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

Hurusheed Abdusosidov1,2, Sergey Chudnikh1,2, Vadim Astashov3, Irina Chekmareva4, Evgeny Kravchenko1

1 A.I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow; 2 A.S. Loginov Moscow Clinical Scientific Centre, Moscow; 3 RUDN University, Moscow; 4 A.V. Vishnevsky National Medical Research Center of Surgery, Moscow, Russia

sogdiana99@gmail.com

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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...
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 longitudinal layer of media externally.

In older patients there are an increase in focuses of intimal endothelium desquamation and myxofibrosis in stroma. In stromal intima 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.

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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 sclerotic-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).

**Table 1. Number of histological examinations**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Normally</th>
<th>Venous disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of cases</td>
<td>Number of GSV fragments</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
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</tr>
<tr>
<td>4</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>120</td>
</tr>
</tbody>
</table>

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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 patients of different age. At the same time degenerative changes in varicose veins contribute to morphological changes that are progressing with age. There are regions of endothelium atrophy and microelastofibrosis in young age and middle age patients with varicose veins while in older and elderly patients desquamation of endothelium and sclerosis were noted.

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

REFERENCES