The Year in Cardiology 2012: valvular heart disease

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Introduction

Growth of the ageing population, advances in imaging techniques, newly available percutaneous interventions, and emphasis on the central role of the Heart Team in risk assessment and treatment selection1 combine to place valvular heart disease (VHD) at the centre of developments in cardiovascular medicine and surgery. However, VHD is poorly researched in comparison with other areas of cardiac disease, both at a basic scientific and clinical level. Until recently, there have been virtually no randomized controlled trials and international guidelines are largely based on expert consensus. Principal limitations to quality research are the diverse nature of patients with VHD, inability to identify individuals at the earliest stages of disease, and a lack of financial support and an appropriate investigational infrastructure.

Guidelines attempt to address this evidence gap and a key publication this year was the joint European Society of Cardiology (ESC) and European Association of Cardiothoracic Surgeons (EACTS) Guidelines on the Management of VHD.2 This concise and practical document provides recommendations on patient evaluation and risk stratification for both surgical and interventional procedures, coupled with emphasis on multimodality imaging and recommendations from the European Association of Echocardiography on the quantification of valve lesions. Evidence-based implementation of surgical mitral valve repair and transcatheter aortic valve implantation (TAVI) feature strongly together with emphasis on the function of the multidisciplinary Heart Team in achieving optimal outcomes for this challenging group of patients.

Medical therapy for valvular heart disease

The pathophysiology of VHD is under-investigated and predictors of disease progression in individual patients poorly understood. Good quality studies examining medical treatment options in early disease are scarce and have been negative to date. Management of asymptomatic patients is therefore challenging and the subject of ongoing controversy. Novel imaging strategies examining the relative contributions of valvular calcification and inflammation suggest new therapeutic targets and a means of assessing their efficacy.3 Furthermore, refined echocardiographic indices integrating valve area and flow-gradient patterns coupled with biomarker assay may allow improved characterization of patients with asymptomatic severe aortic stenosis (AS) and selection of higher risk subjects for early intervention.4

There are no evidence-based effective medical therapies for degenerative mitral regurgitation (MR) and surgery is recommended for severe MR with left ventricular dysfunction and/or symptoms. In a randomized placebo controlled study of beta-blockade (oral metoprolol), outcomes in patients with severe isolated degenerative MR were determined using cardiac magnetic resonance to assess left ventricular systolic and diastolic function, geometry, and volumes.5 At 2 years, modest preservation of ejection fraction and a trend towards reduced need for surgical intervention were demonstrated in the treatment group but no effects on remodeling were observed. While reduction in sympathetic overdrive may have a role in the management of MR, this was a small preliminary trial and larger multicentre studies with clinical endpoints rather than imaging surrogates are required.

Percutaneous treatment of valvular heart disease

Aortic stenosis

Symptomatic severe AS has a bleak natural history and is associated with poor quality of life. Until recently, aortic valve replacement was the only treatment option but many patients are high-risk surgical
candidates. Percutaneous treatment by means of TAVI is an attractive option for such patients and 10 years on from the first case, over 50 000 TAVI procedures have been performed worldwide.

Two-year outcomes of the landmark PARTNER trial published in 2012 confirm the efficacy and safety of TAVI and its established role as an alternative to conventional surgery in high-risk patients. In PARTNER B, TAVI reduced mortality by a remarkable 25% at 2-year follow-up in carefully selected patients with severe AS deemed unsuitable for surgery in comparison with conventional medical therapy with or without balloon aortic valvuloplasty (all cause mortality 43 vs. 68%, \( P < 0.001 \)). This mortality benefit was accompanied by reduced hospitalization, improved symptom class, and quality of life with sustained valvular haemodynamic performance. Moreover, in PARTNER A, 2-year survival rates were equivalent following TAVI or conventional aortic valve replacement in high-risk surgical candidates. Although stroke frequency did not differ between the study groups (addressing concerns regarding a higher incidence of early stroke after TAVI), paravalvular aortic regurgitation (AR) was more frequent after TAVI and associated with increased mortality. While the causal relationship and clinical significance of this association remain uncertain for patients with mild paravalvular AR, there is consensus that moderate/severe AR is of importance. Pre-procedural assessment of annular anatomy by means of multislice CT enables more accurate valve sizing and should reduce the incidence of this complication of TAVI in conjunction with future device technologies.

Quality of life is of at least equivalent importance to survival in the elderly group of patients considered for TAVI. The health status of 628 patients who had undergone TAVI or high-risk aortic valve replacement within PARTNER A was assessed using the Kansas City Cardiomyopathy Questionnaire, the Short Form 12 and the EuroQol 5D, well validated tools which broadly assess symptoms, physical and social limitations, mental state, and ability to self-care. Health status improved substantially after both TAVI and conventional surgery (\( P = NS \)). However, transfemoral TAVI was associated with a more rapid improvement within 1 month of the procedure (\( P < 0.001 \)), compared with either transapical TAVI or conventional valve replacement. These benefits of transfemoral TAVI are of particular relevance in high-risk elderly patients offering the likelihood of rapid mobility, early hospital discharge, brisk convalescence, and the best prospect of maintained independence.

Further studies highlighted the good long-term outcomes of TAVI, and the adverse prognosis associated with new onset left bundle branch block and major vascular complications after the procedure. These findings, coupled with randomized controlled trials and observational data from large national and international registries provided the platform for updated definitions of procedural complications and robust statements within the ESC/EACTS guidelines concerning patient selection, restriction of TAVI to centres with a dedicated Heart Team and on-site cardiac surgery, and avoidance of the procedure in intermediate- and low-risk patients without randomized controlled trials (Figure 1).

**Mitraclip procedure**

Percutaneous treatment of mitral stenosis is long established and 20-year follow-up of a large French cohort with varied clinical and anatomical characteristics undergoing balloon mitral commissurotomy demonstrated good long-term functional results in 30% (strongly determined by age and immediate procedural outcome) and derivation of a simple multifactorial scoring system for estimating individual patient outcome. Careful patient selection based on such scores may justify earlier intervention by expert teams in younger patients with minimal symptoms and favourable valve morphology.

**Mitrif regurgitation**

The mitral valve is more complex in its anatomy, mechanical function, pathophysiology, and interaction with the left ventricular myocardium than its aortic counterpart. These factors and the demonstrated excellence of surgical mitral valve repair provide a more challenging prospect for the percutaneous treatment of MR. Although several devices and techniques are in development, catheter-based duplication of the Alfieri edge-to-edge repair using the Mitraclip is the only one currently commercially available. The initial pivotal EVEREST II randomized controlled trial failed to show convincing benefits of the Mitraclip technique in comparison with surgical repair in all-comers with severe MR. However, subsequent analysis of outcomes in higher risk subjects (predicted surgical mortality >12%) within the trial compared with registry controls receiving medical therapy alone suggests a role for percutaneous treatment of this challenging subgroup. Seventy-eight patients (mean age 77 years, STS-predicted mortality 14%, 50% previous cardiac surgery, 46 functional, 32 degenerative MR) underwent the Mitraclip procedure with a procedural success rate of 96% and significant reduction in MR in 78%. One-month mortality was equivalent in the Mitraclip and comparator groups (7.7 vs. 8.3%, \( P = NS \)) but survival at 1-year follow-up was superior in the Mitraclip group (76 vs. 55, \( P < 0.05 \)) with accompanying improvement in indices of left ventricular remodelling, symptomatic status, quality of life, and rehospitalization for congestive heart failure. Cautious interpretation of this study is required in view of the mixed aetiology of MR and the use of historical controls—randomized studies in better defined populations are planned. For the time being, the Mitraclip procedure may be considered in carefully selected patients with severe MR who are unsuitable for conventional surgery and remain symptomatic despite maximum medical therapy (Figure 2).

**Valve surgery: mitral valve repair in ischaemic mitral regurgitation**

The severity of ischaemic MR is known to affect survival after surgical or percutaneous revascularization. Using observational data from the larger STICH trial (a randomized study comparing coronary artery bypass grafting (CABG) with medical therapy in ischaemic heart failure), Deja et al. investigated whether additional mitral valve repair in patients with ischaemic MR and severely reduced ejection fraction improves survival. Among 1212 patients with an ejection fraction <35% randomized to CABG within the trial, 42 of 91 patients with moderate to severe MR underwent concomitant mitral valve repair. These patients experienced a more complicated immediate post-operative course though in-hospital mortality was
lower and sustained during long-term follow-up (CABG plus mitral valve repair 44%; CABG only 52%; medical therapy 51%; \( P = \text{NS} \)). Additional mitral valve repair at the time of CABG may be helpful in patients with moderate to severe MR and severe left ventricular impairment. However, interpretation is hampered by the observational design and small number of patients with heterogenous clinical characteristics—a formal randomized controlled trial is required and currently underway.

Figure 1. The management of severe aortic stenosis in 2012. Adapted from Vahanian et al \(^2\) with permission. AS, aortic stenosis; AVR, aortic value replacement; BSA, body surface area; LVEF, left ventricle ejection fraction; Med Rx, medical therapy; TAVI, transcatheter aortic value implantation. *see table 4\(^2\) for definition of severe AS. Surgery should be considered (IIaC) if one of the following is present peak velocity >5.5 m/s; severe value calcification + peak velocity progression ≥0.3 m/s/year. Surgery may be considered (IIbC) if one of the following is present markedly elevated natriuretic peptide levels; mean gradient increase with exercise >20 mmHg; excessive LV hypertrophy. The decision should be made by the ‘heart team’ according to individual clinical characteristic and anatomy.
Infective endocarditis

Two key features of the 2009 ESC Guidelines on the Investigation and Management of Infective Endocarditis (IE) were a reassessment of the rationale for preventive antibiotic prophylaxis and the recommendation that this should be restricted to use in high-risk groups, and a move towards earlier surgery in patients with severe valve destruction and/or high risk of...
systemic embolism. Three years later, two key papers support the abolition of antibiotic prophylaxis altogether.

Studies evaluating the role of early surgery in IE have been limited to retrospective single-centre series with inherent selection bias. Two papers comparing rates of in-hospital death and embolism in 76 patients with severe mitral and aortic IE associated with large (>10 mm) vegetations randomized to undergo surgery within 48 h of admission or conventional antibiotic therapy with surgery according to AHA guidelines. Early surgery was associated with a significant reduction in the primary endpoint of in-hospital death and/or major embolic event within 6 weeks of randomization, driven entirely by reduced incidence of major embolism (0/37 vs. 8/39, \( P = 0.005 \)). All primary endpoints in the conventional treatment group occurred before surgery and inclusion of secondary endpoints (congestive heart failure, recurrent IE, repeat hospitalization) widened the benefits of early surgery. All but four patients in the conventional treatment group required valve surgery, the vast majority as inpatients. Although this was a small single-centre study with predominant streptococcal infection, this important paper highlights the high risk of embolism and heart failure in aortic and mitral IE and demonstrates that this risk is lowered with early surgery without increased mortality.

**Concluding remarks**

All in all, therefore, a very productive year and the prospect of a rosy future. New tools and techniques, new guidelines, new interest and energy, and (perhaps most importantly) new robust evidence. 2012 was an excellent year for VHD specialists and their patients—long may it continue.

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**References**


