Ομάδες Εργασίας Καρδιολογίας
SAVR vs TAVR

The jury is still out

Γ.Ε. ΔΡΟΣΟΣ
Χειρουργική Κλινική Θώρακος Καρδιάς
Νοσ. Γ. Παπανικολάου
Θεσσαλονίκη
Screened 3105 patients

77% were screened out

699 were randomly assigned to either TAVR or SAVR,

125 of those 699 patients (17.5%) were alive and had full follow-up to 5-years.

The study reported equivalent 5-year mortalities (67.8% vs 62.4%). Stroke rates (10.4% vs 11.3%), myocardial infarction rates (2.9% vs 5.9%), mean valve area, mean gradient, and left ventricular mass index.

3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement

The US Core Valve study screened 995 patients, randomly allocated 759, and reported equivalent 3-year outcomes for TAVR and SAVR with respect to mortality (32.9% vs 39.1%), stroke rate (8.1% vs 11.8%), and reintervention (2.4% vs 0.4%).

A better effective orifice area was demonstrated for TAVR (1.79 vs 1.53 cm²), but TAVR also carried a higher incidence of moderate to severe paravalvular regurgitation (5.9% vs 0%).

Am Coll Cardiol 2016; Study of the Medtronic CoreValve System
PARTNER 2

In intermediate-risk patients, TAVR was similar to surgical aortic-valve replacement with respect to the primary end point of death or disabling stroke.

TAVR resulted in larger aortic-valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.

NEJM April 28, 2016  Funded by Edwards Lifesciences;
TAVR was a noninferior alternative to surgery in patients with severe aortic stenosis at intermediate surgical risk, with a different pattern of adverse events associated with each procedure.

Surgery was associated with higher rates of acute kidney injury, atrial fibrillation, and transfusion requirements, whereas TAVR had higher rates of residual aortic regurgitation and need for pacemaker implantation. TAVR resulted in lower mean gradients and larger aortic-valve areas than surgery. Structural valve deterioration at 24 months did not occur in either group.

NEJM April 6, 2017 Funded by Medtronic;
These studies, as well as comparable RCT studies of intermediate-risk patients, led to modification of American Heart Association and American College of Cardiology guidelines and European Society of Cardiology guidelines, which now present TAVR and SAVR as equally effective alternative therapies.
The paradox between randomized controlled trials and propensity score–matched real-world data: Moving from dissonance to dialog?

Is it best to report
data from randomized, controlled trials (RCTs),
or
to present data from larger meta-analyses, propensity-scored matched controls, and real-world registry data and registries?

Surprisingly, conclusions from these sets of data appear to be discordant.

B. Z. Atkins, and G. S. Aldea, University of Washington, Seattle, J Thorac Cardiovasc Surg 2018
paravalvular leak
Comparative survival and role of STS score in aortic paravalvular leak after SAVR or TAVR: a retrospective study from the USA

• The first to compare the influence of aortic paravalvular leak (PVL) on survival after TAVR versus SAVR, and was the first to determine the relative influence of aortic PVL on survival in patients with varying level of operative risk.

• During the first year after PVL diagnosis, while either improvement or stable PVL grade was seen in the majority of patients, worsening of PVL grade was more common in the TAVR group

Ratnasari P. et al Mayo Clinic, BMJ Open 2018;
Comparative survival and role of STS score in aortic paravalvular leak after SAVR or TAVR: a retrospective study from the USA

The presence or degree of PVL severity had no influence on survival of patients with high STS score (≥8%).

The presence of greater than mild PVL predicted worse survival in those with STS score <8%.

• Ratnasari P. et al Mayo Clinic, BMJ Open 2018;
Comparative survival and role of STS score in aortic paravalvular leak after SAVR or TAVR: a retrospective study from the USA

Clinical outcomes in patients with PVL following SAVR versus TAVR based on Kaplan-Meier estimates at specific time points

**Overall mortality**
- At 1 year 6.8 vs 17.4
- At 3 years 16.4 vs 41.3
- At 5 years 26.7 vs 69.7

**Rehospitalisation from heart failure**
- At 1 year 4.7 vs 9.3
- At 3 years 9.8 vs 14.6
- At 5 years 9.8 vs 20.2

*Ratnasari P. et al Mayo Clinic, BMJ Open 2018;*
Permanent Pacemaker
Need for Permanent Pacemaker After Surgical Aortic Valve Replacement Reduces Long-Term Survival

- longer intensive care unit stay (89 vs 44 hours, p < 0.0001)
- hospital length of stay (9 vs 6 days, p < 0.0001),
- higher inflation-adjusted hospital cost ($81,000 vs $47,000, p < 0.0001).

Median follow-up was 7.5 years, and patients requiring PPM had significantly worse long-term survival even after risk adjustment with STS predicted risk of mortality (hazard ratio 1.48).

J. Hunter, University of Virginia, Ann Thorac Surg 2018
The need for **PPM** after aortic valve replacement *independently reduces long-term survival*. As **transcatheter** aortic valve replacement *expands to low-risk* patients, the impact of PPM placement on long-term survival warrants *close monitoring*.

J. Hunter, *University of Virginia, Ann Thorac Surg 2018*
Low flow low gradient
Outcome of isolated aortic valve replacement in patients with classic and paradoxical low-flow, low-gradient aortic stenosis

In-hospital mortality was 3% in the CLFLG AS group and 2.3% in the PLFLG AS group.

**One- and five-year mortality** rates were significantly **greater** in the CLFLG AS group (**27% and 42% vs 6% and 20%**) in the PLFLG AS group, respectively, \( P = .001 \).

On follow-up, 90% of the total survivors were in New York Heart Association class I-II, and 51% of the patients in the CLFLGAS group had an improvement in their ventricular function.

Ana Lopez-Marco, Swansea, United Kingdom. JTCVS 2017
Outcome of isolated aortic valve replacement in patients with classic and paradoxical low-flow, low-gradient aortic stenosis

The main findings of the study is that the survivals of patients with PLFLG, who represented one-third of their cohort, were as good as those of patients with high-gradient AS.

On the other hand, patients with classic LFLG AS had worse outcomes than did those with PLFLG AS, reemphasizing the negative impact of low LVEF on outcomes after surgical AVR.

V.Dayan, and P. Pibarot, Quebec, Canada, J Thorac Cardiovasc Surg 2017;154:443-4
Transcatheter Aortic Valve Replacement in Patients With Low-Flow, Low-Gradient Aortic Stenosis: The TOPAS-TAVI Registry.

This multicenter registry included 287 patients with CLASSIC LFLG-AS undergoing TAVR.

Mortality rates were 3.8%, 20.1%, and 32.3% at 30 days, 1 year, and 2 years, respectively.

TAVR was associated with good periprocedural outcomes in patients with LFLG-AS. However, approximately one-third of LFLG-AS TAVR recipients died at 2-year follow-up, with pulmonary disease, anemia, and residual paravalvular leaks associated with poorer outcomes.

LONG TERM RESULTS
5-Year Outcomes of Self-Expanding Transcatheter Versus Surgical Aortic Valve Replacement in High-Risk Patients.

• A total of 797 patients were randomized at 45 U.S. centers, of whom 750 underwent an attempted implant (TAVR = 391, SAVR = 359). The overall mean age was 83 years, and the STS score was 7.4%.
• All-cause mortality rates at 5 years were 55.3% for TAVR and 55.4% for SAVR.
• Major stroke rates were 12.3% for TAVR and 13.2% for SAVR.
• Mean aortic valve gradients were 7.1 ± 3.6 mm Hg for TAVR and 10.9 ± 5.7 mm Hg for SAVR.
• No clinically significant valve thrombosis was observed.
• Freedom from severe SVD was 99.2% for TAVR and 98.3% for SAVR (p = 0.32), and freedom from valve reintervention was 97.0% for TAVR and 98.9% for SAVR (p = 0.04).
• A permanent pacemaker was implanted in 33.0% of TAVR and 19.8% of SAVR patients at 5 years.

• Gleason T et al  CoreValve High Risk Trial Clinical Investigators.  J Am Coll Cardiol. 2018
Worse survival after transcatheter aortic valve implantation than surgical aortic valve replacement: A meta-analysis of observational studies with a propensity-score analysis

- **19 observational studies** with a propensity-score analysis enrolling a total of 6234 patients.
- The arithmetic means of **1-year and 3-year survival rates** were 82.7% and 71.3% after TAVI and 84.8% and 77.9% after SAVR, respectively. A pooled analysis demonstrated a statistically significant 21% increase in the hazard of mortality with TAVI relative to SAVR (**HR, 1.21; 95% CI, 1.05 to 1.39; p = 0.010**).
- Another pooled analysis of 4 RCTs (enrolling a total of 1795 patients) demonstrated no statistically significant difference in mortality between TAVI and SAVR (**HR, 0.92; 95% CI, 0.62 to 1.37; p = 0.69**).


- Our search identified **14 eligible studies** enrolling a total of **4,197** patients reporting a ≥3-year all-cause mortality as an outcome.

- A **pooled analysis** of all the 14 studies demonstrated a statistically significant 54% increase in mortality with TAVI relative to SAVR (HR, **1.54**; 95% CI, 1.31-1.81; P for effect < 0.00001; P for heterogeneity = 0.14; $I^2 = 30\%$).

- Several sensitivity analyses did not substantially change the statistically significant benefit for SAVR. There was no evidence of significant publication bias.

**ALICE (All-Literature Investigation of Cardiovascular Evidence) group.**

*Catheter Cardiovasc Interv*, 2018
Elderly pts and life expectancy
Life expectancy

With life expectancy of more than **17 years at the age of 65 years** and **8.2 years at the age of 80 years** and the quality of life (QOL) of the elderly patient with cardiac disease improving, **QOL may be more important to elderly patients than longer life** and the surgical options for cardiovascular disease in the elderly population cannot be overlooked.

Outcome in elderly patients after AVR with bioprostheses

42 studies including 12,000 patients, with more than 55,000 patient-years of follow-up. Their simulation model shows that:

75-year-old patient after SAVR has an estimated life expectancy of 9.8 years, approximating that of the general population of 10.2 years. During that period, the lifetime risk of bleeding is 7%, that of thromboembolism is 17%, and that of reintervention is 9%.

85–year-old patient with LE in the general population of 5.6 years, the estimated life expectancy after SAVR is 5.0, years with lifetime risks of 4.5% for bleeding, 10.2% for thromboembolism, and 4.3% for reintervention.

S. A. Huygens, Erasmus University, The Netherlands. JTCVS in press
The current low-risk trials of aortic stenosis comparing surgical and transcatheter aortic valve replacement with bioprostheses will include follow-up of all of the approximately 2000 patients enrolled in the trials prospectively out to 10 years. Until the results of those studies become available periodically during the next 10 years, the best information we have for patient counseling is the information published here.

M. Mack, MD  Dallas, Tex.  JTCVS in press
Outcome in elderly patients after AVR with bioprostheses.

This study can be used as a benchmark for the long-term outcomes after TAVI in intermediate surgical risk patients.

Although TAVI is a less-invasive procedure than SAVR, there are also disadvantages.

According to the clinical guidelines, the decision between SAVR and TAVI in elderly patients should be made by a heart team (i.e., multidisciplinary group of health care professionals) according to the individual patient characteristics, procedural risks, values, and preferences.

S. A. Huygens, Erasmus University, The Netherlands. JTCVS in press
Contemporary outcomes of conventional aortic valve replacement in 638 octogenarians: insights from an Italian Regional Cardiac Surgery Registry (RERIC)

- The study population consisted of 638 patients. Mean log-EuroSCORE was 13.0%.
- Overall hospital mortality and stroke rates were 4.5% and 1.3%, respectively. Other post-operative complications included renal failure (4.9%), intubation time >48 h (3.4%), complete atrio-ventricular block (4.4%).
- NYHA III–IV (OR = 2.7; CI 95%:1.2–6.7) emerged as independent predictors of hospital mortality on multivariate analysis.
- At 6 years, octogenarians’ survival rate was similar to the expected survival of the age- and sex-matched regional population.
- Preoperative creatinine > 2.1 (HR = 2.8; CI 95%:1.4–5.9), extra-cardiac arteriopathy (HR = 1.5; CI 95%:1.1–2.1) and peripheral neurological dysfunction (HR = 3.8; CI 95%:1.4–10.4) emerged as independent risk factors for decreased 6 years’ survival.

Marco Di Eusanio, European Journal of Cardio-Thoracic Surgery, 2012,
Cost
The World Health Organization (WHO) has suggested a rough benchmark of 3 times the GDP per capita as an upper threshold for an acceptable level of cost-effectiveness in a given country.

Programs with cost-effectiveness ratios above this range would generally be considered economically unattractive.

Whereas programs with cost-effectiveness ratios below 1 GDP per capita would generally be considered affordable and cost-effective ($50,000 per QALY in an economy with a per capita GDP of the United States).

Determining the health benefits of a medical intervention or program is more difficult (and may be more influential on the results of the analysis) than determining its overall cost.

Incremental health benefits include such things as improvements in symptoms, functional capacity, well-being, and length of life.

One key principle of economic evaluation is that these clinical consequences should be assessed by using patient-centered outcomes, such as symptoms or major clinical events, rather than by changes in surrogate markers (e.g., cholesterol levels).

JACC 2014
• The **Quality-adjusted life-year (QALY)** is the standard measure of outcomes used in economic evaluation. It represents years of survival adjusted for quality of life using a scale of utilities ranging from 0 (equivalent to death) to 1 (perfect health).

• The incremental cost-effectiveness ratio (ICER), which is used to compare a new intervention or program with its alternative (alt.), is expressed symbolically as follows:

\[
\text{ICER} = \left( C_{\text{new}} - C_{\text{alt.}} \right) \left( \text{QALY}_{\text{new}} - \text{QALY}_{\text{alt.}} \right)
\]

where \( C \) indicates the net cost of the intervention/program and \( \text{QALY} \) indicates the quality-adjusted life-years that result from that intervention/program.

JACC 2014
A cost-utility analysis of transcatheter versus surgical aortic valve replacement for the treatment of aortic stenosis in the population with intermediate surgical risk

A fully probabilistic Markov model with 30-day cycles was constructed to estimate the difference in cost and effectiveness (measured as quality-adjusted life years) of transcatheter aortic valve implantation versus surgical aortic valve replacement for intermediate-risk patients over a lifetime time horizon.

Clinical trial data from PARTNER 2 informed the efficacy inputs. Incremental cost-effectiveness ratios were calculated.

Derrick Y. Tam. et al, Toronto, Canada  JTCVS 2018
In the base-case analysis, the **index hospitalization cost** in the TAVI group was $40,274 compared with $29,856 in the SAVR group. With 1.5% global discounting, **the total lifetime cost** was $46,904$4038 and $36,356$7309 in the TAVI and SAVR groups, respectively.

Derrick Y. Tam. et al, Toronto, Canada | JTCVS 2018
A cost-utility analysis of transcatheter versus surgical aortic valve replacement for the treatment of aortic stenosis in the population with intermediate surgical risk

RESULTS

In the base-case analysis, total lifetime costs for TAVR were $10,548 higher than SAVR

When QoL was taken into account, the QALYs gained were $5.63±1.47 and $5.40±1.47 for TAVI and SAVR, respectively.

Thus, the incremental cost was $10,547 and the incremental gain in QALY was 0.23.

This resulted in an ICER of $46,083/QALY after discounting.

Derrick Y. Tam. et al, Toronto, Canada  JTCVS 2018
A cost-utility analysis of transcatheter versus surgical aortic valve replacement for the treatment of aortic stenosis in the population with intermediate surgical risk

• After 2 years, we made the conservative assumption that the rates of complications were assumed to be equivalent in both the TAVI and SAVR arms.

• In addition, after 2 years, mortality rates in the model were based on 2010-2012 age- and gender- specific Canadian life tables given the absence of clinical trial data from the PARTNER 2 study beyond the 2-year follow-up.

• Of note, TAVI was no longer cost-effective when the TAVI valve system cost was increased by $1100 or when ICU LOS increased by 0.3 days.

Derrick Y. Tam. et al, Toronto, Canada JTCVS 2018
A cost-utility analysis of transcatheter versus surgical aortic valve replacement for the treatment of aortic stenosis in the population with intermediate surgical risk

Conclusions:

On the basis of current evidence, **TAVR may be cost-effective** for the treatment of severe aortic stenosis in patients with intermediate surgical risk. **There remains moderate-to-high uncertainty** surrounding the base-case incremental cost-effectiveness ratio.

Derrick Y. Tam. et al, **Toronto, Canada**  JTCVS 2018
Evaluating the best approach to treatment of aortic stenosis

Confidence was only slightly better than the flip of a coin (52.7%-55.4% of modeled scenarios were cost-effective).

True value therefore may hinge on prices at individual facilities, surgeon expertise, and patient views about what makes a good quality of life.

Glen B. Taksler, PhD  Cleveland Clinic,  JTCVS 2018
Initial in-hospital costs were higher in TAVI compared with the SAVR population (40,802 vs 33,354) and higher at 1-year follow-up (total cost: 46,217 vs 35,511; ).

The study did not consider effectiveness, but simply compared the costs of the interventions in a small sample of patients from a single institution over a 1-year time horizon

Drivers of healthcare costs associated with the episode of care for surgical aortic valve replacement versus transcatheter aortic valve implantation.

Micro-costing data from Ontario hospitals

**TAVI, $42,742;** interquartile range, $37,295-$56,196

**SAVR, $21,811;** interquartile range, $18,148-$30,498.

Wijeysundera HC, et al *Open Heart. 2016*
Cost and contribution margin of transcatheter versus surgical aortic valve replacement

Medicare spent $215,770,200 nationally on 4083 patients who underwent TAVR in 2012. Hospital costs were higher for TAVR patients (median, $50,200; interquartile range [IQR], $39,800-$64,300) than for propensity-matched SAVR patients ($45,500; IQR, $34,500-$63,300; P < .01).

Postprocedure hospital length of stay (LOS) length was shorter for TAVR patients (median, 5 days [IQR, 4-8 days] vs 7 days [IQR, 5-9 days]; P < .01), as was total intensive care unit (ICU) LOS (median, 2 days [IQR, 0-5 days] vs 3 days [IQR, 1-6 days]; P < .01).

The median of the differences between payments and costs (contribution margin) was $-3380 for TAVR hospitalizations and $+2390 for SAVR hospitalizations (P < .01).

McCarthy, MD University of Pennsylvania JTCVS 2017
Comparison of transcatheter versus surgical aortic valve implantation in high-risk patients: A nationwide study in France

- **Objective:** To compare the clinical outcomes and direct costs at 5 years between (TAVI) and (SAVR) using real-world evidence.

- **Methods:** We performed a nationwide longitudinal study using data from the French Hospital Information System from 2009 to 2015. We matched, inside hospitals, 2 cohorts of adults who underwent TAVI or SAVR during 2010 on propensity score based on patient characteristics.

- **Outcomes analysis included** mortality, morbidity, and total costs and with a maximum 60-month follow-up

Xavier Armoiry, PharmD, PhD et al Warwick Medical School, Universite Claude Bernard Lyon, Harvard Medical School. JTCVS 2018
Comparison of transcatheter versus surgical aortic valve implantation in high-risk patients: A nationwide study in France

Results: 1598 patients (799 in each group) from 27 centers

• **Higher risk of death was observed after 1 year with TAVI** compared with SAVR (16.8% vs 12.8%, respectively; **HR, 1.33**; 95% confidence interval [CI],) **and was sustained up to 5 years** (52.4% vs 37.2%; **HR, 1.56**; 95% CI,).

• **At 5 years**, the risk of **stroke** was increased (**HR, 1.64**; 95% CI,) **as was myocardial infarction (HR, 2.30; 95% CI,)** and **pacemaker implantation (HR, 2.40; 95% CI,) after TAVI.**

• **The hospitalization costs per patient at 5 years** were **69,083 after TAVI** and **55,687 after SAVR** (**P<.001**).

Xavier Armoiry, PharmD, PhD et al  
Warwick Medical School, Universite Claude Bernard Lyon, Harvard Medical School.  
JTCVS 2018
Comparison of transcatheter versus surgical aortic valve implantation in high-risk patients: A nationwide study in France

CONCLUSIONS

This study showed that patients after TAVI, compared with those who underwent SAVR, harboured a greater risk of mortality and morbidity at 5 years, and had higher costs of hospitalization. These results indicate that more data are needed before considering an enlargement of TAVI indications in people eligible for conventional surgery.

Xavier Armoiry, PharmD, PhD et al Warwick Medical School, Universite Claude Bernard Lyon, Harvard Medical School. JTCVS 2018
ΧΕΙΡΟΥΡΓΙΚΗ ΚΛΙΝΙΚΗ ΘΩΡΑΚΟΣ ΚΑΡΔΙΑΣ
ΝΟΣ ΠΑΠΑΝΙΚΟΛΑΟΥ ΘΕΣΣΑΛΟΝΙΚΗ

Μεμονωμένες αορτικές βαλβίδες  Ιούνιος 2012- Ιανουαριος 2019
Συνολο :441  316βιολογικές 125μηχανικές

Ηλικία 68,1±7,5                  Γυναικες 183 (41,5%)                  Euro score II  2,19±2,7

Θανατοί 11 (2,49%)
ΑΕΕ 3  (0,68%)

RBC transfusion(median) :2 units , Intubation hours(median):7
Prolonged vent>24h: 14(3,17%)

Reexploration hemorrhage 16(3,6%),Sternal infections 9 (2,04%)
AKI 63 (14,28%),Atrial Fib 157(35,6%)
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Figure 2. Number of deaths of any cause, according to the year after hospital discharge
Figure 3. Number of cardiac deaths, according to the year after hospital discharge
Figure 4. % percentage of cardiac death, according to duration of survival after the operation

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The paradox between randomized controlled trials and propensity score–matched real-world data: Moving from dissonance to dialog?

- RCTs were designed to assess specific (limited) patient populations. Generalizations of findings to broader, less-selected populations should be avoided.

- Data from larger propensity score–matched real-world registry studies should inform design of future RCTs and challenge analyses of previous, more focused RCTs.

- Initial sample size may limit interpretation and certainty of longer term clinical outcomes. This is particularly relevant when combined primary end points are used to design the sample size analysis. For example, the PARTNER 3 trial was designed to assess a combined end point of death, neurologic deficits, and hospital readmission.

- B. Z. Atkins, and G. S. Aldea, University of Washington, Seattle, J Thorac Cardiovasc Surg 2018
TAVR is not ready for prime time unrestricted distribution,

To appear in: The Journal of Thoracic and Cardiovascular Surgery
Conclusion

Not so fast my friend

To appear in: The Journal of Thoracic and Cardiovascular Surgery