

A PROSPECTIVE STUDY TO COMPARE HISTOPATHOLOGICAL CHANGES IN SURGICALLY STRIPPED VARICOSE VEINS SPECIMEN AND AUTOPSY CONTROL VEIN SPECIMEN

Sushmitha Nataraj¹, Zeeshan Shaik², Channabasavaraj B³, Ashalatha N⁴, Siddique M Ahmed⁵

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Corresponding Author:

Dr. Sushmitha Nataraj

Email: sushmithan011@gmail.com

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¹Senior Resident, Department of Pathology, BMCRI, Bangalore, India.

²Assistant Professor, Department of Pathology, Shri Atal Bihari Vajpayee Medical College and Research Institute, Bangalore, India.

³Senior Resident, Department of General medicine, BMCRI, Bangalore, India.

⁴Professor, Department of Pathology, BMCRI, Bangalore, India.

⁵Professor and Head of the Department, Department of Pathology, BMCRI, Bangalore, India.

ABSTRACT

Background: Varicose veins are a common manifestation of chronic venous disease characterized by permanent dilatation and tortuosity of superficial veins. Chronic venous hypertension results in progressive structural remodeling of the venous wall, but the associated histopathological changes remain incompletely understood. This study aimed to compare the histopathological features of surgically stripped varicose veins with autopsy control vein specimens. **Materials and Methods:** A prospective cross-sectional study was conducted over three months in the Department of Pathology at a tertiary care teaching hospital. Thirty surgically stripped varicose vein specimens and ten autopsy long saphenous vein specimens serving as controls were evaluated. Clinical details and CEAP classification were recorded. Histopathological assessment was performed using hematoxylin and eosin, Masson's trichrome, and Verhoeff stains. Intimal thickening, internal elastic lamina (IEL) fragmentation, collagen-to-smooth muscle ratio, and fibrosis were assessed using semi-quantitative grading. **Results:** The mean age of patients was 45.3 ± 10.9 years, with a male predominance (70%). Most patients had primary disease with superficial venous reflux (Ep, As, Pr). Moderate intimal thickening (score 2) was observed in 56.7% of cases, while moderate IEL fragmentation (score 2) was present in 66.7%. An increased collagen-to-smooth muscle ratio was noted in 90% of specimens. Grade 3 fibrosis was the most common finding (50%) on Masson's trichrome staining. Compared with autopsy control veins, varicose veins demonstrated marked structural remodelling characterized by intimal hyperplasia, elastic lamina disruption, and increased collagen deposition. **Conclusion:** Varicose veins exhibit characteristic histopathological changes involving all layers of the venous wall, including intimal thickening, elastic lamina fragmentation, increased collagen deposition, and fibrosis. These findings support the role of chronic venous wall remodelling in the pathogenesis of varicose veins and provide a morphological basis for future studies investigating the molecular mechanisms underlying chronic venous disease.

INTRODUCTION

Varicose veins are a spectrum of chronic venous diseases. These are permanently elongated, dilated, tortuous veins leading to pathological circulation. Reversal of blood flow is seen. 23% of US adults are affected with varicose veins.^[1] Varicose veins are equally prevalent in India as that in other parts of western world. In April 2007, 7 surgeons at Chennai created "venous association of India" with aim to promote research and study venous diseases.^[2]

In India varicose veins is more common in males than females, whereas in western nations females are more affected than males. The risk factors include female sex, prolonged standing, immobility, increased intra-abdominal pressure, sports, pregnancy, chronic constipation and many others.^[3]

Varicose veins are indicated by 3-4 mm dilatation of subcutaneous veins and they cause varying degrees of discomfort, heaviness, pain, night cramps, swelling of limbs and excessive fatigue. Apart from conservative management like elevation of limb,

elastic crepe bandage and drugs, most commonly done surgical treatment is Trendelenburg procedure and stripping of veins.^[4]

Many theories initially had concluded that hypoxia and reduced blood flow as the main cause for the disease. But recently studies have disapproved them and lots of research needs to be done in this aspect to know the underlying pathogenesis.

The pathological changes in varicose veins would be assessed by various methods like histopathological and morphometric method, immunohistochemistry(IHC) for smooth muscle cells, matrix metallo proteinases(MMP), (hypoxia inducible factor) HIF levels, smooth muscle cell cultures, increased TGF, fibronectin, VEGF and others. This study highlights the histomorphological changes in varicose veins by routine hematoxylin and eosin stain and special stains like masons trichrome and verhoff.

Objectives

1. To evaluate histopathological changes in surgically stripped varicose vein specimen and autopsy control vein specimen
2. To assess CEAP grading in all the cases.

MATERIALS AND METHODS

A Cross sectional analysis was conducted in the Department of Pathology after approval by ethics committee, at a tertiary care teaching hospital over a three-months period from August 2024 to october 2024. The total sample size was 30. Varicose veins patients who underwent vein stripping and the same specimens received in department of pathology were taken for the study. Only those participants willing to give informed consent were included. Cases of Deep vein thrombosis, venous obstruction from neoplasm and Arterial diseases were excluded from the study. Detailed clinical history was obtained from all study participants, including age, sex, presenting symptoms, and associated risk factors such as occupation, smoking status, pregnancy, and obesity. All patients underwent thorough clinical examination and were classified according to the Clinical-Etiological-Anatomical-Pathophysiological (CEAP) classification system. Clinical classification included C0 (no visible signs of venous disease), C1 (telangiectasia or reticular veins), C2-varicose veins, C3 (edema), C4 (skin and subcutaneous tissue changes, including pigmentation, eczema, or lipodermatosclerosis), C5 (healed ulcer), and C6 (active ulcer). Etiological classification was based on clinical history and categorized as congenital (Ec),

primary (Ep), secondary (Es; post-thrombotic syndrome or trauma), or no venous cause identified (En). Anatomical and pathophysiological classifications were determined using Doppler ultrasonography reports and categorized as superficial (As), deep (Ad), perforator (Ap), or no venous location identified (An), and reflux (Pr), obstruction/thrombosis (Po), combined reflux and obstruction (Pro), or no venous pathophysiology identified (Pn), respectively.

After varicose vein stripping and the same specimen will be taken for histopathological examination in the Department of Pathology. These specimens are received in 10% formalin, after adequate fixation and tissues processing, Appropriate sections of 4-6 micron thick will be taken. It will be stained with hematoxylin and eosin, masson's trichrome and verhoff stain, Stained slides will be scanned with the light microscope. And 10 control long saphenous veins from autopsy(Department of Anatomy) were taken. Intimal thickness was measured and scoring was given as 0- no thickening, score 1 mild thickening, score 2- moderate thickening, score 3- marked thickening. Fragmentation of Internal elastic Lamina was noted and given grade 0- normal, grade 1- mild disruption, grade 2- moderate disruption, grade 3- severe fragmentation/disruption. Collagen: Smooth muscle ratio was noted. Fibrosis was assessed on Masson's Trichrome-stained sections and graded semi-quantitatively according to the extent of collagen deposition within the venous wall. Grade 0 indicated no significant fibrosis, Grade 1 mild fibrosis involving less than 25% of the vessel wall, Grade 2 moderate fibrosis involving 25–50% of the vessel wall, and Grade 3 severe fibrosis involving more than 50% of the vessel wall and grade 4 more than 75% with associated architectural distortion. Similar to study done by Wali et al and Demirkiran M Et al.^[5,6]

RESULTS

A total of 30 patients were included in the study. The mean age was 45.3 ± 10.9 years (range, 20–70 years; median, 44.5 years), and the majority were male (21/30, 70.0%) compared with female (9/30, 30.0%). By occupation, 13 patients (43.3%) were farmers, 11 (36.7%) were engaged in long standing works, 5 (16.7%) in clerical work, and 1 (3.3%) in information technology. Two patients (6.7%) were pregnant at the time of evaluation. Smoking was reported in 20 patients (66.7%), and obesity was present in 16 patients (53.3%).

Table 1: Distribution of Cases According to CEAP Classification (n = 30)

CEAP Classification	Category	Number of Cases (n=30)	Percentage (%)
Clinical (C)	C0 – No visible signs of venous disease	2	6.7
	C1 – Telangiectasia or reticular veins	12	40.0
	C2 – Varicose veins	6	20.0

	C4 – Skin and subcutaneous tissue changes (pigmentation, eczema, lipodermatosclerosis)	3	10.0
	C5 – Healed ulcer	2	6.7
	C6 – Active ulcer	5	16.7
Etiological (E)	Ec – Congenital	7	23.3
	Ep – Primary	15	50.0
	En – No identifiable venous etiology	8	26.7
Anatomical (A)	As – Superficial veins	23	76.7
	Asp – Superficial and perforator veins	4	13.3
	Ap – Perforator veins	2	6.7
	Ad – Deep veins	1	3.3
Pathophysiological (P)	Pr – Reflux	26	86.7
	Pro – Reflux and obstruction	3	10.0
	Pn – No identifiable pathophysiology	1	3.3

With respect to CEAP classification, most of them were C1 Ep As Pr, as given in the table 1.

The mean length of the vein obtained was 50.0 ± 18.4 mm (range, 30–100 mm), with a length of 40 mm being most frequent (13/30, 43.3%), Clots were identified in 8 cases(26.7%).

On the light microscopy, veins from varicose vein patient showed significant changes when compared with the autopsy control veins. Intimal thickness of score 2 was observed in 56.7% cases, fragmentation of Internal elastic Lamina scoring of 2 was noted in 20 cases and most of all the cases 90% showed increased collagen to smooth muscle ratio.

Table 2: Histopathology Findings Summary

Histopathological Parameter	Score	N= 30	Percentage
Intimal Thickness	2	17	56.7%
	3	7	23.3%
	1	6	20.0%
Fragmentation of Internal Elastic lamina	2	20	66.7%
	1	6	20.0%
	3	4	13.3%
Collagen : Smooth muscle Ratio	Increased	27	90.0%
Fibrosis Grading	Grade 3	15	50.0%
	Grade 2	7	23.3%
	Grade 4	4	13.3%
	Grade 0	2	6.7%
	Grade 1	2	6.7%

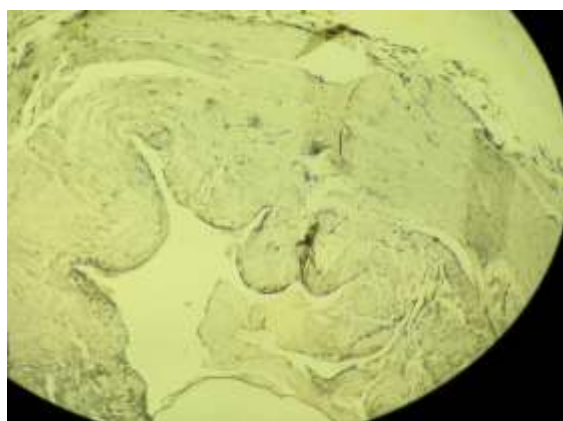


Figure 1: Verhoff stain

DISCUSSION

The present study evaluated the histopathological alterations in surgically stripped varicose veins and compared them with autopsy control long saphenous veins. The majority of patients were middle-aged males, with farmers and individuals involved in prolonged standing occupations constituting the largest occupational group. Smoking and obesity

were also commonly observed. These findings are consistent with the study by Mishra et al,^[3] who reported a higher prevalence of varicose veins among middle-aged males in India, largely attributed to occupational factors and prolonged standing. Most patients belonged to the primary etiology (Ep), superficial venous involvement (As), and reflux (Pr) categories of the CEAP classification, supporting the established role of superficial venous reflux in the pathogenesis of primary varicose veins.

Histopathological examination demonstrated characteristic structural remodelling of the venous wall. Moderate intimal thickening was the most frequent finding, observed in 56.7% of cases, while moderate fragmentation of the internal elastic lamina was seen in 66.7% of cases. Similar findings have been described by Wali et al,^[5] and Demikiran et al,^[6] who reported significant intimal hyperplasia and elastic fibre disruption in varicose veins compared with normal veins. These alterations are could be due to chronic venous hypertension, endothelial injury, and increased matrix metalloproteinase activity, leading to degradation of elastic fibre and progressive thickening of the venous wall. The autopsy control

veins in our study showed preserved venous architecture, highlighting that these changes are disease-related.

A marked increase in the collagen-to-smooth muscle ratio was observed in 90% of cases, and Grade 3 fibrosis was the most common fibrosis grade (50%) on Masson's trichrome staining. These findings indicate progressive extracellular matrix remodelling with replacement of smooth muscle by collagen, resulting in reduced venous elasticity and impaired contractility. Similar observations were reported by Demirkiran et al., who demonstrated increased collagen deposition and extracellular matrix remodelling in patients with chronic venous disease. Our study results were similar to the one done by Naik B et al and noted that among varicose veins as compared to the normal veins, 73% showed increased medial thickening, 47% with focal intimal thickening and 84% showed fragmentation of elastic fibres.^[7]

The inclusion of autopsy-derived control veins is a major strength of the present study, allowing direct comparison with normal venous morphology. The use of routine hematoxylin and eosin stain along with Masson's trichrome and Verhoeff stain enabled us for the assessment of intimal thickening, elastic lamina disruption, and fibrosis. Overall, the findings demonstrate that varicose veins undergo characteristic histopathological remodelling involving all layers of the venous wall. These observations contribute to a better understanding of the pathogenesis of chronic venous disease and provide a morphological basis for future studies evaluating molecular mechanisms and potential therapeutic targets.

Limitations

The present study has certain limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, the study was conducted at a single tertiary care center over a short duration of three months, and therefore may not

represent the broader population. Histopathological assessment was based on semi-quantitative grading, which may be subject to observer variability. Molecular and immunohistochemical markers were not evaluated.

CONCLUSION

Varicose veins showed characteristic histopathological alterations including intimal thickening, fragmentation of the internal elastic lamina, increased collagen-to-smooth muscle ratio, and fibrosis when compared with autopsy control veins. Male sex, prolonged standing occupation, smoking, and obesity were commonly observed among affected patients and may contribute to disease development. These findings support the role of chronic venous wall remodelling in the pathogenesis of varicose veins.

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