

Quantitative assessment of remodeling in thigh blood vessel walls as a part of the complex approach to peripheral arterial disease

D. Stavrev¹, V. Kniajev², G. Marinov¹

¹Department of Anatomy, Histology and Embryology, Medical University, Varna, ²University Clinic of Vascular Surgery, Hospital "St. Anna", Varna,

The data presented for the thickness of the intima and the media of thigh segments of the FA, VF and GSV are part of a complex comparative analysis of morphological remodeling of the vessel wall of the highway in the lower extremity PAD. They can serve as a basis for interpretation and comparison of results obtained by modern imaging methods and tools for visualization and assessment of the vascular system in patients with PAD of the lower limb undergoing surgery, as well as for a selection criterion of adequate venous graft material in the reconstructive surgery for the treatment of PAD of the lower limb

Key words: TASC for PAD, FA, VF, GSV, remodeling

Introduction

Recommendation 76 of The Trans-Atlantic Inter-Society Consensus for the peripheral arterial disease (TASC for PAD) indicates that close cooperation between different disciplines is essential for timely diagnosis and treatment of patients with critical limb ischemia [1]. The therapeutic tactic in this disease requires an integrated approach involving systematic monitoring of general health status, mode of life, and vasoactive antilipidemic drugs, gene therapy and timely surgical intervention. The high effective results from the application of Endovascular Surgery (EVS) initially in the central vascular regions as aorta, coronary and carotid blood vessels [4] creates a natural desire for rapid transfer of these new medical techniques and technologies in a larger range of blood vessels segments [6], including and surgical treatment of PAD [8]. Without ignoring the surgical bypass, as a „gold standard“ for treatment of occlusive disease, EVS, including Percutaneous transluminal angioplasty (PTA) and stent placement are used more often in patients with risk of underlying disorders, and the combination of surgical bypass with PTA increases [3]. At the same time a transfer of EVS from one anatomic region to another requires not only developing new instruments and equipment but also a new approach to the study of morphological changes of the blood vessels subject to intervention. Thus, in the recent years, the remodeling of the blood ves-

sels from the various segments of the vascular system in the various stages of life, more often are the objects of the study [5].

The aim of this study is to trace the process of remodeling of the vascular wall, through objective metric data on thickness of the intima and media of highway vessels of the thigh in different stages of PAD.

Material and methods

The study covered the 139 biopsies taken from the thigh segments of the Femoral artery, the Femoral vein and Great saphenous vein, during the surgery in the University Clinic of Vascular Surgery, Hospital „St. Anna“, Varna, belonging on the 82 patients with PAD of the lower limb. For the control the necropsies from the analogous blood vessels were taken in the Department of Anatomy, Histology and Embryology, Medical University, Varna. The biopsies and the necropsies were fixed in 10 % formaline solution. Representative parts were embedded in Histowax or in Parafin. Using paraffin microtome 7 mm thick sections were prepared. Staining with Haematoxylin-Eosin and the both three-chrome stainings after van Gieson and after Mason were used to evaluate the histological structure.

Measuring the size of vascular sheaths on photomicrography was done through the program Image Tool 3.00 (The University of Texas Health Science Center in San Antonio). The measuring of the thickness of both tunica intima and tunica media, that are clearly distinguishable, both from each other and from adventitia was performed. In the intima the distance was measured between the internal contour of luminal endothelium and the internal contour of the muscle circular layer of the media. In the media the distance was measured between the innermost contour of the circular muscle layer and the outermost contour of the circular muscle layer. In this method sequentially and separately 2600 measurements were conducted. The obtained metric results were documented in worksheets for every one arterial and venous segment, which was measured, according the clinical diagnosis and performed surgery. Mathematical processing of results was done using the Excel program from Microsoft and was calculated in order:

1. minimum and maximum thicknesses measured in fixed number of areas for the every one layer of the every one artery and vein;
2. calculation of average arithmetic value of the thickness of the every one layer of the every one artery and vein – for the individual and for the group;
3. coefficient of variation for the group.

Results

The results of this study based on morphometric analysis showed that in the three studied vessels the intima is most affected layer of the vascular wall by the process of remodeling. This process is expressed more strongly in the AF intima than in VSM and VF intima. Coming in the underlying section of the wall transformation makes the boundaries between tissues lining the wall difficultly discernible.

Therefore, early signs of remodeling of the intima can be analyzed only in areas in which this layer is with sufficiently well preserved structure. In the lower extremity PAD the thickness on the intima of the AF generally increase. Its average thickness in patients with reconstruction exceeds that of the control by 141% against it. In patients with amputation also intima exceeds that of control but only by 131% against it (Fig.1). Thickening of intima of VSM and VF is an essential element in the remodeling of the

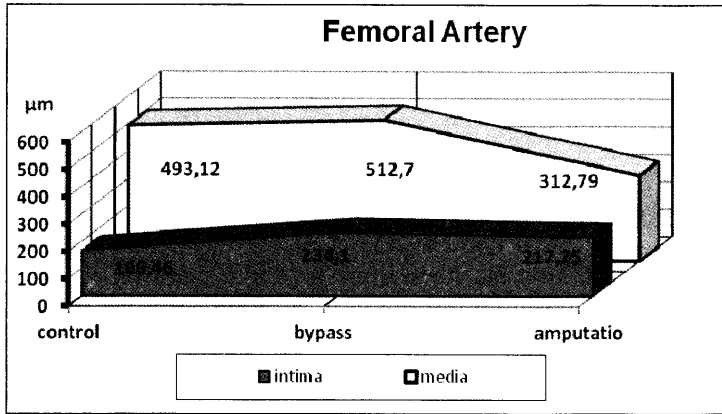


Fig. 1

walls in PAD. Thickness of the intima in the VSM in patients with PAD is uneven and the measured values vary widely. The average thickness of the intima increases and this process is more pronounced in advanced stages of disease. The average thickness of the intima in patients with VSM reconstruction exceeds that of the control by 114% against it. The average thickness of the intima of the VSM in patients with amputation exceeds that of control and is 164% against it (Fig.2). Thickness of the intima of VF in patients with PAD is also uneven and measured values vary widely. In the final stages of PAD the average thickness of the VF intima increases significantly in patients with amputation than that of control, being 167% against it (Fig.3). Comparison of the measured digital characteristics of medium thickness of the intima of the VSM and VF in PAD shows that they have similar values, but their growth is almost two times more intense than that of AF.

The media in AF initially keeps its thickness, but with the progression of PAD significantly reduces. In patients with reconstruction, it is similar to that of control – 104% against it. In patients with amputation the media is significantly thinner – 63% against it. The average thickness of the media of VSM in patients with PAD also increases its thickness and in patients with reconstruction, it is 123% compared to controls. In

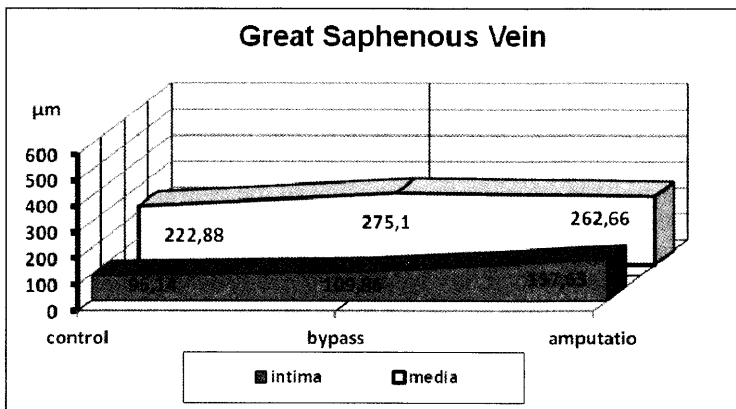


Fig. 2

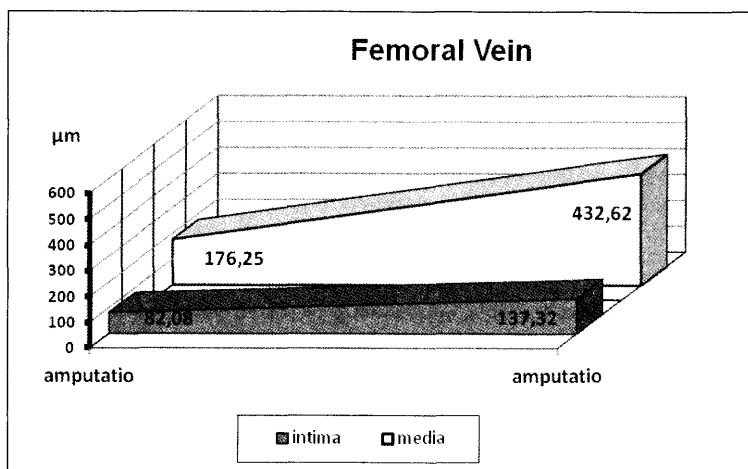


Fig. 3

patients with an amputation, it is 118% compared to controls. The media of VF also greatly increases its thickness and in patients with amputation its average thickness is 245% compared to controls. Thickening of the media of VF wall in patients with amputation is much more pronounced than in the VSM.

Discussion

The process of remodeling of the walls of the thigh vessels at the development of PAD lead to substantial changes in their construction. They have specific quality characteristics in each artery and vein. The proper and accurate interpretation, and evaluation of their effects on the vascular system of the limb, is necessary to be demonstrated through quantitative assessment, first of intima-media thickness. Widespread application of ultrasound measurement of intima-media thickness of carotid arteries, showed the important diagnostic and prognostic value of this approach [2].

1. In all studied patients with PAD, the average thickness of the media of vessels studied is greater than the average thickness of the intima.

2. The intima of the AF in patients who had great amputation is thicker compared to patients with reconstructions, while the media is much thinner.

3. The intima of VSM in patients who had major amputation is thicker compared to patients with reconstructions, while the media did not show significant differences.

4. The thickness of VF intima in patients who had a high amputation showed no significant differences with that of the VSM, while media of VF is thicker.

5. The media is the main and most thick layer of AF, VSM and VF. Our results show, that this layer has a much greater resistance to remodeling of its structure than intima. This resistance can be connected with the fact that media is ontogenetic older than intima.

6. VSM and VF the both had preserved largely its morphological structure and biomechanical properties, and are therefore suitable for use as graft material in reconstructive vascular surgery. In addition, the VF is not only the venous graft with increasing role in the surgery of the lower limb, but it has a great potential for widespread use as material in other vascular segments, too [9, 10].

References

1. Barandon L., L. Leroux, P. Dufourcq, P. Plagnol, C. Deville, C. Duplaa, T. Couffignal, Pessac and Langen, Gene Therapy for Chronic Peripheral Arterial Disease: What Role for the Vascular Surgeon? *An. Vas. Surg.*, 18(6), 2004, 758-765.
2. Collin C. O. Kim - Thanh, H. Beaussier, S. Laurent, P. Boutouyrie. Valeur prédictive de l'épaisseur intima-média de l'artère carotide commune sur le risque de survenue d'événements cardiovasculaires. *Sang Thrombose Vaisseaux*, 20(8), 2008, 393-403
3. De Sanctis J.T. Percutaneous interventions for lower extremity peripheral vascular disease. *Am. Fam. Physician.*, 64(12), 2001, 1965-1972.
4. Hassantash S-A., B. Bikdeli, S. Kalantarian, M. Sadeghian, H. Afshar. Pathophysiology of aortocoronary saphenous vein bypass graft disease. *Asian Cardiovasc. Thorac. Ann.* 16, 2008, 331-336.
5. Kafetzakis, A., G. Kochiadakis, A. et al. Laliotis. Association of subclinical wall changes of carotid, femoral, and popliteal arteries with obstructive coronary artery disease in patients undergoing coronary angiography. *Chest*, 128, 2005, 2538-2543.
6. Met R., U.P. Van Lienden, M.J.W. Koelmay, S. Bipat, D.A. Legemate, J.A. Reekers. Subintimal angioplasty for peripheral arterial occlusive disease: a systematic review. *Cardiovasc. Intervent. Radiol.*, 31, 2008, :687-697.
7. Mizia-Steck, Z. Gąsior¹, B. Zahorska-Markiewicz², M. Holecki², M. Haberk¹, M. Mizia¹, S. Gomułka¹, A. Żak-Gołąb² and A. Gościńska¹ The indexes of arterial structure and function in women with simple obesity: a preliminary study *Heart and Vessels*, 23(4), 2008, 224-229.
8. Puato, M., C. Piergentili, M. Zanardo, et al. Vascular remodeling after carotid artery stenting. *Angiology*, 58,(5), 2007, 565-571.
9. Schulman M.L., L.G. Schulman, A.M. Liedo-Perez. Unusual autogenous vein grafts. *Vasc. Surg.* 26, 1992, 257-264.
10. Stavrev D., G. Marinov, V. Knyazhev. Femoral vein wall remodeling in chronic arterial insufficiency of the lower limb. *Acta Morph. and Anthropol.*, 10, 2005, 78-82.