

The evaluation of annuloplasty in bicuspid aortic valve repair using cardiac magnetic resonance

Marek Jasinski

Uniwersytet Medyczny im Piastow Slaskich we Wroclawiu

Karol Miszalski-Jamka

Slaskie Centrum Chorob Serca

Radoslaw Gocol

Uniwersytet Slaski w Katowicach

Izabella Wenzel-Jasinska

Slaski Uniwersytet Medyczny w Katowicach

Grzegorz Bielicki

Uniwersytet Medyczny im Piastow Slaskich we Wroclawiu

Mikolaj Berezowski

Uniwersytet Medyczny im Piastow Slaskich we Wroclawiu

Kinga Kosiorowska (✉ kosiorowska.kinga@gmail.com)

Uniwersytet Medyczny im Piastów Śląskich we Wrocławiu <https://orcid.org/0000-0002-2768-7362>

Marceli Lukaszewski

Uniwersytet Medyczny im Piastow Slaskich we Wroclawiu

Andrzej Kansy

Instytut Pomnik -Centrum Zdrowia Dziecka

Marek Deja

Slaski Uniwersytet Medyczny w Katowicach

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Abstract

Background: The incompetent bicuspid aortic valve (BAV) can be replaced or repaired using various surgical techniques. This study sought to assess the efficacy of external annuloplasty and postoperative reverse remodeling using cardiac magnetic resonance (CMR) and compare the mid-term results of external and subcommissural annuloplasty.

Methods: Out of a total of 200 BAV repair performed between 2004 and 2018, 21 consecutive patients (median age 54 years) with regurgitation requiring valve repair with annuloplasty without concomitant aortic root surgery were prospectively referred for CMR and transthoracic echocardiography (TTE) one year after the operation. Two aortic annulus stabilization techniques were used: external, circumferential annuloplasty (EA), and subcommissural annuloplasty (SCA).

Results: 11 patients received EA and 10 patients were treated using SCA. There was no in-hospital mortality and all patients survived the follow-up period. CMR showed strong correlation between postoperative aortic recurrent regurgitant fraction and left ventricular end-diastolic volume ($r=0.62$; $p=0.003$) as well as left ventricular ejection fraction ($r=-0.53$; $p=0.01$). Patients treated with EA as compared with SCA had larger anatomic aortic valve area measured by CMR (3.5cm^2 (2.5; 4.0) vs. 2.5cm^2 (2.0; 3.4); $p=0.04$). In both EA and SCA group, aortic valve area below 3.5cm^2 correlated with no regurgitation recurrency. EA (vs. SCA) was associated with lower peak transvalvular aortic gradients (10mmHg (6; 17) vs. 21mmHg (15; 27); $p=0.04$).

Conclusions: The repair of the bicuspid aortic valve provides significant mid-term postoperative reverse remodeling, provided no recurrent regurgitation and durable reduction annuloplasty can be achieved. External, circumferential annuloplasty is associated with better hemodynamics compared to subcommissural annuloplasty.

Background

A bicuspid aortic valve (BAV) is the most common congenital cardiac abnormality affecting 1–2% of the general population. Even though significant insufficiency of the BAV is more common than that of the tri-leaflet aortic valve, it is also accompanied by aortopathy. Such a complex pathology of the bicuspid valve can be nowadays effectively repaired in selected patients¹. To date, there are various techniques of an aortic valve repair described^{2–5} and they are usually chosen based on a surgery-oriented classification of aortic regurgitation (AR)^{6,7}. Of those, annular stabilization is one of the most important factors that may affect the mid-term and long-term results of the entire repair. However, there is no agreed consensus as to which of the annular stabilization techniques provides the best haemodynamics in patients with bicuspid aortic valves.

Over the last few years, the role of cardiac magnetic resonance (CMR) in patients with aortic valve diseases is gradually increasing⁸. CMR is considered the current gold-standard noninvasive method for

quantification of left and right ventricular volumes, mass, global and regional systolic function. Moreover, CMR is able to assess aortic valve and aortic root morphology, mechanism of the dysfunction, and evaluate the degree of aortic regurgitation in a fully quantitative manner.

Therefore, the aim of this study was to analyze the mid-term efficacy of BAV repair and to evaluate the predictors of postoperative reverse remodeling using CMR. Additionally, the study sought to compare in that respect different annuloplasty techniques: external annuloplasty in circumferential fashion and subcommissural annuloplasty.

Methods

Study population

200 consecutive patients (mean age: 43.2 ± 17.5 years; 148 males: 74%) with BAV who underwent BAV repair, were operated on at three surgical centers between 2004 and 2018, under the same clinical setting (MJ). Of these, 24 patients with BAV who developed aortic regurgitation requiring valve repair with annuloplasty without concomitant aortic root surgery were prospectively referred for CMR and transthoracic echocardiography (TTE) one year after the operation. Generally accepted contraindications to magnetic resonance imaging were used. Subsequently, 21 patients have had CMR performed. This study was approved by the Local Ethics Committee. Informed consent was obtained from each subject.

CMR Acquisition Protocol

All CMR examinations were performed on a 1.5T clinical scanner (Signa HDxt, GE Healthcare, Milwaukee, WI). Images were obtained during suspended respiration at end-expiration. For cine imaging balanced steady-state free precession sequence was used. Patients underwent a left ventricular (LV) function study as previously described⁹. Cine images were acquired in three LV long-axis views, LV outflow tract view and a set of multiple contiguous short-axis slices from atrioventricular ring to the apex. Cine imaging of a BAV orifice was performed. The acquisition was repeated several times a few millimeters further and closer from valve orifice to ensure optimal direct planimetry of valve area. Then double oblique cine images were acquired as multiple cross-section and long-axis views in order to visualize aortic root, sinotubular junction (STJ), and ascending aorta. After choosing a plane few millimeters above the tips of aortic cusps (usually at the level of STJ) 2D through-plane phase-contrast sequence was used for quantification of forward and backward flow. Then additional phase-contrast imaging was performed at the level of valve orifice and also few millimeters distal from tips of aortic cusps for maximal velocity assessment. Meticulous care was taken to orient imaging planes perpendicular to the blood flow. Encoding velocity was carefully adjusted to avoid aliasing. All flow sequences were acquired with the region of interest located at the isocenter of the magnet.

CMR data analysis

Images were analyzed with commercial software (Qmass MR, Medis Medical Imaging Systems, Leiden, the Netherlands) by an experienced, observer-blinded to the patients' profile (K.M-J). LV volumes, ejection

fraction, and compacted mass were calculated as previously described⁹. Three-chamber and LV outflow tract cine images were used for aortic annulus assessment. The average diameter of the annulus was calculated from minimal and maximal annulus diameters. Anatomical aortic valve area (AVA) planimetry was performed at the systolic frame (largest aortic valve opening) after careful confirmation of the correct imaging plane. Maximum cross-sectional measurements of the aortic root, STJ, and ascending aorta were performed. From phase-contrast images, forward and backward flow through the aortic valve was measured. Regurgitant volume and regurgitant fraction were calculated. In order to minimize phase offset errors background correction was applied with the region of interest in the stationary tissue (pectoralis muscle).

Transthoracic Echocardiography

All transthoracic echocardiograms were obtained one year after the surgery by an experienced, the same every time, observer-blinded to the patients' profile. Standard echocardiographic parameters of the LV and aortic valve were assessed including the specific bicuspid anatomy, magnitude, and character of the aortic regurgitation, as well as transvalvular aortic gradients.

Surgical Management

All operations were performed through a median sternotomy, with the use of standard cardiopulmonary bypass. In each case, the myocardium was protected with blood cardioplegia. Techniques of aortic valve repair were described previously^{10,15}. Briefly, the first step has been an evaluation of the effective height of leaflets^{10,11}, as well as the central leaflet coaptation. Secondly, the relative lengths of the leaflet free margins were assessed by suturing together and identifying prolapse¹²⁻¹⁶. Raphe management consisted of shaving, plication, or triangular excision followed by direct suturing. Sizing of the aortic graft, as well as the annuloplasty band or ring, were based on the height of the leaflets and the height of the subcommissural triangle between the left and non-coronary sinuses^{12,17}.

Twenty-four consecutive patients fulfilling preselection criteria operated on between 2013 and 2014 by a single surgeon (MJ), were prospectively allocated to one of two groups based on the aortic annulus stabilization technique. Three patients have been excluded due to CMR contraindications. The first group comprised patients who had an external annuloplasty (EA) in circumferential fashion with the use of a Dacron strip made of aortic graft chosen for STJ remodeling and aorta replacement. The external annuloplasty consisted of the placement of a circular, transverse line of 10–12 interrupted pledgeted 2 – 0 braided sutures at the level of the aortic ring below leaflets nadirs, from inside to outside where were supported by a circular band from Dacron strip. The second group had subcommissural annuloplasty (SCA) performed with two braided 2 – 0 sutures enhanced with pledgets to narrow two subcommissural triangles. Additionally, all patients from the EA and SCA group underwent STJ remodeling and replacement of the ascending aorta.

The preselection criteria included: BAV type I anatomy with fused leaflets, moderate to severe aortic regurgitation, an enlarged aortic annulus (median 26 mm (24; 28)) with no aortic root dilatation and

annulus diameter above 28 mm, thus not requiring root replacement and valve reimplantation¹⁶. The groups were comparable in terms of the baseline characteristics including patient age, dimensions of the left ventricle, and aortic annulus diameter. All patients presented with normal left ventricular contractility at baseline.

Statistical analysis

Data are presented as counts (percentages) for categorical variables, and as medians with first and third quartiles of the distributions for continuous variables. Nonparametric tests were used due to the small sample size. For continuous variables, the Mann-Whitney test was performed for unpaired samples. Proportions comparison between groups were analyzed with Fisher's exact test. Correlations between continuous variables were evaluated with the use of Spearman's rank correlation coefficient. All statistical tests were two-sided. A p-value was considered to indicate statistical significance at the nominal 0.05 level. Statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL).

Results

Twenty-one Caucasian patients (median age 54 years (30; 65), 62% men) were included in the study. Of them, 11 patients received EA and 10 patients were treated using SCA. CMR examinations were acquired on average 12.6 (6.6; 14.1) months after the operation. In all patients, the quality of CMR images was sufficient for detailed analyses. Patients' characteristics are summarized in Table 1. Compared with patients who received SCA, EA-treated patients had wider aortic root diameter and larger AVA as measured by CMR (Fig. 1). The latter group had also lower transvalvular peak gradient measured by TTE.

Table 1
Comparison of annuloplasty techniques using CMR and TTE (N = 21).

Characteristics	Overall (N = 21)	SCA (N = 10)	EA (N = 11)	P-value
Demographic parameters				
Age, years	53 (29; 66)	63 (31; 67)	50 (28; 63)	0.46
Gender male, n (%)	13 (62)	5 (50)	8 (73)	0.39
CMR LV volume parameters				
EDV, ml	186 (134; 237)	164 (131; 235)	193 (154; 242)	0.65
ESV, ml	68 (51; 118)	62 (47; 122)	76 (61; 116)	0.65
SV, ml	111 (84; 123)	93 (82; 124)	113 (91; 125)	0.56
EF, %	59 (52; 62)	61 (49; 66)	58 (54; 61)	0.56
LV mass, g	115 (85; 151)	100 (85; 151)	116 (84; 158)	0.71
EDV normalization, n (%)	16 (76)	9 (90)	7 (64)	0.31
EF normalization ($\geq 55\%$), n (%)	15 (71)	7 (70)	8 (73)	0.99
CMR RV volume parameters				
EDV, ml	170 (146; 196)	165 (140; 192)	173 (150; 203)	0.65
ESV, ml	72 (61; 84)	67 (60; 82)	73 (64; 91)	0.35
SV, ml	94 (79; 111)	92 (78; 111)	94 (84; 112)	0.81
EF, %	56 (52; 61)	57 (55; 61)	55 (51; 62)	0.51
CMR aortic valve/root parameters				
Annulus, mm	22.0 (20.5; 26.8)	21.8 (19.8; 26.8)	22.5 (21.0; 27.0)	0.76
AVA planimetry, cm ²	3.0 (2.1; 3.5)	2.5 (2.0; 3.4)	3.5 (2.5; 4.0)	0.04

Values are presented as the number of patients (%) or median (first quartile; third quartile).

AVA - aortic valve area, CMR - cardiac magnetic resonance, EA - external annuloplasty, EDV - end-diastolic volume, EF - ejection fraction, ESV - end-systolic volume, LV - left ventricle, RV - right ventricle, SCA - subcommissural annuloplasty, STJ - sinotubular junction, SV - stroke volume, TTE - transthoracic echocardiography

Characteristics	Overall (N = 21)	SCA (N = 10)	EA (N = 11)	P-value
Aortic root diameter, mm	38.4 (36.4; 41.6)	36.7 (35.8; 39.4)	39.8 (38.1; 43.8)	0.02
Aortic root height, mm	26.0 (23.5; 29.0)	25.5 (23.8; 28.5)	27.0 (23.0; 29.0)	0.61
STJ, mm	30.0 (28.0; 31.0)	30.0 (25.0; 30.0)	30.0 (29.0; 31.0)	0.20
Ascending aorta, mm	32.0 (30.5; 33.5)	32.0 (30.8; 33.3)	32.0 (30.0; 34.0)	0.81
Regurgitant fraction, %	7 (3; 12)	9 (3; 17)	6 (2; 12)	0.81
Regurgitant volume, ml	7 (3; 13)	7 (3; 20)	7 (2; 12)	0.81
Residual aortic insufficiency				0.51
None/mild, n (%)	17 (81)	8 (80)	9 (82)	
Moderate, n (%)	3 (14)	2 (20)	1 (9)	
Severe, n (%)	1 (5)	0 (0)	1 (9)	
TTE parameters				
Interventricular septal thickness at end-diastole, mm	12.0 (11.0; 13.3)	12.3 (11.6; 15.1)	11.5 (11.0; 13.0)	0.17
LV end-diastolic dimension, mm	53.0 (46.5; 59.3)	51.0 (44.0; 60.4)	54.0 (48.0; 58.0)	0.76
LV posterior wall thickness at end-diastole, mm	9.0 (8.0; 10.5)	9.5 (8.0; 11.3)	9.0 (7.0; 9.5)	0.25
Peak gradient, mmHg	16 (9; 24)	21 (15; 27)	10 (6; 17)	0.04
Residual aortic insufficiency				0.99
None/mild, n (%)	17 (81)	8 (80)	9 (82)	
Moderate, n (%)	4 (19)	2 (20)	2 (18)	
Severe, n (%)	0 (0)	0 (0)	0 (0)	
Values are presented as the number of patients (%) or median (first quartile; third quartile).				
AVA - aortic valve area, CMR - cardiac magnetic resonance, EA - external annuloplasty, EDV - end-diastolic volume, EF - ejection fraction, ESV - end-systolic volume, LV - left ventricle, RV - right ventricle, SCA - subcommissural annuloplasty, STJ - sinotubular junction, SV - stroke volume, TTE - transthoracic echocardiography				

There was a strong correlation between postoperative LV end-diastolic volume and severity of residual AR quantified by regurgitant fraction ($r = 0.62$; $p = 0.003$) and regurgitant volume ($r = 0.66$; $p < 0.001$). Similarly, the postoperative LV ejection fraction negatively correlated with the regurgitant fraction ($r = -0.53$; $p = 0.01$) and the regurgitant volume ($r = -0.44$; $p = 0.04$) (Fig. 2).

We also found a moderate correlation between the postoperative anatomical AVA and the severity of residual AR expressed by the regurgitant fraction ($r = 0.43$; $p < 0.05$) and the regurgitant volume ($r = 0.42$; $p = 0.04$). Similarly, the postoperative aortic root diameter is moderately correlated with the regurgitant fraction ($r = 0.44$; $p = 0.04$) and the regurgitant volume ($r = 0.43$; $p = 0.04$) (Fig. 2). However, no significant correlation was observed neither between the annulus diameter and the regurgitant fraction ($r = 0.11$; $p = 0.63$) nor between the annulus diameter and the regurgitant volume ($r = 0.18$; $p = 0.45$).

Of note, the postoperative transvalvular peak gradient measured by TTE significantly negatively correlated with anatomical AVA ($r = -0.44$; $p = 0.04$) and aortic root diameter ($r = -0.63$; $p = 0.002$), but not with aortic annulus diameter ($r = -0.20$; $p = 0.39$).

The agreement between CMR and TTE for residual AR grading was excellent. Both methods yielded the same grade of AR severity in 20 of 21 patients (95%).

Discussion

The presence of a bicuspid aortic valve is associated with a high incidence of valve dysfunction, proximal aortic dilatation, and a higher incidence of acute aortic events. Tzemos et al. observed cardiac events in 25% and aortic dilatation in 45% of 650 patients during a nine-year follow-up¹⁸. Similarly, in the study by Sarano et al. (Olmstead County asymptomatic BAV group) with a 15-year follow-up, 42% of patients experienced cardiac events, and 27% of the examined population required cardiac surgery¹⁹.

Thanasoulis et al. found that predictors of aortic dilatation in 582 patients with BAV included moderate and severe aortic insufficiency and the fusion of right and left leaflets of the aortic valve²⁰. Current recommendations advise the use of valve-sparing operations in patients with isolated aortic valve insufficiency²¹. However, the durability of the repair did not appear to be as good as with the tricuspid aortic valve. This may be related to a connective tissue disorder, which is often an accompanying feature of BAV²².

Progressive annular dilatation caused by annuloaortic ectasia may affect the stability of the repair. Annular stabilization can be achieved by performing annuloplasty during the aortic valve repair operation. The annuloplasty techniques are currently under clinical investigation and it has already been confirmed that suture-based SCA may fail due to late redilatation of the aortic root. Root stabilization with reimplantation provided better stability than SCA alone^{23,24}. Other authors have also shown promising results of internal or external bands and rings^{25,26}. Thus, the present study sought to analyze the results of different annular stabilization strategies.

Our study showed that external stabilization of the ventriculo-aortic junction provided better hemodynamic features, such as transvalvular gradients. Lower transvalvular aortic velocities and gradients after EA, compared to SCA, were associated with significantly larger AVA as measured using CMR. In our opinion, increased transaortic gradients and smaller AVA found in the SCA group may contribute to the future progression of aortic valve degeneration²⁷. Using CMR with four-dimensional flow visualization, it has already been demonstrated that altered transvalvular flow patterns could normalize directly after BAV repair²⁸. We believe that the choice of durable annular stabilization technique is crucial to maintain normal transvalvular flow patterns.

Interestingly, the postoperative transvalvular peak gradient significantly negatively correlated with AVA and aortic root diameter, but not with aortic annulus diameter. Similarly, we found also a significant correlation between the postoperative severity of AR (expressed by a regurgitant fraction and regurgitant volume) with AVA and aortic root diameter, but not with annulus diameter. This suggests that a reduction in anatomical AVA derived from CMR may be a better marker of successful annuloplasty during BAV repair as compared with standard aortic annulus measurements.

Of note, anatomical AVA smaller than 3.5 cm² correlated with no AR recurrency (Fig. 2). Similarly, aortic root diameter below 40 mm was a predictor of durable repair with no postoperative regurgitation. This supports the policy to routinely replace the aortic root during aortic valve repair when its diameter is above 40 mm.

Our study also showed significant reverse remodeling after BAV repair. Normalization of LV ejection fraction and LV end-diastolic volume was achieved in the majority of the patient. However, no significant differences were observed between two annular stabilization strategies. LV reverse remodeling is associated mainly with successful BAV repair considered as a lack of significant postoperative AR. The selection of optimal time-point of operation is also crucial. In patients with moderate or severe aortic insufficiency, the CMR derived aortic regurgitant fraction > 33% and left ventricular end-diastolic volume > 246 ml were combined strongly associated with the development of symptoms or indications for surgery (with 85% sensitivity and 92% specificity)²⁹.

Currently, echocardiography remains the most established imaging modality for assessment and follow-up of patients with valve diseases. However, over the last few years, the role of CMR in patients with valve diseases has been gradually increasing⁸. CMR is considered the current gold-standard method for the precise quantification of left and right ventricular volumes and systolic function. In comparison with echocardiography, a particular strength of CMR is the ability to assess the aortic regurgitant volume and regurgitant fraction in a fully quantitative manner. This allows for adequate monitoring of disease progression over time.

We recognize that our study had limitations. Firstly, we performed a CMR one year after the operation. It has been demonstrated that after BAV repair transvalvular aortic gradients rapidly declined and then increased steadily over a long period of time (> 10 years)²⁷. We cannot be absolutely sure that in the

long-term EA would still demonstrate better haemodynamics compared to SCA. Secondly, the sample size is relatively small. However, due to the excellent quality of images and low inter-observer and inter-study variability, the use of CMR allows a significant reduction in the patient numbers required to prove a research hypothesis. Compared to two-dimensional echocardiography, CMR was shown to reduce the required sample size by several times, even by 81–97%^{30,31}, making the size of our group comparable to similar studies and of adequate statistical power³¹.

Conclusion

In conclusion, the repair of the BAV offers good mid-term results provided durable annuloplasty can be achieved. CMR appears to be a very promising tool for assessing aortic valve repair and subsequent reverse remodeling of the left ventricle. EA in circumferential fashion is associated with better haemodynamics compared to SCA. A reduction in anatomical AVA derived from CMR may be a better marker of successful annuloplasty during BAV repair as compared with standard aortic annulus measurements (Fig. 3).

We believe that results of repair of the BAV may be further improved with more aggressive root stabilization, especially at the level of the ventriculo-aortic junction.

Abbreviations

AR aortic regurgitation

AVA aortic valve area

BAV bicuspid aortic valve

CMR cardiac magnetic resonance

EA external annuloplasty

LV left ventricle

SCA subcommissural annuloplasty

STJ sino-tubular junction

TTE transthoracic echocardiography

Declarations

Ethics approval and consent to participate:

This study was approved by the Ethics Committee of Medical University of Silesia – reference number NN-2-345/08 and KNW-1-146/P/1/0. Informed written consent was obtained from each subject.

Consent for publication:

Not applicable.

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

MJ has made substantial contributions to the conception and design of the work, the acquisition and interpretation of the data, and has drafted the article, KMJ has made contributions to the conception and design of the work, the acquisition and interpretation of the data, and has drafted the article, RG has acquired and analysed data, IWJ has acquired and analysed data, GB has interpreted the data and drafted the work, MB has interpreted the data and drafted the work, KK has interpreted the data, drafted the work and revised it, ML has drafted the work and substantively revised it, AK has made contributions to the conception and design of the work and acquired the data, MD has made contributions to the conception and design of the work and acquired the data. All authors read and approved the final manuscript.

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Figures

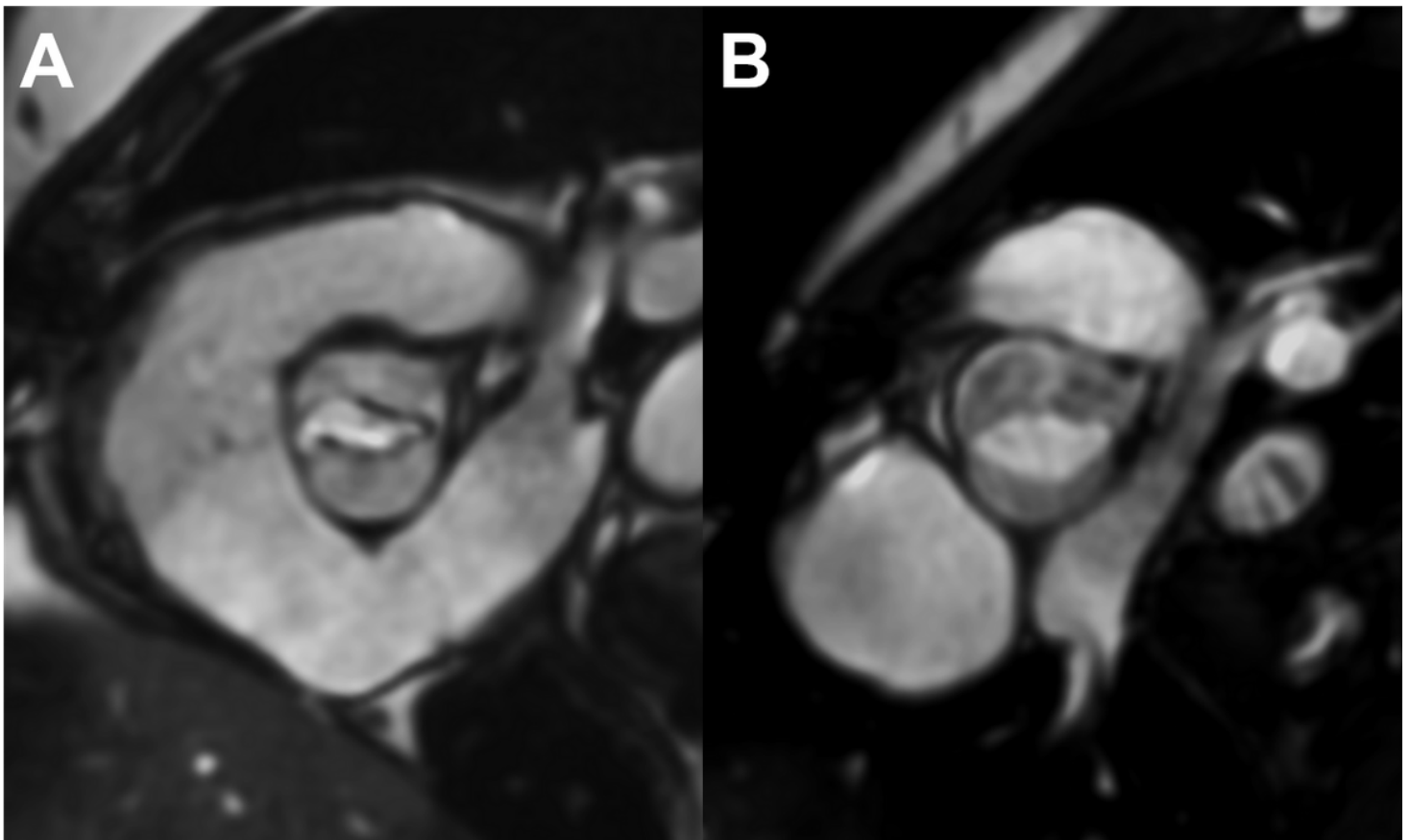


Figure 1

Cardiac magnetic resonance imaging of bicuspid aortic valve at end-systole in two patients treated with subcommissural annuloplasty (A) and external annuloplasty (B). After external annuloplasty (B) larger

aortic valve area was associated with lower transvalvular gradients as compared with subcommissural annuloplasty (A).

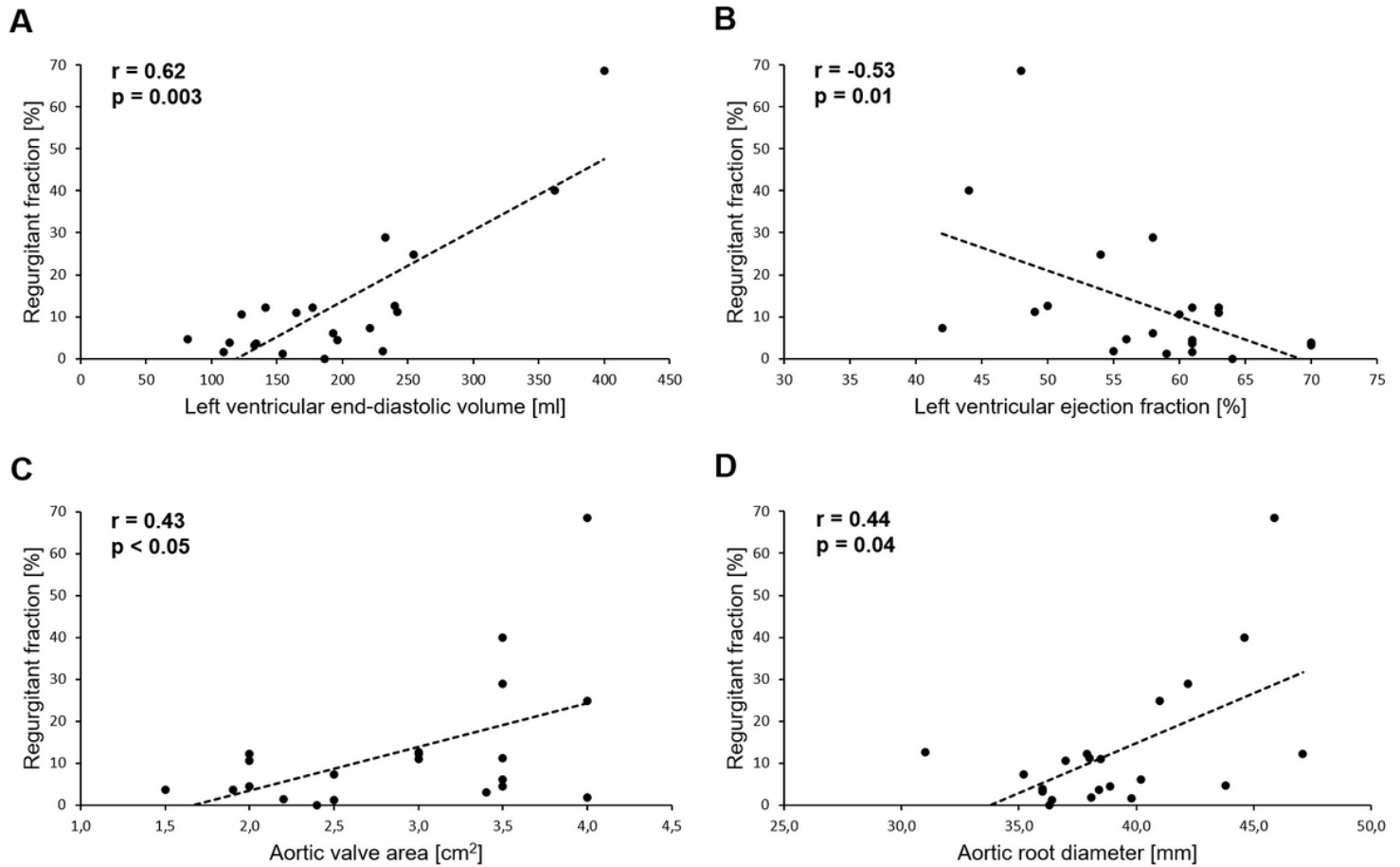


Figure 2

Correlations between severity of residual aortic insufficiency quantified by a regurgitant fraction and several parameters measured postoperatively using cardiac magnetic resonance: A - left ventricular end-diastolic volume, B - left ventricular ejection fraction, C - anatomical aortic valve area, D - aortic root diameter. Degree of each correlation is expressed with Spearman's rank correlation coefficient (r) (N=21).