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Early changes in global longitudinal strain after transcatheter aortic valve replacement

Cambios tempranos del strain *global longitudinal posterior a sustitución valvular aórtica percutánea*

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ABSTRACT

Introduction: aortic stenosis is a prevalent and progressively worsening valvular heart condition associated with elevated rates of morbidity and mortality. While the left ventricular ejection fraction has traditionally served as the standard parameter for assessing systolic function, global longitudinal strain has gained recognition as a more sensitive marker capable of detecting subclinical myocardial impairment, even in individuals with preserved LVEF. Transcatheter aortic valve replacement offers a minimally invasive alternative to surgical valve replacement, particularly in high-risk patients. The Généreux classification stratifies patients with severe AS into stages based on extra-valvular cardiac involvement to better characterize the extent of myocardial damage. While long-term structural improvements after TAVR have been reported, early functional recovery remains underexplored. **Objective:** in this context, we aimed to evaluate early changes in GLS and the E/e' ratio three months after TAVR in patients stratified by the Généreux classification. **Material and methods:** a descriptive, observational, and cross-sectional study was conducted at the *Centro Médico Nacional 20 de Noviembre*. Demographic, echocardiographic, and hemodynamic variables were obtained from institutional electronic medical records. For statistical analysis, the χ^2 test or Student's t-test was used, and Spearman's correlation test was applied to evaluate associations between quantitative variables. **Results:** our study demonstrated a significant improvement in GLS across all stages, including patients with advanced myocardial involvement. In contrast, no significant changes were observed in the E/e' ratio, suggesting that early GLS improvement may not be directly associated with changes in diastolic filling pressures. **Conclusion:** these findings highlight the potential of GLS as an early marker of myocardial recovery following TAVR and support the prognostic value of the Généreux classification in this population.

RESUMEN

Introducción: *la Estenosis Aórtica (EAo) es una valvulopatía prevalente y progresiva, asociada con un aumento en la morbilidad y la mortalidad. Si bien la Fracción de Eyección del Ventrículo Izquierdo (FEVI) ha sido utilizada tradicionalmente para evaluar la función sistólica, el Strain Longitudinal Global (SLG) ha surgido como un marcador más sensible para detectar disfunción miocárdica temprana, incluso en pacientes con FEVI preservada. La Sustitución Valvular Aórtica Percutánea (TAVR, por sus siglas en inglés) ha demostrado ser una alternativa eficaz y menos invasiva que el reemplazo quirúrgico, particularmente en pacientes con alto riesgo. La clasificación de Généreux estratifica a los pacientes con EAo severa en estadios basados en el compromiso cardiaco extravalvular, con el objetivo de caracterizar mejor el grado de daño miocárdico. Aunque se han descrito mejoras estructurales a largo plazo posteriores al TAVR, la recuperación funcional temprana sigue siendo poco estudiada.* ***Objetivo:*** *en este contexto, el objetivo fue evaluar los cambios tempranos en el SLG y el índice E/e' a los tres meses posteriores al TAVR en pacientes estratificados según la clasificación de Généreux.* ***Material y métodos:*** *se realizó un estudio observacional, descriptivo y transversal en el Centro Médico Nacional 20 de Noviembre. Se obtuvieron variables demográficas, ecocardiográficas y hemodinámicas a partir de los expedientes electrónicos institucionales. Para el análisis estadístico, se utilizó la prueba de* χ^2 *o la prueba t de Student y se empleó la prueba de correlación de Spearman para evaluar asociaciones entre variables cuantitativas.* ***Resultados:*** *nuestro estudio demostró una mejoría significativa en el SLG en todos los estadios, incluyendo pacientes con daño miocárdico avanzado. En contraste, no se observaron cambios significativos en el índice E/e', lo que sugiere que la mejoría temprana del SLG podría no estar directamente relacionada con*

Keywords: aortic stenosis, transcatheter aortic valve replacement, global longitudinal strain, echocardiography, Généreux classification.

Palabras clave: *estenosis aórtica, sustitución valvular aórtica percutánea, strain global longitudinal, ecocardiograma, clasificación Généreux.*

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modificaciones en las presiones de llenado diastólico. ***Conclusión:*** *estos hallazgos resaltan el potencial del SLG como un marcador temprano de recuperación miocárdica posterior al TAVR y respaldan el valor pronóstico de la clasificación de Généreux en esta población.*

Abbreviations

AS = Aortic Stenosis
GLS = Global Longitudinal Strain
GLS-LV = Global Longitudinal Strain of the Left Ventricle
LV = Left Ventricle
LVEF = Left Ventricular Ejection Fraction
LVH = Left Ventricular Hypertrophy
SAVR = Surgical Aortic Valve Replacement
TAVR = Transcatheter Aortic Valve Replacement

INTRODUCTION

Aortic Stenosis (AS) is one of the most widespread valvular heart disorders globally. It is defined by the gradual narrowing of the outflow tract from the Left Ventricle (LV) to the aorta. This hemodynamic obstruction induces pressure overload within the LV, subsequently triggering Left Ventricular Hypertrophy (LVH) as an adaptive response. In the absence of timely intervention, AS can progress to impair both systolic and diastolic function, ultimately leading to heart failure and elevated mortality rates.[1,2]

Contemporary clinical guidelines establish two principal criteria for indicating valve replacement: (i) the echocardiographic confirmation of severe aortic stenosis based on parameters such as Maximum Aortic Velocity (Vmax), mean transvalvular pressure gradient, and Aortic Valve Area or its Index (AVAi); and (ii) the presence or absence of symptoms attributable to the valvular pathology, including dyspnea, heart failure, angina, or syncope. Furthermore, preoperative risk assessment primarily considers comorbid conditions while excluding other structural or functional cardiac characteristics from the decision-making framework.[2,3]

To provide a more comprehensive assessment of the hemodynamic impact of severe aortic stenosis, Généreux and colleagues proposed a classification system based on the extent of extra-valvular cardiac damage, using easily obtainable and broadly applicable echocardiographic parameters. This stratification includes five progressive stages: Stage 0 refers to patients with severe AS and no evidence of extra-valvular cardiac involvement; stage 1 includes LV dysfunction (LVEF $< 50\%$, E/e′ ratio > 14, or LVH); stage 2 includes left atrial enlargement, atrial fibrillation, or at least moderate mitral regurgitation; stage 3 includes moderate or more significant tricuspid regurgitation or pulmonary hypertension (sPAP > 60 mmHg); and stage 4 includes right ventricular dysfunction, defined by parameters such as TAPSE < 17 mm or S wave < 9.5 cm/s. When criteria from multiple stages are met, the highest stage is assigned.[3,4]

The underlying hypothesis was that the progression of extra-valvular cardiac damage could have significant prognostic implications. To validate this, data from the PARTNER 2 trial were used, which included 1,661 patients with severe AS who underwent valve replacement (TAVR or surgical). Most patients were in advanced stages (50.8% in stage 2, 24.9% in stage 3, and 8.7% in stage 4), while only 2.8% were classified as stage 0. One-year survival analysis showed a statistically significant and progressive increase in both all-cause and cardiovascular mortality as stages advanced. Multivariate analysis confirmed that the cardiac damage stage was one of the strongest predictors of one-year mortality, with an estimated 40-45% increased risk of death per stage, surpassing other comorbidities such as chronic kidney disease or coronary artery disease. These findings position the Généreux classification as a valuable prognostic tool that could complement current decision-making criteria for AS management.[4]

Surgical Aortic Valve Replacement (SAVR) has traditionally represented the cornerstone treatment for patients with symptomatic severe aortic stenosis. However, in recent decades, Transcatheter Aortic Valve Replacement (TAVR) has gained prominence as a less invasive option, especially advantageous for patients at high surgical risk. Clinical evidence supports the non-inferiority of TAVR relative to SAVR with respect to symptom alleviation and hemodynamic performance while also highlighting its association with expedited recovery and lower perioperative mortality.[5]

LV systolic function has conventionally been evaluated using Left Ventricular Ejection Fraction (LVEF). However, LVEF may remain preserved despite the presence of early myocardial dysfunction. In this regard, a Global Longitudinal Strain of the Left Ventricle (GLS-LV), derived from two-dimensional speckle-tracking echocardiography, has proven to be a more sensitive technique for detecting early impairments in LV systolic mechanics. GLS-LV facilitates the identification of subtle myocardial alterations prior to any measurable reduction in LVEF, thus providing important prognostic insights in patients with aortic stenosis.[6,7]

Myocardial strain analysis is beneficial for assessing ventricular function and as a complementary tool for risk stratification. Even with preserved ejection fraction, these patients may exhibit reduced GLS due to chronic pressure overload impairing longitudinal contractility. This impairment is more pronounced in recently symptomatic patients or those with low-flow, low-gradient variants, where myocardial damage tends to be more severe and sometimes irreversible.[4,6,7]

Several studies have demonstrated improvement in LV longitudinal strain following intervention, especially in patients with concentric hypertrophy. Cimino and colleagues evaluated GLS in 68 patients with concentric and eccentric hypertrophy, showing significant improvement in both groups, with the greatest benefit in patients with eccentric hypertrophy.[8] Significant recovery has also been reported in different AS subtypes, particularly in those with greater postoperative valve area and less prosthesis–patient mismatch.[9] However, in low-flow forms, improvement was only partial, suggesting persistent myopathic involvement.[9,10] Winker and colleagues identified an inverse relationship between GLS recovery and survival.[5,11]

Other echocardiographic parameters, such as the E/e ratio, are used to estimate LV filling pressure and evaluate diastolic function.[6] This ratio is derived from the early diastolic mitral inflow velocity (E wave) and early myocardial displacement velocity at the mitral annulus (e′ wave), measured by tissue Doppler imaging.[6,7] Elevated E/e′ values are associated with diastolic dysfunction and increased left atrial pressure.[6]

In the context of aortic stenosis, E/e′ becomes relevant as a marker of diastolic overload. Disease progression induces LVH, reduced myocardial compliance, and impaired relaxation, all of which lead to increased filling pressures reflected by elevated E/e′ values. This underscores the importance of the E/e′ ratio in AS management, highlighting its clinical relevance.[6,7,10]

After aortic valve replacement, whether surgical or transcatheter, diastolic function has been shown to improve, with progressive reductions in E/e′ ratios. E/e′ has not only prognostic value in AS, but its post-procedural changes also allow assessment of ventricular response and prediction of persistent heart failure risk.[7,8,10]

The safety and efficacy of aortic valve replacement for treating AS are well established. However, premature valve replacement may expose patients to unnecessary periprocedural risks by exchanging native valve disease for prosthetic valve degeneration and thrombosis.[6,7,11]

Recent research has examined changes in GLS following TAVR. One study reported early and significant improvement in GLS, from –8.18 ± 1.81 to –14.52 ± 2.52 one month after TAVR, reaching –16.12 ± 2.69 at one year. This early improvement was not observed in SAVR patients, suggesting that TAVR may facilitate more favorable and rapid LV remodeling.[11,12]

Multiple studies have documented structural changes following TAVR. Liedman et al. demonstrated LVH regression one year after valve implantation, quantified by LV mass index.[7,10] Kempny et al. showed improvement in right ventricular function after one year of TAVR. However, there is a lack of studies evaluating early functional and structural changes following valve replacement. For instance, Kashish et al. reported functional class improvement six months after TAVR.[13,14] Therefore, this study aims to describe early GLS changes after valve replacement according to Généreux classification.

Objective: to assess changes in global longitudinal strain and E/e' ratio before and three months after TAVR in patients with severe aortic stenosis, stratified by the Généreux classification.

MATERIAL AND METHODS

This was a descriptive, observational, retrospective, and cross-sectional study conducted at the *Centro Médico Nacional 20 de Noviembre*. We reviewed institutional electronic medical records of patients who underwent Transcatheter Aortic Valve Replacement (TAVR) between 2015 and 2021. To preserve clinical heterogeneity, patients were not excluded based on clinical conditions or comorbidities. Demographic, echocardiographic, and hemodynamic variables were obtained from the institutional records. The variables analyzed included weight, height, age, sex, and echocardiographic parameters such as Left Ventricular Ejection Fraction (LVEF), Global Longitudinal Strain (GLS), and mean transvalvular gradient. Echocardiographic data were collected before the procedure and six months after valve implantation. All echocardiographic measurements were performed in the institution's echocardiography laboratory using a PHILIPS EPIQ 7 system.

Descriptive statistics were used to summarize the study population, including measures of central tendency and variability for continuous variables, as well as proportions for categorical variables. Continuous variables are presented as mean ± standard deviation. For statistical analysis, the χ^2 test or Student's t-test was applied as appropriate for the type of variable. Correlation analyses were performed using Pearson or Spearman tests, depending on the distribution of the data. Statistical significance was defined as a p-value < 0.05. All analyses were performed using GraphPad Prism, version 9.

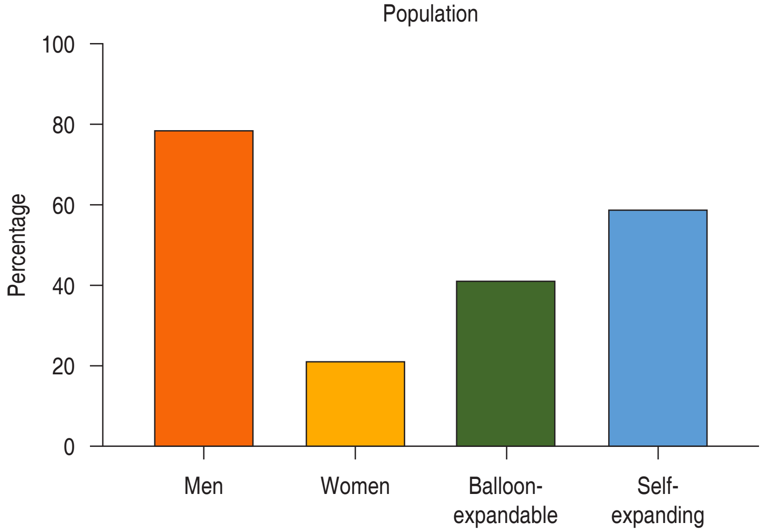

Figure 1: Bar chart showing population distribution by sex and type of transcatheter aortic valve (self-expanding vs balloon-expandable).

RESULTS

A total of 304 patients were analyzed, with a mean age of 75.29 ± 8.19 years; 78.6% (239) were male, and 21.4% (65) were female, with a mean body weight of 69.39 ± 13.88 kg and mean height of 160 ± 9.58 cm. Among the patients, 58.8% (179) received a self-expanding valve, and 41.2% (125) received a balloon-expandable valve. The mean implantation depth was 4.54 ± 0.18 mm *(Figure 1)*.

The pre-TAVR mean transvalvular gradient was 48.32 ± 1.01 mmHg. Three months after valve implantation, the mean transvalvular gradient was 9.93 ± 0.40 mmHg. A correlation analysis was performed between the changes in mean transvalvular gradient (Δ) and GLS (Δ), showing a strong correlation ($r = 0.81$, $p < 0.01$).

Patients were stratified into two groups based on the Généreux classification: those in stages 0, 1, and 2 (mild or minimal cardiac involvement, 36%) and those in stages 3 and 4 (advanced cardiac damage, 64%). GLS was compared before and after TAVR in the group classified as stages 0-2, showing a statistically significant improvement ($p < 0.012$). Similarly, a significant improvement was observed in the group classified as stages 3-4 ($p < 0.002$) *(Figure 2)*.

The E/e ratio was also compared before and after TAVR in both Généreux subgroups. No statistically significant difference was observed

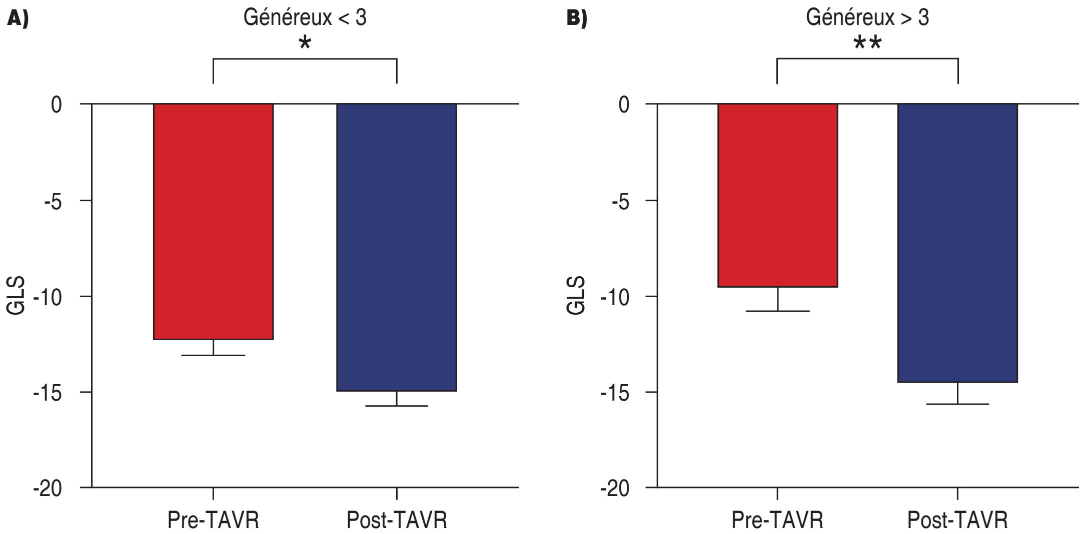

Figure 2: Bar chart of GLS. **A)** Compares GLS before and three months after valve implantation in patients with Généreux classification < 3. **B)** Shows the same comparison in patients classified as Généreux ≥ 3.
GLS = Global Longitudinal Strain. TAVR = Transcatheter Aortic Valve Replacement.
* p< 0.05. ** p < 0.01.

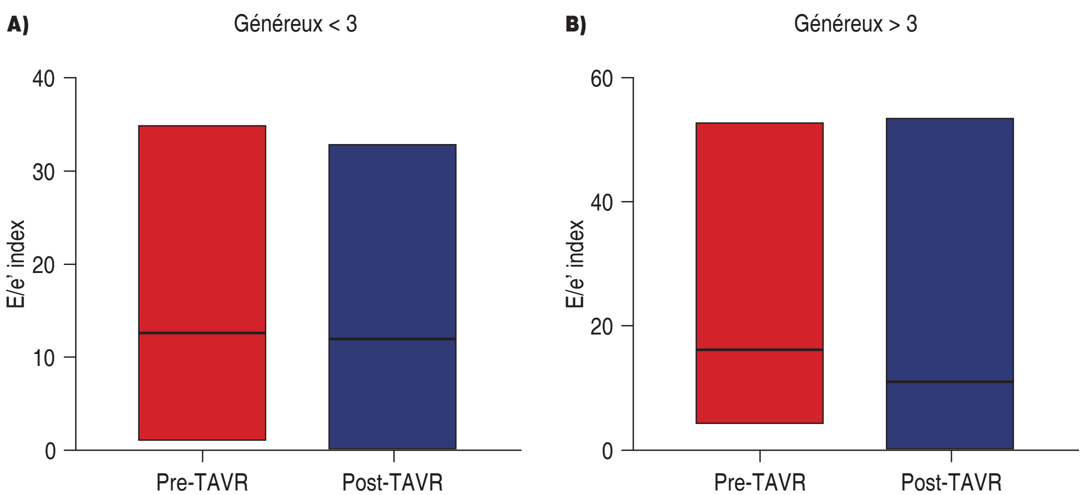

Figure 3: Bar chart of E/e' index. **A)** Shows E/e' before and three months after valve placement in patients with Généreux classification < 3. **B)** Shows the same comparison in patients with Généreux classification ≥ 3.
TAVR = Transcatheter Aortic Valve Replacement.

in patients classified as stage 0-2 (p = 0.19) or stage 3-4 (p = 0.26) *(Figure 3)*.

DISCUSSION

This study analyzed a cohort of 304 patients who underwent TAVR, with a mean age of 75.29 ± 8.19 years, predominantly male (78.6%). The distribution of implanted valve types showed a slight predominance of self-expanding valves (58.8%) over balloon-expandable valves (41.2%). The mean implantation depth was 4.54 ± 0.18 mm, with no reported differences between groups.

To evaluate the presence and progression of myocardial structural damage, patients were stratified using the Généreux classification into groups: those with mild or minimal changes (stages 0-2) and those with advanced changes (stages 3-4). A significant improvement in Global Longitudinal Strain (GLS) was observed after TAVR in both groups, with statistically significant differences in both the less affected myocardial group ($p < 0.012$) and the more structurally compromised group ($p < 0.002$). These findings suggest that TAVR has a positive effect on overall myocardial function, regardless of the degree of pre-existing damage.[4,6,10]

However, analysis of left ventricular filling pressure through the E/e′ index showed no significant differences in either subgroup ($p = 0.19$ for stages 0-2; $p = 0.26$ for stages 3-4). These results indicate that LV filling pressure does not significantly change within three months after TAVR despite improvements in myocardial strain. Furthermore, the lack of statistically significant changes in E/e′ suggests that the observed GLS improvements are unlikely to be directly related to hemodynamic alterations from the valve replacement itself.[6,8]

The findings of this study reinforce the utility of TAVR in improving myocardial function in patients with severe AS, including those with advanced myocardial disease. However, the absence of improvement in diastolic filling parameters highlights the need for additional studies to evaluate the long-term impact of TAVR on diastolic dysfunction and post-procedural ventricular remodeling.[4,6] Future research should also explore the influence of valve type on postoperative hemodynamic changes.

This study is among the first to investigate early changes in ventricular function following valve replacement. Including a large group of patients allows for a comprehensive evaluation of the impact of transcatheter aortic valve replacement on myocardial function. However, additional long-term research is needed to examine the effects of factors such as comorbidities, the initial health of patients, and post-procedural monitoring. Future investigations will be fundamental in establishing the long-term sustainability of the observed myocardial function improvements and delineating the relationship between systolic function recovery and diastolic functional changes.

CONCLUSION

TAVR significantly improves GLS at three months after valve implantation. Our findings confirm the favorable hemodynamic impact of the procedure and demonstrate an early recovery in myocardial contractility, as reflected by improved GLS independent of EF. Notably, when stratifying patients according to the Généreux classification, those in stage 3 or higher (indicating more advanced extra-valvular cardiac damage) showed more significant improvement in GLS than those in earlier stages. This finding highlights the utility of the Généreux classification not only as a prognostic tool but also as a potential indicator of myocardial recovery following TAVR. Unlike prior studies by Généreux, Kempny, and Liedman, which focused on longer-term structural regression, our results provide evidence of early left ventricular contractility response, suggesting that TAVR may trigger functional remodeling processes from early stages — even in patients with advanced extra-valvular involvement.

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