Cardiovascular Magnetic Resonance as a complementary method to Transthoracic Echocardiography for Aortic Valve Area Estimation in patients with Aortic Stenosis: A systematic review and meta-analysis

Theodoros I. Repanas, MSc, Christos A. Papanastasiou, MSc, Georgios K. Efthimiadis, PhD, Nikolaos Fragkakis, PhD, Vassilios Sachpekidis, PhD, Rolf Michael Klein, MD, Haralambos Karvounis, PhD, Theodoros D. Karamitsos, MD, PhD

PII: S1109-9666(20)30098-1

DOI: https://doi.org/10.1016/j.hjc.2020.05.008

Reference: HJC 516

To appear in: *Hellenic Journal of Cardiology*

Received Date: 22 March 2020

Revised Date: 20 May 2020

Accepted Date: 26 May 2020

Please cite this article as: Repanas TI, Papanastasiou CA, Efthimiadis GK, Fragkakis N, Sachpekidis V, Klein RM, Karvounis H, Karamitsos TD, Cardiovascular Magnetic Resonance as a complementary method to Transthoracic Echocardiography for Aortic Valve Area Estimation in patients with Aortic Stenosis: A systematic review and meta-analysis, *Hellenic Journal of Cardiology*, https://doi.org/10.1016/j.hjc.2020.05.008.

Cardiovascular Magnetic Resonance as a complementary method to Transthoracic Echocardiography for Aortic Valve Area Estimation in patients with Aortic Stenosis: A systematic review and meta-analysis

Theodoros I. Repanas, MSc[a]; Christos A. Papanastasiou MSc[b]; Georgios K. Efthimiadis, PhD[b]; Nikolaos Fragkakis, PhD[c]; Vassilios Sachpekidis, PhD[d]; Rolf Michael Klein, MD[a]; Haralambos Karvounis, PhD[b]; Theodoros D. Karamitsos, MD, PhD[b]

[a]*Department of Cardiology, Augusta Hospital Düsseldorf, Academic Teaching Hospital of the University Faculty of Health, Düsseldorf, Germany*

[b]*1st Department of Cardiology, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece*

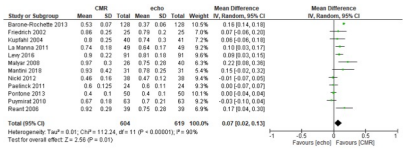
[c]*3rd Department of Cardiology, Hippokration University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece*

[d]*Department of Cardiology, Papageorgiou Hospital, Thessaloniki, Greece*

Address for correspondence and reprints:

Theodoros Karamitsos, PhD

1st Department of Cardiology, AHEPA Hospital, Aristotle University of Thessaloniki,
1 Stilponos Kyriakides Str. Thessaloniki 54636, Greece
Tel: (+30) 2310994832, Fax: (+30) 2310994673
Email: karamits@gmail.com



Abstract

Background: Aortic stenosis (AS) is the most common valvular heart disease. While two-dimensional transthoracic echocardiography (2D-TTE) is the standard imaging modality for AS assessment, cardiac magnetic resonance (CMR) offers a reliable and reproducible alternative. The aim of this study was to compare AVA measurements as determined by TTE and CMR in patients with AS.

Methods: Electronic databases were searched in order to identify studies comparing TTE continuity equation to CMR planimetry for AVA assessment. A meta-analysis of mean difference was conducted using the random effects model. Sensitivity analysis was performed, after excluding studies reporting AVA indexed to body surface area (BSA). Heterogeneity was assessed with I^2.

Results: A total of 12 studies, encompassing 621 patients, were included in our systematic review. In the pooled analysis, measurements of AVA by CMR planimetry were found to be significantly higher than those calculated by the continuity equation in TTE (pooled mean difference: 0.09, 95% CI: 0.01, 0.17, I^2: 93%). The results remained significant, albeit with moderate heterogeneity this time, after excluding from the analysis measurements of AVA indexed to BSA (pooled mean difference: 0.08, 95% CI: 0.03 to 0.13, I^2=61%).

Conclusions: CMR-planimetry slightly overestimates AVA compared to TTE-continuity equation. Although, 2D-TTE should be the primary imaging modality for the estimation of AVA, CMR may be useful when there is discrepancy with the clinical assessment, or when TTE results are discordant or difficult to obtain.

Keywords: aortic stenosis; aortic valve area; cardiovascular magnetic resonance; transthoracic echocardiography

1. Introduction

Aortic stenosis (AS) is the most common valvular heart disease, affecting predominantly the elderly in terms of degenerative calcification of the valve [1]. The estimated prevalence of AS is 4-5% in adults aged over 65, while more than one in eight people above the age of 75 suffer from moderate or severe AS [2,3]. Moreover, 50% of symptomatic patients with severe AS will die within one year of symptom onset without aortic valve replacement, highlighting the eminent need for early diagnosis and accurate grading of the disease [4]. Current guidelines for the treatment of AS recommend valve replacement in all patients with severe AS, when symptoms and/or ventricular decompensation are present [5,6].

Two-dimensional transthoracic echocardiography (2D-TTE) is the most commonly used imaging modality for the quantification and classification of AS severity in everyday clinical practice[7]. However, TTE has limitations (i.e. poor acoustic window, operator-dependency) that render accurate quantification of AS problematic in some cases, especially when discordant results among different stenotic indices are observed. On the other hand, cardiovascular magnetic resonance (CMR) offers a reliable and reproducible alternative for the assessment of aortic valve area (AVA), providing also structural and functional information for the left ventricle [8,9] .

In this study, we aimed to compare AVA measurements as determined by 2D-TTE and CMR in patients with AS.

2. Methods

2.1 Information sources - Search Strategy

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [10]. The electronic databases Medline (Pubmed), Embase and Cochrane Library were searched for eligible studies by two independent reviewers (TR, CP). The search algorithm included the

following keywords and MeSH terms: [(MRI OR CMR OR "cardiac magnetic resonance" OR "cardiovascular magnetic resonance" OR "magnetic resonance imaging") AND "aortic stenosis"]. The reference lists of the included studies were also searched for relevant studies.

2.2 *Eligibility criteria*

A study was deemed to be eligible for this systematic review, if the following inclusion criteria were fulfilled: (i) studies comparing AVA (or AVA indexed to body surface area – BSA) measurements between 2D-TTE and CMR in patients with AS; (ii) AVA was calculated by the continuity equation in TTE and by direct planimetry in CMR with steady state free precession (SSFP) technique; (iii) published in any language up to May, 2019.

2.3 Study selection and data collection

Two independent reviewers (TR, CP) assessed the eligibility of the potentially included studies, according to the inclusion criteria. A study was considered to be eligible, if both reviewers agreed. Pre-specified forms were used to extract the clinical and epidemiological data of the included studies. When studies with duplicated populations were identified, only the larger one was included in the analysis.

2.4 Data synthesis

In this meta-analysis pooled mean difference of AVA measurements with corresponding 95% confidence intervals (CI) were calculated. The random effects model (Mantel-Haenszel method) was used to account for between study heterogeneity. Sensitivity analysis including only AVA measurements (without AVA indexed to BSA) was also performed. Heterogeneity among studies was assessed with I^2 statistic. Values lower than 25% indicated low heterogeneity, while values greater than 75% indicated severe heterogeneity [11]. Funnel plot was used to graphically illustrate the risk of publication bias. All statistic calculations were performed using Revman version 5.3 (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014).

2.5 Risk of bias in individual studies

Quality assessment of the included studies was performed using the quality appraisal tool for studies of diagnostic reliability (QAREL) [12]. Two independent reviewers (TR, CP) answered for each study a QAREL form consisting of eleven items. Each item was answered as "Yes", "No" or "Unclear". A study was considered to be low risk of bias overall, if all key domains were answered as "Yes", otherwise it was judged as moderate or high risk of bias.

3. Results

3.1 Study selection and study characteristics

A total of 2734 studies were identified through searching electronic databases and 41 were assessed for eligibility. Finally 12 studies, encompassing 621 patients, met the inclusion criteria and were included in the meta-analysis [13,14,23,24,15–22]. The detailed flow diagram can be seen at **Figure 1**.

All eligible studies were published after 2002 and conducted in Europe. Six studies had a prospective design [15,16,18,19,22,23], while the rest were retrospective [13,14,17,20,21,24]. CMR examinations were conducted on a 1.5T scanner in all studies, except for the study by Levy et al. [23] which was conducted on a 3T scanner. In three studies, only AVA measurements indexed to BSA were reported [20–22]. The number of enrolled patients ranged from 25 to 128 among the included studies. The mean age of the total population was 73.6 years and 58% were males. Apart from the study by La Manna et al. [18], where data on cardiac function were not reported, in all other eligible studies mean left ventricular ejection fraction was higher than 50%, ranging from 52% to 65%. The number of patients with concomitant aortic regurgitation was reported in six studies (131 out of 244 patients; 53.7%) [13–17,24], while five studies reported data on the presence of bicuspid aortic valve (63 out of 249 patients; 25.3%) [13,15,17,23,24]. Details on baseline characteristics of the included studies are presented in **Table**

1. Visual inspection of the funnel plot did not show publication bias (**Supplementary Figure 1**). Finally, risk of bias was found to be low in most studies (**Supplementary Figure 2**).

3.2 Statistical synthesis of individual results

In the pooled analysis, measurements of AVA by CMR planimetry were found to be significantly higher than those calculated by the continuity equation in TTE (pooled mean difference: 0.07, 95% CI: 0.02, 0.13) (**Figure 2**), with high between-study heterogeneity (I^2=90%). The results remained significant, albeit with moderate heterogeneity, after excluding from the analysis measurements of AVA indexed to BSA (pooled mean difference: 0.08, 95% CI: 0.03 to 0.13, I^2=61%) (**Supplementary Figure 3**).

4. Discussion

This was a systematic review and meta-analysis of studies comparing AVA measurements between 2D-TTE and CMR in patients with AS. The main finding of our study is that CMR planimetry overestimates AVA measurements, compared to those obtained by TTE using the continuity equation method. This finding has important implications for the determination of optimal CMR-based cut-offs for aortic valve replacement.[25]

Our findings are in agreement with previous studies comparing planimetry-based to continuity equation-derived AVAs. Pouleur et al., who studied a mixed population of patients (with or without AS), showed that direct planimetry, performed by CMR or transesophageal echocardiography (TEE), was associated with higher AVA measurements than those derived by TTE-continuity equation (mean AVAs: 2.1±1.7 cm^2 vs. 1.8±1.4 cm^2, p<0.001 for CMR vs. TTE and 2.1±1.6 cm^2 vs. 1.8±1.4 cm^2, p<0.001 for TEE vs. TTE) [26]. This overestimation can be explained by the fact that the echocardiographic calculation of AVA is based on geometrical assumptions. The turning point, which usually accounts for most errors in the calculation of AVA using the continuity equation, is the measurement of left ventricular outflow tract (LVOT) diameter, which is based on the assumption that LVOT has a circular

shape. Importantly, this parameter must be squared to determine LVOT area, thus amplifying any divergence between the calculated effective orifice area and the anatomical orifice area [27,28]. Moreover, poor alignment of the ultrasound beam with aortic flow may further complicate the assessment of AVA leading to imprecise estimations, especially in patients with inadequate acoustic windows. [5].

On the other hand, CMR overcomes the aforementioned limitations, providing reliable and objective measurements of AVA with direct planimetry. The ability of CMR-planimetry to accurately estimate AVA has been validated against TEE and cardiac catheterization. Specifically, Friedrich et al. showed that CMR-planimetry correlated well with hemodynamic measurements of AVA (r: 0.78) [13]. Along those lines, Kupfahl et al. investigated the ability of non-invasive imaging modalities to detect severe AS, as determined by cardiac catheterization. CMR-planimetry had the best performance (sensitivity: 78%, specificity: 89%), compared to TTE-continuity equation (sensitivity: 74%, specificity: 67%) and TEE-planimetry (sensitivity, specificity: 70%) [14].

Apart from its reliability, CMR confers prognostic information in patients with AS. A recent meta-analysis showed that the presence of late gadolinium enhancement (LGE) by CMR was a powerful predictor of all-cause mortality in patients with AS and preserved ejection fraction (pooled OR: 2.56, 95% CI: 1.83 to 3.57) [29]. Similar results have been also reported for novel tissue characterization CMR techniques. Interestingly, Lee et al. found that T1 mapping was significantly associated with adverse outcomes in AS (adjusted HR: 1.28, 95% CI: 1.10 to 1.46, per 20-ms increment) [30]. Although CMR is a valuable imaging tool in the field of valvular heart diseases, further research is needed to establish its role in daily clinical practice.

Our study has some limitations. First, this was a meta-analysis of real world studies and thus should be interpreted within the context of observational research and its inherent

limitations. Second, several of the eligible studies had a retrospective design and included a relatively small number of patients in their analyses with a considerable heterogeneity among the included studies. Third, a substantial proportion of patients in our meta-analysis had concomitant aortic regurgitation. Thus, echocardiographic but not CMR measurements, may have been affected, leading to inaccurate AVA calculations. Fourth, this meta-analysis included studies in AS patients with preserved ejection fraction. Data on AVA calculation by CMR in AS patients with impaired LV function are scarce. Current evidence suggests that CMR planimetry of the aortic valve is adequate in these patients and the need for normalization of flow with pharmacological stress may not always be clinically necessary. Finally, we were not able to make comparisons between other imaging techniques (i.e. CMR-planimetry vs. TEE-planimetry) due to limited data in the existing literature.

Our meta-analysis demonstrates that CMR-planimetry overestimates AVA, compared to TTE-continuity equation a finding that could have major implications for clinical decision-making. There is no doubt that 2D-TTE should be the primary imaging modality for the estimation of AVA. However, CMR may be useful when there is discrepancy with the clinical assessment, or when TTE results are discordant or difficult to obtain. Future studies should explore whether CMR can guide management in patients with AS and identify the ideal AVA cut-off to predict outcomes.

ACKNOWLEDGEMENTS

The authors declare no conflict of interest. This review did not receive any specific grant from any funding agency.

CONTRIBUTIONS

Theodoros I. Repanas: Conceptualization, Design, Electronic search, Data extraction, Formal analysis, Writing - original draft:

Christos A. Papanastasiou: Conceptualization, Design, Electronic search, Data extraction, Formal analysis, Writing - original draft:

Georgios K. Efthimiadis: Writing - Review & Editing

Nikolaos Fragkakis: Writing - Review & Editing

Vassilios Sachpekidis: Conceptualization, Writing - Review & Editing

Rolf Michael Klein: Writing - Review & Editing

Haralambos Karvounis: Writing - Review & Editing, Supervision

Theodoros D. Karamitsos: Conceptualization, Design, Writing - original draft, Writing - Review & Editing, Project administration and Supervision

REFERENCE LIST

1. Iung B, Baron G, Butchart EG, *et al.* A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease. *Eur Heart J* 2003;24:1231–1243.

2. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. *N Engl J Med* 1999;341:142–147.

3. Nkomo VT, Gardin JM, Skelton TN, *et al.* Burden of valvular heart diseases: a population-based study. *Lancet* 2006;368:1005–1011.

4. Leon MB, Smith CR, Mack M, *et al.* Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. *N Engl J Med* 2010;363:1597–1607.

5. Baumgartner H, Falk V, Bax JJ, *et al.* 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739–2791.

6. Kanakakis I. Is TAVR going to be our default choice for treating aortic valve stenosis? *Hell J Cardiol* 2019;60:146–147.

7. Corrigan FE, Zhou X, Lisko JC, *et al.* Mean Aortic pressure gradient and global longitudinal strain recovery after transcatheter aortic valve replacement – A retrospective analysis. *Hell J Cardiol* 2018;59:268–271.

8. Defrance C, Bollache E, Kachenoura N, *et al.* Evaluation of aortic valve stenosis using cardiovascular magnetic resonance comparison of an original semiautomated analysis of phase-contrast cardiovascular magnetic resonance with doppler echocardiography. *Circ Cardiovasc Imaging* 2012;5:604–612.

9. Papanastasiou CA, Kokkinidis DG, Jonnalagadda AK, *et al.* Meta-Analysis of Transthoracic Echocardiography Versus Cardiac Magnetic Resonance for the Assessment of Aortic Regurgitation After Transcatheter Aortic Valve Implantation. *Am J Cardiol*

2019;124:1246–1251.

10. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 2009;6:e1000097.

11. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J* 2003;327:557–560.

12. Lucas NP, Macaskill P, Irwig L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). *J Clin Epidemiol* 2010;63:854–861.

13. Friedrich MG, Schulz-Menger J, Poetsch T, *et al.* Quantification of valvular aortic stenosis by magnetic resonance imaging. *Am Heart J* 2002;144:329–334.

14. Kupfahl C, Honold M, Meinhardt G, *et al.* Evaluation of aortic stenosis by cardiovascular magnetic resonance imaging: comparison with established routine clinical techniques. *Heart* 2004;90:893–901.

15. Reant P, Lederlin M, Lafitte S, *et al.* Absolute assessment of aortic valve stenosis by planimetry using cardiovascular magnetic resonance imaging: comparison with transesophageal echocardiography, transthoracic echocardiography, and cardiac catheterisation. *Eur J Radiol* 2006;59:276–283.

16. Malyar NM, Schlosser T, Barkhausen J, *et al.* Assessment of aortic valve area in aortic stenosis using cardiac magnetic resonance tomography: comparison with echocardiography. *Cardiology* 2008;109:126–134.

17. Puymirat E, Chassaing S, Trinquart L, *et al.* Hakki's formula for measurement of aortic valve area by magnetic resonance imaging. *Am J Cardiol* 2010;106:249–254.

18. Manna A La, Sanfilippo A, Capodanno D, *et al.* Cardiovascular magnetic resonance for the assessment of patients undergoing transcatheter aortic valve implantation: a pilot study. *J Cardiovasc Magn Reson* 2011;13:82.

19. Paelinck BP, Herck PL Van, Rodrigus I, *et al.* Comparison of magnetic resonance imaging of aortic valve stenosis and aortic root to multimodality imaging for selection of transcatheter aortic valve implantation candidates. *Am J Cardiol* 2011;108:92–98.

20. Nickl W, Futh R, Smettan J, *et al.* Assessment of aortic valve area combining echocardiography and magnetic resonance imaging. *Arq Bras Cardiol* 2012;98:234–242.

21. Pontone G, Andreini D, Bartorelli AL, *et al.* Comparison of Accuracy of Aortic Root Annulus Assessment With Cardiac Magnetic Resonance Versus Echocardiography and Multidetector Computed Tomography in Patients Referred for Transcatheter Aortic Valve Implantation. *Am J Cardiol* 2013;112:1790–1799.

22. Barone-Rochette G, Pierard S, Seldrum S, *et al.* Aortic valve area, stroke volume, left ventricular hypertrophy, remodeling, and fibrosis in aortic stenosis assessed by cardiac magnetic resonance imaging: comparison between high and low gradient and normal and low flow aortic stenosis. *Circ Cardiovasc Imaging* 2013;6:1009–1017.

23. Levy F, Iacuzio L, Civaia F, *et al.* Usefulness of 3-Tesla cardiac magnetic resonance imaging in the assessment of aortic stenosis severity in routine clinical practice. *Arch Cardiovasc Dis* 2016;109:618–625.

24. Mantini C, Giammarco G Di, Pizzicannella J, *et al.* Grading of aortic stenosis severity: a head-to-head comparison between cardiac magnetic resonance imaging and echocardiography. *Radiol Med* 2018;123:643–654.

25. Tousoulis D. The evolution in the management of aortic valve disease: From surgical techniques to transcatheter interventions. *Hell J Cardiol* 2016;57:379–381.

26. Pouleur AC, Waroux JBLP De, Pasquet A, *et al.* Planimetric and continuity equation assessment of aortic valve area: Head to head comparison between cardiac magnetic resonance and echocardiography. *J Magn Reson Imaging* 2007;26:1436–1443.

27. Garcia D, Kadem L. What do you mean by aortic valve area: geometric orifice area,

effective orifice area, or gorlin area? *J Heart Valve Dis* 2006;15:601–8.

28. Kouris NT, Tsiapras DP, Olympios CD. Echocardiographic evaluation of aortic valve stenosis: problems and pitfalls. *Hellenic J Cardiol* 2012;53:255–62.

29. Papanastasiou CA, Kokkinidis DG, Kampaktsis PN, *et al.* The Prognostic Role of Late Gadolinium Enhancement in Aortic Stenosis. *JACC Cardiovasc Imaging* 2020;3:385-392.

30. Lee H, Park JB, Yoon YE, *et al.* Noncontrast Myocardial T1 Mapping by Cardiac Magnetic Resonance Predicts Outcome in Patients With Aortic Stenosis. *JACC Cardiovasc Imaging* 2018;11:974–983.

TABLE

Table 1: Demographics and Baseline Characteristics of Included Studies

Author	Country	Study Design	Number of patients	AS severity	Age, years (mean ± SD)	Female (%)	LVEF, % (Mean ± SD)	AR (%)	BAV (%)	CAD (%)	Time interval between Echo and CMR performance
Friedrich et al., 2002	Germany	Retrospective	25	≥ Moderate	64±8	NA	55 ± 12	40	20	64	Within 4 weeks
Kupfahl et al., 2004	Germany	Retrospective	44	Severe	71±9	38.6	63 ± 16	52	NA	NA	10 ± 8 days
Reant et al., 2006	France	Prospective	39	≥ Mild	71.7±7.6	36	NA	66.7	12.8		NA
Malyar et al., 2008	Germany	Prospective	42	≥ Mild	71±8	36	52 ± 13	52	NA	43	1 day
Puymirat et al., 2010	France	Retrospective	63	Severe	72± 10	45	54.4 ± 10.2	56	16	NA	NA
La Manna et al., 2011	Italy	Prospective	49	Severe	80.8± 4.8	57.1	NA	NA	NA	22.4	Within 3-5 days
Paelinck et al. , 2011	UK	Prospective	24	Severe	83.5 (67-88)[a]	66	67.3 (28-83)[a]	NA	NA	NA	NA
Nickl et al., 2012	Germany	Retrospective	38	≥ Moderate	73±9	42	64 ± 12	NA	NA	66	NA
Pontone et al., 2013	Italy	Retrospective	50	Severe	79.6±7.5	46	55.3 ± 13.9	NA	NA	NA	NA
Barone - Rochette et al., 2013	Belgium	Prospective	128	Severe	73±11	41	65 ± 9	NA	NA	NA	Same day
Levy et al., 2016	France	Prospective	91	≥ Moderate	74±10	64	62 ± 10	NA	42	34	Within 24 hours
Mantini et al., 2018	Italy,UK	Retrospective	31	≥ Moderate	69±10	32	63.5 ± 18.6	48.3	16.1	NA	Within 7 days

[a] Mean (range)

AS: Aortic Stenosis; AR: Aortic Regurgitation; BAV: Bicuspid Aortic Valve; CAD: Coronary Artery Disease; CMR: Cardiac Magnetic Resonance; LVEF: Left Ventricular Ejection Fraction; NA: Not Available/Applicable; SD: Standard Deviation; UK: United Kingdom;

FIGURE CAPTIONS

Figure 1: **PRISMA diagram flow chart**.

The selection process is reported according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines

Figure 2: Forrest plot for the association of aortic valve area (AVA) measurements between transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) in patients with aortic stenosis (AS).

Overall CMR planimetry measurements were found to be significantly higher than those calculated by the continuity equation in TTE (pooled mean difference: 0.07, 95% CI: 0.02, 0.13). Between-study heterogeneity was found to be high (I^2=90%).

Supplementary Figure 1: **Funnel plot of studies participating in meta-analysis**.

The funnel plot shows a symmetrical distribution of the participating studies.

Supplementary Figure 2: Risk of bias according to quality appraisal tool for studies of diagnostic reliability (QAREL).

The risk of bias was found to be low in most of the studies participating in meta-analysis.

Supplementary Figure 3: Forrest plot excluding studies with body surface area (BSA) associated aortic valve area (AVA) measurements.

After excluding from the analysis measurements of AVA indexed to BSA it was shown that cardiac magnetic resonance overestimates AVA compared with transthoracic echocardiography in patients with aortic stenosis (pooled mean difference: 0.08, 95% CI: 0.03 to 0.13). Heterogeneity in this subgroup analysis was found to be moderate (I^2=61%).