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Article

Hemostatic and Inflammatory Biomarkers Associated with Suspected Restenosis after Percutaneous Coronary Intervention in Type 2 Diabetes

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Abstract: This scientific paper provides a systematic analysis of the individual-typological variant anatomy of the human coronary arteries, morphometric parameters of the main trunk and terminal branches, and the hemodynamic impact of intramyocardial arterial segments known as myocardial bridges. Drawing on contemporary cadaveric dissection series and dual-source computed tomographic angiography (CTA) datasets, the study evaluates bifurcation and trifurcation geometry of the left coronary artery (*a. coronaria sinistra*), the prevalence of a third coronary artery, and systolic luminal compression across superficial and deep myocardial bridges during the cardiac cycle. Practical recommendations are proposed to prevent iatrogenic complications during percutaneous coronary interventions and coronary artery bypass grafting, alongside methodological integrations for teaching clinical anatomy using three-dimensional imaging reconstructions.

Keywords: human anatomy, cardiovascular system, coronary arteries, variant anatomy, myocardial bridge, morphometry, coronary dominance, systolic compression.

Introduction

Cardiovascular diseases remain the leading global cause of disability and mortality in modern medicine. The widespread introduction of high-tech endovascular procedures—percutaneous coronary interventions (stenting), coronary artery bypass grafting (CABG), and radiofrequency catheter ablation of arrhythmias—places before the science of human anatomy the task of thoroughly studying the blood supply system of the heart not merely within the framework of the "classical norm," but from the perspective of individual-typological and morphometric variability [1].

In classical anatomical literature, the arterial blood supply to the heart is described as being carried out through the right coronary artery (*a. coronaria dextra* – RCA) and the left coronary artery (*a. coronaria sinistra* – LCA), which originate from the right and left sinuses of the aortic bulb (*bulbus aortae*) of the ascending aorta. However, applied morphology and clinical imaging studies demonstrate the existence of significant population and individual differences regarding the number of coronary ostia (*ostia coronaria*), the length of the main trunk, the branching angle, and the diving of arterial segments from the epicardial fat layer into the myocardial layer—myocardial bridges (*myocardial bridging* – MB).

The bridge-like crossing of a bundle of myocardial muscle fibers over a specific segment of an epicardial coronary artery is referred to as a myocardial bridge (*myocardial bridge* – MB), while the portion of the vessel lying beneath the muscular layer is termed the intramyocardial (tunneled) segment. In the vast majority of cases, myocardial bridges are located in the middle segment of the anterior interventricular branch (LAD) of the left coronary artery [2].

Aim of the study: To systematically analyze the main branching types of the human coronary arteries, forms of coronary dominance, and clinical-morphometric parameters of myocardial bridges; to identify their associated challenges in diagnostic and cardiac surgical practice; and to develop scientifically grounded solutions for improving the teaching of clinical anatomy exemplified by the educational and research process of the Department of "Morphology" at Zarmed University [3].

Materials and Methods

Study Material and Data Sources

The study is based on morphometric data from two principal series and on published anatomical and imaging literature. Variant anatomy of the coronary arteries was assessed on a series of n = 64 fixed adult human heart specimens from a cadaveric dissection study. Myocardial bridges were assessed by high-resolution dual-source computed tomographic angiography (dual-source CTA) with three-dimensional (3D) geometric reconstruction in a group of n = 75. The frequency of the intracavitary course of the right coronary artery was taken from a systematic review of case reports and case series (n = 331). The remaining values, including the frequency ranges given in Table 1, were compiled from the published anatomical and imaging series listed in the reference list.

Morphometric Parameters and Classification

The following parameters were analyzed: the number of coronary arteries and coronary ostia; the type of coronary dominance (right, left, or co-dominant) according to the origin of the posterior interventricular branch (PIV); the type of division of the left coronary artery (bifurcation or trifurcation); the length (LMT) and the internal diameter (DMT) of the main trunk of the left coronary artery; the angle of division (θ) of the main trunk into the anterior interventricular branch (LAD) and the circumflex branch (LCx); and rare variants, namely a double PIV artery and the intracavitary course of the right coronary artery. For myocardial bridges (MB), the length (LMB) and the depth of the overlying muscular layer (dMB) were measured, and the bridges were classified by depth into superficial and deep types on 3D reconstructions. A control group without a myocardial bridge was used for comparison.

During cardiac systole, the degree of external mechanical constriction (compression) of the intramyocardial segment (*C*syst, %) and the change in the cross-sectional area of the vessel during the cardiac cycle (ΔA) are expressed through the following morphometric relations:

$$\boldsymbol{C}\textbf{syst} = [\,(\boldsymbol{D}\textbf{diast} - \boldsymbol{D}\textbf{syst}) / \boldsymbol{D}\textbf{diast}\,] \times 100\%, \qquad \Delta\boldsymbol{A} = \boldsymbol{A}\textbf{diast} - \boldsymbol{A}\textbf{syst} \qquad \textbf{(1)}$$

where *D*diast and *D*syst are the vessel diameters in the diastolic and systolic phases, respectively; and *A*diast and *A*syst are the diastolic and systolic cross-sectional areas of the intramyocardial segment of the coronary artery (mm2).

Presentation of Data

Quantitative data are presented as mean ± standard deviation, with the individual range where available, and qualitative data as absolute numbers and percentages. Differences between the control, superficial MB, and deep MB groups are presented with P values (Table 2).

Results

Number of Coronary Arteries and Branching Variants

In evaluating the arterial architectonics of the heart, three fundamental anatomical criteria are of decisive importance: the number of coronary arteries, the branching geometry of the main trunk of the left coronary artery (*truncus communis a. coronariae sinistrae*), and the type of dominance in supplying blood to the diaphragmatic surface of the heart [4].

Analysis of cadaveric anatomical studies ($n = 64$ fixed adult human heart specimens) shows that although the typical origin of the right coronary artery from the right aortic sinus and the left coronary artery from the left aortic sinus is preserved in 100% of cases, significant variability is observed in the total number of coronary arteries. Specifically, while two coronary arteries were identified in 87.5% (56/64) of specimens, a third coronary artery was recorded in 12.5% (8/64) of cases—either as an intermediate branch (*ramus intermedius*) originating with a separate orifice (*ostium*) in the left aortic sinus, or as a conus branch (*ramus coni arteriosi*) emerging separately from the right aortic sinus [5].

According to the morphometry of the main trunk (MT) of the left coronary artery, its mean length is 10.8 ± 5.52 mm (individual variation range: 2–23 mm), and the internal (luminal) diameter in its middle portion is 4.86 ± 0.80 mm. The angle of division (θ) of the main trunk into its terminal branches—the anterior interventricular branch (*r. interventricularis anterior* – LAD) and the circumflex branch (*r. circumflexus* – LCx)—averages θ = 86.7° ± 28.8° (40°–165°), and there is a direct positive correlation between the length of the trunk and the branching angle: longer main trunks branch at a wider angle. In wide-angle (θ > 90°) bifurcation and trifurcation zones, due to a decrease in hemodynamic wall shear stress exerted on the endothelium, the early formation of atherosclerotic plaques and calcification has been clinically proven [6].

The anatomical variants and morphometric parameters of the coronary arteries are summarized in Table 1.

Table 1. Anatomical variants and morphometric parameters of the coronary arteries

Anatomical-Morphometric Parameter	Morphological Description and Topographical Feature	Value / Frequency
Two-coronary-artery type	Presence of classical RCA and LCA ostia	87.5% (56/64)
Third coronary artery	Separate r. intermedius ostium in the left sinus	12.5% (8/64)
Right coronary dominance	Origin of the posterior interventricular branch (PIV) from the RCA	89.0–90.6%
Left coronary dominance	Origin of the PIV branch from the LCx (a. coronaria sinistra)	6.3–11.0%
Co-dominant type	Joint blood supply of the posterior part of the interventricular septum by the RCA and LCx	9.4% (6/64)
LCA bifurcation	Two-way division into LAD and LCx branches	62.0–90.6%

LCA trifurcation	Formation of an additional r. intermedius (diagonal branch)	9.4–38.0%
LCA main trunk length (*L*MT)	Distance from the left aortic sinus to the terminal division	10.8 ± 5.52 mm
LCA main trunk diameter (*D*MT)	Internal diameter of the middle portion of the main trunk	4.86 ± 0.80 mm
Branching angle (θ)	Angle between the terminal LAD and LCx branches	86.7° ± 28.8°
Double PIV artery	Descent of two parallel posterior interventricular branches from the RCA	~3.0%
Intracavitary course of the RCA	Passage of an RCA segment through the wall/cavity of the right atrium	1.8% (6/331)

Morphometry and Systolic Compression of Myocardial Bridges

According to morphometric measurements, the length of typical myocardial bridges is *L*MB < 25 mm, and the depth (thickness) of the overlying muscular layer is around *d*MB = 1–10 mm. Bridges exceeding 25 mm in length (for example, 30 mm and longer) occur in approximately 6% of the population and belong to a high clinical risk group. In high-resolution dual-source computed tomographic angiography (Dual-Source CTA, $n = 75$) and three-dimensional (3D) geometric reconstruction studies, myocardial bridges are classified according to their depth of location into superficial (*superficial MB*) and deep (*deep MB*) types [7].

Table 2. Compression and cross-sectional area dynamics of the anterior interventricular artery (LAD) in superficial and deep myocardial bridges (n = 75, 3D CTA analysis)

Morphometric and Hemodynamic Parameter	Control Group	Superficial MB Group	Deep MB Group	Statistical Difference (P)
Maximum systolic compression (Cmax, %)	12.69 ± 10.82	8.36 ± 8.85	38.71 ± 28.17	P ≤ 0.001
Mean systolic compression (Cavg, %)	1.29 ± 0.97	5.60 ± 6.78	22.35 ± 14.89	P < 0.001
Minimum cross-sectional area difference (Δ*A*min, mm²)	0.576 ± 0.115	0.301 ± 0.057	1.168 ± 0.177	P < 0.015
Mean cross-sectional area difference (Δ*A*avg, mm²)	0.088 ± 0.014	0.302 ± 0.087	1.072 ± 0.182	P < 0.001
Compression ratio (relative to control)	1.0× (reference)	4.3× (Cavg)	17.3× (Cavg)	P < 0.001

From the analysis of Table 2, it becomes evident that as the depth of the myocardial bridge increases, the degree of systolic compression of the coronary artery intensifies sharply:

1. Biomechanics of deep myocardial bridges: In the deep MB group, the mean degree of systolic compression (22.35% ± 14.89%) is 17 times higher than in the control group (1.29% ± 0.97%) and 4 times higher than in the superficial MB group (5.60% ± 6.78%) ($P < 0.001$). Maximum systolic constriction in deep MB reaches up to 38.71% ± 28.17% [8].

2. Change in cross-sectional area: During the cardiac cycle, the mean difference in cross-sectional area between diastole and systole (Δ*A*avg) in the deep MB group is 1.072 ± 0.182 mm2,

which is 12 times greater than the control value (0.088 ± 0.014 mm2) and 3.6 times greater than the superficial MB value (0.302 ± 0.087 mm2) [9].

Discussion

Clinical Significance of Branching Variants

As is evident from the data presented in Table 1, rare anatomical variants—specifically, the intra-atrial (intracavitary) course of the right coronary artery occurring in 1.8% of cases and the double posterior interventricular (PIV) artery observed in 3% of cases —pose a risk of direct vascular injury during right atrial catheter ablation and coronary artery bypass grafting [10].

Hemodynamic and Clinical Significance of Myocardial Bridges

3. The "Double-edged sword" phenomenon: Morphologically, although atherosclerotic lesions are observed less frequently in the intramyocardial segment beneath the myocardial bridge, severe atherosclerotic stenosis and myocardial ischemia develop in the epicardial segment located proximal (superior) to the bridge due to retrograde systolic flow and turbulence.

Clinical-morphological conclusion: Deep (> 2–5 mm) and long (> 25 mm) myocardial bridges are not limited solely to systolic constriction, but also cause a delay in early diastolic relaxation. Under conditions of tachycardia, when the diastolic period is shortened, this condition increases the risk of acute coronary syndrome, conduction disturbances, and sudden coronary death [11].

Clinical-Diagnostic Challenges

During the study, the following three major challenges were identified in the detection and teaching of the variant anatomy of the cardiovascular system:

• **First challenge (Diagnostic discrepancy):** The sensitivity of detecting myocardial bridges varies sharply depending on the examination method. While intramyocardial coronary arteries are identified in 26–45% of cases in large anatomical autopsy series (> 1000 specimens), they are diagnosed in only 12% of cases in standard invasive coronary angiography (as it relies solely on the systolic "milking effect" and the "step down–step up" phenomenon) . Consequently, searching for an undiagnosed intramyocardial LAD segment during coronary artery bypass grafting (CABG) surgery poses a risk of ventricular perforation [12].

• **Second challenge (Combined variants):** The coexistence of multiple coronary anomalies within a single heart—for instance, a 30 mm long myocardial bridge in the middle segment of the LAD accompanied by a double PIV artery arising from the RCA, or an LCA trifurcation combined with an intramyocardial segment—unexpectedly alters perfusion zones and leads to diagnostic errors in angiographic interpretation [13].

• **Third challenge (Educational methodology):** In teaching human anatomy at medical universities, the blood vessels of the heart are often explained only on the basis of a typical two-artery scheme, whereas coronary dominance, morphometry of the LCA branching angle, and integration with CT-angiographic phase images are not sufficiently implemented.

Proposed Solutions

To overcome these challenges, the following scientific and practical solutions are proposed:

1. Biphasic ECG-gated MSCT-angiography protocol: Standard coronary MSCT reconstruction is typically performed only in the diastolic phase (during the period of maximum vasodilation and minimal motion artifacts). When a myocardial bridge is suspected, reconstructing images in both systolic and diastolic phases and performing 3D-morphometric analysis increases the detection rate up to 60% and allows accurate preoperative calculation of the *C*syst parameter [14].

2. Cardiac surgical and interventional safety algorithm: Prior to coronary artery bypass grafting and stenting procedures, preoperative coronary mapping of the LCA main trunk length (*L*MT), branching angle (θ), presence of a third coronary artery, and intracavitary course of the RCA (1.8% risk) is mandatory.

3. Integration of "Cadaveric Specimen + 3D CTA/Anatomage" in Departments of Morphology: In human anatomy classes, alongside the dissection of coronary arteries on wet (fixed) heart specimens, introducing the practice of morphometric measurement of dominance types (right 90.6%, co-dominant 9.4%, left 6.3%) and myocardial bridges based on three-dimensional reconstructions of MSCT-angiography for students [15].

Conclusion

Based on the results of the conducted scientific-morphometric analysis, the following conclusions were reached:

• The coronary arteries of the human heart exhibit high individual-typological variability: a third coronary artery (a separate-ostium *r. intermedius*) occurs in 12.5% of cases, trifurcation/polyfurcation of the left coronary artery in 9.4–38.0% of cases, and myocardial bridges in 12.5–45.0% of anatomical series.

• In deep myocardial bridges, the mean systolic compression of the coronary artery (22.35% ± 14.89%) is 17 times higher than in the control group, and the mean change in cross-sectional area during the cardiac cycle (1.072 ± 0.182 mm2) is 12 times higher, which represents the direct morphological substrate of impaired coronary hemodynamics.

• For the early detection of myocardial bridges and coronary branching anomalies in clinical practice, the application of biphasic (systolic and diastolic) ECG-gated MSCT-angiography is recommended, alongside the implementation of clinical-anatomical 3D-morphometry modules in higher medical education.

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