Transcatheter aortic valve implantation: emerging role in poor left ventricular function severe aortic stenosis?

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Abstract

Transcatheter aortic valve implantation (TAVI) has become an established treatment option for high risk elderly patients with symptomatic severe aortic stenosis. Its role in less high risk patients is being evaluated in clinical trials. Patients with severely impaired left ventricular function may be another group who may benefit from this emerging percutaneous treatment option.

Key words: bicuspid aortic valve, genetics, fibrillin-1, Marfan syndrome, clinical approach

Surgical aortic valve replacement (AVR) has long been recognized as the gold standard treatment for symptomatic severe aortic stenosis improving symptoms, survival and functional class. Recently, transcatheter aortic valve implantation (TAVI) has also become an established procedure for the treatment of higher risk patients with symptomatic severe aortic stenosis.1 These include the frail, elderly patient with multiple co-morbidities and disabilities. TAVI has been shown to successfully reduce aortic valve gradients to a similar degree as conventional AVR but the incidence of paravalvular aortic regurgitation (AR) is significantly higher.2, 3 Compared to conventional AVR, TAVI has a shorter recovery period, avoids a sternotomy and cardiopulmonary bypass, and has a lower risk of bleeding, acute kidney injury, atrial fibrillation and early mortality, but the risk of vascular complications, pacemaker implantations and cardiac perforations are higher.1, 2 Stroke rates were initially reported to be higher following TAVI compared to conventional AVR but recent studies suggest no difference in stroke rates.3

Many patients in the highest risk group who would not previously have been offered surgery are now eligible for TAVI and this has been shown to improve their symptoms, functional class, survival and quality of life compared to best medical treatment; hospital admissions were reduced, although the risk of stroke, vascular complications and need for pacemaker were increased.1, 3-4 In randomized trials, TAVI has been shown to have a similar survival to conventional AVR at up to one year in the highest risk elderly patients; while in those at less high risk, TAVI has been shown to have a lower mortality.3-5 However, the longer-term results of TAVI beyond 5 years is unknown and while TAVI may be suitable for the higher risk elderly patient with multiple co-morbidities who would not be expected to survive beyond 5 years, its role in the lower risk younger patient is uncertain; clinical trials are needed to evaluate this.5

Another group of patients at high risk for conventional AVR is the patient with severely impaired left ventricular (LV) function particularly those with a low gradient, low ejection fraction (LGLFEF) severe aortic stenosis. These include patients with a resting mean aortic valve gradient of less than 30mmHg and an LV ejection fraction of less than 35%.2 Conventional AVR in these patients with cardiopulmonary bypass and cardioplegic arrest of the heart requires meticulous myocardial protection, to avoid the risk of further myocardial injury in an already impaired LV and consequent need for high doses of inotropic support, to failure to wean from cardiopulmonary bypass requiring mechanical circulatory support, with the resulting prolonged stay in intensive care associated with increased morbidity and mortality. Operative mortality in these patients has been reported to be between 5-20% and is better in younger patients with evidence of contractile reserve, minimal coronary disease and no myocardial fibrosis.1, 3-4 An improvement in functional status, ejection fraction and survival has been reported following successful AVR in these patients.3-5 Sutureless valves have been introduced which allows an aortic valve to be implanted without the need to suture it onto the aortic annulus thus reducing the duration of myocardial ischaemia and cardiopulmonary bypass. These valves are increasingly being used in LGLEF aortic stenosis with good results.

Is there also a role for TAVI in these patients? TAVI would of course avoid the need for cardiopulmonary bypass and aortic cross clamping altogether, although there is still a risk of myocardial injury during the period of rapid pacing. Indeed, intra-aortic balloon pump and in some instances more intense mechanical circulatory support may be needed in these patients during TAVI. Unfortunately, most of the TAVI studies to date have excluded patients with severely impaired LV function. An analysis of low flow severe aortic stenosis was performed in the PARTNER Trial but the mean ejection fraction in this group was 49%.10 In this analysis, low flow was associated with increased mortality at two years, with no difference between the TAVI and AVR arms. In a separate observational study, LGLEF severe aortic stenosis with a mean ejection fraction of 32% was associated with increased mortality following TAVI.11 In both studies, low flow, rather than low ejection fraction, were independently predictive of increased mortality at two years. Although TAVI may seem suitable in LGLEF severe aortic stenosis to avoid the need for major surgery, there are several concerns with its use in these patients. Compared with conventional AVR, TAVI has been shown to have a higher
incidence of paravalvular aortic regurgitation (AR).\textsuperscript{1-3} Mild AR has been reported in between 7-63% of patients following TAVI, and moderate or severe AR in between 4-37%\textsuperscript{2, 3, 12-14}. These differences in reported rates of AR may be a reflection of different techniques and methods of assessing and grading AR severity, and possibly of differing techniques of performing the TAVI procedure.\textsuperscript{14} While patients with preserved LV systolic function may be able to tolerate some degree of AR following TAVI, it is uncertain how the severely impaired LV would be able to cope with AR in the long term. The severely hypertrophic LV accustomed to the pressure overload of severe aortic stenosis is often not very compliant and may not cope with the volume overload of aortic regurgitation particularly if LV systolic function is already severely impaired. Indeed, it has been demonstrated that even in those with preserved LV systolic function, paravalvular AR is associated with decreased survival.\textsuperscript{14}

Conventional AVR in LGLEF severe aortic stenosis, although a high risk procedure, has been shown to improve long term survival in younger patients.\textsuperscript{5-9}\textsuperscript{9} The results of TAVI, however, do not extend beyond 5-years. Clearly, the long-term durability and safety of TAVI has to be determined. In addition, indices of reverse LV remodeling in the long term must be carefully studied. Should the presence of paravalvular AR following TAVI adversely affect LV reverse remodeling in the patient with a severely depressed LV, this may ultimately affect their survival and functional status. An observational study did report an improvement in LV ejection fraction at one year following TAVI in LGLEF severe aortic stenosis, however, changes in LV mass or volumes were not reported.\textsuperscript{8} In this non-randomized observational study, the improvement in ejection fraction at one year was better in TAVI patients compared to conventional AVR. However, the improvement in ejection fraction following conventional AVR was better in other observational studies.\textsuperscript{15} Clearly, randomized comparisons are needed including parameters of LV reverse remodeling and clinical outcomes.

TAVI is still a relatively new procedure and just as the results of conventional AVR have improved over the decades since it was first performed, the results of TAVI are likely to improve too with time. Better understanding of pre-procedure sizing of the aortic annulus and its anatomy with CT and 3-D echocardiography assessment, selecting the valve prosthesis of the right size and make, better positioning of the valve prosthesis within the aortic annulus, and improved design of the valve prosthesis itself such as the Sapien 3 prosthesis, will almost certainly reduce the incidence of paravalvular AR with time.\textsuperscript{15, 14}\textsuperscript{14} The indications for TAVI is likely to increase with time and may include the patient with severely impaired LV function and symptomatic severe aortic stenosis. However, clinical evidence for this is necessary and this is likely to come from further analysis of existing registry data and ongoing randomized trials.

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