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Morphological characteristics of the myocardial bridges in the level of the anterior interventricular branch of a human fetal heart

Morfološke karakteristike miokardnih mostova u nivou prednje interventrikularne grane srca ljudskih fetusa

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Abstract

Background/Aim. Myocardial bridges (MB) are narrower or wider fascicles of the atrial or ventricular muscle fibres which form a "bridge" either across the main trunks of coronary arteries or their major subepicardial branches. The aim of this research was to determine and present the exact frequency, morphological, morphometric and histological characteristics of the MB in the level of anterior interventricular branch (AIB) in human fetal hearts. **Methods.** The study was performed on 63 human fetal hearts. Images of the analyzed hearts were captured with a digital camera and afterwards morphometrically evaluated with ImageJ. Characteristic cases of the MB were dissected, sampled and further routinely processed for the subsequent histological analysis. Finally, the obtained morphometric data were statistically analyzed. **Results.** The presence of the MB on the AIB was proven histologically and under the magnifying glass. Myocardial bridges were found in 53.97% of the hearts. The percentage of the hearts with only one MB detected on AIB 88.24% was significantly higher than the percentage of the hearts with two MBs on the AIB (11.76%) ($p < 0.001$). **Conclusion.** We suggest that the MBs are just one anatomical variation of the fetal period as well as of adulthood.

Key words:
fetus; heart; coronary vessels; abnormalities; myocardial bridging.

Apstrakt

Uvod/Cilj. Miokardni mostovi *myocardial bridges* (MB) predstavljaju uzane fascikuluse atrijalnih ili ventrikularnih miokardnih vlakana, koja obrazuju "most" bilo preko glavnih stabala koronarnih arterija, ili preko njihovih subepikardnih grana. Cilj ovog istraživanja je bio da se ustanovi učestalost, morfološke, morfometrijske i histološke karakteristike MB prednje interventrikularne grane (*enterior interventricular bronch* – AIB) srca ljudskih fetusa. **Metode.** Studija je sprovedena na uzorku od 63 srca ljudskih fetusa. Digitalne fotografije analiziranih srca su zatim morfometrijski analizirane uz pomoć Image J sistema. Karakteristični slučajevi MB su disecirani, i dalje rutinski procesirani za potrebe histološke analize. Konačno, dobijeni rezultati morfometrijske analize su statistički obrađeni. **Rezultati.** Prisustvo MB na AIB je verifikovano morfološki (pod lupom) i histološki. Miokardni mostovi su ustanovljeni kod 53,97% slučajeva. Procenat slučajeva sa jednim detektovanim MB na AIB (88,24%) je bio statistički značajno viši u odnosu na procenat slučajeva sa dva MB detektovana na AIB (11,76%) ($p < 0,001$). **Zaključak.** Miokardni mostovi najverovatnije predstavljaju anatomsku varijaciju karakterističnu kako za fetalni, tako i za adultni period života čoveka.

Ključne reči:
fetus; srce; koronarni krvni sudovi; anomalije; miokardni mostovi.

Introduction

Recently, morphologists and clinicians have focused their attention on myocardial bridges across the coronary arteries and/or their branches. Šećerov-Zečević [1] described myocardial bridges (MB) as narrower or wider fascicles of the atrial or ventricular muscle fibres which form a "bridge" either across the coronary arteries' main trunks or their major subepicardial branches. Some of these fibres may wrap around the mentioned arteries and form loops in such way.

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According to Acunã et al. [2], the MBs were first described by Reyman in the 18th century. Subsequent studies pointed to their numerous variations in frequency, localization, length, thickness, direction of fibres and clinical repercussions.

Results of the studies performed on hearts obtained post-mortem showed that the incidence of the MB varies from 15% to 85% in adults [2–8], and about 50% in human fetal material [9,10]. Clinical studies reported that their incidences varied from 0.5% to 40% [6, 11–13].

Depending on their width, the MBs have been usually classified as superficial and deep [5], with the anterior interventricular branch (AIB) of the left coronary arteries as the most frequent location [7, 8, 14, 15]. Deep MBs are usually symptomatic and result in ischemic disease of varying intensity [16]. According to some authors, the MBs are not only characteristic of the human heart, but also of some mammals such as dogs, camels or gorillas [17].

As previous studies showed, the most common localization of the MBs is the AIB [2, 7, 8, 15]. This research aims to determine and to present their exact frequency, morphological, morphometric and histological characteristics in the human fetal hearts.

Methods

The study was performed on 63 human fetal hearts obtained post-mortem (28 males and 35 females) and fixed in 10% buffered formalin. Gestational age of the fetuses ranged from 13 to 28 weeks [18]. They are the part of the collection of the Institute of Anatomy of the Faculty of Medicine, Niš, Serbia. The coronary arteries of the hearts used during this research were injected with Micropaque or Latex. The study was approved by the Ethics Committee of the Faculty of Medicine, University of Niš (No: 01−9002−4).

The anatomical dissection and morphological analysis of the MBs on the AIB was done under the surgical magnifying glass (5×). Anterior thoracic wall of the fetuses (sternum and costal cartilages with adjacent structures) was removed and afterwards hearts with the large blood vessels of is bases were their pulled out of the pericardial sac and inferior middle mediastinum. The anterior descending branch of the left coronary artery was divided into three segments: the first included its segment at the level of the conus arteriosus top and the second and the third segments relatively fit with the halves of the remaining part of the AIB (Figure 1). Morphometric parameters (outer diameter of the AIB, length of the MB) were measured by the Image J [19] on the digital images of the analyzed hearts captured with a digital camera. The morphology and distribution of the MB on the AIB of each case was analyzed under the magnifying glass (5×) and afterwards schematically presented. The histological analysis was performed on the tissue samples of the fetal hearts whose coronary arteries were injected with Micropaque or Latex. The samples were embedded in paraffin and cut into sections 5 μm thick. The obtained sections were stained with haematoxylin eosin (HE) at the Institute of Pathology at our Faculty of Medicine.

The continuous variables were described by means and standard deviations. Frequencies of categorical data were given by absolute numbers and percentages. Differences between the independent groups were tested with the Student's unpaired *t*-test. The χ^2 test was used to compare proportions of categorical variables among the groups. The Pearson's correlation coefficients were used to analyze associations between the continuous variables. The level of significance was set at 0.05. All analyses were performed by the SPSS software [20].

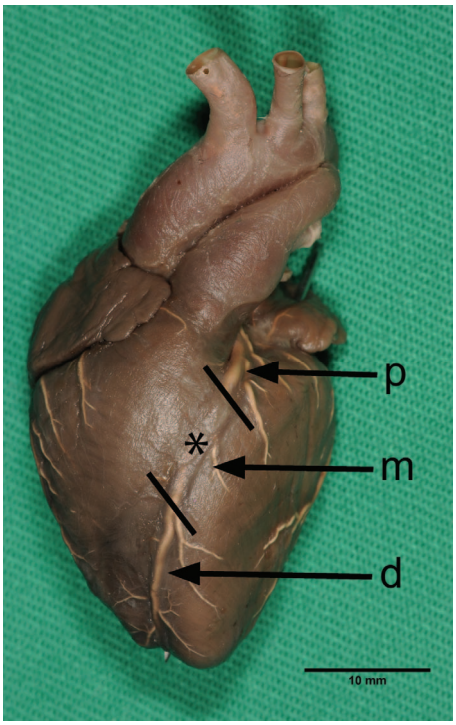

Fig. 1 – The heart of fetus of male gender (gestational age 29 weeks). Sternocostal surface. The coronary arteries were filled with Micropaque. The insert showed anterior interventricular branch (AIB) divided into three segments; proximal (p) (a boundary is a horizontal line to the conus arterios top), middle (m) and distal (d) (horizontal line between the half of the remaining of AIB length to the apex of heart); *myocardial bridge.

Results

The cases were classified into two groups according to the presence of the MBs. The first group included 34 (53.97%) cases with the MBs of which 15 (44.12%) were males and 19 (55.88%) were females. Twenty-nine (46.03%) cases of the second group were without the observed MB across the AIB, 13 (44.83%) were males and 16 (55.17%) were females. The percentage of the male and female cases in the obtained groups were not significantly different ($p > 0.05$). The mean age of the fetuses in the first group was 19.12 ± 3.46 weeks, while in the second group it was 18.00 ± 2.25 weeks of gestation, which was not significantly different ($p > 0.05$).

The total number of the MBs on the AIB observed in the first group was 38. The percentage of the hearts with only one MB detected on the AIB (n = 30 or 88.24%) was significantly higher than the percentage of the hearts with two MB on the mentioned artery (n = 4 or 11.76%) ($p < 0.001$) (Figures 2A and 2B).

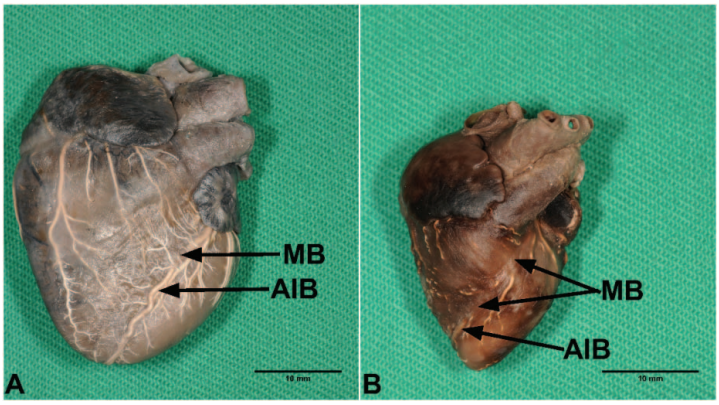

Fig. 2 – Two hearts of fetuses of male gender [gestational age 19 weeks (A) and 17 weeks (B)]. Sternocostal surface. The coronary arteries were filled with Micropaque. The insert A showed one myocardial bridge – MB (arrow) located at the middle segment of the anterior interventricular branch (AIB); The insert B showed double MB (arrows) located at proximal segment, and simultaneously at middle and distal segments of AIB.

Table 1

Myocardial bridges in relation to the arterial localization and gender

Localization	Number of hearts with MB n (%)	Number of hearts with 1 MB n (%)	Number of hearts with 2 MB n (%)	Gender (M/F)
AIB p	6 (17.65)	6 (17.65)	/	3/3
AIB m	9 (26.47)	9 (26.47)	/	3/6
AIB d	1 (2.94)	1 (2.94)	/	0/1
AIB p+m	15 (44.12)*	13 (38.24)	2 (5.88)	7/8
AIB m+d	1 (2.94)	/	1 (2.94)	1/0
AIB p+m+d	2 (5.88)	1 (2.94)	1 (2.94)	1/1
Total	34 (100%)	30 (88.24%)†	4 (11.76%)	15/19

MB – myocardial bridges; AIB – anterior interventricular branch; p – proximal; m – middle; d – distal; p+m – proximal and middle; m+d – middle and distal; p+m+d – proximal, middle and distal; M/F – male/female.
***There is a statistically significance in relation to other localization ($p < 0.05$).**
†There is a statistically significant difference between hearts with one and with double MB ($p < 0.001$).

The coronary dominance of all of the hearts was as follows: 32 (50%) were right dominant, 11 (17.19%) were left dominant and 20 (31.25%) were balanced.

The coronary dominance of the hearts with the MB was as follows: 17 (50%) were right dominant, 5 (14.71%) were left dominant and 12 (35.29%) were balanced.

The morphological analysis showed the presence of 6 morphological types according to the number of the MB present on the different AIB segments. The number of cases included in each morphological type and their percentages are shown on Table 1.

The myocardial bridges were most frequently localized at the proximal and middle segments border and in such way simultaneously covered the parts of both AIB segments (n = 15 or 44.12% of the cases). The percentage of such cases was significantly higher, compared to the cases with localization on the proximal or middle AIB segment separately ($p < 0.05$), as well as the other observed combinations of their localization on the other AIB segments ($p < 0.001$).

The mean length of the MBs in the males (9.67 ± 5.14 mm) was insignificantly ($p > 0.05$) higher than in the females (7.48 ± 3.32 mm).

The presence of MBs on the AIB was proven under the magnifying glass and histologically (Figure 3). Reticular cardiomyocyte as well as numerous lacunae, were noticed in deeper layers of the myocardium.

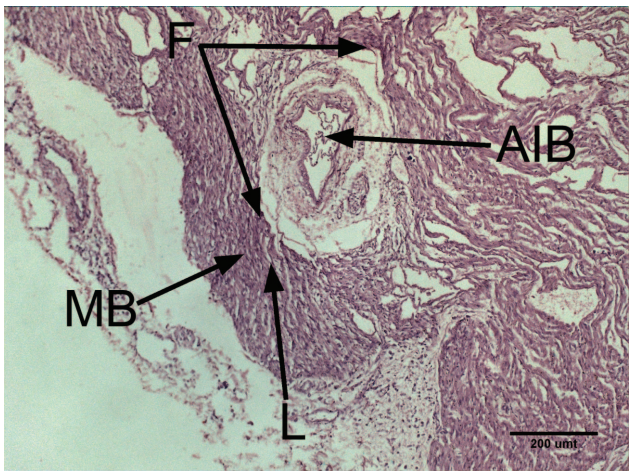

Fig. 3 – Myocardial bridge (MB) seen under the microscope. Obtained section was stained with haematoxylin eosin (HE, x10). The anterior interventricular branch (AIB) over bridged with the MB. The direction of cardiomyocytes was parallel and at a distance from the AIB they were separated into two fascicles (F). Visible parallel flattened lacunae (L).

A relatively irregular direction of cardiomyocytes was observed in some regions of the myocardium. The direction of cardiomyocytes was predominantly parallel and at a certain distance from the AIB they were separated into two fascicles. One fascicle continued posterior and the other travelled in front of the AIB partially enveloping it (visible parallel flattened lacunae). In addition to transversal cardiomyocytes which formed the MB, there were also some oblique and longitudinal cardiomyocytes.

There was a correlation between the length of the MB and gestational age of the fetuses. The length of the MB increased with the gestational age of the fetuses, but this increase was not statistically significant ($\rho = 0.027$; $p > 0.05$).

The mean AIB outer diameter proximally and distally of the MB was compared with the outer diameter of the same segments of the artery in the cases without the MB. Its value was higher in the cases with the MB than in those without the MB, but this difference was not significant ($p > 0.05$).

Discussion

Although the MBs were subjects of various clinical [6, 8, 11–13] and autopsy [3–7, 8, 12] studies, their practical (clinical) significance remained unclear and has not yet been completely resolved.

Some authors reported that segment of the artery under the MB may be protected from atherosclerosis, while proximal segment of a bridged vessel is more susceptible to it [6,13,21,22]. This can be partially supported by an increased axial wall stress just proximal to the MB due to the compression on the over bridged segment [23].

Our study showed that the presence of the MB was not significantly correlated with either of the genders in the evaluated sample. Some authors revealed the presence of insignificant male predominance [2, 7], while in their study, Polacek and Kralove [4] established a significantly higher frequency of the MBs in the male individuals of the Czechoslovakian population. Nevertheless, until today, a rational explanation for differences with respect to gender has never been given.

Incidence of the MBs at the level of the AIB was presented in different ways by many studies. Incidence of the MBs of 53.97%, that we established, is higher than the same of Šećerov [9], who examined the MB on the same artery in fetal hearts (gestational age 3–10 lunar months) and found their incidence of 32.72%. However, the author conducted her research on 55 human fetal hearts among which 28 (50.9%) had one or more MBs in different coronary arteries, and only 18 (32.72%) of them had the MB on the AIB. Concerning the MB location, Cakmak et al. [10] also analyzed their presence in the human fetal hearts (gestational age 6–10 lunar months) and found 50% of all MBs at the level of the AIB. They showed that 18 (46.2%) of the 39 fetal hearts had in total 26 MBs (one or more) on the different branches of coronary arteries. Loukas et al. [7] studied 200 adult hearts and found 81 MB in 34.5% of the hearts, from which 43.2% were on the AIB.

The above cited authors [7, 10] presented incidence of the MBs on the AIB as their percentage in relation to the MBs detected in all investigated branches of coronary arteries and for that reason our results could not be compared to theirs. Nevertheless, Polacek and Krelove [4] reported the presence of the MBs on the AIB in 60% of the adult samples, which coincided with our results. Acunã et al. [2], examined the autopsy material which consisted of 154 hearts (average age 31.5 years) and found the MB in 40.3% of all cases, from which 36.9% were localized on the AIB, which is not in agreement with our findings.

The presence of only one MB on the AIB, was observed in 30 (88.24%) of 34 hearts with the detected MB in our study. Results by Šećerov [9] showed similar frequency of one MB on the same blood vessel. Loukas et al. [7] found that this percentage is 85.5%, but with regard to the number of one MB on all analyzed coronary arteries. Similar to Acunã et al. [2] in their paper, we established that the incidence of only one MB, when all evaluated AIB were taken into the consideration, was 67.74%. Frequency of the double MBs on the AIB detected in this study was 11.76%, which is very similar to the frequency detected by Šećerov [9] (11.11% of the cases) and Loukas et al. [7]. We did not detect the presence of the triple MBs on the AIB.

The angiographic studies suggested that the MBs can be deep and superficial [5] and that they mostly occur in the middle segment of the AIB [7, 8, 14, 15]. Analyzing the distribution of the MBs on the AIB in our study, we determined that their most common localization was in the proximal and middle segment of the AIB simultaneously, with incidence of 44.12% of the samples, which is in agreement with the findings of Reig et al. [24] and Bezerra et al. [25]. Less frequently, we detected the MBs in the middle (26.47%) or in the proximal segment (17.65%) of the vessel.

High variability of the MB length was reported in the literature, ranging from a few up to 50 millimeters [7, 15, 24, 26]. According to our results, the average MB length on the AIB was similar in both sexes (8.57 mm) which corresponded to the findings of Šećerov [9] (3–10 mm). The correlation analysis between the length of the MB and gestational age of the fetuses revealed a weekly increase of the MB length with gestational age, but this increase was not significant. However, an intensity of the increase of the MB length during the postnatal period remains a hypothetical question. Additionally, whether this increase during postnatal period coincides with the frequency of myocardial infarction and other coronary disorders may be the subject of future studies.

In spite of the fact that we established that an outer diameter of the AIB was higher in cases with the MBs than in ones without them, a significant correlation was not statistically confirmed.Taking into consideration that there are no available data in the present literature about this, such findings might be the consequence of a relatively small sample used during this study, and future studies will give definite answer to this dilemma.

Histological organization of the MB in fetal hearts presented by Šećerov [9] did not differ from the one presented in our study. Namely, she showed that muscle fibers of myocardium, after a parallel stream with the AIB, divide into two fascicles stretching, in most cases, perpendicularly upward and beyond the AIB, forming a loop around it, after which they unite again and continue with a parallel course.

Reviewing the literature, it appears that vascular dysfunction at the MBs in adults may cause vasospasm which can lead to the lethal ischemic events, arrhythmias, myocardial infarction and a sudden cardiac death [27, 28]. According to Duygu et al. [28], who conducted their study on 71 patients with the MB (mean age 51 ± 10 years), the myocardial bridge may induce a development of atherosclerotic lesions in a segment of the AIB proximal to MB. They divided the patients into two groups, those with the MB and no atherosclerotic lesions and those with the atherosclerotic coronary artery disease in addition to the MB. After performing the exercise testing of all patients, the authors obtained the following results: stable angina pectoris occurred more frequently in the first group than in the second one (70% *vs* 35% respectively; $p = 0.01$), while acute coronary syndrome appeared more frequently in the second group (65%) than in the first one (30%), ($p = 0.04$). Their treatment depended on length and depth of the MB. The patients with the long and deep MB underwent surgical revascularization, while others received a medical management.

Conclusion

It can be concluded that there was an association between the MBs in the prenatal period and in adulthood. Based on the morphological characteristics of the MBs on the AIB, we suggest that the MBs are just one anatomical variation of the fetal period, as well as of the adulthood. However, since their presence has been noted during adulthood, it is possible that in some cases they could be responsible for some of the vascular dysfunctions and/or genesis of atherosclerosis.

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