

MYOCARDIAL BRIDGES OVER THE RAMUS INTERVENTRICULARIS ANTERIOR AND ITS BRANCHES IN CERCOPITHECUS AETHIOPS SABEUS

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Myocardial bridges (MBs) are structures consisting of heart muscle fibers running above the subepicardially positioned coronary arteries. In the light of previous studies, MBs are most often associated with the ramus interventricularis anterior (RIA) which put this vessel into the focus of our research.

The purpose of the present study was to determine the frequency of occurrence and quantitative analysis of myocardial bridges over the RIA and its lateral branches. The studied material consisted of 55 Cercopithecus aethiops hearts, of both sexes, preserved in formaldehyde solution. Standard anatomical methods were used in the analysis, with the help of a stereomicroscope. The presence of MBs over the RIA was confirmed in a total of 70.9% samples, with no statistically significant differences related to the gender. In 2 hearts (3.6%) multiple bridges were revealed. The length of the bridges varies in the range of 0.5 mm – 31.6 mm, the distance from the origin of RIA varies between 0.5 mm – 25 mm which makes the proximal third of the anterior (paraconal) interventricular groove most frequently tunneled. The lateral branches of RIA were overbridged in 5.4%, with a single muscular band. The length of MBs varied from 6.2 mm – 12.5 mm, and they were localized over the first lateral branch in all cases.

Key words: Cercopithecus aethiops sabeus, coronary arteries, myocardial bridging

INTRODUCTION

Myocardial bridge (MB), intramural coronary artery, mural coronary artery, tunneled artery, coronary artery overbridging, and myocardial loop, are various terms given to the particular heart condition when a portion of the epicardial coronary artery runs under the myocardial fibers for a short distance. It can be found in both humans and certain animals. Polaček and Audrička (1961) and Polaček and Zechmeister (1968) studied the relationship between the coronary arteries and MB in human and animal hearts, and classified the appearance of

coronary arteries into three types: type A (hamster, squirrel, rat, guinea pig, rabbit) in which the coronary arteries are embedded (intramyocardial); type B (dog, cat, non human primates, goat, sheep, man) in which the coronary arteries are predominantly epicardial but possess MBs; and type C (horse, cow, pig) in which the coronary arteries are entirely epicardial, with no heart muscle coverage and thus no MB. On the other hand Berg (1964a) classified pigs, chimpanzees and orangutans as type B, whereas gibbons and gorillas were placed into type C (Chase and Garis, 1939).

The reported prevalence of myocardial bridging phenomenon in humans and animals varies from author to author. The majority of investigators agree that myocardial bridging occurs in animals with coronary type B exclusively, (Polaček and Audrička, 1961; Hadžiselimović *et al.*, 1974), but others reported the MBs over the coronary arteries in pigs (Bertolini *et al.*, 1995), and cows (Santos *et al.*, 2000), belong to the C type. The prevalence varies substantially among studies thus suggesting a lack of fixed rules in the behaviour of coronary arteries in relation to the myocardium, and may in part be attributable to the understanding of the concept of MB.

Our previous studies of coronary artery distribution in non-human primates, conducted mainly on *Macaca fascicularis* (Teofilovski-Parapid *et al.*, 1993; 1998) and *Cercopithecus aethiops sabeus* (Nikolić *et al.*, 2000; 2003; 2007), indicated that blood supply to the monkey hearts is provided by two coronary arteries, occasionally three (Nikolić *et al.*, 2004), running predominantly subepicardially in the corresponding grooves. The direction, branching pattern and supply area of *r. interventricularis paraconalis* is remarkably similar to the *r. interventricularis anterior* in humans (Nikolić *et al.*, 2003). The great resemblance between the non-human primates vascular anatomy and the corresponding one in humans is confirmed by other authors (Filipović *et al.*, 2005; Blagojević *et al.*, 2005). Variable degrees of muscular overbridging in monkey hearts in small series have been reported (Teofilovski-Parapid *et al.*, 1992; 1993; 1994; 1998; Van Nie and Vincent, 1989).

The researches do not present a uniform attitude towards the myocardial bridging phenomenon (Lima *et al.*, 2002; Chen and Lin, 2003). The frequency of MB, their location, morphology and clinical significance arouse some controversies (Nikolić and Teofilovski Parapid, 1995; Nikolić *et al.*, 1996; Mohlenkamp *et al.*, 2002; Bharambe and Arole, 2008). The same thing is with the most of the fundamental questions based in relation to hearts muscle coverage of coronary arteries (Morales *et al.*, 1993), as whether MBs are normal variants of the coronary arteries anatomy (Yamaguchi *et al.*, 1996) or are an anomaly. Angelini *et al.* (2002) proposed that a coronary artery anomaly should be defined as any coronary pattern with a morphological feature encountered in <1%. By determining the incidence of anatomical variations an acceptable definition of normal and anomalous anatomy could be established and the clinical importance of anomalous variants ascertained.

The purpose of this study was to obtain the data on the frequency of occurrence of myocardial bridges, their length and location over the *ramus interventricularis anterior* (RIA) and its lateral branches in *Cercopithecus Aethiops sabeus* hearts.

MATERIAL AND METHODS

Animals

The subjects used in this study were 55 adult *Cercopithecus Aethiops* monkeys imported from East Africa (Kenya, Uganda, Tansania). Their age varied from 3.5 to 6 years (estimated from dentition) and weighted between 4.5 and 5.5 kg. Before the study monkeys were kept in a quarantine for 3 months, after which they were housed in pairs, in a climate-controlled environment (temperature 27°C, 12-h light/dark cycle) and fed *ad libitum*.

The animals were housed at the Institute of Virology Torlak (Belgrade) where all procedures were conducted in accordance with the International Guidelines on the Ethical Use of Animals.

Necropsy

The monkeys were deeply anesthetized by intraperitoneal injection of sodium pentobarbital, and after that euthanized with an intravenous injection of sodium pentobarbital (80 mg/kg). The coronary arteries were injected *in situ* (constant pressure of 18 kPa) through the aortic arch with coloured latex (Group A) or Simgal (methyl methacrylate, Group B).

Tissue preparation

After removal of the periadventitial adipose tissue by careful dissection, the blood vessels were prepared and attention was paid to their course i.e. whether the vessels run intramyocardially, subepicardially, or whether the muscular bridges (MB) or loops were present. Where MBs were found, the location and chosen morphological features such as length, thickness and direction of muscular fibers, were estimated. The vessels were drawn and photographed. The stereomicroscopic examination was performed, also.

Statistical analysis

In statistical evaluation we used descriptive statistical methods (central tendency measures: mean and mode, standard deviation – SD, minimum, maximum) while sexual differences were verified by Student's t-test for paired samples. The testing was performed on a 95% probability level.

The human anatomy terminology is used in this study (Terminologia Anatomica), with some explanations related to the differences in Nomina Anatomica Veterinaria.

RESULTS

The RIA was most frequently one of two terminal branches of LCA, rarely one of three and occasionally one of four LCA terminal branches. The average value of its external diameter at the very origin was 1.31 +/- 0.32 (SD) mm, ranging between 0.5 mm and 2.1 mm. Comparing to gauges of other terminal branches, RIA was most frequently the largest terminal branch of LCA. Descending through the anterior (paraconal) interventricular groove epicardially, towards the heart

apex, it impressed a fissure on the right heart margin and passed on to the diaphragmatic surface of the heart. Occasionally it was possible to follow its epicardial path only on the upper half of the sternocostal surface of the heart where it entered the myocardium.

From the epicardial segment of RIA arose the anterior right ventricular branches, with often prominent vessels directed to the arterial conus, as well as numerous branches entered the anterior part of the septum. Two to three diagonally directed branches arose from the left side of RAI along the anterior surface of the left ventricle, were considered as lateral branches of RIA.

The RIA was the most frequent overbridged coronary vessel in our study. Variable degrees of muscular overbridging of RIA were observed in 39 out of 55 hearts (70.9%), 25 females (71.4%) and 14 male ones (70%). The MB occurred most often as a single muscular band (96.4%), and in 2 hearts as multiple bands (3.6%), in one female (2.8%), and in one male (5%). The total number of MB over the RIA in the research was 41 (Figure 1).

Its predominant localization was the proximal third of the paraconal interventricular groove. The average distance of myocardial bridge from the RIA origin was 6.6 mm (limiting values varied between 0.5 mm to 25 mm).

The length of muscle bridges varied in a wide range between 0.5 mm and 31.6 mm. The shorter structures - up to 10 mm - occurred more often. The average length was 11.7 mm.

The presence of muscular bridging over the lateral branches of the RIA was confirmed in 3 hearts (5.4%), more often in female (5.7%) than in males (5%). In all cases it was a single muscular band (Figure 2).

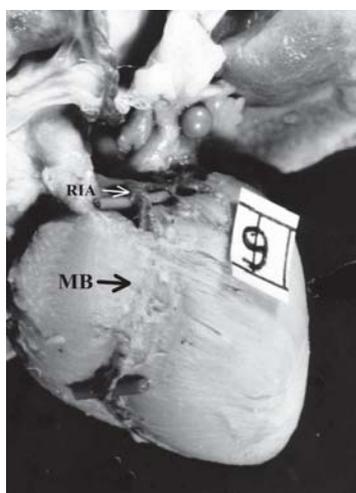


Figure 1. Myocardial bridge (MB) over the *r. interventricularis anterior* (RIA)

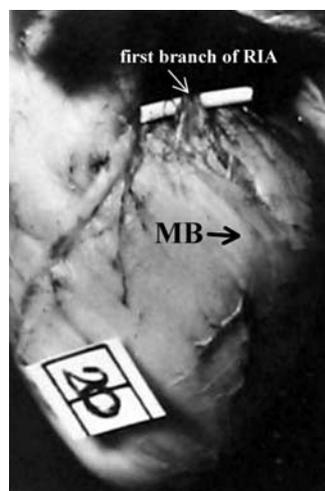


Figure 2. Myocardial bridge (MB) over the first lateral branch of RIA

Its localization was the first lateral branch exclusively. The average length was 8.9 mm, varying between 6.2 mm and 12.5 mm. The shorter structures – up to 10 mm – were found more frequently.

The statistical analysis of the obtained results revealed that the noticed differences between the myocardial overbridging incidence in male and female hearts was not statistically significant (RIA result $X^2=0.908$; $p>0.01$, lateral branch result $X^2=0.911$; $p>0.01$). Likewise, extremely great differences in length of myocardial bridges over these vessels could not be connected to gender.

DISCUSSION

Although, the phenomenon of muscle bridges was the subject of numerous studies, researchers do not share a common view of the frequency of their occurrence, their nature and significance. The incidence of myocardial bridging over the RIA in humans, has been reported to vary between 4.7% (Geringer, 1951) and 100% (Morales *et al.*, 1993), and such large differences may be attributable to the care taken at dissection during necropsy or interpretation of MB (Polaček and Audrlička, 1961; Mohlenkamp *et al.*, 2002).

The incidence of 70.9% of myocardial bridging phenomenon over the RIA in Cas hearts reported in our study, is important for comparative anatomy studies. It can be compared with the incidence of MBs reported in different species. Muscular formations have been described in wild boars with a similar frequency - 57.1% (Nocetti LM *et al.*, 2002), and 80% over the RIA reported by Hadžiselimović *et al.* (1974). Hadžiselimović *et al.* (1974), in their study, reported a prevalence of MBs over the RIA in domestic cats of 100%, while Bombonato *et al.* (1991), found MBs in 50% of examined cat hearts. On the other hand, Hadžiselimović *et al.* (1974) did not find MBs in dog hearts at all, while other authors described them with various frequency, from 15% to 45.6% (Yamaguchi *et al.*, 1996; Amaral and Bombonato, 1996; Tangkawattana *et al.*, 1997; Ozbag *et al.*, 2002). Studying the myocardial bridging phenomenon in bovine hearts authors have obtained varied results. Analysing of bovine hearts of Canchim race, Santos *et al.* (2000), observed MBs in 100%, and among them over the LCA branches in 86.94%, Severino *et al.* (1992) described MBs in 94% of bovine hearts, while over the LCA branches in 85.38%. Shinjo *et al.* (2004), reported the incidence of MBs over the RIA of bovine hearts of 75%, which is similar to our findings in Cas hearts. Myocardial bridging has been revealed in goats and sheep (Ozbag *et al.*, 2002), over the RIA, with a frequency of 60% and 26.6%, respectively.

Results of the current study showed that myocardial bridges over the RIA occur most frequently in the proximal third of the vessel. The length of the bridge varied between 0.5 - 31.6 mm, but the shorter structures i.e. up to 10 mm – occurred more often. The most frequent position of MBs in regard to RIA of the LCA found in our study is similar to that reported by Yamaguchi *et al.*, (1996) in dogs. The position however differs from the one reported in humans. MBs in humans, were seen to be most commonly localized in the middle segment of the RIA (Kosinski *et al.*, 2001; Mohlenkamp *et al.*, 2002; Vanildo *et al.*, 2002; Bharambe and Arole, 2008). According to different authors, the length of bridges in humans,

varies in a wide range (Geiringer, 1951; Kosinski and Grzybiak, 2001). Comparing the length of MBs in different species, Ozbag *et al.* (2002), reported the highest incidence of long MBs among humans, sheep and goats, but shorter structures were more frequent (49%) in dogs. It showed that localization and length of MBs in dogs is very similar to that reported in our study.

Our anatomical study of bridging over the lateral branches of the RIA, have revealed the frequency of 5.4%. MBs were distributed over the first lateral branch exclusively. The lack of studies referring the description, localization and length of MBs over the lateral branches of RIA in different species was obvious. Comparing our results with literature data, we found that Quagliatto *et al.* (2004), reported a case of 12 MBs presented in an adult female mountain lion who have died of natural causes. All 12 MBs were observed over the diagonal branches of the PIVB of the LCA, (the vessel similar to RIA): 3 MBs crossed the first collateral branch, 5 MBs crossed the second collateral branch, and 4 MBs crossed the fifth branch. Comparing morphological characteristics of MBs in humans and certain animals, Ozbag *et al.* (2002) described lateral branches of RIA overbridged in 0.9% in humans, 30.4% in dogs, 5.3% in sheep and none in goats. They classified those hearts as Type II, since the bridges were found over the arteries which are the first grade ramification of the RIA.

The phenomenon of muscular bridges over the coronary artery has also been reported in *Macaca radiata* (Van Nie and Vincent, 1989), *Macaca fascicularis* and *Cercopithecus aethiops*. Teofilovski Parapid *et al.* (1993; 1998), examined 11 hearts of *Macaca fascicularis*, and revealed MBs in 54%, over the LCA branches. The average length of MBs was 5.68 mm, ranging between 0.9 mm – 11.5 mm. The longest MBs were observed over the lateral branches of RIA. They did not report double bridges over the single vessel. The results of the analysis carried out in a small series (29 hearts) of Cas concerning the distribution of MBs over the RIA, delivered data similar to ours (Teofilovski Parapid *et al.*, 1992). As in the majority of descriptions, they found the most common location of MBs over the RIA (69%). The bridges were always single over the vessel, although many researches confirm the possibility of few bridges, which was similar to our findings.

The higher incidence of this anomaly in women than in man has been reported by Chen and Lin (2003). Conversely, Loukas *et al.* (2006) and Kosinski *et al.* (2004), found MBs more frequently in man 85.5% than in women (14.5%). Teofilovski Parapid *et al.* (1992, 1994) could not confirm a statistically significant sexual difference in myocardial bridges distribution in monkey hearts. This was the result of our study, as well.

Our morphological and quantitative study pointed that the myocardial bridges over the RIA and its branches in Cas were a very frequent phenomena, which emphasizes their clinical importance. On the other hand, similarities in frequency and distribution of MBs with humans make these monkeys suitable for use as a non human primate model for coronary artery bridging. The further analysis of the myocardial bridging phenomena in *Cercopithecus aethiops* hearts will be subject of our future research project.

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**MIOKARDNO PREMOŠĆAVANJE PREDNJE MEĐUKOMORNE ARTERIJE
(R. INTERVENTRICULARIS ANTERIOR) I NJENIH GRANA U MALOG ZELENOG
MAJMUNA (CERCOPITHECUS AETHIOPS SABEUS)**

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SADRŽAJ

Fenomen miokardnog premošćavanja subepikardnih koronarnih krvnih sudova je proučavan na 55 srca malog zelenog majmuna (*Cercopithecus aethiops sabeus*). Koristeći standardne metode disekcije, identifikovali smo prisustvo miokardnih mostova (MM) na prednjoj međukomornoj arteriji (RIA) na 39 od 55 srca (70.9%), od kojih su 25 (71.4%) bila srca ženki, a 14 (70%) srca mužjaka, što nije predstavljalo statistički značajnu razliku vezanu za pol ($p > 0.05$). U najvećem broju slučajeva, 96.4% zabeležili smo jedan MM nad RIA, a samo na 2 srca (3.6%) RIA je bila premošćena sa dva MM. Ukupan broj MM u našoj seriji je 41, a njihova najčešća lokalizacija je proksimalna trećina krvnog suda. Dužina MM je varirala između 0.5 mm i 31.6 mm, a češće smo nalazili kraće strukture (do 15 mm). Udaljenost MM od mesta nastanka RIA je varirala od 0.6 mm do 25 mm. MM nad (le-
vim) bočnim granama RIA (*r. laterales*) smo uočili na 3 od 55 srca (5.4%), i to na 2 srca ženki (5.7%) i na 1 srcu mužjaka (5%), što nije predstavljalo statistički značajnu razliku u odnosu na pol ($p > 0.05$). Dužina MM je varirala od 6.2 mm do 12.5 mm. U svim slučajevim smo našli po jedan MM nad prvom bočnom granom RIA.