

Idiopathic dilated cardiomyopathy: computerized anatomic study of relationship between septal and free left ventricle wall

Cardiomiopatia dilatada idiopática: estudo anatômico computadorizado da relação entre o septo e a parede livre do ventrículo esquerdo

Paulo Sérgio Juliani¹, PhD; Éder França da Costa²; Aristides Tadeu Correia¹, MsC; Rosangela Monteiro¹, MsC, PhD; Fabio Biscegli Jatene³, MD, MsC, PhD

DOI 10.5935/1678-9741.20140063

RBCCV 44205-1559

Abstract

Introduction: A feature of dilated cardiomyopathy is the deformation of ventricular cavity, which contributes to systolic dysfunction. Few studies have evaluated this deformation bearing in mind ventricular regions and segments of the ventricle, which could reveal important details of the remodeling process, supporting a better understanding of its role in functional impairment and the development of new therapeutic strategies.

Objective: To evaluate if, in basal, equatorial and apical regions, increased internal transverse perimeter of left ventricle in idiopathic dilated cardiomyopathy occurs proportionally between the septal and non-septal segment.

Methods: We performed an anatomical study with 28 adult hearts from human cadavers. One group consisted of 18 hearts with idiopathic dilated cardiomyopathy and another group with 10 normal hearts. After lamination and left ventricle digital image capture, in three different regions (base, equator and apex), the transversal internal perimeter of left ventricle was divided into two segments: septal and not septal. These segments were measured

by proper software. It was established an index of proportionality between these segments, called septal and non-septal segment index. Then we determined whether this index was the same in both groups.

Results: Among patients with normal hearts and idiopathic dilated cardiomyopathy, the index of proportionality between the two segments (septal and non-septal) showed no significant difference in the three regions analyzed. The comparison results of the indices NSS/SS among normal and enlarged hearts were respectively: in base 1.99 versus 1.86 ($P=0.46$), in equator 2.22 versus 2.18 ($P=0.79$) and in apex 2.96 versus 3.56 ($P=0.11$).

Conclusion: In the idiopathic dilated cardiomyopathy, the transversal dilatation of left ventricular internal perimeter occurs proportionally between the segments corresponding to the septum and free wall at the basal, equatorial and apical regions of this chamber.

Descriptors: Ventricular Remodeling. Cardiomyopathy, Dilated. Heart Failure.

¹Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil.

²Veterinary Physician, private office, Florianópolis, SC, Brazil.

³Faculdade de Medicina da Universidade de São Paulo (FMUSP); Director of InCor-Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo HCFMUSP, São Paulo, SP, Brazil.

This study was carried out in the Instituto do Coração (InCor) of Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil.

Financial support: Fundação Zerbini.

Correspondence Address:

Paulo Sérgio Juliani

Instituto do Coração (InCor) of Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo

Av. Enéas Carvalho Aguiar, 44 - Cerqueira César, São Paulo, SP, Brazil

Zip code: 05403-000

E-mail: psjuliani@usp.br

Abbreviations, acronyms & symbols	
Cm	Centimeters
DCM	dilated cardiomyopathy
Dist AV-AP	Distance from atrioventricular sulcus to the left ventricular apex
ISFC	International Society and Federation of Cardiology
LV	Left ventricle
NSS	Non-septal segment
SAVE	Septal anterior ventricular exclusion
SPSS	Statistical Package for Social Sciences
SS	Septal segment
WHO	World Health Organization

Resumo

Introdução: Uma das características da cardiomiopatia dilatada idiopática é a deformação da cavidade ventricular, a qual contribui para a disfunção sistólica. Poucos trabalhos julgam importante a avaliação dessa deformação ventricular levando em consideração regiões e segmentos do ventrículo, o que pode revelar detalhes importantes do processo de remodelamento, dando suporte a um melhor entendimento do seu papel no comprometimento funcional e ao surgimento de novas estratégias terapêuticas.

INTRODUCTION

Dilated cardiomyopathy (DCM) is the most common among the primary diseases of the myocardium and is featured, in special, by dilation of one or both ventricles and systolic dysfunction^[1]. This is a very interesting model inside a current context of major interest in studies that correlate shape and function of the cardiac pump. The geometrical alterations due to dilation observed in DCM can cause severe functional impairment^[2]. Several authors have studied the effects of these alterations in the left ventricle and developed theories that could explain the reasons for this functional impact. Through exams such as magnetic resonance, for example, verified the influence of geometrical alteration, tending to sphericity, affecting the ventricular torsion during systole or even the ventricular relaxation globally decreasing the cardiac pump performance^[2-5].

However, few studies have evaluated the ventricular chambers splitting them into segments, or observing the changes in size in different places inside the chambers, thus seeking for understanding the real complexity of the geometrical changes in the ill heart. These can give support to the deepening of studies about the influence of the geometrical deformation on cardiac performance as well as the development of more accurate techniques to provide a reverse remodeling^[6-8].

In this context, the aim of this study is to evaluate if, in different regions, increased transverse perimeter of left ventricular chamber in idiopathic dilated cardiomyopathy occurs proportionally between the septal and non-septal segment (free

Objetivo: Verificar se, em regiões diferentes, o aumento do perímetro transversal da câmara ventricular esquerda na cardiomiopatia dilatada idiopática ocorre de maneira proporcional entre o segmento septal e o não septal (parede livre).

Métodos: Foi realizado um estudo anatômico com 28 corações adultos. Um grupo foi constituído por 18 corações com cardiomiopatia dilatada idiopática e outro grupo com 10 corações normais. Em três regiões diferentes (base, equador e ápice), o perímetro interno transversal do ventrículo esquerdo foi dividido em dois segmentos: septal e não septal. Foi criado um índice de proporcionalidade entre esses segmentos. Em seguida verificou-se se esse índice era o mesmo entre os grupos.

Resultados: Entre corações normais e portadores de cardiomiopatia dilatada idiopática, o índice de proporcionalidade entre os dois segmentos (septal e não septal) não apresentou diferença significativa nas três regiões analisadas.

Conclusão: Na cardiomiopatia dilatada idiopática, a dilatação transversal do septo é proporcional à dilatação da parede livre nas regiões basal, equatorial e apical da câmara ventricular esquerda.

Descritores: Remodelação Ventricular. Cardiomiopatia Dilatada. Cardiomiopatias. Insuficiência Cardíaca.

wall), in order to confirm the hypothesis that dilation occurs proportionally between these segments.

METHODS

The selection of the anatomical specimens used and the analysis of results used the current classification system, proposed by the World Health Organization (WHO) and the International Society and Federation of Cardiology (ISFC)^[9]. The Commissions of Science and Ethics from The Heart Institute (*Instituto do Coração (InCor)*) and Ethics for Research Projects Analysis (CAPPesq from the Hospital das Clínicas staff and Faculdade de Medicina da Universidade de São Paulo) approved the studies (protocols no. 2803/06/048 and 501/06, respectively).

Materials

Twenty-eight adult hearts (obtained from necropsy of normal individuals or patients with dilated cardiomyopathy) fixed in 10% formaldehyde were divided into 2 groups, based on their anatomopathological reports. The first group consisted on 18 hearts with idiopathic dilated cardiomyopathy (DCM), from which 13 (72.22%) were originated from male individuals. The hearts weight ranged from 358 to 942 grams, with an average of 595.44 grams. The age ranged from 26 to 64 years old, with an average of 42.44 years old. The exclusion criteria for DCM were: ischemic coronary disease and/or LV aneurisms, congenital heart abnormalities, valve abnormalities, myocardial infiltrative disease, previous heart surgery and the previous use of pacemaker or resynchronization therapy

and/or circulatory assist devices. The second group called NORMAL consisted of 10 cardiomyopathy-free hearts, from which 9 (90%) originated from male individuals. The age ranged from 29 to 70 years old, with an average of 51.4 years old. The weight of those hearts ranged from 212 to 338 grams, with an average of 280.4 grams. The inclusion criteria for the NORMAL group were: non-related cardiopathy *causa mortis*, specimens without macroscopic alterations, particularly valvulopathies, weight up to 340 grams, age between 18 and 75 years old and anatomopathological report certifying normality.

Longitudinal axis measurement and specimen slicing

The longitudinal axis of the heart was measured as follows: with the aid of a millimeter ribbon, a line was drawn near the posterior interventricular sulcus, starting from the atrioventricular sulcus towards the apex. Over this line three dots were marked and used as an anatomic division of the left ventricle (Figure 1):

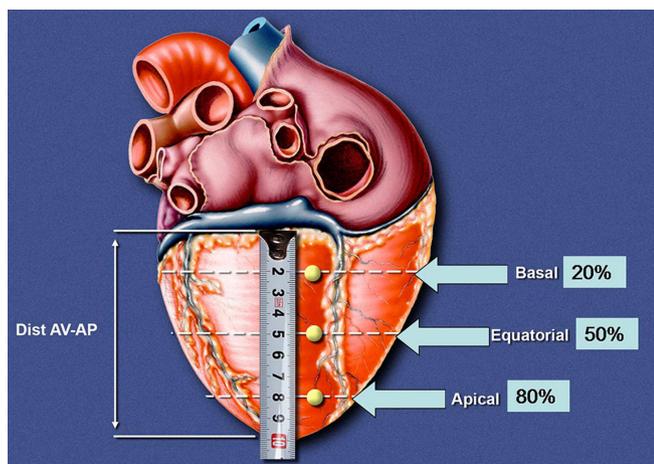


Fig. 1 - Posterior view of a heart with schematic delimitation of dots for ventricular lamination. Basal dot (20%), equatorial dot (50%), apical dot (80%).

DistAV-AP = distance from atrioventricular sulcus to the left ventricular apex

- The equatorial dot at 50% the distance from the atrioventricular sulcus to the apex
- The basal dot 20% far from the atrioventricular sulcus
- The apical dot 80% far from the atrioventricular sulcus

Over the established dots, the transversal section of specimens was proceeded using an electric knife and the following regions were obtained: BASAL, EQUATORIAL and APICAL.

Digital image capture of transversal cuts

The regions originated from the sections were placed on a plain surface of a table, with its basal cut facing upward (Figure 2). The table was equipped with a steel holder to fix a digital imaging device (“Sony Cybershot” model, 3.2 megapixels) to allow the digital image capture of specimens so that those pictures could be obtained from a capture plan precisely placed perpendicularly to the surface. Next to each specimen and as tall as its basal face a centimeter ruler was placed (to be used for calibration purposes on the measurement software). Each region was identified with a small paper tag placed next to it, containing its respective identification.

Computerized digital imaging measurement method

With these digital images, the left ventricular chamber internal perimeter was measured using the software Image Tool for Windows, version 3.00, developed by The University of Texas Health Science Center, USA, disregarding the trabecular relief. The right ventricular chamber vertices were used as a reference to delimitate and measure (in cm) the segment related to the interventricular septum (septal segment – SS), considering the remaining as non-septal segment (NSS) (Figure 2). To analyze the proportionality between segments, the value obtained by the NSS measurement was divided by the SS value in each specimen, thus obtaining the NSS/SS ratio. The values were compared between both groups, corresponding to the ventricular region analyzed (basal, equatorial and apical).

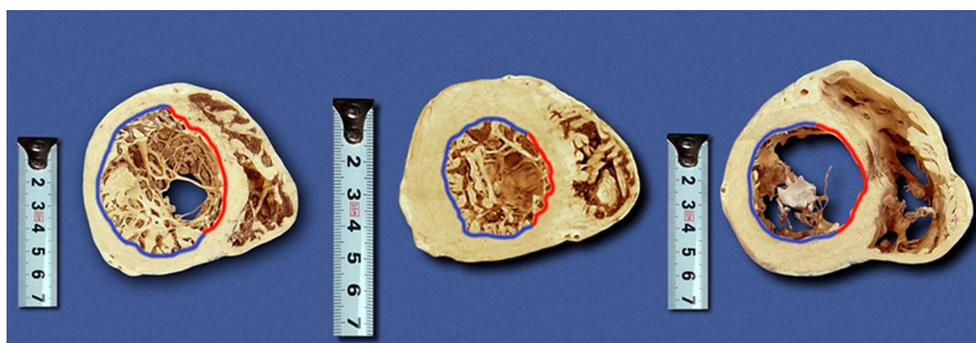


Fig. 2 - From left to right: cranial view, respectively, from equatorial, apical and basal regions of the left ventricle in dilated hearts. The blue line corresponds to the non-septal segment (NSS) and the red line to the septal segment (SS).

Statistical analysis

The descriptive analyses for the quantitative data with normal distribution were performed, showing the mean values along with their respective standard deviations. The condition for normal distribution in each group was evaluated with the Shapiro-Wilk test. The Student’s t-test was used to perform comparisons between NORMAL and DCM groups. A type-I error probability (α) of 0.05 was considered in every inferential analyses. The inferential and descriptive statistical analyses were performed by using the SPSS software, version 17 (SPSS 17.0 for Windows).

RESULTS

The null hypothesis was test taking into consideration that the proportionality between NSS and SS in each LV slice region would be the same between both groups. The mean values for the variables measured in both groups, as well as the NSS/SS ratio are displayed in Table 1. The NSS/SS ratios calculated for the normal hearts were 2 for the base, 2.2 for the equator and 3 for the apex. Therefore in the base, equator and apex, the free wall is respectively 100%, 120% and 200% bigger than the septum. Likewise, the NSS/SS ratios calculated for the dilated hearts were 1.9 for the base, 2.2 for the equator and 3.6 for the apex. Thus, in the base, equator and apex, the free wall on dilated ones is respectively 90%, 120% and 260% bigger than the septum. In the statistical analysis comparing the NSS/SS ratios in the basal, equatorial and apical regions of both groups no significant difference was found ($P=0.46$, $P=0.79$ and $P=0.11$, respectively). Figure 3 represents this analysis.

Figure 3 shows that in the comparison analysis of the NSS/SS ratio mean values in the three ventricular regions between NORMAL and DCM no statistically significant differences were found ($P>0.05$).

DISCUSSION

Methodology

In spite of the constant technological innovations that allow higher and higher accuracy of the structure and *in situ* cardiac function assessment a lot of factors still bring important limitations to these methodologies, as it occurs in the cine nuclear magnetic resonance imaging that, despite providing an excel-

lent anatomical definition among tissues, it cannot be used in some situations, such as in patients with uncompensated heart failure who do not tolerate the apnea needed for the exam and others who would eventually suffer from claustrophobia, as well as arrhythmia carriers and in those who make use of brain metal implants, pacemaker or cardioversor – defibrillator^[10,11]. Therefore, for the proposed evaluation, the anatomical method was chosen, as it still presents the best way to study the left ventricular geometry^[2]. The trabecular relief exclusion during ventricular chamber perimeter measurement does not change significantly the values checked^[7].

Ventricular Geometry

The importance of the geometrical study and its impact on the heart functioning as a pump can be demonstrated by Laplace’s law ($T=P.pR$, where T =tension or ventricular muscle strength, P =intracavitary pressure, $P=3.1416$, R =chamber radius)^[12]. It clarifies the interrelationship between the ventricle shape and the forces exerted on it.

Several studies have pointed out the ventricular sphericity as the main cause of lower heart performance on DCM^[3,4,13], bringing a simplistic view to the existing phenomena in this pathology. With the aim of searching a better detailing of this process, the choice was to analyze the left ventricle in segments rather than considering it a spatial geometric figure. It was shown previously that each segment presents distinct behavior during the ventricular remodeling process^[7].

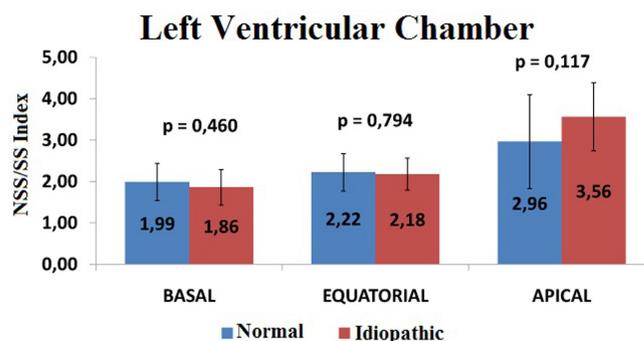


Fig. 3 - Comparison of mean values of the NSS/SS ratios from basal, equatorial and apical regions of the left ventricular chamber in both groups

Table 1. Descriptive results (averages) for the variables measured (cm) in both groups, as well as the NSS/SS ratio of 3 regions analyzed.

		VE								
		Septal Segment (SS)			Non-Septal Segment (NSS)			NSS / SS		
		Basal	Equatorial	Apical	Basal	Equatorial	Apical	B	E	A
Normal	Averages	3.4	3.5	2.2	6.5	7.5	6.1	2	2.2	3
DCM	Averages	6	6	2.7	11	12.9	6.9	1.9	2.2	3.6

Possible applications

The surgical strategies developed so far aiming at reestablishing a “physiological geometry” in the LV do not take enough into consideration this distinct segmental behavior of the left ventricle remodeling process. The first technique performed in non-ischemic cardiopathy, developed by Batista et al.^[12] based on the perception of the clinical improvement in patients submitted to aneurysmectomies and cardiomyoplasties, took into consideration the total increase in the ventricular chamber, applying Laplace’s theory, and consisted of a muscle slice removal from the LV lateral wall. Other techniques that seek to provide the geometry restructuring (Dor, SAVE, Overlapping) reinforce that this logic is true. However, these once again derive from the usual understanding of such geometrical alteration behavior (the sphericity theory). Transoperative mortality, myocardial infarction risk and cardiomyopathy progression after these procedures were problems pointed out^[14-17], a fact that perhaps has discouraged further studies.

In the development of surgical strategies, besides the doubts about the LV dilation behavior throughout its longitudinal axis (basal, equatorial and apical regions) there are also those related to the proportion of the septal wall dilation versus non-septal or free wall. The understanding of the segmental geometrical alterations in DCM can help determine the prognostic and allow the application of early therapeutic measures, even in more accurate interventions that may cause directly a more anatomic remodeling of the left ventricular chamber^[2,12,18].

In general, when establishing the surgical strategies to remodel the distorted LV in idiopathic DCM we should take into account the arrangement of the myocardial fibers^[18,19] as well as the restoring or maintenance of proportion rates among regions (base, equator and apex)^[7] and LV segments (septum and non-septal or free wall). We do not know how important the morphological relationship between the septum and non-septal or free wall is to LV performance.

As this relationship is kept in DCM, we assume that the surgical strategies for LV geometry restoring in this disease might contemplate not only the normal anatomic relationship reestablishment among the perimeters of basal, equatorial and apical regions^[7], but also the maintenance of the relationship between the septum and non-septal or free wall, that is, in the case of ventriculectomies, it could be supposed to be more cautious to exclude the proportional segments from the septum and free wall instead of just, as performed so far, taking out segments from the free wall or even septum or free wall disproportional segments. Therefore, it is clear that the understanding of the segmental geometrical alterations in DCM can help determine the prognosis and allow the application of early therapeutic measures, also in more accurate interventions that directly cause a more anatomic remodeling of the left ventricular chamber^[2,12,18].

CONCLUSION

In idiopathic dilated cardiomyopathy, the left ventricular chamber perimeter transversal dilation occurs proportionally between the segments corresponding to the septum and the free wall, in the basal, equatorial and apical regions of this chamber.

Authors' roles & responsibilities	
PSJ	Analysis and/or interpretation of data, final approval of manuscript, conception and design of the study, conduct of operations and/or experiments, drafting of the manuscript and critical review of the content
EFC	Analysis and/or interpretation of data, Final approval of manuscript, conception and design of the study, drafting of the manuscript and critical review of the content
ATC	Statistical analysis, final approval of manuscript, analysis and/or interpretation of data, conduct of operations and / or experiments
RM	Analysis and/or interpretation of data, final approval of manuscript, Conception and design of the study, drafting of the manuscript and critical review of the content
FBJ	Analysis and/or interpretation of data, final approval of manuscript, Conception and design of the study, drafting of the manuscript and critical review of the content

REFERENCES

- Hare JM. The dilated, restrictive and infiltrative cardiomyopathies. In: Braunwald E. Braunwald’s heart disease – A textbook of cardiovascular medicine. Philadelphia: Saunders Elsevier. 2012. p.1561-81.
- Gómez-Doblas JJ, de Tereza E, Lamas GA. Geometria ventricular e insuficiência cardíaca. Rev Esp Cardiol. 1999;52(1):47-52.
- Tumkosit M, Martin CG, Bayram E, Morgan TM, Lane KS, Rerkpattanapipat P, et al. Left ventricular spherical remodeling and apical myocardial relaxation: cardiovascular MR imaging measurement of myocardial segments. Radiology. 2007;244(2):411-8.
- van Dalen BM, Kauer F, Vletter WB, Soliman OI, van der Zwaan HB, Ten Cate FJ, et al. Influence of cardiac shape on left ventricular twist. J Appl Physiol (1985). 2010;108(1):146-51.
- Nikitin NP, Loh PH, de Silva R, Witte KK, Lukaschuk EI, Parker A, et al. Left ventricular morphology, global and longitudinal function in normal older individuals: a cardiac magnetic resonance study. Int J Cardiol. 2006;108(1):76-83.
- Hueb AC, Jatene FB, Moreira LF, Pomerantzeff PM, Kallás E, de 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.

7. 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: Universidade de São Paulo; 2009.
8. Dalva, M. Estudo do remodelamento ventricular e dos anéis valvares na cardiomiopatia dilatada: avaliação anátomo-histopatológica [Tese de doutorado]. São Paulo: Universidade de São Paulo; 2012.
9. Report of the WHO/ISFC task force on the definition and classification of cardiomyopathies. *Br Heart J.* 1980;44(6):672-3.
10. Nigri M, Rochitte C E, Tarasoutchi F, Grinberg M. A ressonância magnética como método propedêutico em valvopatia. *Arq Bras Cardiol.* 2006;87(4):534-7.
11. Parga JR, Avila LF, Bacal F, Moreira LF, Stolf NG, Ramires JA, et al. Partial left ventriculectomy in severe idiopathic dilated cardiomyopathy: assessment of short-term results and their impact on late survival by magnetic resonance imaging. *J Magn Reson Imaging.* 2001;13(5):781-6.
12. Batista RJV, Santos JLV, Franzoni M, Araujo ACF, Takeshita N, Furukawa M, et al. Ventriculectomia parcial: um novo conceito no tratamento cirúrgico de cardiopatias em fase final. *Rev Bras Cir Cardiovasc.* 1996;11(1):1-6.
13. Bockeria LA, Gorodkov AJ, Dorofeev AV, Alshibaya MD, RESTORE Group. Left ventricular geometry reconstruction in ischemic cardiomyopathy patients with predominantly hypokinetic left ventricle. *Eur J Cardiothorac Surg.* 2006;29 Suppl 1:S251-8.
14. Bocchi EA, Esteves-Filho A, Bellotti G, Bacal F, Moreira LF, Stolf N, et al. Left ventricular regional wall motion, ejection fraction, and geometry after partial left ventriculectomy. Influence of associated mitral valve repair. *Eur J Cardiothorac Surg.* 2000;18(4):458-65.
15. Starling RC, McCarthy PM, Buda T, Wong J, Goormastic M, Smedira NG, et al. Results of partial left ventriculectomy for dilated cardiomyopathy: hemodynamic, clinical and echocardiographic observations. *J Am Coll Cardiol.* 2000;36(7):2098-103.
16. Moreira LFP, Bacal F, Benício A, Bocchi EA, Higuchi ML, Stolf NAG, et al. Fatores prognósticos e evolução da função ventricular em 5 anos de seguimento da ventriculectomia parcial esquerda no tratamento da cardiomiopatia dilatada. *Rev Bras Cir Cardiovasc.* 2001;16(4):275-88.
17. Ueno T, Sakata R, Iguro Y, Yamamoto H, Ueno M, Matsumoto K. Mid-term changes of left ventricular geometry and function after Dor, SAVE, and Overlapping procedures. *Eur J Cardiothorac Surg.* 2007;32(1):52-7.
18. Buckberg GD, RESTORE Group. Form versus disease: optimizing geometry during ventricular restoration. *Eur J Cardiothorac Surg.* 2006;29 Suppl 1:S238-44.
19. Torrent-Guasp F, Kocica MJ, Corno AF, Komeda M, Carreras-Costa F, Flotats A, et al. Towards new understanding of the heart structure and function. *Eur J Cardiothorac Surg.* 2005;27(2):191-201.