Cardiac and vascular changes after transcatheter or surgical aortic valve replacement in low-risk aortic stenosis

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EDITORIAL

Cardiac and Vascular Changes After Transcatheter or Surgical Aortic Valve Replacement in Low-Risk Aortic Stenosis

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In patients with symptomatic severe aortic stenosis, transcatheter aortic valve replacement (TAVR) has been demonstrated to reduce risk of mortality and stroke for up to 2 years as compared with surgical aortic valve replacement (SAVR).[1] TAVR is associated with reduced risk of bleeding complications, acute kidney injury, and onset of atrial fibrillation. However, the risks of pacemaker implantation and major vascular complications are higher with TAVR than SAVR. These are important considerations for the heart team when selecting the appropriate treatment for patients with symptomatic severe aortic stenosis. In patients with low operative risk, who are generally younger and in whom SAVR is associated with excellent outcomes, other factors need to be taken into consideration as well when deciding on treatment.

One of those factors in younger patients is the higher frequency of bicuspid aortic valve stenosis, a condition that traditionally has been excluded from randomized clinical trials. In the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, of 170 959 eligible TAVR procedures, 3.2% were performed in patients with bicuspid aortic valve.[2] A modestly higher incidence of moderate and severe paravalvular regurgitation after TAVR has been reported with bicuspid aortic valve as compared with tricuspid aortic valve anatomy (2.7% versus 2.1%; P=0.006). Among patients with tricuspid aortic valve stenosis, residual paravalvular regurgitation remains more common after TAVR than SAVR. Advances in transcatheter valve technology have resulted in reduced incidence of moderate and severe paravalvular regurgitation. In PARTNER 3 (Placement of Aortic Transcatheter Valve Trial) using the SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA),[3] there were no differences between TAVR and SAVR in rates of moderate and severe paravalvular regurgitation (0.8% and 0% at 30 days, respectively), although mild paravalvular regurgitation was observed more frequently in TAVR than in SAVR (28.8% versus 2.9%; P<0.001). In contrast to previous studies, the presence of mild paravalvular regurgitation was not associated with increased all-cause mortality. However, the effect of mild paravalvular regurgitation on long-term outcomes needs to be defined carefully, and long-term data on progression of regurgitation will be important.

The development of conduction abnormalities and need for permanent pacemaker implantation are additional important factors that should be considered in patients with low surgical risk. The association between permanent pacemaker implantation after TAVR and all-cause death at 1 year remains controversial.[4] The development of pacemaker-induced left ventricular systolic dysfunction or lead-induced severe tricuspid regurgitation and right heart failure have been described. Both tricuspid regurgitation and right heart failure have been associated with poor prognosis after TAVR and SAVR.[5,6]

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Another question relates to the durability of transcatheter aortic valves. The life expectancy of patients with low surgical risk is longer than that of patients with inoperable disease or high or intermediate operative risk. Long-term durability assessment from earlier trials was confounded by a high competing hazard of death. PARTNER 3 and the Evolut Low Risk Trial include the use of sequential echocardiograms and postprocedural computed tomography to monitor the hemodynamic performance and structural integrity of transcatheter and surgical valves over 10 years of follow-up.[3,7] These data will be extremely important given that patients with low surgical risk constitute ≈50% of all patients with aortic stenosis.[8] In the meantime, comprehensive information on hemodynamic performance of transcatheter and surgical valve bioprostheses as well as left and right ventricular function at short-term and midterm follow-up is important.

In this issue of *Circulation*, the echocardiographic substudy of PARTNER 3 including patients with low surgical risk by Pibarot and coworkers[9] shows that valve hemodynamics, mean transvalvular gradient, effective aortic valve area, and patient–prosthesis mismatch were comparable between TAVR and SAVR at 30-day and 1-year follow-up. However, TAVR was associated with lower valvulo-arterial impedance (indicating lower left ventricular afterload) and greater reduction in left ventricular hypertrophy when compared with SAVR at 1 year. Changes in valvulo-arterial impedance after TAVR or SAVR have not been studied extensively, and its association with clinical outcomes is controversial. Whereas high valvulo-arterial impedance at baseline has been associated with increased risk of all-cause mortality after TAVR,[10] high valvulo-arterial impedance after TAVR has not been similarly associated with a higher mortality.[11] Valvulo-arterial impedance has not been demonstrated to change acutely after TAVR, probably related to its dependence on both the valvular and the vascular components of the left ventricular afterload, which are competitively influenced by the treatment.[12] Instead, other measures of vascular function have shown that the vascular tree becomes stiffer after TAVR with rise in continuous and pulsatile vascular load and blood pressure requiring antihypertensive treatment escalation. Increased valvulo-arterial impedance partly reflects the vascular behavior, and one could hypothesize that sustained high valvulo-arterial impedance could reduce the benefits of aortic valve replacement. This needs to be elucidated in longer-term follow-up studies.

The present article also provides information on right ventricular function and presence of tricuspid regurgitation,[9] factors that have been associated with worse outcomes among patients with severe aortic stenosis.[13] Whereas right ventricular systolic function remained unchanged after TAVR, it decreased after SAVR and remained significantly worse at 1-year follow-up as compared with TAVR. The percentage of patients with tricuspid annular plane systolic excursion (TAPSE) <16 mm was significantly higher after SAVR as compared with TAVR (51% versus 14%; $P<0.001$). The percentage of patients with moderate and severe tricuspid regurgitation was significantly higher after SAVR versus TAVR (5.5% versus 1.7%; $P<0.001$). A higher probability of impaired right ventricular function after SAVR as compared with TAVR has been described.[5] However, most of the included patients had intermediate or high operative risk and may have had additional comorbidities that could influence right ventricular systolic function. In patients undergoing TAVR, particularly with balloon-expandable valves, in which rapid pacing is essential to valve implant, postprocedure right ventricular dysfunction has been described,[14] but this was believed to be transient, a finding that appears to be confirmed by the current study.[9] Coisne et al[15] reported impaired TAPSE in 617 patients undergoing SAVR immediately after the intervention. At 1 year of follow-up, significant but incomplete recovery of TAPSE was observed, which is concordant with the findings of the current study.[9] TAPSE after SAVR was not associated with the occurrence of cardiovascular death, cardiac hospitalization, acute heart failure, or stroke.[15] This could indicate that after the pericardium is opened, changes in right ventricular geometry may invalidate the measurement of TAPSE as a measure of right ventricular function, or alternatively that the magnitude of the recovery in TAPSE after SAVR is sufficient to prevent major cardiovascular events. Three-dimensional modalities such as three-dimensional transthoracic echocardiography and cardiovascular magnetic resonance imaging are not influenced by geometric assumptions and may be more appropriate modalities than TAPSE to assess right ventricular function. Potential differences in the evolution of prevalent versus incident right ventricular dysfunction after aortic valve replacement and its effect on long-term outcomes have remained largely unexplored and are important questions that may help in decision making.

Pibarot et al[9] showed that both high valvulo-arterial impedance and low TAPSE at 30 days were independently associated with increased risk of the composite end point of mortality, stroke, and rehospitalization at 1 year in both arms. Whether the present echocardiographic findings at 30-day and 1-year follow-up remain associated with outcomes at 2-year follow-up and beyond needs to be analyzed.

Imaging data are important in understanding how TAVR and SAVR improve the clinical outcomes of patients with severe aortic stenosis and helping to refine the indications for these therapies. Long-term follow-up will confirm whether the observed differences with regard to short-term and intermediate-term imaging findings are relevant to clinical outcomes, and whether

they should be factored into decision-making when choosing the appropriate therapy for patients with severe aortic stenosis.

ARTICLE INFORMATION

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REFERENCES

1. Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, Pilgrim T, Petrinic T, Nikolakopoulou A, Salanti G, et al. Transcatheter aortic valve implantation vs surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. *Eur Heart J.* 2019;40:3143–3153. doi: 10.1093/eurheartj/ehz275
2. Halim SA, Edwards FH, Dai D, Li Z, Mack MJ, Holmes DR, Tuzcu EM, Thourani VH, Harrison JK, Brennan JM. Outcomes of transcatheter aortic valve replacement in patients with bicuspid aortic valve disease: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *Circulation.* 2020;141:1071–1079. doi: 10.1161/CIRCULATIONAHA.119.040333
3. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, et al; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med.* 2019;380:1695–1705. doi: 10.1056/NEJMoa1814052
4. Auffret V, Puri R, Urena M, Chamandi C, Rodriguez-Gabella T, Philippon F, Rodés-Cabau J. Conduction disturbances after transcatheter aortic valve replacement: current status and future perspectives. *Circulation.* 2017;136:1049–1069. doi: 10.1161/CIRCULATIONAHA.117.028352
5. Cremer PC, Zhang Y, Alu M, Rodriguez LL, Lindman BR, Zajarias A, Hahn RT, Lerakis S, Malaisrie SC, Douglas PS, et al. The incidence and prognostic implications of worsening right ventricular function after surgical or transcatheter aortic valve replacement: insights from PARTNER IIA. *Eur Heart J.* 2018;39:2659–2667. doi: 10.1093/eurheartj/ehy251
6. McCarthy FH, Vemulapalli S, Li Z, Thourani V, Matsouaka RA, Desai ND, Kirtane A, Anwaruddin S, Williams ML, Giri J, et al. Association of tricuspid regurgitation with transcatheter aortic valve replacement outcomes: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *Ann Thorac Surg.* 2018;105:1121–1128. doi: 10.1016/j.athoracsur.2017.11.018
7. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, et al; Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med.* 2019;380:1706–1715. doi: 10.1056/NEJMoa1816885
8. Otto CM, Kumbhani DJ, Alexander KP, Calhoon JH, Desai MY, Kaul S, Lee JC, Ruiz CE, Vassileva CM. 2017 ACC expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol.* 2017;69:1313–1346. doi: 10.1016/j.jacc.2016.12.006
9. Pibarot P, Salaun E, Dahou A, Avenatti E, Guzzetti E, Annabi M-S, Toubal O, Bernier M, Beaudoin J, Ong G, et al. Echocardiographic results of transcatheter versus surgical aortic valve replacement in low-risk patients: the PARTNER 3 trial. *Circulation.* 2020;141:1527–1537. doi: 10.1161/CIRCULATIONAHA.119.044574
10. Katsanos S, Yiu KH, Clavel MA, Rodés-Cabau J, Leong D, van der Kley F, Ajmone Marsan N, Bax JJ, Pibarot P, Delgado V. Impact of valvuloarterial impedance on 2-year outcome of patients undergoing transcatheter aortic valve implantation. *J Am Soc Echocardiogr.* 2013;26:691–698. doi: 10.1016/j.echo.2013.04.003
11. Nagura F, Kataoka A, Hara M, Kozuma K, Watanabe Y, Nakashima M, Hioki H, Kawashima H, Nara Y, Shirai S, et al; OCEAN-TAVI Investigators. Association between valvuloarterial impedance after transcatheter aortic valve implantation and 2-year mortality in elderly patients with severe symptomatic aortic stenosis: the OCEAN-TAVI registry. *Heart Vessels.* 2019;34:1031–1039. doi: 10.1007/s00380-018-01329-2
12. Yotti R, Bermejo J, Gutiérrez-Ibañes E, Pérez del Villar C, Mombiela T, Elízaga J, Benito Y, González-Mansilla A, Barrio A, Rodríguez-Pérez D, et al. Systemic vascular load in calcific degenerative aortic valve stenosis: insight from percutaneous valve replacement. *J Am Coll Cardiol.* 2015;65:423–433. doi: 10.1016/j.jacc.2014.10.067
13. Généreux P, Pibarot P, Redfors B, Mack MJ, Makkar RR, Jaber WA, Svensson LG, Kapadia S, Tuzcu EM, Thourani VH, et al. Staging classification of aortic stenosis based on the extent of cardiac damage. *Eur Heart J.* 2017;38:3351–3358. doi: 10.1093/eurheartj/ehx381
14. Axell RG, White PA, Giblett JP, Williams L, Rana BS, Klein A, O'Sullivan M, Davies WR, Densem CG, Hoole SP. Rapid pacing-induced right ventricular dysfunction is evident after balloon-expandable transfemoral aortic valve replacement. *J Am Coll Cardiol.* 2017;69:903–904. doi: 10.1016/j.jacc.2016.12.011
15. Coisne A, Modine T, Outteryck F, Mouton S, Pilato R, Ridon H, Richardson M, Duva-Pentiah A, Madika AL, Ledieu G, et al. Clinical significance of right ventricular longitudinal function parameters after aortic valve replacement. *J Am Coll Cardiol Cardiovasc Imaging.* 2018;11:651–652. doi: 10.1016/j.jcmg.2017.06.016