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A 20-Year Autopsy Study of Myocardial Bridging Among Sudden Deaths

Ahmad Shafiie Ahmad Amran[1,2], Faridah Mohd Nor[1], Mohamed Swarhib Shafee[1], Nadiawati Abdul Razak[3]*

[1] Forensic Unit, Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, Cheras, 56000 Kuala Lumpur, Malaysia.
[2] Department of Forensic Medicine, Hospital Miri, Jalan Cahaya Miri 98000 Sarawak Malaysia.
[3] Forensic Medicine Unit, Faculty of Medicine and Defense Health, National Defense University of Malaysia, Kuala Lumpur, Malaysia.

*Corresponding author's email: drnadiawati@yahoo.com

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ABSTRACT

Myocardial bridging (MB) is a condition, where the cardiac muscle overlies the intramyocardial segment of the major epicardial coronary artery. This study aims to analyse the demographics and anatomical characteristics of MB within a pool of 2093 sudden cardiac-related death cases examined at the Forensic Unit of Universiti Kebangsaan Malaysia Medical Centre between 2000 and 2019. In this cross-sectional study, postmortem data collected were gender, racial affiliations, MB anatomical properties, and association with cardiac pathologies entered into the statistical software SPSS version 25 for analysis. The prevalence of MB was 12.9%. It was commoner in males (91.5%). MB was predominant between age 21-40 years old (50.2%). Chinese race showed the highest number of recorded MB cases (24.3%) among local races. MB was mostly found in left anterior descending (LAD) artery (98.2%), with the commonest length of 11-20mm (44.6%), depth of 1-5mm (49.8%), and distance from the ostium of 21-40mm (54.0%). The prevalence of isolated MB (43.2%) was nearly comparable to that of MB with cardiac pathologies (56.8%). MB was mostly associated with atherosclerosis (50.1%) and atheroma formation was mostly proximal to MB (78.3%). MB is a common occurrence and commonly found in the LAD as a single entity. It has a higher preponderance in the male gender among the adult population. In conclusion, the findings not only contribute

to a deeper understanding of MB but also hold potential implications for identifying and managing risks related to sudden cardiac-related deaths. It is a pathological condition at a certain length and depth whether it exists as an isolated entity or associated with cardiac pathologies. Atherosclerosis tends to form proximal to MB and might pose a risk for myocardial infarction.

INTRODUCTION

Myocardial bridging (MB) is a condition where the cardiac muscle overlies the intramyocardial segment of the major epicardial coronary artery. It is synonymously described as a myocardial bridge, an intramural coronary artery, a mural coronary artery and a tunnelled artery (Angelini et al., 2002; Bourassa et al., 2003). The medical fraternity is still divided in terms of whether MB is a congenital anomaly or just a common anatomical variant. The prevalence of MB greatly varies based on autopsy data as well as radiography data. For the autopsy, several studies showed a prevalence between 2% to 85.7% (Desseigne et al., 1991; Poláček, 1961).

Even though MB might be found as a single entity, its association with certain cardiac pathologies has been reported such as coronary atherosclerosis, MI, hypertrophic cardiomyopathy or even sudden death (Srettabunjong, 2016; Zhu et al., 2012). Patients with underlying MB are mostly asymptomatic but some of them present with recurrent chest pain or syncope (Abdou, 2011; Daana et al., 2006). The presence of MB is clinically significant if it can be proved that the patient presents with angina and MI, and the coronary angiography record shows >70% systolic compression (Mookadam et al., 2009).

Regarding coronary atheroma formation, MB has been said to promote proximal atherosclerosis whereby the bridged segment of the coronary artery is protected from atherosclerotic plaque formation (Akishima-Fukasawa et al., 2018; Nakaura et al., 2014; Uusitalo et al., 2015). MB is most commonly found in a single coronary artery which is the LAD artery even though some people might have more than one bridging in other coronary arteries (Lujinović et al., 2013).

In the Malaysia setting, so far there is still no study has been done on MB except for two case reports, both in 2010 and 2019 respectively (Ngow & Wan Khairina, 2010; Rohani et al., 2019). Both cases were based on living patients and radiographical imaging findings. Hence, as a starting point, this study will serve as a preliminary study in examining the demographic and anatomical properties of MB in medico-legal autopsies of sudden death cases brought into the Forensic Unit, Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The objectives of this study were to study the prevalence of isolated MB and the prevalence of MB associated with cardiac pathologies.

MATERIALS AND METHODS

The sample population comprised autopsy cases of sudden death cases received at the Forensic Unit, UKMMC between the years 2000 and 2019 (20-year-study). All cases had fulfilled the inclusion criteria i.e. sudden death from cardiac disease including all males and females, regardless of racial affiliations. Additional inclusion criteria were added during data collection as a pending cause of death for autopsy cases with MB is the only positive finding. The exclusion criteria were sudden death other than a cardiac disease, traumatic death with incidental finding of MB, and death of another manner i.e. accidental, suicidal, and homicide cases. All cases were taken from postmortem reports, and the data were analysed by descriptive statistics. The calculation is based on the total number of sudden death cases with MB in relation to the total number of medicolegal autopsies over 20 years and with the total number of sudden death cases with cardiac origin. The socio-demographic data assessed were gender, age groups, and racial affiliations.

Racial affiliations were divided into categories of Malay, Chinese, Indian, others (Malaysian local natives) and foreigners. The description of coronary artery involvement with MB, the length, the depth, and the distance of MB from the ostium. The presence of MB in one or more coronary arteries was also included. MB was also described as isolated MB or associated with cardiac pathologies such as atheroma formation, MI, or hypertrophic cardiomyopathy (HCM). Concerning atheroma formation in MB, its relation to MB in the coronary artery was described and identified. This study was intended to find the relation of MB to gender, age, and racial affiliations and the relation of MB to association with cardiac pathologies (atheroma formation, MI, HCM). The collected data were tabulated and statistically analysed using SPSS version 25. The significance of the difference was tested using the chi-square test. A P value <0.05 was considered statistically significant (S). The study was approved by the UKM Research Ethics Committee (Ref No: UKM PPI.800-11/1/5/JEP-2019-354).

RESULTS

Prevalence

From 2000 to 2019, a total of 6270 medico-legal autopsies had been conducted in UKMMC. Based on the inclusion and exclusion criteria, a total of 2093 cases were selected. Among those cases, MB was recorded in 271 cases which made the prevalence of MB 12.9% over total cardiac-related death and 4.3% over total medico-legal autopsy cases. Throughout the 20 years of data, the range of prevalence of cardiac-related death was from 2.0% to as high as 31.7% (Table 1).

Demographic data

Among those cases with MB, males (91.5%, n=248) showed higher preponderance than females (8.5%, n=23). From the data, it showed that MB was most commonly found between 21 to 40 years old (50.2%, n=136) and was less common in the age group of 1 to 20 years old (3.3%, n=9). It showed that from the record the Chinese races were highest in several cases for recorded MB as compared to other local racial affiliations (24.3%, n=66). MB was present in a quite significant number of foreigner cases which had been autopsied in UKMMC (39.5%, n=107) (Table 2). Single MB was found to appear significantly more frequently in males than females, in young age (1-20 years) and adults (21-40 years) and Indian and Malaysian local natives. However, generalization could not be made to the real population as there were limited data available for age groups and racial affiliations for analysis and comparison (Table 6).

Anatomical properties of MB

In 271 cases that presented with MB, a total of 273 MB was recorded with the majority of them possessing single MB (99.3%, n=269) with only 2 cases with double bridging found (0.7%, n=2). MB tends to develop in the LAD artery (98.2%, n=266) as compared to other coronary arteries. Out of 271 cases with MB, there was a variable number of total MB for length (N=258), depth (N=239) and distance from ostium (N=263) as cases without recorded values were omitted from the calculation. It had been found that MB length was from 11mm to 20mm in most of the cases (44.6%, n=115). In nearly half of the cases, the depth of MB from epicardial fat was to be from 1mm to 5mm (49.8%, n=119). More than half of the MB recorded was located between 21mm to 40mm from the ostium (54.0%, n=142) (Table 3).

MB association with cardiac pathologies

It had been shown in this study that isolated MB (43.2%, n=117) was almost equally equivalent to MB associated with cardiac pathologies (56.8%, n=154). Among those cardiac pathologies, atherosclerosis was more predominantly associated with MB whether present alone or mixed with other cardiac pathologies (50.1%, n=138) (Table 4). Regarding atheroma formation, the data is collected based on its formation in the coronary artery where the MB was present

regardless of its location pertaining to MB. It showed that more than two-thirds of the data had shown the development of atheroma was proximal to the location of MB (78.3%, n=108). For the remaining cases of MB with atherosclerosis, it was not recorded in the autopsy draft whether the atheroma was located within the bridging segment of the coronary artery or distal to it (Table 5). It was noticed that single MB was highly significantly presented as either isolated MB or associated with atheroma formation in the involved coronary artery. However, a similar conclusion did not apply to other cardiac pathologies as available data was limited for analysis and comparison (Table 7).

Table 1: Prevalence of myocardial bridging cases over 20 years.

Year	Autopsy cases	Cardiac-related death	Cardiac-related death with MB	Prevalence over autopsy cases	Prevalence over cardiac-related death
2000	215	38	1	0.5	2.6
2001	262	45	1	0.4	2.2
2002	240	49	1	0.4	2.0
2003	265	42	9	3.4	21.4
2004	279	60	19	6.8	31.7
2005	285	73	13	4.6	17.8
2006	321	116	11	3.4	9.5
2007	235	69	7	3.0	10.1
2008	204	65	9	4.4	13.9
2009	277	85	16	5.8	18.8
2010	263	93	16	6.1	17.2
2011	284	101	17	6.0	16.8
2012	331	116	15	4.5	12.9
2013	333	118	18	5.4	15.3
2014	370	155	17	4.6	11.0
2015	392	187	26	6.6	13.9
2016	360	161	25	6.9	15.5
2017	412	161	16	3.9	9.9
2018	446	165	15	3.4	9.1
2019	496	194	19	3.8	9.8
Total	6270	2093	271	4.3	12.9

Table 2: Demographic characteristics of autopsy cases with myocardial bridging.

Personal Identification	No. of cases (%), N=271
Sex	
Male	248 (91.5)
Female	23 (8.5)
Age group	
1-20	9 (3.3)
21-40	136 (50.2)
41-60	112 (41.3)
61-80	14 (5.2)
Racial Affiliations	
Malay	59 (21.8)
Chinese	66 (24.3)
Indian	33 (12.2)
Others	6 (2.2)
Foreigners	107 (39.5)

Table 3: Anatomical properties of myocardial bridging.

Anatomical properties of myocardial bridging	No. of cases (%)
Single MB (N=271)	
LAD	266 (98.2)
RCA	3 (1.1)
Double MB	
LAD+RCA	2 (0.7)
MB length (mm, N=258)	
1-10	69 (26.7)
11-20	115 (44.6)
21-30	43 (16.7)
31-40	18 (7.0)
41-50	7 (2.7)
>50	6 (2.3)
MB depth (mm, N=239)	
1-5	119 (49.8)
6-10	97 (40.6)
11-15	16 (6.7)
16-20	5 (2.1)
>20	2 (0.8)
MB distance (mm, N=263)	
1-20	64 (24.3)
21-40	142 (54.0)
41-60	46 (17.5)
61-80	10 (3.8)
>80	1 (0.4)

Table 4: Myocardial bridging association with cardiac pathologies.

	No. of cases (%), N=271
Isolated MB	117 (43.2)
MB associated with	
Atherosclerosis (AS)	116 (42.8)
Myocardial infarction (MI)	9 (3.3)
Cardiomyopathy (CM)	7 (2.6)
Mixed	22 (8.1)

Table 5: Atheroma formation in relation to myocardial bridging.

	No. of cases (%), N=138
Proximal to MB	108 (78.3)
Unknown relation to MB	30 (21.7)

DISCUSSION

MB is one of the medical entities that has been a topic of debate for many years people tend to discuss as simply as whether it is an anomaly or just a common variant of coronary artery or to an extent conducting a study on assessing its physiological role in promoting myocardial ischaemia in a heart (Tarantini et al., 2018). One of the topics of interest in MB is the study of its prevalence which has been conducted widely all around the globe, using autopsy or radiography.

Most prevalence of MB found in the works of literature was based on the direct dissection of the formalin-fixed heart with the given value from 34.5% to as high as 85.7% (Loukas et al., 2006; Poláček, 1961). However, a retrospective study of the relationship between MB and sudden death in a series of 930 medico-legal cases in 1991 showed a prevalence of only 2% MB among those cases (Desseigne et al., 1991). The prevalence of MB in this study was 4.3% over total medico-legal cases was considered comparable to that study. The prevalence of MB over total cardiac-related death which is the main focus of this study was 12.9% which was not in agreement with those studies with direct heart dissection mentioned earlier. There was no specific prevalence pattern over the 20 years of our data collection.

We could appreciate that the male gender always showed higher preponderance than the female gender in terms of the presence of MB in the coronary artery. From this study, the male gender was more predominant with 248 (91.5%) cases out of 271 cases of sudden death with MB. In 2006, a study on the relationship of MB to coronary artery dominance by Loukas M. et al on 200 human hearts showed that MB was present in 69 hearts and among those number, 59 hearts were from a male body which made up about 85.5% (Loukas et al., 2006). Furthermore, Akishima-Fukusawa Y. et al 2018 conducted a study on 150 human hearts regarding MB's influence on atherosclerosis development in the LAD of the normal heart. The data from that study showed MB was present in 93 hearts and from that number, the heart which originated from a male was 65 hearts (Akishima-Fukasawa et al., 2018).

Sudden death cases with MB came from an adult age group which was between 21 to 40 years old as seen in this study. This is in accordance with a study by Morales A.R. et al the mean age of the study population was 31.0 (Morales et al., 1993). However, our data was not correlated with few studies in terms of age range where their range of mean age was from 51.0 to 71.4 (Akishima-Fukasawa et al., 2018; Kim et al., 2010; Micić-Labudović et al., 2015;

Mookadam et al., 2009).

For anatomical properties of MB, our data showed MB was mostly dominant in the LAD, followed by the Right Coronary Artery (RCA) then in both coronaries. These findings are in agreement with a few studies that demonstrated similar findings (Job et al., 2016; Loukas et al., 2006; Swaroop et al., 2014). It has been supported by Lujinovic A. et al who demonstrated that single bridging is commoner than more than one bridging (Lujinović et al., 2013). Even though MB might be present as triple bridging in certain people, our data did not accord with that fact. However, a study by Loukas M. et al observed two hearts with triple bridging among 69 human hearts with bridging (Loukas et al., 2006). An almost similar finding was recorded in 2014 when Swaroop N. et al observed two human hearts with triple bridging among 35 human hearts that present with MB (Swaroop et al., 2014). Nevertheless, the highest case recorded for triple bridging was from a study by Ferreira A.G et al way back in 1991 with a total of five human hearts (5.5%) presented with triple bridging among 50 human hearts MB (Ferreira et al., 1991).

In terms of MB parameters such as the length, depth from epicardial fat and distance from ostium, all literature found were discussing mainly the former two of the parameters most probably because both of them have more physiological effects on coronary blood flow and cause ischaemia in the myocardium. Our study observed that MB length was most commonly measured from 11mm to 40mm and its depth was from 1mm to 5mm. The commonest location of MB in our study was at the middle of LAD (21mm-40mm). Our data is supported by a study in 1961 where the recorded length and depth for MB were from 10mm to 20mm and a maximum depth of 5mm respectively (Poláček, 1961). This is later supported by Lujinovic A. et al the study observed a mean length and depth for MB was 14.64mm and 1.23mm respectively (Lujinović et al., 2013). In 2015, another study by Micić-Labudović J. et al found that the average length for MB was 21.85mm and its depth was 3.74mm which is again in agreement with our study (Micić-Labudović et al., 2015). Mookadam F. et al observed that mid-LAD MB was the commonest pattern with 54.4% among his study population and this finding is almost similar to our result with 54.0% MB located in the middle part of LAD (Mookadam et al., 2009).

To prove that MB at a certain length and depth would contribute to myocardial lesions we used a study by Morales A.R. et al back in 1993 as an example. This study involved 39 human hearts with MB in LAD which was then divided into Group 1 and Group 2. Group 1 consisted of 22 hearts with myocardial lesions whether observed grossly and/or microscopically, while Group 2 consisted of 17 hearts without myocardial lesions. The myocardial lesions could be any one or more of the following; interstitial fibrosis, replacement fibrosis, contraction band necrosis, and/or increased vascular density in areas of focal fibrosis. Group 1 had an average length and depth of 2.4cm and 0.31cm respectively. Meanwhile, Group 2 had an average length and depth of 1.9cm and 0.18cm respectively. From these, it had been suggested that deep intramural LAD was abnormal rather than a normal anatomical variant due to its association with myocardial lesions (Morales et al., 1993).

One of the objectives of this study was to study the prevalence of isolated MB and the prevalence of MB associated with cardiac pathologies. It is evident from this study that isolated MB was almost equally prevalent to MB associated with cardiac pathologies with a value of 43.2% out of 271 sudden cases with MB. Therefore, its role in contributing to sudden death cases is not neglectable.

A study of isolated MB was performed using corrected TIMI frame count (CTFC) in 2013, in which a higher CTFC value indicated a decrease in coronary blood flow volume, and

a lower CTFC indicated a normal coronary flow. Results showed significantly higher CTFC in LAD, compared to the control group, which proved that coronary blood flow in MB patients was reduced in comparison to normal coronary arteries (Daoud & Wafa, 2013).

Another related study was conducted by Mookadam F. et al in 2009 on the clinical relevance of isolated MB by reviewing their coronary angiography reports. The severity of MB was categorized into three groups characterized by percentages of systolic compression on LAD, which are group I (< 50% compression), group II (50–70% compression) and group III (compression ≥70%), and these groups were followed up for 12 months. The study revealed that patients with systolic compression of ≥ 70% were associated with angina and MI. It was concluded that MB was not a benign variation of coronary anatomy based on the findings (Mookadam et al., 2009).

The above finding was in agreement with a study in 2010 by Kim S.S. et al. where 308 patients with isolated MB were followed up for about 37 months. The findings on unstable angina pectoris and MI were common presentations in patients with MB, which was in agreement with the study by Mookadam F. et al. It was also shown that patients with MB had a higher incidence of readmission compared to the control group, where the predictors of readmission were long (length) MB and spontaneous vasospasm on the coronary angiogram (Kim et al., 2010).

From this study, we found that MB was mostly associated with atheroma formation with a total of 138 cases out of 275 cases of sudden death cases with MB, whether the atheroma is isolated or associated with MI or cardiomyopathy. Our study observed that atheroma formation proximal to MB was recorded in at least 108 cases out of 138 cases with a percentage of 78.3%. Our data is in agreement with a study by Nakaura T. et al. in 2014 where the study observed that MB in the mid-LAD is considered a significant independent risk factor for coronary atherosclerosis formation in proximal LAD, other than age and diabetes mellitus in 188 patients by MDCT angiography (Nakaura et al., 2014).

Findings on atheroma formation at the proximal segment of the LAD artery or proximal to the MB entrance were also supported by Uusitalo V. et al. and Akishima-Fukasawa Y. et al (Akishima-Fukasawa et al., 2018; Uusitalo et al., 2015). However, according to Sun J.L. et al., MB is not a significant risk factor for coronary atherosclerosis, when compared to traditional cardiovascular risk factors, even though the study had agreed on the role of MB in promoting proximal atherosclerosis (Sun et al., 2013). The bridged segment of the coronary artery usually was spared or protected from atherosclerotic plaque formation (Nakaura et al., 2014) but it was not observed in this study as it was not clearly stated in the record whether the bridged segments of the coronary artery were spared or not.

We had observed a few cases of sudden death with MB where they were associated with atherosclerosis and MI at the same time. There was one study by Ishikawa Y. et al. in 2009 to see the anatomic properties of MB that predispose to MI which could support our observation. This study involved 100 autopsied MI hearts which were divided into MI hearts with MBs [(MI+)(MB+) group] and MI hearts without MBs [(MI+)(MB-) group]. The control group for the study was 200 normal hearts, 100 with MBs [(MI-)(MB+) group] and 100 without MBs [(MI-)(MB-) group]. It was observed that MB with greater thickness and greater MB muscle index was more significant in the (MI+)(MB+) group than the (MI-)(MB+) group. (MI+)(MB+) group had shown a greater intima-media ratio within 1.0 cm of the left coronary ostium than the other groups. It has been proved that from this study MB muscle index is associated with a shift of coronary artery disease more proximally in a proximal

LAD with MB, thus increasing the risk of MI (Ishikawa et al., 2009).

In this study, a few cases of sudden death cases with MB were associated with cardiomyopathy, which is most probably referring to hypertrophic cardiomyopathy (HCM) based on the heart weight in the autopsy draft. This association might be incidental and of no significant relevance based on the study in 2003 by Sorajja P. et al. where follow-up of 425 HCM patients (64 patients with MB) for about 7 years had observed no increased risk of death, including sudden cardiac death among HCM patients with MB as compared to HCM patients without bridging (Sorajja et al., 2003).

In another study in 2009, an assessment of 255 hearts comprised of 115 hearts with HCM and 140 controls, it was observed that MB was a frequent component of phenotypically expressed HCM, but no evidence of systemic association with HCM-related sudden death. Nevertheless, their finding could exclude the possibility of MB contributing to increased risk in certain patients (Basso et al., 2009).

That study was further supported by a retrospective study in 2014 by Tian T. et al.. The data was collected among 298 adult patients who were diagnosed with HCM from 1999 to 2011 and 34 of them presented with MB based on coronary angiography. With average follow-up for 4 years, it was observed that the presence of bridging in HCM patients was not evidently associated with all-cause death, cardiovascular death, sudden cardiac death, or deterioration of heart failure. Therefore, despite of common presentation of MB in HCM patients, it was not a predictor for adverse clinical outcomes (Tian et al., 2014).

MB is a quite common occurrence in our population and is commonly found as a single entity in the LAD. It seems that it has a higher preponderance in male gender among the adult age group. It is a pathological condition at a certain length and depth whether it exists as an isolated entity or is associated with cardiac pathologies, especially atherosclerosis. Atherosclerosis tends to form proximal to MB and might pose a risk for MI.

CONCLUSION

This study has illuminated the demography and anatomical properties associated with MB. The segment of a coronary artery proximal to a segment with MB is at increased risk of atherosclerosis. It was noticed that single MB was highly significantly presented as either isolated MB or associated with atheroma formation in the involved coronary artery. The findings not only contribute to a deeper understanding of MB but also hold potential implications for identifying and managing risks related to sudden cardiac-related deaths. This extensive research stands as a valuable resource, providing a nuanced perspective on this critical aspect of forensic medicine and cardiovascular health.

CONFLICT OF INTEREST

All the authors don't have any conflict of interest. No benefits have been received from a commercial party related directly or indirectly to the study.

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