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Morphological and Histological changes in coronary arteries due to Myocardial bridges

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Abstract

Background:
Myocardial bridges are muscular structures consisting of cardiac muscle fibers that pass above the coronary arteries and their branches. Myocardial bridges and their clinical implications are uncertain and many patients are generally asymptomatic. Smaller segments of myocardial bridges may remain asymptomatic for a longer duration and remain undiagnosed. However, longer and deeper myocardial bridge segments and may compress the underlying coronary segment and hamper blood supply have clinical symptoms.

Objectives: To study the histology and morphology of coronary arteries, pre-bridge, under-bridge and post-bridge segments, containing myocardial bridges.

Material and Method: The present study was a Descriptive Cross Sectional study carried out for a period of one and a half year on 60 adult cadaveric hearts. After locating the myocardial bridge ,they were dissected, cleaned and numbered. Arteries proximal and distal to myocardial bridges were identified and coloured by the use of brush and fabric colour. Specimens showing myocardial bridges were photographed. The tissues obtained during the morphological study were further processed and stained with Haematoxylin and Eosin(H&E) for further study.

Result: Out of 60 hearts, 22 (36.6%) hearts were having myocardial bridges, either in single or both major coronary arteries. All 22 cadaveric hearts had a myocardial bridge in Anterior Interventricular branch of Left coronary artery (LCA). On examining them histologically under a microscope, the average thickness of Tunica Intima was higher in the study group in both the pre-bridge and post-bridges segments. The average thickness of Tunica Media was also more in the pre-bridge and post-bridge segments compared to under bridge segment.On comparing the ratio of the Tunica Intima / Tunica Media there was hyperplasia seen in pre-bridge myocardial segments.

Conclusion: This study concludes that there was a marked intima hyperplasia in the pre-bridge segment and post-bridge segment compared to under bridge segment. The hyperplasia is more in the pre-bridge segment compared to post-bridgesegment.

Key words: Myocardial bridges, Hyperplasia of coronary artery, Histological changes in Myocardial bridges.

INTRODUCTION:

Right and Left Coronary Arteries supply blood to the Heart. Mostly, coronary arteries and their branches run through the subepicardial tissue and supply the myocardium but there may be a few variations to this rule like coronary arteries may also penetrate the myocardium and then reappear on the surface [1].Myocardial bridges are structures of cardiac muscle fibers that may pass above the coronary arteries and their branches[2]. Cardiac muscles covering the myocardial segment

of an epicardial coronary artery are called as myocardial bridge and the artery traversing within the myocardium is called a tunneled artery[1].Tunneled artery has their own clinical effects.
Coronary arteries have certain features that are not found in arteries elsewhere. Coronary arteries are muscular arteries. They differ somewhat, from the usual type of muscular arteries. Usually, the endothelium of the muscular arteries lies directly on the internal elastic lamina. But in coronary arteries, sub endothelial tissue is also present.

Clinical Implications:
Myocardial bridges and their clinical implications are uncertain and many patients are asymptomatic. Smaller segments may remain asymptomatic for a longer duration and remain undiagnosed. However, longer and deeper myocardial bridge segments may compress the underlying coronary segment and hamper blood supply and give rise to clinical symptoms[3]. However, myocardial bridges are associated with myocardial ischemia, myocardial infarction, coronary artery spasm, conduction abnormalities, ventricular arrhythmias and sudden death[4-10].

Conversely, it has also been suggested that myocardial bridges have a protective role against atherosclerosis as compared to non-bridged vessels[11-14].

Although myocardial bridges may protect the bridged arterial segment, however, there is a significant increase in the incidence of atherosclerosis in the vessel segment proximal to the myocardial bridges [15,16].There are few studies which suggest the near absence of atheromatous changes in the tunnel coronary segment in comparison to the pre-bridge segment of the coronary artery which has higher incidences of atheromatous changes [17-19].

There are very few studies done on the effect of myocardial bridges on coronary arteries in human hearts.The present work was therefore designed to study the morphology and histology of coronary arteries containing myocardial bridges in cadaveric hearts. The section covered by myocardial bridges as well as the pre-bridge segments and post-bridge segments were examined to determine whether there were any histo-morphometric changes in the segments and to study the impact of myocardial bridges on these segments.

Material and Method:
The present study was a Descriptive Cross Sectional study carried out for a period of one and a half year in the Department of Anatomy, Gandhi Medical College, Bhopal after obtaining ethical clearance from the Institutional Ethical Committee (Ethical No 20155-56/MC/7/2014 dated 29/07/14). A total of 60 adult cadaveric hearts were included in the study irrespective of age and sex. All the hearts studied were obtained from adult cadavers. All the hearts were cadaveric hearts procured during dissection in the department. Hearts were collected, cleaned and numbered before keeping them separately with all the aseptic precautions in 10% formalin.

Inclusion criteria: In the present study, adult hearts were included which have visible coronary arteries. Besides this, the heart having a single myocardial bridge artery was included. In the case of multiple bridges, the segment that was the post-bridge segment of the first bridge will be pre-bridge segment to the second bridge. Under these circumstances, it will be not possible to classify the proximal and distal segments.

Methodology:
Once a myocardial bridge was located, it was dissected, cleaned and numbered. The exact location from the beginning till the end of the myocardial bridge was defined. Both the pre-bridge and post-bridge segments of the coronary arteries were identified and coloured by the use of brush and fabric colour. Specimens having myocardial bridges were photographed by Sony digital camera of 12 mega pixel intensity from various angles.

The Coronary arteries showing the presence of myocardial bridges were further dissected for histological studies. The arteries dissected out had the following segments- one pre-myocardial bridge segment, one under bridge myocardial segment and one post myocardial bridge segment. all three components of the Tunneled artery were taken. We also took 25% i.e 10 hearts without a myocardial bridge for control purposes from the hearts having no myocardial bridges. The control arteries were divided into three segments, namely- upper one-third, middle one-third and lower one-third.
Each tissue was placed in a separate bottle of 10% formalin and labelled.

Histological Study [20]:
The tissues obtained during the morphological study were further processed with Haematoxylin and Eosin(H&E) stain for further study.

Detail microscopic study was also carried out to examine the histology of coronary arteries in various segments. Changes in normal histological patterns due to Myocardial Bridges were studied. Thickness of Tunica intima (TI) and Tunica media (TM) were measured with the help of an ocular micrometer. Thickness of TI and TM in each segment was noted and then means thickness was calculated and recorded

Statistical Analysis:
All the data were transferred into MS Excel software version 10 and the following statistics were applied. Descriptive statistics in the form of Mean, Percentage, Proportion and Standard Deviation (SD). Chi-square Test was applied to find out the difference between the two qualitative data ($p<0.05$ at CI of 95%). Unpaired Student T Test (Two-tailed) was applied to find out the difference between two quantitative data($p<0.05$ at CI of 95%)

Result:
In the present study, out of 60 adult cadaveric hearts, 22 (36.67%) hearts showed the presence of myocardial bridges in single or both major coronary arteries. All 22 cadaveric hearts had myocardial bridges in Anterior Interventricular branch of Left coronary artery (LCA) while only three cadaveric heart shad myocardial bridges in the Anterior Interventricular Artery as well as the Posterior Interventricular branch of Right Coronary Artery (RCA). The incidence of myocardial bridge was higher in the Left coronary artery (36.67%) compared to right coronary artery (5%) and this difference was statistically significant .The overall incidence of myocardial bridges in the cadaveric heart was 36.67% (Fig 1-3). On analysis of Table 1 it is evident that the distribution of myocardial bridges over the AIV artery was highest in middle one third (33.3%) followed by proximal one third(11.67%). The mean length of myocardial bridge in LCA was 18.42mm(± 1.24) and in RCA it was 15.53mm(± 0.41) and this difference was also statistically significant.

Table 1: Morphological characteristics of myocardial bridges present in LCA and RCA

Characteristics		**LCA**	**RCA**
Incidence	Number (N=60)	22 (36.67%)	3 (5%)
	P Value	χ^2=7.445; df=1; p=0.0064	
Location	Proximal 1/3*	7 (11.67%)	0
	Middle 1/3*	20 (33.33%)	1 (1.67%)
	Distal 1/3*	1 (1.67%)	2 (3.33%)
	P Value**	χ^2=11.10; df=2; p=0.0039	χ^2=0.667; df=2; p=0.414
Length	length	18.42 ± 1.24	15.53 ± 0.41
	P Value	T=3.943 Df=23.0 P =<0.001	

Note: *Six hearts showed two bridges over a different segment of Anterior Interventricular Artery (AIV) i.e of the total 22 hearts there are 28 bridges in AIV.
** P value is calculated separately to show the most common location of the Myocardial Bridge in both LCA and RCA.

In the Left Coronary Artery (LCA) six hearts showed two bridges while in Right Coronary artery showed a single bridge. Therefore, out of 60 hearts, histological studies were focused on 16(26.66%) hearts having a single myocardial bridge on the Left Anterior Descending. On doing the histological examination, the thickness of Tunica intima in Pre-bridge segment, Under- bridge segment & Post- bridge segment were 3.03mm(±0.56), 0.587mm(±0.12)and 1.493mm(± 0.82) respectively. It was noted that the average thickness of Tunica Intima was higher in both the pre-bridge and post-bridge segments. The average thickness of Tunica intima in control group were 1.01mm(±0.42), 0.7mm(0.004) & 0.5mm(±0.009) in proximal one third, middle one third and Distal one third respectively. (Fig 4-10) (Table 2)

Table 2: Histological Characteristics of Study and Control artery

Artery	**Study**	**Control**	**P value**
Tunica intima			
Pre-bridge vs Proximal 1/3 segment	3.031± 0.56	1.01±0.42	T=14.02; df=38.6; p value=0.002
Under bridge vs Middle 1/3 segment	0.587 ± 0.12	0.7± 0.004	T=4.79; df=41; p value =0.99
Post- bridge vs Distal 1/3 segment	1.493 ± 0.82	0.5 ±.009	T= 6.774; Df=45.5; P value=<0.001
Tunica Media			
Pre-bridge vs Proximal 1/3 segment	1.768 ± 0.04	2.2 ± 1.03	T=1.677; Df-14.5; P value=0.047
Under bridge vs Middle 1/3 segment	1.1 ± 0.14	1.6 ± 0.07	T=1.649 Df=45.5;

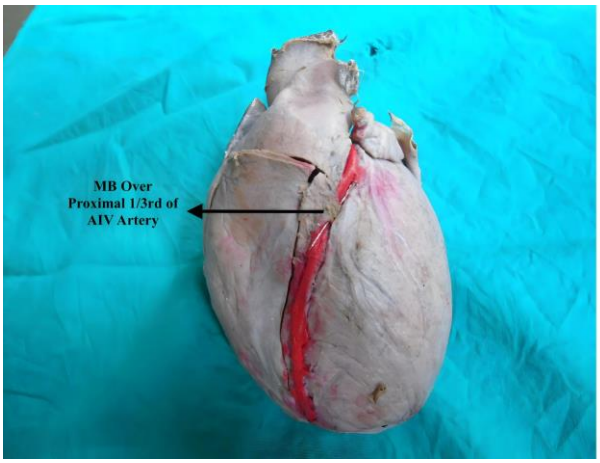
			P=1.15
Post- bridge vs Distal 1/3 segment	0.993 ± 0.015	1.3 ± 0.824	T= 1.48; Df=14.5; P value=0.039

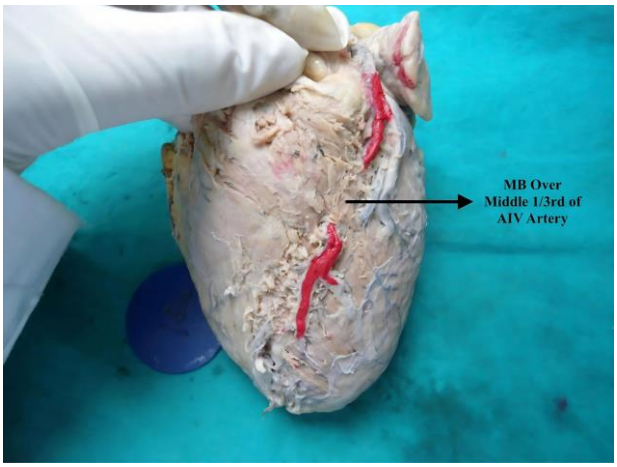
On doing a comparison of the Tunica Intima of the pre-bridge segments of the study arteries with the Tunica intima of the upper one-third of the control arteries there was a marked hyperplasia in the Tunica Intima of the pre-bridge segment of the study arteries and this difference was statistically significant. Similar hyperplasia was also noted in the post-bridge segment of the study group compared to the control group and there was a statistically significant difference noted (Table 2).

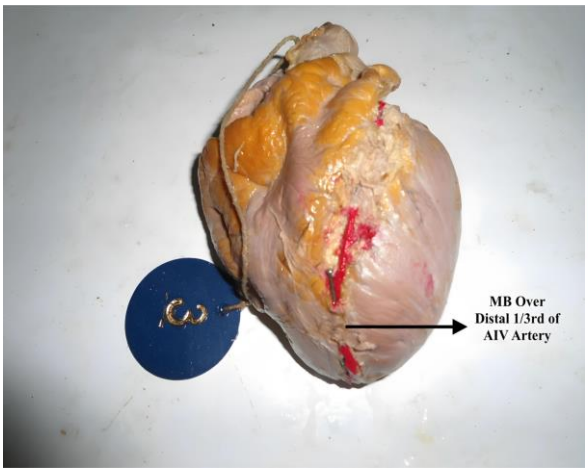
The average thickness of Tunica media was more in all segments of the control group compared to the study group.
The ratio of intima-media thickness in our study in the pre-bridge, the under-bridge and the post-bridge segments were 1.718, 0.53409 and 1.503 respectively. In the control group, the ratio of the thickness of tunica intima to media in proximal 1/3, middle 1/3 and distal 1/3 segments are 0.4545, 0.4375 and 0.3846 respectively.On comparing the ratio of the Tunica Intima / Tunica Media in the study and control group, it was noted that there was hyperplasia of the Tunica Intima in the study group in pre-bridge segments and post bridge segments compared to the control group. (Fig 11-13) (Table 3)

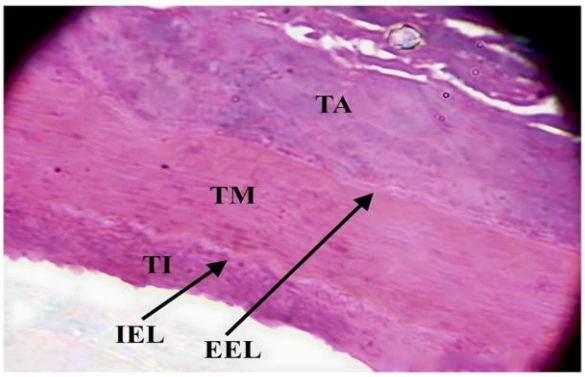
Table 3: Showing the ratio of Tunica Intima and Tunica Media in the study and control Group

Segment	**Study**	**Control**	**P value**
Proximal 1/3 segment	1.718	0.454	χ^2=0.7846; df=1; p=0.3757
Middle 1/3 or under segment	0.534	0.437	χ^2=0.0085; df=1; p=0.9264
Distal 1/3 segment	1.503	0.384	χ^2=0.4372; df=1; p=0.5085

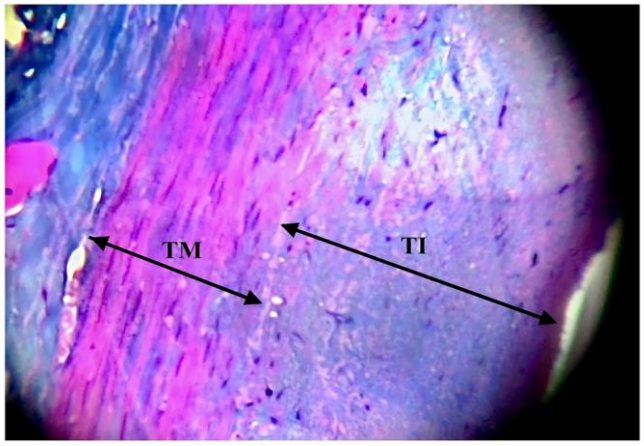




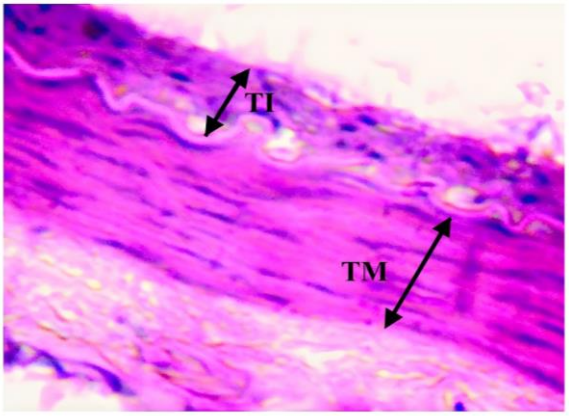




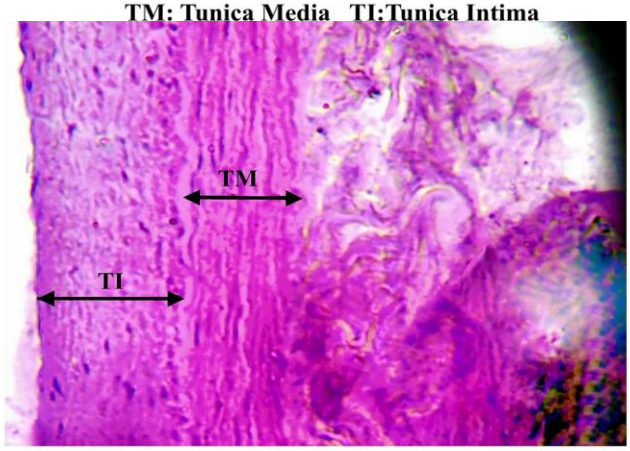
TA: Tunica Adventitia TM: Tunica Media TI: Tunica Intima EEL: External Elastic Lamina IEL: Internal Elastic Lamina



TM: Tunica Media TI:Tunica Intima



TI: Tunica Intima TM: TunicaMedia



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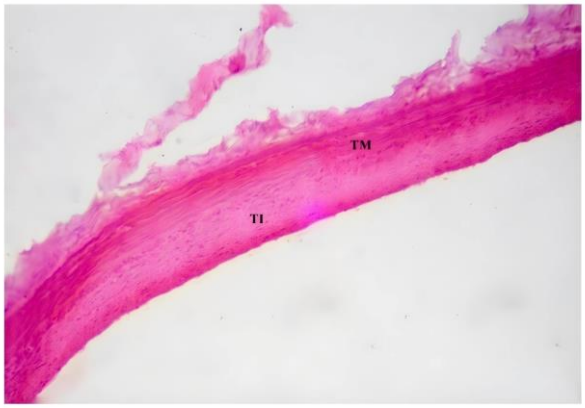
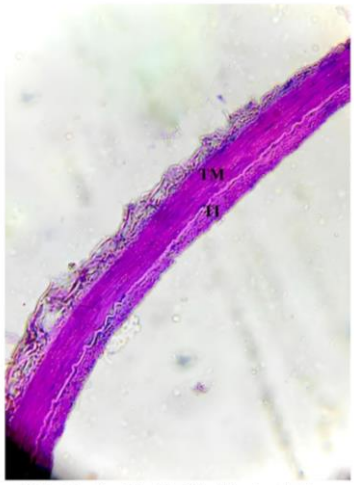
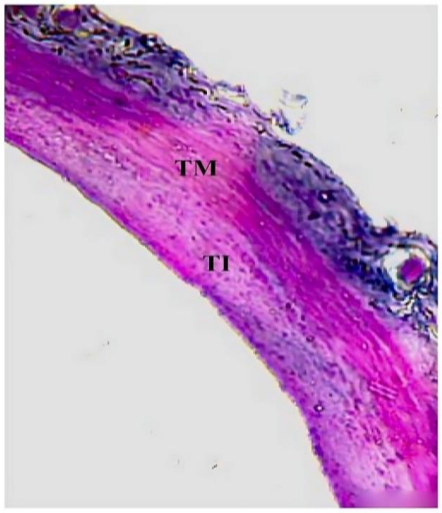


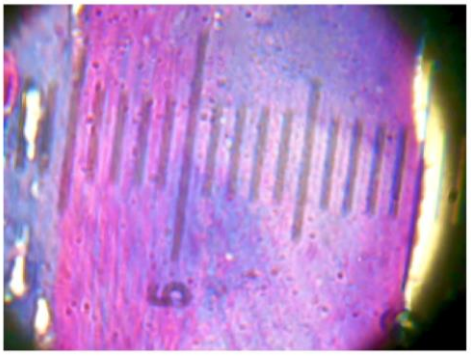
TM:Tunica Media TI: Tunica Intima

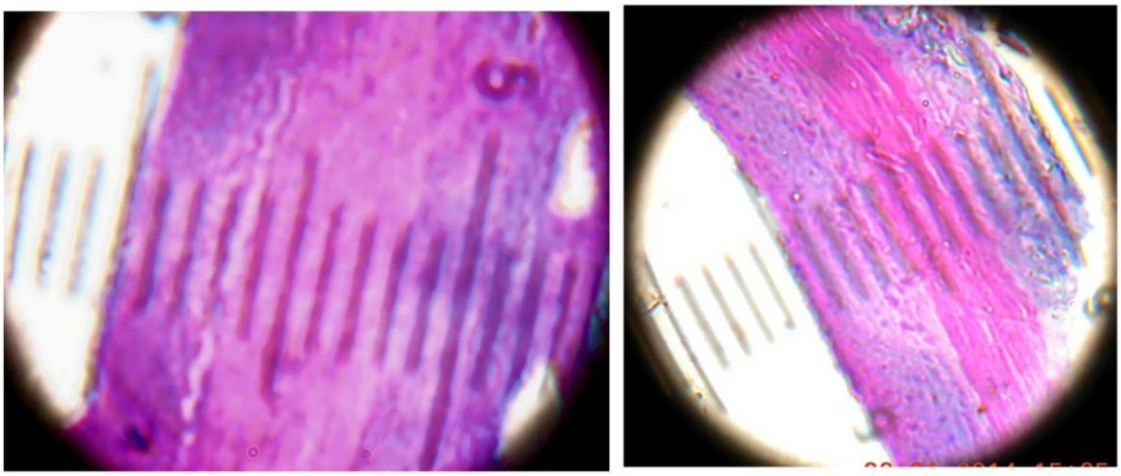


TM: Tunica Media TI: Tunica Intima



TM: Tunica Media TI: Tunica Intima





Discussion:

The prevalence of myocardial bridges reported in the present study was comparable with the results of other researchers. The prevalence of myocardial bridges in the present study was 36.67%. This is similar to the studies carried out by different researchers like Chodomella JRR[3], Loukas et al[11], Kosinski et al[13],Saidi H et al[19], and Stefanet al[21]. However, the prevalence was higher than the findings reported by Geiringer et al[15] and lower than that of Ferreira et al[22]. This difference could be attributed to the fact that there was variation in the number of hearts examined.

Myocardial Bridges were found on Left Anterior Descending in 22 of the 60 hearts. Five hearts with multiple bridges over LAD were not included in the study due to technical reasons. For the control hearts without Myocardial Bridge, three independent vessel samples from each of the segments (proximal 1/3, middle 1/3 and distal 1/3) were examined.
In the present study, the mean thickness of tunica intima of the pre-bridge segment was 5.17 times the intima of the under-bridge segment, as the mean thickness of tunica intima of the pre-bridge and the under-bridge segment were 3.0375 and 0.5875 micrometer respectively.

In a study by Shinjo et al[17] on bovine hearts, the histological analysis showed that the intimal layer was thick and well developed in the pre-bridge segment and contain elastic fibers. Saidi H et al[23] studied the tunica intima of the pre-bridge and that of the post-bridge coronary vessels and found that the pre-bridge appeared thicker (thickest proximally) than that of under-bridge segments. When compared with the sub endothelial zone of the pre-bridged segment to the under-bridged vessels segment, the pre-bridged segment contained abundant connective tissue including elastic fibers. In the present study the mean thickness of tunica intima in the pre-bridge, the under-bridge and post bridge segment were 3.0375, 0.5875 and 1.49375 micrometer respectively. Therefore, there is a marked intimal hyperplasia that occurs in the pre-bridge segments while intima is thinnest in the under-bridge segment. In the present study, the mean thickness of tunica media of the pre-bridge, the under-bridge and the post-bridge bridge segment were 1.768, 1.1, and 0.99375 micron meters respectively.

Ishikawa et al[24]) studied the intima-media ratio and development of atherosclerotic plaque. In the study, he measured the area of intima and media using a visual 32 image analysis system to assess the extent of atherosclerosis. The area ratio of the intima-to-media was defined as the intima-media ratio. By this method, the intima-media ratio was usually 0.2 to 0.8 in almost normal LAD and < 1.5 in LAD segments that had diffuse intimal thickness. In the patients with myocardial infarction having a Myocardial Bridge, the intima-media ratio in the under-bridge segment was significantly lower than in the pre-bridge segment. The ratio of the post-bridge segment to the under-bridge was also lower than that of the pre-bridge segment. The ratio of intima-media thickness in our study in the pre-bridge, the under-bridge and the post-bridge segments were 1.718, 0.53409 and 1.503 respectively. In the control group, the ratio of the thickness of tunica intima to media in proximal 1/3, middle 1/3 and distal 1/3 segments are 0.4545, 0.4375 and 0.3846 respectively. These findings correlate well with the findings of Ishikawa et al[24].

Risse and Weiler[25]reported that the intima of the tunnelled artery is significantly thinner than that of the pre-bridge segment of the artery. Furthermore, changes in the endothelial cell morphology indicated that the Intima beneath the myocardial bridge could be protected by hemodynamic factors such as high shear stress.

We also observed that the under-bridged segment of the coronary artery tends to have a reduced tunica intima as compared to the proximal and distal segments. Conversely, the bridge protects the under-bridge segment from atherosclerosis, manifesting with a reduced intima even in comparison to the distal zone. Compression of the tunnelled segment may be associated with increased resistance to follow and reduced mural tension for any given tension as deduced from the Laplace principle [25,27].

Limitation of our study is that we have taken cadaveric hearts so we are unaware of any history of coronary artery disease in the cadaver. So, the cause of death cannot be correlated with the coronary artery disease due to myocardial disease.

Conclusion:

The present study concludes that the myocardial bridges are quite common in the cadaveric hearts. The results of the current study show that Myocardial Bridges occur most frequently over the AIV branch of LCA.

The study also concludes that there is a marked intima hyperplasia in the proximal segment and distal segment compared to under bridge segment. The hyperplasia is more in the proximal segment compared to the distal segment. On comparison of ratios with the control group, there is an increase in ratio in the arteries having myocardial bridges.

It was also seen that the tunica media is more thickened compared to intima in the bridged segment.

The present study concluded that the Myocardial Bridge is an important protective factor against atherosclerosis in the under-bridge segment. In contrast, there is an increased incidence of atherosclerosis in the pre-bridge segment. This is attributed to the fact that there is a marked intimal hyperplasia in the pre-bridge segment compared to the under-bridge segment.

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"The authors sincerely thank those who donated their bodies to science so that anatomical research could be performed. Results from such research can potentially increase mankind's overall knowledge which can then improve patient care. Therefore, these donors and their families deserve our highest gratitude"[28].

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