

New contribution to the study of ventricular remodeling and valve rings in dilated cardiomyopathy: anatomical and histological evaluation

Nova contribuição ao estudo do remodelamento ventricular e dos anéis valvares na cardiomiopatia dilatada: avaliação anátomo-histopatológica

Moise Dalva¹, MD, PhD; Aristides Tadeu Correia²; Natalia de Freitas Jatene¹; Paulo Hilário Nascimento Saldiva³, MD, PhD; Fabio Biscegli Jatene¹, MD, PhD

DOI: 10.5935/1678-9741.20140064

RBCCV 44205-1579

Abstract

Introduction: Idiopathic dilated cardiomyopathy causes great impact but many aspects of its pathophysiology remain unknown.

Objective: To evaluate anatomical and histological aspects of hearts with idiopathic dilated cardiomyopathy and compare them to a control group, evaluating the behavior of the perimeters of the atrioventricular rings and ventricles and to compare the percentage of collagen and elastic fibers of the atrioventricular rings.

Methods: Thirteen hearts with cardiomyopathy and 13 normal hearts were analysed. They were dissected keeping the ventricular mass and atrioventricular rings, with lamination of segments 20%, 50% and 80% of the distance between the atrioventricular groove and the ventricular apex. The sections were subjected to photo scanning, with measurement of perimeters. The atrioventricular rings were dissected and measured digitally to evaluate their perimeters, later being sent to the pathology

laboratory, and stained by hematoxylin-eosin, picrosirius and oxidized resorcin fuccin.

Results: Regarding to ventricles, dilation occurs in all segments in the pathological group, and the right atrioventricular ring measurement was higher in idiopathic dilated cardiomyopathy group, with no difference in the left side. With respect to collagen, both sides had lower percentage of fibers in the pathological group. With respect to the elastic fibers, there was no difference between the groups.

Conclusion: There is a change in ventricular geometry in cardiomyopathy group. The left atrioventricular ring does not dilate, in spite of the fact that in both ventricles there is lowering of collagen.

Descriptors: Heart. Mitral Valve. Tricuspid Valve. Cardiomyopathy, Dilated.

¹Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, InCor-HCFMUSP, São Paulo, SP, Brazil.

²Surgical Anatomical Museum of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, InCor-HCFMUSP, São Paulo, SP, Brazil.

³Pathology Department of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, InCor-HCFMUSP, São Paulo, SP, Brazil.

This study was carried out at Hospital das Clínicas of the Faculdade de Medicina da Universidade de São Paulo, InCor-HCFMUSP, São Paulo, SP, Brazil.

No financial support.

Correspondence address:

Moise Dalva

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo InCor-HCFMUSP

Rua Dr. Enéas de Carvalho Aguiar, 44 – Cerqueira César – São Paulo, SP, Brazil - Zip Code: 05403-000

E-mail: moise.dalva@gmail.com

Abbreviations, acronyms and symbols	
RVR	Right ventricular ring
LVR	Left ventricular ring
CAPPesq	Ethics Committee for Research Project Analysis
DCM	Dilated cardiomyopathy
idDCM	Idiopathic dilated cardiomyopathy
iscDCM	Ischemic dilated cardiomyopathy
DistAV-AP	Distance of atrioventricular groove to the left ventricular apex
SD	Standard deviation
USP	University of São Paulo
HCFMUSP	Clinics Hospital of the Faculty of Medicine, University of São Paulo
HE	hematoxylin-eosin
CHF	congestive heart failure
INCOR	Heart Institute
ISFC	International Society and Federation of Cardiology
MAGPs	Microfibrils associated with glycoproteins
MMPs	Metalloproteinases
RFO	Weigert Resorcin-fuchsin with previous oxidation by oxone
SPSS	Statistical package for the social sciences
SVOC	Coroner's Service of São Paulo
USA	United States of America
WHO	World Health Organization

Resumo

Introdução: A cardiomiopatia dilatada idiopática (CMDId) é causadora de grande impacto, porém aspectos de sua fisiopatologia são desconhecidos.

INTRODUCTION

Congestive heart failure (CHF) is the entity causing major impact in terms of morbidity and mortality, and its main cause is dilated cardiomyopathy (DCM), which in its various etiologies, constitute a serious public health problem, with an estimated prevalence of 4-8 cases per 100,000 people per year and an estimated incidence of 36.5 per 100,000 people^[1].

The key pathophysiological aspect of such entities is the severe systolic dysfunction caused by the loss of efficiency of the heart to act as hydraulic pump. Although myocellular component is present in an important way, other mechanisms such as the remodeling and activation of the renin-angiotensin-aldosterone system are factors contributing to the perpetuation of the presentation^[1].

Ventricular remodeling characterized by both right and left morphogeometrical changes, provides vicious cycle of functional deterioration, since the heart loses its original anatomical conformation, which is critical to its efficiency. In this context, the valve insufficiency caused primarily by expansion of the atrioventricular rings is of paramount importance^[1], but

Objetivo: Avaliar aspectos anatomo-histológicos de corações com CMDId comparando-os a corações normais, com medidas perimetrais dos anéis atrioventriculares direito (AVD) e esquerdo (AVE) e dos ventrículos direito (VD) e esquerdo (VE) e a porcentagem de fibras colágenas e elásticas dos anéis.

Métodos: Foram avaliados 13 corações de cadáveres portadores de CMDId e 13 corações normais, que foram dissecados mantendo-se os anéis atrioventriculares e a massa ventricular, com laminação em segmentos correspondentes a 20%, 50% e 80% da distância entre o sulco atrioventricular e o ápice ventricular. Os cortes foram submetidos à digitalização fotográfica, sendo comparadas as medidas. Os anéis foram dissecados, medidos e enviados ao laboratório de anatomia patológica, sendo realizadas colorações por meio de hematoxilina-eosina, picrossírius e resorcina fuccina oxidada.

Resultados: Com relação aos ventrículos, no grupo CMDId ocorre dilatação nos segmentos apical, equatorial e basal. A medida do AVD foi maior no grupo CMDId, não havendo diferença no AVE entre os grupos. Com relação ao percentual de fibras colágenas, há diminuição no grupo CMDId em relação ao grupo normal. Com relação às fibras elásticas, não houve diferença entre os grupos.

Conclusão: Ocorre alteração da geometria ventricular com dilatação no grupo CMDId. Na CMDId observou-se aumento no perímetro do AVD. Não se observou aumento do perímetro do AVE. Houve diminuição percentual na área total de colágeno tanto no AVD quanto no AVE em corações com CMDId.

Descritores: Coração. Valva Mitral. Valva Tricúspide. Cardiomiopatia Dilatada.

despite this relevant fact, the rings expansion mechanism is not completely understood^[2-4].

The presence of valvular insufficiency may contribute to increased morbidity in heart valve disease patients^[5] or those presenting a DCM of various etiologies^[6]. There is a tendency to consider the valve tissues as inert, because of its simple histological structure and sparse cell population, however, this fact seems less reasonable in light of the huge mechanical load imposed on these structures throughout life and the consequent need for maintenance of its tissue integrity at the cost of balance between collagen production and degradation^[7].

Although the presence of myocytes and coronary circulation are capital for the functioning of the heart as a pump, the components of the extracellular matrix (ECM), particularly the collagen fibers of types I and III are recognized as fundamental to the maintenance of the cardiac cycle^[8]. Among its many functions, the most important are to provide structural framework for myocytes and vessels as well as provide the body resistance and resilience properties, providing systolic and diastolic tone, helping the heart to maintain its conformation^[8-12].

The breakdown of these fibers may occasionally persist even after removal of the underlying disease in many situations. In patients with disease of the mitral valve with secondary tricuspid insufficiency, there can be no normalization of tricuspid regurgitant flow even with the correction of mitral valve disease^[13]. This fact raises controversy in the literature about the real necessity of repair of the tricuspid valve ring when it is secondarily dilated^[13], and to what extent the non-standardization of reflux may be associated with irreversible histological changes in atrioventricular rings. This fact is of crucial importance, given the fact that about half of patients with mitral valve disease requiring surgery presents significant tricuspid insufficiency^[14]. The authors who advocate not performing repair insist on the fact that the correction of mitral lesion leads to normalization of the afterload of the right ventricle by reducing the pressure of the pulmonary vascular bed^[15]. In contrast, those who advocate the realization of repair of the tricuspid ring support the fact that the ring expansion cannot be naturally reversible in advanced cases, despite the total correction of the mitral valve^[16,17]. This fact could possibly be due to microscopic structural changes in the atrioventricular rings with occurrence of collagenolysis and replacement of collagen fibers for tissue of other nature, compromising its integrity.

The anatomical concept that the fibrous skeleton of the heart does not dilate has been refuted^[2,3,18], and its enlargement has been proved in cases of severe heart failure due to dilated cardiomyopathy of ischemic (iscDCM) or nonchagasic idiopathic (idDCM) etiologies^[2,3]; however, it does not exist in the literature comparative histological study of right and left atrioventricular rings in cases of idDCM in light of this new concept. At the same time, available knowledge about the role played by ECM in terms of control and regulation of this process is still scarce so that there is broad field of research being done in this area.

Objective

The aims of this study are:

1-Evaluating and comparing the perimeters of the right and left ventricles in different segments and right and left atrioventricular rings in normal hearts and patients with IdDCM.

2- Comparing the percentage by area of collagen and elastic fibers of the right and left atrioventricular rings between the normal hearts and patients with idDCM.

METHODS

The design of this study was initially submitted to and approved by the Institutional Research Ethics Committee.

Material

Specimens of normal and dilated hearts were studied. Normal hearts came from the Coroner's Service of São Paulo

(SVOC-USP), and dilated hearts from the Anatomic Pathology Laboratory of the Heart Institute of the Clinics Hospital, University of São Paulo (InCor-HC USP).

A total of 26 specimens were grouped as follows:

Group 1 - (idDCM) Composed of 13 hearts from individuals with idDCM

Group 2 - (NORMAL) Composed of 13 hearts from individuals without cardiomyopathy and considered normal

After collection, samples were fixed in formalin, followed by removal of large vessels and the atria, leaving only the atrioventricular rings and ventricular mass.

After the steps of preparation and assessment of parts, cross-sections of ventricular mass were performed, starting from the atrioventricular groove towards the apex of the heart (DistAV-AP). The cross-sections were performed at a level corresponding to 80% (baseline), 50% (equatorial) and 20% (apical) from this distance, following being photographed with a digital camera (Sony, model Cyber Shot DSC W 200) which was set at a table through a bucky 15 cm distally from the parts. The images were transferred to a computer where measurements were performed with the software Image Tool, (Department of Dental Diagnostic Science of the University of Texas Health Science Center, San Antonio, USA). All parts were photographed next to a rule which served as a reference for measurements.

After the completion of the photographs, the right and left atrioventricular rings were completely dissected, but were not separated, keeping them together by the central fibrous body. The rings were placed in boxes and sent to the pathology department, following being waxed and laminated, and performed histological sections of 5 micrometers thick and used the following staining methods:

- Hematoxylin-eosin (HE) - Standard coloring in pathology services, and is used for identification of technical artifacts and histopathological changes that eventually could compromise analysis by other methods.

- Picrosirius - coloring used to study collagen fibers.

- Weigert's resorcinol-fuchsin with previous oxidation by oxone (RFO) - coloring used to study elastic fibers

Quantitative morphometric analysis was performed by means of digital image analysis using system consisting of optical microscope Leyca DMR (Leyca Microsystems Wetzlar GmbH, Germany) connected to a computer by a video camera.

Histological sections of the right and left atrioventricular rings were photographed at 15 points randomly selected from an increase of 100 times, and the captured images were analyzed using the software Image Pro Plus version 4.1 (Media Cybernetics - Silver Spring, MD, USA) that quantifies the area occupied by fibers and then quantifies the total area, and then it was possible to calculate the percentage of collagen and elastic fibers of each photographed spot. For each ring was used the percentage average of the fibers of the fifteen points photographed.

After obtaining the macroscopic data, comparisons of the average ventricular circumference of each segment were performed (apical and basal Equatorial) between idDCM and normal groups and the right and left ventricles as well as comparisons of means of ventricular perimeter between each segment (Apical, Equatorial and Basal) within each group (idDCM and NORMAL). The perimeters of the right and left atrioventricular rings were also compared.

Regarding the microscopic data, the average of the percentages comparisons were performed by area of collagen and elastic fibers of the right and left atrioventricular rings between each group (idDCM and NORMAL).

Regarding the statistics, descriptive analyzes were performed, presenting means along with the related standard deviations (\pm SD) and minimum and maximum values. The assumptions of normal distribution in each group and the homogeneity of variances between groups were assessed, respectively, with the Shapiro-Wilk test and the Levene test. The inferential analysis for ventricular perimeter was performed using analysis of variance (ANOVA) for repeated measures to compare the means of each segment between the groups (intergroup factor). The t test was used to evaluate the average perimeters of the right and left atrioventricular rings and the mean percentage of elastic and collagen fibers of the rings. The descriptive and inferential

statistical analyzes were performed using SPSS version 13 (SPSS 13.0 for Windows).

RESULTS

One of the objectives was to assess the perimeters of the right and left ventricles (apical, equatorial and basal segments) for each group (idDCM and NORMAL), but the point for section of the apical segment (20%) did not include the right ventricular cavity of hearts from idDCM the NORMAL groups and in most cases. Thus, in the right ventricles of the hearts from idDCM and NORMAL groups were analyzed only the perimeters of the equatorial and basal segments.

Descriptive data for variables of right ventricle perimeters (equatorial and basal segments) and left (apical, equatorial and basal segments) for each group are presented in Tables 1 and 2 and the descriptive results for the perimeters of variables of right and left atrioventricular rings for each group are presented in Tables 3 and 4.

The descriptive results for the variables percentages by area of collagen fibers of the right and left atrioventricular rings for each group are shown in Tables 5 and 6, and the descriptive results for the variables percentages by area of elastic fibers of the right and left atrioventricular rings for each group are presented in Tables 7 and 8.

Table 1. Descriptive measures of equatorial and basal perimeter variables in idDCM and NORMAL (mm) right ventricle groups.

Groups	Segment	N	Mean	Standard deviation	Minimum	Maximum
idDCM	Equatorial	13	170.812	44.60938	84.36	242.99
	Basal	13	223.339	29.03743	190.58	287.34
NORMAL	Equatorial	13	112.66	20.58866	74.78	142.72
	Basal	13	173.38	24.82283	123.59	216.54

idDCM: Idiopathic dilated cardiomyopathy

Table 2. Descriptive measures of variables apical, equatorial and basal perimeter in idDCM and NORMAL (mm) left ventricle groups.

Groups	Segment	N	Mean	Standard deviation	Minimum	Maximum
idDCM	Apical	13	101.5862	38.23844	56.34	180.79
	Equatorial	13	191.3458	30.37638	146.81	254.45
	Basal	13	181.9777	35.22137	140.39	261.37
NORMAL	Apical	13	59.93	18.70348	23.62	86.57
	Equatorial	13	120.3235	17.89946	93.17	144.8
	Basal	13	116.6919	15.00732	93.42	143.5

idDCM: Idiopathic dilated cardiomyopathy

Table 3. Descriptive measures of variables RVR ring perimeter in idDCM groups and Normal (mm).

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	13	120.1915	15.33305	94.85	141.78
NORMAL	13	104.0046	13.88195	75.77	128.89

RVR=Right ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

Table 4. Descriptive measures of variables LVR perimeter in idDCM and Normal (mm) groups.

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	12	108.3233	13.76889	87.35	128.01
NORMAL	13	97.2723	16.40091	69.02	118.09

RVR=Right ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

Table 5. Descriptive measures of variables collagen fibers of RVR in idDCM and NORMAL groups (percentage).

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	13	19.2332	14.19502	1.51	60.73
NORMAL	13	38.5756	21.51783	13.43	88.89

RVR=Right ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

Table 6. Descriptive measures of variables collagen fibers of LVR in idDCM and NORMAL groups (percentage).

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	13	22.0962	12.85746	1.44	59.55
NORMAL	13	38.4603	14.75941	14.85	59.55

LVR=Left ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

Table 7. Descriptive measures of variables elastic fibers of RVR in idDCM and NORMAL groups (percentage).

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	13	19.5032	11.33865	8.12	45.4
NORMAL	13	17.5873	13.42513	0.29	43.46

RVR=Right ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

Table 8. Descriptive measures of variables of elastic fibers of LVR in idDCM and NORMAL groups (percentage).

Groups	N	Mean	Standard deviation	Minimum	Maximum
idDCM	13	21.0929	11.16968	7.13	43.78
NORMAL	13	18.1184	13.63213	1.26	50.78

LVR=Left ventricular ring; idDCM: Idiopathic dilated cardiomyopathy

In the mean comparison analysis of right ventricular perimeters of equatorial and basal segments between NORMAL and idDCM groups, statistically significant differences were found ($P<0.05$) in all studied segments.

In the mean comparison analysis of the right atrioventricular perimeters of the rings between idDCM and NORMAL groups statistically significant difference was found ($P<0.05$).

In the mean comparison analysis of left ventricular apical perimeters of equatorial and basal segments between idDCM and NORMAL groups, statistically significant differences were found ($P<0.05$) in all segments.

The results of the Post-Hoc test with Bonferroni correction for multiple comparisons showed statistically significant differences for all comparisons, except with respect to the com-

parison between equatorial and basal ventricular perimeters.

In the mean comparison of the perimeters analysis of left atrioventricular rings between the idDCM and NORMAL groups, there was no significant statistical difference ($P > 0.05$).

In the mean comparison analysis of the collagen fibers of the right and left atrioventricular rings between the idDCM and NORMAL groups, there was a statistically significant difference ($P < 0.05$).

In the mean comparison analysis of the elastic fibers of the right and left atrioventricular rings between the idDCM groups and NORMAL, there was no statistically significant difference ($P > 0.05$).

DISCUSSION

The medical understanding of the CHF has undergone substantial change since the first records of this entity, which can be traced in writings attributed to Hippocrates, and we can identify its historical evolution, which progressed in symmetry with the advancement of scientific knowledge^[19].

From a functional standpoint, the loss of pumping function occurs due to energy dissipation, a fact derived from mechanisms as increased heart weight, ventricular dilation, and thrombi in the heart chambers and dilation of atrioventricular rings^[1].

The ECM had its role reviewed in the genesis of idDCM. Initially, its components were taken as part of passive support in which the myocytes are intertwined, but recent studies point to the fact that these components play an active role in all phases of the normal cardiac cycle, for giving the heart fundamental properties such as resistance, resilience and elasticity, with consequent amendment of these features in pathological cardiac cycle, whose main characteristic is ventricular remodeling, which can be observed in macroscopic and microscopic level^[8,20].

The normal myocardial collagen comprises predominantly Type I (corresponding to about 80% of the total collagen mass) and III, which form a three dimensional network structure which includes valves, chordae tendineae and perivascular interstitial collagenous components, which is organized in bundles. They are called epimysium (which covers each muscle fiber individually), perimysium (covering myocytes groups) and endomysium (found between each myocyte)^[8].

Regarding the behavior of the collagen fibers in cardiomyopathies, studies show conflicting results, and there may be increased^[21] or decrease^[20] of the collagenous component as well as breakdown of normal structure. Weber et al.^[8], in histological study analyzing three hearts of patients who died due to idDCM, reported that there was a decrease of type I collagen (tougher) and increased collagen type III (less resistant) compared to the normal pattern and loss of normal functional architecture of collagenous fibers. They found that the increase in the less resistant collagen is likely

responsible for the remodeling mechanism, with decreased contractile efficiency.

This discrepancy results seem to be related in part to the methodology used and partly due to the fact that collagen may take different forms in the case of normal myocardial collagen or fibrosis.

Although myocardial ECM changes have already been investigated in cases of idDCM, two factors remain unknown, namely any modification of the histological composition of the ECM of right and left atrioventricular rings and the behavior of the collagen fibers in terms of balance among its production, degradation and organization. These facts motivated the present study.

From a macroscopic point of view, it was noted that there dilatation in both ventricles of the idDCM group, albeit with distinct morphology, since the expansion of the RVR accompanies the expansion of the equatorial and basal ventricular segments, contrary to what happens in LVR which presents no significant expansion compared to the control group, although there was dilation of equatorial and basal segments at left. In relation to LVR, these findings confirm the results of Juliani^[22] and Hueb et al.^[2,3], who claim to not be the degree of left ventricular dilation that determines the degree of dilation of the mitral ring, since they occur independently. This statement has always been a matter of controversy in the literature. In a study that examined the measure of LVR in 102 hearts, 78 of which had left ventricular dilation, Bulkley & Roberts^[23] conclude that the isolated expansion of the left ventricular rarely causes failure in the left atrioventricular valve. They mention that the contrary affirmative has long been regarded as true, as postulated by great names of cardiology, as Flint and Osler in books dated end of the nineteenth century.

The association of left atrioventricular valve insufficiency increases the morbidity and mortality of patients with CHF caused by idDCM^[1]. Although often seen as secondary only to ventricular remodeling and it is therefore classified as "functional", recent studies indicate that possibly there are intrinsic components to the valve structure as a whole that acting differently can be responsible for the observed failure^[4,6]. The valve leaflets, although considered to be only inert, because apparently they are not committed in cases of idDCM, contrary to what happens in other types of valvular regurgitation, present their own characteristics that must be taken into account, such as afferent and efferent innervation, intrinsic contractile properties, and spatial orientation of collagenous fibers that allows optimal distribution of mechanical stress, so that the remodeling of the leaflets possibly plays an intrinsic role in the genesis of valve failure, as demonstrated by Timek et al.^[4] in experimental study in sheep. This fact comes against the results observed in our study, since there was no statistically significant dilation of the LVR, which seems to confirm the fact that it is not only the possible expansion of the ring that

causes failure. The fact that there was dilation statistically significant of the RVR may optionally be associated to a lack of a full collagenous ring around the right atrioventricular orifice, unlike what occurs on the left side, where this hole is effectively surrounded by strong collagenous ring, which may reduce the propensity for ring dilation.

According Juliani^[22], there was cross left ventricular dilation in idDCM, which is mainly caused by changes in the baseline and equatorial segments. The fact that dilation of LVR can be a significant component of the ventricular remodeling process because anatomically the ring is part of the ventricle containing it, and because of its non-expansion may not occur changes in ventricular anatomic configuration, with tapering of its superior portion. This fact occurs only at left because at right occurs dilation of the basal, equatorial and RVR segments, a fact that gives rise to a different ventricular conformation and morphology of the wider top. These findings seem to corroborate the results of Hueb^[3], who observed the fact that impairment of RVR valve accompanies the enlargement of the right ring, which does not occur on the left.

The proportionality between the different types of collagen seems to represent major role in maintaining normal geometric conformation of the heart^[8]. Although the amount of total collagen in the myocardium may increase, due mainly to the replacement of such fibers by scar tissue, with a consequent functional breakdown, there appears to be evidence points to the fact that the ECM of myocardium composition may vary according to the anatomic location. Gunja-Smith et al.^[24] in study comparing 8 hearts with idDCM extracted from heart transplant recipients, with 12 normal hearts, stated emphatically that “it deals with a simplification to assume that every heart has a similar composition.”

In this study, we assessed the ECM regarding its collagenous and elastic components exclusively in the region of the atrioventricular rings. As far as we know, there is no similar study in literature, a reason that can possibly explain the inconsistencies found with respect to the total amount of collagen, because in this study we noted, under microscopic inference analysis, that the percentage amount of total collagen fibers was significantly lower in idDCM group relative to the control group in both atrioventricular rings.

Study limitations

With regard to the selection of the sample, although we had calculated the power to explain any change found in macroscopic terms such as above 80%, it was not possible to calculate it in microscopic terms, since there are no studies in the literature about the specific change in EMC of atrioventricular rings in idDCM that would serve as the basis to a similar calculation. The possibility of a pilot study was not contemplated by the impossibility of obtaining more

participants, since the only available were effectively used in the study. This limitation may eventually be overcome from studies in animal models, since there are already developed models for this purpose.

Microscopic analysis was limited by issues relating to staining methods used, especially in relation to the study of elastic fibers. Staining with the use of resorcin-fuchsin oxidized allows evaluating the totality of the elastic fibers present, but it does not adequately provide for differentiation between three different types of such fibers (oxytalan, elastic and mature). Studies with use of alternative colors, such as Verhoeff method for exclusive coloring mature elastic fibers and Weigert resorcin-fuchsin, for recognizing the mature and elastic fibers may help elucidate the elastic behavior of the system qualitatively and not only quantitative.

Regarding the collagen fibers, the methodology used allowed the quantification of the total fibers present, however, it did not allow the differentiation of different types of fibers present, so that it could not be assessed the quantity of the collagen studied that was composed of healing material and fibrosis.

In the present study, there was the aim to investigate the variation of the total quantity of collagen and elastic fibers in different anatomic regions of the heart, which could lead to the confirmation of the hypothesis that the ECM structure varies according to the anatomical region, presenting a standard of increase of some structures and decrease in others.

Final considerations

The anatomical variation of the atrioventricular ring in terms of presence of ECM has been demonstrated. Angelini et al.^[25] analyzed after autopsy the left atrioventricular junction in 13 subjects, 7 of them free of heart disease and 6 patients with mitral valve prolapse and concluded that except for the intertrigonal distance, where lies the mitral-aortic continuity, there is great ECM array arrangement, with the presence of variable size fibrous portions permeating areas where atrial myocardium and the ventricular myocardium are located, and further found that the amount of collagen in the ring ranged thick and easily identifiable portions and also thin portions.

This same hypothesis was raised by Juliani^[22], who in anatomical study that examined 43 human hearts, 18 of them from deceased patients by idDCM, when establishing the independence of the left atrioventricular ring dilatation with respect to dilation of ventricular segments, postulated that “One hypothesis would be that the forming tissue of the mitral ring is richer in fibrous matrix, particularly the region of shortest inter-trigonal distance, than the ventricular muscle, so even suffering the “pressure” of ventricular dilation, in addition to being subject the same etiologic agents that determine the left ventricular dilation in idDCM and iscDCM, its rate of expansion occurs differently.”

CONCLUSION

The results showed that:

1) There was an increase of ventricular perimeters in idDCM group compared to the normal group at right and left in different segments evaluated. The perimeter of the RVR was higher in idDCM group compared to the NORMAL group, with no significant difference in relation to LVR between the two groups.

2) With regard to the percentage by area of collagen fibers, the right and left atrioventricular rings showed lower percentage of fibers in idDCM group compared to the control group. Regarding the percentage by area of elastic fibers, there was no difference between groups.

Authors' roles & responsibilities	
MD	Analysis and/or interpretation of data, statistical analysis, final approval of the manuscript, conception and design of the study, implementation of operations and/or experiments, manuscript writing or critical review of its contents
ATC	Analysis and/or interpretation of data, statistical analysis, final approval of the manuscript, conception and design of the study, implementation of operations and/or experiments, manuscript writing or critical review of its contents
NFJ	Implementation of operations and/or experiments
PANS	Conception and design, manuscript writing or critical review of its contents
FBJ	Analysis and/or interpretation of data, final approval of the manuscript, study design, manuscript writing or critical review of its contents

REFERENCES

- Hare JM. The dilated, restrictive and infiltrative cardiomyopathies. In: Libby P, Bonow RO, Mann DL, Zipes DP, eds. Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed. Philadelphia: Saunders Elsevier; 2008. p.1739-62.
- Hueb AC, Jatene FB, Moreira LFP, Pomerantzeff PMA, Miotto BM, Chabelmann RC, et al. Estudo comparativo do anel valvar mitral e do ventrículo esquerdo na cardiomiopatia dilatada. Rev Bras Cir Cardiovasc. 2001;16(4):354-63.
- Hueb AC, Jatene FB, Moreira LF, Pomerantzeff PM, Kallás E, Oliveira SA. Ventricular remodeling and mitral valve modifications in dilated cardiomyopathy: new insights from anatomic study. J Thorac Cardiovasc Surg. 2002;124(6):1216-24.
- Antoniali F, Braile DM, Potério GMB, Costa CE, Lopes MM, Ribeiro GCA, et al. Proporção entre os segmentos do anel da valva tricúspide normal: um parâmetro para realização de anuloplastia valvar. Braz J Cardiovasc Surg. 2006;21(3): 262-71.
- Matsuyama K, Matsumoto M, Sugita T, Nishizawa J, Tokuda Y, Matsuo T. Predictors of residual tricuspid regurgitation after mitral valve surgery. Ann Thorac Surg. 2003;75(6):1826-8.
- Breda JR, Palma JHA, Teles CA, Branco JNR, Catani R, Buffolo E. Miocardiopatia terminal com insuficiência mitral secundária: tratamento com implante de prótese e remodelamento interno do ventrículo esquerdo. Braz J Cardiovasc Surg. 2006;21(3):283-8.
- Henney AM, Parker DJ, Davies MJ. Collagen biosynthesis in normal and abnormal human heart valves. Cardiovasc Res. 1982;16(11):624-30.
- Weber KT. Cardiac interstitium in health and disease: the fibrillar collagen network. J Am Coll Cardiol. 1989;13(7):1637-52.
- Montes GS, Junqueira LC. The use of the Picrosirius-polarization method for the study of the biopathology of collagen. Mem Inst Oswaldo Cruz. 1991;86(Suppl 3):1-11.
- Melo ECM, Lemos M, Ximenes Filho JA, Sennes LU, Saldiva PHN, Tsuji DH. Distribution of collagen in the lamina propria of the human vocal fold. Laryngoscope. 2003;113(12):2187-91.
- Buhler RB, Sennes LU, Mauad T, Melo EC, Silva LF, Saldiva PH. Collagen fiber and versican distribution within the lamina propria of fetal vocal folds. Laryngoscope. 2008;118(2):371-4.
- Sakae FA, Imamura R, Sennes LU, Mauad T, Saldiva PH, Tsuji DH. Disarrangement of collagen fibers in Reinke's edema. Laryngoscope. 2008;118(8):1500-3.
- Sagie A, Schwammenthal E, Padial LR, Vasquez de Prada JA, Weyman AE, Levine RA. Determinants of functional tricuspid regurgitation in incomplete tricuspid valve closure: Doppler color flow study of 109 patients. J Am Coll Cardiol. 1994;24(2): 446-53.
- Dreyfus GD, Corbi PJ, Chan KM, Bahrami T. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair? Ann Thorac Surg. 2005;79(1):127-32.
- Braunwald NS, Ross J Jr, Morrow AG. Conservative management of tricuspid regurgitation in patients undergoing mitral valve replacement. Circulation. 1967;35(4 Supp):I63-9.
- Cohen SR, Sell JE, McIntosh CL, Clark RE. Tricuspid regurgitation in patients with acquired, chronic, pure mitral regurgitation. II. Nonoperative management, tricuspid valve anuloplasty, and tricuspid valve replacement. J Thorac Cardiovasc Surg. 1987;94(4):488-97.
- Groves PH, Lewis NP, Ikram S, Maire R, Hall RJ. Reduced exercise capacity in patients with tricuspid regurgitation after

-
- successful mitral valve replacement for rheumatic mitral valve disease. *Br Heart J.* 1991;66(4):295-301.
18. McCarthy PM. Does the intertrigonal distance dilate? Never say never. *J Thorac Cardiovasc Surg.* 2002;124(6):1078-9.
19. Katz AM. The "modern" view of heart failure: how did we get here? *Circ Heart Fail.* 2008;1(1):63-71.
20. Spinale FG. Myocardial matrix remodeling and the matrix metalloproteinases: influence on cardiac form and function. *Physiol Rev.* 2007;87(4):1285-342.
21. Nunes VL, Ramires FSA, Pimentel WS, Fernandes F, Ianni BM, Mady C. O papel do acúmulo de colágeno no interstício miocárdico na sobrevida dos pacientes com cardiomiopatia dilatada idiopática e chagásica. *Arq Bras Cardiol.* 2006;87(6):757-62.
22. Juliani PS. Avaliação morfogeométrica do ventrículo esquerdo e do anel valvar mitral na cardiomiopatia dilatada isquêmica ou idiopática: estudo comparativo computadorizado [Tese de doutorado]. São Paulo: Faculdade de Medicina, Universidade São Paulo; 2008.
23. Bulkley BH, Roberts WC. Dilatation of mitral annulus. A rare cause of mitral regurgitation. *Am J Med.* 1975;59(4):457-63.
24. Gunja-Smith Z, Morales AR, Romanelli R, Woessner JF Jr. Remodeling of human myocardial collagen in idiopathic dilated cardiomyopathy. Role of metalloproteinases and pyridinoline cross-links. *Am J Pathol.* 1996;48(5):1639-48.
25. Angelini A, Ho SY, Anderson RH, Davies MJ, Becker AE. A histological study of the atrioventricular junction in hearts with normal and prolapsed leaflets of the mitral valve. *Br Heart J.* 1988;59(6):712-6.