Prognostic value of preprocedural LV global longitudinal strain for post-TAVR-related morbidity and mortality: a meta-analysis

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ORIGINAL RESEARCH

Prognostic Value of Preprocedural LV Global Longitudinal Strain for Post-TAVR-Related Morbidity and Mortality

A Meta-Analysis

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ABSTRACT

BACKGROUND Left ventricular ejection fraction (LVEF) demonstrates limited prognostic value for post-transcatheter aortic valve replacement (TAVR) outcomes. Evidence regarding the potential role of left ventricular global longitudinal strain (LV-GLS) in this setting is inconsistent.

OBJECTIVES The aim of this systematic review and meta-analysis of aggregated data was to evaluate the prognostic value of preprocedural LV-GLS for post–TAVR-related morbidity and mortality.

METHODS The authors searched PubMed, Embase, and Web of Science for studies investigating the association between preprocedural 2-dimensional speckle-tracking–derived LV-GLS and post-TAVR clinical outcomes. An inversely weighted random effects meta-analysis was adopted to investigate the association between LV-GLS vs primary (ie, all-cause mortality) and secondary (ie, major cardiovascular events [MACE]) post-TAVR outcomes.

RESULTS Of the 1,130 identified records, 12 were eligible, all of which had a low-to-moderate risk of bias (Newcastle-Ottawa scale). On average, 2,049 patients demonstrated preserved LVEF (52.6% ± 1.7%), but impaired LV-GLS (−13.6% ± 0.6%). Patients with a lower LV-GLS had a higher all-cause mortality (pooled HR: 2.01; 95% CI: 1.59-2.55) and MACE (pooled odds ratio [OR]: 1.26; 95% CI: 1.08-1.47) risk compared with patients with higher LV-GLS. In addition, each percentage point decrease of LV-GLS (ie, toward 0%) was associated with an increased mortality (HR: 1.06; 95% CI: 1.04-1.08) and MACE risk (OR: 1.08; 95% CI: 1.01-1.15).

CONCLUSIONS Preprocedural LV-GLS was significantly associated with post-TAVR morbidity and mortality. This suggests a potential clinically important role of pre-TAVR evaluation of LV-GLS for risk stratification of patients with severe aortic stenosis. (Prognostic value of left ventricular global longitudinal strain in patients with aortic stenosis undergoing Transcatheter Aortic Valve Implantation: a meta-analysis; CRD42021289626) (J Am Coll Cardiol Img 2023;16:332-341)

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Transcatheter aortic valve replacement (TAVR) has become the method of choice to treat symptomatic, severe aortic stenosis (AS) in older patients with intermediate and high surgical risk.[1,2] The indication for aortic valve replacement is based on symptomatology and systolic dysfunction of the left ventricle (LV), reflected by an ejection fraction of <50%.[1,2] Interpretation of AS symptoms in older patients remains challenging,[3] posing a strong emphasis on early detection of LV systolic dysfunction to facilitate timely replacement of the native calcified aortic valve. The concentric remodeling of the LV, induced by the persistent increase in afterload caused by AS, can mask decrements in left ventricular ejection fraction (LVEF) until very late in the AS disease process.[4] Consequently, LVEF has limited value for risk stratification within the older population with AS.

In the past years, several studies have demonstrated that myocardial deformation assessment via 2-dimensional (2D)-speckle tracking represents a reliable method to evaluate clinical and subclinical systolic dysfunction.[5-7] LV global longitudinal strain (LV-GLS) may indicate subtle changes in LV mechanics already present during early stages of AS, even when LVEF is preserved.[4] Previous studies have examined whether impaired LV-GLS is associated with post-TAVR outcomes, both in symptomatic and asymptomatic patients with AS.[8,9] Similarly, studies have explored the relation between preprocedural LV-GLS and post-TAVR outcomes. However, studies have reported conflicting results, which in part may relate to studies being underpowered and/or using various methodological approaches. Pooling of these studies may provide better insight into the potential prognostic value of preprocedural LV-GLS for post-TAVR morbidity and mortality.

Therefore, we systematically reviewed the current published reports and performed a comprehensive meta-analysis of aggregated data to evaluate the prognostic value of LV-GLS for post-TAVR outcomes. We hypothesize that preprocedural LV-GLS is associated with post-TAVR-related morbidity and mortality in patients with severe AS. Identifying patients at high risk for developing clinical outcomes after TAVR allows for timely recognition, intervention, and intensified follow-up.

ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

AS = aortic stenosis

LV = left ventricle

LVEF = left ventricular ejection fraction

LV-GLS = left ventricular global longitudinal strain

MACE = major cardiovascular events

TAVR = transcatheter aortic valve replacement

METHODS

This meta-analysis was reported according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses checklist.[10] The protocol of this meta-analysis is registered within the PROSPERO system (CRD42021289626).

INFORMATION SOURCES AND SEARCH STRATEGY. A systematic search of published reports was performed in 3 bibliographic databases, including PubMed, Embase (Ovid), and Web of Science, from January 2001 to April 2022. The search strategy included a combination of the following terms: strain, speckle tracking, TAVR, mortality, and cardiovascular events. Supplemental Table 1 highlights the search strategy that was used within the selected bibliographic databases. Reference lists of relevant papers were thoroughly screened for additional studies.

ELIGIBILITY CRITERIA. To be eligible for inclusion in this systematic review and meta-analysis, papers had to: 1) include patients with AS who underwent TAVR; 2) quantify the LV-GLS using 2D-speckle tracking before TAVR; 3) investigate the association between preprocedural LV-GLS vs primary (ie, all-cause mortality) and secondary (ie, major adverse cardiovascular events [MACE], ie, incident rehospitalization, stroke, heart failure, myocardial infarction, revascularization or death) postprocedural outcomes; 4) define follow-up time as the interval between pre-TAVR and the end of follow-up (determined by either occurrence of an event or the duration of the study); 5) be written in English and be published in a peer-reviewed journal; and 6) be performed in adults.

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Linda Gillam, MD, served as the Guest Editor for this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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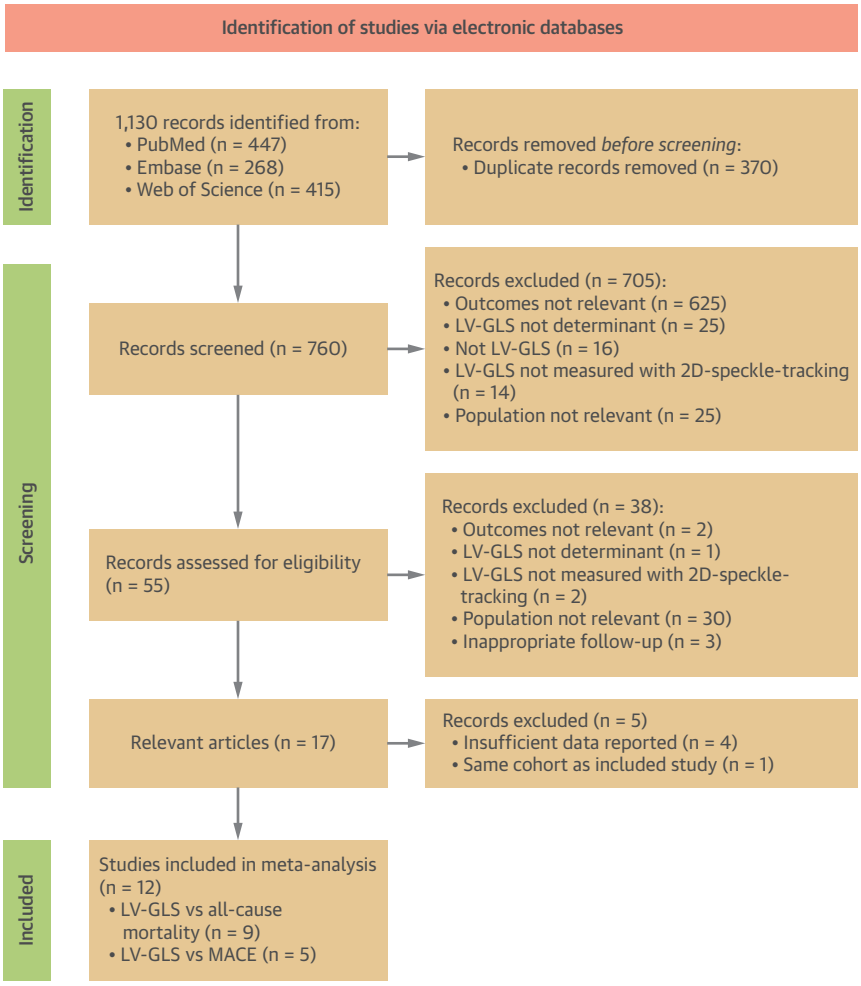
FIGURE 1 Flowchart of Study Screening Process



The PRISMA (Preferred Reporting Items for Systemic Reviews and Meta-Analyses) flow diagram highlights the number of records identified, included and excluded, and the reasons for exclusions, through the different phases of the systematic review and meta-analysis.
2D = 2 dimensional; LV-GLS = left ventricular global longitudinal strain; MACE = major adverse cardiovascular events.

Studies addressing bicuspid valves were excluded. In addition, reviews, case studies, and conference abstracts were excluded, but no further restrictions regarding study design were applied.

DATA SELECTION AND EXTRACTION. Study selection was performed by 2 independent researchers (N.A.S., O.vI.). All titles and abstracts of the retrieved papers were screened for the inclusion and exclusion criteria. Subsequently, full texts of the relevant manuscripts were retrieved and reviewed. The results from both researchers were compared and discussed until consensus was reached. In case of continued disagreement, a third researcher was consulted (D.H.J.T.). After consensus was reached, the included studies were then summarized within a preformatted data sheet, in which report (ie, author and year), study (ie, sample characteristics, criteria used for AS), patient (ie, disease and surgical risk status, presence of comorbidities, measures of cardiac function), survival (ie, outcome measure, number of events, follow-up duration, prognostic value of LV-GLS), and measurement (ie, echo and analysis software vendor) characteristics were described. Authors were contacted whenever insufficient aggregate data were reported. When multiple manuscripts from the

TABLE 1 Population Characteristics of the Included Studies

First Author	Design	Outcome	n	Women	Age (y)	AVA (cm²)
Erhart et al[20]	Retrospective cohort	All-cause mortality	146	49	81.8 (78.6-85.8)	0.79 (0.65-0.90)
Gegenava et al[26]	Retrospective cohort	All-cause mortality	210	50	80 ± 7	0.7 ± 0.2
Kjønås et al[19]	Prospective cohort	All-cause mortality	218	45	81.5 ± 6.8	NR
Pedersen et al[21]	Retrospective cohort	All-cause mortality	252	51	79.3 ± 6.7	0.67 ± 0.16
Poulin et al[25]	Retrospective cohort	All-cause mortality	105	42	82.1 ± 7.8	0.68 ± 0.17
Povlsen et al[28]	Prospective cohort	All-cause mortality	411	46	80.1 ± 7.1	0.7 ± 0.3
Sato et al[29]	Retrospective cohort	All-cause mortality	209	42	81 ± 10	NR
Shimoni et al[27]	Retrospective cohort	All-cause mortality Hospitalization/cardiac death	110	62	83 (6)	0.73 ± 0.16
Anastasius et al[22]	Prospective	HF hospitalization and death	109	51	81 ± 7.3	0.7 (0.2)
Ferreira et al[24]	Retrospective cohort	All-cause mortality MACE: all-cause mortality, stroke and HF hospitalization	89	56	82.1 ± 5.9	0.6 ± 0.2
Reskovic Luksic et al[23]	Retrospective cohort	MACE: mortality and HF hospitalizations	62	63	84.5 ± 6.6	0.77 ± 0.21
Suzuki-Eguchi et al[30]	Retrospective cohort	MACE: mortality and HF/stroke hospitalization	128	66	83.7 ± 4.2	0.65 ± 0.18

TABLE 1 Continued

First Author	Mean Transaortic Gradient (mm Hg)	NYHA Functional Class ≥III	HTN	DM	CAD	LVEF	LV-GLS	Follow-Up (mo)
Erhart et al[20]	37.5 (30.0-46.3)	41	80	25	53	56.0 (46.8-62.3)	−17.0 (−18.93 to −14.80)	24.3 (18.6-24.3)
Gegenava et al[26]	41 ± 18	57	76	26	60	46 ± 10	−14 ± 4	31 (17-48)
Kjønås et al[19]	NR	NR	68	28	67	49 ± 12	−11 ± 4	33 ± 8
Pedersen et al[21]	43 ± 17	51	74	24	38	51 ± 11.2	−12.7 ± 3.7	19 (10)
Poulin et al[25]	49 ± 15	88	82	29	66	53.8 ± 11.8	−12.6 ± 3.9	38.5 (29.2-48.7)
Povlsen et al[28]	39 ± 16	78	73	18	NR	50 ± 13	−14.0 ± 5.2	25.1 (19.4)
Sato et al[29]	47 ± 15	94	84	41	84	50 ± 14	−12.0 ± 3.7	44.2 (27.0-55.0)
Shimoni et al[27]	45 ± 12	14	90	36	38	55 ± 8.7	−13.4 ± 3.4	57 (35)
Anastasius et al[22]	42.9 ± 13.2	82	96	34	41	62 (13)	−15 ± −3.5	14.1 (11.4-25.4)
Ferreira et al[24]	57.0 ± 16.8	72	87	28	52	56.7 ± 10.0	−13.0 ± 3.8	13.4 (6.4-32.2)
Reskovic Luksic et al[23]	46.8 ± 17.3	61	71	26	44	64.5 ± 8.0	−16.7 ± 2.4	42.0 ± 22.8
Suzuki-Eguchi et al[30]	50 ± 18	NR	73	27	34	62 ± 13	−15 ± 4.4	19.4 (NR)

Values are median (IQR), mean ± SD, or n (%), unless otherwise indicated. When the lower and upper bounds of the IQR were not available, the width of the IQR was presented. Pedersen et al[21] and Povlsen et al[28] showed overlap in patients, so Pedersen et al[21] represents solely the unique patients of this cohort. Shimoni et al[27] provided data regarding an extended cohort. Kjønås et al[19] provided data regarding an extended follow-up.

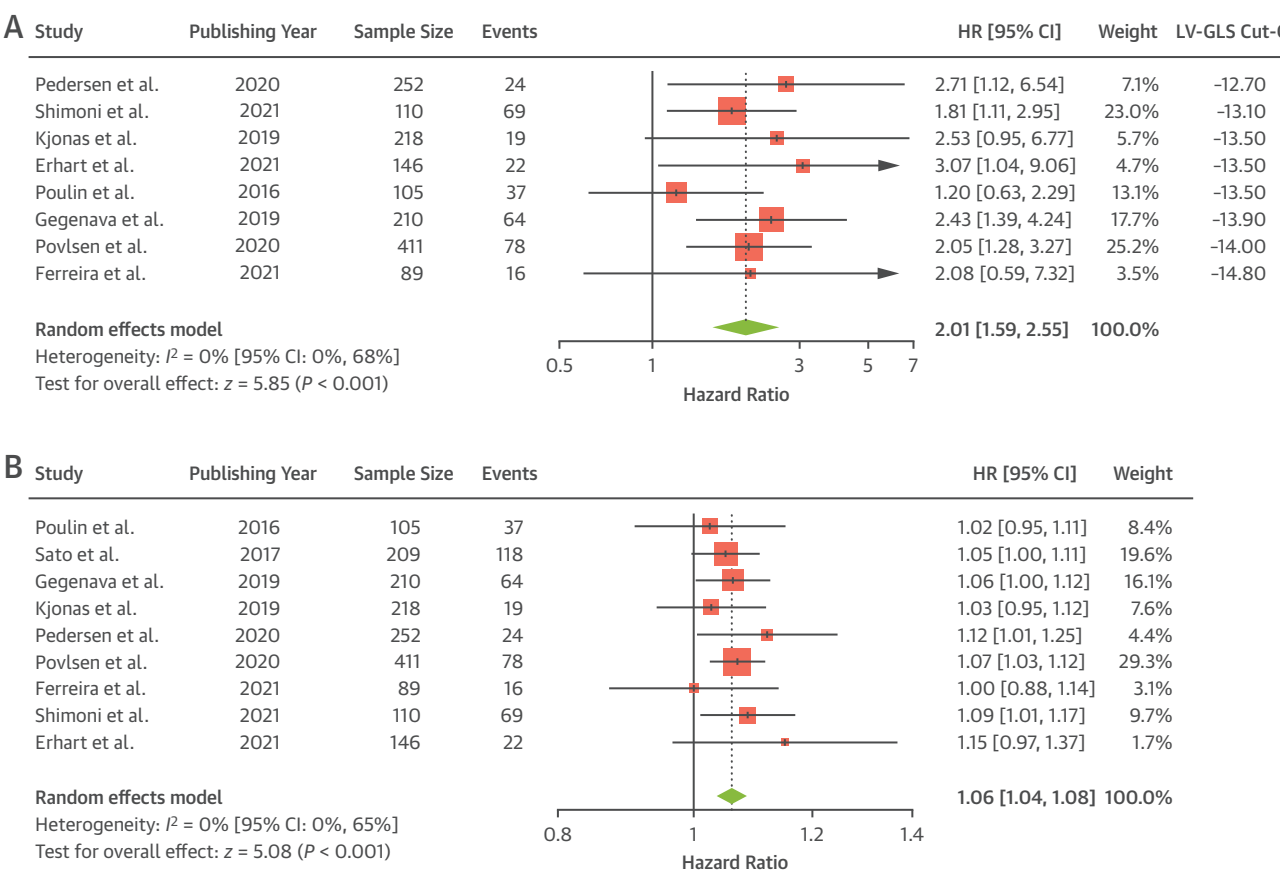
CAD = coronary artery disease; DM = diabetes mellitus; LV-GLS = left ventricular global longitudinal strain; HF = heart failure; HTN = hypertension; LVEF = left ventricular ejection fraction; MACE = major cardiovascular events; NR = not reported; NYHA = New York Heart Association.

same research group were included with overlapping time ranges, authors were asked to send data from unique patients only, to prevent patients from appearing twice in the meta-analysis.

RISK OF BIAS ASSESSMENT. The risk of bias of included studies was independently rated by 2 researchers (N.A.S., O.v.I.) using the Newcastle-Ottawa Scale.[11] Results were discussed until consensus was reached, where a third researcher (D.H.J.T.) was consulted in case of continued disagreement. Included studies were rated on 3 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 are reflecting a high, intermediate, and low risk of bias respectively.

SYNTHESES OF RESULTS. Unadjusted HRs and corresponding 95% CIs were extracted from included studies that included all-cause mortality as their outcome measure, and unadjusted ORs and corresponding 95% CIs were extracted from studies that included MACE as their outcome measure. Transformation of HRs and ORs using the natural logarithm was performed to allow accurate estimation of the 95% CI for the pooled estimate. An inverse variance-weighted random effects model was subsequently used to pool per % LV-GLS decrease HRs for all-cause mortality following the DerSimonian and Laird

FIGURE 2 Forest Plot for the Association Between Preprocedural LV-GLS and Post-TAVR All-Cause Mortality



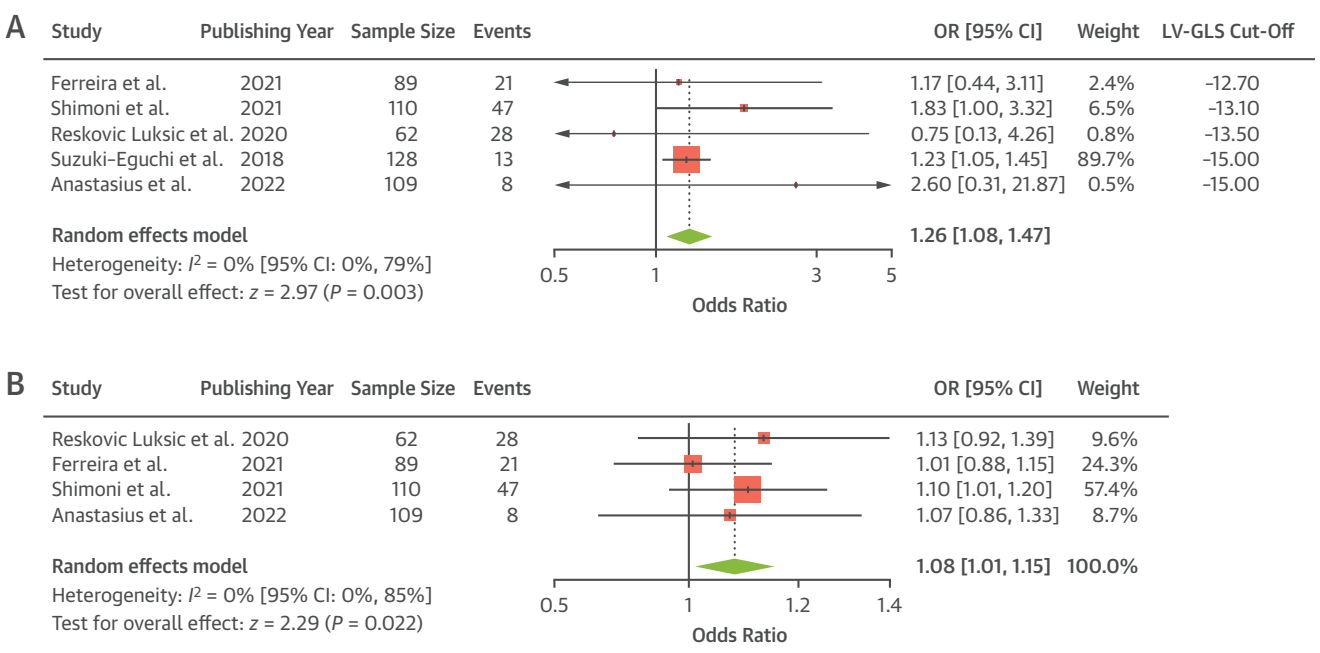
LV-GLS on a dichotomous **(A)** (ie, high vs low LV-GLS) and continuous **(B)**, per percentage point decrease in LV-GLS [toward 0%]) scale vs all-cause mortality. Sato et al[29] did not present data regarding the association between LV-GLS (on a dichotomous scale) and all-cause mortality, so this study was removed from **A**. Weights are obtained via the random effects analysis. TAVR = transcatheter aortic valve replacement; other abbreviation as in Figure 1.

approach.[12] In an individual analysis, we explored trends when LV-GLS was presented on a dichotomous scale (ie, impaired vs preserved LV-GLS) for all-cause mortality and MACE separately. The median LV-GLS was used as a cutoff to dichotomize LV-GLS if between −12% and −15%. If this criterion was not satisfied, authors were contacted to share the HR/OR corresponding to an LV-GLS of −13.5%. To evaluate heterogeneity present within the included studies, we used the I^2 test, with >50% indicating significant heterogeneity. Subgroup analyses were performed to evaluate the influence of design type (ie, prospective vs retrospective design) and risk of bias. Inverted funnel plots and Egger's test were used to exploratively evaluate the presence of publication bias. Analyses were performed in R version 4.1.2 (R Foundation for Statistical Computing) using the meta-package (version 5.1-1),[13] in which a 2-tailed value of $P = 0.05$ was used to claim statistical significance. Data are presented as mean ± SEM, median (IQR), or frequency and proportion, as appropriate.

RESULTS

SEARCH RESULTS. In total, 1,130 studies were identified after applying the specified search string in PubMed, Embase, and Web of Science. Screening of the titles and abstracts with respect to the inclusion and exclusion criteria, combined with the removal of duplicates, resulted in the exclusion of 1,075 papers. Subsequent assessment of the full text of the remaining 55 papers resulted in further exclusion of 38 papers, leaving 17 relevant studies. To overcome methodological constraints in pooling of the data,

FIGURE 3 **Forest Plot for the Association Between Preprocedural LV-GLS and Post-TAVR MACE**



LV-GLS on a dichotomous **(A)** (ie, high vs low LV-GLS) and continuous **(B)** (ie, per percentage point decrease in LV-GLS [toward 0%]) scale vs MACE. Suzuki-Eguchi et al[30] did not present data regarding the association between LV-GLS (on a continuous scale) and MACE, so this study was removed from **B**. Weights are obtained via the random effects analysis. OR = odds ratio; other abbreviations as in Figures 1 and 2.

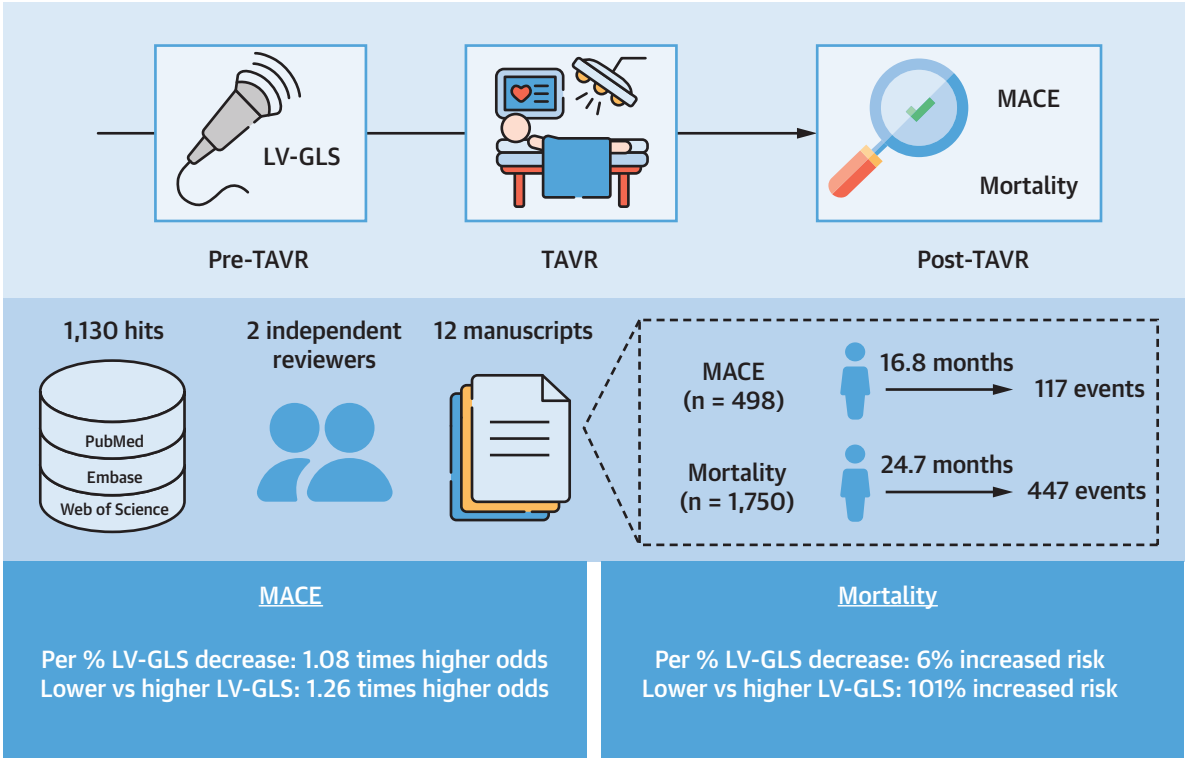
authors were contacted to provide aggregate data for the association between LV-GLS (ie, per percentage point decrease and/or high vs low LV-GLS) vs primary (ie, all-cause mortality) and secondary (ie, MACE) outcomes. Five studies originally met the requirements for inclusion, but were excluded because: 1) the paper did not report sufficient data to allow analysis and the authors were not able to share the required data;[14-17] or 2) the study covered the same cohort[18] as another included study.[19] Authors of 9 publications provided unpublished data.[19-27] Taken together, this resulted in the inclusion of 12 studies in the meta-analysis of which 9 evaluated the association of preprocedural LV-GLS with all-cause mortality (n = 1,750)[19-21,24-29] and 5 with MACE (n = 498),[22-24,27,30] respectively. **Figure 1** visualizes the sequential steps performed previously.

POPULATION CHARACTERISTICS. Preprocedural characteristics of the included studies are depicted in **Table 1**. The analytical cohort of the 12 included studies comprised 2,049 unique patients (49.8% women) with AS who underwent TAVR. Mean age was 81.1 ± 0.5 years and New York Heart Association (NYHA) functional class ≥III was reported in 66.0%. Mean aortic valve area was 0.70 ± 0.02 cm^2 with a mean transaortic pressure gradient of 43.6 ± 1.8 mm Hg. Comorbidities were frequent (prevalence of hypertension 77.7%, diabetes 27.1%, coronary artery disease 54.6%). On average, patients demonstrated preserved LVEF (mean: 52.6% ± 1.7%) but impaired LV-GLS (mean: −13.6% ± 0.6%). In terms of risk of bias, 5 studies had an intermediate risk of bias (Newcastle-Ottawa Scale = 6) and the remaining studies showed a low risk of bias (Newcastle-Ottawa Scale ≥7) (Supplemental Table 2).

LV-GLS VS CLINICAL OUTCOMES. During a median follow-up of 24.7 (IQR: 22.5-32.9) months, overall all-cause mortality was 25.5% (n = 447). Patients with a lower preprocedural LV-GLS had a higher risk of all-cause mortality compared with patients with a higher LV-GLS (pooled HR 2.01 [95% CI: 1.59-2.55]; P < 0.001; I^2 = 0% [95% CI: 0%-68%]; P = 0.74) (**Figure 2A**). Each 1% lower LV-GLS (ie, toward 0%) was associated with an increased mortality risk after TAVR (pooled HR: 1.06 [95% CI: 1.04-1.08]; P < 0.001; I^2 = 0% [95% CI: 0%-65%]; P = 0.79) (**Figure 2B**).

In addition, during a median follow-up of 16.8 (IQR: 13.6-36.7) months, MACE occurred in 117 patients (23.5%). Patients with a lower preprocedural LV-GLS had a higher odds of MACE compared with patients with a higher LV-GLS (pooled OR: 1.26 [95% CI: 1.08-1.47]; P = 0.003; I^2 = 0% [95% CI: 0%-

CENTRAL ILLUSTRATION **Preprocedural LV-GLS is Associated With Post-TAVR Mortality and MACE**



Stens NA, et al. J Am Coll Cardiol Img. 2023;16(3):332-341.

LV-GLS = left ventricular global longitudinal strain; MACE = major adverse cardiovascular events; TAVR = transcatheter aortic valve replacement.

79%]; $P = 0.67$) (**Figure 3A**). In addition, each 1% decrease in LV-GLS was associated with an increased odds of MACE after TAVR (pooled OR: 1.08 [95% CI: 1.01-1.15]; $P = 0.022$; $I^2 = 0\%$ [95% CI: 0%-85%]; $P = 0.67$) (**Figure 3B**).

Subgroup analyses suggested no significant differences in prognostic value of LV-GLS for all-cause mortality between prospective and retrospective studies, and between studies with a low and moderate risk of bias (Supplemental Table 3). Explorative assessment of publication bias for the association between preprocedural LV-GLS (on a continuous and dichotomous scale) and all-cause mortality via inverted funnel plots and Egger's tests suggested no publication bias (Supplemental Figure 1).

DISCUSSION

The aim of this meta-analysis was to evaluate the prognostic value of LV-GLS for post-TAVR morbidity and mortality in patients with severe, symptomatic AS undergoing TAVR. First, despite different cutoff values when LV-GLS was modeled on a dichotomous scale, those with a lower preprocedural LV-GLS demonstrated a significantly higher post-TAVR risk for all-cause mortality (101% increased risk) and odds for MACE (1.26 times higher odds) compared with individuals with a higher LV-GLS. In addition, we found that every percentage point decline in LV-GLS was associated with an increased risk for post-TAVR all-cause mortality (6% higher risk) and odds for MACE (1.08 times higher odds). Taken together, our meta-analysis demonstrates that LV-GLS is significantly associated with post-TAVR outcomes (**Central Illustration**), which suggests an important role for the preprocedural evaluation of LV-GLS for risk stratification of patients with severe symptomatic AS for clinical outcomes post-TAVR.

Assessment of systolic dysfunction has been considered the mainstay of risk stratification in

patients with AS. Current guidelines advocate the presence of an impaired LVEF as a gatekeeper for aortic valve replacement.[1,2] However, the recovery of LV function after TAVR varies widely and more sensitive methodologies to detect subclinical LV dysfunction are warranted. Speckle tracking has emerged as a relevant method to quantify subclinical and clinical systolic dysfunction. Unfortunately, studies that used LV-GLS as a prognostic factor for events post-TAVR were often limited by a small sample size, causing most studies to conclude that LV-GLS has no significant prognostic value. The ability to pool aggregate data from 2,049 individuals within our meta-analysis effectively overcomes this limitation. Indeed, in our meta-analysis we found that preprocedural LV-GLS was significantly associated with post-TAVR all-cause mortality in patients with severe, symptomatic AS.

Compared with all-cause mortality, the association between preprocedural LV-GLS and post-TAVR cardiovascular morbidity has been less extensively described in published reports. The pooling of the 5 included studies reinforces both the limitation of relatively small sample sizes, but also the potential benefit of meta-analyses to provide better insight into these areas. Our meta-analysis showed that preprocedural LV-GLS is also significantly related to post-TAVR morbidity. It should be noted that an OR is dependent on the number of events and the sample size,[31] which may explain the observation that the pooled effect is largely determined by 2 individual studies. Nevertheless, reports have highlighted that the preprocedural LV-GLS correlated with the improvement in NYHA functional class[32] and complication rate directly following TAVR.[33] To further support our observations, previous work using computed tomography angiography reinforced that a lower LV-GLS is related to a higher risk of all-cause mortality and heart failure hospitalizations.[34] Although it remains premature to make definitive conclusions, the presented evidence, paired with recent reports, suggests that LV-GLS also has potential for risk stratification of patients with severe AS for post-TAVR morbidity. This warrants future studies to elaborate on the association between preprocedural LV-GLS and post-TAVR morbidity.

The observation that LV-GLS is associated with morbidity and mortality in patients undergoing TAVR raises the question about the potential underlying physiological mechanism. In essence, AS transcends the definition of an isolated valvular disease with its considerable implications for cardiac function and structure. Compensatory LV hypertrophy develops in response to the persistent pressure overload induced by the stenotic aortic valve, as an attempt to compensate and normalize LV wall stress and systolic function. Because the subendocardial myocytes are susceptible to reductions in coronary blood flow,[35] the accompanied myocardial ischemia mainly affects longitudinally oriented muscle fibers. If pressure overload persists, irreversible myocardial fibrosis and a reduction in myocardial (longitudinal) function may occur. This may explain why global LV afterload, LV mass, and replacement fibrosis are independently associated with LV-GLS in patients with AS.[36,37] In addition, transthyretin cardiac amyloidosis is often coexisting in patients with AS.[38] In patients with cardiac amyloidosis, the degree of deposed myocardial amyloid fibrils strongly correlated with longitudinal strain in all segments in a 17-segment model.[39] Also others found that LV-GLS is more impaired in patients with AS with concurrent transthyretin cardiac amyloidosis compared with those with isolated AS.[40] These processes may contribute to the ability of LV-GLS to predict post-TAVR all-cause mortality.

Although our meta-analysis revealed that a dichotomous cutoff has prognostic value, substantial variation in using cutoff values was present between these studies. This raises questions on its applicability, but also what would represent the optimal LV-GLS cutoff for prognosis of post-TAVR outcomes in patients with severe symptomatic AS. Variation in cutoffs was minimized by setting a range of LV-GLS for the dichotomous analysis (ie, between −12% and −15%). Because no clear trend was observed in a change in HRs in relation to the increase in cutoff values (**Figure 2**), it seems unlikely that the variation in cutoffs explained the large interstudy variability that we observed when LV-GLS was modeled on a dichotomous scale. Alternatively, differences in the patient's risk profile may play an important role in this large interstudy variability. Although all studies included patients with severe, symptomatic AS, differences in comorbidity prevalence (ie, hypertension, diabetes, coronary artery disease) and/or disease status (ie, mean transvalvular gradient, NYHA functional class) may affect the association between LV-GLS and post-TAVR mortality. In addition, data regarding the degree of myocardial fibrosis and cardiac amyloidosis were not present, even though these entities are frequently encountered in patients with AS.[38,40,41] This should be acknowledged when interpreting our data.

STUDY LIMITATIONS. First, in asymptomatic patients with more than moderate AS, the association

between % decline LV-GLS and mortality appears to follow a nonlinear shape.[8] The exact shape of the dose-response curve between preprocedural LV-GLS and post-TAVR all-cause mortality remains to be clarified.[28,34] In other words, each additional decrease in % LV-GLS would be highly informative on demonstration of a linear pattern in symptomatic patients who undergo TAVR. Insufficient data were available to elaborate on the shape of the dose-response curve. Another limitation is that most of the included studies were retrospective cohort studies, and all studies reported univariate HRs. This highlights that residual confounding may be present, which could affect the pooled estimates in either direction.[42]

CONCLUSIONS

This meta-analysis showed that preprocedural LV-GLS as measured by 2D-speckle tracking is significantly associated with TAVR-related outcomes in patients with severe, symptomatic AS, irrespective of how LV-GLS was modeled. Even though LVEF is commonly used in patients with AS for risk stratification and adopted as a gatekeeper for aortic valve replacement, LVEF seems to remain preserved until late in the AS disease process because of compensatory mechanisms in cardiac structure. Indeed, LVEF seems largely preserved in patients with severe, symptomatic AS from the studies we included in our meta-analysis. In contrast to LVEF, alterations in LV-GLS seem to occur early in the disease process of AS, potentially even preceding changes in LVEF. Addition of evaluation of LV-GLS to current guideline-based assessment of LVEF may provide clinicians with better risk stratification for patients undergoing TAVR.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In this meta-analysis of 12 studies including 2,049 patients with severe, symptomatic AS, we demonstrate that preprocedural LV-GLS is significantly associated with post-TAVR outcomes. This suggests an important role for the evaluation of LV-GLS for risk stratification of patients with severe symptomatic AS for clinical outcomes post-TAVR.

TRANSLATIONAL OUTLOOK: Alterations in LV-GLS seem to occur early in the disease process of AS, potentially even preceding changes in LVEF. Addition of evaluation of LV-GLS to current guideline-based assessment of LVEF may therefore provide clinicians with improved risk stratification, allowing for timely recognition, intervention, and intensified follow-up.

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KEY WORDS aortic stenosis, echocardiography, morbidity, mortality, strain, transcatheter aortic valve replacement

APPENDIX For supplemental tables and a figure, please see the online version of this paper.