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AGE-RELATED MORPHOLOGICAL CHANGES IN INTIMA OF GREAT SAPHENOUS VEIN IN HEALTH AND IN VENOUS DISEASE

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ABSTRACT — Aim: To study and evaluate degree of morphological changes in intima of great saphenous vein (GSV) in patients of different age groups in health and in venous disease.
Materials and methods: We investigated autopsy material of GSV in 60 deceased patients and postoperative material of GSV in 80 patients with venous disease. Four age groups were formed: young age, middle age, older and elderly age. Totally there were 280 GSV fragments. Histological, morphometric, electron microscopic and biochemical studies were performed.
Results: Our results are mainly consistent with the reference data. However, we carried out a comparative study of intima structure in norm and with venous disease in patients of different age. At the same time due to age-related decline in varicose veins morphological changes are progressing. There are areas of endothelium atrophy and signs of fibrotic replacement in young and middle age patients with venous disease, whereas in older and elderly patients desquamation of endothelium and sclerosis were observed.
Conclusion: Progressive degeneration in older and elderly patients with varicose veins promotes morphological changes of GSV and progression of the disease on histological and ultrastructural level that worsens endothelial dysfunction.

KEYWORDS — great saphenous vein (GSV), intima, varicose veins, chronic venous insufficiency, degenerative changes.

INTRODUCTION

Despite advances in medicine and science, some issues on development and pathogenesis of varicose disease (VD) still remain disputable. All over the world the prevalence of varicose veins in elderly people over 60 years of age has been increasing. The reference literature contains extensive data on morphology of venous walls; however we could hardly come across studies dealing withage-related morphological changes in intima of great saphenous vein in patients with VD.

Aim:

To study and evaluate degree of age-related morphological changes of GSV intima in norm and with venous disease.

MATERIALS AND METHODS

The autopsy material of the veins in 60 deceased patients without pathological changes in the wall of the investigated veins of the lower extremities was studied. Age groups of deceased and patients were assigned in accordance with the WHO classification: group 1 (young people); Group 2 (middle-aged people); Group 3 (older people), Group 4 (elderly people). Each group included 15 cases. In 80 patients with 4–6 clinical stages of chronic venous insufficiency (CVI) of lower extremities (CEAP classification), we estimated postoperative material of GSV and divided the fragments between four age groups. Pieces of GSV were obtained from the area located in the upper and middle third of the thigh and the saphenofemoral junction. A total of 280 fragments of GSV were examined (Table 1).

The histochemical study was carried out on paraffin sections stained with hematoxylin and eosin and by Van Gieson. We studied volume fraction (VF) of intima using a morphometric study. In 19 patients we performed ultrastructural study of 133 GSV fragments using a JEM 100 CX electron microscope (JEOL, Japan) at an accelerating voltage of 80 kV. Statistical data processing included the calculation of the arithmetic average (M), its error (m). The significance of the differences was judged by the value of the Student t-test and was considered significant at $P < 0.05$.

RESULTS AND DISCUSSION

In young patients with varicose veins intima is thicker compared to norm. Mostendothelial cells are flattened with heavily elongated cytoplasm and thin side branches. Desquamation of GSV endotheliocytes is focal. The base of thick intima consists of mesenchymal matrix with signs of fatty infiltration; rare

Table 1. *Number of histological examinations*

Groups	Normally		Venous disease	
	Number of cases	Number of GSV fragments	Number of patients	Number of GSV fragments
1	15	30	20	40
2	15	30	20	40
3	15	30	20	40
4	15	30	20	40
Total	60	120	80	160

smooth muscle cells (SMCs) and fibroblasts. During an ultrastructural study the continuity of the endothelial lining persisted. At the same time ultrastructural changes were detected in endotheliocytes which indicates dysregulation of intracellular bioenergy and reducing the activity of metabolic processes in cells. The basal membrane was unevenly thick, in most regions rather thin and discontinuous or absent. Endotheliocytes with total destruction of all intracellular organelles and membrane structures were detected. The subendothelial layer is thin, friable and composed by the connective tissue with separate SMCs that were swollen with fragments of collagen and elastic fibers.

In healthy middle-aged and older patients we observed unevenness of GSV wall thickness. In patchy regions the intima made up of a layer of endothelial cells and a very thin subendothelial layer. In thicker parts of GSV wall subendothelial layer is well expressed with friable smooth muscle cells and elastic net with elastic membrane and longirudinal layer of media externally.

There are an increase in the length of endothelium atrophy and progressing myoelastosis in VD. In intimal stroma there are separate scattered myocytes. It is worth noting that the nature of ultrastructural changes in the wall of GSV depends on the duration of the disease so in patients of middle-aged group suffering from varicose disease for 10 years, the desquamation of the endothelium was determined on a greater length of the venous wall.

In older patients there are an increase in focuses of intimal endothelium desquamation and myelofibrosis in stroma. In stromal intima prevailed connective tissue elements, SMCs and dystrophic fibroblasts. Ultrastructural intima changes in patients of this group are more pronounced and characterized by invagination atrophy lysis of destructively modified endothelial layer.

In elderly patients the thickness of intima was more than 2 times less than that of more young patients. Intima is rarely lined with elongated and highly blended endothelial cells. The elastic net is very rare and has no distinct boundaries. There are increase of endothelial desquamation of intima and preserved endotheliocytes are swollen and damaged. Ultrastructural study confirms the progression of sclerotically-degenerative changes in the form of destruction of the endothelial layer. The basal membrane at the same time was swollen, fragmented, stratified and vacuolar. There are SMCs focal lysis and the destruction of the miofilaments especially in the nuclear zone.

Quantitative analysis of the structure of the intima of the GSV wall with the help of methods of morphometry normally and in varicose diseases in people of different age groups showed that in the normal conditions despite the degenerative changes occurring in the structure of the intima the volume fraction in all age groups has practically equal values and only in senile patients have reliably insignificant ($p > 0.09$) decrease. In groups of young and middle-aged patients a statistically reliable increase in VF of intima was found compared with the patients of elderly and senile age groups ($p < 0.001$). In the group of senile patients the volume fraction of intima is reduced to a greater extent (3.2 times) compared with the patients of young and middle-aged groups. (Fig. 1).

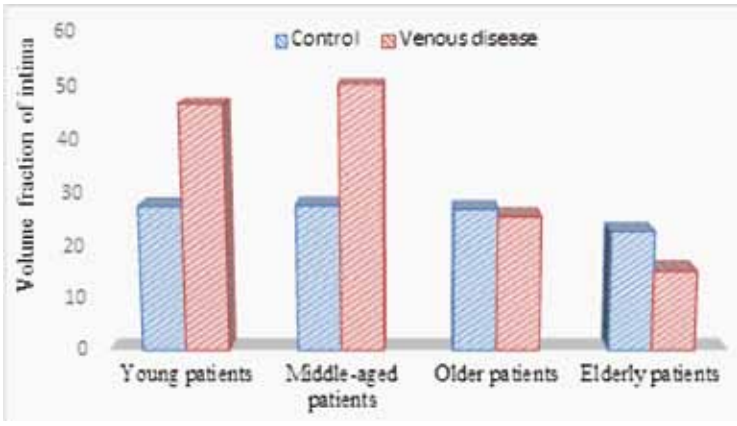

Fig. 1. *VF indexes of GSV intima in people of different age groups normally and in varicose disease (M±m) (VFin %%).*

DISCUSSION

According to some authors the primary cause of the venous disease of the lower limbs are morphological changes in the venous wall primarily in the intima thickness due to deregulation of the components of the connective tissue as well as changes in the structure of the media resulting in transformation of smooth muscle cells. [1, 2, 3] Other authors conclude that endothelial dysfunction plays an important role in chronic venous insufficiency (CVI). This fact is explained by disruption of the morpho-functional state of endothelial cells, which leads to an inflammatory cascade with subsequent pathological changes in the walls of the veins.[4, 5, 6, 7]

CONCLUSION

The results of our study are mainly consistent with the reference literature.However we focused on comparative estimate of intima structure in norm and in venous disease in patientsof different age. At the same timedegenerative changes in varicose veins contribute to morphological changes that are progressingwith age. There are regions of endothelium atrophy and microelastofibrosis in young age and middle age patients with varicose veins while in older and elderly patientsdesquamation of endothelium and sclerosis were noted.

Thus,degenerative processes in older and elderlypatients with varicose veins affect the morphology of GSV and the disease progression on histological and ultrastructural levels, which in its turnaggravates endothelial dysfunction.

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