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·基础研究·

高流体静力压下大隐静脉和脾静脉管壁滋养血管对比研究

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摘　要

目的：观察高流体静力压对大隐静脉和脾静脉管壁滋养血管的影响。

方法：收集曲张大隐静脉和高压性脾静脉标本（疾病组），以及正常大隐静脉和脾静脉标本（正常对照组）。采用 CD34 免疫组化染色与 Masson 染色，计算各组管壁滋养血管的数量和平均截面积，并定量分析。

结果：形态学观察显示，两个疾病组管壁滋养血管均较各自的对照组明显增生。定量分析显示，两个疾病组的滋养血管数量、平均截面积在中膜或外膜，均明显大于各自的正常对照组（均 $P<0.05$）；脾静脉外膜滋养血管数量疾病组与其正常对照组差值明显大于大隐静脉，大隐静脉外膜滋养血管疾病组与其正常对照组平均截面积差值明显大于脾静脉（均 $P<0.05$），但两种血管间以上差值在中膜中的差异均无统计学意义（均 $P>0.05$）。

结论：高流体静力压下大隐静脉和脾静脉管壁滋养血管明显增生，两者变化存在异质性，大隐静脉中以管径增大为主，脾静脉中以数量增多为主。

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关键词　流体静力压；隐静脉；脾静脉；滋养血管

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Comparative study of vasa vasorum in the wall of the great saphenous vein and splenic vein under high hydrostatic pressure

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ABSTRACT

Objective: To observe the impact of high hydrostatic pressure on vasa vasorum in the walls of the great saphenous vein and splenic vein.

Methods: The specimens of great saphenous varicose vein and portal hypertension-splenic vein (disease groups), along with the specimens of normal great saphenous vein and splenic vein (normal control groups)

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were collected. CD34 immunohistochemical staining and Masson staining were performed to calculate the number and cross-sectional area of the vasa vasorum in each group of vessel walls, and quantitative analysis was also conducted.

Results: Morphological observation showed that there was remarkable vasa vasorum proliferation in both disease groups compared with their paired normal control groups. Quantitative analysis showed that the number and cross-sectional area of the vasa vasorum in either adventitia or tunica media in both disease groups were significantly higher than those in their paired normal control group (all $P<0.05$); the difference in number of the adventitial vasa vasorum between disease group and normal control group of the splenic vein was significant higher than that of the great saphenous vein, while the difference in average cross-sectional area of the adventitial vasa vasorum between disease group and normal control group of the greater saphenous vein was significantly higher than that of the splenic vein (both $P<0.05$), but both the differences in the tunica media between the two vessels had no statistical significance (both $P>0.05$).

Conclusion: Under high hydrostatic pressure, the vasa vasorum is proliferated in the wall of the great saphenous vein and splenic vein, but its proliferation pattern has heterogeneity, which presented in the great saphenous vein mainly as enlargement of lumen size while in splenic vein mainly as increase of number.

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KEYWORDS Hydrostatic Pressure; Saphenous Vein; Splenic Vein; Vasa Vasorum

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所谓滋养血管是指营养血管壁的微小动静脉，主要分布在血管壁外膜和中膜外层[1]。研究[2-3]表明，冠状动脉粥样硬化斑块的滋养血管渗透性增加，血流减少，白细胞黏附和渗出增加。近期对静脉管壁滋养血管的研究主要集中在下肢慢性静脉功能不全和移植的大隐静脉[4-6]。资料[7]显示，动脉管壁滋养血管存在着异质性，即不同血管床外膜滋养血管存在不同分布结构。前期笔者[8]对浅表血栓性静脉炎管壁滋养血管研究发现，外膜滋养血管数量和密度明显增多。本研究对高流体静力压下大隐静脉和脾静脉管壁滋养血管的密度和平均截面积进行对比分析，探讨不同静脉管壁滋养血管的异质性。

1 资料与方法

1.1 一般资料

标本来源：所有病例由潍坊医学院人类研究伦理委员会批准。⑴ 疾病组：选取标本来自我院2009年6月—2012年6月间住院的患者。其中行高位结扎剥脱加旋切治疗的大隐静脉曲张患者20例，男12例，女8例；平均43（23~46）岁；术前经彩色多普勒超声检查，确诊为原发性大隐静脉曲张，按CEAP分类选取C_2~C_3；病程5~8年。行脾大部切除大网膜胸骨后固定术治疗的门静脉高压症患者14例，男8例，女6例；平均年龄42（21~44）岁；确诊为乙型肝炎后肝硬化，肝功能Child分级为A、B级，伴有脾功能亢进；病程为5~8年。⑵ 正常对照组：创伤后下肢行截肢术而大隐静脉无损伤者20例，男14例，女6例，年龄40(22~45)岁；外伤性脾破裂脾静脉无损伤者14例，男9例，女5例；平均年龄39（20~43）岁，共34例。

1.2 实验方法

制备石蜡切片：术中取膝关节下方大隐静脉主干3~4 mm和脾门处脾静脉主干2~3 mm各1段，共68份标本，用10%福尔马林固定，常规脱水、包埋、4 μm厚连续切片，备1张行苏木精－伊红（HE）染色。

1.2.1 Masson染色和免疫组化 每个标本切片15份，每5份1组进行Masson染色及CD34免疫组化。免疫组化：pH8.5，EDTA抗原修复，0.3% H_2O_2和山羊血清封闭，免疫组织化学采用SP法。一抗4 ℃孵育过夜（鼠抗人CD34单克隆抗体标记内皮

细胞），DAB 显色，苏木素复染，常规脱水、封片。阴性对照以 PBS 代替一抗，光镜下进行血管壁组织形态学分析。

1.2.2 滋养血管计数　光镜（200 倍）下，采用 3、6、9、12 四点法，计数 10 个视野中管壁中膜和外膜滋养血管数量并取平均值，分别计算滋养血管数量差值（疾病组 – 正常对照组）。截面积测量：每 1 组取 5 张照片，用 Image-Pro Plus 图像处理获得滋养血管截面积，取平均值，分别计算滋养血管平均截面积差值（疾病组 – 正常对照组）。判断标准：光镜下大隐静脉滋养血管管径在 5~75 μm 范围；脾静脉滋养血管管径在 5~65 μm 范围。CD34 试剂盒由北京中杉生物技术有限公司提供，Masson 染色试剂由珠海贝索生物技术有限公司提供。光学显微镜用日本产奥林巴斯 BX51 型。

1.3 统计学处理

采用 SPSS 16.0 统计软件，数据用均数 ± 标准差（$\bar{x} \pm s$）表示，差值计量资料采用两独立样本 t 检验，P<0.05 为差异有统计学意义。

2 结　果

2.1 各组光镜下滋养血管的分布情况

大隐静脉疾病组滋养血管：外膜和中膜外层增多，呈密集线性排列，中膜内层和内膜呈零星散在分布；大隐静脉正常对照组滋养血管：外膜呈稀疏散在分布，中膜外层偶见，内膜未见。脾静脉疾病组滋养血管：外膜和中膜外层增多，呈密集线性排列，中膜内层和内膜呈零星散在分布。脾静脉正常对照组滋养血管：外膜呈稀疏散在分布，中膜外层偶见，内膜未见（图 1–2）。

2.2 滋养血管密度和平均截面积差值的定量比较

两个疾病组的滋养血管数量、平均截面积在中膜或外膜，均明显大于各自的正常对照组（均 P<0.05）。脾静脉管壁外膜滋养血管数量差值明显高于大隐静脉，差异有统计学意义（P<0.05）；大隐静脉外膜膜滋养血管平均截面积差值明显高于脾静脉，差异有统计学意义（P<0.05）。两种血管中膜滋养血管密度差值和平均截面积差值差异无统计学意义（P>0.05）（表 1）。

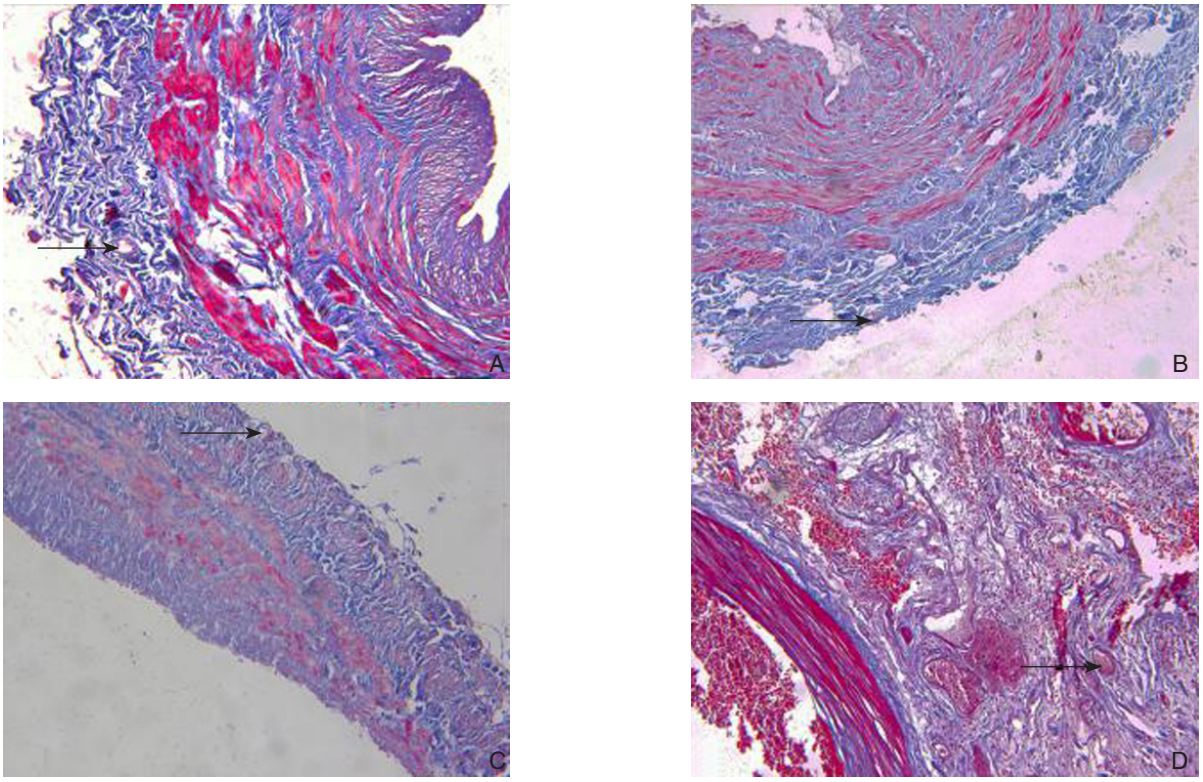

图 1　各组血管 Masson 染色（×200）　A：大隐静脉疾病组；B：大隐静脉正常对照组；C：脾静脉疾病组；D：脾静脉正常对照组

Figure 1　Masson staining for each group　A: Disease group of the great saphenous vein; B: Normal control group of the great saphenous vein; C: Disease group of the splenic vein; D: Normal control group of the splenic vein

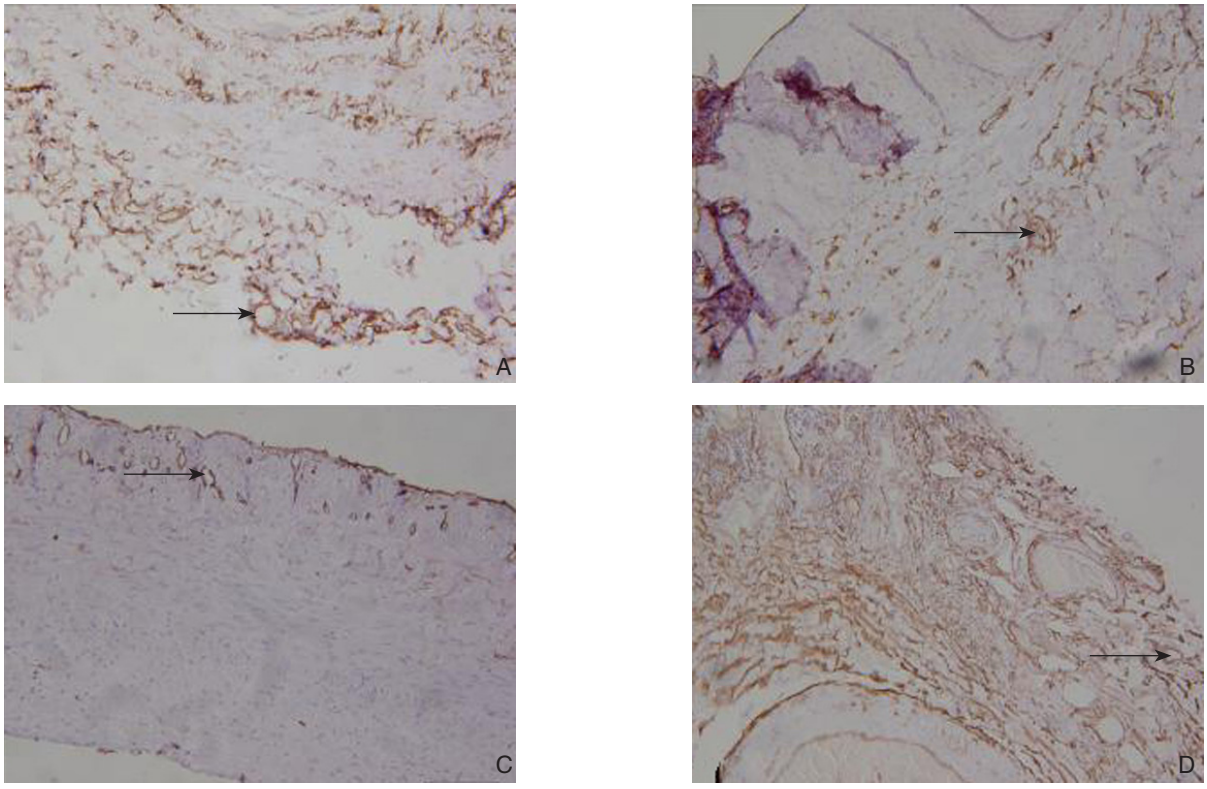

图 2 各组血管 CD34 免疫组化染色（×200） A：大隐静脉疾病组；B：大隐静脉正常对照组；C：脾静脉疾病组；D：脾静脉正常对照组

Figure 2 Immunohistochemical for CD34 in each group (×200) A: Disease group of the great saphenous vein; B: Normal control group of the great saphenous vein; C: Disease group of the splenic vein; D: Normal control group of the splenic vein

表 1 两种静脉管壁滋养血管平均数量和平均截面积差值的定量比较

Table 1 Quantitative comparison of the difference in average number and cross-sectional areas of vasa vasorum between the two types of veins

参数	大隐静脉		脾静脉	
	疾病组	正常对照组	疾病组	正常对照组
中膜				
血管密度（个 /HP）	1.90 ± 2.60[1)]	0.80 ± 1.05	3.80 ± 2.62[1)]	2.20 ± 1.81
平均截面积（μm^2）	164.92 ± 21.53[1)]	127.36 ± 24.63	148.26 ± 52.89[1)]	124.23 ± 48.82
血管密度差值	1.10 ± 2.60		1.60 ± 2.62	
截面积差值	37.56 ± 21.53		24.03 ± 52.89	
外膜				
血管密度（个 /HP）	15.20 ± 9.07[1)]	8.20 ± 5.45	23.60 ± 7.62[1)]	9.40 ± 4.43
平均截面积（μm^2）	742.01 ± 381.10[2)]	533.19 ± 96.11	377.44 ± 188.14[1)]	318.50 ± 132.33
血管密度差值	7.00 ± 9.07[2)]		14.20 ± 7.62	
截面积差值	208.82 ± 381.10[2)]		58.94 ± 188.14	

注：1）与各自正常对照组比较，$P<0.05$；2）与脾静脉比较，$P<0.05$

Note: 1) $P<0.05$ *vs*. paired normal control group; 2) $P<0.05$ *vs*. splenic vein

3 讨 论

追溯至 19 世纪初期，Voigt[9] 率先提出滋养血管结构概念。1876 年 Köester[10] 首先描述动脉粥样硬化斑块新生血管形成。所谓滋养血管包括动脉滋养血管，毛细血管网，静脉滋养血管 [11]。血管壁平滑肌细胞小于 29 层，滋养血管分布在管壁外膜层，大于 29 层，管壁外膜滋养血管可穿入中膜外层 [12]。血管壁外膜和中膜层的营养和氧气由滋养血管提供，内膜由管腔内血流以弥散形式提供。滋养血管可为运送的营养物质提供交换面积，并能吸收血管壁周围组织的代谢物质 [13]。大的滋养血管壁含有平滑肌，中的滋养血管仅有内皮构成。静脉壁滋养血管较动脉壁多，大动脉管壁滋养血

管可由外膜进入中膜外层，有的延伸至中膜全层[14]。在生理和病理状态下，血管壁本身具有较强的代偿适应性，可通过血管增生方式来提供血管壁的营养[15]。当血管腔内氧分压下降时，滋养血管可代偿性膨胀。因此，急性缺氧时，大的动脉和肌性静脉管壁滋养血管会增多以补偿所需营养[16]。研究[17]发现，大隐静脉管壁滋养血管沿主干平行纵轴分布，静脉管壁滋养血管数量和密度比动脉多。曲张静脉和浅表血栓性静脉炎管壁滋养血管明显增多[18]。可见，缺氧和静脉高压可诱导静脉壁内膜和中膜增厚，继发滋养血管增多，以适应管壁重塑的病理需求[19]。

关于动静脉管壁滋养血管形态、密度及功能的研究文献已有报道，主要涉及动脉粥样硬化斑块、正常大隐静脉、慢性静脉功能不全 3 个方面。Galili 等[7]采用微计算机扫描技术，对不同血管床外膜滋养血管结构特征（血管壁面积、血管数量、血管密度）进行观察分析，发现冠状动脉滋养血管最多，肾动脉次之，腹主动脉最少，认为动脉管壁滋养血管存在异质性。一组研究资料显示，采用传统技术（静脉骨骼化）和非接触血管技术获取大隐静脉，光镜和电镜下观察发现，非接触技术获取的静脉管壁滋养血管数量明显增多，提示此方法可完整地保留管壁外膜滋养血管[20]。Kachlík 等[21-22]和 Lametschwandtner 等[23]研究证实，大隐静脉管壁中膜分疏松内层和致密外层，厚度相似，内外层之间存在滋养血管网。外膜滋养血管伴随结缔组织纤维呈纵向分布，中膜外层围绕平滑肌细胞层呈环形分布。静脉管壁高压时，滋养血管可出现膨胀或延伸。文献[24]报道，下肢曲张静脉和浅表血栓性静脉炎管壁内膜和中膜增生，滋养血管明显增多，内膜则保持无血管化。认为血管壁滋养血管增多是一种损伤代谢情况下继发性血管反应。由此表明，曲张静脉时，由于管壁微循环流量降低，氧分压下降，在维持血管壁的完整性方面滋养血管起决定性作用[25]。

本研究发现，曲张大隐静脉和高压性脾静脉管壁滋养血管具有如下分布特征：(1) 两组外膜层滋养血管数量明显增多，并呈密集线性分布；(2) 滋养血管穿入中膜全层，呈零星散在分布；(3) 高压性脾静脉管壁外膜滋养血管密度与其对照组的差值明显高于曲张大隐静脉与其对照组的差值；(4) 大隐静脉平均截面积与其对照组的差值明显高于高压性脾静脉。结果提示，高血流动力因素（高流体静力压、高跨壁压、高移动静脉压）与静脉管壁机械力的动力传感和动力传导有关，容易触发管壁新生血管形成[26-28]。静脉缺氧是静脉高压并存因素，可引起管壁炎症改变和管壁重塑效应[29-31]。管壁滋养血管的增多和延伸，可补偿内膜和中膜增生所造成的血供不足，维护其血管壁的完整性和功能性。脾静脉管壁外膜滋养血管密度差值高，可能与脾静脉内膜和中膜差值增厚明显有关[32]。外膜高密度的滋养血管可能是维持高压性静脉管壁氧供的基本条件。大隐静脉管壁外膜滋养血管平均截面积差值高，说明在下肢静脉高压时滋养血管膨胀是一种病理适应形式。滋养血管单位面积反映微血管密度，并与血管壁氧供需求有关[22]。笔者认为，曲张大隐静脉和高压性脾静脉处于两种不同的静脉高压环境（下肢静脉高压和门静脉高压），血氧含量不同[33-34]，高压的代偿变化不同（大隐静脉膨胀、扭曲、延长；脾静脉膨胀、瘤样变）[35-36]，管壁的厚薄不同[37-38]，故在高流体静力压下两种静脉管壁滋养血管存在异质性，即脾静脉以数量增多为主，大隐静脉以管径增大为主。本研究证实，静脉管壁滋养血管密度和形态的变化取决于静脉高压（流体静力压、跨壁压、移动静脉压）的程度及管壁对营养和氧气的需求。

参考文献

[1] Baikoussis NG, Apostolakis EE, Papakonstantinou NA, et al. The implication of vasa vasorum in surgical diseases of the aorta[J]. Eur J Cardiothorac Surg, 2011, 40(2):412–417.

[2] Gössl M, Versari D, Hildebrandt HA, et al. Segmental heterogeneity of vasa vasorum neovascularization in human coronary atherosclerosis[J]. JACC Cardiovasc Imaging, 2010, 3(1):32–40.

[3] Rademakers T, Douma K, Hackeng TM, et al. Plaque-associated vasa vasorum in aged apolipoprotein E-deficient mice exhibit proatherogenic functional features in vivo[J]. Arterioscler Thromb Vasc Biol, 2013, 33(2):249–256.

[4] Tonar Z, Kural T Jr, Kochov á P, et al. Vasa vasorum quantification in human varicose great and small saphenous veins[J]. Ann Anat, 2012, 194(5):473–481.

[5] Dreifaldt M, Souza D, Bodin L, et al. The vasa vasorum and associated endothelial nitric oxide synthase is more important for saphenous vein than arterial bypass grafts[J]. Angiology, 2013, 64(4):293–299.

[6] Sepehripour AH, Jarral OA, Shipolini AR, et al. Does a 'no-touch' technique result in better vein patency?[J]. Interact Cardiovasc Thorac Surg, 2011, 13(6):626–630.

[7] Galili O, Herrmann J, Woodrum J, et al. Adventitial vasa vasorum heterogeneity among different vascular beds[J]. J Vasc Surg, 2004,

　

40(3):529–535.

[8] Chu H, Yan F, Zhao J, et al. Assessment of vasa vasorum in the walls of thrombophlebitic saphenous vein[J]. Int Angiol, 2013, 32(5):459–464.

[9] Voigt CA. De systemate intermedio vasorum ejusque radicibus. Microscopico-anatomica. Vindobonae,Ueberreuter, 1840.

[10] Köester W. Endarteriitis and arteriitis[J]. Berl Klin Wochenschr, 1876, 13:454–455.

[11] Schoenenberger F, Mueller A. On the vascularization of the bovine aortic wall[J]. Helv Physiol Pharmacol Acta, 1960, 18:136–150.

[12] Wolinsky H, Glagov S. Nature of species differences in the medial distribution of aortic vasa vasorum in mammals[J]. Circ Res, 1967, 20(4):409–421.

[13] Williams JK, Heistad DD. Structure and function of vasa vasorum[J]. Trends Cardiovasc Med, 1996, 6(2): 53–57.

[14] Dashwood MR, Anand R, Loesch A, et al. Hypothesis: a potential role for the vasa vasorum in the maintenance of vein graft patency[J]. Angiology, 2004, 55(4):385–395.

[15] Wheater PR, Burkitt HG, Daniels VG. In Functional Histology[M]. London, UK: Churchill Livingstone, 1987:121–128.

[16] Heistad DD, Armstrong ML, Amundsen S. Blood flow through vasa vasorum in arteries and veins: effects of luminal PO2[J]. Am J Physiol, 1986, 250(3 Pt 2):H434–442.

[17] Minnich B, Lametschwandtner A, Kachlik D, et al. Spatial arrangement of vasa vasorum of the human great saphenous vein: scanning electron microscopy and 3D-morphometry of vascular corrosion casts[J]. Microsc Microanal, 2005, 11(Suppl 2):174–175.

[18] Lefebvre D, Lescalie F. Vascularization of the wall of the superficial veins. Anatomic study of the vasa vasorum[J]. J Mal Vasc, 1996, 21(Suppl C): 245–248.

[19] Langheinrich AC, Kampschulte M, Buch T, et al. Vasa vasorum and atherosclerosis-Quid novi?[J]. Thromb Haemost, 2007, 97(6):873–879.

[20] Dreifaldt M, Souza DS, Loesch A, et al. The "no-touch" harvesting technique for vein grafts in coronary artery bypass surgery preserves an intact vasa vasorum[J]. J Thorac Cardiovasc Surg, 2011, 141(1):145–150.

[21] Kachl í k D, Lametschwandtner A, Rejmontov á J, et al. Vasa vasorum of the human great saphenous vein[J]. Surg Radiol Anat, 2003, 24(6):377–381.

[22] Kachlík D, Baca V, Stingl J, et al. Architectonic arrangement of the vasa vasorum of the human great saphenous vein[J]. J Vasc Res, 2007, 44(2):157–166.

[23] Lametschwandtner A, Minnich B, Kachlik D, et al. Three-dimensional arrangement of the vasa vasorum in explanted segments of the aged human great saphenous vein: scanning electron microscopy and three-dimensional morphometry of vascular corrosion casts[J]. Anat Rec A Discov Mol Cell Evol Biol, 2004, 281(2):1372–1382.

[24] Kachlík D, Stingl J, Sosna B, et al. Morphological features of vasa vasorum in pathologically changed human great saphenous vein and its tributaries[J]. Vasa, 2008, 37(2):127–136.

[25] Maurice G, Wang X, Lehalle B, et al. Modeling of elastic deformation and vascular resistance of arterial and venous vasa vasorum[J]. J Mal Vasc, 1998, 23(4):282–288.

[26] Recek C. Venous pressure gradients in the lower extremity and the hemodynamic consequences[J]. Vasa, 2010, 39(4):292–297.

[27] Zamboni P, Lanzara S, Mascoli F, et al. Inflammation in venous disease[J]. Int Angiol, 2008, 27(5):361–369.

[28] Atta HM. Varicose veins: role of mechanotransduction of venous hypertension[J]. Int J Vasc Med, 2012, 2012:538627. doi: 10.1155/2012/538627.

[29] Lim CS, Kiriakidis S, Paleolog EM, et al. Increased activation of the hypoxia-inducible factor pathway in varicose veins[J]. J Vasc Surg, 2012, 55(5):1427–1439.

[30] Lim CS, Gohel MS, Shepherd AC, et al. Venous hypoxia: a poorly studied etiological factor of varicose veins[J]. J Vasc Res, 2011, 48(3):185–194.

[31] Chu HB, Yan F, Zhao JH, et al. Assessment of the infiltration of inflammatory cells in the walls of thrombotic varicose veins[J]. Angiology, 2013, 64(1):69–72.

[32] 褚海波 , 边小维 , 徐永波 , 等 . 高血流动力对大隐静脉和脾静脉血管重塑的影响 [J]. 中华普通外科学文献杂志 (电子版), 2011, 5(2):100–103.

[33] MacPhail CM, Monnet E, Gaynor JS. Evaluation of splanchnic oxygen extraction ratio as an index of portal vein pressure in dogs[J]. Am J Vet Res, 2002, 63(1):15–18.

[34] Murphy MA, Hands L. Is arteriovenous shunting involved in the development of varicosities? A study of the intraluminal pressure and oxygen content in varicose veins[J]. Phlebology, 2008, 23(3):137–141.

[35] Raffetto JD, Khalil RA. Mechanisms of varicose vein formation: valve dysfunction and wall dilation[J]. Phlebology, 2008, 23(2):85–98.

[36] Yang Z, Zhang L, Li D, et al. Pathological morphology alteration of the splanchnic vascular wall in portal hypertensive patients[J]. Chin Med J (Engl), 2002, 115(4):559–562.

[37] Li T, Ni JY, Qi YW, et al. Splenic vasculopathy in portal hypertension patients[J]. World J Gastroenterol, 2006, 12(17):2737–2741.

[38] Jian FG, Chu HB, Liu GZ, et al. Morphological characteristics of the walls of thrombophlebitic saphenous vein[J]. Phlebology, 2013. [Epub ahead of print].

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