Myocardial Bridge Associated with Cardiovascular Injuries in Bovines Adult of Canchim Race

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Abstract

Background: The influence that myocardial bridge exercises over blood stream in the course of arterial segment under the bridge has been discussed by the scientific community.

Objective: To compare ultrastructural muscle tissue of myocardial bridge and the ventricular wall; to analyze the degree of injury to the tunica intima of the arterial segments, and look for possible changes that may precede or initiate the process of atherosclerotic lesions.

Methods: Forty Canchim bovine hearts were studied regarding alterations of the tunica intima from coronary arteries on the different myocardial bridge segments. For the microscopic examination, hematoxylin-eosin and fuchsin-resorcin staining following conventional microscope techniques were made. For the electronic microscopic examination, myocardial Bridge segments from twelve Canchim bovine hearts were collected from the ventricle wall and coronary artery and were processed according to conventional techniques.

Results: In the light microscopy, a higher frequency of lesions on prepontine and postpontine segments of the tunica intima was observed, compared to the pontine segment. Tunica intima thickenings were followed by a disarrangement on the internal elastic limitant lamina. These cells often presented their cytoplasmas engorged by lipidic drops, making up the so-called foam cells. Electronic microscopy revealed that the muscular fibers of the myocardial bridge are usually joined in a straight and smooth way presenting lateral branches with a greater number of mitochondria in the ventricular muscle than in the bridge.

Conclusion: There are few differences between the muscle tissues studied; intimae lesions are less frequent in pontine regions compared to pre and post-pontine regions. (Arq Bras Cardiol 2012;98(1):22-28)

Keywords: Myocardial bridging/pathology, atherosclerosis, cattle, animal experimentation, mitochondria, heart.

Introduction

The heart has been awakening a special interest of researchers for a long time, making it an important organ for different kinds of approach. The influence that myocardial bridge exercises over the blood stream in the course of arterial segment under the bridge has been widely discussed by the scientific community.

Brodsky et al[1] and Kilic et al[2] suggest that myocardial bridging may be an independent risk factor for the development of myocardial ischemia and interstitial fibrosis. Santos et al[3] affirm that the muscular fibers of the bridge segment form angles with the longitudinal axis of arterial vessels holding a 46° average, being predominantly oblique to them, and trying to follow its longitudinal axis. Some authors[4-7] report that the presence of myocardial bridge can influence the arterial tissue through hemodynamic force changes, caused by the bridge muscle contraction. Yamaguchi et al[8] propose that the bridge muscle have features close to the skeletal striated muscle and Masuda et al[9] affirm that the atherosclerosis extension in the coronary intimae is less significant under the myocardial bridge compared with the proximal and distal segments, and reinforce a suspicion that coronary arteries intimae behavior could be changed by the presence of myocardial bridge. Based on this suspicion, we propose to investigate possible influences of myocardial bridge over the coronary arteries intimae features, as well as possible differences between the bridge tissue and the sub-epicardical cardiac muscle.

Methods

This material was acquired from slaughters carried out in different industrial establishments, with special permission from the Federal Inspection Service of the Agriculture Ministry, coming from animals without pathological cardiac processes, proved by *anti* and *post-mortem* examination, according to the procedure provided in the specific legislation in force.

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Light Microscopy

Forty Canchim bovine hearts from 25 males and 15 females with an approximate age of 30 to 48 months were used in this research. Fragments of myocardial bridges were located on the paraconal interventricular branches of the left coronary artery. Those fragments were constituted by prepontine, pontine and postpontine vessel segments and by the neighboring cardiac muscle tissue, which were fixed on 10% formaldehyde aqueous solution for a 72-hour period and then reduced into $1cm^3$ blocks, in order to individualize the said segments. The material was submitted to dehydration in progressive series of alcohol degree, clarified in xilene and paraffin, where sections of 7μm of thickness were immediately performed. Those sections were re-hydrated in order to be stained through the Hematoxylin-Eosin (HE) and Fuchsin-resorcin methods. After laminas had been prepared and stained, the surfaces of both the normal tunica intima and the damaged tunica intima were measured in all arterial branches from prepontine, pontine and postpontine segments, in order to obtain the percentage of the damaged area on the several regions of each vessel. For those measurements, digitalized images analyzed through the software HL image 97 were used.

Eletronic Microscopy

Twelve Canchim female bovine hearts, approximately thirty to forty-eight months old, were used for this research. For the electronic technical microscope, segments from the interventricular paraconal branch of the left coronary were collected. These were formed by the prepontine, pontine, and postpontine vessels, together with the muscle forming the myocardial bridge and segments from the sub-epicardical ventricle muscle from the ventricle wall. After being disconnected, they were fixed in a 2.5% glutaraldehyde solution tampon in a 0.1M (pH-7.2) sodium cacodylate solution, for forty-eight hours. After this, the material was washed in a 0.1M (pH-7.2) sodium cacodylate tampon, three times for fifteen minutes each, and was then post-fixed in a 0.1% Osmium Tetroxide plus 1.25% Potassium Ferrocyanide solution, for ninety minutes. Afterwards, the material was submitted to dehydration in crescent row levels of Alcohols and Propylene Oxide, included in epon resin, and later ultra-slim cuts were made. These cuts were contrasted using uranyl acetate and lead citrate, and afterwards analyzed and photographically documented by the Zeiss EM-109 electronic microscope.

The results of these two methodologies have been statistically handled. According to the results of analysis of variance, there was comparison of means by the Tukey test (a=5%), allowing comparison of treatments. The percentage of both statistical tests was transformed into arcsine, given the predispositions of the analysis of variance.

Results

Microscopic findings

The alterations on the tunica intima of the paraconal interventricular branches of the left coronary artery were viewed as thickenings of this layer where cells with light cytoplasm, and disarrangement and/or duplication on the internal elastic limitant lamina, were observed (Figure 1).

The percentages of the damaged area on the prepontine, pontine and postpontine segments from paraconal interventricular branches of the left coronary artery were statistically analyzed, where the variables position and sex were observed. The F test (Table 1) was significant for position, emphasizing that there is a variation on frequency and lesion degree between the arterial segments studied. The same test was not significant for the variable sex; in other words, the presence of lesions does not depend on this variable.

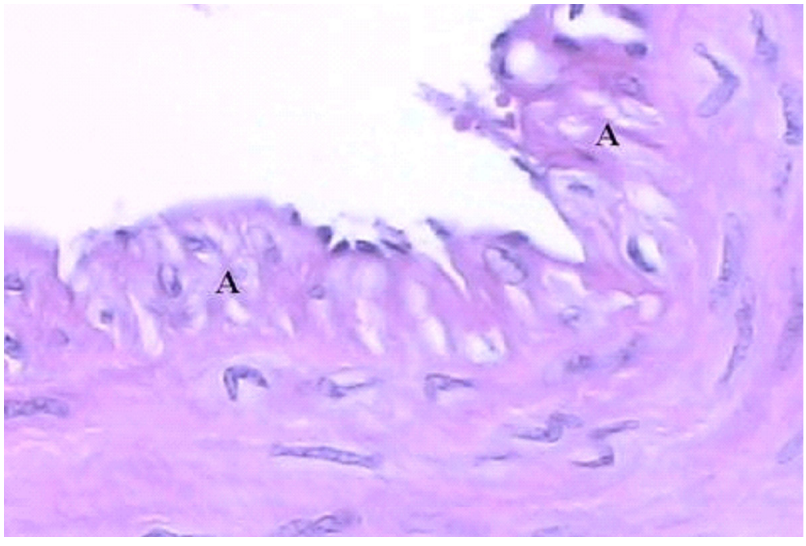

Figure 1 – *Microscopic cross-section of the interventricular branch paraconal of the left coronary artery, stained through the Hematoxylin-Eosin method, presenting thickenings in whole extension of the tunica intima, where cells with light cytoplasm are observed (A). Magnification (400x).*

Table 1 – Analysis of variance of the tunica intima lesion percentages of the paraconal interventricular branches of the left coronary artery of animals of different sexes on the prepontine, pontine and postpontine segments

C. Variation	G.L.	Q.M.	F
Sex (S)	1	630.4924	0.79 NS
Error (A)	28	797.2693	
Position (P)	2	2822.4686	18.64 *
Interaction P x S	2	69.9801	0.46 NS
Error (B)	56	151.4259	
C.V. for Sex = 73.96 C.V. for Position= 32.23			

*G.L - degree of freedom; Q.M - mean square; F - Analysis of Variance; * - significant by the F test (α=1%); NS - not significant by the F test (α=5%).*

The Tukey test (Tables 2 and 3) was found to be significant for the position variable, assuring that there is a higher frequency of lesions on the prepontine and postpontine segments from the tunica intima in the left coronary artery, when compared to the pontine segment. However, when the prepontine and postpontine segments are compared to each other, no significant difference on the lesion degree was found.

Electronic microscope technique

Ultrastructural aspects of the muscular fibers

In longitudinal cuts, it was possible to observe that muscular fibers of the myocardial bridge are usually joined in a straight and smooth way. These fibers are predominantly stuck on each other by means of an intercalated disc. These longitudinal cuts also revealed the sarcoplasm-reticulum-tube system forming triads, both in the bridge muscle and in the muscle from the ventricle wall, but dyad forms were the most common ones (Figure 2).

The myocardial fibers from the sub-epicardical ventricle wall showed, lengthways, an ellipsoid course, presenting lateral branches. Through the morphometric data, it was possible to evaluate the average and standard deviation relating to the area occupied by mitochondria, T tube and sarcoplasm-reticulum found in the bridge muscle, as well as in the muscle from the sub-epicardical ventricle wall (table 4). The mitochondria area was compared measuring both tissues and the statistical analysis showed a significant difference, sustaining that it is smaller in the bridge tissue than in the common cardiac tissue. However, the statistical analysis did not present significant differences when the T tube and sarcoplasm-reticulum area was compared in both tissues (table 4).

Ultrastructural aspects of the left coronary artery tunica intima

It was not possible to observe ultrastructural differences in the three arterials segments analyzed. The lesions observed in the tunica intima from the paraconal interventricular branch of the left coronary artery, irrespective of the kind of segment evaluated, were described as the tunica intima thickening with or without clear lesions of endothelium. In the thickening region, collagen fibrils, smooth muscular cells and some extracellular lipidic drops were found (Figure 3). The most intensive thickenings were usually accompanied by a disarrangement of the internal elastic limitant lamina, which were broken up or often duplicated (Figure 3).

In lesion regions, the endothelium was occasionally broken up. But when it was entirely composed of cells in polygonal or prolongation shapes, it presented a high level of micropinocytosis, even in areas not damaged. Cytoplasm lipidic drops were often observed in endothelium cells of lesion regions, but these were also apparently normal with a smaller frequency. Smooth muscular cells found in the thickened tunica intima were mostly rounded shaped tending towards polygonal shape with a greater amount of organelles compared to the muscular cells of the tunica media, often presenting cytoplasm lipid drops (Figure 3).

Table 2 – Tukey test establishing differences between sex on the incidence of tunica intima lesions of paraconal interventricular branches of the left coronary artery

Sex	Average
Male	40.8226 A
Female	35.5290 A

Equal letters (A) are similar averages.

Table 3 - Tukey test establishing differences on the incidence of tunica intima lesions of paraconal interventricular branches of the left coronary artery over several segments

Segment	Average
Distal	43.8230 A
Proximal	43.7285 A
Beneath	26.9758 B

Equal letters are similar averages and different letters are averages different from each other.

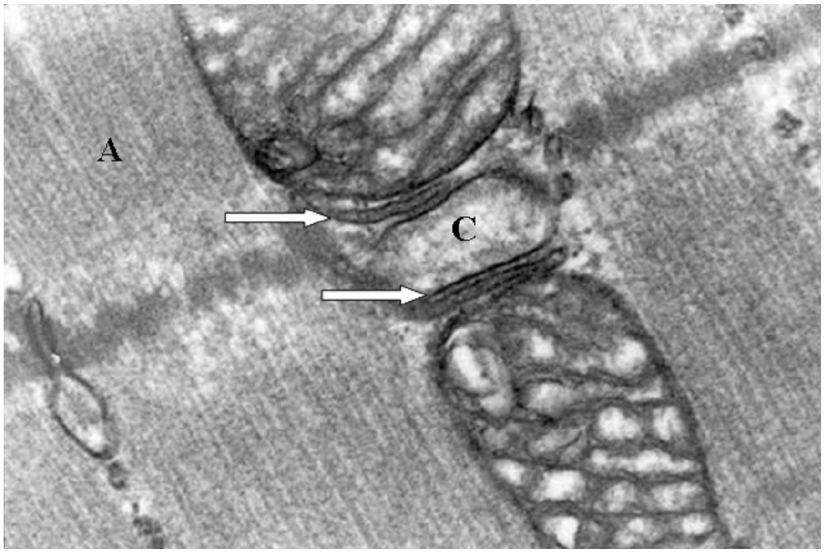

Figure 2 - *Photomicrography of bridge muscular tissue in a longitudinal cut, presenting myofibrils (A), mitochondria (B), T tube (C) and sarcoplasm-reticulum (→), both in a triad shape. (Increased 78000x).*

Table 4 – Variable for the mitochondria % (Q.M.1), T tube % (Q.M.2) and Sarcoplasm-Reticulum % (Q.M.3) analysis

Change rate	G.L.	Q.M.1	Q.M.2	Q.M.3
Treatments	1	193.62*	0.75 NS	0.99 NS
Error	20	12.57	0.63	2.71
Change rate		10.41	10.32	20.22
Average		34.05	7.73	8.15

*G.L - degree of freedom; Q.M - mean square; * - Significant by the F test (α=1%); NS – Not significant by the F test (α=5%); Data transformed into Arc Sen SQRT (X+0.50).*

Some smooth muscular cells were occasionally observed in the tunica intima and even in the tunica media with their cytoplasm engorged by lipidic drops, making up the so-called foam cells (Figure 4).

Discussion

In spite of the fascination caused by the heart study on researchers, we are too far from affirming that it is an entirely known structure. In the context of Animal Anatomy, it is possible to confirm that systematic reports are still beginning mainly when it comes to myocardial bridges or the possible influences that these bridges can exert on coronary stream.

Thus, we observe that classical writers[10] studied the topography of coronary arteries only regarding the characterization of their course and ramifications, without addressing the subject we have proposed. In this study, the statistical analysis allows us to assure that there are variations on the frequency of lesions present on the tunica intima of the left coronary artery branches, when prepontine and postpontine segments are compared to the pontine segment, as well as the non occurrence of significant variations on the appearance of these lesions between the males and females studied. Those results are consistent with those results from other authors[9,11-19], once all results assure that the lesion present at the tunica intima of these arteries along the pontine segment is smaller than those lesions observed on the other two segments. It was also possible to observe that when prepontine and postpontine segments are compared to each other, no significant difference on the lesion degree was found. Zoghi et al[20] add that the endothelial function is impaired in patients with MB and there is an increased tendency for atherosclerosis proximal to the bridge in patients with MB. The endothelial dysfunction is more severe in patients with atherosclerosis proximal to the bridge.

In a previous study, Santos et al[3] observed the angle generated between the muscular fiber and the longitudinal axis of the respective arterial vessels, which ranged from 11° to 168°, with median value of 46°; this fact established an oblique position for those fibers, tending to be longitudinal in relation to the axis of these vessels. Those results are consistent with other results reporting that the myocardial bridge alignment generates a longitudinal force along the fiber axis with minimum constriction of

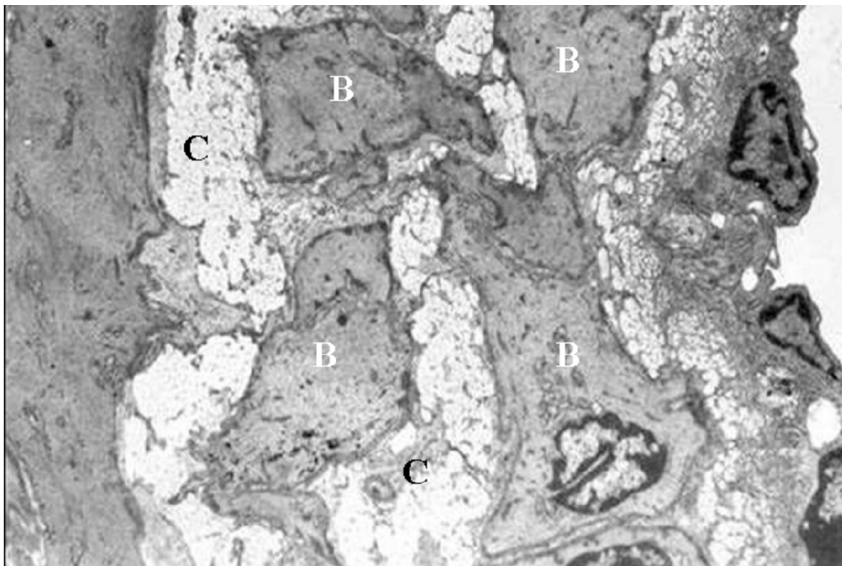

Figure 3 - *Photomicrography of tunica intima, with preserved endothelium, smooth muscular cells in a polygonal shape (B), duplication of the internal elastic limitant (C). (Increased 5000x).*

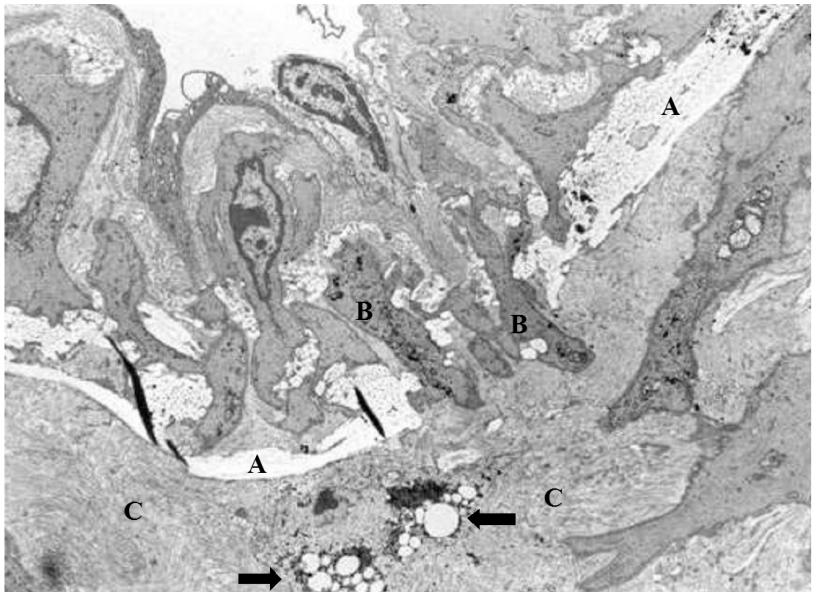

Figure 4 - *photomicrography of intima tunica, presenting the foam cell in the media tunica (→), internal elastic limitant (A), smooth muscular cells (B) and changed extra cellular matrix (C). (Increased 5000x).*

the coronary artery[21], and with results reporting that the presence of the myocardial bridge may influence the arterial tissue through haemodynamic forces alterations through its contractions[5]. Therefore, the highest obliquity of fibers[3], as well as the environment in which this artery is involved[21-23] could be a compensatory disposition mechanism in order to avoid possible lesions caused by haemodynamic forces alterations in the vessels.

Although several authors describe the myocardial bridge macroscopy, microscopic and ultra-structural aspects of these are still scarce[24-32].

The ultrastructural analysis of the myocardial bridge from the sub-epicardical muscular tissue reveal that muscular fibers are joined in a straight and smooth way, as described by Yamaguchi et al[8]. However, this research reported a similar amount of lateral branches in the bridge and in the parietal musculature, against the observations presented by the same authors.

As reported by Yamaguchi et al[8], the joining between the bridge muscular fibers was performed by the intercalated disc and the conclusion-terminal connection using collagen fibrils, which the authors called nipple joints. It is important to consider that this research has not found nipple joints in the ventricle wall of the Canchim bovine cardiac muscle, and the muscular cells found in the myocardial bridge did not form cellular joints side by side as were described by the said author. These authors also say that the sarcoplasm-reticulum-tube system of bridge muscular fibers was usually presented in a triad shape and these fibers, in cross-section, were personally disconnected by the conjunctive tissue[8]. Our results partially agree with his, because there was also such a triad-shaped system, however, these were not anatomically similar to those found in the skeletal muscle, since in addition to the fact that the sarcoplasma-reticulum does not form expansions around the T-tubule, which became severely dilated, these structures looked alike in the heart muscle of the ventricular wall. The bridge muscular fibers that we observed were also personally disconnected by the conjunctive tissue according to these authors[8], but it is important to emphasize that it was also found in the parietal cardiac musculature. However, the results found are consistent with those reported by these authors when they affirm that some structural aspects of the myocardial bridge tissue went astray from the common cardiac structure[8], because the statistical analysis revealed that there is a higher number of mitochondria present in the parietal cardiac tissue than in the bridge tissue. Moreover, there was not a significant difference when the occurrence of T tube and sarcoplasm-reticulum is compared between the tissues observed.

Whatever the ultrastructural aspects of the tunica intima left coronary artery analysis, we did not find any changes in the endothelium cells anatomy such as the changes pointed by Ishikawa et al[13], who described the polygonal shapes of these cells in the pre-bridge and post-bridge segments, while in the bridge segment these cells presented an elongated shape.

Regarding the changes in the tunica intima, the results of this research are consistent with Cheville[33] and Stary et al[34], who described several kinds of lesions which would precede or would start the atherosclerosis process. According to them, the most intensive thickenings of this layer caused disarrangements of the internal elastic lamina broken up and/or duplicated and these, were usually followed by endothelium damages. The invasion of lesion areas by collagen and muscular cells that reproduced and presented lipidic drops was also possible to observe.

The shape and huge amount of organelles observed in the smooth muscular cells of tunica intima lesion regions and the absence of fibroblasts suggest that these cells are involved with the increase of extra cellular matrix (collagen fibers and glycoprotein). A small amount of foam cells was observed both in the tunica intima and in the tunica media, as described by other authors[33-35].

Conclusions

The tunica intima lesions visible to the light microscopy are less frequent on the paraconal interventricular branches of the left coronary artery on regions covered by myocardial bridges compared to prepontine and postpontine regions.

There are few differences between the ultrastructure of the bridge muscular tissue and sub-epicardical parietal muscular tissue.

The injuries found in the tunica intima of interventricular paraconal branch of the left coronary artery, irrespective of the position evaluated, are similar to the lesions that precede the formation of atherosclerotic plaque.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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