

CASE SERIES

# Subclinical Right Ventricular Dysfunction in Patients with Severe Aortic Stenosis: A Retrospective Case Series

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## ABSTRACT

**Introduction:** There is scarce information about right ventricle (RV) function in patients with secondary pulmonary hypertension (PH) undergoing transcatheter aortic valve implantation (TAVI). We aim to identify possible RV abnormalities in patients referred for TAVI with severe aortic stenosis (sAS) and secondary PH.

**Methods:** Objective measures of RV function, as well as noninvasive estimates of pulmonary artery systolic pressures (PASP) were obtained from 30 sAS patients undergoing percutaneous valve intervention.

**Results:** Sixteen (53%) evaluated patients had some degree of PH. As expected, left ventricular mass index ( $281 \pm 75 \text{ g/m}^2$ ) and left atrial volume index ( $89 \pm 23 \text{ mL/m}^2$ ) values were significantly elevated. Even though RV end-systolic ( $8 \pm 4 \text{ cm}^2$ ) and end-diastolic ( $17 \pm 4 \text{ cm}^2$ ) areas were normal as well as RV fractional area

change values ( $57 \pm 16\%$ ); both longitudinal measures of RV systolic function such as tricuspid annular plane systolic excursion ( $1.9 \pm 0.5 \text{ cm}$ ) and systolic velocity ( $10 \pm 2 \text{ cm/s}$ ) were clearly reduced with just mild elevations in PASP ( $54 \pm 7 \text{ mmHg}$ ).

**Conclusions:** Subclinical RV dysfunction is present in patients with sAS and secondary PH undergoing TAVI. Whether longitudinal measures of RV systolic function could predict clinical outcomes in these patients needs to be further explored.

**Keywords:** Echocardiography; Pulmonary hypertension; Severe aortic stenosis; Subclinical right ventricular dysfunction

## INTRODUCTION

Improved survival of the population has raised our attention to degenerative calcified aortic stenosis (AS), the most common form of acquired valvular heart disease in the Western world. Depending on the source, from 3% to 7% of patients older than 65 years of age has a moderate to severe degree of AS; a prevalence that is projected to increase with aging of the population [1].

Since symptomatic severe AS is lethal with high 2-year mortality, surgical aortic valve replacement has been traditionally offered to these patients in order to improve survival.

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However, up to 50% of patients with symptomatic AS are usually not referred to a surgeon due to the presence of significant comorbidities [2]. Moreover, older age and left ventricular dysfunction have been reported as additional reasons for which patients were denied surgery rather than their associated comorbidities.

The advent of transcatheter aortic valve implantation (TAVI) procedures has broadened the opportunity to many patients to undergo this intervention if considered at high risk for traditional surgical replacement. In a recent review, surgery for AS and TAVI were compared and TAVI was found to have similar or better early and midterm outcomes for adults with AS, including those at low to intermediate risk [3]. Therefore, it is important to characterize better these patients in order to determine which patients would benefit the most.

Most recently, right ventricular (RV) dilatation has been associated with postoperative outcomes in patients undergoing TAVI. Furthermore, in inoperable AS patients treated with TAVI, the presence of moderate or severe tricuspid regurgitation and RV dilatation have been independently associated with increased 1-year mortality [4]. Finally, the presence of secondary pulmonary hypertension (PH) and RV failure in AS patients has been also associated with an increased perioperative risk [5].

There is paucity of data regarding RV function in patients with severe AS and mild degrees of secondary PH being considered for possible TAVI. We, therefore, examined patients referred for TAVI to describe RV echocardiographic measurements to determine possible RV abnormalities in the presence of PH secondary to severe AS (sAS).

## METHODS

In this retrospective case series, echocardiographic data from patients with sAS and preserved left ventricular systolic function from 2009 through 2011 were collected. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

The University of Cincinnati College of Medicine Institutional Review Board Committee approved data collection for this study.

Inclusion criteria required that all patients at the time of the echocardiographic study were in normal sinus rhythm. In addition, there had to be good visualization of the left and right ventricular endocardium for tracing of end diastolic and systolic cavity. Patients with atrial fibrillation or rhythm abnormalities, mitral annular calcification, mitral valve stenosis, or previous valvular replacement surgery were excluded.

Two-dimensional echocardiographic studies were performed using commercially available systems (Vivid 7 and 9; GE Medical Systems, Milwaukee, WI, USA). The following echocardiographic parameters were measured: (A) aortic valve gradient and aortic dimensional index; (B) pulmonary artery systolic pressure (PASP); (C) LV ejection fraction, mass index, as well as end-systolic and end-diastolic volumes; (D) Left atrial volume index; (E) RV fractional area change, systolic velocity, end-systolic and end-diastolic area; (F) tricuspid annular plane systolic excursion (TAPSE), TA tissue Doppler systolic velocity (TA TDI s'), maximum tricuspid regurgitation velocity and right atrial pressure. The commercially available software Merge Cardio Workstation (Merge Healthcare) was used to calculate all echocardiographic measurements determined by a single observer. Categorical data are presented as frequencies and continuous data are presented as mean  $\pm$  standard deviation.

## RESULTS

In this preliminary study, a complete transthoracic echocardiogram with adequate left and right endocardial border resolution to allow determination of end systolic and diastolic measurements as well as TA-motion with M-mode and tissue Doppler of tricuspid valve and inferior vena cava were performed in 30 patients [mean age  $82 \pm 11$  years, 12 men (40%)] with severe aortic stenosis. Ninety-seven percent of the study population were older than 65 years. After evaluating PASP

measurements, we found that 16 (53%) individuals had PH.

Echocardiographic parameters of PH patients are listed in Table 1. The mean aortic valve gradient of the studied population was  $56 \pm 20$  mmHg and the dimensional index was  $0.2 \pm 0.1$ . As expected, in this sAS patient population both left ventricular mass index ( $281 \pm 75$  g/m<sup>2</sup>) and left atrial volume index ( $89 \pm 23$  mL/m<sup>2</sup>) values were significantly elevated. RV end systolic ( $8 \pm 4$  cm<sup>2</sup>) and end diastolic ( $17 \pm 4$  cm<sup>2</sup>) areas, as well as RV fractional area change values were within the normal range ( $57\% \pm 16\%$ ). However, longitudinal measures of RV systolic function such as tricuspid annular plane systolic excursion ( $1.9 \pm 0.5$  cm) and TA TDI s' ( $10 \pm 2$  cm/s) were clearly reduced with just mild elevations in PASP ( $54 \pm 7$  mmHg).

## DISCUSSION

These preliminary results appear to suggest that subclinical RV dysfunction is present in sAS patients with mild degrees of PH, which is clinically critical considering that PH is not only an independent predictor of late TAVI mortality [6], but also increases operative mortality while reducing long-term survival [7]. Furthermore, subclinical RV dysfunction has been identified as an adverse predictor of clinical outcomes in PH patients [8].

The prevalence of severe pulmonary hypertension in patients with severe aortic valve stenosis has been reported as high as 29% using invasive hemodynamic monitoring prior to surgical aortic valve replacement (SAVR) [9]. Recent data from Barbash et al., showed that pulmonary hypertension was a frequent co-morbidity found

**Table 1** Echocardiographic data of the study population

Variables	Mean value ( $\pm$ SD)	Range
Aortic valve gradient (mmHg)	56 (20)	28–99
Aortic dimensional index	0.2 (0.1)	0.1–0.3
PASP (mmHg)	54 (7)	45–66
LVEF (%)	66 (19)	32–92
LV-end systolic volume (cm <sup>3</sup> )	37 (31)	5–102
LV-end diastolic volume (cm <sup>3</sup> )	100 (43)	45–192
LV mass index (g/m <sup>2</sup> )	281 (75)	175–437
LA volume index (ml/m <sup>2</sup> )	89 (23)	46–130
RV-end systolic area (cm <sup>2</sup> )	8 (4)	4–19
RV-end diastolic area (cm <sup>2</sup> )	17 (4)	11–27
RV fractional area change (%)	57 (16)	29–79
TAPSE (cm)	1.9 (0.5)	1.1–2.6
TA TDI s' (cm/s)	10 (2)	6–13
MaxTR (cm/s)	3.3 (0.2)	3.0–3.8
RAP (mmHg)	11 (3)	10–19

*PASP* pulmonary artery systolic pressure, *LV* left ventricle, *LA* left atrium, *RV* right ventricle, *TAPSE* tricuspid annular plane systolic excursion, *TA TDI s'* tricuspid annular tissue Doppler imaging systolic velocity, *MaxTR* maximum tricuspid regurgitation velocity, *RAP* right atrial pressure

in patients with severe aortic stenosis referred for TAVR. In addition, these investigators found that significantly elevated pulmonary artery pressures at baseline was a poor prognostic factor when performing preprocedural assessment of the patients [10]. The prevalence of PH in our case series (56%) was higher than previously published by these authors.

Musa and collaborators have recently explored the impact of TAVI and SAVR upon RV function in patients with sAS using cardiovascular magnetic resonance [11]. Interestingly, they found that TAVI had no adverse impact on RV function and volume. Unfortunately, we lack post-TAVI echocardiographic information for most of patients included in our study. Nevertheless, further studies are encouraged to determine whether or not TAVI has any adverse beneficial impact upon right ventricular echocardiographic parameters.

Even though there have been some variations in terms of what is expected as normal with regards to longitudinal measures of RV systolic function, our laboratory has consistently shown the linear relationship between these measures and RV fractional area change. In prior reported studies, a TAPSE >2 cm and a TD TDI  $s'$  >12 cm/s correlated with a RV fractional area change >55% [12, 13].

Some limitations need to be acknowledged in our study. First, this is a retrospective case series study; however, the main goal was met. Second, there was only a small number of patients included for analysis. Third, the original database missed important data, such as strain imaging and invasive hemodynamic information. Furthermore, based on the pre-specified exclusion criteria no assumptions can be made on how atrial fibrillation or rhythm abnormalities, mitral annular calcification, mitral valve stenosis, or prior valvular replacement surgery could affect the reliability of our study findings.

## CONCLUSION

Reductions in longitudinal measures of RV systolic function suggestive of subclinical RV dys-

function could affect clinical outcomes in sAS patients, despite normal reference standard values for RV size and fractional area change in mild degrees of PH. Additional studies are now required to determine whether subclinical RV dysfunction in sAS patients with mild PH undergoing TAVI might not only be an indirect measurement of AS severity, but also an important tool in predicting overall clinical outcomes.

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**Disclosures.** Dagmar F. Hernandez-Suarez and Angel López-Candales have nothing to declare.

**Compliance with ethics guidelines.** This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors. The University of Cincinnati, College of Medicine Institutional Review Board Committee approved data collection for this study.

**Data availability.** The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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