CAT – FINAL **Jay Kolasinac**
RT 7 WK 2 PICO

Brief description of patient problem/setting (summarize the case <u>very</u> briefly)

74M, with history of CAD, HLD, DM, and HTN, is admitted to the hospital for chest pain. Patient is deemed to have severe aortic stenosis. When informed he will undergo TAVR, the patient responds, "So you are not going to open me up?" "What are the outcomes of this new method of valve replacement years from now?"

<u>Search Question:</u>

In elderly patients diagnosed with severe aortic stenosis, is TAVR (transcatheter aortic valve replacement) associated with better long-term outcomes compared to SAVR (surgical aortic valve replacement)?

<u>Question Type:</u> What kind of question is this? (boxes now checkable in Word)

☐Prevalence	☐Screening	☐Diagnosis
☒Prognosis	☒Treatment	☐Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)? **Please explain your choices.**

Since my question is related to a treatment method, RCTs would be studies that I would look for. Prospective studies as well as retrospective studies would also be taken into consideration although quality of evidence not as high as the others mentioned above.

<u>PICO search terms:</u>

P	**I**	**C**	**O**
Severe aortic stenosis	TAVR	SAVR	Increased survival
Elderly	Transcatheter aortic valve replacement	Surgical aortic valve replacement	Decreased rates of survival
Adults			Similar rates of survival
			Valvular outcomes

<u>Search tools and strategy used:</u>

Database	**Terms**	**Filter**	**# of Articles**
PubMed	Aortic stenosis TAVR SAVR	Medline, last 10 years	384
	Aortic stenosis Transcatheter aortic valve replacement Surgical aortic valve replacement	Medline, last 10 years	2,015

	TAVR outcomes	Medline, last 10 years	295
ScienceDirect	Aortic stenosis TAVR SAVR	Last 10 years, research articles	476
	Aortic stenosis Transcatheter aortic valve replacement Surgical aortic valve replacement	Last 10 years, research articles	1,952
	TAVR outcomes	Last 10 years, research articles	1,720
Cochrane Library	Aortic stenosis TAVR SAVR	Last 10 years	70
	Aortic stenosis Transcatheter aortic valve replacement Surgical aortic valve replacement	Last 10 years	1
	TAVR outcomes	Last 10 years	355 (trials)
Wiley Online Library	Aortic stenosis TAVR SAVR	Last 5 years, journal article	338
	Aortic stenosis Transcatheter aortic valve replacement Surgical aortic valve replacement	Last 5 years, journal article	1,314
	TAVR outcomes	Last 5 years, journal article	874

The search results yielded lots of articles. Many of them were very specific to an aspect about TAVR/SAVR that did not necessarily relate to my PICO question which was probably do to using the complete spelling of the procedures as opposed to the acronym. Had to sort through articles that related to health outcomes and not other aspects such as cost, etc.

Results found:

Article 1

Citation:

Siontis, G. C. M., Praz, F., Pilgrim, T., Mavridis, D., Verma, S., Salanti, G., … Windecker, S. (2016). *Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials. European Heart Journal, 37(47), 3503–3512.* doi:10.1093/eurheartj/ehw225

https://pubmed.ncbi.nlm.nih.gov/27389906/

Article Type:

Meta Analysis

Abstract:

Aims: In view of the currently available evidence from randomized trials, we aimed to compare the collective safety and efficacy of transcatheter aortic valve implantation (TAVI) vs. surgical aortic valve replacement (SAVR) across the spectrum of risk and in important subgroups.

Methods and results: Trials comparing TAVI vs. SAVR were identified through Medline, Embase, and Cochrane databases. The primary outcome was death from any cause at 2 years. We performed random-effects meta-analyses to combine the available evidence and to evaluate the effect in different subgroups. This systematic review and meta-analysis is registered with PROSPERO (CRD42016037273). We identified four eligible trials including 3806 participants, who were randomly assigned to undergo TAVI (n = 1898) or SAVR (n = 1908). For the primary outcome of death from any cause, TAVI when compared with SAVR was associated with a significant 13% relative risk reduction [hazard ratio (95% CI): 0.87 (0.76-0.99); P = 0.038] with homogeneity across all trials irrespective of TAVI device ($P_{interaction}$ = 0.306) and baseline risk ($P_{interaction}$ = 0.610). In subgroup analyses, TAVI showed a robust survival benefit over SAVR for patients undergoing transfemoral access [0.80 (0.69-0.93); P = 0.004], but not transthoracic access [1.17 (0.88-1.56); P = 0.293] ($P_{interaction}$ = 0.024) and in female [0.68 (0.50-0.91); P = 0.010], but not male patients [0.99 (0.77-1.28); P = 0.952] ($P_{interaction}$ = 0.050). Secondary outcomes of kidney injury, new-onset atrial fibrillation, and major bleeding favoured TAVI, while major vascular complications, incidence of permanent pacemaker implantation, and paravalvular regurgitation favored SAVR.

Conclusion: Compared with SAVR, TAVI is associated with a significant survival benefit throughout 2 years of follow-up. Importantly, this superiority is observed irrespective of the TAVI device across the spectrum of intermediate and high-risk patients, and is particularly pronounced among patients undergoing transfemoral TAVI and in females.

Article 2

Citation:

Deeb, G. M., Reardon, M. J., Chetcuti, S., Patel, H. J., Grossman, P. M., Yakubov, S. J., … Popma, J. J. (2016). *3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement. Journal of the American College of Cardiology, 67(22), 2565–2574.* doi:10.1016/j.jacc.2016.03.506

https://pubmed.ncbi.nlm.nih.gov/27050187/

Article Type:

RCT

Abstract:

Background: In patients with severe aortic stenosis at increased risk for surgery, self-expanding transcatheter aortic valve replacement (TAVR) is associated with improved 2-year survival compared with surgery.
Objective: We sought to determine whether this clinical benefit was sustained over time.
Methods: Patients with severe aortic stenosis deemed at increased risk for surgery by a multidisciplinary heart team were randomized 1:1 to TAVR or open surgical valve replacement (SAVR). Three-year clinical and echocardiographic outcomes were obtained in those patients with an attempted procedure.
Results: A total of 797 patients underwent randomization at 45 US centers; 750 patients underwent an attempted procedure. Three-year all-cause mortality or stroke was significantly lower in TAVR patients (37.3% versus 46.7% in SAVR; p = 0.006). Adverse clinical outcome components were also reduced in TAVR patients compared with SAVR patients, including all-cause mortality (32.9% versus 39.1%, respectively; p = 0.068), all stroke (12.6% versus 19.0%, respectively; p = 0.034), and major adverse cardiovascular or cerebrovascular events (40.2% versus 47.9%, respectively; p = 0.025). At 3 years aortic valve hemodynamics were better with TAVR patients (mean aortic valve gradient, 7.62 ± 3.57 mm Hg versus 11.40 ± 6.81 mm Hg in SAVR, p < 0.001), although moderate or severe residual aortic regurgitation was higher in TAVR patients (6.8% versus 0.0% in SAVR; p < 0.001). There was no clinical evidence of valve thrombosis in either group.
Conclusion: Patients with severe aortic stenosis at increased risk for surgery had improved 3- year clinical outcomes after TAVR compared with surgery. Aortic valve hemodynamics were more favorable in TAVR patients without differences in structural valve deterioration

Article 3

Citation:

Latif, A., Lateef, N., Ahsan, M. J., Kapoor, V., Usman, R. M., Cooper, S., … Khouzam, R. (2020). *Transcatheter Versus Surgical Aortic Valve Replacement in Patients with Cardiac Surgery: Meta-Analysis and Systematic Review of the Literature. Journal of Cardiovascular Development and Disease, 7(3), 36.* doi:10.3390/jcdd7030036

https://pubmed.ncbi.nlm.nih.gov/32927705/

Article Type:

Meta-Analysis and Systematic Review

Abstract:

The number of patients with severe aortic stenosis (AS) and a history of prior cardiac surgery has increased. Prior cardiac surgery increases the risk of adverse outcomes in patients undergoing aortic valve replacement. To evaluate the impact of prior cardiac surgery on clinical endpoints in patients undergoing transcatheter aortic valve replacement (TAVR) versus surgical aortic valve replacement (SAVR), we performed a literature search using PubMed, Embase, Google Scholar, and Scopus databases. The clinical endpoints included in our study were 30-day mortality, 1–2-year mortality, acute kidney injury (AKI), bleeding, stroke, procedural time, and duration of hospital stay. Seven studies, which included a total of 8221 patients, were selected. Our study found that TAVR was associated with a lower incidence of stroke and bleeding complications. There was no significant difference in terms of AKI, 30-day all-cause mortality, and 1–2-year all-cause mortality between the two groups. The average procedure time and duration of hospital stay were 170 min less ($p \leq 0.01$) and 3.6 days shorter ($p < 0.01$) in patients with TAVR, respectively. In patients with prior coronary artery bypass graft and severe AS, both TAVR and SAVR are reasonable options. However, TAVR may be associated with a lower incidence of complications like stroke and perioperative bleeding, in addition to a shorter length of stay.

Article 4

Citation:

Abi Khalil, C., Ignatiuk, B., Erdem, G., Chemaitelly, H., Barilli, F., El-Shazly, M., … Bonaros, N. (2021). Aortic valve function post-replacement of severe aortic stenosis by transcatheter procedure versus surgery: a systematic review and metanalysis. Scientific Reports, 11(1). doi:10.1038/s41598-021-91548-x

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8184892/

Article type:

Meta Analysis and Systematic Review

Abstract:

Transcatheter aortic valve replacement (TAVR) has shown to reduce mortality compared to surgical aortic valve replacement (sAVR). However, it is unknown which procedure is associated with better post-procedural valvular function. We conducted a meta-analysis of randomized clinical trials that compared TAVR to sAVR for at least 2 years. The primary outcome was post-procedural patient prosthesis-mismatch (PPM). Secondary outcomes were post-procedural and 2-year: effective orifice area (EOA), paravalvular gradient (PVG) and moderate/severe paravalvular leak (PVL). We identified 6 trials with a total of 7022 participants with severe aortic stenosis. TAVR was associated with 37% (95% CI [0.51–0.78) mean RR reduction of post-procedural PPM, a decrease that was not affected by the surgical risk at inclusion, neither by the transcatheter heart valve system. Postprocedural changes in gradient and EOA were also in favor of TAVR as there was a pooled mean difference decrease of 0.56 (95% CI [0.73–0.38]) in gradient and an increase of 0.47 (95% CI [0.38–0.56]) in EOA.

Additionally, self-expandable valves were associated with a higher decrease in gradient than balloon ones (beta= 0.38; 95% CI [0.12–0.64]). However, TAVR was associated with a higher risk of moderate/severe PVL (pooled RR: 9.54, 95% CI [5.53–16.46]). All results were sustainable at 2 years.

Article 5

Citation:

Tarus, A., Tinica, G., Bacusca, A., Artene, B., Popa, I. V., & Burlacu, A. (2020). *Coronary revascularization during treatment of severe aortic stenosis: A meta-analysis of the complete percutaneous approach (PCI plus TAVR) versus the complete surgical approach (CABG plus SAVR). Journal of Cardiac Surgery.* doi:10.1111/jocs.14814

https://pubmed.ncbi.nlm.nih.gov/32667080/

Article type:

Meta Analysis

Abstract:

Background: The management of patients with coexisting severe aortic stenosis (AS) and coronary artery disease (CAD) is still facing a great deal of uncertainty when it comes to choosing between the entire surgical versus the complete percutaneous approaches, after accurately balancing risks versus outcomes.

Aim: To evaluate clinical outcomes and mortality of transcatheter aortic valve replacement (TAVR) plus percutaneous coronary intervention (PCI) compared with surgical aortic valve replacement (SAVR) plus coronary arteries bypass grafting (CABG) procedures in patients with concomitant AS and CAD.

Methods: Electronic databases of PubMed, EMBASE, and SCOPUS were searched for relevant articles assessing outcome parameters of interest. The study endpoints were the rate of overall myocardial infarction and stroke within 30 days and the rate of 30-day mortality and 2-year mortality between patients with TAVR/PCI and those with SAVR/CABG.

Results: Random-effect meta-analysis did not reveal any significant difference between 30-day safety outcomes: myocardial infarction (TAVR/PCI vs SAVR/CABG: odds ratio [OR]: 0.52; 95% confidence interval [CI]: 0.20-1.33; I 2 = 0%), stroke (TAVR/PCI vs SAVR/CABG: OR: 0.88; 95% CI: 0.45-1.73; I 2 = 0%). No significant difference in 30-day mortality (OR: 0.72; 95% CI: 0.43-1.21; I 2 = 0%) and 2- year mortality (OR: 1.50; 95% CI: 0.77-2.94; I 2 = 81%) rate was noted between patients with TAVR/PCI and those with SAVR/CABG.

Conclusions: When comparing the total percutaneous and total surgical treatment, no significant difference in short-term safety outcomes or early and late mortality was observed. More evidence is needed to guide the clinical decision.

Article 6

Citation:

Tam, D. Y., Vo, T. X., Wijeysundera, H. C., Ko, D. T., Rocha, R. V., Friedrich, J., & Fremes, S. E. (2017). *Transcatheter vs Surgical Aortic Valve Replacement for Aortic Stenosis in Low-Intermediate Risk Patients: A Meta-analysis. Canadian Journal of Cardiology, 33(9), 1171–1179.* doi:10.1016/j.cjca.2017.06.005

https://pubmed.ncbi.nlm.nih.gov/28843328/

Article type:

Meta Analysis

Abstract:

Background: Transcatheter aortic valve replacement (TAVR) has emerged as the treatment of choice for patients with severe aortic stenosis (AS) at high surgical risk; the role of TAVR compared to surgical aortic valve replacement (SAVR) in the low-intermediate surgical risk population remains uncertain. Our primary objective was to determine differences in 30-day and late mortality in patients treated with TAVR compared to SAVR at low-intermediate risk (Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM)<10%).

Methods: Both Medline and Embase were searched from 2010 to March 2017 for studies that compared TAVR to SAVR in the low-intermediate surgical risk population, restricted to randomized clinical trials and matched observational studies. Two investigators independently abstracted the data and a random effects meta-analysis was performed.

Results: Four RCTs (n=4042) and nine propensity-score matched observational studies (n=4192) were included in the meta-analysis (n=8234). There was no difference in 30-day mortality between TAVR and SAVR (3.2% vs 3.1%, pooled risk ratio: 1.02, 95% confidence interval (CI): 0.80,1.30; P=0.89, I2 =0%) or mortality at 1.5-year median follow-up (incident rate ratio: 1.01, 95%CI: 0.90,1.15;P=0.83, I2 =0%). There was a higher risk of pacemaker implantation and greater than trace aortic insufficiency in the TAVR group while the risk of early stroke, atrial fibrillation, acute kidney injury (AKI), cardiogenic shock and major bleeding was higher in the SAVR group.

Conclusions: While there was no difference in 30-day and late mortality, the rate of complications differed between TAVR and SAVR in the low-intermediate surgical risk population.

Summary of Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Biases
Siontis et al., (2016)	Meta-Analysis	Outcomes during a period of at least 1-	The primary outcome was death from any	TAVR was associated with	First, the main analysis is focused on 2

		year or longer of follow-up. We identified four eligible trials including 3806 participants, who were randomly assigned to undergo TAVI (n=1898) or SAVR (n=1908).	cause at 2 years; cerebrovascular event (any stroke or transient ischemic attack), stroke, myocardial infarction, kidney injury, new-onset AF, major bleeding, major vascular complications, valve endocarditis, permanent pacemaker implantation, and the echocardiographic outcome of paravalvular regurgitation (moderate or severe) were secondary outcomes	13% relative risk reduction TAVR: Favored in outcomes including kidney injury, new onset AF, and major bleeding SAVR: favored in outcomes including major vascular complications, incidence of permanent pacemaker, and paravalvular regurgitation. Mortality benefits with TAVI over SAVR are consistent across the spectrum of intermediate to high-risk without evidence of heterogeneity according to the TAVI heart valve system	years of follow-up. Excess mortality during long-term follow-up due to non-valvular causes of death may conceal the therapeutic effect of valvular replacement. The competing effect of non-valve-related mortality in a predominantly elderly and high risk patient population may camouflage potential differences between the two treatment strategies and bias potentially important between/group differences towards the null.
Deeb et al., (2016)	RCT	Patients were randomly assigned to TAVR or SAVR in a 1:1 manner. A total of 750 patients were included	The primary outcome was 3-year clinical outcomes: all-cause mortality, all stroke, major stroke, all-cause	Three year clinical outcomes were available in 228 of 246 (92.7%) eligible patients who	It is uncertain whether the crimping – recrimping of the transcatheter valve will have an impact on long-term

		in the as treated patient population. TAVR was attempted in 391 patients and surgery was attempted in 359 patients.	mortality or major stroke, major adverse cardiovascular events, defined as death from any cause, myocardial infarction, any stroke or re-intervention; vascular complications, pacemaker implantation, life-threatening or disabling bleeding, valve thrombosis and valve endocarditis.	were alive in the TAVR group and 179 of 194 (92.3%) eligible patients who were alive in the SAVR group. There was a 20.1% relative reduction in the occurrence of all-cause mortality or stroke at 3 years in TAVR patients compared with surgical patients.	bioprosthesis durability. The 3-year follow-up is limited and longer 10-year studies are needed to understand the longer-term durability in patients at lower risk with longer life expectancies.
Latif et al., (2020)	Meta-Analysis and Systematic Review	A total of seven studies (3 randomized trials, 4 cohort) including 8221 patients (4055 in the TAVR group and 4166 in the SAVR group) were included in the analysis.	30-day mortality, 1–2-year mortality, post-operative stroke, major bleeding, mean length of hospital stay, discharge to home from the hospital, post-operative acute renal failure, and pacemaker implantation	There was no significant difference between the two groups regarding 30-day all cause mortality. Five studies reported 1–2-year all-cause mortality. There was no significant difference between the two groups regarding 1-2 year all cause mortality. TAVR was associated with lower incidence of stroke. TAVR	: First, this was a cohort study/trial-level meta-analysis as we did not have access to individual patient data and thus, the reason for individual decisions was unknown. Second, most of the studies included patients in the TAVR group who were deemed to be high risk with high STS-PROM (Society of thoracic surgeons-predicted risk of mortality) and

				was associated with lower incidence of bleeding complications. There was no statistical difference between both groups in AKIs.	EuroSCORE (European system for cardiac operative risk evaluation), putting them at higher risk for mortality and post-procedural complications. Finally, baseline characteristics were not similar in all included studies and the used access site for TAVR was not mentioned in all studies
Abi Khalil et al., (2021)	Meta-Analysis and Systematic Review	We performed a systematic literature search for randomized controlled trials (RCTs) using 3 databases: Medline, Embase and the Cochrane library, from the 1st of January 2002 till the 20th of December 2019. There were 6 articles included totaling 7020 participants, 3511 randomized to TAVR and 3509 randomized to sAVR.	The primary outcome was post-procedural patient prosthesis-mismatch (PPM). Secondary outcomes were post-procedural and 2-year: effective orifice area (EOA), paravalvular gradient (PVG) and moderate/severe paravalvular leak (PVL).	Tere was a 37% mean relative risk reduction (RR=0.63, 95% CI [0.51–0.78]) in post-procedural PPM in favor of TAVR. The effective orifice area, the transvalvular gradients and the patient-prosthesis mismatch favor transcatheter aortic valve replacement over surgery for the treatment of severe aortic stenosis in our	Although the overall risk of bias was low, there are still some possibilities of outcome measurement bias in the studies, especially for the measurement of echocardiographic parameters that are operator- and technique-dependent. Although surgical prostheses do not variate a lot, some degree of heterogeneity on the grounds of prostheses differences cannot be

				metanalysis. Tis benefit is counterbalanced by higher rates of paravalvular regurgitation.	excluded. s. Finally, with only 6 trials included in our meta-analysis, it was not possible to perform a meta-regression that takes into account confounding factors like age, gender and cardiovascular risk factors.
Tarus et al., (2020)	Meta-Analysis	Three articles were selected for final meta-analysis. Among the included one was an RCT, one national observational, prospective, multicenter, cohort propensity score match study and one a prospective registry analysis. The final analysis included a total of 1380 patients. Only patients with combined AS and CAD were selected in all studies, those with concomitant interventions on other valves or	The endpoints were the rate of overall myocardial infarction and stroke within 30 days and the rate of 30-day mortality and 2-year mortality between patients with TAVR/PCI and those with SAVR/CABG.	First, there is no difference in 30-day myocardial infarction, stroke rate, and survival in PCI plus TAVR versus CABG plus SAVR groups. Second, 2-year survival is not different based on treatment strategy. In the third place, the number of post-procedural permanent pacemaker implantations is significantly higher after TAVR/PCI procedure (which is consistent with the higher	First, it includes only three studies with a high heterogeneity according to the study design, only one randomized control trial, and others an observational propensity score match study and prospective registry analysis. Second, we calculated the 2-year mortality from the Kaplan-Meier survival curve in one study, and this can cause some inaccuracies, which is probably reflected in high I 2 value. Finally, the revascularization

		other surgical procedures were excluded.		reported number of pacemakers after TAVR itself).	strategy in the TAVR group was nonuniform, ranging from simultaneous to less than 12 months of PCI prior procedure. All these impose precaution in interpreting current results.
Tam et al., (2017)	Meta-Analysis	Our final selection included 13 articles 4 RCTs (4042 patients) and 9 propensity matched observational studies (4192 patients).	The primary outcome of our study as early (30-days or in-hospital) and late (>30-days) mortality while secondary outcomes were early (30-days or in-hospital) and late (>30-days) stroke, clinically relevant periprocedural complications rates and hospital length of stay.	Early and late mortality – no significant difference in early mortality nor late mortality seen between the SAVR and TAVR groups. Significant decrease in early stroke seen in TAVR vs SAVR patients. No difference in the rate of stroke was seen between the TAVR and SAVR groups at a follow up of 2 years (late). TAVR group seen to have significant reduction in a-fib, cardiogenic shock, AKI, myocardial infarction and	While we included only observational studies that used propensity matching to adjust for known confounders, the weakness of any observational study includes the lack of randomization and the inability to control for unknown confounders.

				major/life-threatening bleeding. SAVR group had less AI, paravalvular leak, major vascular complications, and permanent pacemaker insertion. Decrease length of stay seen in the TAVR group.	

Conclusions:

1. Siontis et al., (2016) - Compared with SAVR, TAVI is associated with a significant survival benefit throughout 2 years of follow-up. Importantly, this superiority is observed irrespective of the TAVI device across the spectrum of intermediate and high-risk patients, and is particularly pronounced among patients undergoing transfemoral TAVI and in females.

2. Deeb et al., (2016) - Patients with severe aortic stenosis at increased risk for surgery had improved 3- year clinical outcomes after TAVR compared with surgery. Aortic valve hemodynamics were more favorable in TAVR patients without differences in structural valve deterioration.

3. Latif et al., (2020) - Our study found that TAVR was associated with a lower incidence of stroke and bleeding complications. There was no significant difference in terms of AKI, 30-day all-cause mortality, and 1–2-year all-cause mortality between the two groups. The average procedure time and duration of hospital were less in patients with TAVR. However, TAVR may be associated with a lower incidence of complications like stroke and perioperative bleeding, in addition to a shorter length of stay.

4. Abi Khalil et al., (2021) - TAVR was associated with 37% mean reduction of post-procedural PPM. Postprocedural changes in gradient and EOA were also in favor of TAVR. However, TAVR was associated with a higher risk of moderate/severe PVL. All results were sustainable at 2 years.

5. Tarus et al., (2020) - This meta-analysis demonstrates that there is no significant difference in short-term safety outcomes using the total percutaneous or total surgical treatment in patients with severe native AS and CAD. Likewise, there is no difference in early and late mortality.

6. Tam et al., (2017) - This meta-analysis of low-intermediate STS-PROM risk patients demonstrated no differences in perioperative mortality and median 1.5-year mortality and supports the use of TAVR in this population. While TAVR was confirmed to be non-inferior to SAVR in mortality, the duration of follow-up was limited in all studies. As such, longer follow-up is required to ascertain the benefits of TAVR compared to SAVR in the intermediate surgical risk population – particularly as transcatheter valves are tested in lower risk populations.

Overarching conclusion: Both the TAVR and SAVR treatment options for severe aortic stenosis are seen to have similar and no significant differences in early and late mortality. However, TAVR is associated with fewer post-procedural complications, bleeding, stroke, in addition to shorter length of stays in the hospital. More research needs to be conducted to establish longer term outcomes between the two groups (5+ and 10 years +)

Clinical Bottom Line:

Weight of the evidence:

1. Latif et al., (2020) – I would rate this article with the highest weight of evidence because it was published last year and included a total of seven studies (3 randomized trials, 4 cohort) including 8221 patients (4055 in the TAVR group and 4166 in the SAVR group). Its primary outcomes were 30-day all-cause mortality and 1-2-year all-cause mortality. It included the 2nd highest number of participants in its meta-analysis/systematic review (just shy by about 13 patients compared to the other article). Its recent publication, large sample size, and various outcomes studied places this article at the top.
2. Abi Khalil et al., (2021) – This article is the most recently published out of all the others. This meta-analysis/systematic review included 6 RCTs totaling a sample size of 7,022 participants where 3,511 randomized to TAVR and 3,509 randomized to SAVR. This study included the largest amount of RCTs compared to the others but only focused on valvular outcomes between the two groups.
3. Tam et al., (2017) –It is still considered quality evidence being a meta-analysis, having the largest sample size of 8,234 participants - 4 RCTs (4042 patients) and 9 propensity matched observational studies (4192 patients). However, the article was published 4 years ago which makes it relatively old compared to some of the others.
4. Siontis et al., (2016) – Being one of the relatively oldest articles amongst the others, it still included 4 RCTs and possessed a decent sample size of 3,806 participants (TAVR 1,898 and SAVR 1,908). Being that is older, does not posses as much weight as the newer articles who have greater sample sizes.
5. Tarus et al., (2020) – Although this article was a meta-analysis, the articles chosen in the analysis included only 1 RCT along with a one national observational, prospective, multicenter, cohort propensity score match study and one a prospective registry analysis. Although recently published, it does not hold as much weight as the other articles which included only RCTs and much more of them.

6. Deeb et al., (2016) – This article was not a meta-analysis or systematic review and was only a RCT which ranks it the lowest amongst the rest of the articles. It had the lowest number of participants of 750 where 391 were in the TAVR group and 359 in the SAVR group. Although having the smallest sample size compared to the other articles, it made the largest statement out of all of the other articles stating there was a 3-year all cause mortality reduction seen in the TAVR group compared to the SAVR group. It also the oldest of all the articles.

Magnitude of any effects:

1. Siontis et al., (2016) - We identified four eligible trials including 3806 participants, who were randomly assigned to undergo TAVI (n = 1898) or SAVR (n = 1908). For the primary outcome of death from any cause, TAVI when compared with SAVR was associated with a significant 13% relative risk reduction [hazard ratio (95% CI): 0.87 (0.76–0.99); P =0.038] with homogeneity across all trials irrespective of TAVI device (Pinteraction =0.306) and baseline risk (Pinteraction = 0.610). In subgroup analyses, TAVI showed a robust survival benefit over SAVR for patients undergoing transfemoral access [0.80 (0.69–0.93); P =0.004], but not transthoracic access [1.17 (0.88–1.56); P =0.293] (Pinteraction =0.024) and in female [0.68 (0.50–0.91); P =0.010], but not male patients [0.99 (0.77–1.28); P = 0.952] (Pinteraction =0.050). Secondary outcomes of kidney injury, new-onset atrial fibrillation, and major bleeding favoured TAVI, while major vascular complications, incidence of permanent pacemaker implantation, and paravalvular regurgitation favoured SAVR.
2. Deeb et al., (2016) - Underwent randomization at 45 US centers; 750 patients underwent an attempted procedure. Three-year all-cause mortality or stroke was significantly lower in TAVR patients (37.3% versus 46.7% in SAVR; p = 0.006). Adverse clinical outcome components were also reduced in TAVR patients compared with SAVR patients, including allcause mortality (32.9% versus 39.1%, respectively; p = 0.068), all stroke (12.6% versus 19.0%, respectively; p = 0.034), and major adverse cardiovascular or cerebrovascular events (40.2% versus 47.9%, respectively; p = 0.025). At 3 years aortic valve hemodynamics were better with TAVR patients (mean aortic valve gradient, 7.62 ± 3.57 mm Hg versus 11.40 ± 6.81 mm Hg in SAVR, p < 0.001), although moderate or severe residual aortic regurgitation was higher in TAVR patients (6.8% versus 0.0% in SAVR; p < 0.001). There was no clinical evidence of valve thrombosis in either group,
3. Latif et al., (2020) - Seven studies reported 361 cases of 30-day all-cause mortality in patients undergoing TAVR versus SAVR in previous cardiac surgery patients. There were 125 events out of 4055 (3.0%) that occurred in the TAVR group and 136 events out of 4166 (3.26%) that occurred in the SAVR group. There was no significant difference between the two groups (OR 0.87 [95% CI: 0.56–1.37], p = 0.54). Five studies reported 1–2-year all-cause mortality. There were 126 out of 663 (19%) events that occurred in the TAVR group, while 108 out of 659 (16.4%) events occurred in the SAVR group. There was no significant difference (OR = 1.15 [95% CI: 0.71–1.86], p = 0.57) between the two groups. Five studies reported data on the number of patients experiencing bleeding complications. There were 557/4055 (13.7%) patients in the TAVR group that had bleeding events, while 1252/4166

(30.0%) patients in the SAVR experienced bleeding events. TAVR was associated with lower incidence of bleeding complications (OR = 0.36 [95% CI: 0.21–0.59], $p \leq 0.01$) compared with the SAVR group. Seven studies reported data on AKI. There were 699/4055 (17.2%) patients who suffered AKI in the TAVR group, while 860/4166 (20.6%) patients suffered AKI in the SAVR group. There was no statistical difference between both groups (OR = 0.71 [95% CI: 0.49–1.02], p = 0.06). Three studies reported data on the average procedure time and our study reported TAVR lasting 170 min less than SAVR (Mean difference = −170.95 [95% CI: −249.37, −92.53], $p \leq 0.01$). Four studies reported the duration of hospital stay. TAVR was associated with shorter hospital stay (3.6 days [95% CI: −5.43, −1.95], $p < 0.01$) as compared to patients with SAVR, respectively.

4. Abi Khalil et al., (2021) - Tere was a 37% mean relative risk reduction (RR=0.63, 95% CI [0.51–0.78]) in post-procedural PPM in favor of TAVR. This benefit was observed in high and low surgical risk groups (Fig. 2a), as well as in balloon and self-expendable valves (Fig. 2b) although at different magnitude. The rest of echocardiographic measures were also in favor of TAVR, except for the PVL. We observed a pooled mean decrease of 0.56 (95%CI [0.73–0.38]) in gradient. Sub-group analysis showed no difference in gradient between TAVR and sAVR across categories of surgical risk on inclusion (Fig. 3a) (p=0.625). However, self-expendable valves were associated with a larger decrease in gradient than balloon ones (Fig. 3b) (β=−0.38; 95% CI [−0.64, −0.12]). We also observed an overall increase of 0.47 (95% CI [0.38–0.56]) in EOA. However, the postoperative EOA did not difer between self-expandable and balloon expandable valves. Te latter was consistent across subgroups (Fig. 4a,b). Finally, TAVR was associated with an almost tenfold increase in the risk of moderate/severe PVL (pooled RR: 9.54, 95% CI [5.53–16.46]), that was noticed in both subgroups. A similar trend was observed at 2 years. We noted a pooled mean decrease of 0.59 (95%CI [0.29–0.89]) in gradient that was independent of the patient's surgical risk at inclusion (Supplementary Fig. 1a). However, self-expandable valves were associated with a larger gradient decrease as compared to balloon expandable ones (β=−0.62; 95%CI [−0.85, −0.40]) (Supplementary Fig. 11). Additionally, there was a pooled mean increase of 0.46 (95% CI [0.25–0.67]) in EOA that was significant in all surgical risk categories.
5. Tarus et al., (2020) - Random-effect meta-analysis did not reveal any significant difference between 30-day safety outcomes: myocardial infarction (TAVR/PCI vs SAVR/CABG: odds ratio [OR]: 0.52; 95% confidence interval [CI]: 0.20-1.33; I 2 = 0%), stroke (TAVR/PCI vs SAVR/CABG: OR: 0.88; 95% CI: 0.45-1.73; I 2 = 0%). No significant difference in 30-day mortality (OR: 0.72; 95% CI: 0.43-1.21; I 2 = 0%) and 2- year mortality (OR: 1.50; 95% CI: 0.77-2.94; I 2 = 81%) rate was noted between patients with TAVR/PCI and those with SAVR/CABG.
6. Tam et al., (2017) - Overall, there was no difference in surgical risk between the TAVR and SAVR arm (standardized mean difference: -0.15, 95%CI: -0.55,0.22; P=0.44) When TAVR was compared to SAVR, there was no significant difference in early (in-hospital or 30 day) mortality in the pooled results (Figure 1 – 3.2% vs 3.1%, pooled RR: 1.02 95%CI: 0.80, 1.30; P=0.99, I2 =0%). There was a significant decrease in early stroke in the TAVR group (3.0%) compared to SAVR (3.9%) in the pooled analysis (Online Figure 4 – pooled RR: 0.76 95%CI: 0.60, 0.97; P=0.03, I 2

=0%). In the TAVR group, there was a significant reduction in the pooled relative risk of atrial fibrillation (11.2% vs 35.2%, P<0.00001, I2 =0%), cardiogenic shock (1.6% vs 4.4%, P<0.00001, I2 =0%), acute kidney injury AKIN 2 or 3, (2.4% vs 5.5%, P=0.0002, I2 =53%) and major or life-threatening bleeding (9.9% vs. 23.2%, P<0.00001, I2 =94%). There was an increased risk of greater than trace aortic insufficiency or paravalvular leak (25% vs 4.0%, P=0.003, I2 =63%), major vascular complications (7.1% vs 1.9%, P<0.0001, I2 =80%) and permanent pacemaker insertion (15.6% vs. 4.9%, P<0.00001, I2 =79%) in the TAVR group. There was less myocardial infarction in the TAVR group (Online Figure 8 – 0.8% vs. 1.3%, P=0.05, I2 =0%). There was a decrease in the length of stay in the TAVR group of 3.23 days (Online Figure 9 – MD: -3.23 days, 95%CI -4.79, -1.68;P<0.0001, I^2=93%).

Clinical Significance:

- Patients with severe aortic stenosis may replace their aortic valves either surgically or by using multiple catheters making TAVR a more favorable intervention for high-risk surgical patients. However, 3/6 articles concluded that there was no significant difference in all-cause mortality between the two interventions in the short term (up to 2 years). 2/6 articles concluded there is significant difference in the TAVR group vs SAVR group regrading all-cause mortality up to 2- and 3-years post procedure. However, these articles were ranked much lower than the others. Most of the articles agreed that TAVR provided fewer post-procedural complications, bleeding, decreased rates of stroke, better overall aortic valve hemodynamics in addition to shorter length of stays in the hospital. It is difficult to confidently conclude which method has a favorable all-cause mortality in the short term. Longer studies need to be conducted to further evaluate longer-term all-cause mortality rates (5-years and 10-years +)

Any other considerations important in weighing this evidence to guide practice – If the evidence you retrieved was not enough to conclude an answer to the question, discuss what aspects still need to be explored and what the next studies will have to answer/provide:

- In the short term, 1-2 years, it seems that there are no differences in all-cause mortality, but we can see that there are some advantages to TAVR, mentioned above, that SAVR seems to not provide. None of the articles provide high quality evidence that can definitively conclude the longer-term outcomes seen 5 or 10 years from procedure date. We need more evidence and studies that provide longer term outcomes between the two groups. A big consideration here is that typically, patients who undergo aortic valve replacements, are at an advanced age already, typically 75+. To conduct studies that may demonstrate some type of long-term improvement in mortality, or any type of benefit, there can be some conflict simply because life expectancy is not that high at that age to begin with, and comorbid conditions are more present the older someone gets. Researchers may consider explore which type of patient and which chronic conditions will have the least impact on the overall benefit of the TAVR in the long run.