

# Transcatheter aortic valve implantation in Italy: an uneven growth

Giulia Masiero and Giuseppe Musumeci\*

USC Cardiologia, Ospedale Santa Croce e Carle Cuneo, via M. Coppino, 26, Cuneo, Italy

## KEYWORDS

TAVI (transcatheter valve aortic implant);  
SAVR (surgical aortic valve replacement);  
SAS (severe aortic stenosis)

Transcatheter aortic valve implantation (TAVI) is the treatment of choice in patients with severe symptomatic aortic stenosis who are not suitable for surgery. The procedure has become the preferred strategy in patients at intermediate/high surgical risk with favourable clinical and anatomical characteristics. The collected scientific evidences, as well as the technologic innovations shaping the newer devices, allowed for a progressive reduction of the procedure-related complications as a well as a simplification of the procedure itself, promoting the gradual expansion of the indication for TAVI with the consequent increase in the estimated number of procedures performed each year. There are significant geographic and socio-economic disparities in the use of TAVI around the world and in Italy as well, reflecting an application of the procedure directly related to the economic prosperity of the Health System of the Country examined. The Italian situation, similar to the worldwide reality, reveals an uneven application of the procedure, signalling a disparity in the socio-economic and organizational capabilities of each single region. Standardization of patient selection for treatment, and of the clinical pathway for TAVI are crucial for an homogeneous integration of this new technology in the current Health Care System.

## Premise

Aortic valve stenosis (AS) represents the most common valvulopathy in Europe and North America, with a growing prevalence due to the progressive ageing of the population.<sup>1</sup> The incidence rate of severe AS is equal to 4.4°/oo/year in the general population over the age of 65; among these, however, more than 40% of patients with asymptomatic severe AS present contraindications to the traditional valve replacement surgery (SAVR, surgical aortic valve replacement). Over the past 15 years, transcatheter aortic valve implantation (TAVI) has proved superior in terms of survival, compared to medical therapy, in inoperable elderly subjects and not lower, compared to surgery, in patients at intermediate/high risk, for this reason, it is facing exponential growth and diffusion.<sup>2</sup> In this context, an annual growth of 7% of potential TAVI candidates is expected, exceeding, in Europe only, 120 000 patients/

year.<sup>3</sup> The accumulated scientific evidence, the introduction of new generation prostheses with the reduction of cardiac, cerebral, and especially vascular complications, and the progressive simplification of the procedure are also favouring the progressive expansion of indications for percutaneous correction of aortic valvulopathy, addressing patients of advanced age with low surgical risk or correction of moderate symptomatic aortic stenosis or severe insufficiency.<sup>4</sup> In such a scenario, the estimate of the procedural volume predicts a further annual growth of 50%.<sup>3</sup> Recent studies, however, have found profound geographical and socio-economic disparities in the degree of access and use of TAVI in the world that translate into a gradient of penetration of the method directly correlated to the economic prosperity of the health system of the country examined.<sup>4</sup> We therefore propose an overview of the current state of the art of TAVI, providing a brief account of the most recent innovations and future perspectives and analysing in more detail the penetration of this method in the Italian national reality.

\*Corresponding author. Email: giuseppe.musumeci@gmail.com

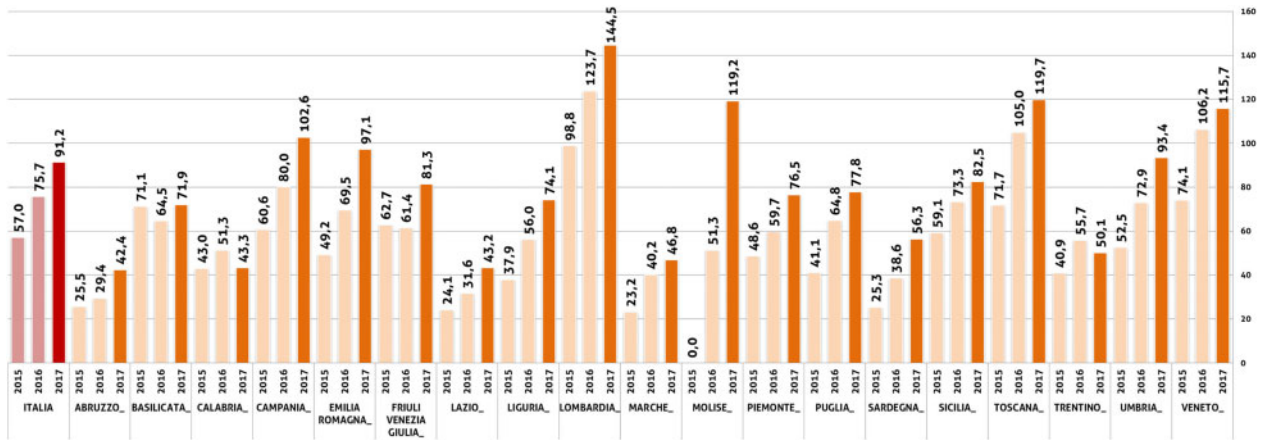
**Table 1** Integrated approach for the evaluation of the operative risk of the patient suffering from asymptomatic severe aortic valve stenosis

	Pro-TAVR	Pro-SAVR
Clinical characteristics	STS/EuroSCORE II >4%, logistic EuroSCORE I >10% Age ≥75 years Other severe comorbidities not included in the STS score, previous cardiac surgery, frailty, reduced mobility, and other conditions that limit post-procedural rehabilitation	STS/EuroSCORE II <4%, logistic EuroSCORE I <10% Age <75 years Suspect of endocarditis
Anatomical and technical aspects	Favourable access for trans-femoral TAVI Aspects of disfavour for SAVR: sequelae of thoracic irradiation, porcelain aorta, presence of patent aorto-coronary bypass risky in the case of sternotomy, expected mismatch prosthesis-patient, severe thoracic deformations or scoliosis	Unfavourable access (any) for TAVI Aspects that are unfavourable for TAVI: short distance between coronary arteries and aortic annulus, size of the aortic annulus outside the range for TAVI, morphology of the aortic or valvular root (bicuspid aortic valve, degree and distribution of calcifications) unfavourable for TAVI, presence of thrombi in the aorta or left ventricle
Cardiac conditions in addition to aortic stenosis requiring assessment for possible combined intervention	—	Severe CAD, severe primitive, or tricuspid mitral valve disease, ascending aortic aneurysm or hypertrophy of the septum requiring surgical treatment

## State of the art

After the first pioneering TAVI implant, which took place in 2002, numerous randomized studies and observational registers of comparison between medical therapy or traditional surgery followed, which enrolled, starting from 2007, more than 15 000 patients demonstrating the superiority of the method in terms of survival, compared to medical therapy, in inoperable subjects and non-inferiority, compared to surgery, in patients at intermediate/high risk.<sup>4</sup> The sub-analyses of the most recent studies involving patients of an average age of not less than 80 years but at intermediate surgical risk (Society of Thoracic Surgeon, STS-PROM, average score between 4 and 8) have also shown, if the trans-femoral approach was applied, the superiority of percutaneous implant compared to surgical solution.<sup>5</sup> In light of these evidences, the most recent European guidelines on the treatment of AS favour the trans-femoral percutaneous treatment of elderly patients suffering from a non-negligible surgical risk, however, submitting the choice between TAVI and SAVR to a multidisciplinary evaluation by a Heart Team (IC class recommendation) that must analyse clinical and anatomical elements, procedural technical aspects and further comorbidities that may need surgical correction to select the safest and most effective treatment for the individual patient<sup>5</sup> (Table 1). At present, the percutaneous approach is in fact still burdened by a higher rate of vascular complications, implantation of pacemakers, and paravalvular leaks, than the surgical technique, with a severity strictly related to the type of device used and the selection of the patient; on the other hand, with surgery, severe bleeding,

acute renal failure, and atrial fibrillation of new occurrence are more frequent, while there are no differences in terms of stroke.<sup>2</sup> The decades of clinical experience accumulated in the field of TAVI along with a conspicuous investment in terms of clinical research are however favouring a progressive simplification and the achievement of a greater safety of the procedure through: technical implementations of the valve and the release system, the development of dedicated imaging programmes for effective pre-procedural planning, the use of a more minimalist procedural approach such as the use of mild sedation and transthoracic echocardiographic guidance. These innovations have, in fact, allowed the progressive reduction of cardiac, cerebral, and especially vascular complications, authorizing the expansion of the possible indications of TAVI to patients of advanced age at low surgical risk or to the correction of moderate symptomatic aortic stenosis or severe insufficiency. On the other hand, the limits still related to the method (the durability of the device due to structural degeneration processes, the non-negligible risk of ischaemic stroke, and the need for a permanent pacemaker, the treatment of complex anatomies such as bicuspid aortic valve) represent the stimulus for the further innovations necessary for the opening of the TAVI market to the treatment of patients of a younger age.<sup>1</sup> Despite these developments, the global spread of TAVI presents a marked geographical dis-homogeneity due to different socio-economic factors that favour a penetration of the method directly correlated to the economic prosperity of the health system of the country examined. These factors include the high costs of the device that weigh on health spending, the need for adequate infrastructure, the



**Figure 1** Number of transcatheter aortic valve implants per million inhabitants, in Italy, from 2015 to 2017. Alto Adige and Valle d'Aosta do not perform transcatheter aortic valve implantation. *Source:* GISE data Think Heart 2018.

absence of dedicated Heart-Teams, the presence of peculiar anatomical characteristics of the population. An analysis conducted in 2011 among 11 European countries has indeed demonstrated a variation in the number of TAVI procedures per million inhabitants/year between 6.1 implants in Portugal and 88.7 in Germany.<sup>4</sup>

## Transcatheter aortic valve implantation in Italy

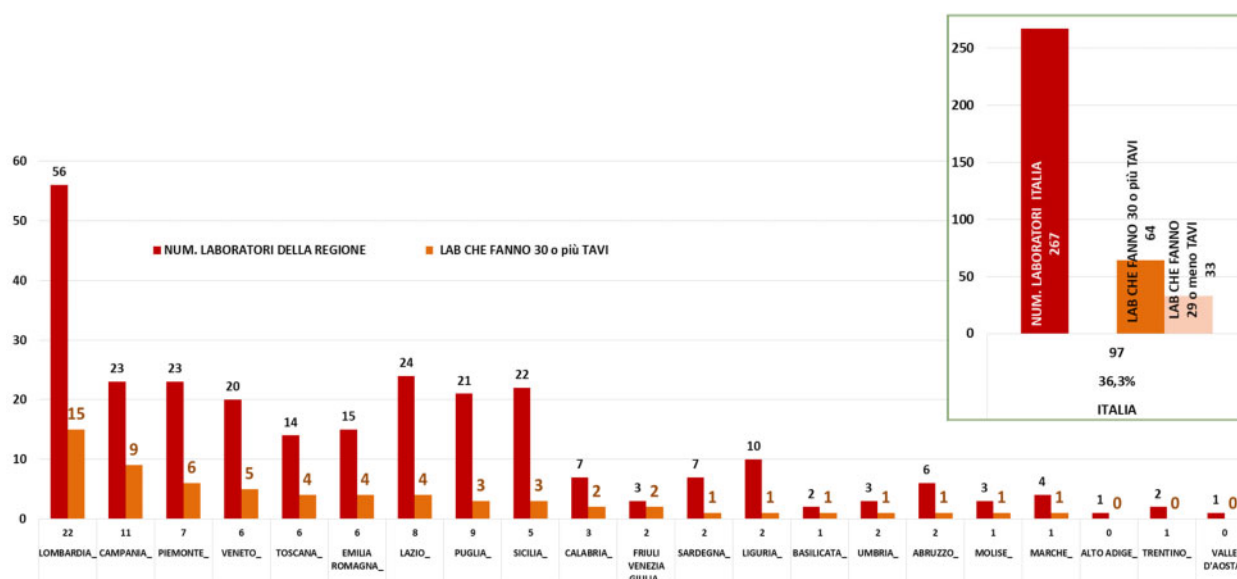
From 2007 to 2017, in Italy, the number of TAVI procedures performed has grown exponentially to reach 5528 procedures in the year 2017, registering a 21% increase compared to the previous year in analogy with the growth trend observed in others European countries.<sup>6</sup> The activity report of the Italian Society of Interventional Cardiology GISE, has collected in 2017 the data of 267 centres equal to 98.5% of the associated centres and made it possible to point out the situation of our country regarding the application of this method:

- The number of cath-labs that perform TAVI in Italy is 97, almost all of which at centres with cardiac surgery in the centre and in 19% of cases in a hybrid room; in 5% of centres without Cardiac Surgery, the procedures were carried out in affiliated facilities.
- The significant increase in the number of procedures/year performed was driven by the increase recorded in some more virtuous regions such as Lombardy which in 2017 performed 144 TAVI per million inhabitants followed by Tuscany, Molise, and Veneto, with 120, 119, and 116 interventions per million inhabitants, respectively (*Figure 1*).
- The average number of TAVI performed per cath-lab was 57 procedures/year and more than 60% of the centres reported an average volume of more than 30 procedures/year. The regions with the highest concentration of cath-labs with the highest annual procedural volume were the following: Lombardy, Campania, Piedmont, and Veneto; on the contrary, Marche, Molise, Abruzzo, Umbria, Basilicata, and

Sardinia presented the lowest concentration of high-volume centres (*Figure 2*).

- The privileged vascular access was the femoral one, accounting for 90% of the cases.
- Regarding the type of device used, a fair majority of expandable valves were recorded (mainly CoreValve, Lotus, Portico, and Symetis, respectively in 49%, 6%, 5%, and 4% of cases) compared to those mounted on balloon (Edwards Sapien in 33% of cases) in the absence of significant differences among regions.

The OBSERVANT study was the first study aimed at assessing the appropriateness, efficiency, and efficacy of SAVR and TAVI procedures in the treatment of aortic stenosis in Italy.<sup>7-9</sup> It is an observational, prospective, multicentre study that between December 2010 and June 2012 enrolled 5707 surgical patients, 1652 TAVIs performed with transfemoral approach and 259 TAVIs performed with transapical approach, for a total of 7799 patients; 61 surgical centres and 34 cath-labs participated in the enrolment process. The choice between SAVR and TAVI was based on the clinical judgement of local Heart-teams. Patients who underwent SAVR presented a significantly lower risk profile with a correspondingly lower average logistic EuroSCORE value than the TAVI groups. The risk class most represented in the TAVI group was between 5% and 10% and in particular, about half of the patients who underwent trans-femoral TAVI presented a logistic EuroSCORE level <10%. The propensity-matched analysis of patients over 80 years of age at intermediate surgical risk showed no differences between surgical treatment and percutaneous treatment in terms of short- and medium-term survival, highlighting however different rates and types of complications between the two groups.<sup>10</sup> Patients who underwent TAVI were in fact burdened with higher rates of vascular complications, para-valvular leaks, and pacemaker implantation; surgically treated patients reported peri-procedural stroke, acute renal failure, shock, bleeding, and increased trans-prosthetic gradients with greater frequency. In December 2016, phase II of this study was launched in order to enroll a new TAVI series, also with different risk profiles compared to the previous one, and to evaluate whether



**Figure 2** Proportion of catheterization laboratories (Cath-Labs) performing more than 30 transcatheter aortic valve implantation/year at regional level. Source: GISE data Think Heart 2018.

the use of new generation devices, together with the progress in terms of operator's expertise, were able to modify the results in the comparison between SAVR and TAVI.<sup>11</sup>

With 91 procedures per 1 000 000 inhabitants, our country ranks among the last European health systems in terms of volume of TAVI implanted/year, with a very uneven and not always regulated distribution on the national territory. Only 9 out of 20 were the regions that issued resolutions of council or departments to address documents and/or indications on reimbursement. The lack of unambiguous identification of the procedure in the hospital discharge record and the DRG with the often inadequate reimbursement of the procedure, puts our country in a situation of disadvantage compared to the main advanced health systems, and conditions the different adoption in the Italian regions. The research project 'Costs, cognitive abilities and quality of life of transcatheter aortic valve implantation and surgical aortic valve replacement' (CCQ, ClinicalTrials.gov ID: NCT01852552) had the objective of estimating, in the four participating regions (Piedmont, Emilia-Romagna, Lazio, and Sicily), the different costs of hospitalization index of patients suffering from severe aortic stenosis treated with SAVR or TAVI, and the assistance given at 1 year of follow-up for both procedures.<sup>12</sup> This analysis was carried out on 372 patients enrolled consecutively from December 2012 to September 2015, evaluating the cost of the hospitalization index both with a full-costing approach, according to the hospital's perspective, and through the hospitalization rates provided by the tariff nomenclature of the Regional Health Service (SSR) in force. With regard to TAVI, the average cost of hospitalization index was almost doubled compared to the cardiac surgery intervention (equal to €32 120/€35 958 for the TAVI procedure, trans-femoral and trans-apical, and €17 441 for SAVR, respectively) against comparable costs according to the SSRG perspective (respectively equal to €29 989, €39 148, and €32 020), both characterized by a great interregional variability. If, on the

one hand, the price of the valve device continues to represent the largest share responsible for the cost of the procedure, the great variability found between the total cost of hospitalization is attributable to the different average peri- and post-procedural unit costs, to the different organizational methods and reimbursement mechanisms adopted, as well as to the types of patients subjected to treatment.

### Minimum requirements for transcatheter aortic valve implantation Hospitals and operators in Italy

In order to effectively invest in technological innovation such as TAVI it is necessary to evaluate carefully the local context of use in order to promote the most appropriate ways to integrate the new technology into the current care offer. The fundamental objective is therefore to define the organization of both selection phases of patients eligible for treatment (e.g. presence of a Heart Team), and design the new path in which the procedure is inserted (e.g. availability of hybrid room and resort to intensive care). This standardization also makes it possible to achieve a reduction in the dis-homogeneity of costs due to differences not only in the services provided but also in the organizational methods of the procedures adopted which otherwise risk determining inequality of access for the population. In order to regulate the use of TAVI in Italy, the Italian Society of Interventional Cardiology (SICI-GISE) has recently proposed an updated version of the minimum requirements for centres and operators performing this procedure on the national territory.<sup>6</sup> This document, first of all redefined the structural requirements for the TAVI centres so that they are carried out exclusively in centres equipped with a cardiac surgery service, for adequate planning of the procedural strategy by the Heart Team, and to be prepared for the small percentage of complicated procedures (<1%), in



