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EDITORIAL COMMENT

Trailing behind: Limitations on transcatheter aortic valve implantation in Portugal☆

Na cauda do cometa. Limitações para implantação de válvulas aórticas percutâneas transcatéter em Portugal

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Transcatheter aortic valve implantation (TAVI) is an unparalleled therapeutic innovation in cardiology. The first valve was developed by Andersen et al. in 1989, but two decades passed before the first randomized trial was performed, in which at 24-month follow-up, there was an absolute reduction in mortality from 51% under medical therapy to 31% with TAVI.[1–4] Following the first implantation in humans by Cribier et al. in 2002, Webb et al. introduced the retrograde approach in 2005 and Walther et al. the transapical approach in 2006, which sparked a meteoric rise in use of the technique.[5–7] These developments have reduced 30-day mortality to 6.5–9.7%,[8–10] and it is still progressing, concomitantly with significant gains in quality of life.[11,12]

There are considerable differences in Europe in access to TAVI for severe aortic stenosis, particularly in Portugal.[13,14] The prevalence of aortic stenosis increases with age, and based on an estimated prevalence of 3.4% among the 924 000 Portuguese aged over 75, around 32 000 will have severe stenosis, of whom 75% (24 000) will be symptomatic.[15] Assuming that around 40% of those considered inoperable and 80% of those at high surgical risk are eligible for TAVI, this amounts to 4600 individuals.[16] However, the data for Portugal show that 265 TAVI procedures were performed in the last five years, only 5% of potential candidates.

Portugal has the lowest annual rate of TAVI per million population in the European Union – seven compared to an average of 45. Adoption of the 2012 guidelines of the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery could help bring Portugal more in line with the rest of Europe in the use of this new technique.[17] There are 3 areas in which the guidelines are of particular relevance to aortic stenosis:

(1) Screening and diagnosis, which needs to be earlier and more accurate:
   (a) in terms of primary health care, paying particular attention to symptoms that are extremely common in the elderly, such as exertional dyspnea, asthenia and dizziness;
   (b) in terms of echocardiographic assessment, which is hampered in many cases by the lack of Doppler study;
(2) Appropriate therapeutic indications, favoring surgical or percutaneous valve replacement over medical therapy alone:

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a. appropriate referral on the part of cardiologists, including of patients with severe aortic stenosis who appear asymptomatic and particularly those with comorbidities that reduce their quality of life and/or prevent referral for surgical valve replacement[18];
b. on the part of cardiac surgeons, when stratifying the potential benefit of conventional surgery and determining operative risk, which is higher in the elderly and women, and in cases of left ventricular dysfunction, comorbidities, higher functional class, pulmonary hypertension or coronary artery disease, and emergency operation[19];
c. predictors of risk in TAVI, the subject of much research into anatomical evaluation for selection of vascular access and type of prosthesis, especially of the aortic annulus, which is rarely circular and often deformed by severe calcification.

(3) Organization and expertise of multidisciplinary teams using the latest technology available within budgetary constraints:
   (a) establishment of a multidisciplinary 'heart team' including cardiologists, cardiac surgeons, imaging specialists, interventional cardiologists, anesthetists, geriatricians, heart and lung specialists, nursing staff and rehabilitation specialists;
   (b) patient-centered management on an individual basis, with preference given to conventional surgery but, when appropriate, respecting patients' wishes for the least invasive approach (the PARTNER trial showed that 8% of patients withdrew their consent for conventional surgery compared to 0.3% in the TAVI group[2]);
   (c) prosthesis characteristics, an area that is developing rapidly within two main types of delivery and release systems (self-expanding and balloon-expandable) and two types of biological material (bovine or porcine pericardium) currently available, in four sizes suitable for annulus diameters of 18–29 mm;
   (d) assessment of the economic burden to society through studies of improvements in quality of life and cost-effectiveness.[20]

The article by Sousa et al. in this issue of the *Journal* focuses on the penultimate point, concluding that all currently available vascular approaches and three sizes of two types of prosthesis – Medtronic CoreValve and Edwards Sapien – give a significantly wider range of anatomical alternatives, making TAVI an almost universal treatment option.

The study population was a reasonable size, reflecting the experience of the team that began TAVI procedures at the Centro Hospitalar de Vila Nova de Gaia in August 2007, when they performed the first implantation of a self-expanding CoreValve prosthesis via transfemoral access in the Iberian Peninsula.[21]

Few anthropometric data are presented to indicate that most patients had small annulus diameters, which is to be expected since the mean height of the Portuguese population is 165.5 cm, shorter than the European Union average of 169.9 cm.[16]

The study was retrospective and focused on the data that was most relevant to the study's objectives, using two complementary imaging techniques.

Determining the aortic annulus diameter is essential in procedure planning in order to minimize paravalvular leak,[22] embolization (0.5–8% of cases), annulus rupture (although rare), and need for permanent pacemaker (3–40%), which appears to be more frequent with larger valves.[22–25] As stated above, the aortic annulus is often oval and much effort has gone into developing software to increase the accuracy of valve area measurements, which is increasingly important in the choice of prosthesis size.[26,27] Three-dimensional transesophageal echocardiography (3D TEE) has advantages over transthoracic echocardiography and two-dimensional TEE in this respect.[28] Sousa et al. used TEE by preference, although they do not state whether this was performed prior to or during the procedure, nor what proportion of patients underwent 3D TEE. The study did not assess the anatomy of the ascending aorta or the coronary sinuses, the proximity of the coronary arteries to the valve plane, the degree and distribution of aortic and mitral calcification, or left ventricular outflow tract diameter. Although there are no unequivocal exclusion criteria, information on sinus of Valsalva dimensions or severe septal hypertrophy with intraventricular gradient would have been relevant to the study's objectives since it might have excluded implantation of at least one of the types of prosthesis assessed.

The main predictors of major vascular complications, which occur in 4–20% of cases, are the relationship between the caliber of the introducer and the native artery, vessel calcification and operator experience.[29] Sousa et al. assessed femoral artery diameters by multidetector computed tomography but ignore the importance of calcification, which is critical, although the center does have wide experience of this imaging technique.[30] It would be of interest to know what equipment was used and the type and reproducibility of the protocol, together with data on the degree and distribution of calcification, particularly circumferential, and on 3D assessment of aortic and iliofemoral anatomy.

The important point is that there were solutions to cover 98.6% of the patients. The study showed that this was only possible based on a multiple device strategy, since each type of prosthesis could not treat 2.8% and 6.2% of cases, respectively. Moreover, use of multiple approaches significantly extended this treatment option to a further 5.2% of patients.

One remark is that the term ''anatomically suitable'' slightly overestimates the real number of candidates. Detailed anatomical evaluation for planning the procedure will usually exclude some patients, for example due to vessel tortuosity in a transfemoral approach or the association of calcification and proximity of the coronary arteries in a transapical approach.

Since 98.6% of implantations were with a single type of prosthesis, nothing can be concluded as to the link between anatomical variables and the type of valve and access chosen. It would be interesting to analyze the prognostic implications of these procedure-related variables in terms of adverse events according to the standardized endpoint definitions proposed by the

Valvular Academic Research Consortium,[29] in which device success is defined as correct positioning of the device and mean anterograde valve gradient of <20 mmHg, with no moderate or severe prosthetic valve regurgitation, and absence of procedural mortality.[31] Early (30-day) safety criteria are defined as absence of mortality, stroke, life-threatening bleeding, stage 2 or 3 acute renal failure (contrast nephropathy), coronary artery obstruction requiring intervention, major vascular complications, and valve-related dysfunction requiring repeat procedure.

In conclusion, the study by Sousa et al. is original because it shows that anatomy is not a limiting factor with current percutaneous aortic valves if multiple devices and multiple access approaches are considered. The most important factors now governing the treatment of aortic stenosis are screening, diagnosis, comorbidities, multidisciplinary therapeutic management, technological advances and cost. Each represents a challenge that, if overcome, may eventually mean that even patients at low or intermediate surgical risk can be treated by TAVI.

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