Aortic valve and aneurysms

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The aorta is the highway in the human circulation, and accordingly any functional or structural change is associated with severe symptoms or even a fatal outcome. The aortic valve is the door to the aorta and it opens up to 3 billion times in a lifetime. If not perfectly built by nature, e.g., in bicuspid valve disease, or tricuspid valves with raphe, aortic sclerosis and eventually stenosis are the result. Similarly, the aorta itself can change with age and remodel, and eventually develop aneurysms in its thoracic or abdominal part. This issue of the journal is devoted to the aortic valve and in particular the management of patients after valve implantation, as well as the treatment of abdominal aortic aneurysms, a common and potentially fatal disease particularly in male smokers.

This focus issue begins, however, with a timely Clinical Review article on a slightly different topic, i.e., 'Sudden cardiac death in the young: the molecular autopsy and a practical approach to surviving relatives' by Chris Semsarian from the Royal Prince Alfred Hospital in Camperdown, NSW, Australia. Sudden cardiac death of a young, apparently fit and healthy individual is a particularly devastating event for the patient’s family and treating physicians alike. While coronary artery disease and acute myocardial infarction are the most common causes of sudden cardiac death in older populations, genetic cardiac conditions comprise a substantial proportion of such cases in those aged ≤40 years. These include arrhythmogenic disorders such as the long QT syndromes, and inherited cardiomyopathies, namely hypertrophic cardiomyopathy. In up to 30% of young sudden cardiac death, no apparent cause of death can be found, i.e., so-called ‘autopsy negative’ or ‘sudden arrhythmic death syndrome’. Management of families following sudden cardiac death begins with a concerted effort to identify the cause of death in the decedent, based on either pre-morbid clinical details or the pathological findings at post-mortem. Where no cause can be found, genetic testing of DNA extracted from post-mortem blood, i.e., the molecular autopsy, may identify underlying mechanisms in up to 30% of cases. The authors stress the fact that optimal care of families with a sudden cardiac death amongst their loved ones requires dedicated and appropriately trained staff in a multidisciplinary cardiac genetic clinic.

The first paper of this issue is dedicated to the natural history of transcatheter aortic valve implantation (TAVI) valves after implantation. In the ageing Western population, aortic stenosis has become increasingly common, particularly in the elderly. Due to the high operative risk in these frequently frail patients, TAVI or transcatheter aortic valve replacement (TAVR; for our US readers) has been developed. With appropriate pre-operative assessment including sophisticated imaging, modern valves, and experienced operators, the results have become increasingly better and peri-interventional mortality has declined. As a result, the European Society of Cardiology (ESC) Guidelines on valvular heart disease assigned TAVI a I B–C recommendation in patients selected by an experienced Heart Team. This has stirred enthusiasm to use this minimally invasive technique also in patients of lesser age and in those of medium operative risk. The true longevity of these bioprosthetic valves, however, remains unknown.

Thus, the first clinical research paper entitled 'Transcatheter heart valve failure: a systematic review' by Nicolo Piazza from the McGill University Health Centre in Montreal, Canada, accompanied by an Editorial by Jan-Malte Sinning from the Heart Center Bonn, Germany, serves an unmet need. The paper provides a comprehensive description of transcatheter heart valve failure. Between December 2002 and March 2014, a total of 70 publications reported 87 individual cases of TAVI failure. Similar to surgical bioprosthetic heart valve failure, 34 cases of prosthetic valve endocarditis with a similar microbiological profile to surgical cases, 13 structural valve failures, and 15 valve thromboses were noted. Structural valve failure occurred mostly due to leaflet calcification and was predominantly treated in two-thirds of cases by a redo procedure. Valve thrombosis occurred at a mean 9 months post-implantation and was successfully treated by prolonged anticoagulation in three-quarters of the cases. Furthermore, two novel causes of valve failure were identified, i.e., 18 cases of late valve embolization mandating surgery in 80%, and 7 cases of valve compression following cardiopulmonary resuscitation. Potential risk factors for late valve embolization appear to include low prosthesis implantation, valve undersizing, or underexpansion, and bicuspid and non-calcified anatomy. The authors conclude that transcatheter valves are susceptible to failures noted already with surgical bioprostheses, as well as unique causes of failure specific to their specific design. TAVI bioprostheses compression and late embolization represent complications previously unreported.

Unlike TAVI bioprostheses, surgically implanted mechanical valves do require lifelong anticoagulation with vitamin K antagonists. Surprisingly, novel oral anticoagulants do not work in this indication. The second paper 'Telemedicine-guided, very low-dose international normalized ratio self-control in patients with mechanical heart valve implants' by Armin Zittermann from the Heart Center North-Rhine Westfalia in Germany therefore addresses this important topic. The authors studied the efficacy...
and safety of international normalized ratio (INR) self-control with electronically guided transfer of INR values in patients after mechanical valve replacement. In total, 1304 patients undergoing aortic valve replacement, 189 undergoing mitral valve replacement, and 78 undergoing double valve replacement were randomly assigned to low-dose self-control with an INR target range for aortic valve replacement of 1.8–2.8 and 2.5–3.5 for mitral or double valve replacement, or very low-dose self-control once a week and twice a week with an INR target range for aortic valve replacement of 1.6–2.1 and 2.0–2.5 for mitral or double valve replacement. Two-year freedom from bleedings in the low-dose group was 96.3% (and significantly lower) than in the very low-dose once a week (98.6%) and the low-dose twice a week group (99.1%). The corresponding values for thrombotic events were 99.0, 99.8, and 98.9%, respectively, and were statistically comparable. The risk-adjusted composite of grade III complications was in the per-protocol population, with the low-dose group as reference, 0.307 for the very low-dose once a week group and 0.241 for the very low-dose twice a week group. The authors conclude that telemedicine-guided very low-dose INR self-control is comparable with low-dose INR in thrombotic risk, and is superior in bleeding risk. Weekly testing is sufficient. Given the small number of mitral and double valve replacements, however, the results are only valid for those receiving mechanical valves in the aortic position.

The vast majority of patients today have calcified aortic stenosis. Thus, research into the mechanisms of this condition is of great importance. The third Basic Science manuscript ‘Expression of smooth muscle cell markers and co-activators in calcified aortic valves’ by Najma Latif et al. from the Imperial College School of Science in London is based on the fact that similar risk factors and mediators are involved in calcific aortic stenosis and atherosclerosis. Since normal valves harbour a low percentage of smooth muscle cells, the authors hypothesized that the smooth muscle cell phenotype participates in the pathogenesis of calcific aortic stenosis and analysed 12 normal and 22 calcified aortic valves for smooth muscle cell markers and expression of co-activators of their gene expression, i.e. myocardin and myocardin-related transcription factors. Transforming growth factor-β1 (TGFβ1) was used to up-regulate smooth muscle cell markers and co-activators in interstitial cells. Smooth muscle cell markers and co-activators, myocardin, myocardin-related transcription factors-A and -B, demonstrated an increased incidence and aberrant expression around calcified nodules in all 22 calcified valves as well as in surface and microvessel endothelial cells. Smooth muscle cell markers and myocardin-related transcription factors-A were abundant in calcified valves. TGFβ1 up-regulated the expression of some smooth muscle cell markers, as well as myocardin-related transcription factors-A in interstitial cells. In the fibrobra layer of calcified valves, bundles of smooth muscle cells and smooth muscle-derived foam cells were noted. The authors conclude that smooth muscle cell markers and co-activators such as myocardin and myocardin-related transcription factors are aberrantly expressed in calcified valves. TGFβ1 was able to up-regulate these markers in interstitial cells. Smooth muscle cells were abundantly present in calcified regions of the leaflets, suggesting that they play a role in the development of calcific aortic stenosis.

The fourth Basic Science paper ‘The effect of aortic morphology on peri-operative mortality of ruptured abdominal aortic aneurysm’ by Janet T. Powell and colleagues from the Imperial College London is devoted to a frequent aortic disease. Of note, the ESC recently published their guidelines on this issue. An important development in the management of patients is the introduction of endovascular aneurysm repair (EVAR), which is much less invasive for patients than the classical surgical approach. Whether a patient with a ruptured abdominal aortic aneurysm is eligible for endovascular aneurysm repair is currently debated among experts. Aneurysm shape and extent may help in the decision to use endovascular repair rather than open surgical repair. The influence of six morphological parameters, maximum aortic diameter, aneurysm neck diameter, length, and conicality, proximal neck angle, and maximum common iliac diameter, on mortality and reinterventions within 30 days was therefore investigated in patients randomized before morphological assessment in the Immediate Management of the Patient with Rupture: Open Versus Endovascular strategies (IMPROVE) trial. Among 458 patients who had either endovascular or surgical repair, there were 155 deaths and 88 re-interventions within 30 days of randomization. Of note, aneurysm neck length was shorter in those undergoing open repair and was inversely associated with mortality for open repair. There were no convincing associations of morphological parameters with reinterventions. The authors conclude that in patients with ruptured abdominal aortic aneurysms, short aneurysm necks adversely influence mortality after open repair and preclude conventional endovascular repair. This may help explain why observational studies, but not randomized trials, have shown an early survival benefit for endovascular repair. The importance of these findings is further discussed in an Editorial by Johnny Steuer from the Section of Vascular Surgery in Stockholm, Sweden.

The editors hope that this issue of the European Heart Journal will be received with interest by its readers.

References


