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Ten years of transcatheter aortic valve implantation in the NOTION study: the good and the bad

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Transcatheter aortic valve implantation (TAVI) has transformed the treatment of severe aortic stenosis, becoming a preferred option for patients at high and moderate surgical risk and for individuals over 75 years of age. The NOTION study represents the first randomized clinical trial to reach a 10-year follow-up in patients at low surgical risk, comparing TAVI with surgical valve replacement (SAVR). The results show comparable clinical outcomes between TAVI and SAVR in terms of all-cause mortality, stroke, and myocardial infarction. TAVI demonstrated a better haemodynamic profile and a lower incidence of structural valve deterioration (SVD), but showed higher rates of pacemaker requirement and paravalvular leakage compared with surgical replacement. The trial highlights the excellent durability of transcatheter bioprostheses, although new-generation devices and advanced techniques could further reduce adverse events. The study confirms the increasing role of TAVI even in younger patients, but further long-term data will be needed to evaluate its full potential.

Introduction

Transcatheter aortic valve implantation (TAVI) has revolutionized the treatment of severe acquired aortic valve stenosis. The most recent European guidelines recommend TAVI rather than surgical aortic valve replacement (SAVR) in patients at high surgical risk and, if eligible, at moderate risk. Additionally, transcatheter replacement is recommended in patients older than 75 years, regardless of surgical risk.[1] In the 2022 American Heart Association guidelines, transcatheter aortic valve replacement is recommended in patients 65 years or older.[2] In the USA, approximately half of patients younger than 65 years treated for isolated aortic stenosis are treated with TAVI.[3]

Surgery continues to be recommended for younger, lower-risk patients, primarily because of the lack of long-term outcome data for transcatheter valves. Due to the longer life expectancy of these patients, an evaluation of the long-term durability of transcatheter bioprostheses compared with surgical bioprostheses is necessary.

The NOTION study

The Nordic Aortic Valve Intervention (NOTION) trial was the first clinical trial to reach 10 years of follow-up in patients at low surgical risk undergoing TAVI.[4]

It is a randomized, multicentre, non-blinded trial that randomized patients between TAVI and SAVR. All patients aged 70 years or older with severe symptomatic aortic stenosis were considered for inclusion in the study. No specific surgical risk profile was required, as long as patients were anatomically suitable for both procedures, as determined by echocardiography and, in some cases, computed tomography.

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Patients requiring acute treatment, presence of other significant cardiovascular disease, or major organ failure were excluded from the study.

Patients assigned to the TAVI group received a first- or second-generation self-expanding CoreValve bioprosthesis (Medtronic Inc., Minneapolis, MN, USA), using transfemoral access in most cases. Surgery patients were treated with a complete sternotomy and standard implantation of a porcine or bovine stented bioprosthesis, without annular augmentation techniques. The specific type of bioprosthesis was left to the discretion of the surgeon.

The primary outcome of the study is a composite of all-cause mortality, stroke, or myocardial infarction at 1 year. This article reports these composite outcomes and all components at 10 years post-operatively.

Other relevant clinical outcomes include:

- Transient ischaemic attack.
- New onset of atrial fibrillation.
- Need for permanent pacemaker implantation.
- Endocarditis.

Echocardiographic outcomes include:

- Effective orifice area (EOA) of the bioprosthesis.
- Mean transprosthetic gradient.
- Degree of central regurgitation.
- Paravalvular leaks (PVLs).

Bioprosthesis durability was classified according to the Valve Academic Research Consortium-3 criteria, distinguishing between bioprosthetic valve failure (BVF) and bioprosthetic valve dysfunction.[5]

For the intention-to-treat population, 280 patients were enrolled, of whom 145 were assigned to the TAVI group and 135 were assigned to the SAVR group.

There were no significant differences in baseline characteristics between the two groups at the time of surgery. The mean age was 79.1 ± 4.8 years, 47% of patients were female, and the mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 3.0 ± 1.7%, indicating a low-risk cohort.

During the study:

- Four patients died before the procedure.
- Three patients in the TAVI group crossed over to the SAVR group after a TAVI attempt.
- Three patients in the SAVR group did not receive a bioprosthesis.

Thus, the as-implanted population included 274 patients:

- 139 were treated with TAVI.
- 135 were treated with SAVR.

At 10 years, follow-up was completed by 98.9% of patients (two patients in the TAVI group and one patient in the SAVR group were lost). Of them, 36.1% (101 patients) were still alive. Echocardiographic data at 10 years were available for 81.2% of the live patients.

At 10 years, there were no statistically significant differences in all-cause mortality in the intention-to-treat population [TAVI: 62.7%; SAVR: 64.0%; hazard ratio (HR): 1.0; 95% CI 0.7–1.3; $P = 0.8$]. There were also no significant differences between the two groups in the composite outcome (all-cause mortality, stroke, or myocardial infarction) (TAVI: 65.5%; SAVR: 65.5%; HR: 1.0; 95% CI 0.7–1.3; $P = 0.9$). Furthermore, no significant differences were observed in the individual components of the composite outcome.

The occurrence of atrial fibrillation was statistically more frequent after surgical valve replacement (TAVI: 52.0%; SAVR: 74.1%; $P < 0.01$), while permanent pacemaker implantation was more frequent after transcatheter replacement (TAVI: 44.7%; SAVR: 14.0%; $P < 0.01$).

The initial increase in EOA and reduction in transprosthetic gradient observed after both procedures remained significant within the two groups during follow-up. However, during all follow-up assessments, the increase in EOA and reduction in gradient were more evident in patients in the TAVI group than in those in the SAVR group.

In the TAVI group, a higher frequency of moderate/severe PVL was found at 10 years (TAVI: 25.4%; SAVR: 2.5%; $P < 0.01$). No association was observed between the presence of moderate/severe PVL at 3 months after surgery and mortality at 10 years.

At 10 years, in the as-implanted population, severe structural valve deterioration (SVD) occurred more frequently in patients who underwent surgical valve replacement (TAVI: 1.5%; SAVR: 10.0%; HR: 0.2; 95% CI 0.04–0.7; $P = 0.02$). The same was true for non-structural valve dysfunction (NSVD) (TAVI: 20.5%; SAVR: 43.0%; $P < 0.01$). There were no significant differences between the two groups in BVF (TAVI: 9.7%; SAVR: 13.8%; HR: 0.7; 95% CI 0.4–1.5; $P = 0.4$) and reinterventions (TAVI: 4.3%; SAVR: 2.2%; $P = 0.3$).

No patients had clinical valve thrombosis, and rates of infective endocarditis were similar between the two groups.

The good and the bad

The 10-year results of the NOTION trial provide a unique assessment of the durability and clinical and echocardiographic outcomes of TAVI and SAVR in patients at low surgical risk.

This study reinforces the role of TAVI as a valid option for patients at low surgical risk and provides reassuring data in a world where transcatheter treatment is no longer reserved exclusively for elderly patients.

In fact, no significant difference was observed in the rates of all-cause mortality, stroke, or myocardial infarction between the two groups. After both procedures, the EOA significantly increased and the transprosthetic gradient decreased, with better results in the TAVI group compared with the SAVR group. In addition, severe structural valve dysfunction (SVD) was less frequent in the TAVI group compared with the SAVR group.

A further finding in favour of percutaneous treatment was the lower rate of new-onset atrial fibrillation in patients undergoing TAVI compared with those undergoing SAVR, mainly in the immediate post-operative period. The rates of bioprosthesis endocarditis and reintervention were very low and similar between groups. These results are consistent with those of other studies comparing TAVI and SAVR at 4 and 5 years of follow-up.

In the trials 'Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years (PARTNER 3)', '4-Year Outcomes of Patients With Aortic Stenosis in the Evolut Low Risk Trial' and 'Self-expanding Transcatheter vs. SAVR in Intermediate-Risk Patients: 5-Year Outcomes of the SURTAVI Randomized Clinical Trial', TAVI showed a durability and clinical outcome profile similar to surgery, with a better haemodynamic profile.[6–8]

However, in the comparison between percutaneous and surgical approaches to aortic valve replacement, not all results were in favour of the former.

Patients undergoing TAVI more frequently presented with conduction disturbances, requiring the implantation of a permanent pacemaker. These data confirm that reported by the Evolut Low Risk and SURTAVI studies, in which self-expanding supranular bioprostheses were used, while in Partner 3, in which balloon-expandable intranular prostheses were used, no significant difference was found in the rates of definitive pacemaker implantation.

Echocardiographic detection of PVLs was also significantly more frequent in patients undergoing TAVI, as demonstrated by the other studies previously cited. However, in the NOTION study, no association was found between the presence of moderate/severe PVL at 3 months after surgery and 10-year mortality.

Furthermore, the rate of mild or greater PVLs found in this study (53% at 5 years) was higher than that found in more recent studies using new-generation delivery systems and bioprostheses (15.3 and 20.8% after 4 and 5 years, respectively).[6,7]

The NOTION study was conducted from 2009 to 2013, and in recent years, there have been numerous innovations in the field of delivery devices, valve bioprostheses, and implantation techniques. Among these, commissural alignment should be mentioned, which led to safer implantation of the prosthesis, ensuring access to the coronary arteries even in the case of higher valve implantation and, therefore, potentially reducing the rate of PVLs and rhythm alterations.[9]

It can be concluded that the NOTION study, like other trials that have evaluated the long-term results of transcatheter prostheses, has demonstrated the excellent durability of these prostheses, with clinical results comparable to surgically implanted prostheses, with a better haemodynamic profile but with higher rates of definitive pacemaker implantation and PVLs. These latter results, however, were obtained with older-generation devices and in a small patient population; therefore, the role of TAVI in younger patients will have to be reevaluated also in the light of the data that we will acquire in the future from more recent studies and with larger populations.

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Data availability

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Disclaimer

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