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

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Running title:
Myocardial bridges
Morphological characteristics of the myocardial bridges in the level of the anterior interventricular branch of a human fetal heart

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 coronary arteries’ main trunks or their major subepicardial branches. The aim of this research was to determine and present the exact frequency, morphological, morphometric and histological characteristics of 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 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, obtained morphometric data were statistically analyzed.

Results. Myocardial bridges were found in 53.97% of the hearts. 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 AIB (11.76%) (p < 0.001). Presence of MB on the AIB was proven histologically and under the magnifying glass.

Conclusion. We suggest that MBs are just one anatomical variation of the fetal period, as well as of adulthood.

Key words: fetus, heart, anterior interventricular branch, myocardial bridge.

Morfološke karakteristike miokardnih mostova prednje interventrikularne grane humanog fetalnog srca

Apstrakt

Uvod/Cilj. Miokardni mostovi (MB) predstavljaju uzane fascikuluse atrijalnih ili ventrikularnih miokardijalnih vlakana, koja obrazuju “most” bilo preko glavnih stabala koronarnih arterija, ili preko njihovih subepikardijalnih grana. Cilj ovog istraživanja je bio da se ustanovi učestalost, morfološke, morfometrijske i histološke karakteristike MB prednje interventrikularne grane (AIB) srca humanih fetusa. Metode. Studija je sprovedena na 63 humana fetalna srca. Digitalne fotografije analiziranih srca su zatim morfometrijski
analizirane uz pomoću ImageJ sistema. Karakteristični slučajevi MB su disecirani, i dalje rutinski procesirani za potrebe histološke analize. Konačno, dobijeni rezultati morfometrijske analize su statistički analizirani. **Rezultati.** Miokardni mostovi su detektovani 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). Prisustvo MB na AIB je verifikovano morfološki (pod lupom) i histološki. **Zaključak.** Miokardni mostovi najverovatnije predstavljaju anatomsku varijaciju karakterističnu kako za fetalni, tako i za adultni period života čoveka.

**Ključne reči:** fetus, srce, prednja interventrikularna grana, miokardni most
Introduction

Recently, morphologists and clinicians have focused their attention on myocardial bridges across the coronary arteries and/or their branches. Šećerov-Zečević 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.

According to Ballesteros 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 MB varies from 15 to 85% in adults, and about 50% in human fetal material. Clinical studies reported that their incidences varied from 0.5 to 40%.

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

As previous studies have shown that the most common localization of MB is the AIB, this research aims to determine and to present its exact frequency, morphological, morphometric and histological characteristics of MB in 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. They are the part of the collection of the Institute of Anatomy of the Faculty of Medicine, Niš, Serbia. Coronary arteries of the hearts used during this research were injected with Micropaque or Latex. Study was approved by the Ethical Committee of the Faculty of Medicine, University of Niš (No: 01–9002–4).

Anatomical dissection and morphological analysis of MB on AIB was done under the surgical magnifying glass. Anterior thoracic wall of the fetuses (sternum and costal cartilages with adjacent structures) was removed and afterwards hearts with the large blood vessels of its base were pulled out of the pericardial sac and inferior middle mediastinum. Anterior descending branch of the left coronary artery was divided into three segments: the
first which included its segment at the level of the conus arteriosus top; second and the third segments relatively fit with the halves of the remaining part of the AIB (Fig.1). Morphometric parameters (outer diameter of AIB, length of MB) were measured by ImageJ on the digital images of the analyzed hearts captured with digital camera. Morphology and distribution of MB on AIB of each case was analyzed under the magnifying glass (5×) and afterwards schematically presented. Histological analysis was performed on the tissue samples of the fetal hearts whose coronary arteries were injected with Micropaque or Latex. Samples were embedded in paraffin and cut into sections 5 µm thick. 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 independent groups were tested with the Student’s unpaired t-test. A chi-square test was used to compare proportions of categorical variables between groups. Pearson correlation coefficients were used to analyze associations between continuous variables. The level of significance was set at 0.05. All analyses were performed with SPSS software.

Results

Cases were classified into two groups according to the presence of MB. The first group included 34 cases (53.97%) with MB of which 15 (44.12%) were males and 19 (55.88%) were females. Twenty nine cases of the second group (46.03%) were without observed MB across AIB (13 (44.83%) were males and 16 (55.17%) were females). Percentage of the male and female cases in the obtained groups were not significantly different (p > 0.05).

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).

Total number of MB on the AIB observed in the first group was 38. Percentage of the hearts with only one MB detected on 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) (Fig. 2A and 2B).

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 MB was as follows: 17 (50%) were right dominant, 5 (14.71%) were left dominant and 12 (35.29%) were balanced.
Morphological analysis showed the presence of 6 morphological types according to the number of the MB present on different AIB segments. Number of cases included in each morphological type and their percentages are shown on Table 1.

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).

Mean length of MB in males (9.67 ± 5.14 mm) was insignificantly (p > 0.05) higher than in females (7.48 ± 3.32 mm).

Presence of MB on the AIB was proven under the magnifying glass and histologically (Fig. 3). Reticular cardiomyocyte, as well as numerous lacunae, were noticed in deeper layers of the myocardium. 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 MB, there were also some oblique and longitudinal cardiomyocytes.

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

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

**Discussion**

Although MBs were subjects of various clinical studies, their practical (clinical) significance remained unclear and has not yet been completely resolved. Some authors have 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. This can be partially supported by increased axial wall stress just proximal to the MB due to the compression on the over bridged segment.
Our study showed that the presence of MB was not significantly correlated with either of the genders in the evaluated sample. Some authors revealed the presence of insignificant male predominance, while Polacek et al., in their study established significantly higher frequency of MB in male individuals of Czechoslovakian population. Nevertheless, until today rational explanation for differences with respect to gender has never been given.

Incidence of MB at the level of AIB was presented in different ways by many studies. Incidence of MB of 53.97%, that we established, is higher than the same of Šećerov, who examined 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 MB on AIB. Concerning MB location, Cakmak et al. also analyzed their presence in human fetal hearts (gestational age 6 – 10 lunar months) and found 50% of all MB at the level of AIB. They showed that 18 (46.2%) of the 39 fetal hearts had in total 26 MBs (one or more) on different branches of coronary arteries. Loukas et al. 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 presented incidence of MB on AIB as their percentage in relation to the MB detected in all investigated branches of coronary arteries and for that reason our results could not be compared to theirs. Nevertheless, Polacek et al. reported the presence of MB on AIB in 60% of the adult samples, which coincided with our results. Ballesteros et al., examined autopsy material which consisted of 154 hearts (average age 31.5 years) and found MB in 40.3% of all cases, from which 36.9% were localized on AIB, which is not in agreement with our findings.

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

Angiographic studies suggested that MB can be deep and superficial and that they mostly occur in the middle segment of AIB. Analyzing distribution of MB on AIB in our
study, we determined that their most common localization was in the proximal and middle segment of AIB simultaneously, with incidence of 44.12% of the samples, which is in agreement with the findings of Reig et al.\textsuperscript{24} and Bezerra et al.\textsuperscript{25} Less frequently, we detected MB in the middle (26.47%) or in the proximal segment (17.65%) of the vessel.

High variability of MB length has been reported in the literature, ranging from a few up to 50 millimeters\textsuperscript{7,15,24,26}. According to our results, average MB length on AIB was similar in both sexes (8.57 mm) which corresponded to the findings of Šečerov\textsuperscript{9} (3 – 10 mm).

Correlation analysis between the length of MB and gestational age of the fetuses revealed weekly increase of MB length with gestational age, but this increase was not significant. However, intensity of the increase of 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 AIB was higher in cases with MBs than in ones without them, 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 for this dilemma.

Histological organization of the MB in fetal hearts presented by Šečerov\textsuperscript{9} does not differ from the one presented in our study. Namely, she showed that muscle fibers of myocardium, after a parallel stream with AIB, divide into two fascicles and stretched, in most cases, perpendicularly upward and beyond 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 MB in adults may cause vasospasm which can lead to lethal ischemic events, arrhythmias, myocardial infarction and sudden cardiac death\textsuperscript{27,28}. According to Duygu et al.\textsuperscript{28}, who conducted their study on 71 patients with MB (mean age 51 ± 10 years), myocardial bridge may induce development of atherosclerotic lesions in a segment of AIB proximal to MB. They divided the patients into two groups, those with MB and no atherosclerotic lesions and those with atherosclerotic coronary artery disease in addition to MB. After performing 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 group (70% vs 35%, \(p = 0.01\)), while acute coronary syndrome appeared more frequently in the second group (65% vs 30%, \(p = \)).
Their treatment depended on length and depth of MB. The patients with long and deep MB underwent surgical revascularization, while others received medical management. Finally, from our results, it can be concluded that there is an association between MB in prenatal period and in adulthood. Based on morphological characteristics of MB on AIB, we suggest that 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 vascular dysfunctions and/or genesis of atherosclerosis.

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References


Table 1.

Myocardial bridges in relation to arterial localization and gender.

<table>
<thead>
<tr>
<th>Localization</th>
<th>Nº of hearts with MB (%)</th>
<th>Nº of hearts with 1 MB (%)</th>
<th>Nº of hearts with 2 MB (%)</th>
<th>Gender (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIB p</td>
<td>6 (17.65)</td>
<td>6 (17.65)</td>
<td>/</td>
<td>3/3</td>
</tr>
<tr>
<td>AIB m</td>
<td>9 (26.47)</td>
<td>9 (26.47)</td>
<td>/</td>
<td>3/6</td>
</tr>
<tr>
<td>AIB d</td>
<td>1 (2.94)</td>
<td>1 (2.94)</td>
<td>/</td>
<td>0/1</td>
</tr>
<tr>
<td>AIB p+m</td>
<td>15 (44.12)†</td>
<td>13 (38.24)</td>
<td>2 (5.88)</td>
<td>7/8</td>
</tr>
<tr>
<td>AIB m+d</td>
<td>1 (2.94)</td>
<td>/</td>
<td>1 (2.94)</td>
<td>1/0</td>
</tr>
<tr>
<td>AIB p+m+d</td>
<td>2 (5.88)</td>
<td>1 (2.94)</td>
<td>1 (2.94)</td>
<td>1/1</td>
</tr>
<tr>
<td>Total</td>
<td>34 (100%)</td>
<td>30 (88.24%)†</td>
<td>4 (11.76%)†</td>
<td>15/19</td>
</tr>
</tbody>
</table>

Myocardial bridges (MB); Anterior interventricular branch (AIB); Proximal (p); Middle (m); Distal (d); Proximal and middle (p+m); Middle and distal (m+d); Proximal, middle and distal (p+m+d); Male/Female (M/F);

† There is statistical significance in relation to other localization (p < 0.05).

† There is statistical significance between hearts with one and with double MB (p < 0.001).
**Figure legends**

Fig. 1 – Heart of fetus of male gender (gestational age 29 weeks). Sternocostal surface. Coronary arteries were filled with Micropaque. Insert showed 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). MB (*).

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

Fig. 3 – Myocardial bridge seen under the microscope. Obtained section was stained with haematoxylin eosin. The anterior interventricular branch (AIB) over bridged with myocardial bridge (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).
Fig. 1