

Should all aortic stenosis patients older than 80 years undergo TAVR rather than SAVR?



GREGORY MISHKEL, MD, FRCPC, FACC, FSCAI

*Executive Medical Director,
Prairie Heart Institute
Springfield, Illinois*

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VIKAS AGGARWAL, MD, FACC

*Advanced Interventional Fellow
Prairie Heart Institute
Springfield, Illinois
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Transcatheter aortic valve replacement (TAVR) has seen worldwide adoption for the treatment of senile degenerative aortic stenosis (AS). More than 200,000 global implantations have been accomplished, and TAVR volumes are projected to increase fourfold over the next 10 years.¹⁻³ In large measure, this growth is driven by two phenomena. First, AS is a disease of the elderly, and the geriatric demographics are growing as medical advances extend lives. Second, AS is prevalent and undertreated. An estimated 550,000 individuals in the United States have severe AS, and the vast majority are aged 70 years or older; yet, only approximately 88,000 surgical aortic valve replacements (SAVRs) are performed annually.³⁻⁵ Despite the fact that surgery can be safely performed in octogenarians, many patients either remain undiagnosed or untreated, in some measure related to patient or physician reluctance to offer SAVR.⁶ Regardless of published success rates, the elderly and their physicians do not relish open heart surgery

and in many cases have deferred treatment in the past, despite the high mortality associated with severely symptomatic AS.

As a result of the PARTNER (Edwards Lifesciences) and CoreValve (Medtronic) trials, we now have two commercially available TAVR platforms approved for high- or prohibitive-risk indications. The average age in both of these pivotal studies was 83 years, and benefits of TAVR versus surgery were seen across all age ranges. The 1-year outcomes have been sustained out to 2 to 5 years now, with predictors of mortality generally unassociated with age.^{7,8} Early concerns regarding paravalvular leak, increased rates of stroke, vascular access complications, and durability have substantially been mitigated over the course of extended follow-up, by improved patient and device selection, and with newer generations of commercial products (Sapien 3, Edwards Lifesciences; Evolut R, Medtronic).⁹⁻¹¹

Are we ready to cross the threshold and routinely offer TAVR to all octogenarians regardless of their risk stratification score, understanding that surgical results in today's era can be accomplished with a single-digit mortality rate? Will the TAVR experience mirror endovascular aortic aneurysm repair, which in its infancy was only offered to patients at high surgical risk but is now the default strategy in > 80% of patients with abdominal aortic aneurysms, even in the United States? While we await the results of the randomized PARTNER 2 and SURTAVI intermediate-risk trials, we can gain insight into this question by looking to European real-world and trial results, as well as to newer data available here in the United States.

The all-comers Nordic Aortic Valve Intervention (NOTION) trial randomized 280 relatively low-risk patients (mean STS score, 3) with a mean age of 79 ± 5 years to either SAVR or TAVR.¹² A self-expanding CoreValve device was implanted without any need for

transapical or transaortic access within 2 hours (using local anesthesia only in 20%) in 98% of the randomized TAVR patients. Across an entire spectrum of in-hospital outcomes, TAVR patients had significantly fewer complications, but admittedly, at the expense of higher pacemaker and perivalvular leak rates. At 1 year, there was no difference in clinically relevant outcomes for the SAVR and TAVR patients.¹² These results are even more remarkable when realizing that the NOTION trial was initiated only 2 years after TAVR was widely introduced in Europe, used a first-generation product, and came prior to the adoption of CT sizing rather than echocardiographic measurements of annular perimeter. These results are generally concordant with many European registries that more liberally enroll patients than those described in the United States commercial indications. In Germany, where TAVR has its greatest penetration, the use of SAVR has been plateauing since 2006. More recently, there has been a decrease in the absolute number of isolated SAVR procedures, with > 40% of all AS patients now treated with TAVR.^{13,14}

In the United States, we have the 30-day results of the nonrandomized Sapien 3 valve data set. More than 1,000 elderly (mean age, 81.9 years) intermediate-risk (median STS score, 5.2) patients underwent TAVR and showed a 30-day all-cause mortality and disabling stroke rate of 1.1% and 1%, respectively, and a paravalvular leak rate of 2.5%.⁹ By the time this article is published, the results of the randomized portion of this trial will be known, and if TAVR is indeed noninferior to SAVR, we will see further widespread adoption of TAVR, particularly for the elderly, regardless of their risk status.



PAUL J. PEARSON, MD, PhD

Chief, Division of Cardiovascular Surgery
Owen L. Coon Chair of Cardiothoracic Surgery
NorthShore University HealthSystem
Evanston, Illinois

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SAVR, first performed by Harkin and Starr in 1960, revolutionized the treatment of AS, which was previously a fatal disease. The safe application of open heart surgery in the elderly population, as first reported in 1966 by Denton Cooley¹ (at that time, defined as patients older than 60 years) has expanded to the current era in which the Mayo Clinic reports outstanding outcomes in select patients older than 90 years with SAVR.² It needs to be stated that SAVR is an excellent treatment with excellent outcomes. Debates about SAVR versus TAVR get sidetracked because they tend to debate the wrong issue. SAVR and TAVR are separate tools (tactics) to treat AS by valve replacement (the strategy). In the current era, each has different indications and applications, and both are necessary to comprehensively treat a population with valvular heart disease. To advocate for TAVR does not discount the important role for SAVR in select patients.

That being said, with the current technology available and based on current scientific data, TAVR should be the initial therapy offered to patients older than 80 years with isolated AS. The data supporting this assertion are compelling. For example, results from the Nordic Aortic Valve Intervention Trial (NOTION) randomizing nearly 300 patients who are older than 70 years and deemed low risk for SAVR showed no significant differences in the composite 1-year endpoints of rate of mortality from any cause, stroke, or myocardial infarction between those undergoing TAVR and those undergoing SAVR.³ Although the TAVR group had more conduction abnormalities and greater aortic regurgitation, the SAVR group had more episodes of major bleeding, cardiogenic shock, and new-onset or worsening atrial fibrillation. Some might parse such results by stating that TAVR is not inferior to SAVR, but the reality for a patient is that if two therapies are noninferior and one is less invasive, then the less invasive therapy is superior.

In a slightly higher-risk population than NOTION, TAVR was shown to outperform SAVR in the CoreValve pivotal trial.⁴ Of the 795 patients randomly assigned to SAVR or TAVR, a significant difference emerged at the 1-year primary endpoint of all-cause mortality: 14.2% for TAVR compared with 19.1% for SAVR. Analysis also demonstrated that the 1-year rate of heart attack, stroke,

1. Horne A Jr, Reineck EA, Hasan RK, et al. Transcatheter aortic valve replacement: historical perspectives, current evidence, and future directions. *Am Heart J*. 2014;168:414-423.
2. Stolkler JM, Patel AV, Lim MJ, Hauptman PJ. Estimating the adoption of transcatheter aortic valve replacement by US interventional cardiologists and clinical trialists. *Clin Cardiol*. 2013;36:691-697.
3. Carabello BA, Paulus WJ. Aortic stenosis. *Lancet*. 2009;373:956-966.
4. Supino PG, Borer JS, Preibisz J, Bornstein A. The epidemiology of valvular heart disease: a growing public health problem. *Heart Fail Clin*. 2006;2:379-393.
5. Bouma BJ, van Den Brink RB, van Der Meulen JH, et al. To operate or not on elderly patients with aortic stenosis: the decision and its consequences. *Heart*. 1999;82:143-148.
6. Thourani VH, Suri RM, Gunter RL, et al. Contemporary real-world outcomes of surgical aortic valve replacement in 141,905 low-risk, intermediate-risk, and high-risk patients. *Ann Thorac Surg*. 2015;99:55-61.
7. Kapidia SR, Leon MB, Makkar R, et al. 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomized controlled trial. *Lancet*. 2015;385:2485-2491.
8. Reardon MJ, Adams DH, Kleinman NS, et al. 2-year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2015;66:113-121.
9. Kodali S. Clinical and echocardiographic outcomes at 30 days with the Sapien 3 TAVR system in inoperable, high-risk and intermediate-risk AS patients. Presented at: ACC Scientific Sessions; March 15, 2015; San Diego, CA.
10. Data on file, Medtronic, Inc. Comparison of CoreValve to CoreValve Evolut/Evolut R. Significant PVL defined as ≥ moderate PVL.
11. Medtronic. IFU M054712T001.
12. Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers NOTION randomized clinical trial. *J Am Coll Cardiol*. 2015;65:2184-194.
13. Beckmann A, Hamm C, Figulla HR, et al. The German Aortic Valve Registry (GARY): a nationwide registry for patients undergoing invasive therapy for severe aortic valve stenosis. *Thorac Cardiovasc Surg*. 2012;60:319-325.
14. Buellfeld L, Gerckens U, Erbel R, et al. Age-stratified baseline and outcome characteristics of patients undergoing transcatheter aortic valve implantation: results from the German multicenter registry. *J Invasive Cardiol*. 2012;24:531-536.

or related death was significantly lower for TAVR at 20.4%, compared with 27.3% for SAVR.

From a procedural perspective, the systemic impact of TAVR on a patient is significantly less than with SAVR. For example, at our institution, patients who undergo transfemoral access for TAVR (the majority of cases) undergo conscious sedation, thereby eliminating the risks and side effects of endotracheal intubation and general anesthesia. Early unrestricted activity and ambulation is the rule after TAVR. Indeed, when counseling TAVR patients about the expected length of their hospital stay and recovery after TAVR, I commonly state that what will determine their hospital stay are those factors that make them a TAVR candidate, not the procedure per se. When I counsel patients prior to SAVR, recovery from the procedure is the focus. Also, while researchers evaluating SAVR in the past have justifiably focused on endpoints such as survival or stroke, new literature documenting common themes of patients recovering after heart valve replacement surgery use such terms as *suffering weakness* and *struggling to resume normality*.⁵

Finally, valves implanted by TAVR typically have significantly lower postprocedure gradients than SAVR.³ In patients being treated for AS, gradients are the ultimate issue. Moderate patient-prosthesis mismatch (PPM) is present in up to one-quarter of patients after SAVR.⁶ PPM is associated with decreased survival, lower freedom from heart failure, and incomplete left ventricular mass regression. In addition, because of the disturbed prosthetic valve performance associated with PPM due to high transvalvular gradients, PPM is associated with stenosis-type structural valve deterioration after SAVR.⁷ One could infer that the low gradients typically associated with TAVR would mitigate these complications and possibly improve the durability of the prosthesis.

Just as percutaneous intervention revolutionized the role of coronary artery bypass grafting in treating coronary artery disease, TAVR is revolutionizing the role of SAVR for treating patients with AS. In patients older than 80 years, the data and patient experience dictate that it should be the initial therapy of choice.



**VINOD H. THOURANI,
MD, FACC, FACS**

*Professor of Surgery and Medicine
Chief of Cardiothoracic Surgery,
Emory Hospital Midtown*

*Co-Director, Structural Heart and Valve Center
Emory University School of Medicine
Atlanta, Georgia*

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JESSICA FORCILLO, MD, MSc, FRCS

*TAVR fellow, Emory University Hospital Centers
Atlanta, Georgia*

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The treatment of patients who are older than 80 years has become a daily reality for physicians managing AS. Moreover, this proportion of the elderly population is expected to expand dramatically over the next 20 years. As members of the heart team, cardiac surgeons are particularly confronted by the aspect of assessing the risks and benefits of surgical procedures in these elderly patients. Currently, existing risk scores such as the Society of Thoracic Surgeons (STS) score and the EuroSCORE I and II tend to overestimate the surgical risk in this elderly population.¹ Articles published in the literature don't appropriately reflect the heterogeneous health and functional well-being seen in real patients overall. Accordingly, it is difficult to make absolute recommendations and accurate surgical risk predictions in that population. Epidemiological data suggest that age is among the most powerful predictors of operative mortality, increasing exponentially from 1.7% at age 50 to 8.3% at age 80. However, data from the National Cardiovascular Network have challenged the importance of age as a predictor. This study included 67,764 patients undergoing conventional cardiac surgery. They have shown that the mortality rate in octogenarians without significant comorbidity was surprisingly low at 5%, but was still higher than the younger patients who had a 3% mortality rate.² Different outcomes may be explained by "biological" as opposed to "chronological" age, as defined further by indicators of frailty and/or a constellation of medical issues.³ We have previously shown that SAVR in patients with no organ dysfunction do exceedingly well, but when multiple systems are affected, the out-

1. Bowles LT, Hallman GL, Cooley DA. Open-heart surgery on the elderly. Results in 54 patients sixty years of age or older. *Circulation*. 1966;33:540-544.

2. Murashita T, Greason KL, Suri RM, et al. Aortic valve replacement for severe aortic stenosis in the nonagenarian patient. *Ann Thorac Surg*. 2014;98:1593-1597.

3. Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers NOTION randomized clinical trial. *J Am Coll Cardiol*. 2015;65:2184-2194.

4. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-1798.

5. Berg SK, Zwissler AD, Pederson BD, et al. Patient experiences of recovery after heart valve replacement: suffering weakness, struggling to resume normality. *BMC Nurs*. 2013;12:23.

6. Walther T, Rastan A, Falk V, et al. Patient prosthesis mismatch affects short- and long-term outcomes after aortic valve replacement. *Eur J Cardiothorac Surg*. 2006;131:1036-1044.

7. Flammeng W, Herregods MC, Vercauteren M, et al. Prosthesis-patient mismatch predicts structural valve deterioration in bioprosthetic heart valves. *Circulation*. 2010;121:2123-2129.

comes are significantly worse in a patient in the same age group.⁴ Indeed, these factors or predictors of frailty exist, but their exact weight in terms of mortality and morbidity is not, at the present time, well defined.

Since the introduction of TAVR in 2002, the management of severe AS received a significant face-lift with this less invasive treatment modality for AS. These once-novel technologies have now become standard and well-established techniques, with implantations in over 400 hospitals within the United States. The Sapien valve (Edwards Lifesciences) received US Food and Drug Administration approval in 2011 for inoperable patients and in 2012 for high-risk patients based on the PARTNER IA and IB studies.^{5,6} The initial study randomized 358 patients to either medical treatment or TAVR. The mean age was similar between groups (medical group: 83.2 ± 8.3 years; TAVR: 83.1 ± 8.6 years). At 1 year, the authors noted that TAVR significantly reduced mortality rates from any cause, the composite endpoint of death from any cause, or repeat hospitalization and cardiac symptoms despite the higher incidence of major strokes and major vascular events.⁵ Those results were sustained up to 5 years.⁷ The second study compared 699 high-risk patients who underwent TAVR versus conventional SAVR. This study showed similar rates of survival at 1 year.⁶ With similar results between TAVR and SAVR at 5 years, the percutaneous option has practically replaced conventional surgery in high-risk patients.⁸ The second most important trial is the CoreValve pivotal trial, which led to this valve receiving US Food and Drug Administration approval in 2014. The trial randomized 795 high-risk patients to either self-expandable TAVR or SAVR. The results showed that TAVR patients had a lower mortality rate from any cause at 1 year compared to the surgical group (14.2% vs 19.1%), further solidifying the role of TAVR in high-risk patients.⁹

Quite interestingly, the mean age for almost all patients undergoing TAVR in the randomized trials and in the TVT (Transcatheter Valve Therapy) United States database is 81 to 83 years. Consequently, some have hypothesized whether all AS patients older than 80 years should have TAVR rather than SAVR. In a compassionate and totally empathic point of view, with our minimalist TAVR pathway at Emory University, I would answer “yes,” since approximately 70% of our patients are discharged within 1 to 2 days, and the majority do not require an intensive care unit stay.¹⁰ However, there remain many questions regarding the use of a TAVR valve universally. The question of valve thrombosis, pacemaker rates, and paravalvular leaks are still concerning and have dampened the enthusiasm for some physicians. Moreover, major costs are associated with these new devices, and it still remains a societal choice regarding

health expenses. Therefore, in patients with a low surgical risk score (STS score of < 3% to 4%), we still believe that the data do not allow for adoption of TAVR quite yet. In 2016, we expect randomized trials to begin evaluation in this patient population.

The critical decision in terms of TAVR or SAVR in those aged 80 or older lies within the auspices of the valve heart team. The multidisciplinary team, enhanced preoperative risk-evaluation scoring systems, and objective assessment that includes frailty parameters will strongly contribute to excellent procedural results.

1. Christensen K, Doblhammer G, Rau R, Vaupel JW. Aging populations: the challenges ahead. *Lancet*. 2009;374:1196-1208.
2. Alexander KP, Anstrom KJ, Muhlebaier LH, et al. Outcomes of cardiac surgery in patients ≥ 80 years: results from the national cardiovascular network. *J Am Coll Cardiol*. 2000;35:731-738.
3. Afzal J, Karunanathan S, Eisenberg MJ, et al. Role of frailty in patients with cardiovascular disease. *Am J Cardiol*. 2009;103:1616-1621.
4. Thourani VH, Chowdhury R, Gunter RL, et al. The impact of specific preoperative organ dysfunction in patients undergoing aortic valve replacement. *Ann Thorac Surg*. 2013;95:838-845.
5. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597-1607.
6. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-2198.
7. Kapadia SR, Leon MB, Makkar RR, et al. 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385:2485-2491.
8. Mack MJ, Leon MB, Smith CR, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385:2477-2484.
9. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-1798.
10. Jensen HA, Condado JF, Devireddy C, et al. Minimalist transcatheter aortic valve replacement: the new standard for surgeons and cardiologists using transfemoral access? *J Thorac Cardiovasc Surg*. 2015;150:833-839.



**NICOLAS M. VAN MIEGHEM,
MD, PhD, FESC**

*Department of Interventional Cardiology
Thoraxcenter
Erasmus Medical Center*

Rotterdam, The Netherlands

*Disclosures: Has received research grants from
Medtronic, St. Jude Medical, Edwards Lifesciences,
Boston Scientific Corporation, and Claret Medical.*

Despite the fact that current ACC/AHA guidelines only recommend TAVR for patients with symptomatic severe AS who are inoperable or at high operative risk, I believe TAVR is the treatment of first choice for most patients who are aged 80 years or older.¹ As a matter of fact, this philosophy is already in place in many centers throughout Europe. A recent report from the vast German experience between 2007 and 2013 stipulates the effect of TAVR on contemporary practice. Compared to SAVR, TAVR is used in older patients with a higher operative risk. Furthermore, it has become clear that, over the years, the number of octogenarians undergoing surgery is rapidly declining.²

Randomized trials in patients with at least a high operative risk have already demonstrated TAVR's superiority over SAVR from a patient and health economic perspective. Indeed, TAVR seems to be associated with faster ambulation, shorter in-hospital stay, earlier gain in quality of life, and improved short-term survival up to 1 year.^{3,4}

TAVR purists often bring up the unknown transcatheter heart valve durability to slow down TAVR adoption and implementation in patients who have a longer life expectancy. We should put this argument in proper perspective if we discuss octogenarians. A healthy 80-year-old person with a pristine past medical history has an estimated lifespan of 8 to 9 years.⁵⁻⁷ In reality, up to 20% of all octogenarians are considered frail. Frailty is a diminished ability to overcome stressors. This also includes a major surgical operation including sternotomy, aortotomy, and use of cardiopulmonary bypass. Recovery time will inevitably be prolonged, and complications may linger. It may take months to fully recover and regain full mobility and independence at an older age.

Initial transcatheter heart valves were limited by their unfavorable profile, and the early experience partially

suffered from paravalvular regurgitation and cerebroembolic and access site complications. The latest generation of repositionable and retrievable transcatheter heart valves with sealing technology and refined accessories, such as innovative access sheaths and cerebral embolic protection devices, have properly addressed these issues. TAVR has become a relatively straightforward and safe procedure under local anesthesia with same-day ambulation and short hospital stay. Thus, it is arguably the ideal option for elderly AS patients who cherish their independence and quality of life. ■

1. Nishimura RA, Otto CM, Bonow RO et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63:2438-2488.
2. Reinohl J, Kaier K, Reinecke H, et al. Effect of availability of transcatheter aortic-valve replacement on clinical practice. *N Engl J Med*. 2015;373:2438-2447.
3. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790-1798.
4. Reynolds MR, Magnuson EA, Lei Y, et al. Cost-effectiveness of transcatheter aortic valve replacement compared with surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results of the PARTNER (Placement of Aortic Transcatheter Valves) trial (cohort A). *J Am Coll Cardiol*. 2012;60:2683-2692.
5. Ahmed N, Mandel R, Fain MJ. Frailty: an emerging geriatric syndrome. *Am J Med*. 2007;120:748-753.
6. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146-M156.
7. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc*. 2012;60:1487-1492.