Meta-Analysis of Transthoracic Echocardiography Versus Cardiac Magnetic Resonance for the Assessment of Aortic Regurgitation After Transcatheter Aortic Valve Implantation

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Residual aortic regurgitation (AR) is a major complication after transcatheter aortic valve implantation (TAVI). Although the echocardiographic assessment of post-TAVI AR remains challenging, cardiac magnetic resonance (CMR) allows direct quantification of AR. The aim of this study was to review the level of agreement between 2-dimensional transthoracic echocardiography (2D TTE) and CMR on grading the severity of AR after TAVI, and determine the accuracy of TTE in detecting moderate or severe AR. Electronic databases were searched in order to identify studies comparing 2D TTE to CMR for post-TAVI AR assessment. Kappa coefficient was used to determine the level of agreement between the 2 imaging modalities. CMR was used as the reference standard in order to assess the diagnostic accuracy of 2D TTE. Seven studies were included in this systematic review. Six studies reported a low correlation between 2D TTE and CMR (kappa coefficient ranging from −0.02 to 0.41), whereas one study showed good agreement with a kappa coefficient of 0.72. Given the heterogeneity in the included studies the diagnostic accuracy of TTE was evaluated by estimating the hierarchical summary receiver operator characteristic curve. The area under the curve for detection of moderate or severe AR with TTE was 0.83 (95% confidence interval 0.79 to 0.86). In conclusion, despite the reported significant disconcordance between TTE and CMR grading of AR, TTE has sufficient ability to discriminate moderate or severe AR from mild or none AR after TAVI in the clinical setting. CMR should be considered when TTE results are equivocal. **(Am J Cardiol 2019;124:1246−1251)**

Transcatheter aortic valve implantation (TAVI) has evolved into an indispensable therapeutic option for patients with severe aortic stenosis, who cannot undergo, or who is considered at high risk for surgical aortic valve replacement.[1,2] Despite the marked improvements in prosthetic valve design and procedural techniques, aortic regurgitation (AR)—mainly secondary to paravalvular leak (PVL)—remains a major postprocedural complication. Significant post-TAVI AR (moderate or severe) is independently associated with higher mortality rates.[3,4] Two-dimensional transthoracic echocardiography (2D TTE) is the most commonly used imaging modality for AR assessment following TAVI.[5] Several echocardiographic parameters have been proposed for the quantification of AR severity post-TAVI.[6,7] However most of these indices are primarily used to assess native AR and may be less accurate for the assessment of eccentric PVL jets due to the acoustic shadowing from the valve stent, notwithstanding other limitations of echocardiography (e.g., poor acoustic windows, operator-dependency).[8] By contrast to echocardiography, cardiac magnetic resonance (CMR) confers more accurate and reproducible quantitative measurements of AR severity using phase-contrast velocity mapping.[9−12] With this study, we aim to (1) review the degree of concordance between CMR and TTE for post-TAVI AR assessment, and (2) determine the ability of 2D TTE to detect identify moderate or severe AR.

Methods

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses.[13] A study was considered to be eligible for this review, if the following inclusion criteria were fulfilled: (1) primary research comparing 2D TTE to CMR for post-TAVI AR assessment, irrespective of the imaging parameters assessed;

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(2) studies reporting kappa coefficient or data that could be used for its calculation to determine the agreement between TTE and CMR on grading of AR severity, (3) studies published in any language until April 6, 2018. The electronic databases Medline (PubMed) EMBASE and Cochrane CENTRAL Library were searched for relevant studies. We searched electronic databases using a search algorithm, composed of the following medical subject headings: (1) CMR OR "cardiac magnetic resonance" and (2) TAVI OR "transcatheter aortic valve implantation" OR TAVR OR "transcatheter aortic valve replacement". The results of these 2 independent searching themes were combined using the Boolean operator "AND."

Two independent reviewers (CAP, AKJ) assessed the eligibility of the potentially included studies according to the prespecified inclusion and exclusion criteria. An article was deemed to be eligible, if both reviewers agreed. A third reviewer (EO) was involved when needed in order consensus to be reached. Data extraction was performed independently by 2 reviewers (CAP, DGK) based on prespecified forms with epidemiological and clinical information.

Baseline characteristics of the patient population were presented as mean values ± standard deviation (SD) for continuous variables or absolute and relative frequencies for categorical variables. The level of agreement between CMR and TTE was reported using the Cohen's kappa statistic with corresponding 95% confidence interval (CI).[14] When kappa coefficient and 95% CI were not directly available, they were calculated using appropriate formulas.[15] The level of agreement was considered to be: poor if $k < 0.20$, fair if $k = 0.21$ to 0.40, moderate if $k = 0.41$ to 0.60, good if $k = 0.61$ to 0.80, almost perfect if $k = 0.81$ to 1.0. Given that kappa coefficient is affected by the distribution of the outcome of interest, prevalence index was calculated. When conflict between kappa and percent agreement was detected because of prevalence or bias effect, prevalence-adjusted-bias-adjusted-kappa was calculated.[16]

Greater than mild residual AR has been proven to be the turning point toward increased mortality.[4,17] Therefore, we assessed the diagnostic accuracy of 2D TTE in detecting moderate/severe AR after TAVI. For this purpose, CMR was used as the reference standard. Given the significant heterogeneity in the parameters assessed for AR classification across the included studies, the overall diagnostic performance of TTE was evaluated by estimating the hierarchical summary receiver operator characteristic curve, without interpreting summary sensitivity and specificity, which are clinically meaningless in this case.[18] Publication bias was not assessed given the low number of the included studies (<10).[19] All analyses were performed with Stata 13.0 (StataCorp, College Station, Texas).

Results

A total of 424 studies were screened and 9 full-text articles were assessed for eligibility. Seven studies met the inclusion criteria and were finally included in our systematic review.[11,20–25] A detailed flow diagram is shown in Figure 1. As expected, patients had a high surgical risk profile and suffered from moderate-to-severe symptoms of heart failure. Details on baseline characteristics of the included studies are shown in Table 1. AR assessment was performed at various time intervals ranging from 5 to 180 days postoperatively. Different imaging parameters, recommended by either American Society Echocardiography or VARC-2, were adopted by each study for the assessment of AR severity with TTE. Finally, different cut-off values of regurgitant fraction, measured by CMR, were used as reference standards for grading the severity of post-TAVI AR (Table 2).

The Cohen's kappa coefficient ranged from −0.02 to 0.72. Poor and fair agreement were indicated by 3 [22,24,25] and 2 studies,[11,20] respectively, whereas moderate and good agreement were each indicated by one study.[21,23] Data on the diagnostic performance of TTE for the detection of moderate-to-severe post-TAVI AR are presented in Table 3.

Three of the included studies in the systematic review were excluded from statistical analysis.[21–23] Two of them did not provide data for the sensitivity and specificity of TTE[21,22] whereas the other one used TTE as the reference standard for AR classification.[23] Using the remaining 4 studies in our hierarchical summary receiver operating characteristic analysis, the area under the curve (AUC) for detecting moderate or severe with TTE was 0.83 (95% CI 0.79 to 0.86; Figure 2).

Discussion

This is the first systematic review and meta-analysis of studies reporting on the level of agreement between CMR and 2D TTE for grading AR severity after TAVI. The major findings of our study are the following: (1) 2D TTE generally correlates poorly with CMR for AR assessment post-TAVI, with wide variation in the level of agreement (kappa coefficient ranging from −0.02 to 0.72); (2) despite the significant disconcordance between the 2 imaging modalities over all grades of AR, 2D TTE has a good ability to discriminate moderate or severe from mild or no AR (AUC 0.83).

The poor and variable correlation between the 2 imaging modalities is most likely due to the limited quantitative accuracy of echocardiography compared with the direct quantification of AR offered by CMR. Despite the numerous studies that have explored the importance of residual AR after TAVI, a unanimous grading system of validated echocardiographic parameters remains challenging. In an attempt to achieve uniformity in the assessment of postprocedural AR, VARC-2 proposed a multiparametric and multiwindow approach, which classified AR severity into 3 categories (mild, moderate, and severe) according to semiquantitative and qualitative indices.[6] Recently, Pibarot et al proposed a multimodality approach based mainly on echocardiography and secondarily on complementary imaging methods (cineangiography, invasive hemodynamic assessment, and CMR), with a recommendation for a 5-class scheme (mild, mild to moderate, moderate, moderate to severe, and severe).[26] Although this approach may improve the accuracy of AR grading providing a better classification of debatable jets, it has inherent limitations. First, the recommended echocardiographic parameters in both approaches are based on experts' consensus without being validated in well-conducted, real-world registries. Moreover, a recent study, which analyzed more than 1,000 echocardiographic

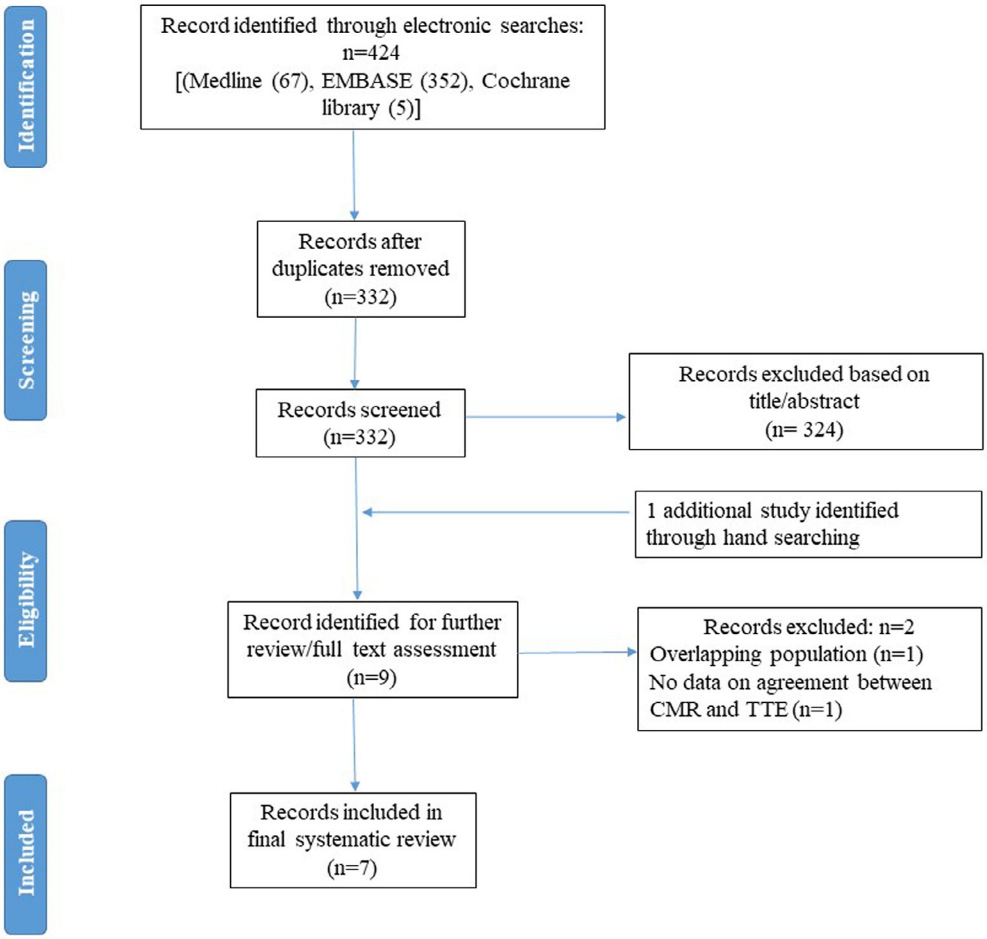

Figure 1. PRISMA flow chart. The selection process is reported according to preferred reporting items for systematic reviews and meta-analyses guidelines.

data from 5 TAVI registries, demonstrated that the combination of the VARC-2 parameters was feasible in only half of the cases.[27]

In contrast, CMR appears to be an attractive alternative, which fills the gaps of echocardiography. Phase-contrast velocity mapping allows precise and objective measurements of AR severity by measuring forward and backward blood volume through the aortic valve, enabling the calculation of regurgitant volume, and fraction. Considering the pathophysiological changes and the subsequent concentric hypertrophy that occurs in patients with pre-existing severe aortic stenosis, regurgitant fraction may be more accurate than regurgitant volume for assessing the severity of AR.[12] Compared with TTE, CMR provides much lower interobserver (120.3% ± 62.3% vs 1.7% ± 1.1%) and intraobserver variabilities (75.2% ± 55.9% vs 1.9% ± 1.9%) for quantification of AR fraction after TAVI, suggesting that the highly accurate and reproducible CMR not only improves the quantification of post-TAVI AR, but also exhibits a significant prognostic role in this patient population.[20] Ribeiro et al demonstrated that higher regurgitant fraction, as determined by CMR post-TAVI, was independently associated with increased all-cause mortality and the combined end point of mortality and rehospitalization for heart failure (hazard ratios 1.18, 95% CI 1.08 to 1.30 and 1.19, 95% CI 1.15 to 1.23, for each 5% increase in regurgitant fraction (RF) respectively).[12] Interestingly, a cut-off value of 30% was the best predictor of poor clinical outcomes (AUC 0.678 for 2-year mortality and AUC 0.679 for the combined end point of mortality and rehospitalization for heart failure). The superiority of CMR in predicting adverse events in patients who developed post-TAVI AR was also confirmed by the study of Hartlage et al.[28] Greater than mild AR, as determined by a CMR value higher than 20%, was associated with a higher incidence of the combined end point (all-cause mortality, heart failure hospitalization, recurrent heart failure symptoms necessitating repeat invasive therapy at 1-year follow-up), while the stratification of AR by echocardiography did not show significant predictive value.

Limited data exist on the level of agreement between CMR and other imaging modalities for the quantification of post-TAVR AR severity. Altiok et al reported a modest-to-moderate agreement between 3D TTE and CMR with a kappa coefficient of 0.446.[20] Similarly, Frick et al showed a moderate correlation between angiographic analysis of AR severity and CMR derived regurgitant fraction ($r = 0.42$, $p < 0.01$).[29] Although these results suggest a slightly better agreement compared to 2D TTE, the level of agreement is at best moderate. Further research is needed to

Table 1
Characteristics of included studies and demographics of TAVI population

First author	Country	Patients	Study design	Age, years (Mean)	Male	DM	HTN	NYHA class (Mean)	Edwards SAPIEN XT valve	STS score	Logistic euroscore
Altiok et al[20]	Germany	71	Prospective	81	45%	32%	81%	3	55%	–	21%
Crouch et al[21]	Australia	56	Prospective	84	61%	39%	90%	3	100%	9%	–
Hayek et al[22]	USA	18	Retrospective	85	67%	–	–	–	7%	–	–
Orwat et al[11]	Germany	59	Prospective	82	41%	–	–	3	–	6%	20%
Ribeiro et al[25]	Canada	50	Prospective	79	56%	30%	82%	–	78%	6%	22%
Salaun et al[23]	France	30	Prospective	81	47%	30%	63%	3	–	–	16%
Sherif et al[24]	Germany	16	Prospective	79	50%	–	–	–	–	–	–
Mean (weighted)				82	51%	33%	81%	3	69%	7%	20%

DM = diabetes mellitus; HTN = hypertension; NYHA = New York Heart Association; STS = Society of Thoracic Surgery.

Table 2
Correlation between TTE and CMR grading of AR severity

First author	Time of imaging, days after TAVI	Echocardiographic parameters assessed for grading AR severity	Classification of AR severity based on CMR-RF measurement	Cohen's kappa coefficient (95% CI)	PI
Altiok et al[20]	180	(i) diastolic flow reversal in descending aorta, (ii) circumferential extent of AR, (iii) Rvol,[17] RF, (v) EROA	none/mild: <19%, moderate: 19-29%, severe: ≥30%	0.357 (0.106−0.608)*/0.158 (−0.029 − 0.344)†	0.7‡ 0.73§
Crouch et al[21]	5	(i) visual assessment of the number of jets, (ii) jet(s) width, (iii) circumferential extent for AR,[17] aortic flow reversal	none/trivial: <8%, mild: 9-20%, moderate: 21-39%, severe >40%	0.41 (0.273−0.547)	–
Hayek et al[22]	6	(i) diastolic flow reversal in the descending aorta, (ii) circumferential extent of AR, (iii) Rvol,[17] RF, (v) EROA	mild: <30%, moderate: 30-50%, severe >50%	0.21 (NA)†/0.19 (NA)¶/ −0.02 (NA)**	–
Orwat et al[11]	69	(i) diastolic flow reversal in the descending aorta, (ii) circumferential extent of prosthetic valve AR	none/trace: 10%, mild: 10−20%, moderate: 20−40%, severe: > 40%	0.33 (0.15−0.51)	0.17
Ribeiro et al[25]	7	(i) visual assessment of the number of jets, (ii) jet(s) width, (iii) extent of AR	none/trace: <5%, mild: 5%−19%, moderate: 20%−29%, severe: ≥30%	0.06 (−0.14−0.262)	0.28
Salaun et al[23]	5	(i) number of regurgitant jets, (ii) jet(s) width, (iii) circumferential extent of AR	none/mild: <14%, moderate/severe: >14%	0.72 (0.429−1)	0.46
Sherif et al[24]	28	Width and area of AR jet(s)	mild: <15%, moderate: 16-30%, moderate-severe: 31-50%, severe: >50%	0.12 (−0.257−0.501)	0.31

AR = aortic regurgitation; CI = confidence interval; CMR = cardiac magnetic resonance; EROA = effective regurgitant orifice area; PABAK = Prevalence-Adjusted-Bias-Adjusted-Kappa; PI = prevalence index; RF = regurgitant fraction; Rvol = regurgitant volume; TAVI = transcatheter aortic valve implantation.

* Kappa statistic for agreement in AR grading between CMR-RF and multiparametric analysis of VARC-2.

† Kappa statistic for agreement in AR grading between CMR-RF and TTE-RF.

‡ PABAK: 0.63.

§ PABAK: 0.52.

¶ Kappa statistic for agreement in AR grading between CMR-RF and TTE-Jet width.

** Kappa statistic for agreement in AR grading between CMR-RF and TTE-Circumferential extent.

explore the accuracy of these methods and establish them in the diagnostic algorithm of AR grading.

Our study has some limitations. First, this was a systematic review of real-world studies, and therefore carries the inherent limitations of observational research. Importantly, there was a significant heterogeneity in the design of included studies. More specifically, different echocardiographic parameters and cut-off values of CMR derived regurgitant fraction were used to assess AR severity, whereas the assessment was performed at different time intervals after the TAVI procedure.

Our systematic review demonstrated that TTE measures of AR correlate poorly with CMR post-TAVI across all grades of AR. However, TTE has a good ability to discriminate mild from moderate or severe AR. Therefore, we recommend TTE for the initial evaluation of AR severity in all patients post TAVI, whereas CMR should follow only where there is discrepancy with the clinical assessment, when TTE results are equivocal or difficult to obtain. Further prospective studies are needed to identify the optimal diagnostic approach associated with improved outcomes for patients who develop post-TAVI AR.

Table 3
Diagnostic performance of TTE for the detection of moderate/severe post-TAVI AR

	Altiok et al[20]	Crouch et al[21]	Hayek et al[22]	Orwat et al[11]	Ribeiro et al[25]	Salaun et al[23]	Sherif et al[24]
Sensitivity	46%	–	–	19%	75%	–	33%
Specificity	93%	–	–	95%	98%	–	90%

AR = aortic regurgitation; TAVI = transcatheter aortic valve implantation; TTE = transthoracic echocardiography.

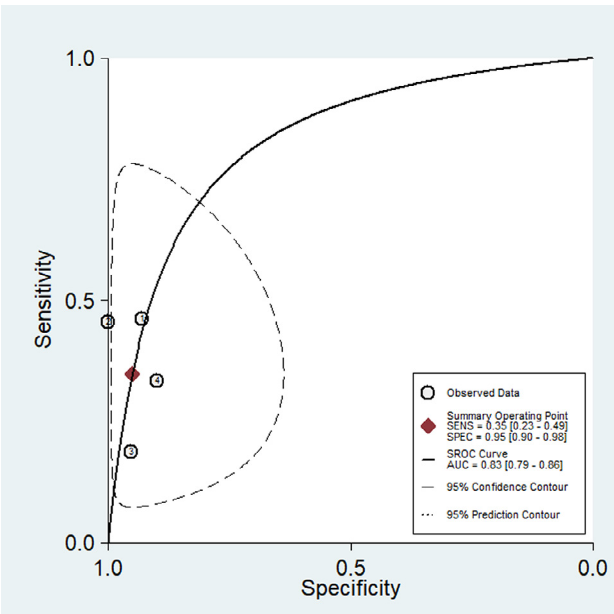

Figure 2. Hierarchical summary receiver operating characteristic (HSROC) curve of 2D TTE in the detection of moderate/severe aortic regurgitation (AR). Each circle represents a study. The curve represents the summary receiver operating characteristic curve for 2D TTE.

Disclosures

The authors have no conflicts of interest to disclose.

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1. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–1607.
2. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–2198.
3. Hayashida K, Lefevre T, Chevalier B, Hovasse T, Romano M, Garot P, Bouvier E, Farge A, Donzeau-Gouge P, Cormier B, Morice MC. Impact of post-procedural aortic regurgitation on mortality after transcatheter aortic valve implantation. *JACC Cardiovasc Interv* 2012;5:1247–1256.
4. Tamburino C, Capodanno D, Ramondo A, Petronio AS, Ettori F, Santoro G, Klugmann S, Bedogni F, Maisano F, Marzocchi A, Poli A, Antoniucci D, Napodano M, De Carlo M, Fiorina C, Ussia GP. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. *Circulation* 2011;123:299–308.
5. Pislaru SV, Nkomo VT, Sandhu GS. Assessment of Prosthetic Valve Function After TAVR. *JACC Cardiovasc Imaging* 2016;9:193–206.
6. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg* 2012;42:S45–S60.
7. Zamorano JL, Badano LP, Bruce C, Chan KL, Goncalves A, Hahn RT, Keane MG, La Canna G, Monaghan MJ, Nihoyannopoulos P, Silvestry FE, Vanoverschelde JL, Gillam LD. EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. *Eur Heart J* 2011;32:2189–2214.
8. Hahn RT, Nicoara A, Kapadia S, Svensson L, Martin R. Echocardiographic imaging for transcatheter aortic valve replacement. *J Am Soc Echocardiogr* 2018;31:405–433.
9. Crouch G, Bennetts J, Sinhal A, Tully PJ, Leong DP, Bradbrook C, Penhall AL, De Pasquale CG, Chakrabarty A, Baker RA, Selvanayagam JB. Early effects of transcatheter aortic valve implantation and aortic valve replacement on myocardial function and aortic valve hemodynamics: insights from cardiovascular magnetic resonance imaging. *J Thorac Cardiovasc Surg* 2015;149:462–470.
10. Myerson SG, d'Arcy J, Mohiaddin R, Greenwood JP, Karamitsos TD, Francis JM, Banning AP, Christiansen JP, Neubauer S. Aortic regurgitation quantification using cardiovascular magnetic resonance: association with clinical outcome. *Circulation* 2012;126:1452–1460.
11. Orwat S, Diller GP, Kaleschke G, Kerckhoff G, Kempny A, Radke RM, Buerke B, Burg M, Schulke C, Baumgartner H. Aortic regurgitation severity after transcatheter aortic valve implantation is underestimated by echocardiography compared with MRI. *Heart* 2014;100:1933–1938.
12. Ribeiro HB, Orwat S, Hayek SS, Larose E, Babaliaros V, Dahou A, Le Ven F, Pasian S, Puri R, Abdul-Jawad Altisent O, Campelo-Parada F, Clavel MA, Pibarot P, Lerakis S, Baumgartner H, Rodes-Cabau J. Cardiovascular magnetic resonance to evaluate aortic regurgitation after transcatheter aortic valve replacement. *J Am Coll Cardiol* 2016;68:577–585.
13. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647.
14. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960;20:37–46.

15. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)* 2012;22:276–282.
16. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. *Phys Ther* 2005;85:257–268.
17. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, Thomas M, Kovac J, Spyt T, MacCarthy PA, Wendler O, Hildick-Smith D, Davies SW, Trivedi U, Blackman DJ, Levy RD, Brecker SJ, Baumbach A, Daniel T, Gray H, Mullen MJ. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol* 2011;58:2130–2138.
18. Leeflang MMG, Deeks JJ, Takwoingi Y, Macaskill P. Cochrane diagnostic test accuracy reviews. *Syst Rev* 2013;2. 82-82.
19. Ioannidis JP, Trikalinos TA. The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. *CMAJ* 2007;176:1091–1096.
20. Altiok E, Frick M, Meyer CG, Al Ateah G, Napp A, Kirschfink A, Almalla M, Lotfi S, Becker M, Herich L, Lehmacher W, Hoffmann R. Comparison of two- and three-dimensional transthoracic echocardiography to cardiac magnetic resonance imaging for assessment of paravalvular regurgitation after transcatheter aortic valve implantation. *Am J Cardiol* 2014;113:1859–1866.
21. Crouch G, Tully PJ, Bennetts J, Sinhal A, Bradbrook C, Penhall AL, De Pasquale CG, Baker RA, Selvanayagam JB. Quantitative assessment of paravalvular regurgitation following transcatheter aortic valve replacement. *J Cardiovasc Magn Reson* 2015;17:32.
22. Hayek S SF, Oshinski J, Lerakis S. Multiparametric assessment of post-transcatheter aortic valve replacement paravalvular regurgitation grading by transthoracic echocardiography and cardiac magnetic resonance. *J Clin Exp Cardiolog* 2014;5.
23. Salaun E, Jacquier A, Theron A, Giorgi R, Lambert M, Jaussaud N, Hubert S, Collart F, Bonnet JL, Habib G, Cuisset T, Grisoli D. Value of CMR in quantification of paravalvular aortic regurgitation after TAVI. *Eur Heart J Cardiovasc Imaging* 2016;17:41–50.
24. Sherif MA, Abdel-Wahab M, Beurich HW, Stocker B, Zachow D, Geist V, Tolg R, Richardt G. Haemodynamic evaluation of aortic regurgitation after transcatheter aortic valve implantation using cardiovascular magnetic resonance. *EuroIntervention* 2011;7:57–63.
25. Ribeiro HB, Le Ven F, Larose E, Dahou A, Nombela-Franco L, Urena M, Allende R, Amat-Santos I, Ricapito Mde L, Thebault C, Clavel MA, Delarochelliere R, Doyle D, Dumont E, Dumesnil JG, Pibarot P, Rodes-Cabau J. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment and quantification of aortic regurgitation in patients undergoing transcatheter aortic valve implantation. *Heart* 2014;100:1924–1932.
26. Pibarot P, Hahn RT, Weissman NJ, Monaghan MJ. Assessment of paravalvular regurgitation following TAVR: a proposal of unifying grading scheme. *JACC Cardiovasc Imaging* 2015;8:340–360.
27. Abdelghani M, Spitzer E, Ren B, Serruys PW, Soliman OI. Real-world feasibility of the VARC-recommended multiparametric approach for the assessment of post-TAVI aortic regurgitation. *Int J Cardiol* 2016;223:220–221.
28. Hartlage GR, Babaliaros VC, Thourani VH, Hayek S, Chrysohoou C, Ghasemzadeh N, Stillman AE, Clements SD, Oshinski JN, Lerakis S. The role of cardiovascular magnetic resonance in stratifying paravalvular leak severity after transcatheter aortic valve replacement: an observational outcome study. *J Cardiovasc Magn Reson* 2014;16:93.
29. Frick M, Meyer CG, Kirschfink A, Altiok E, Lehrke M, Brehmer K, Lotfi S, Hoffmann R. Evaluation of aortic regurgitation after transcatheter aortic valve implantation: aortic root angiography in comparison to cardiac magnetic resonance. *EuroIntervention* 2016;11:1419–1427.