Aortic stenosis: expanding treatment options

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Aortic stenosis has markedly increased in prevalence and incidence as the life expectancy of citizens of Western societies has increased substantially. Indeed, we learned that there are patients with high-gradient, low-flow low-gradient, and even paradoxical low-flow low-gradient aortic stenosis. While surgical valve replacement was the treatment of choice for decades, transcatheter aortic valve implantation or TAVI has become an increasingly safe, effective, and attractive treatment option in patients at high risk for surgery. A downside of, in particular, the first-generation TAVI valves is the relatively high prevalence of paravalvular leaks with impact on clinical outcome. However, as outlined by Fabian Nietlispach and colleagues from the University Heart Center in Zurich, Switzerland in the review ‘Percutaneous paravalvular leak closure: chasing the chameleon’, a catheter-based approach can also solve this problem. The authors note that paravalvular leaks occur after both surgical and transcatheter valve replacement or implantation, respectively. This can lead to haemolysis and heart failure, and may increase the risk of endocarditis. Recently, proper adjudication of such leaks has been well defined, setting the basis for proper management. Percutaneous closure has significantly less morbidity than re-operation and is therefore often the therapy of choice. Percutaneous paravalvular leak closure can make an important difference for patients and can improve patient prognosis.

Whether and in what patient population TAVI is superior to surgical valve replacement remains an ongoing debate. In a FAST TRACK paper entitled ‘Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials’, Stephan Windecker and colleagues from the University Hospital Bern in Switzerland note that in light of current evidence available from randomized trials, they aimed to compare the collective safety and efficacy of TAVI vs. surgical aortic valve replacement across the spectrum of risk and in important subgroups. Trials comparing TAVI vs. surgical aortic valve replacement were identified through Medline, Embase, and Cochrane databases. The primary outcome was death from any cause at 2 years. The authors then identified four eligible trials including 3806 participants, who were randomly assigned to undergo TAVI (n = 1898) or surgical aortic valve replacement (n = 1908). For the primary outcome of death from any cause, TAVI as compared with surgical aortic valve replacement was associated with a significant 13% reduction (hazard ratio (HR) 0.87, 95% confidence interval (CI) 0.76–0.99; P = 0.038) with homogeneity across all trials irrespective of TAVI device (P for interaction = 0.306) and baseline risk (P for interaction = 0.610). In subgroup analyses, TAVI showed a robust survival benefit over surgical aortic valve replacement for patients undergoing transfemoral access (HR 0.80, 95% CI 0.69–0.93; P = 0.004), but not trans-thoracic access (HR 1.17, 95% CI 0.88–1.56; P = 0.293) (P for interaction = 0.024), and in female (HR 0.68, 95% CI 0.50–0.91; P = 0.010) but not male patients (HR 0.99, 95% CI 0.77–1.28; P = 0.952) (P for interaction = 0.050). Secondary outcomes of kidney injury, new-onset atrial fibrillation, and major bleeding favoured TAVI, while major vascular complications and incidence of permanent pacemaker implantation favoured surgical aortic valve replacement. The authors conclude that compared with surgical aortic valve replacement, TAVI is associated with a significant survival benefit throughout 2 years of follow-up. Importantly, this superiority is observed irrespective of the TAVI device across the spectrum of intermediate and high-risk patients, and is particularly pronounced among patients undergoing transfemoral TAVI and in females. This work is put into further perspective by an Editorial by Stephen J.D. Brecker from St. Georges Hospital in London, UK.

For decision-making in any cardiac conditions, the natural history of untreated individuals should be known. Unfortunately, current estimates of the natural history and prevalence of aortic stenosis are based on historical studies with potential sources of bias. Indeed, today such patients are at least in part much older, more fragile, and may have more co-morbidities such as diabetes, hypertension, and renal failure, but also inflammatory diseases such as psoriasis or even transthyretin amyloidosis. Furthermore, particularly in older subjects, aortic stenosis may be underdiagnosed as doctors and patients explain their declining exercise capacity with age. In a study entitled Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort...
As mentioned above, aortic stenosis and transthyretin cardiac amyloidosis are both frequent in the elderly. The combination of these two diseases has never been investigated. In a EHJ Brief Communication ‘Aortic stenosis and transthyretin cardiac amyloidosis: the chicken or the egg?’, Thibaud Damy and colleagues from the Henri-Mondor Teaching Hospital in Créteil, France aimed to describe patients with concomitant aortic stenosis and transthyretin cardiac amyloidosis. Six French cardiology centres identified retrospectively 16 cases of mainly male patients with severe or moderate aortic stenosis associated with transthyretin cardiac amyloidosis with a mean age of 79 years hospitalized during the last 6 years. Two-thirds were in NYHA class III–IV, one-third had carpal tunnel syndrome, and more than half had atrial fibrillation. Interventricular septum thickness was 18 mm, left ventricular ejection fraction 50%, and global longitudinal strain −7%. Median NT-proBNP averaged 4382 pg/mL and 91% had elevated cardiac troponin levels. Overall, 88% had severe aortic stenosis, of whom the majority had low-gradient aortic stenosis. Diagnosis of transthyretin cardiac amyloidosis was histologically proven in one-third, and was based on strong cardiac uptake of bone tracer at scintigraphy in the rest. Of these patients, 81% had wild-type transthyretin cardiac amyloidosis, one had mutated Val122I, and in 19% genetic testing was unavailable. Valve replacement was surgical in 63% and with TAVI in 13%. Overall mortality was of 44% during follow-up. The authors conclude that a combination of aortic stenosis and transthyretin cardiac amyloidosis—albeit probably rare—may occur in elderly patients particularly those with a low-flow low-gradient aortic stenosis, and is associated with a bad prognosis. Diagnosis of transthyretin cardiac amyloidosis in aortic stenosis is relevant to discuss specific treatment and management that may become available in the future.

In a second EHJ Brief Communication ‘Iron alters valvular interstitial cell function and is associated with calcification in aortic stenosis’ Magnus Back and colleagues from the Karolinska University Hospital in Stockholm, Sweden remind us that iron accumulates in aortic valves after intraleafflet haemorrhages. Uptake by valvular interstitial cells then stimulates proliferation, extracellular remodelling, and calcification of the valvular tissue, suggesting that valvular iron uptake favours aortic stenosis progression. Iron metabolism has raised great interest in heart failure, and its molecular mechanisms are increasingly understood, thus opening up novel avenues for future treatment options.

This issue ends with a Special Article on the ‘The 200th anniversary of the stethoscope: can this low-tech device survive in the high-tech 21st century?’ by Albert Bruschke and colleagues from Leiden University Medical Center in Leiden, The Netherlands.

In 1816, Laennec discovered that auscultation of the heart and lungs could be performed effectively by placing a hollow cylinder, initially made of a roll of paper, between the chest of the patient and the ear of the examiner. This was the first step in the development of the stethoscope, which was a breakthrough in the diagnosis and

**Figure 1** Venn diagram demonstrating the distribution of single and multiple left-sided valve abnormalities in OxVALVE participants with newly diagnosed valvular heart disease. The outer rectangle represents the full cohort (n = 2500) and the area of each circle is proportional to the number of participants with different manifestations of left-sided valvular heart disease. Numbers denote the number of participants in each group. (from d'Arcy JL, Coffey S, Loudon MA, Kennedy A, Pearson-Stuttard J, Birks J, Frangou E, Farmer AJ, Mant D, Wilson J, Myers G, Prendergast BD. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. See pages 3515–3522.)
management of cardiac and pulmonary patients. Technical improvements of the stethoscope followed, and in cardiac patients auscultation soon became a major diagnostic tool. In the second half of the 20th century, new powerful non-invasive diagnostic modalities were developed and the interest in auscultation declined. Thus, the auscultatory skills of students and physicians decreased to a disappointingly low level. Nevertheless, the time-honoured stethoscope, despite its limitations, still has potential as a patient-friendly, effective, and economical instrument in medical practice.

The editors hope readers of this issue of the European Heart Journal will find it of interest.

References


