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# Morphometric evaluation of the left atrioventricular valve complex and its clinical relations

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#### ORIGINAL ARTICLE

## Morphometric evaluation of the left atrioventricular valve complex and its clinical relations

Buse Naz Çandır et al., Anatomy of the left atrioventricular valve complex

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#### ABSTRACT

**Background:** In this study, it was aimed to evaluate morphometrically and morphologically the left fibrous ring, mitral leaflets, tendinous cords, and papillary muscles, which are the components of the left atrioventricular valve complex (LAVC), and to reveal their clinical relationships.

**Materials and methods:** A total of 120 human hearts were examined at the Forensic Medicine Institute. Cases aged 30 years and older, less than 24 hours after their death, were included in the study. Heart length, width, height/width ratio, anteroposterior and mediolateral diameters of the annulus, annular area, length and width of leaflets, number and attachment sites of tendinous cords, number, shape, length, the width of papillary muscles, and distances to various points were recorded to determine their spatial configurations. As well as the measurement data of LAVC components in cases with and without cardiovascular disease

(CVD), the relationships of these data with the demographic characteristics of the cases are also explained.

**Results:** In the diagnostic performance test (ROC analysis), it was determined that body mass index (> 26.7), heart weight (> 414 g), heart height/width ratio ( $\leq$  1.24), mitral valve width (> 99.96 mm), left ventricular wall thickness (> 15.08 mm), annular area (> 619.37 mm<sup>2</sup>) and mediolateral diameter of the annulus (> 30.71 mm) are important diagnostic criteria in determining CVD if they are outside the specified reference values.

**Conclusions:** This study provides anatomical information about LAVC, as well as recommendations for diagnosis and surgical treatment planning. We therefore believe that our findings will be useful to clinicians.

Keywords: left atrioventricular valve complex, left fibrous ring, mitral leaflets, tendinous cords, papillary muscles, cardiovascular disease

#### INTRODUCTION

The Mitral Valve (MV) is one of the four main valve structures of the heart, located between the left atrium (LA) and left ventricle (LV). The left atrioventricular valve complex (LAVC), on the other hand, is a structure complex consisting of left fibrous ring (LFR), anterior mitral leaflet (AML), posterior mitral leaflet (PML), tendinous cords (TC), and superior papillary muscle (SPM) and inferior papillary muscle (IPM) of the left ventricle. LAVC is one of the most complex mechanical structures of the human body [19], and it is not just a passive flap protecting the left atrioventricular orifice, but a set of components that work actively and in coordination throughout the cardiac cycle [5, 11, 15]. The ability of the LAVC to function effectively and accurately depends on the biomechanical and structural integrity of its components.

MV dysfunction have variable etiology and might result from pathological changes in any component of LAVC [19]. Bringing the pathological mitral valve back to normal functioning requires understanding the structure and dysfunction caused by the disease [5]. There are many studies in the literature investigating the structure of LAVC through bymostly studying cadavers formalin fixed heart specimens or by imaging methods, but unlike previous studies, unfixed fresh hearts were used in this study. It was aimed to examine the morphometric and morphological aspects of the LAVC components and the LV as a whole in these heart specimens, to compare these characteristics in healthy and pathological cases, and in this way, to uncover various characteristics that can be associated with clinical outcomes.

#### MATERIALS AND METHODS

The prospective study was carried out between January 2021 and November 2022 at the Forensic Medicine Institute after ethics committee approval (IRB: 2021/376). Inclusion criteria for the study was age (over 30) and absence of thoracic or cardiac trauma (penetrating, firearm etc.). Exclusion criteria were time (autopsy performed more than 24 hours postmortem), burns, foreign nationalities, and identification or history of previous cardiac surgery/intervention. One hundred and twenty cases met inclusion and exclusion criteria.

The cases with cause of deaths unrelated to the heart and cases that showed pathological findings/artefacts related to cardiopulmonary resuscitation or postmortem changes were considered as healthy. A total of 31 cases that showed pathological cardiac findings during macroscopic and histopathologic examinations were considered as "Cardiovascular Disease" (CVD). These findings included increase in heart size, severe subepicardial fattening, and myocardial infarction (pearlescent-white discoloration, fibrosis, aneurysm, granulation and trabecular changes).

Morphometric evaluations were made with a 0.01 mm precision digital caliper (Insize 1112-150, Insize Co. Ltd, Germany). Area and angle measurements were made by using the Image J Program (http://rsbweb.nih.gov/ij). Measurement references are explained in Table 1. All evaluations were made by two experienced researchers and the two measured values were averaged. Measurements were repeated in case of more than 10% differences between the two values.

#### **Statistical analysis**

The conformity of the variables to the normal distribution was examined by using the Shapiro-Wilk Test. If the variables fit the normal distribution, mean  $\pm$  standard deviations were used, if they did not fit the normal distribution, median values were presented with minimum and maximum values. The Independent Samples *t* Test or Mann–Whitney U-Test was used for comparisons between two groups according to the results of the normality test. If the number of groups was three or more, the ANOVA test or the Kruskal–Wallis test was used. Categorical variables were specified as n (%) and were compared between groups by using the Pearson Chi-Square Test, Fisher's Exact Chi-Square Test, and Fisher's Freeman-Halton Test. Logistic Regression Analysis was performed to determine the factors influencing the

pathological results of the cases. The established Logistic Regression Model was found to be significant (p < 0.001). Receiver-Operator Characteristic (ROC) Analysis was made to investigate the diagnostic performance of the parameters and the SPSS (IBM Corp. Released 2012; IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA), and MedCalc Programs were used for statistical analysis and p < 0.05 was considered statistically significant.

#### RESULTS

Among the 120 subjects that were included in the study, 21.67% (n = 26) were female and 78.33% (n = 94) were male. The mean age of women was  $44.3 \pm 14.4$  years, and the mean age of men was  $54.5 \pm 15.6$  years ( $52.3 \pm 15.8$  years for all cases). The cases were divided into three groups as those who were 30–44 years old (n = 41, 32.5%), 45–59 years old (n = 40, 33.3%), and 60 years and older (n = 39, 34.2%) considering cardiovascular risk factors. Also, according to their body mass index (BMI) values, the cases were divided into three groups as low, normal, and high (< 18.5 (n = 6, 5%), 18.5–24.9 (n = 41, 34.2%), and > 24.9 (n = 73, 60.8%), respectively). Among the 31 pathological cases, 2 (6.45%) were female, 29 (93.55%) were male, and among the 89 non-pathological cases, 24 (26.97%) were female and 65 (73.03%) were male. The mean age of the pathological cases was 60.16 ± 13.34 and the mean age of the nonpathological group was 49.58 ± 15.78 years.

The death events of the cases are presented in Table 2. In this respect, a difference was detected between the pathological conditions of the cases (p = 0.003). It was detected in the subgroup analysis that the rate of death because of being hanged by the neck was higher in the non-pathological group, and the rate of deterioration of health and falling ill was found to be higher in the pathological cases (p < 0.05).

The measurements of the heart and LV, LFR (Fig. 1), mitral leaflets (Fig. 2), CT, PM numbers and measurements (Fig. 3) and the comparison of these measurements with the demographic characteristics and pathological conditions of the cases are presented in Tables 3–8, respectively. Additionally shapes and origin regions of papillary muscles (PMs) are shown in Fig. 4 and 5.

Logistic regression analysis was made to determine the risk factors affecting the presence of disease in the cases included in the study (Tab. 9). Independent variables were included in the regression model by using the forward selection method.

The results of ROC analysis applied to determine the pathology groups showed that BMI, heart weight, heart length/width ratio, MV width, VS wall thickness, annulus

mediolateral (ML) diameter, and annular area values can be used as diagnostic markers in determining the pathology groups, but the annulus anteroposterior (AP) diameter cannot be used in this respect (p = 0.547) (Tab. 10).

#### DISCUSSION

#### Heart and left ventricle measurements

According to Gray's [25], the length and width of the heart were defined as 12 cm and 8.5 cm and mean heart weight was 280–340 g in men and 230–280 g in women, respectively. Mohammadi et al. [17] examined the heart sizes in 550 cadavers and found the mean heart length as  $11.41 \pm 2.15$  cm, heart width as  $8.21 \pm 4.38$  cm, and heart weight as 248.96 g in men and 242.74 g in women. They stated that these values were associated with the age, height and body weight of the cadavers, but not with gender and BMI. We believe that the age difference between the sample groups explains the difference between the two studies (Tab. 3). Also, the length/width index  $\leq$  1.24 were more likely to have CVD.

When studies in different races were reviewed, it was found that the MV width was 7 to 10.1 cm on average in healthy individuals [17]. In this study, the mean MV width in healthy subjects was found to be 9.5 cm (Tab. 3), and it was noted that cases with this value > 99.96 mm were more likely to be pathological.

For the heart to maintain its normal physiology, the wall thickness must be proportional to the systolic pressure and ventricular width [8, 14]. It was reported that available data on this structural anatomy are limited [27]. Our findings are consistent with previous studies [14] and also it was seen that the probability of CVD was high in cases with LV wall thickness > 15.08 mm.

LVIT and LVOT are markers reflecting the preload and afterload of the heart. Especially LVOT carries a risk of stenosis or obstruction because it has a narrower and more complex channel or tunnel structure [23], causing a decrease in the compliance (flexibility) and diastolic function of the LV, depending on the degree of obstruction [2] and this might result in heart failure, stroke or sudden cardiac death [2, 23]. Although the LVIT and LVOT distances are well defined, there is no definite consensus on the reference point for LVOT diameter measurement, and this may be because LVOT obstruction may be at the valvular or subvalvular level [26]. Therefore, diameter measurements were performed at both levels in this study. LVIT and LVOT distances and diameters were found to be related with the pathological conditions of the cases (p < 0.001).

#### Left fibrous ring

The LFR is the key structure in replacement surgeries [6], and it has been reported that providing an appropriate ratio between the AP and ML diameters of the LFR is extremely important for the prevention of mitral regurgitation [15]. In direct annuloplasty techniques (Cardioband, Mitraline, etc.), it is observed that the AP diameter of the annulus is focused on the placement of anchors to reduce the size of the mitral annulus [1], and anchor disengagement has been reported in a considerable number of cases [16]. In this study, it was observed that only the ML diameter of the annulus was associated with pathological groups (p = 0.001) and could be used as a marker in the diagnosis of CVD (Tab. 10). Therefore, clinical trials that investigate the potential of ML diameter in surgeries to reduce mitral annulus dimensions may be planned.

Annular area is 4–6 cm<sup>2</sup> in healthy adults [18]. While an annular area smaller than 2 cm<sup>2</sup> indicates mitral stenosis [18], the annular area may increase significantly in mitral regurgitation [5, 7]. In these cases, the original shape of the ring and its sphincter feature change, resulting in increased stress on the mitral leaflets [7]. As expected, the annular area was larger in pathological cases in this study. It was also found that the probability of CVD is higher in cases with an annular area value > 619.37 mm<sup>2</sup>.

#### **Mitral leaflets**

Mitral leaflets are divided into anterior (AML), posterior (PML), and lateral sections (commissuras) according to their shape and annular connections [5, 11]. Carpentier [4] defined three mussel-like structures of the PML as P1 laterally, P2 in the middle, and P3 medially, and the corresponding regions in the AML as A1, A2, and A3. Commissural structures are named anterolateral commissure (ALC) (A1–P1) and posteromedial commissure (PMC) (A3–P3) according to this locations.

The length of the leaflet tissue is critical for the leaflets to be tightly coapted and to maintain the proper position [5]. In all cases, P2 width was greater than P1 (pathological p < 0.001, non-pathological p < 0.001) and P3 (pathological p < 0.001, non-pathological p < 0.001) and P3 (pathological p = 0.018, non-pathological p < 0.001), and P3 width was greater than P1 (pathological p = 0.018, non-pathological p < 0.001). Similarly, P2 height was found to be higher than P1 (pathological p = 0.002, non-pathological p < 0.001) and P3 (pathological p < 0.001, non-pathological p < 0.001). It was determined that the height of P1 was higher than P3 in non-pathological cases (p = 0.01), and

no differences were detected between the heights of the two structures in pathological cases. Also, PMC width and height were found to be greater than ALC (p = 0.009 and p = 0.022 in pathological cases, p < 0.001 and p < 0.001 in non-pathological cases, respectively). Although our findings were similar to Krawczyk et al. [12] stated that, unlike this study, there was no statistically significant difference between P3 and P1 widths. We think that this difference is due to the fact that they work with fixed hearts.

In addition, the annular widths of P1 and P3 and the height of the AML were greater in pathological cases than in non-pathological cases. Since coaptation between P1–P2–P3 is known to be as important as coaptation between AML and PML [13], leaflet tissue that prevents proper coaptation may be P1 and P3, as in the cases in this study. Accordingly, in the percutaneous end-to-end mitral valve repair technique (such as MitraClip, PASCAL) [1], a single clip placed in the A2–P2 position may be insufficient. Furthermore, the length in the AML may cause a mismatch in the A2–P2 leaflets, resulting in clip-related leaflet damage. Therefore, consideration of the information presented may help the surgeon to select the appropriate length and number of clips, increase the likelihood of success of the technique, and prevent potential complications.

#### **Tendinous cords**

There is wide variability in the anatomy and branching patterns of TC. In the present study, the anatomical classification was preserved and TC were defined in two groups as TTC and FTC. Gray's [24] reported MV-related FTCs in approximately 50% of all people, and Krawczyk et al. [11] reported that it was present in almost all cases (95%). The presence of FTC was detected in all (100%) of the 120 cases evaluated here. The number of FTC originating from SPM was  $5.3 \pm 2.5$  and IPM was  $9.2 \pm 3.8$ , respectively. Krawczyk et al. [11] reported that an average of  $3.5 \pm 2.2$  FTC originated for SPM and an average of  $5.4 \pm 2.7$  for IPM. Also, as in their results, it was found that FTC originating from IPM were more numerous than SPM.

A significant number of ruptures of artificial chordae used for mitral valve repair have been reported in the literature [25]. They concluded that increasing the number of neochordae, and sizing them to the correct length for a more durable mitral valve repair [25]. This is because TC interfere with the mitral leaflets structure, contribute to their fibrous skeleton, and, because of their complex arrangement, provide an even distribution of stress on the mitral leaflets [15]. We think that not only disconnected TTCs but also disconnected FTCs should be considered in the planning of artificial CT in order to ensure proper stress distribution of neo-chordae on the leaflets. Because FTCs, like TTCs, also participate in leaflet stress and their number is quite high as seen in this study. However, when the studies are analyzed, we think that they are ignored and therefore, they fail to create the correct leaflet stress. In addition, although the number of new cords is focused in the literature, we think that the implant location of these cords (Tab. 6) is also important in creating appropriate leaflet stress.

#### **Papillary muscles**

PMs contract during ventricular systole, and pull the leaflets into the ventricles through TC, preventing the backflow of blood into the atria. Dysfunction of PMs causes the leaflets to not close properly during ventricular systole and causes blood to flow back into the atrium. There are many types of surgeries such as resection, repositioning, and realignment to restore the normal physiological function of PMs [9]. If there is more than one PM, the number of options for deciding the direction and degree of realignment increases and facilitates the maintenance and restoration of normal physiological function [9]. Our findings regarding papillary muscle and apex numbers and sizes are consistent with the literature [9, 11]. In addition, it was reported that PMs grow in length to meet the chronically increased workload or in width to create more tension in pathological conditions [8]. This study confirms this by showing that PM was longer in pathological hearts (SPM p = 0.005, IPM p < 0.001).

The location of the PMs in the LV is defined as its spatial configuration. The spatial location of PMs can be described mathematically, especially by considering measurements such as their distance from the mitral annulus or mitral coaptation [20]. In this context, different annulo-papillary distances were defined in many studies. Sakai et al. [22] made 4 different measurements from PM apex to annulus at 2, 4, 8, and 10 o'clock directions. Kim et al. [10] defined the distance from the ends of the PMs to the AAM as "tethering distance". Krawczyk et al. [11] evaluated the highest PM apex-LFR distance. Although different annulo-papillary distances were defined, researchers agree that annulo-papillary continuity is important for the normal functioning of the LV and proper coaptation, and this relationship must be maintained in valve replacement, and thus the risk of post-op complications can be reduced [10, 20]. However, we think that the data may be insufficient in cases where PM reconstruction and/or repositioning is required in studies where the apex is defined as the reference point. Therefore, in this study, the distances of the midpoint of the bases of the PMs to the AAM and the coaptation line (Tab. 1), as well as the highest apex-LFR distances of the PMs were recorded (Tab. 8).

The shape of PMs affects the passage of blood through the LV [3]. It was reported that conical, broad-based, distant from the center of the ventricular cavity, and narrow apex muscles best facilitate cardiovascular physiology with minimal obstruction to blood flow [9]. For this reason, there are many studies investigating and categorizing PM shapes [3, 21]. While Bhadoria et al. [3] classified PMs as broad apex, pyramidal, fan-shaped and cone-shaped, Saha et al. <sup>[21]</sup>, similar to this study (Fig. 4), determined 5 muscle shapes: cone, bifurcated, trifurcated and flat-top. Furthermore, the location of the PMs has primary importance for normal cardiovascular physiology, as it influences the alignment of the TC and the direction of traction on the ventricular wall [9]. For this reason, the origin regions of the papillary muscles from the ventricular wall were examined and, similar to the literature [21], it was observed that both muscle groups mostly originated from the middle 1/3 part (Fig. 5).

#### CONCLUSIONS

The fixation process is a chemical reaction and it must be taken into account that it may cause changes in the size and shape of the structure, which might cause differences in measurements. We think that our data will be closer to live when compared to the studies performed on fixed hearts in the previous literature.

The present study includes the morphometric and morphological data of the LAVC components in cases with and without CVD, and also includes the comparison with the demographic characteristics of the cases. Accordingly, all parameters related to the heart and left ventricle (heart weight, heart length, heart width, MV width, left ventricular and apex wall thicknesses, LVIT–LVOT distances and diameters), ML diameter of annulus and annular area, P1 and P3 leaflet width, AML height and papillary muscle dimensions were found to increase in cases with CVD. Heart length and width , and age and BMI of the individuals' were identified as the main risk factors for the presence of CVD. BMI, heart weight, heart length/width ratio, MV width, LV wall thickness, annular area and ML diameter of annulus were found to be important diagnostic criteria in the determination of CVD. In conclusion, this study provides anatomical information and recommendations for proper coaptation, preservation of left ventricular function and correction of technical errors reported in previous studies in mitral valve repair and replacement surgeries. Therefore, we believe that our findings will help clinicians in the diagnosis, treatment plan and management of the surgical process of pathologies involving the LAVC and will shed light on increasing the success rate of new techniques.

#### Article information and declarations

#### Data availability statement

Original contributions are included in the manuscript and further questions can be directed to the corresponding author.

#### **Ethics statement**

The study was reviewed and approved by an Ethics Committee.

#### **Author contributions**

**BN Candir:** project development, data collection, data analysis, manuscript writing/ editing. **C Ergin:** project development, data collection. **K Yilar:** data collection, project development. **O Coskun:** project development, data collection. **E Kara:** data collection, data management. **A Kale:** manuscript editing, data analysis. **N Bozbuga:** project development, manuscript editing. **A Ozturk:** project development, manuscript editing. **O Gayretli:** project development, data collection, manuscript writing/editing.

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**Conflict of interest:** The authors declare that they have no conflict of interest.

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#### Table 1. Measurement references

|            | Parameters   | Measurement references   |
|------------|--|--|
|            | Heart length [mm]  | Vertical distance from the highest point of the left auricle of heart to the apex<br>of heart in the sagittal plane<br>The largest horizontal distance between the right atrium and left ventricle in  |
|            | Heart longth/width                                       | the coronal plane  |
| cle        | ratio  | The ratio of the length of the heart to the width of the heart   |
| ntri       | MV width [mm]  | Width measurement of the MV at LFR level   |
| nd Left Ve | LV wall thickness<br>[mm]<br>Apex wall thickness<br>[mm] | Transverse wall thickness measurement 2 cm inferior to the point where the MV attaches to the lateral wall of the left ventricle<br>Thickness measurement of the deepest point of the left ventricle (which coincides with the apex of heart from the outside) |
| eart a     | LVIT [mm]  | Distance from the MV to the deepest point of the left ventricle (apex of heart)  |
| H          | LVOT [mm]  | Distance from deepest point of left ventricle (apex of heart) to AV  |
|            | LVOT 1st diameter<br>[mm]                                | Distance from the septal wall of the left ventricle to the ventricular surface of the AML, at the level of the bases of the semilunar leaflets of aortic valve   |
|            | [mm]   | the AML, 0.5 cm below the bases of the semilunar leaflets of aortic valve  |
| brous      | AP diameter of annulus [mm]                              | Distance measurement of the LFR in the anteroposterior direction   |
| eft fil    | ML diameter of annulus [mm]                              | Distance measurement of the LFR in the mediolateral direction  |
| ringI      | Annular Area [mm <sup>2</sup> ]                          | LFR area measurement   |
| Mitral     | Annular distance of mitral leaflets [mm]                 | Attachment line distances of AML, PML (P1, P2, P3) ALC and PMC to LFR  |
| leaflets   | Height of mitral<br>leaflets [mm]                        | The distance from the midpoint of the annular distances of the AML, PML (P1, P2, P3), ALC, and PMC to the midpoints of their free edges  |
| snou       | Number of TTC  | Number of TTC originating from each muscle   |
| sTendi     | Origin and attachment sites of TC                        | Origin and insertion sites of TC   |
| cord       | Number of FTC  | Number of FTC in left ventricle  |
| muscles    | Number of muscles  | Each muscle with its own base, trunk, and one or more apex was considered<br>a PM. Muscles belonging to the SPM and IPM groups were numbered from<br>the LVOT to the free wall of the left ventricle.  |
| llary      | Number of apexes   | Number of apex in each muscle  |
| Papil      | Height of muscle<br>[mm]                                 | Length measurement from base to highest apex of each muscle group  |
|            | Width of muscle [mm]                                     | Width measurement in horizontal plane of the base part, where the muscle group connects to the left ventricle  |

| Highest apex-LF<br>d <del>istance [mm]</del>  | R Vertical distance of the   | highest apex of each mus  | scle group to the LFR   |
|---|--|---|---|
| Distance betwee<br>bases [mm]   | en Horizontal distance be<br>group<br>muscle groups                                | Non-pathological<br>tween the midpoints of<br>group<br>(n = 90)                   | the bases of the SPM-IPM  |
| Be hanged by the i  | neck 0   | 13 (14.61%)   | PM-IPM muscle groups  |
| P Gunshot wound<br>Cerebral hemorrh   | re The distance of the n<br>age 0  | nid70677877677 the bases of 1 (1.12%)   | f the muscle groups to the (1)  |
| P <b>Mall copthe gr</b> ound<br><sup>(</sup> Deterioration of h   | The <b>₫i∢€a¤5%)</b> f the m<br>ealth 8 (25.81%)<br>tenumous corus attacn          | nidpotn87%) the bases of<br>4 (4.49%)<br>on the ventricular surface               | f the muscle groups to the<br>e rough areas where the<br>s of the leaflets) |
| Drug poisoning<br>International of the second s | y = 0  | $\frac{1}{4}$ (1.12%)<br>4 (4.49%)  | nts of the bases of the SPM   |
| Shapes yf muscles a<br>intoxication<br>Be found dead  | licoholne <sub>1</sub> (one appex), bifur<br>(more than three apex)<br>10 (32.26%) | cca <u>terb (ந</u> ரை apex), trifurc<br>). and flat-top (with no s<br>16 (17.98%) | ated (three apex), truncated significant height difference                  |
| O <b>Pgistoperegione</b> s (<br><sup>I</sup> Fall ill<br>— Drowning in water  | of The <b>l@</b> ft ventricle was<br>7 (22.58%)<br>originated.                     | di <b>t/i(ded</b> 28k)ng its length<br>8 (8.99%)                                  | into three sections: upper,<br>ich 1/3 part each muscle                     |
| Traffic accident<br>Falling from heigh  | 1 (3.23%)<br>at 1 (3.23%)  | 14 (15.73%)<br>9 (10.11%)   | MV — mitral<br>valve; AV — aortic<br>valve; LV — left                       |
|   |  |   | -   |

ventricle; LVIT — left ventricular inflow tract; LVOT — left ventricular outflow tract; LFR

— left fibrous trigone; AML — anterior mitral leaflet; PML — posterior mitral leaflet; ALC

— anterolateral commissure; PMC — posteromedial commissure; TC — tendinous cords;

TTC — true tendinous cord; FTC — false tendinous cords; PM — papillary muscle; SPM — superior papillary muscle; IPM — inferior papillary muscle; AAM — anterior annular midpoint.

Table 2. Death event of the cases

Data are expressed as numbers n (%).

|  | Sex                             |   |                            | Age                                     |   |   |                            | BMI                                     |   |                                   |                            | Pathological condition            |   |                                     |  |
|--|---------------------------------|---|----------------------------|---|---|---|----------------------------|---|---|-----------------------------------|----------------------------|-----------------------------------|---|-------------------------------------|--|
|  | Fema<br>le<br>(n =<br>26)       | Mal<br>e<br>(n =<br>94)                 | p<br>v<br>a<br>l<br>u<br>e | < 45<br>(n =<br>41)                     | 45-<br>59<br>(n =<br>40)                | 60<br>and<br>olde<br>r (n<br>=<br>39)   | p<br>v<br>a<br>l<br>u<br>e | Low<br>(n =<br>6)                       | Nor<br>mal<br>(n =<br>41)               | Hig<br>h<br>(n =<br>73)           | p<br>v<br>a<br>l<br>u<br>e | Pat<br>holo<br>gic<br>(n =<br>31) | Non<br>-<br>pat<br>holo<br>gic<br>(n =<br>89) | p<br>v<br>al<br>u<br>e              |  |
| He<br>art<br>wei<br>ght                            | 279<br>(175:<br>449)            | 407<br>(240<br>:735<br>)                | <<br>0<br>0<br>0<br>1<br>c | 320.<br>41 ±<br>76.8<br>4               | 426.<br>25 ±<br>112.<br>75              | 425.<br>38 ±<br>112.<br>43              | <<br>0<br>0<br>0<br>1<br>g | 306.<br>67 ±<br>93.5<br>1               | 340.<br>93 ±<br>87.2<br>5               | 424.<br>10 ±<br>114.<br>18        | <<br>0<br>0<br>0<br>1<br>g | 503.<br>52 ±<br>98.9<br>3         | 350.<br>20 ±<br>87.7<br>9                     | <<br>0.<br>0<br>0<br>1 <sup>d</sup> |  |
| He<br>art<br>len<br>gth                            | 88.94<br>(75.5<br>3:107.<br>67) | 101.<br>75<br>(81.<br>45:1<br>82)       | <<br>0<br>0<br>0<br>1<br>c | 98.3<br>6<br>(75.<br>53:1<br>18.6<br>4) | 101.<br>13<br>(79.<br>31:1<br>82)       | 99.1<br>7<br>(83.<br>65:1<br>19.1<br>4) | 0<br>5<br>2<br>2<br>f      | 87.3<br>2<br>(81.<br>31:1<br>17.6<br>9) | 95.3<br>2<br>(75.<br>53:1<br>20.8<br>0) | 101.<br>82<br>(79.<br>31:1<br>82) | 0<br>0<br>0<br>3<br>f      | 107.<br>67<br>(88.<br>51:1<br>82) | 96.2<br>8<br>(75.<br>53:1<br>19.1<br>4)       | <<br>0.<br>0<br>0<br>1 <sup>c</sup> |  |
| He<br>art<br>wid<br>th                             | 74.16<br>(62.6<br>6:97.3<br>5)  | 85.5<br>0<br>(61.<br>42:1<br>15.0<br>4) | <<br>0<br>0<br>0<br>1<br>c | 77.3<br>2<br>(64.<br>91:1<br>12.5<br>8) | 83.0<br>6<br>(62.<br>66:1<br>15.0<br>4) | 85.4<br>2<br>(61.<br>42:1<br>12.4<br>0) | 0<br>0<br>1<br>0<br>f      | 82.0<br>8 ±<br>8.42                     | 79.7<br>5 ±<br>10.1<br>9                | 85.9<br>7 ±<br>10.6<br>0          | 0<br>0<br>1<br>0<br>g      | 93.7<br>7 ±<br>8.68               | 80.1<br>2 ±<br>8.97                           | <<br>0.<br>0<br>0<br>1 <sup>d</sup> |  |
| He<br>art<br>len<br>gth/<br>wid<br>th<br>rati<br>o | 1.21<br>(1.02:<br>1.45)         | 1.20<br>(0.9<br>9:2.<br>24)             | 0<br>6<br>3<br>3<br>c      | 1.24<br>(1.0<br>2:1.<br>45)             | 1.20<br>(0.9<br>9:2.<br>24)             | 1.14<br>(1.0<br>1:1.<br>38)             | 0<br>0<br>1<br>6<br>f      | 1.09<br>(1:1.<br>25)                    | 1.23<br>(1.0<br>2:1.<br>45)             | 1.18<br>(0.9<br>9:2.<br>24)       | 0<br>0<br>2<br>0<br>f      | 1.14<br>(0.9<br>9:2.<br>24)       | 1.22<br>(1:1.<br>45)                          | 0.<br>0<br>0<br>9 <sup>c</sup>      |  |
| MV<br>wid<br>th                                    | 90.44<br>±<br>13.25             | 100.<br>58 ±<br>12.8<br>6               | 0<br>•<br>0<br>0<br>1<br>d | 92.5<br>3 ±<br>10.1<br>9                | 102.<br>31 ±<br>14.8<br>1               | 100.<br>50 ±<br>13.5<br>3               | 0<br>0<br>0<br>2<br>g      | 102.<br>92 ±<br>10.6<br>6               | 93.7<br>5 ±<br>13.8<br>0                | 100.<br>60 ±<br>13.0<br>8         | 0<br>•<br>0<br>2<br>3<br>g | 105.<br>73 ±<br>12.4<br>8         | 95.8<br>2 ±<br>13.0<br>3                      | <<br>0.<br>0<br>0<br>1 <sup>d</sup> |  |
| LV<br>wal  | 11.54<br>± 1.55                 | 13.2<br>7 ±                             | <<br>0                     | 12.3<br>2 ±                             | 13.1<br>3 ±                             | 13.2<br>7 ±                             | 0                          | 12.4<br>8                               | 12.1<br>5                               | 13.3<br>2                         | 0                          | 34.1<br>6 ±                       | 30.9<br>6 ±                                   | <<br>0.                             |  |

**Table 3.** Heart and left ventricle measurements

| l<br>thic<br>kne<br>ss                    |                                | 2.05                                    | 0<br>0<br>1<br>d           | 1.62                                    | 2.43                                    | 2.03                                    | 0<br>8<br>4<br>g      | (10.<br>63:1<br>5.97<br>)              | (8.9<br>6:16<br>.54)                   | (8.2<br>2:19<br>.55)                    | 0<br>0<br>2<br>f             | 5.10                                    | 4.26                                    | 0<br>0<br>1 <sup>d</sup>            |
|---|--------------------------------|---|----------------------------|---|---|---|-----------------------|--|--|---|------------------------------|---|---|-------------------------------------|
| Ap<br>ex<br>wal<br>l<br>thic<br>kne<br>ss | 1.93<br>(1.06:<br>5.54)        | 2.60<br>(1.0<br>9:5.<br>59)             | <<br>0<br>0<br>0<br>1<br>c | 2.27<br>(1.1<br>6:4.<br>96)             | 2.54<br>(1.0<br>6:5.<br>59)             | 2.59<br>(1.0<br>9:5.<br>54)             | 0<br>2<br>2<br>3<br>f | 2.71<br>(1.6<br>7:3.<br>29)            | 2.24<br>(1.0<br>6:5.<br>59)            | 2.68<br>(1.0<br>9:5.<br>54)             | 0<br>0<br>2<br>1<br>f        | 3.02<br>(1.7<br>5:5.<br>12)             | 2.31<br>(1.0<br>6:5.<br>59)             | 0.<br>0<br>0<br>2 <sup>c</sup>      |
| LVI<br>T                                  | 71.05<br>(54.8<br>9:92.5<br>6) | 79.8<br>8<br>(28.<br>39:1<br>10.7<br>0) | <<br>0<br>0<br>0<br>1<br>c | 77.7<br>8 ±<br>9.84                     | 78.6<br>9 ±<br>9.80                     | 75.8<br>0 ±<br>14.0<br>3                | 0<br>5<br>1<br>5<br>g | 62.5<br>8<br>(56.<br>17:7<br>8.07<br>) | 75.6<br>4<br>(28.<br>39:9<br>6.49<br>) | 80.0<br>5<br>(57.<br>97:1<br>10.7<br>0) | <<br>0<br>0<br>0<br>1<br>f   | 84.3<br>4<br>(63.<br>63:1<br>10.7<br>0) | 75.6<br>6<br>(28.<br>39:1<br>01.5<br>0) | <<br>0.<br>0<br>0<br>1 <sup>c</sup> |
| LV<br>OT                                  | 71.79<br>(55.6<br>4:83.9<br>8) | 76.1<br>2<br>(18.<br>91:1<br>07.7<br>0) | 0<br>0<br>1<br>6<br>c      | 75.6<br>5<br>(60.<br>20:1<br>02.1<br>6) | 76.6<br>2<br>(55.<br>64:1<br>03.4<br>6) | 71.5<br>0<br>(18.<br>91:1<br>07.7<br>0) | 0<br>1<br>2<br>8<br>f | 60.6<br>3<br>(55.<br>08:7<br>6.23<br>) | 74<br>(18.<br>91:1<br>03.4<br>6)       | 78.6<br>5<br>(54.<br>05:1<br>07.7<br>0) | < 0<br>0<br>0<br>0<br>1<br>f | 82.4<br>7<br>(60:<br>107.<br>70)        | 74<br>(18.<br>91:9<br>9.42<br>)         | <<br>0.<br>0<br>0<br>1 <sup>c</sup> |
| LV<br>OT<br>1st<br>dia<br>met<br>er       | 12.07<br>(8.13:<br>31.59<br>)  | 14.9<br>0<br>(5.9<br>5:27<br>.94)       | 0<br>•<br>0<br>2<br>9<br>c | 12.0<br>1<br>(8.1<br>3:31<br>.59)       | 15.4<br>6<br>(9.3<br>3:26<br>.15)       | 15.1<br>9<br>(5.9<br>5:27<br>.94)       | 0<br>0<br>0<br>1<br>f | 14.2<br>3<br>(8.8<br>8:25<br>.03)      | 12.4<br>9<br>(8.1<br>3:27<br>.94)      | 15.4<br>2<br>(5.9<br>5:31<br>.59)       | 0<br>1<br>2<br>0<br>f        | 16.3<br>4<br>(10.<br>01:2<br>6.15<br>)  | 13.5<br>7<br>(5.9<br>5:31<br>.59)       | <<br>0.<br>0<br>0<br>1 <sup>c</sup> |
| LV<br>OT<br>2nd<br>dia<br>met<br>er       | 14.33<br>(8.17:<br>33.13<br>)  | 17.5<br>5<br>(10.<br>55:2<br>8.46<br>)  | 0<br>0<br>0<br>1<br>c      | 15.8<br>5<br>(8.1<br>7:33<br>.13)       | 17.5<br>0<br>(12.<br>19:2<br>7.50<br>)  | 18.4<br>1<br>(10.<br>55:2<br>8.46<br>)  | 0<br>0<br>0<br>4<br>f | 17.1<br>3<br>(10.<br>73:2<br>5.88<br>) | 16.5<br>7<br>(11.<br>67:2<br>8.46<br>) | 18.3<br>8<br>(8.1<br>7:33<br>.13)       | 0<br>1<br>2<br>9<br>f        | 19.1<br>2<br>(13.<br>89:2<br>7.89<br>)  | 16.3<br>9<br>(8.1<br>7:33<br>.13)       | <<br>0.<br>0<br>0<br>1 <sup>c</sup> |

Data are expressed as median (minimum:maximum) and mean ± standard deviation in grams for heart weight and in mm for other parameters. <sup>c</sup>Mann–Whitney U test, <sup>d</sup>the independent samples t-test; <sup>f</sup>Kruskal–Wallis test; <sup>g</sup>ANOVA test. MV — mitral valve; LV — left ventricle; LVIT — left ventricular inflow tract; LVOT — left ventricular outflow tract.

|   | Sex<br>F<br>M                                    |  | Age                        |                                |                                |                                   | BMI                            |                                |                                |                                | Pathological condition             |                                |                                       |                        |
|---|--|--|----------------------------|--------------------------------|--------------------------------|-----------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|------------------------------------|--------------------------------|---------------------------------------|------------------------|
|   | F<br>e<br>m<br>al<br>e<br>(<br>n<br>=<br>2<br>6) | M<br>al<br>e<br>(<br>n<br>=<br>9<br>4<br>) | p<br>v<br>a<br>l<br>u<br>e | < 45<br>(n =<br>41)            | 45–59<br>(n =<br>40)           | 60<br>and<br>older<br>(n =<br>39) | p<br>v<br>a<br>l<br>u<br>e     | Low<br>(n =<br>6)              | Nor<br>mal<br>(n =<br>41)      | High<br>(n =<br>73)            | p<br>v<br>a<br>l<br>u<br>e         | Patho<br>logic<br>(n =<br>31)  | Non-<br>patho<br>logic<br>(n =<br>89) | p<br>v<br>al<br>u<br>e |
| A<br>P<br>di<br>a<br>m<br>ete<br>r<br>of<br>an<br>nu<br>lus | 1<br>9.<br>7<br>6<br>±<br>3.<br>2<br>4           | 2<br>2.<br>6<br>3<br>±<br>5.<br>0<br>9     | 0.<br>0<br>1<br>d          | 19.59<br>(13.3<br>3:34.4<br>7) | 22.50<br>(12.3<br>5:35.8<br>4) | 23.03<br>(11.6<br>2:33.<br>59)    | 0.<br>0<br>0<br>3 <sup>f</sup> | 26.25<br>(16.0<br>9:33.<br>59) | 20.55<br>(15.4<br>5:31.<br>78) | 22.08<br>(11.6<br>2:35.8<br>4) | 0<br>3<br>4<br>0 <sup>f</sup>      | 22.70<br>(11.6<br>2:35.8<br>4) | 21.23<br>(12.3<br>5:34.4<br>7)        | 0.<br>5<br>2<br>9°     |
| M<br>L<br>di<br>a<br>m<br>ete<br>r<br>of<br>an<br>nu<br>lus | 3<br>0.<br>9<br>±<br>5.<br>2<br>8                | 3<br>2.<br>2<br>6<br>±<br>4.<br>3          | 0.<br>0<br>3<br>6<br>d     | 30.35<br>±<br>4.22             | 32.73<br>±<br>5.39             | 32.34<br>±<br>4.10                | 0.<br>0<br>4<br>8<br>g         | 35.20<br>(21.5<br>4:38.<br>36) | 31.07<br>(21.6<br>8:43.<br>52) | 31.53<br>(23.6<br>7:47.4<br>4) | 0<br>•<br>1<br>5<br>5 <sup>f</sup> | 34.16<br>±<br>5.10             | 30.96<br>±<br>4.26                    | 0.<br>0<br>0<br>1<br>d |
| A   | 5<br>2   | 6<br>3                                     | 0.<br>0                    | 538.3<br>6                     | 644<br>(352.                   | 637.7<br>9                        | 0.<br>0                        | 736.5<br>1                     | 560.5<br>3                     | 619.3<br>7                     | 0                                  | 657.8<br>4<br>(347.            | 578.1<br>4<br>(319.                   | 0.<br>0<br>3           |

| D i | -  | -  |   | 1     | 1     | •     |                | <u> </u> | 1     | 1                    | 1.1         | • .•  | •     | -<br>- |
|-----|----|----|---|-------|-------|-------|----------------|----------|-------|----------------------|-------------|-------|-------|--------|
|     | 1  | 1  |   |       |       |       |                |          |       |                      |             |       |       |        |
|     | 7  | 5  |   |       |       |       |                |          |       |                      |             |       |       |        |
| cu  | 6. | 2. |   | ,     |       |       |                |          |       | ,                    |             |       |       |        |
| еа  | 3  | 6  | d | )     | )     | 2.18) |                | 2.18)    | 4.17) | )                    | $6^{\rm f}$ | )     | )     |        |
| Ar  | 1  | 1  | 1 | 26.75 | 60.97 | 66:99 | 5 <sup>f</sup> | 16:99    | 66:90 | 60.97                | 2           | 60.97 | 26.75 | 9°     |
| ar  | ±  | ±  | 0 | 79:10 | 16:10 | (319. | 0              | (352.    | (319. | ( <u>82</u><br>79:10 | 1           | 56:10 | 66:10 |        |
| 11] | 2  | 5  |   | (324. |       |       |                |          |       | (324.                |             |       |       |        |
|     | 1  | 6  |   |       |       |       |                |          |       |                      |             |       |       |        |
|     | 0. | 3. |   |       |       |       |                |          |       |                      |             |       |       |        |

Data are expressed as median (minimum:maximum) and mean  $\pm$  standard deviation in mm for diameter measurements and mm<sup>2</sup> for area measurements.

<sup>c</sup>Mann–Whitney U test; <sup>d</sup>the independent samples t-test; <sup>f</sup>Kruskal–Wallis test; <sup>g</sup>ANOVA test; AP — anteroposterior; ML — mediolateral.

**Table 5.** Mitral leaflets measurements

|                                    | Sex                       |                           |                             | Age                       |                           |                             |                        | BMI                        |                            |                           |              |
|------------------------------------|---------------------------|---------------------------|-----------------------------|---------------------------|---------------------------|-----------------------------|------------------------|----------------------------|----------------------------|---------------------------|--------------|
|                                    | Female<br>(n =<br>26)     | Male<br>(n = 94)          | p<br>val<br>ue              | < 45<br>(n =<br>41)       | 45–59<br>(n = 40)         | 60 and<br>older<br>(n = 39) | p<br>val<br>ue         | Low<br>(n = 6)             | Normal<br>(n = 41)         | High<br>(n =<br>73)       | p<br>va<br>u |
| AML<br>annu<br>lar<br>dista<br>nce | 32.34 ±<br>4.54           | 35.41 ±<br>4.53           | 0.0<br>03 <sup>d</sup>      | 33.05 ±<br>4.14           | 35.73 ±<br>5.27           | 35.51 ±<br>4.18             | 0.0<br>16 <sup>g</sup> | 37.27 ±<br>5.83            | 34.07 ±<br>5.28            | 34.91 ±<br>4.20           | 0.<br>64     |
| PMC<br>annu<br>lar<br>dista<br>nce | 6.11<br>(3.75:1<br>2.20)  | 6.75<br>(3.72:11<br>.90)  | 0.0<br>87°                  | 6.23<br>(3.84:1<br>2.20)  | 7.13<br>(3.75:11<br>.90)  | 6.50<br>(3.72:9.<br>41)     | 0.0<br>64 <sup>f</sup> | 5.50<br>(3.98:8.1<br>3)    | 6.23<br>(3.72:10.<br>60)   | 6.88<br>(3.75:1<br>2.20)  | 0.<br>08     |
| P3<br>annu<br>lar<br>dista<br>nce  | 12.21<br>(5.97:2<br>0.60) | 15.30<br>(7.21:3<br>0.00) | 0.0<br>31°                  | 12.32<br>(7.40:2<br>4.30) | 15.25<br>(7.21:3<br>0)    | 16.10<br>(5.97:2<br>8.79)   | 0.0<br>19 <sup>f</sup> | 13.65<br>(9.34:23.<br>70)  | 13.20<br>(7.25:30<br>)     | 15.50<br>(5.97:2<br>5.70) | 0.<br>8:     |
| P2<br>annu<br>lar<br>dista<br>nce  | 23.91 ±<br>6.61           | 25.58 ±<br>7.88           | 0.3<br>25 <sup>d</sup>      | 24.17 ± 6.91              | 26.02 ±<br>8              | 25.49 ±<br>8                | 0.5<br>36 <sup>g</sup> | 26.86 ±<br>7.60            | 24.00 ±<br>7.25            | 25.77 ±<br>7.84           | 0.<br>29     |
| P1<br>annu<br>lar<br>dista<br>nce  | 8.82<br>(4.93:1<br>9.80)  | 10.37<br>(4.77:2<br>9.35) | 0.0<br>51°                  | 9.19<br>(5.01:1<br>9.84)  | 10.09<br>(4.93:2<br>2.12) | 10.59<br>(4.77:2<br>9.35)   | 0.2<br>22 <sup>f</sup> | 8.73<br>(8.04:29.<br>35)   | 8.77<br>(4.77:19.<br>80)   | 10.57<br>(4.93:2<br>2.12) | 0.<br>20     |
| ALC<br>annu<br>lar<br>dista<br>nce | 4.56<br>(3.12:9.<br>52)   | 5.64<br>(3.17:1<br>0.88)  | 0.0<br>19 <sup>c</sup>      | 5.49<br>(3.12:1<br>0.88)  | 5.85<br>(3.74:9.<br>85)   | 5.28<br>(3.17:9.<br>02)     | 0.1<br>09 <sup>f</sup> | 4.65<br>(3.74:5.4<br>7)    | 5.15<br>(3.12:9.8<br>5)    | 5.80<br>(3.33:1<br>0.88)  | 0.<br>0:     |
| AML<br>heigh<br>t                  | 22.89 ±<br>3.01           | 26.27 ±<br>3.69           | <<br>0.0<br>01 <sup>d</sup> | 24.96 ±<br>4.23           | 25.79 ±<br>3.47           | 25.88 ±<br>3.71             | 0.4<br>88 <sup>g</sup> | 24.89 ±<br>3.58            | 24.56 ±<br>4.08            | 26.14 ±<br>3.59           | 0.<br>9!     |
| PMC<br>heigh<br>t                  | 7.45<br>(3.69:1<br>1.65)  | 7.91<br>(4.57:1<br>5.25)  | 0.0<br>32°                  | 7.74<br>(4.56:11<br>.62)  | 7.80<br>(4.57:1<br>5.25)  | 7.87<br>(3.69:1<br>2.61)    | 0.8<br>62 <sup>f</sup> | 7.20<br>(4.57:8.6<br>2)    | 8.02<br>(4.56:11.<br>98)   | 7.74<br>(3.69:1<br>5.25)  | 0.<br>38     |
| P3<br>heigh<br>t                   | 9.20<br>(5.37:1<br>3.26)  | 10.25<br>(7.08:1<br>9.39) | 0.0<br>01 <sup>c</sup>      | 9.69<br>(6.54:1<br>4.58)  | 10.06<br>(7.41:1<br>8.70) | 10.26<br>(5.37:1<br>9.39)   | 0.2<br>37 <sup>f</sup> | 10.14<br>(8.53:10.<br>61)  | 9.77<br>(6.82:15.<br>73)   | 9.92<br>(5.37:1<br>9.39)  | 0.<br>15     |
| P2<br>heigh<br>t                   | 12.35<br>(9.92:1<br>6.89) | 13.42<br>(8.17:2<br>1.30) | 0.0<br>04 <sup>c</sup>      | 13.58<br>(9.96:1<br>8.80) | 12.56<br>(8.17:2<br>1.30) | 13.20<br>(9.92:1<br>9.79)   | 0.3<br>62 <sup>f</sup> | 12.98<br>(10.22:1<br>8.53) | 13.21<br>(10.21:1<br>7.73) | 13.15<br>(8.17:2<br>1.30) | 0.<br>34     |

| P1<br>heigh<br>t | 10.25 ±<br>2.21  | 11.27 ±<br>2.09  | 0.0<br>32 <sup>d</sup> | 10.85<br>(6.77:1<br>5.58) | 10.51<br>(7.50:1<br>6.31) | 11.13<br>(6.75:1<br>5.99) | 0.6<br>54 <sup>f</sup>   | 11.76 ±<br>1.73   | 11.11 ±<br>1.90   | 10.96 ±<br>2.32 | 0.<br>61 |
|------------------|------------------|------------------|------------------------|---------------------------|---------------------------|---------------------------|--------------------------|-------------------|-------------------|-----------------|----------|
| ALC<br>heigh     | 10.22<br>(6.75:1 | 11.03<br>(7.50:1 | 0.0<br>14 <sup>c</sup> | 6.48<br>(3.81:11          | 6.46<br>(4.03:1           | 6.87<br>(4.33:1           | 0.2<br>$88^{\mathrm{f}}$ | 6.46<br>(5.07:8.4 | 6.32<br>(3.81:11. | 6.70<br>(4.03:1 | 0.<br>29 |
| t                | 5.58)            | 6.31)            | 11                     | .07)                      | 0.68)                     | 0.66)                     | 00                       | 4)                | 07)               | 0.68)           |          |

Data are expressed as median (minimum:maximum) and mean ± standard deviation in mm. <sup>c</sup>Mann–Whitney U Test; <sup>d</sup>the independent samples t-test; <sup>f</sup>Kruskal–Wallis test; <sup>g</sup>ANOVA Test. ALC — anterolateral commissure; AML — anterior mitral leaflet; BMI — body mass index; PMC — posteromedial commissure.

|                 |                      | Patholo      | Pathological group (n = 31) |         |         |              |   | Non-pathological group (n<br>= 89) |         |         |                        |  |
|-----------------|----------------------|--------------|-----------------------------|---------|---------|--------------|---|------------------------------------|---------|---------|------------------------|--|
| Origin<br>sites | Attachme<br>nt sites | Mean<br>± SD | Medi<br>an                  | Mi<br>n | Ma<br>x | Mean<br>± SD | 1 | Medi<br>an                         | Mi<br>n | Ma<br>x | val<br>ue              |  |
|                 | AML                  | 4.9 ±<br>2.4 | 4                           | 2       | 14      | 5.3<br>2.5   | ± | 5                                  | 2       | 14      | 0.8<br>01 <sup>c</sup> |  |
| SPM             | ALC                  | 1.3 ±<br>0.5 | 1                           | 1       | 3       | 1.2<br>0.5   | ± | 1                                  | 1       | 3       | 0.1<br>21 <sup>c</sup> |  |
|                 | P1                   | 3.1 ±<br>1.2 | 3                           | 1       | 6       | 3.2<br>1.4   | ± | 3                                  | 1       | 10      | 0.9<br>13 <sup>c</sup> |  |
|                 | P2                   | 2.7 ±<br>1.2 | 2                           | 1       | 5       | 2.4<br>1.1   | ± | 2                                  | 1       | 6       | 0.2<br>65°             |  |
|                 | AML                  | 4.8 ±<br>1.4 | 5                           | 2       | 7       | 5.0<br>1.4   | ± | 5                                  | 2       | 9       | 0.6<br>23 <sup>c</sup> |  |
| IDM             | РМС                  | 1 ± 0.2      | 1                           | 0       | 1       | 1.1<br>0.3   | ± | 1                                  | 1       | 3       | 0.0<br>58 <sup>c</sup> |  |
| IPM             | P3                   | 3.1 ±<br>1.3 | 3                           | 1       | 6       | 3.3<br>1.5   | ± | 3                                  | 1       | 8       | 0.7<br>07 <sup>c</sup> |  |
|                 | P2                   | 2.4 ±<br>1.5 | 2                           | 1       | 7       | 2.7<br>1.3   | ± | 2                                  | 1       | 7       | 0.1<br>22 <sup>c</sup> |  |

| Table 6. | Tendinous | cords | measurements |
|----------|-----------|-------|--------------|
| raore or | renamous  | corab | measurement  |

Data expressed as numbers (n). <sup>c</sup>Mann–Whitney U test. SPM — superior papillary muscle; IPM — inferior papillary muscle; AML — anterior mitral leaflet; ALC — anterolateral commissure; PMC — posteromedial commissure.

|     |   | Patho | ologica | l group | (n = 31 | .) | Non-pathological group (n = 89) |    |   |   |    |  |
|-----|---|-------|---------|---------|---------|----|---------------------------------|----|---|---|----|--|
|     |   | SPM   |         |         |         |    |                                 |    |   |   |    |  |
|     |   | 1     | 2       | 3       | 4       | Т  | 1                               | 2  | 3 | 4 | Т  |  |
|     | 1 | 12    | 2       | 0       | 0       | 14 | 29                              | 7  | 1 | 1 | 38 |  |
|     | 2 | 9     | 1       | 0       | 0       | 10 | 24                              | 6  | 1 | 0 | 31 |  |
| IPM | 3 | 5     | 0       | 0       | 1       | 6  | 10                              | 6  | 0 | 0 | 16 |  |
|     | 4 | 1     | 0       | 0       | 0       | 1  | 3                               | 1  | 0 | 0 | 4  |  |
|     | Т | 27    | 3       | 0       | 1       | 31 | 66                              | 20 | 2 | 1 | 89 |  |

Data are expressed as numbers (n). SPM — superior papillary muscle; IPM — inferior papillary muscle; T — total.

|                                | Sex                        |                           | Age                         |                            |                            |                             | BMI                    |                            |                            |                           |
|--------------------------------|----------------------------|---------------------------|-----------------------------|----------------------------|----------------------------|-----------------------------|------------------------|----------------------------|----------------------------|---------------------------|
|                                | Female<br>(n =<br>26)      | Male<br>(n = 94)          | p<br>val<br>ue              | < 45<br>(n =<br>41)        | 45–59<br>(n = 40)          | 60 and<br>older<br>(n = 39) | p<br>val<br>ue         | Low<br>(n = 6)             | Normal<br>(n = 41)         | High<br>(n<br>73)         |
| SPM<br>muscle<br>number        | 1 (1:3)                    | 1 (1:4)                   | 0.9<br>34°                  | 1 (1:2)                    | 1 (1:4)                    | 1 (1:4)                     | 0.4<br>81 <sup>f</sup> | 1 (1:2)                    | 1 (1:3)                    | 1 (1:4)                   |
| SPM<br>apex<br>number          | 3 (1:5)                    | 3 (1:9)                   | 0.7<br>36°                  | 3 (1:5)                    | 3 (1:9)                    | 3 (1:6)                     | 0.0<br>10 <sup>f</sup> | 3 (2:3)                    | 3 (1:5)                    | 3 (1:9)                   |
| SPM<br>height                  | 33.07<br>(19.46:4<br>8.56) | 33.70<br>(3.13:68<br>.43) | 0.3<br>69°                  | 33.17<br>(3.13:47<br>.29)  | 35.56<br>(19.06:5<br>8.64) | 32.56<br>(13.48:6<br>8.43)  | 0.3<br>10 <sup>f</sup> | 28.48<br>(16.12:4<br>2.91) | 31.93<br>(3.13:42<br>.40)  | 35.63<br>(19.46:<br>8.43) |
| SPM<br>width                   | 17.34<br>(11.35:2<br>6.43) | 18.13<br>(8.46:44<br>.69) | 0.5<br>66°                  | 17.04<br>(11.02:3<br>5.16) | 19<br>(10.49:4<br>4.69)    | 16.69<br>(8.46:39<br>.55)   | 0.1<br>10 <sup>f</sup> | 19.32<br>(14.20:2<br>5.03) | 16.25<br>(8.46:44<br>.69)  | 18.26<br>(10.33:<br>9.55) |
| SPM<br>highest<br>apex-<br>LFR | 15.96<br>(7.91:26<br>.18)  | 21.55<br>(0:31.29<br>)    | <<br>0.0<br>01 <sup>c</sup> | 19.66<br>(7.91:31<br>.29)  | 20<br>(0:26.67<br>)        | 22.29<br>(4.26:30<br>.37)   | 0.0<br>79 <sup>f</sup> | 19.19<br>(13.10:2<br>2.44) | 20.16<br>(7.91:30<br>.21)  | 21.60<br>(0:31.2<br>)     |
| IPM<br>muscle<br>number        | 2 (1:4)                    | 2 (1:4)                   | 0.9<br>29°                  | 2 (1:4)                    | 2 (1:4)                    | 1 (1:4)                     | 0.1<br>41 <sup>f</sup> | 1.50<br>(1:3)              | 2 (1:3)                    | 2 (1:4)                   |
| IPM<br>apex<br>number          | 4.50<br>(2:6)              | 4 (2:8)                   | 0.6<br>39°                  | 4 (2:7)                    | 4 (3:6)                    | 4 (2:8)                     | $0.6$ $11^{ m f}$      | 4 (3:8)                    | 4 (2:7)                    | 4 (2:6)                   |
| IPM<br>height                  | 29.34 ±<br>5.89            | 33.66 ±<br>7.54           | 0.0<br>08 <sup>d</sup>      | 32.56<br>(19.46:5<br>2.24) | 31.64<br>(15.62:4<br>9.11) | 33.91<br>(17.13:5<br>9.57)  | 0.7<br>54 <sup>f</sup> | 25.14<br>(22.87:3<br>7.24) | 30.49<br>(17.13:4<br>5.56) | 34.28<br>(15.62:<br>9.57) |
| IPM<br>width                   | 16.53<br>(9.93:21<br>.75)  | 19.14<br>(9.99:38<br>.16) | 0.0<br>07 <sup>c</sup>      | 18.70<br>(11.70:3<br>6.23) | 18.48<br>(9.93:38<br>.16)  | 18.20<br>(9.99:25<br>.89)   | 0.8<br>72 <sup>f</sup> | 15.38<br>(9.99:20<br>.01)  | 18.70<br>(10.71:3<br>8.16) | 18.69<br>(9.93:3<br>.23)  |
| IPM<br>highest<br>apex-<br>LFR | 20.20 ±<br>4.57            | 23.43 ±<br>4.71           | 0.0<br>02 <sup>d</sup>      | 21.94<br>(13.06:4<br>1)    | 22.94<br>(14.69:2<br>9.92) | 23.85<br>(10.49:3<br>2.21)  | 0.5<br>23 <sup>f</sup> | 18.20<br>(10.49:2<br>0.06) | 23.96<br>(13.06:3<br>0.82) | 23<br>(12.04:<br>1)       |
| Distance<br>Between<br>Bases   | 17.30<br>(5.33:29<br>.71)  | 19.11<br>(9.17:41<br>.07) | 0.0<br>16 <sup>c</sup>      | 17.62 ±<br>4.82            | 19.86 ±<br>5.60            | 20.54 ±<br>5.90             | 0.0<br>93 <sup>g</sup> | 22.70<br>(14.92:2<br>6.31) | 20.01<br>(10.44:4<br>1.07) | 18.02<br>(5.33:3<br>.47)  |
| Distance<br>Between<br>Apexes  | 24.75 ±<br>7.02            | 25.72 ±<br>7.13           | 0.5<br>39 <sup>d</sup>      | 24.08<br>(10.70:3<br>7.37) | 24.99<br>(12.06:4<br>3.02) | 27.63<br>(12.07:4<br>1.28)  | 0.1<br>13 <sup>f</sup> | 21.25 ±<br>4.62            | 19.76 ±<br>5.05            | 18.91<br>5.88             |
| SPM-<br>AAM                    | 50.63 ±<br>6.45            | 48.19 ± 6.02              | 0.0<br>74 <sup>d</sup>      | 49.94 ±<br>6.51            | 47.50 ±<br>5.84            | 48.68 ±<br>6.04             | 0.2<br>05 <sup>g</sup> | 45.37<br>(43.34:6<br>1.27) | 49.13<br>(38.03:6<br>8)    | 48.79<br>(35.17:<br>8.70) |
| IPM-                           | 49.66                      | 49.19                     | 0.3                         | 50.13                      | 48.31                      | 50.09                       | 0.1                    | 53.89                      | 48.59                      | 49.71                     |

### Table 8. Papillary muscles measurements

| AAM                         | (42.04:7<br>5)          | (35.96:7<br>2.84)          | 02 <sup>c</sup>        | (35.96:7<br>5)             | (37.20:6<br>3.60)          | (40.22:7<br>2.84)          | $09^{\mathrm{f}}$           | (43.75:7<br>2.84)          | (35.96:7<br>5)             | (38.25:<br>8.76)          |
|-----------------------------|-------------------------|----------------------------|------------------------|----------------------------|----------------------------|----------------------------|-----------------------------|----------------------------|----------------------------|---------------------------|
| SPM-<br>coaptatio<br>n line | 40.89 ±<br>7.31         | 40.06 ± 5.85               | 0.5<br>44 <sup>d</sup> | 41.04 ± 6.58               | 38.87 ±<br>6.12            | 40.81 ± 5.68               | 0.2<br>27 <sup>g</sup>      | 39.54<br>(37.16:5<br>4.95) | 38.49<br>(29.47:5<br>9.37) | 38.89<br>(28.81:<br>5.90) |
| IPM-<br>coaptatio<br>n line | 42.40 ±<br>7.53         | 41.71 ± 6.38               | 0.6<br>39 <sup>d</sup> | 41.72<br>(29.84:5<br>8.26) | 39.43<br>(29.53:5<br>4.93) | 41.55<br>(30.25:5<br>9.02) | 0.4<br>73 <sup>f</sup>      | 47.52 ±<br>7.79            | 41.55 ±<br>7.13            | 41.57<br>6.09             |
| Intermus<br>cular<br>Angle  | 21.76<br>(12.13:4<br>4) | 23.25<br>(11.51:4<br>5.41) | 0.0<br>50°             | 21.77<br>(11.51:3<br>6.20) | 22.89<br>(12.17:4<br>3.44) | 26.29<br>(14.64:4<br>5.41) | <<br>0.0<br>01 <sup>f</sup> | 25.85<br>(18.23:4<br>2.64) | 24.09<br>(12.13:4<br>5.41) | 22.57<br>(11.51:4)        |

Data are expressed as median (minimum:maximum) and mean ± standard deviation in degrees for angle measurement and mm for other measurements. <sup>c</sup>Mann–Whitney U test; <sup>d</sup>the independent samples t-test; <sup>f</sup>Kruskal-Wallis test; <sup>g</sup>ANOVA test. SPM — superior papillary muscle; IPM — inferior papillary muscle; LFR — left fibrous ring; AAM — anterior annular midpoint; PM — papillary muscle.

Table 9. Logistic regression analysis

|        |   |         | 95%      | confidence |  |  |  |
|--------|---|---------|----------|------------|--|--|--|
|        |   |         | interval |            |  |  |  |
|        | Odds  | l       | Lower    | Upper      |  |  |  |
|        | ratio   | p-value | bound    | bound      |  |  |  |
| Heart  | 1.07  | 0.040   | 1.00     | 1 15       |  |  |  |
| length | 1.07  | 0.049   | 1.00     | 1.10       |  |  |  |
| Heart  | 1 1 -   | 0.000   | 1.05     | 1.00       |  |  |  |
| width  | 1.15  | 0.002   | 1.05     | 1.20       |  |  |  |
| Age    | 1.08  | 0.002   | 1.03     | 1.13       |  |  |  |
| BMI    | 1.25  | 0.004   | 1.07     | 1.45       |  |  |  |
|        | Model χ <sup>2</sup> = 69.49; <b>p-value</b> < <b>0.001</b> |         |          |            |  |  |  |
|        | $R^2 = 0.633$   |         |          |            |  |  |  |
|        | Hosmer and Lemeshow Test p = 0.992                          |         |          |            |  |  |  |
|        | n = 120   |         |          |            |  |  |  |

|--|

|                                 | AUC   | p<br>value | Cut-off<br>point | Sensitivity<br>% | Selectivity<br>% | PPV<br>% | NPV<br>% |
|---------------------------------|-------|------------|------------------|------------------|------------------|----------|----------|
| BMI                             | 0.731 | <<br>0.001 | > 26.7           | 71               | 69.7             | 44.9     | 87.3     |
| Heart weight [g]                | 0.878 | <<br>0.001 | > 414            | 83.9             | 78.7             | 57.8     | 93.3     |
| Heart length/width ratio        | 0.658 | 0.006      | ≤ 1.24           | 87.1             | 41.6             | 34.2     | 90.2     |
| MV width [mm]                   | 0.701 | <<br>0.001 | > 99.96          | 64.5             | 69.7             | 42.6     | 84.9     |
| LV wall thickness [mm]          | 0.730 | <<br>0.001 | > 15.08          | 41.9             | 97.8             | 86.7     | 82.9     |
| Annulus ML diameter<br>[mm]     | 0.696 | <<br>0.001 | > 30.71          | 87.1             | 49.9             | 37.5     | 91.7     |
| Annular area [mm <sup>2</sup> ] | 0.625 | 0.003      | > 619.37         | 67.7             | 62.9             | 38.9     | 84.8     |

AUC — area under the ROC curve; PPV — positive predictive value, NPV — negative predictive value; BMI — body mass index; MV — mitral valve; LV — left ventricle; ML — mediolateral.



Figure 1. Left fibrous ring measurements. A — anterior; P — posterior; L — lateral; M — medial; LA — left atrium; AP — anteroposterior; ML — mediolateral; AV — aortic valve; AML — anterior mitral leaflet.



**Figure 2.** Mitral leaflets measurements. Blue arrows — height of leaflets, black lines between red dots — annular distance of leaflets. AML — anterior mitral leaflet; ALC — anterolateral commissure; PMC — posteromedial commissure.



**Figure 3.** Papillary muscle measurements. Black vertical arrows — muscle height; black horizontal arrows — muscle width; black dots — the midpoint of the muscle bases; black triangles — highest apex points; red dots — anterior annular midpoints; green arrows — distance between bases and distance between apexes; red arrows — muscle base-anterior annular midpoint distance; red angle — intermuscular angle; yellow arrows — muscle base-coaptation line distance; blue arrows — highest apex-annulus distance. AV — aortic valve; LV — left ventricle; Co — coaptation line.



**Figure 4.** Shape characteristics of papillary muscles. Arrowheads — apex of papillary muscles. C — cone; B — bifurcated; Trif — trifurcated; Trun — truncated; FT — flat-top; SPM — superior papillary muscle; IPM — inferior papillary muscle.



**Figure 5.** Origin regions of papillary muscles. U — upper; M — middle; L — lower; SPM — superior papillary muscle; IPM — inferior papillary muscle.