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TAVI the frontier of interventional cardiology 40 years after the first ballon angioplasty

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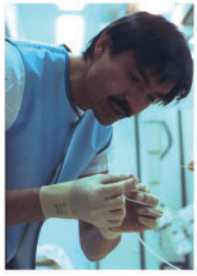

Forty years ago on 16 September 1977, Andreas R. Grüntzig performed his seminal procedure that led to the development of interventional cardiology as a novel discipline of cardiology.[1] Ever since, the spectrum of catheter-based interventions has been expanded from coronary[2–4] to valvular heart disease. Indeed, valvular heart disease has enjoyed an impressive revival of interest recently, thanks to the introduction of transarterial valve implantation or TAVI[5] and catheter-based interventions at the mitral[6,7] and, most recently, the tricuspid valve.[8] This has also revitalized the discussion on the use of surgical valves. Mechanical valves are still frequently used for surgical aortic valve replacement, but continue to be associated with bleeding risks,[9] because of the requirement for anticoagulation with vitamin K antagonists, while bioprosthetic valves do not require that, but are at risk of structural valve deterioration requiring re-operation.[10]

The decision as to what valve to use in patients undergoing surgery for aortic stenosis is extensively discussed in a review entitled '**Mechanical vs. bioprosthetic aortic valve replacement**' by Stuart J. Head and colleagues from the Erasmus University Medical Center in Rotterdam, The Netherlands.[11] These risk and benefit considerations of mechanical and bioprosthetic valves has led to American and European guidelines[12] on valvular heart disease recommending the use of mechanical prostheses in patients younger than 60 years of age. Despite these recommendations, the use of bioprosthetic valves has increased in all age groups. A systematic review applying propensity matching or multivariable analysis to compare the usage of mechanical vs. bioprosthetic valves found either similar outcomes between the two types of valves or favourable outcomes with mechanical prostheses, particularly in younger patients. Indeed, current evidence does not support lowering the age threshold for implanting a bioprosthesis. Heart Teams and patients should be cautious in pursuing more bioprosthetic valve use until its benefit is clearly proven in middle-aged patients.

Risk factors to develop aortic stenosis primarily involve age and structural defects of valve structure. In a first clinical research article entitled '**Overall and abdominal obesity and incident aortic valve stenosis: two prospective cohort studies**', Susanna C. Larsson and colleagues from the Institute of Environmental Medicine in Stockholm, Sweden examined the association of overall and abdominal obesity with aortic stenosis incidence in the Cohort of Swedish Men and the Swedish Mammography Cohort, involving 71 817 men and women who were free of cardiovascular disease.[13] During a mean follow-up of 15 years, 1297 incident aortic stenosis cases were ascertained. Both overall and abdominal obesity, measured as body mass index (BMI) and waist circumference, respectively, were associated with the incidence of aortic stenosis, with similar associations in men and women. Compared with BMI 18.5–22.5 kg/m^2, the multivariable hazard ratios were 1.24 for overweight, i.e. a BMI of 25.0–29.9 kg/m^2, and 1.81 for obesity, i.e. a BMI $\geq$30 kg/m^2. The hazard ratio for substantially large waist circumference in men $\geq$102 cm and in women $\geq$88 cm compared with normal waist circumference was 1.30. Impressively, the proportion of aortic stenosis cases estimated to be attributed to overweight and obesity combined was 10.8%. Thus, it would need to be shown whether a large proportion of the cases may be prevented if the population maintained a healthy BMI. Among others, this issue is discussed in an **Editorial** by Patrick Mathieu from the Laval Hospital in Quebec, Canada.[14]

Transarterial valve implantation or TAVI is increasingly used not only in inoperable patients and those at high risk of surgery,[15] but also in those at intermediate risk.[16] Recently, it has been noted that high attenuation leaflet thrombosis or HALT develops in certain patients after TAVI.[17] However, the clinical importance of these computed tomography or CT findings remains uncertain. Although some patients develop pressure gradients, strokes occur extremely rarely, if at all, in such patients.[18] The SAVORY registry enrolled 75 patients treated by TAVI and 30 with surgical aortic valve replacement with two 4D CT scans fully interpretable for HALT and hypoattenuation affecting motion as well as unchanged antithrombotic medication

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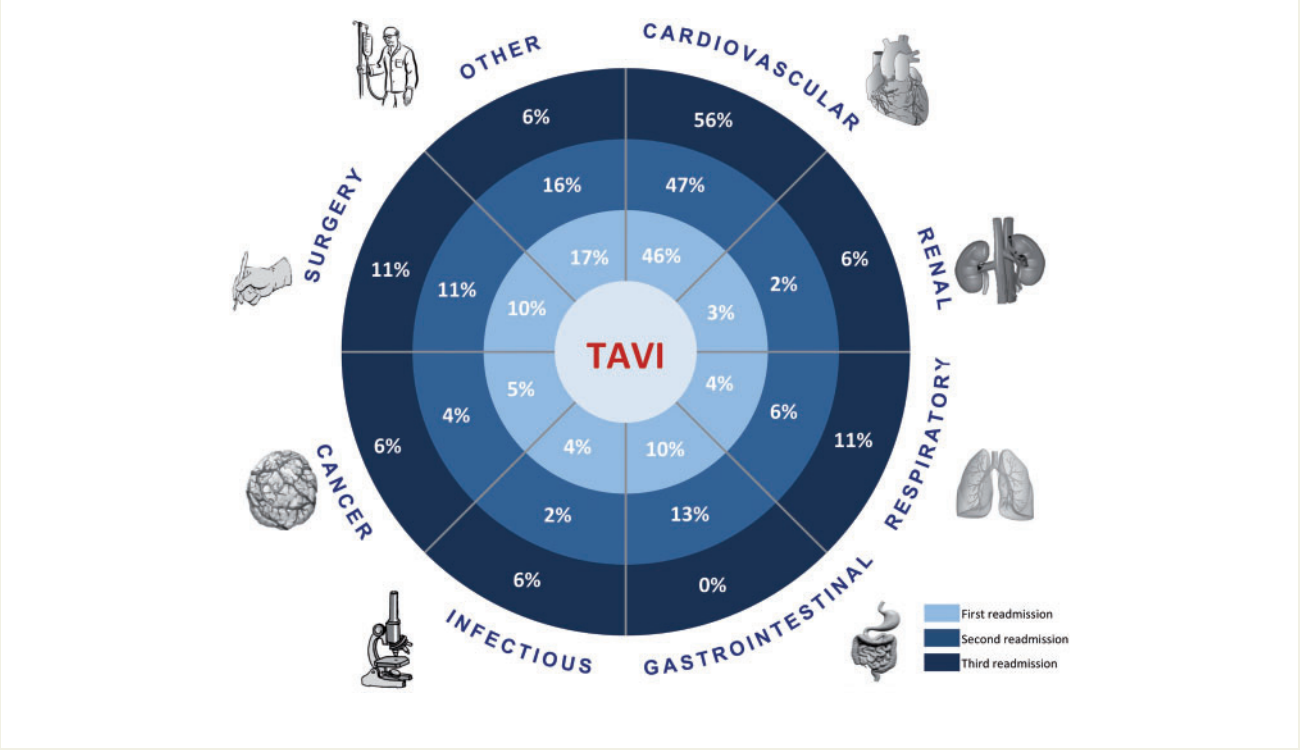

Figure 1 Causes of hospital readmission by timing of occurrence. Distribution of causes of hospital readmission according to the timing of their occurrence since discharge after the procedure. (From Franzone A, Pilgrim T, Arnold N, Heg D, Langhammer B, Piccolo R, Roost E, Praz F, Räber L, Valgimigli M, Wenaweser P, Jüni P, Carrel T, Windecker S, Stortecky S. Rates and predictors of hospital readmission after transcatheter aortic valve implantation. See pages: 2211–2217).

between the scans. Lars Sondergaard and colleagues from the Rigshospitalet in Copenhagen, Denmark report their results in their manuscript '**Natural history of subclinical leaflet thrombosis affecting motion in bioprosthetic aortic valves**'.[19] The analysable population of 84 patients had a first and second CT scan at 140 and 298 days after valve implantation, respectively. HALT was noted in 38% and hypoattenuation affecting motion in 20%. Both findings were dynamic, showing progression in 16% and regression in 11%. Compared with antiplatelet therapy, progression was less likely among patients on oral anticoagulation with vitamin K antagonists or non-VKA oral anticoagulants with an odds ratio of 0.014. However, maintenance on chronic oral anticoagulation was not a significant predictor of regression. These findings were similar for transcatheter and surgical bioprosthetic aortic valves. No patients developed symptoms of valve dysfunction, and leaflet thickening was not associated with clinical events. Thus, subclinical leaflet thrombosis appears common after TAVI or surgical aortic valve replacement and may progress from normal leaflet through high attenuation leaflet thrombosis to the more severe hypoattenuation affecting motion. Moreover, the phenomenon can develop and regress at variable intervals after valve implantation. Anticoagulants may have a protective effect, but HALT can also regress without anticoagulation therapy. These provocative findings are put into a clinical context in an interesting **Editorial** by Jeroen J. Bax from the Leiden University Medical Center in The Netherlands.[20]

Be that as it may, patients do experience various other events after TAVI, including death.[21–23] This may be in part related to the advanced age ond co-morbidities of these patients. Stefan Stortecky and colleagues from the University Hospital Bern in Switzerland sought precisely to analyse reasons for, timing of, and predictors of hospital readmissions after TAVI in their paper entitled '**Rates and predictors of hospital readmission after transcatheter aortic valve implantation**'.[24] Of 868 patients alive at discharge in their single-centre registry, one in four were readmitted within 1 year. Compared with patients not requiring readmission, those with at least one readmission more frequently were male and more often had atrial fibrillation and higher creatinine levels. For the 308 readmissions, cardiovascular causes accounted for 46% with heart failure, while non-cardiovascular readmissions occurred for surgery in 12%, gastrointestinal disorders in 10%, malignancy in 5%, respiratory diseases in another 5%, and chronic kidney failure in 3% (*Figure 1*). Male gender and stage 3 kidney injury were independent risk factors for any hospital readmission, whereas previous myocardial infarction and in-hospital life-threatening bleeding were associated with cardiovascular readmissions. The event rate for mortality was significantly increased after readmissions for any cause, with a relative risk of 4.3. Thus, hospital readmission after TAVI are frequent and are associated with an increase in mortality. These findings are discussed in a comprehensive **Editorial** by Devraj Sukul from the University of Michigan Health System in Ann Arbor, Michigan, USA.[25]

An important issue during the evaluation of patients considered for TAVI is concommitant mitral regurgitation, the quantification of which remains challenging.[26,27] Jeroen J. Bax and colleagues from the Leiden University Medical Center in The Netherlands evaluated the concept of integrating echocardiography and CT for grading mitral regurgitation severity in their paper entitled '**Integrated imaging of echocardiography and computed tomography to grade mitral regurgitation severity in patients undergoing transcatheter aortic valve implantation**'.[28] Specifically, an integrated parameter was developed that combines the true cross-sectional mitral regurgitant orifice area as assessed with multidetector CT with flow data from echocardiography. Systolic multidetector CT data of 73 patients, referred for TAVI who also had mitral regurgitation, were evaluated. The mitral regurgitant orifice area was multiplied by the velocity time integral of the mitral regurgitation jet on echocardiography for the calculation of the integrated regurgitant volume. Multidetector CT analysis showed a mean mitral regurgitant orifice area of 11.3 ± 7.4 mm^2 and a mean integrated integrated regurgitant volume of 21.4 ± 14.7 mL/beat, whereas echocardiography showed a mean effective regurgitant orifice area and integrated regurgitant volume of 13.3 ± 8.2 mm^2 and 23.9 ± 13.6 mL/beat, respectively. Compared with echocardiography, grading based on integrated mitral integrated regurgitant volume resulted in reclassification of 10% of the patients from severe to non-severe mitral regurgitation and 14% of the patients from non-severe to severe mitral regurgitation. Thus, integrated mitral regurgitant volume is a quantitative parameter of mitral regurgitation severity by combining the true cross-sectional mitral regurgitant orifice area assessed with multidetector CT and Doppler mitral haemodynamics, which results in a clinically meaningful reclassification of the severity of mitral regurgitation in some patients with severe aortic stenosis undergoing TAVI. The clinical applicability of these findings are evaluated in an **Editorial** by Jan-Malte Sinning from the Heart Center Bonn in Germany.[29]

The introduction of TAVI has brought cardiologists and cardiac surgeons closer together than ever. Today, every patient with valvular heart disease should be discussed in a interdisciplinary group of physicians experienced in the field. The requirements of such a Heart Team are defined by the ESC Working Group on Valvular Heart Disease and the European Association for Cardiothoracic Surgery in a Viewpoint entitled '**Standards defining a "Heart Valve Centre"**'.[30] The experts state that such teams should include cardiologists with competencies in valve disease, cardiac imagers, cardiac anesthesiologists, surgeons and interventional cardiologists with training and experience in valvular heart disease, but also extracardiac specialists. as appropriate. Good results are usually associated with high individual and centre volumes, but this relationship is complex and it is more important to report outcome data, which must be available for external audit.[31] Results of both the immediate 30-day post-operative period and at least 1- and 5-year follow-up should be reported according to the Valve Academic Research Consortium recommendations. The authors further stress that there should be structured training programmes available for staff involved in the periprocedural care of patients and these should be overseen by national or international professional societies. 'Heart Valve Centres' should be involved in technical innovation and research, and in developing prospective databases and registries.

The editors hope that this issue of the *European Heart Journal* will be of interest to its readers.

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