Valve interventions—a word of caution

The possibility of repairing or replacing the valves of the heart in a percutaneous, minimally invasive manner is an attractive alternative to open-heart surgery. Within the past decade, several approaches have been developed for this purpose. Transcatheter aortic valve implantation (TAVI), the first of these approaches to be introduced, has been used for the treatment of aortic stenosis since 2002. Currently, two devices for aortic valve implantation are on the market, the Edwards SAPIEN® valve (Edwards Lifesciences Inc., Irvine, CA) and the CoreValve® (CoreValve Inc., Irvine, CA). A percutaneous strategy for mitral valve repair in patients with mitral regurgitation, with the MitraClip® valve (Evalve Inc., Menlo Park, CA), has also been employed in Europe and its use in US clinical settings is imminent. Percutaneous pulmonary valve implantation has been tested and similar strategies for tricuspid valve replacement have begun to be investigated.

Generally, untreated severe valvular heart diseases are fatal and medical therapy is not sufficient to prevent the progression of disease. Open-heart surgery is an established procedure that has good probability of success in a substantial proportion of patients, but percutaneous interventions could be valuable, minimally invasive options, for example in patients for whom surgery is a high-risk procedure. The safety and efficacy of percutaneous approaches for valve implantation and repair, however, have not been fully clarified.

Early reports have highlighted the specific risks of TAVI relatively to conventional surgery. These risks include stroke (with the risk of stroke estimated to be as high as 10% in some studies), vascular and cardiac injury, and valve misplacement. Such concerns led the AHA and expert groups to recommend, in 2008, that percutaneous and minimally invasive approaches for treatment of valvular heart disease remain investigational.

Two years later, the results of the EVEREST I and EVEREST II trials on the MitraClip® system (Feldman, T. *et al. J. Am. Coll. Cardiol.* **54**, 686–694; 2009), those of the longest follow-up outcomes study on the Edwards SAPIEN® valve (Rodés-Cabau, J. *et al. J. Am. Coll. Cardiol.* **55**, 1080–1090; 2010), and those of a pilot study on pulmonary valve implantation (Vezmar, M. *et al. JACC Cardiovasc. Interv.* **4**, 439–448; 2010) were reported and caused considerable excitement amongst the cardiology community. These reports indicate that these percutaneous intervention techniques have rates of success and safety that are comparable to those of conventional surgery. Notably, in the study by Rodés-Cabau and colleagues, the risk of stroke associated with TAVI at the 30-day follow-up (2.3%) was much smaller than that reported in previous studies and seems equivalent to that associated with open-heart surgery for aortic valve replacement.

Although these findings are exciting, caution about these techniques is still justified because the issues around the safety of percutaneous valvular interventions are not fully resolved. In particular, two independent studies on TAVI have shown that this procedure is associated with a high number of new brain lesions, as assessed by diffusion-weighted MRI (Kahlert, P. *et al. Circulation* **121**, 870–878; 2010 and Ghanem, A. *et al. J. Am. Coll. Cardiol.* **55**, 1427–1432; 2010). In the first of these studies, 84% of the 32 patients who underwent TAVI with either the Edwards SAPIEN® valve or the CoreValve® had new foci of restricted diffusion after this intervention, whereas only 48% of the 21 patients who underwent open-heart surgery had such lesions ($P = 0.011$). In the second study, 72.7% of the 22 patients who completed the imaging test had new brain lesions after implantation of the Edwards SAPIEN® valve. In both studies, these presumably embolic lesions were not associated with persistent impairment of neurological function in the overwhelming majority of patients, as assessed 3 months after intervention. The rates of mortality and stroke did not significantly differ from those of conventional surgery in the study by Kahlert and colleagues, which corroborates the findings of Rodés-Cabau and colleagues. Nevertheless, the appearance of these apparently functionally silent foci in patients who underwent TAVI raises concerns that the procedure might have a yet unknown impact on cognitive function.

Longer follow-up assessments that include a variety of measures of cognitive impairment are warranted to clarify this question. As the authors of these studies acknowledge, the clinical significance of their findings will also need to be assessed in larger populations and through randomized side-by-side comparisons between TAVI, or other percutaneous approaches, and open-heart surgery.

The potential neurological consequences of available interventions for valvular replacement or repair clearly need to be thoroughly investigated. The inclusion of MRI and measures of cognitive function in the design of future trials assessing these techniques is a possible way forward.

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Competing interests
The authors declare no competing interests.