. 18 cases (78.2%) were in the age group of 21-30 years. This is in agreement with few Indian studies were the most prevalent age group was 21-40 years. [12] and in with contrast to most of the studies that have shown a steep increase in the prevalence of VV with age, most predominantly in age group 41-60 yrs [4,13] Also ,in the study by D Ketan *et al* [14] the most commonly affected age group was between 51-70 years. Since VV is a chronic condition, there occurs an accumulation of cases with increasing age group. Our

study is a hospital based study rather than a population-based study, so the incidence of VV is higher in young age group patients

Our study shows that the greater proportion of varicose veins were seen in male (16 out of 23,69.5%) as compared to female (7 out of 23,30%) as also observed in other studies probably due to occupationally related risk factors. [12,13] Several other studies on the contrary found a female preponderance among cases. [15-19] Among the 7 female cases studied, 5(21.7%) female were multiparous. One study supported our finding that risk of VV formation increases with parity. [20]

Proportion of varicose veins cases with history of smoking in this study was 34.7 % which was lower than 45.6% reported in an Edinburgh study. [16] Smokers had 1.8 times greater risk in studies done in Finland [2] and France. [21]

In this study family history of varicose veins was reported only one case (4.3 %) compared to other studies (12,13) where it was reported in 12% to 25% cases and increased risk has been noticed elsewhere in other studies. [2] Genetic etiology on venous function and in varicosity has been established too in genetic studies. [22,23] Although the evidence of genetic predisposition for varicose veins is still not highly conclusive, a family history of CVI was reported by 95.5% of the patients in a study by Porciunculla *et al.* [24]

Bilateral presentation of varicose veins was seen in 9.4% to 26% cases in other studies [3,12,13,25] compared to 32.1% observed in this study

Under the CEAP classification, proportion of cases in other studies with C1 was 22% [16], with C2 was 31% to 51.4% [12,16,18,26] , with C3 was 28.6% to 51% (12,16,18,26), with C4 was 11.4% to 28% [12,16,26] , with C5 was 2.9% [12] and with C6 was 17.1% [12] in comparison to ours where more cases were concentrated in C2 andC3 clinical grade, since our study is a hospital based study.

The most predominant presentation in our study was swelling followed by pain.Pain was the second most frequent complaint in the present study reported in 49.2% cases compared to other studies where it was reported between 37.5 to 80%. [12,13,19,27] Edema of the limbs was reported in 42.5% to 65.5% in varicose veins cases elsewhere [16,19,27] compared to 48% reported in this study. Other symptoms like heaviness of legs 53.5%, cramps 53.0%, lipodermatosclerosis 39.0%, superficial thrombophlebitis 33.5%, cellulitis 12.5% and bleeding 9.1% reported in a study done in Malaysia was more than our observations. [19] Another study done in Finland reported itching in 26% cases compared to 20% observed in this study. [27] These skin conditions are usually complications due to late referral of chronic venous insufficiency and ulceration, making cure difficult. [16] This highlights the importance of early diagnosis and management among high risk patients in the settings.In a study done in Bagalkot, India the commonest complication was wound infection (25%) followed by haematoma (6.25%) [12] These complications can be avoided by good nursing care and antibiotic support.

The results of our study show that there is marked intimal hypertrophy in varicose veins,which is either diffuse or zonal and cushion type.The normal arrangement of the intimal SMC was distrupted with loss of demarcation between circular and longitudinal muscle layer,followed by increased thickening of tunica media.This was due to infilteration of extracellular collegen in the tunica media. Ferrerira S [28] also found the thickening of the venouswalls, especially in distal positions and in tunic intima ,to be main and most frequent histological alteration in varicose veins but contradicts that of Mashiah et al who did not observe any changes in the tunica intima.

Our study showed deficiency of both intimal and medial SMCs which were replaced by fibrous tissue.This is inagreement with the view of some previous investigators [9] but contradicts that of others who reported muscle hypertrophy with disorganization of the connective tissue support.

Conclusion

The present study suggests that the main abnormalities in the wall of varicose vein is intimal hypertrophy,thining of muscle layer .So,the role of the SMC and its abnormalities should be further investigated.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

References

1. Eberhardt RT, Raffetto JD. Chronic venous insufciency. Circulation 2014; 130:333-346
2. Beebe-Dimmer JL, Pfeifer JR, Engle JS, Schottenfeld D. The epidemiology of chronic venous insufficiency and varicose veins. Ann Epidemiol 2005;15:175-84.
3 Robertson L, Evans C, Fowkes FG. Epidemiology of chronic venous disease. Phlebology 2008; 23: 103-111
4. Das K, Ahmed S, Abro S, Arain MS, Vericose veins; outcome of surgical management and recurrences, Postgraduate Med J 2014;21:509-13.
5. Schoonover JP, King JT, Gray C, Campbell K, Sherman C. 3 alternatives to standard varicose vein treatment, J Fam Pract 2009;58; 522-26.
6. van Korlaar I, Vossen C, Rosendaal F, Cameron L, Bovill E, Kaptein A. Quality of life in venous disease .Thrombo Haemost. 2003;90: 27-35.
7. Mallick R, Lal BK,Daugherty C. Relationship between patient-reported symptoms,limitations in daily activities, and psychological impact in varicose veins. J Vasc Surg Venous Lymphat Disord 2017;5(2):224-37.
8. Andreotti L, Cornmelli D, Banchi G, Guarnieri M, Serantoni C. Collagen, elastin and sugar content in primary varicose veins. Ric Clin Lab 1978;8:273-85.
9. Rose SS, Ahmed A. Some thoughts on the etiology of varicose veins. J Cardiovasc Surg l986;27:534-43.
10. Maurel E, Azema C, Deloly J, Bouissou H. Collagen of the normal and the varicose human saphenous vein: a biochemical study. Clin Chim Acta 1990; 193:27-37.
11. Mirji P, Emmi S, Joshi CJ. Study of clinical features and management of varicose veins of lower limb. J Clin Diagn Res 2011;5: 1416-20.
12.. Sahu S, Bhushan S, Sachan P. Clinco-anatomical and radiological study ofvaricose veins of lower limb and their management outcomes. Internet Journal of Surgery. 2012;28 (2) :2-9.
13. Nitin J , Abhishai B, Thouseef MF,Devi MU, Ayesha Abna A, et al. A multicenter review of epidemiology and management of varicose veins for national guidance. Annals of Medicine and Surgery2016;8:21-27.
14. Dayma K, Modi V, Kalpita S, Adeesh J. Risk factors associated with varicose veins and health seeking behavior among patients of varicose veins compared to patients with other surgical conditions. International Journal of Scientific Research 2020; 9: 1-4.
15. Lins EM, Barros JW, Appolonio F, Lima EC, Junior MB, Anacleto E. Epidemiologic profile of patients who underwent varicose vein surgery of the lower limbs. J Vasc Bras.2012;11: 301 - 4.
16. Robertson L, Lee AJ, Gallagher K, Carmichael SJ, Evans CJ, McKinstry BH, et al. Risk factors for chronic ulceration in patients with varicose veins: a case control study. J Vasc Surg 2009;49:1490-98.
17. Seidel AC,Campos MB,Campos RB,Harada DS,Rossi RM,Cavalari Junior P,et al. Associacao entre sintomas,veias varicosas e refluxo na veia safena magna aoeco. Doppler J Vasc Bras 2017;16(1):4-10.
18 Tonev AO, Genadiev SG, Dimitrov SG, Zahariev TT, Nachev GK. A retrospective study of 100 patients with varicose veins treated with radiofrequency ablation and stripping. Phlebolymphology 2013; 20 (3) : 150-54
19. Murli NM, Navin ID. Classical varicose vein surgery in a diverse ethnic community. Med J Malays 2008;63: 193-98
20. Lim CS, Davies AH. Pathogenesis of primary varicose veins. Br J Surg 2009;96:1231-42
21. Gourgou S, Dedieu F, Sancho-Garnier H. Lower limb venous insufficiency and tobacco smoking: a case control study, Am J Epidemiol 2002;155: 1007-15.
22. Brinsuk M, Tank T, Luft FC, Busjahn A, Jordan J. Heritability of venous function in humans, Arterioscler. Thromb. Vasc. Biol. 2004;24: 207-11.
23. Ng MYM, Andrew T, Spector TD, Jeffery S. Linkage to the FOXC2 region of chromosome 16 for varicose veins in otherwise healthy, unselected sibling pairs. J Med Gen 2005;42: 235-39
24. Moacir P, Dafne L, Rodrigo A, Celina P, Alexandre F, Nelson W. Clinical, ultrasonographic and histological findings in varicose vein surgery. Revista da Associação Médica Brasileira 2018; 64:729-35.
25. Barros FS, Perez JMG, Zandonade E. Evaluation of pelvic varicose veins using color Doppler ultrasound: comparison of results obtained with ultrasound of the lower limbs, transvaginal ultrasound and phlebography. J Vasc Bras 2010;9:15-23.
26. Ziegler S. Chronic venous disease is highly prevalent in hospital employees. Phlebolymphology 2006;13(3): 150-55.
27. Suominen SV, Heikkinen M, Saaristo R, Zeitlin R, Vainio J, Nordback I, Salenius JP. The profile of leg symptoms, clinical disability and reflux in legs with previously operated Varicose disease. Scand J Surg 2005;94: 51-55.
28. Garrido M, Santos Ferreira C, Sales EA. Varizes de membros inferiores: Patologia. In: Maffei FHA, Lastória S, Yoshida WB, Rollo HA. Doenças vasculares periféricas. 3rd. ed. Rio de Janeiro; Medsi; 2002; 2. pp.1511-20