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ORIGINAL ARTICLE

The influence of transcatheter aortic valve replacement on left atrial mechanics: a systematic review and meta-analysis

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Abstract

Aims

The morphology and function of the left atrium (LA) are intimately tied to left ventricular loading conditions. Data pertaining to the effect of transcatheter aortic valve replacement (TAVR) on LA function and geometry are scarce. The aim of the study was to quantify associations between TAVR and LA remodelling by pooling available data from published observational studies.

Methods and results

A systematic review and meta-analysis were performed. Studies reporting serial LA speckle-tracking echocardiographic (STE) data, before and after TAVR, were included. Other outcome data included LA area and indexed volume (LAVi) and standard chamber measurements. Outcomes were stratified by timing of follow-up echocardiography: early (<6 months) or late (≥6 months). Twelve studies were included, comprising 1066 patients. The mean reduction in LAVi was 2.72 mL/m^2 [95% confidence interval (CI) 1.37–4.06, $P < 0.01$]. LA reservoir function improved overall by a mean difference (MD) of 3.71% (95% CI 1.82–5.6, $P < 0.01$), although there was significant heterogeneity within the pooled studies ($I^2 = 87.3\%$). Significant improvement in reservoir strain was seen in both early follow-up (MD 3.1%, $P < 0.01$) and late follow-up studies (MD 4.48%, $P = 0.03$), but heterogeneity remained high ($I^2 = 65.23$ and 94.4%, respectively). Six studies reported a change in LA contractile function, which recovered in the early follow-up studies (MD 2.26, $P < 0.01$), but not in the late group (MD 1.41, $P = 0.05$). Pooled improvement in LA booster function was 1.96% (95% CI 1.11–2.8, $P < 0.01$).

Conclusion

TAVR is associated with significant negative LA remodelling, and an improvement in LA mechanics, quantified by STE. The prognostic implications of these findings require further study.

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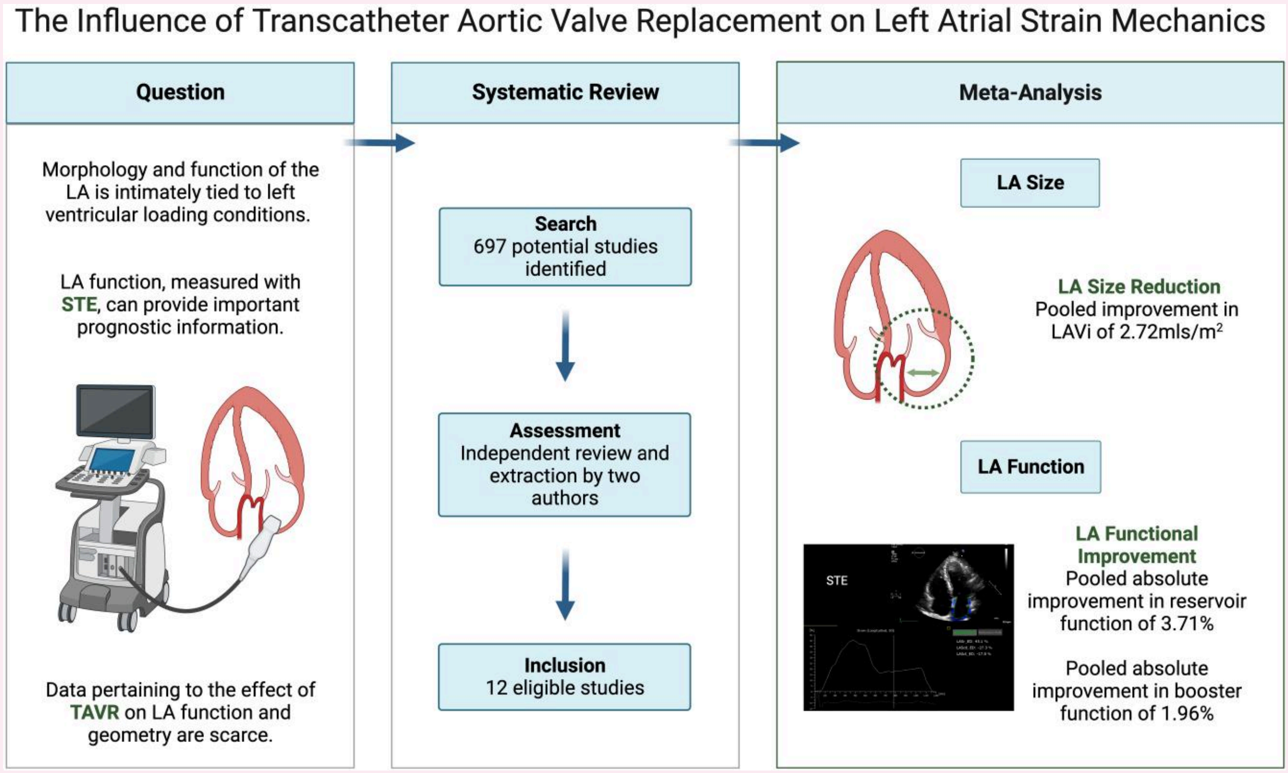
Graphical Abstract



LA, left atrium; STE, speckle-tracking echocardiography; TAVR, transcatheter aortic valve replacement.

Keywords aortic stenosis • transcatheter aortic valve replacement • left atrium • strain • left atrial function

Introduction

Progressive aortic stenosis (AS) is associated with hypertrophic remodelling of the left ventricle, ultimately leading to reactive fibrosis and impaired ventricular function, which is associated with a poor prognosis.[1] Advances in echocardiographic techniques, specifically speckle-tracking echocardiography (STE), have facilitated more granular assessment of tissue deformation and mechanical cardiac function. STE reveals early myocardial dysfunction in patients with significant AS prior to symptom development or overt deterioration in systolic function, quantified by the left ventricular ejection fraction (LVEF).[2] Owing to this robust sensitivity to subtle impairments in ventricular function, strain imaging also provides important prognostic information.[3] Left atrial (LA) strain imaging can be employed to quantify the phases of LA function during the cardiac cycle. LA mechanical function can be divided into three key phases: (i) reservoir phase: collection of pulmonary venous flow during ventricular systole; (ii) conduit phase: passive transit of blood to the left ventricle during early ventricular diastole; and (iii) contractile/booster phase: active contraction of the atrium during late ventricular diastole.[4] The triphasic strain curve produced by STE during the cardiac cycle quantifies LA distensibility and contractility during these phases. LA mechanical function, measured with STE, has demonstrated independent prognostic discriminatory power for a range of cardiomyopathic states and valvular diseases, including aortic stenosis.[5–7] Impaired LA function also predicts major adverse cardiac events.[8] However, the potential reversibility of LA mechanical dysfunction following transcatheter aortic valve replacement (TAVR), and the potential prognostic implications are scarcely reported. As such, we sought to quantify these associations by pooling available data from published observational studies.

Methods

This systematic review was registered with PROSPERO (CRD42023485102) and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility

To be eligible for inclusion, studies needed to report serial LA strain measurements, as quantified by STE, both before and after transcatheter aortic valve implantation (TAVI). Prospective and retrospective studies were included.

Search strategy

A systematic search of PubMed, Embase, and Web of Science was conducted using combinations of the following MeSH and keyword terms: transcatheter aortic valve implantation; TAVI; transcatheter aortic valve replacement; TAVR; left atrial strain; atrial strain; strain. The full search strategy is available in Supplementary data online, *Table S1*. The databases were queried from their inception until October 2023. To ensure comprehensive capture, an additional manual reference check of pertinent literature, including recent review articles, was performed.

Data extraction and management

A standardized, pre-piloted form was used to extract data from the included studies. Two reviewers (T.M. and L.B.) independently extracted data. Discrepancies were discussed following a cross-check. The extracted data included information pertaining to study type, methodology, strain software, and population characteristics. Echocardiographic variables of interest were the aortic valve area (AVA), mean aortic valve gradient, LVEF, LA area, LA volume indexed to body surface area (LAVi), and LA function, quantified by STE.

Assessment of bias

Studies were assessed for risk of bias and methodological quality using the Newcastle–Ottawa tool for assessing risk of bias in cohort studies.[9] The included studies were rated on three different domains, including the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome. The quality score ranges from 0 to 9 points, where 1–3, 4–6, and 7–9 points reflect a high, intermediate, and low risk of bias, respectively.

Data analysis

Analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria). Changes in LA strain parameters from baseline were stratified by duration of follow-up (<6 and ≥6 months). Where continuous data were reported as median and interquartile range (IQR), means were estimated according to the method described by Luo *et al.*,[10] and standard deviations according to the method described by Wan *et al.*[11] Due to the paucity of studies and the heterogeneity of outcome reporting, some results are presented qualitatively with relevant figures. Where data were sufficiently homogeneous to permit pooling and meta-analysis, differences were expressed as the mean difference (MD) with a 95% confidence interval (CI) for continuous outcomes. Studies reporting peak atrial longitudinal strain (PALS), according to the recommendations of the EACVI/ASE/Industry Task Force,[12] which corresponds to reservoir function, were pooled with studies specifically reporting reservoir function. The Hedges random-effects model was used, which has utility in correcting for bias in small sample sizes. Heterogeneity was assessed using the I^2 statistic, with an $I^2 > 50\%$, indicating significant heterogeneity. Potential bias was also visualized using funnel plots. Where significant heterogeneity existed, meta-regression was performed. A two-tailed value of $P = 0.05$ was used to claim statistical significance.

Results

A total of 697 studies were identified from the search. Following duplicate removal and initial screening for eligibility, 61 full-text studies were retrieved for assessment. Forty-nine studies were excluded, leaving 12 studies for final inclusion (*Figure 1*).

Baseline characteristics

The characteristics of the included studies are outlined in *Table 1*. The pooled cohort totalled 1066 patients. The average age of participants was 80.8 years. The median LVEF and AVA were 53.7% (IQR 53–58.8) and 0.71 cm^2 (IQR 0.69–0.73), respectively. Seven of the 12 studies reported early follow-up data, and most participants underwent TAVR with a self-expanding valve, compared with a balloon-expandable valve. Six studies utilized EchoPAC strain software, ahead of TomTec and QLab (used in two studies each). All studies demonstrated intermediate risk of bias.

LA geometry

Eleven of the 12 studies reported change in LAVi (*Figure 2*). The mean overall reduction in LAVi was 2.72 mL/m^2 following TAVI (95% CI 1.37–4.06, $P < 0.01$, low heterogeneity: $I^2 = 0\%$). When stratified by duration of follow-up (early or late), a significant change was seen in both early and late follow-up groups (see Supplementary data online, *Figures S1* and *S2*).

LA function

All studies reported reservoir indices, albeit six studies referred to this as PALS, and six specifically as reservoir strain. LA reservoir function improved overall by an MD of 3.71% (*Figure 3*; 95% CI 1.82–5.6, $P < 0.01$), although there was significant heterogeneity within the pooled studies ($I^2 = 87.3\%$). Significant improvement in reservoir strain was seen in both early follow-up (MD 3.1%, $P < 0.01$) and late follow-up studies (MD 4.48%, $P = 0.03$), but heterogeneity remained high ($I^2 = 65.23$ and 94.4%, respectively). Funnel plot visualization demonstrated some asymmetry, although this was not statistically significant ($P = 0.12$, Supplementary data online, *Figure S3*). Meta-regression was performed to test the influence of the following study characteristics: baseline LVEF, proportion of study participants with atrial fibrillation (AF), mean study age, and strain software used. Using a Knapp and Hartung adjustment (given mixed continuous and categorical variables), meta-regression did not reveal a statistically significant influence of these variables (F statistic = 1.12, $P = 0.55$) with significant residual heterogeneity ($I^2 = 84.5\%$). Although not significant, there was a trend towards greater improvement in reservoir function with lower baseline LVEF (see Supplementary data online, *Figure S4*).

Six studies reported a change in LA booster/contractile function, which recovered in the early follow-up studies (MD 2.26, $P < 0.01$), but not in the late group (MD 1.41, $P = 0.05$). Pooled improvement in LA booster function was 1.96% (*Figure 4*; 95% CI 1.11–2.8, $P < 0.01$, low heterogeneity: $I^2 = 0\%$). Five studies reported conduit indices. There was a high level of heterogeneity ($I^2 = 90.1\%$). The mean improvement in conduit strain was 2.23%, but this was not statistically significant (*Figure 5*; 95% CI −0.56 to 5.02, $P = 0.12$). No significant difference was observed when the studies were stratified. Meta-regression was not performed owing to the low number of studies reporting this metric.

Discussion

The aim of our study was to quantify improvement, if any, in LA mechanical function following TAVR, as quantified by STE. The key findings of this meta-analysis are that, following TAVR, the LA negatively remodels (reduces in size), and this is associated with improved distensibility, as quantified by an improvement in reservoir function. We identified a significant overall improvement in LAVi (2.72 mL/m^2), which was not individually demonstrated by all but one study, highlighting the utility of meta-analysis. LA dilation and dysfunction are clearly highly prevalent in the TAVR population. In all studies, the mean baseline LAVi values were abnormal by current consensus criteria (>34 mL/m^2), as were the mean baseline reservoir strain values (<39.4%).[25] Although LVEF was generally preserved, diastolic dysfunction was highly prevalent, but only one group clearly stratified diastology, according to contemporary guidelines.[18] Spethmann *et al.*[18] found that all patients had some degree of diastolic dysfunction, but nearly half improved by one grade, and some completely normalized. Interestingly, Poulin *et al.*[19] did not replicate this finding despite the similar sample size, and D'Ascenzi *et al.*[17] did not find an association between diastolic function (or its post-TAVR change) and the observed improvement in LA strain. It has been suggested that LA strain may be more appropriate than contemporary markers of filling pressures, such as *E*/*e*′.[18]

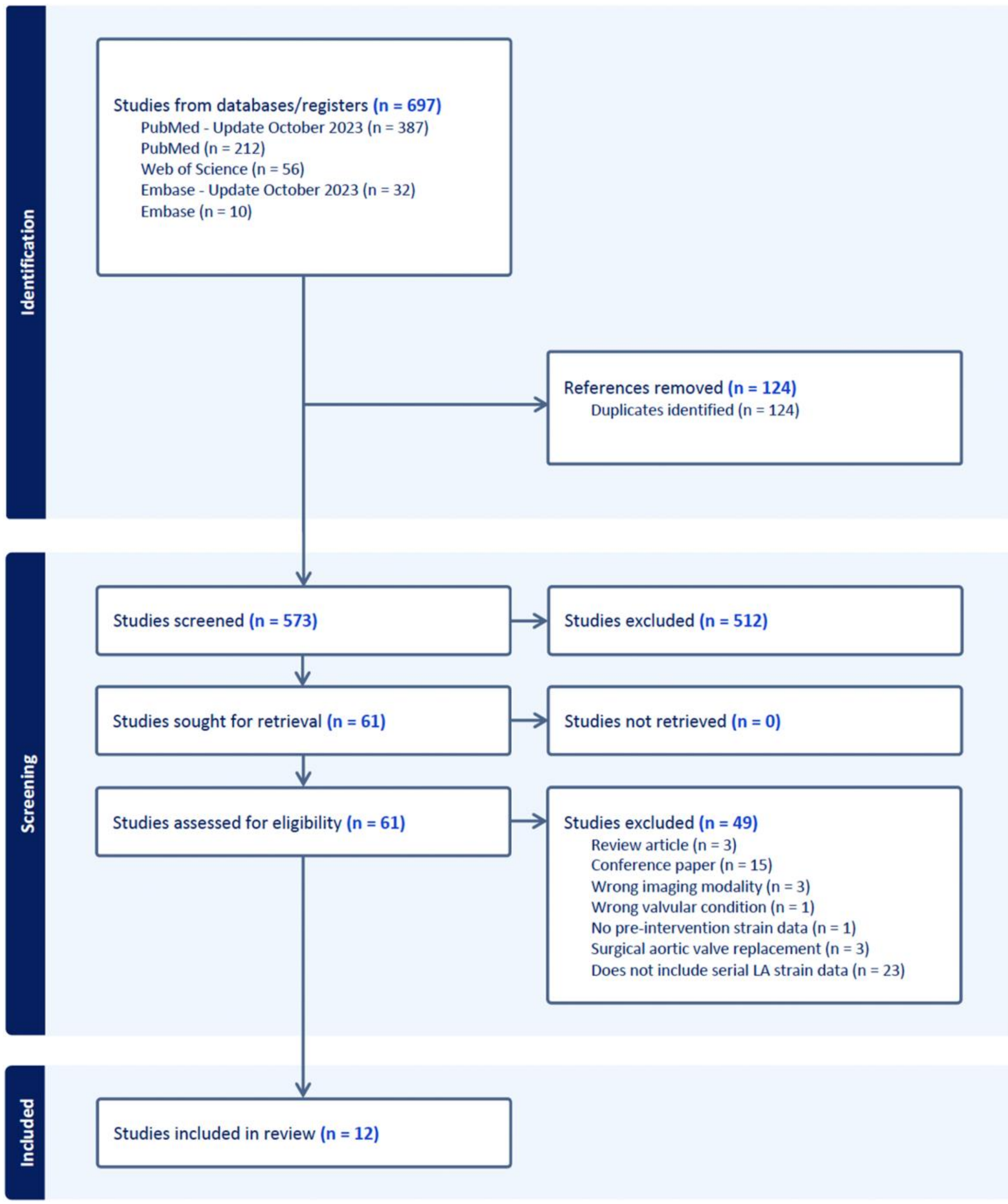


Figure 1 PRISMA flow chart for record screening and assessment. The initial search yielded 697 studies, of which 12 were eligible for inclusion.

Regardless, further research elucidating the link between diastolic function and LA functional recovery is needed.

The reversal of left ventricular hypertrophy following aortic valve replacement, and the prognostic implications, have been studied exhaustively.[26] However, cardiac adaptation to aortic stenosis is non-uniform; not all patients demonstrate reactive hypertrophy to the chronic pressure load of aortic stenosis, and not all patients favourably remodel the following treatment.[27] Nor is pathological cardiac change confined to the valve or left ventricle—important prognostic information is contained within the LA. Both LA reverse remodelling and improvement in LA strain indices following TAVR have shown association with improved survival, albeit in a small cohort.[23] It is also well known that dilation of the LA and impairment in mechanical function are associated with an increased risk of stroke and stroke related to incident AF.[28,29] It has recently been reported that LA strain and strain rate are also predictive of new onset AF following AVR, both transcatheter and surgical.[19,30] Poulin *et al*. found that LA early diastolic strain rate, a marker of conduit function, was associated with new AF following TAVR, raising the question of whether improvement in LA strain following TAVR might be associated with stroke risk reduction. This is currently unknown and requires further research.

Table 1 Baseline characteristics of the included studies

Study	*n*	Strain software	Longest follow-up	Age	Male (%)	LVEF (%)	AF (%)	TAVI type	AVA (cm^2)	Mean gradient (mmHg)	LAVi (mL/m^2)	*E/A*	*E/e′*	LA reservoir strain (%)	Risk of bias
Anastasius *et al.* (2022)[13]	109	QLab	Early (<6 months)	81	49	62	33	58% SEV	0.7	44	47	NR	NR	18	Intermediate
Coyle *et al.* (2023)[14]	25	EchoPAC	Early (<6 months)	80.6	76	54.32	36	NR	NR	NR	NR	0.8	16.05	12.78	Intermediate
Sabatino *et al.* (2021)[15]	100	EchoPAC	Late (≥6 months)	81.2	48	53.7	0	71% SEV	0.75	47.9	48.1	0.72	13.5	15.3	Intermediate
Spethmann *et al.* (2014)[16]	54	EchoPAC	Late (≥6 months)	79.3	38.9	53.6	NR	85.2% SEV	0.74	43.3	43.6	1.16	17.4	21.5	Intermediate
D'Ascenzi *et al.* (2013)[17]	32	EchoPAC	Early (<6 months)	80.9	54	52.9	0	61% BEV	NR	52.3	47.3	0.83	12.5	14.4	Intermediate
Spethmann *et al.* (2013)[18]	32	EchoPAC	Early (<6 months)	76.6	43.8	53.3	21.9	75% SEV	0.73	41.7	41.3	1.36	18.7	24	Intermediate
Poulin *et al.* (2017)[19]	52	NR	Early (<6 months)	81	54	58	0	83% BEV	0.7	50	51	1.1	11.8	21	Intermediate
D'Andrea *et al.* (2015)[20]	55	NR	Late (≥6 months)	78.6	54.5	48.8	23.1	100% SEV	0.58	52.1	41.6	NR	NR	14.2	Intermediate
Medvedofsky *et al.* (2019)[21]	213	TomTec	Late (≥6 months)	83	42	61	0	NR	0.67	49	49	NR	NR	19	Intermediate
Roslan *et al.* (2022)[22]	112	TomTec	Late (≥6 months)	80	49.1	53.02	NR	56.2% SEV	0.68	49.94	52.96	NR	NR	17.44	Intermediate
Weber *et al.* (2021)[23]	150	QLab	Early (<6 months)	82	42	63	0	50% SEV	0.72	42.2	42.2	1.0	19.89	21.96	Intermediate
Parasca *et al.* (2023)[24]	132	EchoPAC	Early (<6 months)	76.6	52.5	51.4	31.1	100% BEV	0.72	57.6	55.3	1.2	NR	12.4	Intermediate

BEV, balloon-expandable valve; NR, not reported; SEV, self-expanding valve.

Several covariates may contribute to heterogeneity of the included studies, including inter-vendor variability, LA strain nomenclature, prevalence of AF, and differences in the type of valve prosthesis (which can influence residual transaortic gradient and left ventricular reverse remodelling). Meta-regression demonstrated that baseline LVEF, AF, age, and strain software accounted for some, but not all, of the heterogeneity. Also, measurement of reservoir function is influenced by the apical excursion of the mitral annulus in the systole. Therefore, any improvement in this phenomenon afforded by TAVR could influence this observation. Ten of the 12 studies reported a normal mean left ventricular function at baseline; hence, theoretically, a significant change in mitral annular excursion following TAVR might not be expected.

LA strain nomenclature warrants highlighting. It is important to note that measurement of LA strain can be referenced to either the onset of the QRS complex (end of ventricular diastole) or the beginning of the P wave (beginning of atrial systole, late ventricular diastole). This has important implications for the magnitude of deformation measured, and how each phasic component is calculated. For example, peak positive strain corresponds to conduit function when timed to the P wave, and reservoir strain when timed to the QRS. Further confusion arises when LA mechanical phases are labelled according to events in the *left ventricle*. For example, Sabatino *et al*. report 'LA systolic strain', which corresponds to QRS-gated peak positive strain, and, therefore, the reservoir phase. Weber *et al*. report LA global peak longitudinal strain, corresponding to the same phase. Indeed, 6 of the 12 studies in this meta-analysis reported peak LA longitudinal strain or equivalent, and 5 reported specific reservoir, conduit, and contractile strain values. Coyle *et al*. used PALS nomenclature but did not specify whether P wave or QRS gating was implemented. The authors infer that PALS reflects reservoir function, suggesting that they used QRS gating. The remaining studies reporting PALS also utilized QRS referencing. Presently, standardized strain referencing to the QRS, and labelling according to the *LA cycle*, is recommended.[12,31]

Future directions

LA geometry and function are well-described prognostic discriminators for multiple left heart conditions. For patients with aortic stenosis, both LA size and function have demonstrated independent incremental prognostic information[32,33]; however, current studies quantifying LA function using strain imaging are limited in both number and sample size. Moreover, the independent prognostic value of LA functional recovery following TAVR and whether intervention at an earlier stage may afford biologically plausible protection from the known consequence of adverse LA remodelling, such as new onset AF, are yet to be demonstrated in large prospective cohorts. Assessment of LA function with strain imaging may provide more sensitive assessments of left ventricular diastolic function and improve our ability to identify patients at risk for adverse outcomes. Incorporating these parameters of LA structure and function in the assessment of patients with aortic stenosis may ultimately improve risk stratification and selection for therapy. Prospective data are very much needed.

Limitations

Although 10 of the 12 studies were prospective in design, most studies did not report several other covariates known to influence left ventricular remodelling following TAVR, such as paravalvular leak. All studies were observational cohort studies, and we did not analyse patient-level data. Nevertheless, the strength of our study lies in the pooling of multiple studies yielding a combined cohort of 1066 patients, representing the only meta-analysis of LA strain dynamics following TAVR to date.

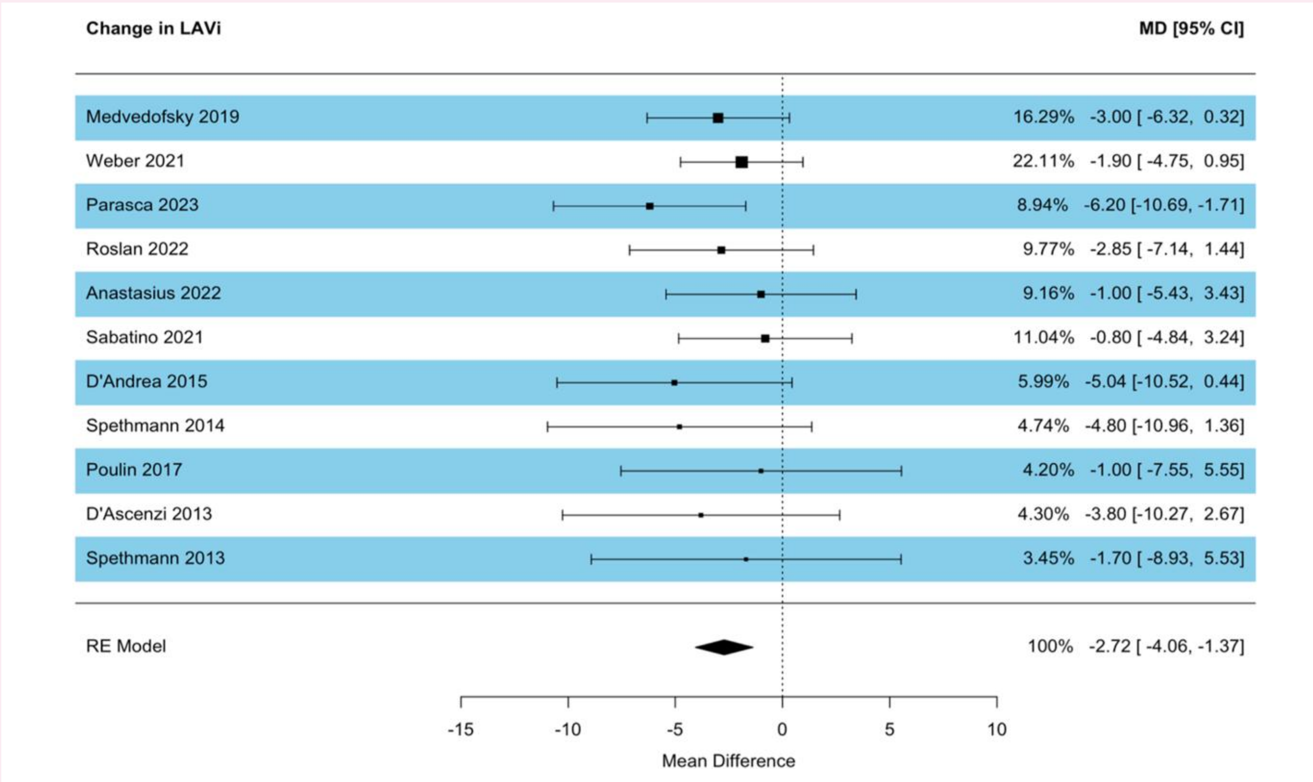


Figure 2 Forest plot of studies reporting changes in LAVi (mL/m^2). Studies are listed in descending order of sample size.

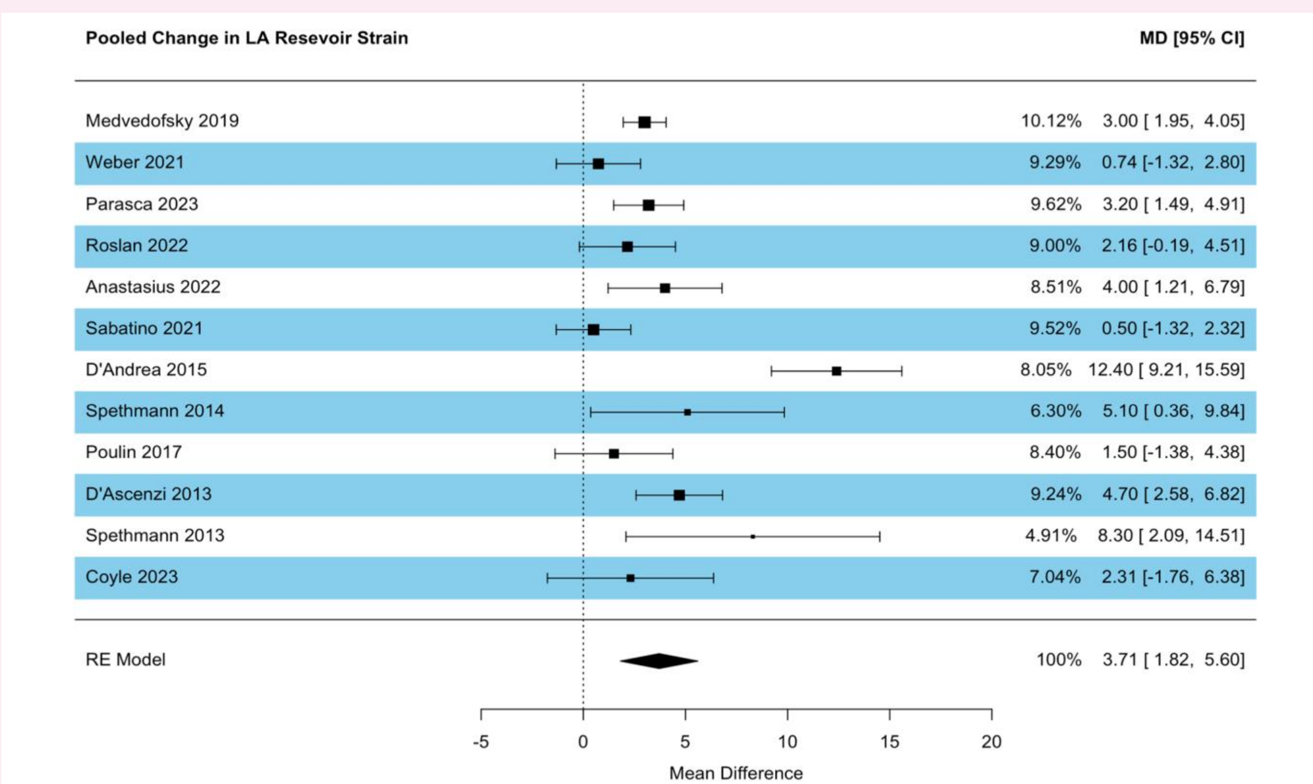


Figure 3 Forest plot of studies reporting changes in LA reservoir strain. Studies are listed in descending order of sample size.

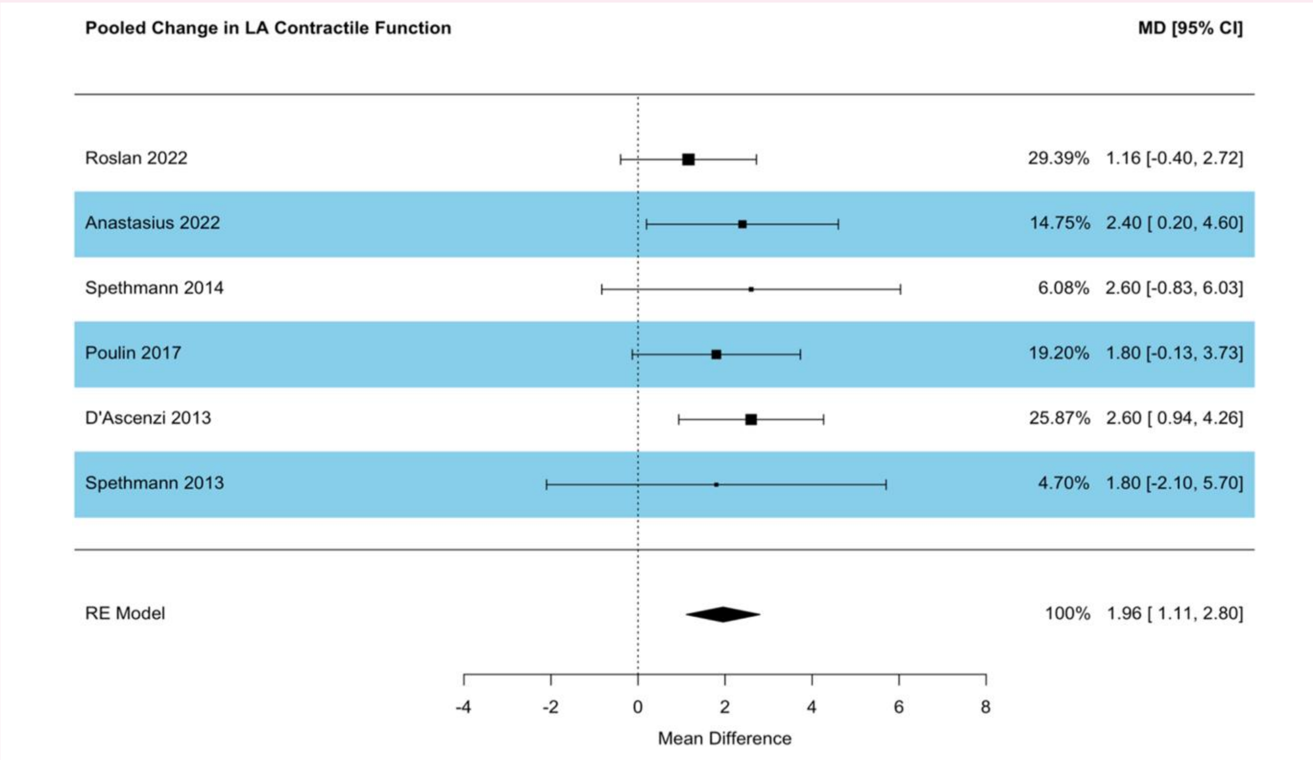


Figure 4 Forest plot of studies reporting change in contractile/booster function. Studies are listed in descending order of sample size.

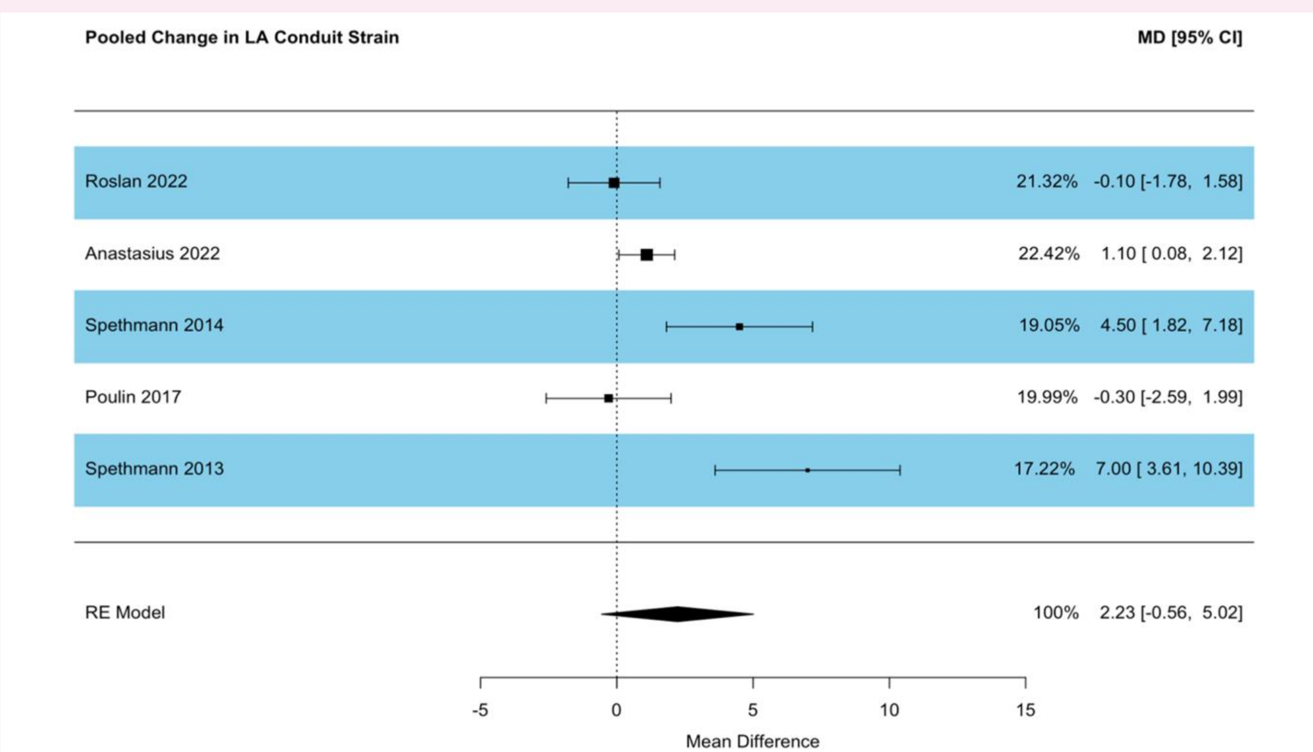


Figure 5 Forest plot of studies reporting changes in conduit strain. Studies are listed in descending order of sample size.

Conclusion

The LA plays a critical role in modulating left ventricular filling and function. STE can be used to quantify LA mechanical function and has demonstrated independent prognostic power across a range of cardiac conditions, including aortic stenosis. Hitherto, scarcely described is the extent of LA reverse remodelling following TAVR. This meta-analysis of 12 observational studies revealed significant negative LA remodelling following TAVR, and an improvement in LA mechanics, quantified by STE. The prognostic implications of these findings require further study.

Supplementary data

Supplementary data are available at *European Heart Journal – Imaging Methods and Practice* online.

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Conflict of interest: M.N.'s laboratory has received an NVIDIA Corporation Academic Hardware Grant. The remaining authors have nothing to disclose.

Data availability

Data are available upon reasonable request from the authors.

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