

## Original article

## Tricuspid but not Mitral Regurgitation Determines Mortality After TAVI in Patients With Nonsevere Mitral Regurgitation



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## ABSTRACT

**Introduction and objectives:** Many patients undergoing transcatheter aortic valve implantation (TAVI) have concomitant mitral regurgitation (MR) of moderate grade or less. The impact of coexistent tricuspid regurgitation (TR) remains to be determined. We sought to analyze the impact of moderate vs none-to-mild MR and its trend after TAVI, as well as the impact of concomitant TR and its interaction with MR. **Methods:** Multicenter retrospective study of 813 TAVI patients treated through the transfemoral approach with MR  $\leq 2$  between 2007 and 2015.

**Results:** The mean age was  $81 \pm 7$  years and the mean Society of Thoracic Surgeons score was  $6.9 \pm 5.1$ . Moderate MR was present in 37.3% of the patients, with similar in-hospital outcomes and 6-month follow-up mortality to those with MR  $< 2$  (11.9% vs 9.4%;  $P = .257$ ). However, they experienced more rehospitalizations and worse New York Heart Association class ( $P = .008$  and  $.001$ , respectively). Few patients (3.8%) showed an increase in the MR grade to  $> 2$  post-TAVI. The presence of concomitant moderate/severe TR was associated with in-hospital and follow-up mortality rates of 13% and 34.1%, respectively, regardless of MR grade. Moderate-severe TR was independently associated with mortality (HR, 18.4; 95%CI, 10.2–33.3;  $P < .001$ ).

**Conclusions:** The presence of moderate MR seemed not to impact short- and mid-term mortality post-TAVI, but was associated with more rehospitalizations. The presence of moderate or severe TR was associated with higher mortality. This suggests that a thorough evaluation of the mechanisms underlying concomitant mitral and tricuspid valve regurgitation should be performed to determine the best strategy for avoiding TAVI-related futility.

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### La insuficiencia tricúspide, y no la insuficiencia mitral, determina la mortalidad en pacientes que presentan insuficiencia mitral no grave previa a TAVI

## RESUMEN

**Introducción y objetivos:** Muchos pacientes sometidos a implante percutáneo de válvula aórtica (TAVI) presentan insuficiencia mitral (IM) de grado moderado o menor. El impacto de la insuficiencia tricuspídea (IT) sigue sin resolverse. Se analiza el impacto de la IM moderada frente a leve-ausente y su evolución, y de la IT concomitante y su interacción con la IM.

**Métodos:** Estudio retrospectivo multicéntrico de 813 pacientes tratados con TAVI entre 2007 y 2015 con IM  $\leq 2$  y abordaje transfemoral.

**Resultados:** La edad media fue  $81 \pm 7$  años y el *Society of Thoracic Surgeons-score* fue de  $6,9 \pm 5,1$ . El 37,3% presentó IM moderada, con resultados comparables intrahospitalarios y de mortalidad a 6 meses frente a IM  $< 2$  (11,9 frente a 9,4%;  $p = 0,257$ ). Sin embargo, experimentaron más rehospitalizaciones y peor clase de la *New York Heart Association* ( $p = 0,008$  y  $0,001$ , respectivamente). Solo un 3,8% demostró un aumento en el grado de IM  $> 2$  tras el TAVI. La presencia de IT moderada/grave se asoció con una mortalidad

## Palabras clave:

Insuficiencia mitral

Insuficiencia tricuspídea

Implante percutáneo de válvula aórtica

Enfermedad multivalvular

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intrahospitalaria y de seguimiento del 13 y el 34,1%, independientemente del grado de IM. La IT moderada-grave fue predictor independiente de mortalidad (HR = 18,4; IC95%, 10,2-33,3;  $p < 0,001$ ).

**Conclusiones:** La presencia de IM moderada no supuso mayor mortalidad a corto-medio plazo tras el TAVI, pero asoció más rehospitalizaciones. La presencia de IT moderada/grave implicó mayor mortalidad. Esto sugiere que una evaluación minuciosa de los mecanismos subyacentes entre ambas insuficiencias valvulares debe realizarse para determinar la mejor estrategia para evitar la futilidad relacionada con TAVI.

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## Abbreviations

MR: mitral regurgitation  
 PHT: pulmonary hypertension  
 TAVI: transcatheter aortic valve implantation  
 TR: tricuspid regurgitation

## INTRODUCTION

Aortic stenosis is the most frequently treated heart valve disease in our society, followed by mitral regurgitation (MR).<sup>1</sup> Double valve replacement may cause up to a 5-fold increase in risk for cardiac surgery compared with single valve replacement, which has limited the surgical management of dual-valve disease to less than 30% of the patients with these conditions.<sup>2</sup> This is despite the recommendation for double valve intervention by clinical practice guidelines if both valves are severely diseased.<sup>3,4</sup> Transcatheter aortic valve implantation has emerged as an alternative treatment strategy for patients with multivalvular disease, but the impact of significant concomitant MR has received limited evaluation in the main TAVI trials.<sup>5,6</sup> Several studies, however, have suggested heightened mortality when significant MR persists following TAVI.<sup>7–10</sup>

In many patients undergoing TAVI, concomitant MR—when present—is usually of mild-to-moderate severity. There is a paucity of data on the implications of coexistent MR of varying severity in the post-TAVI population, which may be present in up to 70% of these patients. Additionally, although some studies have assessed the impact of tricuspid regurgitation (TR) and pulmonary hypertension (PHT) post-TAVI,<sup>11–15</sup> the role played by right-heart hemodynamics in the outcomes of concomitant nonsignificant mitral disease is currently unknown. A better understanding of the interplay between dual-valve (and dual-sided) disease could shed further light on TAVI-related outcomes, including TAVI-related futility, which ultimately could impact decision-making strategies for such patients, while also raising further speculation on alternative percutaneous treatment strategies. The aim of this study was: *a*) to analyze the clinical impact of moderate vs none-to-mild MR and its variations following TAVI; and *b*) to determine the impact of concomitant TR in TAVI recipients with no, mild, or moderate MR.

## METHODS

### Study Population

Between August 2007 and January 2015, 1110 consecutive patients underwent TAVI in 6 different centers. The effect of moderate (3+) and severe (4+) MR has previously been reported in this study cohort.<sup>8</sup> In the present analysis, we included 813 patients without prior mitral prostheses, with moderate (grade 2) MR severity or less with severe aortic stenosis. Only patients treated via the transfemoral approach were included. All patients were

previously accepted for TAVI by a multidisciplinary team and subsequently each patient was evaluated to determine the most appropriate valve type/size and approach. Finally, clinical outcomes according to Valve Academic Research Consortium 2 (VARC-2) criteria were evaluated at each clinical visit.<sup>16</sup>

### Imaging Evaluation

All patients underwent complete 2-dimensional and color-Doppler echocardiography at baseline, before discharge, and at 1- and 6-months post-TAVI. All images were digitally stored. Off-line retrospective analysis of the grade and etiology of MR and TR was performed by an experienced echocardiographer blinded to further data of the post-TAVI outcomes. Other parameters included left ventricular indices (end-diastolic and end-systolic diameters, left ventricular ejection fraction obtained by biplane Simpson's method), determination of the organic or functional/ischemic origin of the MR, mitral and aortic annular diameters, tenting height and area when indicated, and pulmonary artery systolic pressure. Baseline measurements were graded following the recommendations of the European Association of Echocardiography.<sup>17</sup>

Tricuspid regurgitation and MR grade were assessed following the European and American Guidelines on Echocardiography<sup>3,4</sup> and accordingly classified as follows: 0 (none), 1+ (mild), 2+ (nonsignificant moderate), 3+ (significant moderate), and 4+ (severe). Patients were classified into 2 groups according to the grade of baseline MR following the same guidelines<sup>3,4</sup>: *a*) none or mild (0 and 1+), and *b*) nonsignificant moderate MR (2+). Patients with significant moderate (3+) or severe MR (4+) were excluded from this study. For statistical purposes, any decrease of 1 or more grades was considered an improvement of the MR. Pulmonary artery systolic pressure was estimated by echocardiography as previously described elsewhere<sup>3</sup> and the remaining echocardiographic parameters, including assessment of the function of other valves and the left ventricle, followed the recommendations of scientific societies.<sup>3,4</sup>

### Statistical Analysis

Data are expressed as absolute frequency and percentage for qualitative variables. Quantitative variables are described as mean  $\pm$  standard deviation or median (25th–75th interquartile range) depending on their distribution. Group comparisons according to the grade and improvement of MR were analyzed using the Student *t* test or its nonparametric equivalent, the Mann-Whitney *U* test for continuous variables, and the chi-square test or Fisher exact test for categorical variables. Statistical significance was defined as a *P* value  $< .05$ . Multivariate analysis was performed to determine independent predictors of 6-month overall mortality. Survival curves for 6-month overall and cardiac mortality were compared using a log rank test according to the MR grade and as affected by the TR for each grade.

All analyses were conducted using the statistical package IBM SPSS Statistics, version 20.0.

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