tumor growth and metastasis. One of the mechanisms by which PSIs exert their antineoplastic effect is by reducing VEGFC expression and reducing endothelial cell sensitivity to this factor. The results of this study indicate that determination of the level of VEGFC gene expression in tumor tissue from patients who have developed cancer after HTx could help identify those with a potentially better response to the antineoplastic effects of PSIs, which would facilitate decision-making on the choice of immuno-suppressive regimen to prescribe. More studies are needed to corroborate these findings.

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Concomitant or Staged Transcatheter Treatment for Severe Combined Aortic and Mitral Valve Disease

Tratamiento percutáneo simultáneo o secuencial de la valvulopatía aórtica y mitral grave combinada

To the Editor,

Aortic stenosis (AS) and mitral regurgitation (MR) are the most prevalent valvular heart diseases in Western countries.1 The rate of concomitant significant MR in patients with severe AS ranges between 2% and 33%.2 Double-valve surgery has been associated with higher morbidity and mortality compared with isolated surgical aortic valve surgery, especially in elderly patients.3 However, this approach remains the standard of care for patients with combined mitral-aortic valve disease.

Transcatheter aortic valve replacement (TAVR) and transcatheter mitral valve repair, particularly edge-to-edge repair with the MitraClip device (Abbott Vascular, Inc. Santa Clara, CA, United States) have emerged as a treatment option for patients deemed inoperable or at high surgical risk. The combination of the 2 transcatheter therapies would appear to be a viable approach for managing high-risk patients with concomitant AS and MR. This systematic review seeks to analyze the safety and feasibility of combined transcatheter mitral-aortic valve treatment.

A comprehensive, systematic review was performed of published data in the English language describing double-valve (aortic and mitral) transcatheter therapy. A computerized search was conducted to identify all relevant studies from the PubMed, EMBASE, and Google Scholar databases using the following terms: “TAVR”, “TAVI”, “transcatheter/percutaneous aortic valve”, “transcatheter/percutaneous aortic valve replacement/implantation”, “transcatheter/percutaneous mitral valve repair”, “MitraClip”, and “transcatheter/percutaneous double-valve treatment/intervention”.

A total of 10 articles (Table of the supplementary material) describing 33 patients (mean age 79 ± 3 years, 69.7% male) were included. Baseline clinical characteristics and echocardiographic data are summarized in the Table. All patients were considered to be inoperable or at high risk for surgery. The indication for transcatheter aortic valve replacement was predominantly severe native AS, whereas 4 (12.1%) patients underwent TAVR to treat a degenerated surgical bioprosthesis. Moderate-to-severe MR was present before TAVR in all but 1 patient, who had an iatrogenic mitral chord rupture during TAVR, resulting in severe MR.

The procedural details and in-hospital outcomes are described in Table. Transcatheter mitral valve repair was performed using the MitraClip system in all patients. Transcatheter aortic valve replacement was performed before the MitraClip procedure in 29 patients (87.9%); 27 of them were discharged after TAVR and had the MitraClip procedure at a mean of 172 ± 344 days post-TAVR. In 3 patients (9.0%), both valves were treated during the same intervention. Only 1 patient (3.0%) underwent MitraClip implantation before the TAVR procedure. Mitral regurgitation was significantly
Table
Baseline, Procedural Characteristics, In-hospital and Follow-up Outcomes

<table>
<thead>
<tr>
<th>Baseline clinical characteristics</th>
<th>N = 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>79.4 ± 3.1</td>
</tr>
<tr>
<td>Male</td>
<td>23/33 (69.7)</td>
</tr>
<tr>
<td>NYHA class III-IV</td>
<td>28/29 (96.6)</td>
</tr>
<tr>
<td>Logistic EuroSCORE, %</td>
<td>27.0 ± 13.0</td>
</tr>
<tr>
<td>STS score, %</td>
<td>8.7 ± 6.9</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>15/33 (45.5)</td>
</tr>
<tr>
<td>Prior surgical AVR</td>
<td>4/33 (12.1)</td>
</tr>
</tbody>
</table>

Baseline echocardiography
- LVET, %: 39.8 ± 7.0
- Mean aortic valve gradient, mmHg: 42.7 ± 19.5
- Aortic valve area, mm²: 0.72 ± 0.15
- Functional mitral regurgitation: 13/30 (43.3)

Procedural characteristics
- TAVR before MitraClip: 29/33 (87.9)
- Simultaneous TAVR and MitraClip: 3/33 (9.1)
- TAVR after MitraClip: 1/33 (3.0)
- Mean time between procedures, d: 172 ± 344

TAVR
- Device success: 32/33 (97.0)
- Balloon expandable valve: 14/32 (43.7)
- Transfemoral approach: 22/33 (67.9)
- Valve-in-valve: 4/33 (12.1)

Procedural complications
- Need for permanent pacemaker implantation: 8/33 (24.2)
- Need for second valve implantation: 1/33 (3.0)
- Mitral chord injury: 1/33 (3.0)
- Acute kidney injury not requiring hemodialysis: 1/33 (3.0)

Transcatheter mitral valve repair (MitraClip)
- Technical success: 28/30 (93.3)
- Length of hospital stay, days: 5 ± 1
- ≥ 2+ MR post-MitraClip: 7/19 (36.9)

Procedural complications
- Cardiac tamponade: 1/33 (3.0)
- Clip embolization: 0/33 (0)
- Minor bleeding from access side: 1/33 (3.0)
- Transfusion (≥ 1 blood units): 1/33 (3.0)
- Length of hospital stay, d: 5 ± 1

In-hospital outcomes
- Patients with any complication: 11/33 (33)
- In-hospital MACE (death, MI, stroke): 3/33 (9.1)
- Death: 2/33 (6)
- Major stroke: 1/33 (3)
- Myocardial infarction: 0/33 (0)
- Conversion to open heart surgery: 1/33 (3.0)

Follow-up
- Follow-up, d (range): 179.4 (14-390)
- NYHA class at last follow-up ≥ III: 7/27 (25.9)
- Rehospitalization: 5/33 (15.2)
- 6-month mortality: 4/27 (14.8)

AVR, aortic valve replacement; CABG, coronary artery bypass graft; LAA, left atrial appendage; LVET, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; MR, mitral regurgitation; NYHA, New York Heart Association; TAVR, transcatheter aortic valve replacement; STS, Society of Thoracic Surgeons.

According to Mitral Valve Academic Research Consortiums endpoint definitions (MR reduced by at least 1 class or grade from baseline and to no more than moderate [2+] in severity).

This patient required transfusion of 2 blood units.

Patients died 21 and 69 days after second procedure, respectively.

Data available in all patients.

Data from 6 months of follow-up are available for 27 patients (17, 21, 50, and 69 days). Another patient died 419 days after MitraClip repair.

Reduced in most patients, achieving MR grade ≤ 2+ in 28 out of 30 (93.3%) after the procedure.

Follow-up information (ranging from 14 days to 390 days) was available in the 27 patients; 3 patients (9.7%) out of the 31 who were discharged after MitraClip implantation died from a cardiac cause on days 17, 50, and 419 post-MitraClip repair. New York Heart Association (NYHA) functional class was reported for 27 patients; among these, 20 (60.6%) were in NYHA class I-II at the last follow-up. Five patients (15.2%) had to be rehospitalized due to heart failure. One patient underwent cardiac surgery with conventional aortic and mitral valve replacement as a consequence of aortic valve prosthesis migration and recurrent severe MR secondary to single mitral leaflet detachment. The main complications associated with both procedures are summarized in the Table.

This systematic review indicates that transcatheter double-valve treatment appears to be safe and feasible for high-surgical-risk patients with severe AS and concomitant severe MR. The in-hospital mortality appears to be slightly higher than that described in contemporary MitraClip registries.4,5 TAVR did not seem to increase the periprocedural risk or interfere with MitraClip implantation. One of the patients who died underwent TAVR and MitraClip implantation in a single session. The other case of in-hospital mortality was in a very high-risk patient (logistic EuroSCORE, 65%), who was in a critical clinical condition.

Recent studies have suggested that significant concomitant MR improves in approximately 50% to 60% of patients post-TAVR, especially MR of functional etiology.4 In this population at high-risk of periprocedural complications, it is important to decide the need for the 2 (aortic and mitral) procedures and their optimal timing, avoiding unnecessary risks in patients who could potentially show MR improvement during follow-up. Although there is no conclusive evidence in the literature regarding which strategy (staged vs single mitral and aortic procedure) is associated with superior outcomes, in our opinion, a staged approach addressing the aortic valve first would likely be the most appropriate strategy. After TAVR, a comprehensive clinical follow-up is essential for the early identification of patients who are unlikely to show spontaneous MR improvement in order to offer the possibility of transcatheter mitral repair. Based on the available data, we propose an algorithm (Figure) that could guide the clinical decision-making process in such patients.

Several limitations of the present review warrant consideration. First, inherent to all systematic reviews is the issue of publication bias, which could have limited the extent of clinical experience with combined transcatheter treatment for combined mitral and aortic valve disease available in the literature. Second, patients’ baseline characteristics, echocardiographic findings, and procedural-related data were reported heterogeneously among publications.

In conclusion, transcatheter double-valve treatment appears to be safe and feasible for high-surgical-risk patients with severe AS and concomitant severe MR. Larger studies are needed
Patients with severe AS and concomitant significant MR at high or prohibitive surgical risk

Transcatheter aortic valve replacement (TAVR)

3-month clinical and echocardiographic follow-up

MR < 3+ and NYHA I-II

No

MRI ≥ 3+ and NYHA III-IV

Yes

Degenerative MR and/or predictors of persistent MR*

6-month clinical and echocardiographic follow-up

MR < 3+ or NYHA I

No

MR ≥ 3+ and NYHA II-IV

Yes

MitraClip

1-year follow-up

Figure. Algorithm for the management of severe aortic stenosis and concomitant significant mitral regurgitation for high-surgical-risk patients. AS, aortic stenosis; MR, mitral regurgitation; NYHA, New York Heart Association.
to confirm the safety and to establish the most appropriate timing for this double treatment strategy in this challenging group of patients who combine significant aortic and mitral valve disease.

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SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at http://dx.doi.org/10.1016/j.rec.2017.05.001

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Paravalvular Leak Correction: Searching for a Balance Between Surgical and Percutaneous Techniques

Corrección de fugas paravalvulares: buscando el equilibrio entre las técnicas quirúrgicas y percutáneas

To the Editor,

Paravalvular leak (PVL) is a complication after valve replacement surgery, with an incidence ranging from 2% to 10% in the aortic position and from 7% to 17% in the mitral position.1 Although most cases have a benign course, 1% to 5% of linked might be linked to serious clinical consequences such as heart failure or hemolytic anemia.1,2 Mortality following re-do surgery has been reported to be high (10%-15%) and rises with the number of previous surgeries.2 Percutaneous treatment of PVL has emerged as a promising alternative to surgery,3 although data comparing the results of surgical vs percutaneous PVL correction are scarce. The purpose of the present study was to describe the outcomes of surgical and percutaneous PVL correction in a contemporary series of patients. Between January 2006 and December 2015, all patients undergoing isolated PVL through either surgery or the percutaneous approach at our institution were analyzed. The selection of percutaneous or surgical treatment was at the discretion of the treating medical team. However, percutaneous PVL correction became available in 2012 and was performed by experienced operators. Since then, all technically feasible PVLs were initially approached by percutaneous techniques after a Heart Team discussion. To avoid bias, corrective procedures other than isolated PVL, such as combined interventions with coronary revascularization or adjunctive treatment of another cardiac valve, were excluded from the analysis. Patients with active endocarditis were excluded. All patients gave informed consent before the intervention.

A total of 50 patients (32 percutaneous and 18 surgical) underwent isolated PVL correction and were therefore included in the study (Table). Procedural success was achieved in 94% and 87% of the surgical and percutaneous patients, respectively. Major adverse events and in-hospital mortality were balanced between groups and patients undergoing percutaneous correction had shorter admission periods. At 1-year of follow-up, no significant differences between groups were found in all-cause mortality, hospital readmissions for PVL symptoms, and reintervention (Table).

The main findings of the present study were: a) both percutaneous and surgical PVL correction techniques were associated with a high rate of procedural success (> 85%) with a trend toward more complete sealing in patients undergoing surgery; b) in-hospital major adverse events were comparable between groups; c) patients treated with percutaneous techniques had shorter in-hospital admissions; and d) at 1-year of follow-up, clinical outcomes remained balanced between groups.

In our series, surgical patients showed a trend toward more complete PVL sealing but procedural success with percutaneous techniques was still high and similar to that achieved with surgery. These results are in agreement with those of previous publications reporting similar outcomes after percutaneous PVL correction.3 Although our surgical in-hospital mortality might be considered high (11%), it reflects the high surgical risk of the treated population and is in agreement with previous series reporting mortalities between 6% and 22%.1,3 However, it is important to highlight that surgical PVL repair might be the only therapeutic alternative, especially in large or multiple PVLs. Communication within the Heart Team and discussion about the technical complexity of percutaneous repair as well as the proposed