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Systemic Vascular Load in Calcific Degenerative Aortic Valve Stenosis

Insight From Percutaneous Valve Replacement

Raquel Yotti, MD, PhD,* Javier Bermejo, MD, PhD,* Enrique Gutiérrez-Ibañes, MD,* Candelas Pérez del Villar, MD,* Teresa Mombiela, MD,* Jaime Elízaga, MD, PhD,* Yolanda Benito, DCS, DVM,* Ana González-Mansilla, MD, PhD,* Alicia Barrio, DCS, MBIOL,* Daniel Rodríguez-Pérez, PhD,† Pablo Martínez-Legazpi, MENG, PhD,‡ Francisco Fernández-Avilés, MD, PhD*

ABSTRACT

BACKGROUND Systemic arterial load impacts the symptomatic status and outcome of patients with calcific degenerative aortic stenosis (AS). However, assessing vascular properties is challenging because the arterial tree's behavior could be influenced by the valvular obstruction.

OBJECTIVES This study sought to characterize the interaction between valvular and vascular functions in patients with AS by using transcatheter aortic valve replacement (TAVR) as a clinical model of isolated intervention.

METHODS Aortic pressure and flow were measured simultaneously using high-fidelity sensors in 23 patients (mean 79 ± 7 years of age) before and after TAVR. Blood pressure and clinical response were registered at 6-month follow-up.

RESULTS Systolic and pulse arterial pressures, as well as indices of vascular function (vascular resistance, aortic input impedance, compliance, and arterial elastance), were significantly modified by TAVR, exhibiting stiffer vascular behavior post-intervention (all, $p < 0.05$). Peak left ventricular pressure decreased after TAVR (186 ± 36 mm Hg vs. 162 ± 23 mm Hg, respectively; $p = 0.003$) but remained at >140 mm Hg in 70% of patients. Wave intensity analysis showed abnormally low forward and backward compression waves at baseline, increasing significantly after TAVR. Stroke volume decreased (−21 ± 19%; $p < 0.001$) and correlated with continuous and pulsatile indices of arterial load. In the 48 h following TAVR, a hypertensive response was observed in 12 patients (52%), and after 6-month follow-up, 5 patients required further intensification of discharge antihypertensive therapy.

CONCLUSIONS Vascular function in calcific degenerative AS is conditioned by the upstream valvular obstruction that dampens forward and backward compression waves in the arterial tree. An increase in vascular load after TAVR limits the procedure's acute afterload relief. (J Am Coll Cardiol 2015;65:423–33) © 2015 by the American College of Cardiology Foundation. Open access under CC BY-NC-ND license.

Calcific degenerative aortic valve stenosis (AS) has become endemic in Western countries. For a given degree of valve obstruction, systemic arterial properties may impact the symptomatic status and outcome of these patients (1–3). In AS, left ventricular (LV) afterload is abnormally high because concentric remodeling and hypertrophy are insufficient to compensate for the

From the *Department of Cardiology, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, and Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain; †Department of Mathematical Physics and Fluids, Facultad de Ciencias, Universidad Nacional de Educación a Distancia, Madrid, Spain; and the ‡Mechanical and Aerospace Engineering Department, University of California San Diego, San Diego, California. This study was supported by Instituto de Salud Carlos III, Ministerio de Economía y Competitividad, Spain, grants PIS09/02602, PIS012/02878, RD12/0042, CM12/00273 (to Dr. Perez del Villar), and CM11/00221 (to Dr. Mombiela). Drs. Mombiela, González-Mansilla, and del Villar were partially supported by grants from the Fundación para Investigación Biomédica Gregorio Marañón, Spain. Dr. Martínez-Legazpi was supported by U.S. National Institutes of Health grant 1R21 HL108268-01. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. This work was presented in part at the Scientific Sessions of the American Heart Association, 2012, Los Angeles, California, November 4 to 7; abstract A15474.
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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

BCW = backward compression wave

C = compliance

E_a = systemic arterial elastance

FCW = forward compression wave

SVI = stroke volume index

TAVR = transcatheter aortic valve replacement

WIA = wave intensity analysis

Z = impedance

Z_c = characteristic impedance

additive effects of valvular obstruction and vascular load (4). Thus, vascular stiffness may be a source of LV systolic and diastolic dysfunctions in patients with moderate degrees of valve obstruction (3). This mechanism helps explain abnormally high morbidity and mortality rates in patients with AS for whom classical obstruction indices fail to predict outcomes (2).

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Characterizing intrinsic properties of the arterial tree remains particularly challenging in AS because of the difficulties of uncoupling valvular and vascular functions in vivo (5). Acute and chronic interventions on either compartment cause reciprocal changes in the other. For instance, changes in vascular resistance caused by vasodilators (6,7) and exercise (8) induce significant modifications in valve hemodynamics. Likewise, valve interventions may acutely impact arterial function (9).

Although attempts have been made to quantify vascular load in AS noninvasively (2,4), a rigorous quantification of arterial hemodynamics entails simultaneous measurements of central aortic pressure and flow (10). Use of this invasive approach in a small number of subjects has suggested that steady and pulsatile loads are increased in symptomatic degenerative calcific AS, particularly during exercise (8). However, measurements of vascular load might be conditioned by upstream valvular obstruction.

This study was designed to characterize the interaction between valvular and vascular function in patients with calcific degenerative AS. We hypothesized that transcatheter aortic valve replacement (TAVR) offers a useful clinical model of isolated valvular intervention to unmask underlying valvular-vascular interactions of AS. Therefore, we analyzed the acute changes induced by TAVR to understand how valve obstruction impacts vascular function, using state-of-the-art methods, including frequency domain and wave intensity analyses (WIA) of high-fidelity data.

METHODS

STUDY POPULATION. We studied 23 consecutive patients with severe symptomatic calcific degenerative AS undergoing TAVR (**Table 1**). Patients were either in sinus rhythm or permanent right ventricular (RV) pacing (n = 3). No patient had significant aortic regurgitation (AR), and 7 patients had an ejection fraction of ≤45%. Low-gradient AS (mean: <40 mm Hg) was present in 9 patients and concomitant low-flow (stroke volume [SV] index of <35 ml/m^2) in 3 patients. Sixteen patients (74%) had a pre-procedural diagnosis of hypertension requiring pharmacotherapy. Antihypertensive agents were withheld 12 h before the procedure. After TAVR, patients were initially kept on their pre-procedural antihypertensive therapy. The local Institutional Review Board approved the study protocol and all subjects provided written informed consent.

TABLE 1 Baseline Clinical and Demographic Data (N = 23)

Age, yrs	79 ± 7
Female	11 (47)
Body surface area, m^2	1.68 ± 0.15
NYHA functional class III or IV	9 (39)
Logistic EuroSCORE	10 ± 7
Coronary heart disease	10 (43)
Chronic kidney disease	7 (30)
Mitral regurgitation (grade > mild)	7 (30)
Cardiovascular risk factors	
Hypertension	17 (74)
Diabetes	11 (48)
Dyslipidemia	12 (52)
Smoking	4 (17)
Taking cardiovascular treatment	
ACEIs/ARBs	17 (74)
Diuretics	17 (73)
Beta-blockers	9 (39)
Aldosterone receptor antagonists	4 (17)
Calcium antagonists	2 (9)
Nitrates	1 (4)
Statins	14 (61)

Values are mean ± SD or n (%).

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association.

STUDY PROTOCOL AND FOLLOW-UP. Procedures were performed using the femoral approach under local anesthesia and conscious sedation with low doses of midazolam (2 to 5 mg, intravenous) and fentanyl (2 μg/kg, intravenous); additional boluses (1 mg and 50 μg, respectively) were used if necessary to maintain patient comfort during the procedure. Special care was taken to ensure a constant level of sedation during pre- and post-procedural measurements. A pacing wire and a thermodilution Swan-Ganz catheter were placed in the RV and in the main pulmonary artery, respectively. The self-expanding valve (Corevalve, Medtronic, Inc., Minneapolis, Minnesota) transfemoral implantation procedure (11) was successful in all patients. Mild residual AR was present in 10 patients (grade 1 in 9 patients and grade 2 in 1 patient). Aortic and LV pressures were simultaneously recorded before and after TAVR, using