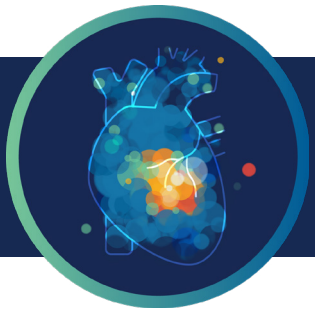
MEDPACE

EXPERT INSIGHTS: Q&A WITH PROF. DEAN KEREIAKES



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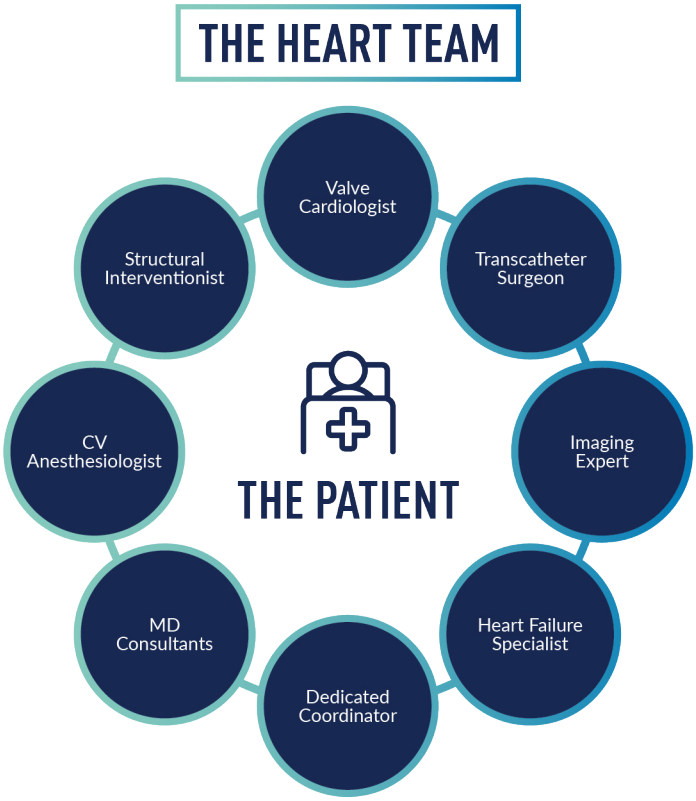
Access the full publication: **Transcatheter or Surgical Treatment of Aortic Valve Stenosis**

To those unfamiliar with the term "Heart Team", could you explain what this is and what are, in your opinion, the qualities intrinsic to a well-performing heart team that makes decisions in the very best interests of the patients they serve with structural heart disease?

The Heart Team provides a multi-disciplinary, collaborative approach to the decision making process regarding care for specific patients. The participants, which include multidisciplinary physicians as well as nursing coordinator constituents, meet on a regular basis to discuss the diagnosis and appropriate treatment for individual patients. All diagnostic and cardiovascular imaging studies are presented by individual experts and the patient's risk stratification for surgery is determined in real-time by the Cardiothoracic Surgical attendings. All patients have been seen in advance by the structural interventional cardiologist, cardiothoracic surgeon and dedicated nurse coordinator prior to the meeting. A shared decision making process with the patient has been entered into by both the surgeon and structural interventionist prior to the meeting.

Suggested components of this team are illustrated in the figure below:



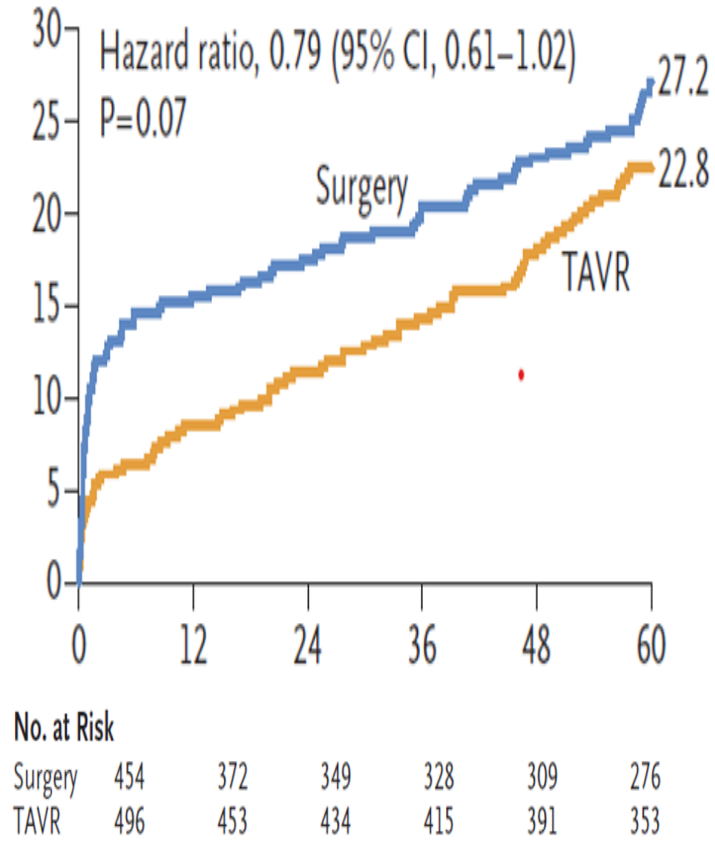
In plain language, how would you explain the results of the DEDICATE trial to a young symptomatic patient with severe aortic stenosis at low surgical risk, as you discuss treatment options with them in your hospital clinic?

First, DEDICATE involved 38 clinical sites in Germany that enrolled patients with symptomatic, severe aortic valve stenosis who were 65 years old or older. All patients were determined to be either low (STS score 2 or less) or intermediate (STS score >2-4) risk for surgical aortic valve replacement by the multi-disciplinary heart team. Patients with prior cardiac surgery, bicuspid aortic valves or clinically significant coronary artery disease

requiring revascularization were excluded. Patients were randomly assigned 1:1 to receive treatment with either transcatheter aortic valve replacement (TAVR; 97.3% transfemoral access) or surgical aortic valve replacement (SAVR; 51% full and 38.7% partial sternotomy).

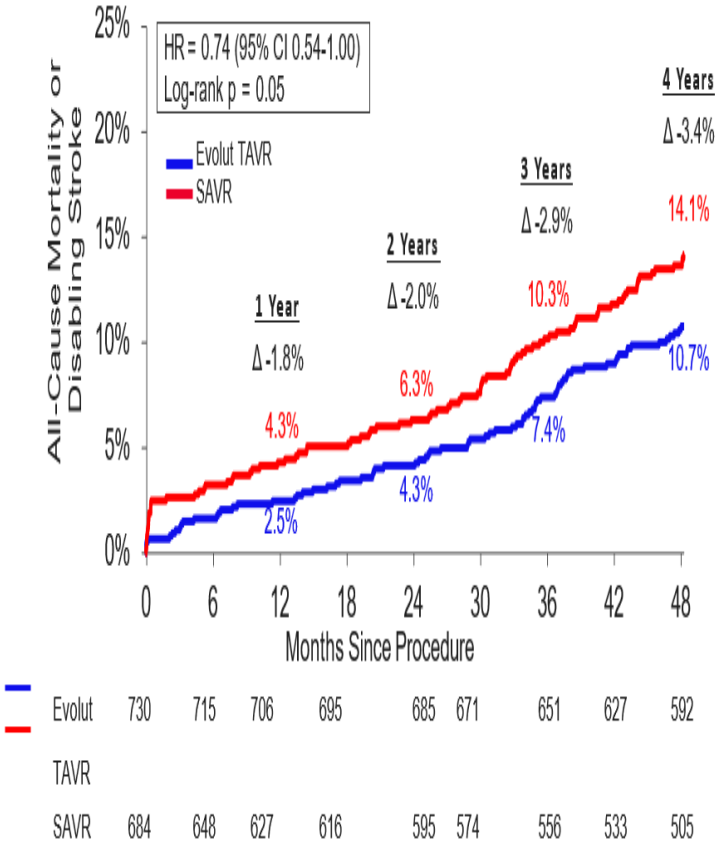
The primary endpoint for analysis was the occurrence of death (all cause) or non-fatal stroke at 1 year follow-up. The primary analysis was on the basis of intention to treat. Although TAVR was determined to be non-inferior to SAVR for the primary endpoint, from a patient's perspective TAVR was associated with a 60% relative reduction in death, 40% relative reduction in stroke and 50% relative reduction in the composite primary endpoint. Cerebral embolic protection was used during TAVR in only 5.1% of patients. Balloon expandable TAVR valves were used in 61.4% and self-expanding valves in 35.1% of patients, respectively. Conscious sedation was used in 75% of the procedures. Atrial fibrillation (new onset) was significantly more frequent in the SAVR treatment group (30.8% vs 12.4%) and the need for permanent pacemaker was increased in the TAVR treatment group (11.8% vs 6.7%). These results are similar to and extend prior randomized clinical trial comparisons of TAVR vs. SAVR in lower risk surgical patients (PARTNER III and Evolut Low Risk; **Figures 1 and 2**).

Partner 3: 5-year follow-up SAVR vs TAVR



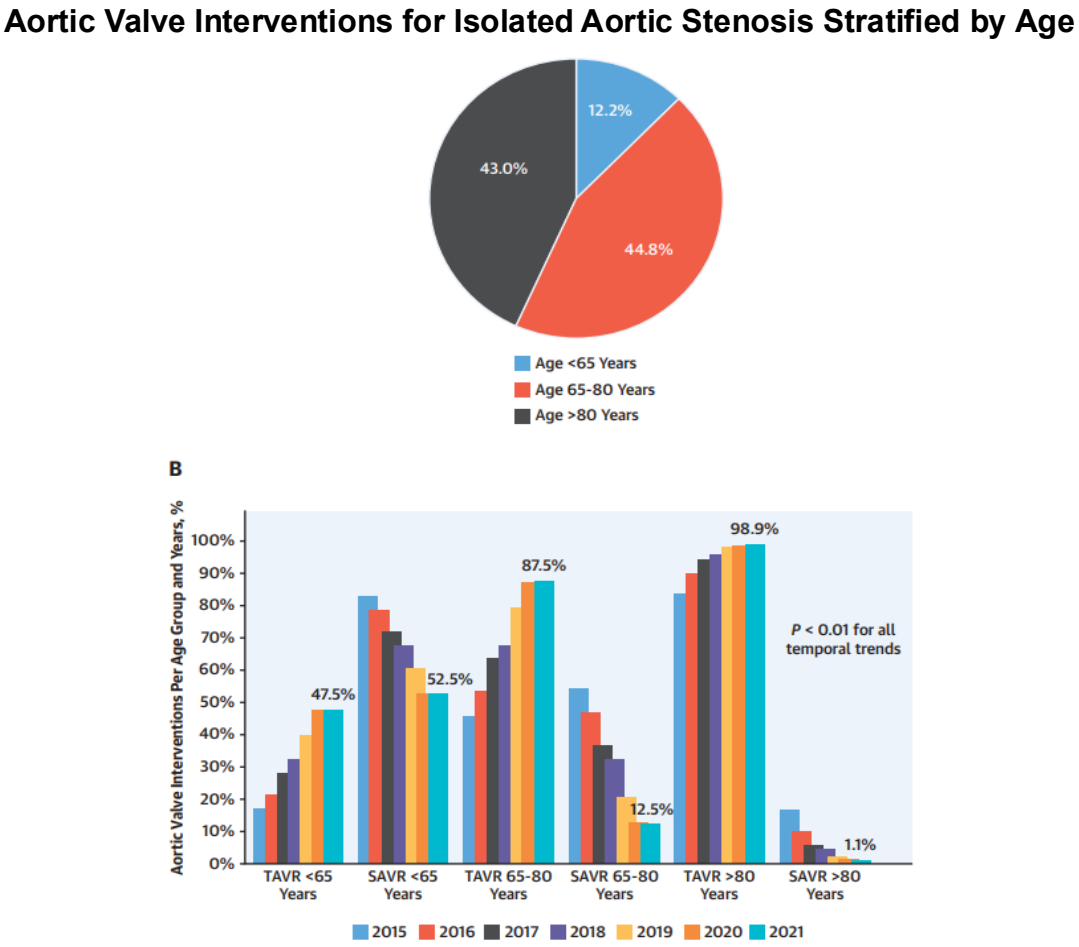
(Figure 1) Mack, Leon et al NEJM 2023 DOI: 10.1056/NEJMoa2307447

EVOLUT LOW RISK: 4 Year Results SAVR vs TAVR

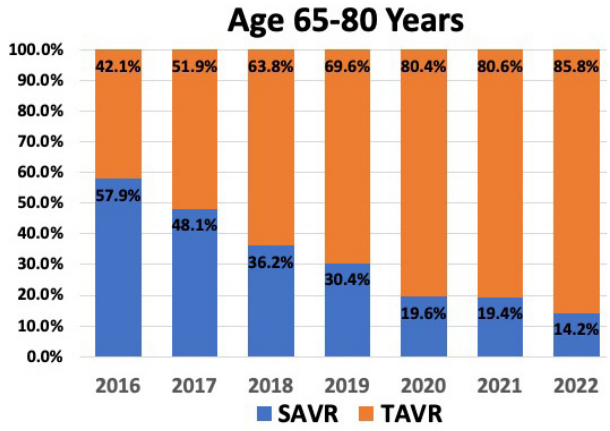


(Figure 2) Forest JK, et al J Am Coll Cardiol. 2023 Nov 28;82(22):2163-2165.

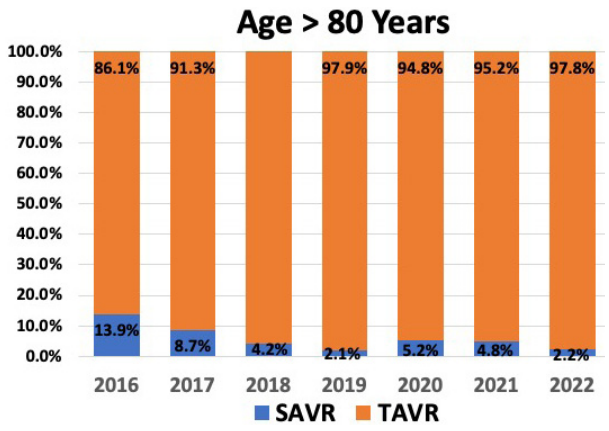
The primary analysis in DEDICATE is even more meaningful in the context that 96 of the patients randomly assigned to SAVR either crossed over to TAVR (70) or withdrew from the trial (26) while only 16 patients randomly assigned to TAVR either crossed over to SAVR (12) or withdrew from the trial (4). This significant discrepancy would tend to minimize the relative benefit of TAVR vs SAVR. These results have been supported by trends in clinical practice which have demonstrated that the vast majority of subjects with symptomatic severe aortic stenosis greater than 65 years of age are currently undergoing TAVR in comparison to SAVR **(Figures 3-5)**.



(Figure 3) Sharma T, et al. *J Am Coll Cardiol.* 2022;80(21):2054-2056.



(Figure 4) Gupta T, et al. / Journal of the Society for Cardiovascular Angiography & Interventions doi.org/10.1016/j.jscai.2024.101861



(Figure 5) Gupta T, et al. / Journal of the Society for Cardiovascular Angiography & Interventions doi.org/10.1016/j.jscai.2024.101861

The choice of TAVR valve prosthesis, vascular access and surgical technique were left to the discretion of the heart team at each participating site in the DEDICATE trial. Is there a danger of introducing selection and operator bias which may be detrimental to the validity of the trial's outcomes with this type of study design?

This trial has evaluated "real world" clinical practice as performed in those centers, in that geography and in that timeframe. As clinical practice is dynamic over time, the results may vary to some degree over time. Nevertheless, the results of DEDICATE remain contemporary at this time with the vast majority of TAVR procedures using conscious sedation, transfemoral access and balloon expandable TAVR devices. The use of cerebral embolic protection was minimal and remains limited in clinical practice. Further, the consistency of findings in DEDICATE when compared with the other randomized controlled trials in lower risk patients noted above, suggests that the results may be more globally extrapolatable to other geographies.

How generalizable are the results of this study globally, given that it was performed at multiple sites in Germany alone, and therefore as the authors describe, in line with standard clinical practice of many "Western" countries?

As noted in the answer to the earlier question, the results of DEDICATE are consistent with other low risk randomized controlled trials. Over time, one might expect the results in the TAVR treatment group to improve further due to the progressive increase in use of conscious sedation as well as cerebral embolic protection in many centers.

The evidence demonstrating the safety and efficacy of TAVI for severe AS in those at high, intermediate and low surgical risk appears to be overwhelming. Do you see a future where the implementation of TAVI extends to those with moderate, symptomatic calcific aortic valve stenosis?

This specific question is being addressed in the PROGRESS Trial (NCT04889872) which randomly assigns patients with moderate aortic stenosis who are asymptomatic to receive either watchful waiting clinical follow-up until they become symptomatic or TAVR. The biggest challenges to the further expansion of TAVR to younger, less symptomatic patients with aortic valve stenosis are valve durability and coronary access. In considering lifetime management of aortic stenosis patients who are under the age of 75, they will likely require 2 valves during their lifetime. Multiple novel technologies are being evaluated to enhance both transcatheter as well as surgical valve durability. Similarly, access to the coronaries is being addressed through structural valve iterations.