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RESEARCH ARTICLE

Arteriolar Atherosclerosis and Pathological Intussusceptive Remodeling in Heart Disease

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ABSTRACT

Background. Microvascular dysfunction is a major contributor to morbidity and mortality in various cardiovascular diseases. In patients with congenital heart disease (CHD), rheumatic heart disease (RHD), ischemic heart disease (IHD), structural remodeling of intramyocardial arterioles may play an important role in the development of microvascular dysfunction and progressive cardiac impairment.

Materials and Methods. Right atrial appendage specimens were obtained during cardiac surgery. Tissue samples were processed for light microscopy (LM) and transmission electron microscopy (TEM) after embedding in epoxy resin. Histological and ultrastructural analyses were performed to evaluate arteriolar remodeling.

Results. Intramyocardial arterioles demonstrated a distinct pattern of pathological intussusceptive growth, which differs from physiological intussusceptive angiogenesis. The formation of de novo arterioles from pre-existing vessels occurred through mechanisms involving vascular invagination and the formation of transluminal tissue pillars (intussusceptive pillars). Vessel lumina varied considerably during this process, and several de novo arterioles could simultaneously arise from a single pre-existing arteriole. Atherosclerosis observed in advanced stages of CHD, RHD, and IHD indicates that pathological intussusceptive arteriolar growth is involved in vascular remodeling in all examined patients. These changes were most pronounced in patients with PVS and CAD. According to a five-point semiquantitative grading system, the severity of pathological microvascular growth reached 4 points, indicating marked structural remodeling.

Conclusions: Pathological intussusceptive arteriolar growth appears to represent a previously underrecognized mechanism of microvascular remodeling in cardiovascular diseases. This process may contribute to microvascular dysfunction and progressive myocardial impairment associated with advanced atherosclerotic disease.

Keywords: CHD, RHD, IHD, arteriolar atherosclerosis; intussusceptive remodeling; LM; TEM

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Introduction

Cardiovascular diseases comprise a broad spectrum of disorders, including CHD, RHD, and IHD. Despite their different etiologies, advanced stages of these diseases are commonly associated with impaired myocardial perfusion, reduced oxygen and nutrient delivery, and progressive heart failure. In patients with CHD[3] and RHD[2], myocardial ischemia may develop even in the absence of significant epicardial coronary artery lesions, whereas coronary arteriosclerosis represents the principal pathological substrate of IHD.

Increasing evidence suggests that many patients with angina and myocardial ischemia do not exhibit obstructive coronary artery disease but instead present with abnormalities of the coronary microcirculation. Coronary microvascular dysfunction (CMD)[25] has therefore emerged as an important mechanism contributing to myocardial ischemia and adverse cardiovascular outcomes.

The myocardial vascular supply is provided by an extensive vascular network consisting of epicardial coronary arteries, intramyocardial arteries, arterioles, and capillaries.[9] The coronary microcirculation, comprising arterioles and capillaries, plays a central role in myocardial oxygen delivery and metabolic regulation.[9,10, 1] The structural organization of the microvascular network determines vessel diameter, length, branching pattern, blood flow velocity, wall shear stress, and tissue oxygenation, thereby maintaining adequate myocardial perfusion.[9,6,21,22]

Coronary microvascular dysfunction encompasses a broad spectrum of structural and functional abnormalities affecting the coronary microvasculature. These alterations impair coronary blood flow regulation and contribute to myocardial ischemia despite angiographically normal or minimally diseased epicardial coronary arteries.[7,21]

Under physiological conditions, coronary arterioles possess thin vascular walls consisting of endothelial cells, a single layer of smooth muscle cells, and a minimal amount of connective tissue surrounding a relatively narrow lumen. During disease progression, arterioles undergo structural remodeling characterized by smooth muscle cell hypertrophy, thickening of the vascular wall, extracellular matrix deposition, reduced vascular elasticity, and altered hemodynamic properties. These changes are accompanied by activation of vascular growth mechanisms and progressive atherosclerosis.[19]

Morphological remodeling of coronary arterioles has been described in CAD;[16,17,18,20] however, the mechanisms responsible for pathological arteriolar growth remain poorly understood. Furthermore, direct investigation of coronary arteriolar remodeling and capillary alterations is difficult in clinical studies because myocardial tissue is rarely available for detailed morphological examination.[23]

Patients with advanced CHD, RHD, and IHD frequently require open-heart surgery. During these procedures, a portion of the right atrial appendage is routinely excised, providing valuable myocardial tissue for histopathological investigation. Tissue specimens embedded in epoxy resin, including both archived collections and newly obtained biopsies, are suitable for high-resolution examination using both light microscopy (LM) and transmission electron microscopy (TEM). These techniques enable detailed visualization of coronary arterioles and identification of arteriosclerotic lesions and structural remodeling.

The present study aimed to investigate the morphological mechanisms of pathological arteriolar remodeling in the myocardium of patients with CHD, RHD, and IHD, with particular emphasis on pathological intussusceptive arteriolar growth as a potential mechanism contributing to coronary microvascular dysfunction.

Materials and Methods

Small fragments of the right atrial appendage were obtained from patients undergoing routine cardiac surgery, including one patient with congenital heart disease (CHD), two patients with rheumatic heart disease (RHD), and six patients with ischemic heart disease (IHD).

Immediately after excision, biopsy specimens were fixed in a cold mixture of paraformaldehyde and glutaraldehyde, followed by post-fixation in osmium tetroxide (OsO_4). The tissues were dehydrated through a graded series of ethanol and acetone and embedded in epoxy resin.

Semi-thin sections (approximately 1 µm) and ultrathin sections (approximately 50 nm, 500 Å) were prepared using a Reichert ultramicrotome. Ultrathin sections were double-stained with uranyl acetate and lead citrate and examined using a Philips EM 10 transmission electron microscope (TEM). Semi-thin sections were stained with 1% Azure II and examined using a digital light microscope (LM) equipped with a ×40 objective and ×10 ocular.[15]

All light microscopic images were analyzed to evaluate the pathological growth of myocardial microvessels, with particular attention to intussusceptive arteriolar growth.

A semi-quantitative assessment of arterioles was performed using a 5-point scale to evaluate pathological microvascular growth of the intussusceptive type.[18]

The study was approved by the Institutional Review Board and Bioethics Committee of Yerevan State Medical University and was conducted in accordance with the ethical principles of the Declaration of Helsinki and the European Community Directive 2001/20/EC.

Aim of the Study

The aim of this study was to visualize, using TEM and LM, the ultrastructural and histopathological changes of myocardial arterioles, including atherosclerotic alterations, in patients with CHD, RHD and IHD.

In addition, we aimed to evaluate the pathological growth of arterioles by the intussusceptive mechanism and to compare the severity of arteriolar atherosclerotic alterations among the three groups of cardiac diseases. Finally, we sought to assess how these microvascular changes may contribute to impaired myocardial perfusion and influence the clinical condition of patients.

Results

CONGENITAL HEART DISEASE (CHD)

Light microscopic examination of myocardial biopsy specimens obtained from the right atrial appendage of a patient

with congenital heart disease (CHD), specifically critical pulmonary valve stenosis (PVS), demonstrated marked structural alterations of the intramyocardial arterioles (Figure 1). The patient was 20 years old, and the right ventricular systolic pressure exceeded 100 mmHg, indicating severe right ventricular pressure overload.

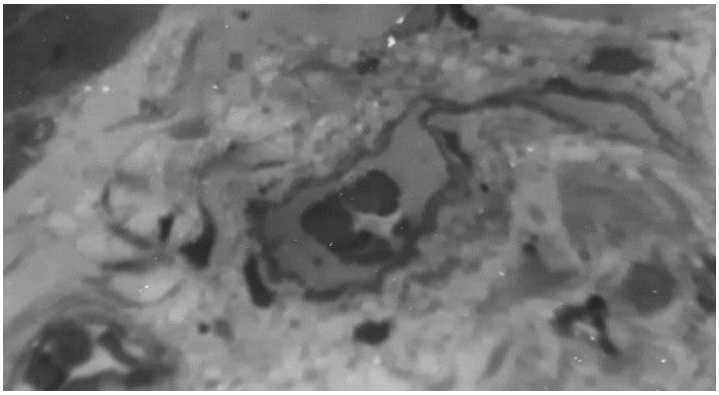

Fig.1 Pillar formation LM x 40

The thickness of the arteriolar wall varied from mild to pronounced thickening. Hyperplasia of the cellular components of the vascular wall was observed. The luminal diameter of the arterioles ranged from small to medium caliber.

Numerous transluminal invaginations of opposing endothelial walls were identified, frequently accompanied by pillar formation, where the opposite walls of the arteriole came into contact within the vascular lumen. These morphological features are characteristic of intussusceptive growth (Figure 1).

Newly formed arterioles of different diameters and irregular configurations were observed in large numbers, indicating active de novo arteriolar formation through the intussusceptive mechanism. According to our semiquantitative scoring system, pathological arteriolar growth in this specimen was graded as 4 points, representing the highest degree of intussusceptive remodeling.

RHEUMATIC HEART DISEASE (RHD)

TEM examination of collection material obtained from a patient with rheumatic heart disease (RHD), presenting with mitral valve stenosis and insufficiency, demonstrated characteristic ultrastructural changes of the myocardial microvasculature (Figure 2). The patient was 40–42 years old.

Electron microscopy revealed two closely adjacent arterioles sharing a short segment of a common basement membrane. This ultrastructural finding suggests the formation of two independent arterioles de novo through the intussusceptive process, in which one wall of the pre-existing arteriole progressively invaginates into the vascular lumen and eventually separates to form two distinct vascular profiles.

In one of the newly formed arterioles, the process of intussusceptive angiogenesis was still ongoing. Progressive transluminal invagination of the opposing vascular walls toward each other was observed within one vascular profile, whereas a mature intraluminal tissue pillar had already formed in another arteriole (Figure 2).

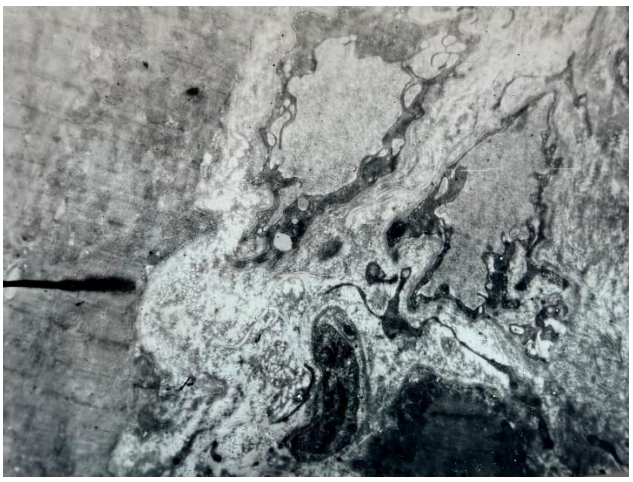

Fig.2 Formation of De Nova Arteriolas TEM x 8000

The vascular walls were tortuous and exhibited irregular thickness. Small endothelial invaginations were present in several regions. A rare morphological finding was the visualization of a vascular profile in the process of complete separation into two independent arterioles. According to the semiquantitative scoring system, pathological microvascular growth was graded as 3–4 points.

These observations provide ultrastructural evidence supporting active intussusceptive remodeling of the myocardial microcirculation in rheumatic heart disease.

RHEUMATIC MITRAL VALVE INSUFFICIENCY

Semi-thin epoxy sections provided a broader overview of myocardial arteriolar remodeling.

Most vessels undergoing intussusceptive remodeling were small- and medium-sized arterioles. Numerous vessels contained well-developed intraluminal pillars dividing the vascular lumen into two unequal compartments. Mild thickening and tortuosity of the arteriolar wall were frequently observed.

Large arterioles participated in intussusceptive remodeling considerably less often. Only isolated large arterioles contained pseudovascular profiles suggestive of ongoing de novo vessel formation. Fig 3

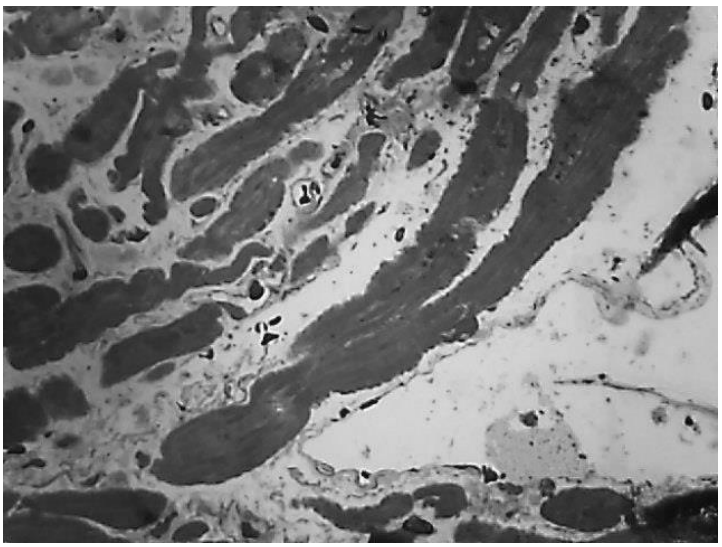

Fig.3 Bridge formation in a small arteriolas LM x 40

The pathological growth score was 3 points.

ISCHEMIC HEART DISEASE (IHD)

Light microscopic examination of myocardial biopsy specimens from patients with IHD demonstrated structural remodeling of intramyocardial arterioles with varying degrees of severity.

Patient 1

The patient was a 46-year-old male with stenocardial tension, post infract cardiosclerosis. Semi-thin epoxy sections demonstrated arterioles with variable wall thickness, ranging from mildly to markedly thickened vessels. One large arteriole demonstrated active de novo arteriolar formation (Figure 4).

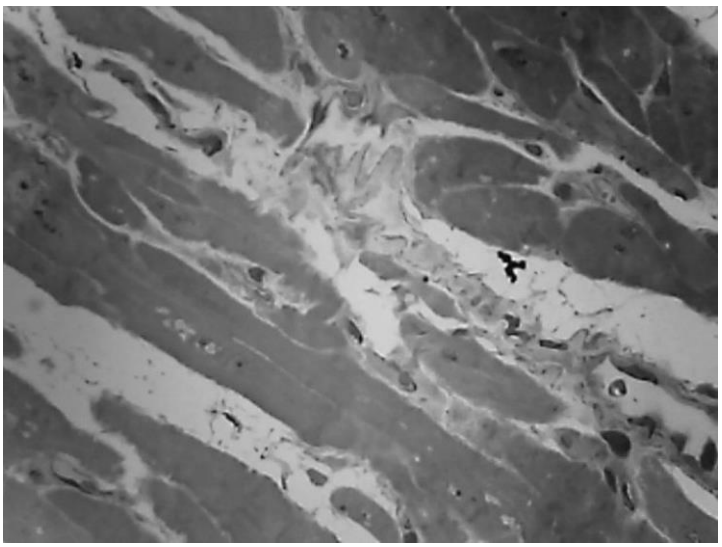

Fig.4 De nova arteriolas formation by pillar and invagination LM x40

Two vascular profiles of different diameters were identified. Several small vascular profiles sharing a common vascular wall were adjacent to the larger arteriole. In addition, repeated invaginations into the vascular lumen suggested ongoing formation of a new small arteriole.

Such findings were uncommon. Small arterioles also demonstrated active intussusceptive remodeling accompanied by tortuous vascular walls. The pathological growth score was 3–4 points.

CHRONIC ISCHEMIC HEART DISEASE (CIHD)

A 63-year-old patient with CIHD stenocardium of tension and rest (collection material) demonstrated advanced remodeling of the myocardial microcirculation.

Most large arterioles exhibited marked wall thickening with variable luminal diameters. Numerous areas of severe luminal narrowing were observed, in some vessels progressing to slit-like lumina between opposing vascular walls (Figure 5).

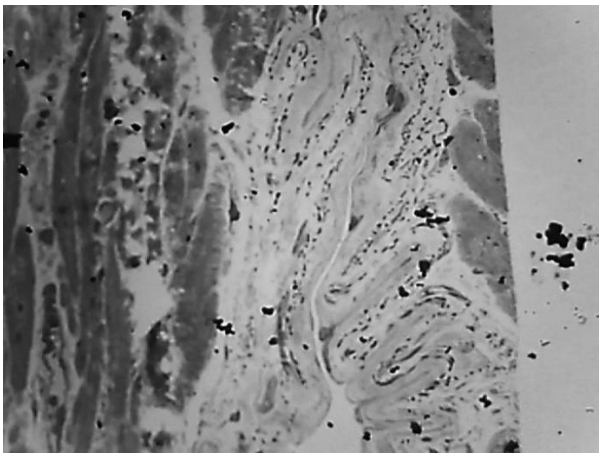

Fig 5. A slit-like lumen in arteriole LM x40

Several large arterioles appeared to divide into two separate vascular profiles through progressive approximation of the opposing walls followed by pillar formation.

Occasionally, newly separated arterioles were identified as two closely adjacent vascular profiles with extremely narrow lumina. According to the pathological grading system, intussusceptive microvascular remodeling was graded as 3–4 points.

CORONARY ARTERY DISEASE (CAD)

Four patients aged 50–65 years demonstrated varying degrees of pathological intussusceptive remodeling. Semi-thin epoxy sections revealed arterioles of different calibers. Larger arterioles frequently exhibited elongated luminal profiles, marked wall thickening, and proliferation of vascular smooth muscle cells.

In medium-sized arterioles, wall thickening was less pronounced. Large arterioles often developed complex convolutions of the vascular wall at the ends of elongated luminal profiles (Figure 6). These vascular convolutes consisted of several interconnected compartments and occasionally almost completely replaced the normal vascular lumen.

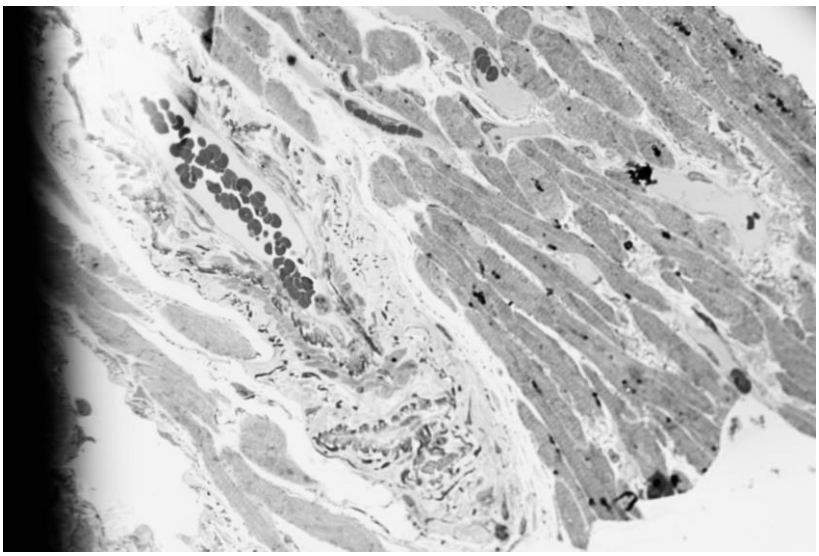

Fig 6. Convolute in a large arteriole wall. LM x 40

A pronounced tendency toward de novo arteriolar formation was observed. This was evidenced by closely adjacent vascular profiles of different diameters, sometimes sharing a common wall or appearing as recently separated daughter vessels.

In some patients, numerous newly formed arterioles were present. Another characteristic finding was pathological inward growth of the arteriolar wall into the vascular lumen, resulting in the formation of pseudo arterioles (Figure 7).

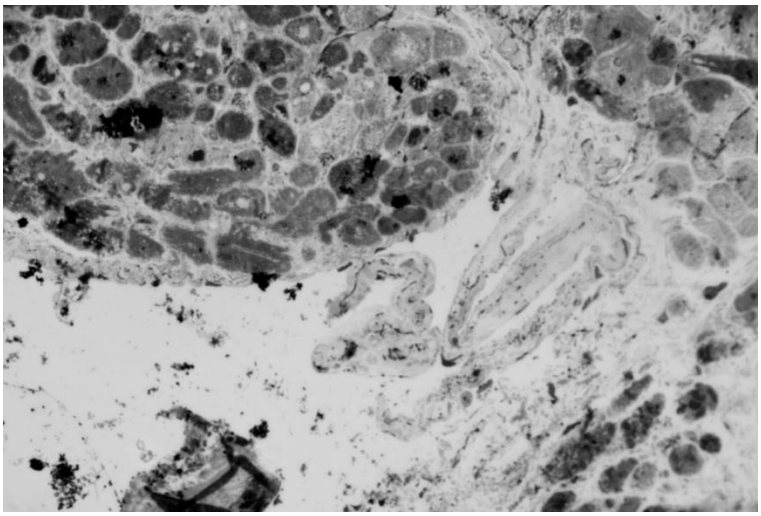

Fig 7. Pseudo arteriola, De Nova formation. LM x 40

According to the pathological grading system, two patients demonstrated Grade 4 intussusceptive remodeling, whereas the remaining patients showed Grade 3–4 changes.

Discussion

Heart pathology encompasses structural, functional, and biochemical abnormalities that impair the heart's ability to pump blood effectively. Although IHD and CAD are closely related, they are not synonymous. Atherosclerotic plaque may be present, indicating CAD, but it may not be sufficiently severe to induce myocardial ischemia.[12] Nevertheless, our

understanding of the pathophysiological cause-and-effect relationships involving the coronary microcirculation remains limited. Likewise, the mechanisms underlying post-ischemic coronary microvascular dysfunction remain controversial.[22,23,14]

Arterioles are the principal structural components of the coronary microvasculature (CMV). These resistance vessels, measuring 100 µm in diameter or less, are responsible for regulating coronary blood flow. Under physiological conditions, arterioles continuously adjust their luminal diameter in response to metabolic demand, thereby maintaining adequate myocardial perfusion. In ischemic heart disease, growth factors play a crucial role in vascular remodeling. Structural alterations, including smooth muscle hypertrophy and hyperplasia within the vascular wall, increase vascular resistance and impair coronary perfusion.[1,24]

Our findings demonstrate that, with the progression of atherosclerosis, arterioles undergo marked structural remodeling characterized by enhanced plasticity. Pronounced smooth muscle cell hyperplasia accompanies this process. We observed that arterioles participate in pathological growth through a mechanism resembling intussusceptive remodeling.[17,18,20] Although this process shares several features with intussusceptive angiogenesis, it also exhibits important differences.

Intussusceptive angiogenesis is a well-characterized mechanism of vascular growth in which new capillaries are generated from pre-existing vessels. During this process, intraluminal tissue pillars are formed, resulting in longitudinal splitting of the original vessel into two newly formed vessels.[8] Experimental studies of physiological arteriogenesis have demonstrated similar mechanisms.[15,13] Intussusceptive angiogenesis is generally considered a rapid process.[4,11,14] However, investigations of ischemic skeletal muscle have shown that intussusceptive vascular remodeling may proceed more slowly and involve larger arterioles. Similarly, arteriolar atherosclerosis in the myocardium demonstrates gradual remodeling during the prolonged course of chronic disease. These structural changes may represent adaptive responses but are also likely to influence disease progression and vascular responses to hemodynamic stress.[23]

Our results indicate that pathological arteriolar growth through intussusceptive remodeling involves a broad spectrum of morphological mechanisms. These include the formation of intraluminal pillars, bridge formation, and invagination of one side of the vessel wall toward the opposite wall. In many vessels, two or even all three mechanisms occur simultaneously. The formation of pillars, bridges, and invaginations results in asymmetric division of the arteriolar lumen and the generation of de novo arterioles with markedly different luminal diameters, ranging from very small to relatively large vessels. Fig 1,2,3,4

In chronic IHD, progressive thickening of the arteriolar wall frequently leads to slit-like lumina in larger arterioles, thereby impairing blood flow and contributing to myocardial ischemia. Fig 5 In patients with congenital heart disease (CHD) and rheumatic heart disease (RHD), sustained intussusceptive growth is observed predominantly in small arterioles, although de novo vessel formation is also present. In contrast, patients with IHD, particularly those with CAD, exhibit active intussusceptive remodeling involving both large and small arterioles, accompanied by a substantially greater number of newly formed (de novo) arterioles.

A characteristic feature of CAD is the formation of complex intramural convolutions within the walls of large arterioles. These structures consist of multiple interconnected chambers that interfere with normal blood flow. CAD is also associated with pronounced degenerative changes of the arteriolar wall. The severity of these pathological alterations was

consistently observed across all patients with arteriolar atherosclerosis but was most pronounced in CAD. These findings were quantitatively confirmed using a five-point histopathological scoring system for microvascular pathological growth.

Conclusion

In conclusion, myocardial specimens obtained from patients undergoing cardiac surgery for advanced stages of CHD, RHD and IHD demonstrated consistent evidence of arteriolar atherosclerosis. Pathological endovascular remodeling, distinct from classical intussusceptive angiogenesis, was identified across all disease groups but was most pronounced in patients with CAD and PVS. This remodeling was characterized by the formation of intraluminal pillars, bridges, invaginations, and de novo arterioles of variable calibers, accompanied by smooth muscle cell hyperplasia, progressive luminal narrowing, and degenerative vascular changes. These structural alterations likely impair coronary microvascular perfusion and may represent an important contributor to myocardial dysfunction and the development of heart failure in patients with advanced cardiac disease.

References

1. Al Rifai, A., Kabach, M., Nieves, J., Pino, J. E., & Chait, R. (2018). Microvascular coronary artery disease: Review article. US Cardiology Review, 12(1), 1–7. https://doi.org/10.15420/usc.2017:27:1
2. Faccini, A., Kaski, J. C., & Camici, P. G. (2016). Coronary microvascular dysfunction in chronic inflammatory rheumatoid diseases. European Heart Journal, 37(23), 1799–1806. https://doi.org/10.1093/eurheartj/ehw018
3. Faccini, A., Micheletti, A., Negura, D. G., Giugno, L., Butera, G., Carminati, M., Giamberti, A., & Chessa, M. (2018). Heart failure in grown-up congenital heart disease. Minerva Cardioangiologica, 66(3), 329–336. https://doi.org/10.23736/S0026-4725.18.04591-7
4. Arpino, J.-M., Yin, H., Prescott, E. K., Staples, S. C. R., Nong, Z., Li, F., et al. (2021). Low-flow intussusception and metastable VEGFR2 signaling launch angiogenesis in ischemic muscle. Science Advances, 7(48), eabg9509. https://doi.org/10.1126/sciadv.abg9509
5. Cai, W., & Schaper, W. (2008). Mechanisms of arteriogenesis. Acta Biochimica et Biophysica Sinica (Shanghai), 40(8), 681–692. https://doi.org/10.1111/j.1745-7270.2008.00436.x
6. Chilian, W. M. (1997). Coronary microcirculation in health and disease: Summary of an NHLBI workshop. Circulation, 95(2), 522–528. https://doi.org/10.1161/01.CIR.95.2.522
7. Crea, F., & Montone, R. A. (2023). Pathophysiology of coronary microvascular dysfunction. Vascular Pharmacology, 153, 107239. https://doi.org/10.1016/j.vph.2023.107239
8. Djonov, V., Baum, O., & Burri, P. H. (2003). Vascular remodeling by intussusceptive angiogenesis. Cell and Tissue Research, 314(1), 107–117. https://doi.org/10.1007/s00441-003-0784-3
9. Fonseca, D. A., Antunes, P. E., & Cotrim, M. D. (2016). The morphology, physiology and pathophysiology of coronary microcirculation. In H. Lenasi (Ed.), Microcirculation Revisited: From Molecules to Clinical Practice (pp. 15–47). IntechOpen. https://doi.org/10.5772/64537
10. Gianni-Barrera, R., Butschkau, A., Uccelli, A., Certelli, A., Valente, P., Bartolomeo, M., Groppa, E., Burger, M. G., Hlushchuk, R., Heberer, M., Schaefer, D. J., Gürke, L., Djonov, V., Vollmar, B., & Banfi, A. (2018). PDGF-BB regulates splitting angiogenesis in skeletal muscle by limiting VEGF-induced endothelial proliferation. Angiogenesis, 21(4), 883–900. https://doi.org/10.1007/s10456-018-9634-5
11. Arpino, J. M., Yin, H., Prescott, E. K., Staples, S. C. R., Nong, Z., Li, F., et al. (2021). Low-flow intussusception and metastable VEGFR2 signaling launch angiogenesis in ischemic muscle. Science Advances, 7(48), eabg9509. https://doi.org/10.1126/sciadv.abg9509
12. Kaski, J. C., Crea, F., Gersh, B. J., & Camici, P. G. (2018). Reappraisal of ischemic heart disease. Circulation, 138(14), 1463–1480. https://doi.org/10.1161/CIRCULATIONAHA.118.031373
13. Ranjbar, K., & Fayazi, B. (2019). Vascularisation of skeletal muscle. In M. T. Valarmathi (Ed.), Muscle Cells – Recent Advances and Future Perspectives. IntechOpen. https://doi.org/10.5772/intechopen.85903
14. Konijnenberg, L. S. F., Damman, P., Duncker, D. J., Kloner, R. A., Nijveldt, R., van Geuns, R. J. M., Berry, C., Riksen, N. P., Escaned, J., & van Royen, N. (2020). Pathophysiology and diagnosis of coronary microvascular dysfunction in ST-elevation myocardial infarction. Cardiovascular Research, 116(4), 787–805. https://doi.org/10.1093/cvr/cvz301
15. Kukurtchyan, N. S., & Karapetyan, G. R. (2014). Staining method of histological material (Patent of the Republic of Armenia No. 2844 A)
16. Kukurtchyan, N. S., & Karapetyan, G. R. (2021). Heart microvessels research at ischemic heart disease at open heart surgery. European Journal of Biomedical and Pharmaceutical Sciences, 8(8), 71–75.

17. Kukurtchyan, N. S., & Karapetyan, G. R. (2024). Visualisation and evaluation study of some patients' arteriosclerotic microvessels with coronary artery disease at coronary artery bypass grafting. Medical Research Archives, 12(3). https://doi.org/10.18103/mra.v12i3.5095
18. Kukurtchyan, N., Karapetyan, G., Kocharyan, A., Voskanyan, M., Hovhannisyan, M., Farsiyan, N., Sahakyan, I., & Tumasyan, N. (2025). Microvessels' atheroscleroses study and evaluation of some patients with coronary artery disease at open heart surgery in Armenia. Medical Research Archives, 13(1). https://doi.org/10.18103/mra.v13i1.6210
19. Heil, M., & Schaper, W. (2004). Influence of mechanical, cellular, and molecular factors on collateral artery growth (arteriogenesis). Circulation Research, 95(5), 449–458. https://doi.org/10.1161/01.RES.0000141145.78900.44
20. Kukurtchyan, N., Karapetyan, G., Kocharyan, A., Voskanyan, M., & Hovhannisyan, M. (2025). Morphological findings of arteriolar atherosclerosis and prognosis in patients undergoing artery bypass grafting in Armenia. Medical Research Archives, 13(10). https://doi.org/10.18103/mra.v13i10.7045
21. Padro, T., Manfrini, O., Bugiardini, R., Canty, J. M., Cenko, E., De Luca, G., Duncker, D. J., Eringa, E. C., Koller, A., Tousoulis, D., Trifunovic, D., Vavlukis, M., de Wit, C., & Badimon, L. (2020). ESC Working Group on Coronary Pathophysiology and Microcirculation position paper on coronary microvascular dysfunction in cardiovascular disease. Cardiovascular Research, 116(4), 741–755. https://doi.org/10.1093/cvr/cvaa003
22. Pries, A. R., & Reglin, B. (2017). Coronary microcirculatory pathophysiology: Can we afford it to remain a black box? European Heart Journal, 38(7), 478–488. https://doi.org/10.1093/eurheartj/ehv760
23. Sorop, O., van de Wouw, J., Chandler, S., Ohanyan, V., Tune, J. D., Chilian, W. M., Merkus, D., Bender, S. B., & Duncker, D. J. (2020). Experimental animal models of coronary microvascular dysfunction. Cardiovascular Research, 116(4), 756–770. https://doi.org/10.1093/cvr/cvaa002
24. Taqueti, V. R., & Di Carli, M. F. (2018). Coronary microvascular disease: Pathogenic mechanisms and therapeutic options. JACC State-of-the-Art Review. Journal of the American College of Cardiology, 72(21), 2625–2641. https://doi.org/10.1016/j.jacc.2018.09.042
25. Scarica, V., Rinaldi, R., Animati, F. M., Manzato, M., & Montone, R. A. (2025). Coronary microvascular dysfunction: Pathophysiology, diagnosis, and therapeutic strategies across cardiovascular diseases. EXCLI Journal, 24, 454–478. https://doi.org/10.17179/excli2025-8285