

## EDITORIALS



## Transcatheter Aortic-Valve Implantation — At What Price?

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In 2000, Bonhoeffer et al. described transvenous placement of a pulmonary-valve prosthesis and speculated that similar technology might be used in other cardiac valves, including the aortic position.<sup>1</sup> Two years later, the first transcatheter insertion of an aortic-valve prosthesis was performed by Cribier et al.<sup>2</sup> Transcatheter aortic-valve implantation has developed rapidly, and two relatively mature technologies are in clinical use: the SAPIEN Transcatheter Heart Valve (Edwards Lifesciences) and the CoreValve Revalving System (Medtronic). In contrast to surgical valve replacement, in which the diseased, calcified cusps are removed, these and other catheter-based techniques in development rely on forcibly spreading the stenotic aortic-valve cusps and anchoring the stented bioprosthesis without sutures.

In this issue of the *Journal*, Smith et al.<sup>3</sup> report the results of a cohort in the Placement of Aortic Transcatheter Valves (PARTNER) trial, which tested the hypothesis that transcatheter aortic-valve replacement (with transfemoral or transapical placement) would be noninferior to surgical replacement in the 1-year survival of patients with severe aortic-valve stenosis and high operative risk. Perioperative rates of death were low for these patients. In the intention-to-treat population, 30-day mortality was 3.4% in the transcatheter group and 6.5% in the surgical group ( $P=0.07$ ), and the 1-year overall mortality was 24.2% versus 26.8%, confirming noninferiority.

However, the avoidance of a sternotomy by transfemoral or transapical aortic-valve implantation appears to come at the price of some potentially serious vascular and technical complications and increased hazards of embolic stroke and paravalvular leakage. The technical problems and imperfect seating of the prosthesis may be eliminated or largely overcome by increased operator experience and refinement of the implantable device. Newer, more flexible, and smaller delivery systems should increase the number of

patients who are eligible for transfemoral insertion and may decrease vascular injury.

But the increased risk of stroke associated with transcatheter replacement, as compared with surgical replacement, is a special concern. Smith and colleagues report a 5.5% risk of stroke or transient ischemic attack within 30 days after transcatheter replacement, and this risk increased to 8.3% after 1 year. In contrast, among patients undergoing surgical replacement, early and late risks of neurologic injury were 2.4% and 4.3%, respectively ( $P=0.04$  for both comparisons). Are these increased risks of neurologic injury consistent with other studies? And if so, how did a procedure in which the risk of neurologic complications is twice that of surgical replacement become adopted so widely and rapidly? Perhaps most important, what are the mechanisms of stroke and how might these be mitigated?

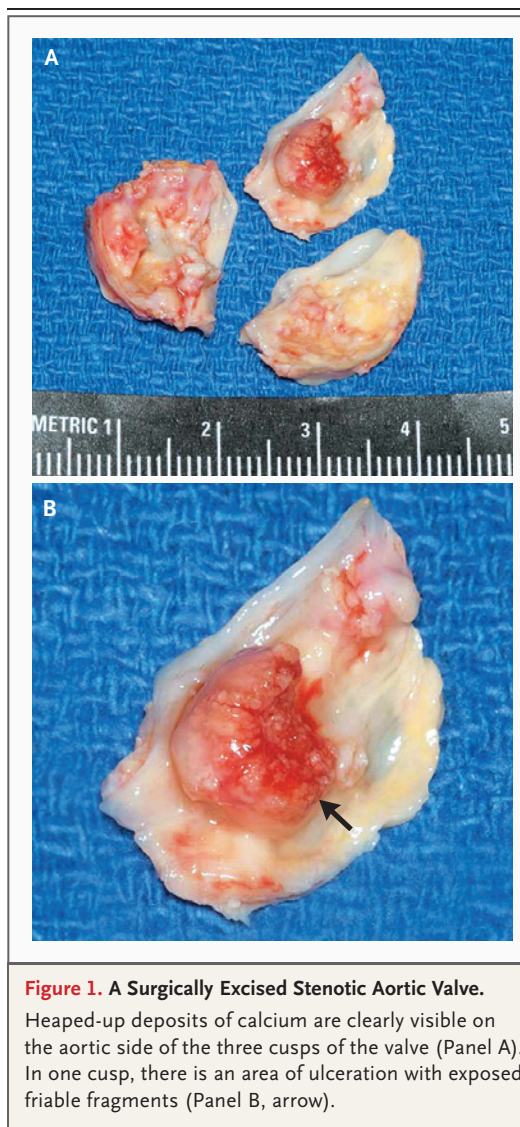
Despite efforts to standardize definitions,<sup>4</sup> the reported risk of clinically apparent neurologic complications with transcatheter replacement has varied from 0 to 11% in series that include single institutions and registries.<sup>5-7</sup> The 5.5% early risk of stroke or transient ischemic attack in the PARTNER trial is consistent with previous studies and is similar to the 6.7% risk in patients who were not candidates for surgery.<sup>8</sup> In most centers, transcatheter replacement has been used in patients who are at high operative risk, and the same clinical characteristics that increase such risk for patients (e.g., previous surgery, atherosclerotic vascular disease, and systemic hypertension) also increase the risk of stroke with any major cardiovascular intervention. Thus, the 1-in-20 occurrence of stroke or transient ischemic attack after transcatheter replacement might be considered a complication that comes with the territory in treating elderly patients with multiple coexisting conditions.

However, previous outcome studies of transcatheter replacement have not provided a com-

parison with similar patients undergoing surgical replacement, and in this respect, the study by Smith et al. is highly revealing. For patients who would not be candidates for surgical replacement, such an increased rate of neurologic complications might be acceptable, but for those who are candidates for either transcatheter or surgical replacement, the findings present a dilemma in balancing the risks of increased neurologic complications against the benefits of avoiding sternotomy and cardiopulmonary bypass.

It is not surprising that neurologic complications occur with transcatheter replacement in patients with senescent (degenerative) aortic-valve stenosis. Deposits of calcification in aortic-valve cusps are usually covered by endothelium, but dilatation of the valve may lead to fracture of the calcified portion and exposure to the circulation. Some patients have friable ulcerations of calcified cusps that are especially prone to embolization (Fig. 1). Indeed, the simple passage of a catheter across a stenotic calcified aortic valve for left ventricular pressure measurement can cause emboli. Omran et al.<sup>9</sup> found new focal abnormalities on magnetic resonance imaging (MRI) in 22% of patients undergoing retrograde left ventricular catheterization for assessment of aortic-valve stenosis; most of these abnormalities were silent, with only 3% of patients showing neurologic signs or symptoms. Kahlert and associates<sup>10</sup> reported new defects on cerebral MRI in 84% of patients undergoing transcatheter replacement, but these defects were not associated with clinical events or neurocognitive dysfunction during 3 months of follow-up. In other studies, this high rate of new cerebral emboli after transcatheter replacement was found to be similar for both transfemoral and transapical approaches during SAPIEN valve implantation.<sup>11</sup> It seems clear that calcific atherosclerotic emboli are common during catheter and device manipulation of a stenotic aortic valve.

Continued surveillance of patients in this study will be critically important to determine the durability of the transcatheter prosthesis and to assess the risk of late thromboembolic events. The insertion of a prosthesis without removal of the diseased aortic valve creates an irregular zone around the stent that may predispose to thrombus formation. This concern might explain the investigators' use of dual antiplatelet therapy in patients undergoing transcatheter replacement. In contrast, antiplatelet therapy



with aspirin alone seems adequate for those undergoing surgical replacement who have no additional risk factors for thromboembolism.<sup>12</sup>

Technological refinement of transcatheter valves and adjunctive procedures, such as the use of embolic protection devices,<sup>13</sup> will facilitate transcatheter replacement and may improve outcomes, but these new devices should be evaluated in controlled trials with randomization against current standard techniques. The future introduction of prostheses for surgical replacement should be held to the high standard of clinical evaluation demonstrated in this evaluation of transcatheter aortic-valve implantation.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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1. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet* 2000;356:1403-5.
2. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation* 2002;106:3006-8.
3. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187-98.
4. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *J Am Coll Cardiol* 2011;57:253-69.
5. Masson JB, Kovac J, Schuler G, et al. Transcatheter aortic valve implantation: review of the nature, management, and avoidance of procedural complications. *JACC Cardiovasc Interv* 2009;2:811-20.
6. Nuis RJ, Piazza N, Van Mieghem NM, et al. In-hospital complications after transcatheter aortic valve implantation revisited according to the Valve Academic Research Consortium definitions. *Catheter Cardiovasc Interv* 2011 May 11 (Epub ahead of print).
7. Lefèvre T, Kappetein AP, Wolner E, et al. One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. *Eur Heart J* 2011;32:148-57.
8. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597-607.
9. Omran H, Schmidt H, Hackenbroch M, et al. Silent and apparent cerebral embolism after retrograde catheterisation of the aortic valve in valvular stenosis: a prospective, randomised study. *Lancet* 2003;361:1241-6.
10. Kahlert P, Knipp SC, Schlamann M, et al. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation: a diffusion-weighted magnetic resonance imaging study. *Circulation* 2010;121:870-8.
11. Rodés-Cabau J, Dumont E, Boone RH, et al. Cerebral embolism following transcatheter aortic valve implantation: comparison of transfemoral and transapical approaches. *J Am Coll Cardiol* 2011;57:18-28.
12. Sundt TM, Zehr KJ, Dearani JA, et al. Is early anticoagulation with warfarin necessary after bioprosthetic aortic valve replacement? *J Thorac Cardiovasc Surg* 2005;129:1024-31.
13. Nietlispach F, Wijesinghe N, Gurvitch R, et al. An embolic deflection device for aortic valve interventions. *JACC Cardiovasc Interv* 2010;3:1133-8.

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