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Review Article

"TAVI: Valve in valve. A new field for structuralists? Literature review"

Dimitrios A. Vrachatis [a, *], Michail Vavuranakis [b], Styliani Tsoukala [a], Sotiria Giotaki [c], Theodore G. Papaioannou [d], Gerasimos Siasos [d], Gerasimos Deftereos [a], Georgios Giannopoulos [a], Konstantinos Raisakis [a], Dimitrios Tousoulis [d], Spyridon Deftereos [c], Manolis Vavuranakis [b]

[a] Department of Cardiology, General Hospital of Athens, "G.Gennimatas", Athens, Greece
[b] 3rd Department of Cardiology, National and Kapodistrian University of Athens, Athens, Greece
[c] 2nd Department of Cardiology, National and Kapodistrian University of Athens, Greece
[d] 1st Department of Cardiology, National and Kapodistrian University of Athens, Greece

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ABSTRACT

Transcatheter aortic valve implantation (TAVI) led to the foundation of the subspecialty of structural heart interventions and created an emerging area of clinical and technical issues. Soon after TAVI introduction into clinical practice, boundaries were expanded with utilization of valve-in-valve (V-i-V) techniques. V-i-V comprised a diverse subset of patients including TAVI within TAVI, TAVI within a degenerated surgically implanted bioprosthesis, or even TAVI-in-TAVI-in-surgical bioprosthesis. In the present review, we summarize the available literature and present initial experience on the field in Greece.

1. TEXT

In the past decade, the first steps of Transcatheter Aortic Valve Implantation (TAVI) in clinical practice spread enthusiasm in the cardiological community. Today, it is commonly accepted that TAVI led to the foundation of the subspecialty of structural heart interventions. Indeed, through this fascinating journey, a series of clinical and technical issues regarding TAVI emerged.[1–4]

Various technical issues and complications urged pioneer "structuralists" to discover solutions.[5] For example, the lack of truly repositionable and/or retractable devices was early recognized and initially tackled with either utilization of off-label bailout maneuvers[6–8] or implantation of a second valve within the first (Valve-in-Valve; V-i-V). As expected, biomedical engineers soon provided the community with bioprosthetic devices for transcatheter implantation with upgraded capabilities.

However, the early V-i-V experience (literally TAVI-in-TAVI) had already extended the field of potential indications. In early 2007, a TAVI procedure for the treatment of a failing surgically implanted aortic bioprosthesis was reported by Wenaweser, P. et al.[9] Interestingly, the same year, Ruiz C. et al announced proper bioprosthesis functionality after a three-year follow-up of a patient treated (in a bailout basis) with TAVI-in-TAVI in 2005.[10] Remarkably, according to the authors, at that time, this patient was the one with the longest available follow-up after implantation of a self-expandable aortic bioprosthesis (CoreValve).

Today, the advent of V-i-V procedures in clinical practice is more than evident. Temporal trends indicate an increase in V-i-V utilization,[11] while the available data show that such procedures may become the best option in the future. Technical concerns are yet to be confronted and a significant responsibility lies over cardiac teams that shall—in an individualized basis—match the proper patient with the proper treatment.

It is important to understand that there is no typical candidate for a V-i-V procedure. This population is highly heterogenic as each patient has a different type of surgically implanted bioprosthesis (size; stented vs. stentless; individual device characteristics), specific patient-device characteristics (i.e., patient prosthesis mismatch), and a different mode of device failure (stenosis; regurgitation; mixed). Indeed, V-i-V as a means of TAVI-in-TAVI has mostly been reported in the acute setting as a rescue procedure for improper function of the

* Corresponding author. Dimitrios A. Vrachatis.
E-mail address: dvrachatis@gmail.com (D.A. Vrachatis).
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initially implanted bioprosthesis. In the future, it is expected that bioprosthesis implanted with TAVI will probably present with characteristics of degeneration that require V-i-V.

2. Reintervention after SAVR: Initial TAVI-in-SAVR data

To date, the largest study to evaluate outcomes of V-i-V procedures is the "*Valve-in-Valve International Data Registry*" study.[12] Dvir D. et al in a semi-prospective manner followed 459 patients (age 78 years; 59% males; median Logistic EuroSCORE 29%) who underwent V-i-V with a SAPIEN (54%; balloon expandable; Edwards Lifesciences) or a CoreValve (46%; self-expandable; Medtronic) device. V-i-V procedure was required due to a failing bioprosthesis implanted surgically (surgical aortic valve replacement; S-AVR) that presented as stenotic (39%), regurgitant (30%), or mixed. Overall 1-year survival was ~83% (i.e., ~17% all-cause mortality). Independent 1-year mortality predictors were as follows: a) baseline stenotic surgical implant (HR 3.07), b) transapical V-i-V access (HR 2.25), c) small surgically implanted valve (i.e., label ≤21 mm; HR 2.04), and d) STS score (per 1% increment; HR, 1.01). Survival was comparable between the two utilized devices (SAPIEN; CoreValve).

In a meta-analysis by Chen H-L and Liu K,[13] published in 2016, 861 patients from 17 studies were analyzed. Except for the international V-i-V registry (459 patients), the rest of the studies included ≤50 patients. Findings in most of the included studies were in line with the aforementioned results. Thirty-day mortality was relatively consistent among the reported results. A wider range was observed in one-year mortality.

In the same direction, in May 2017, the results of the PARTNER II registry were published.[14] In this prospective, multicenter registry, a total of 365 patients were treated with transcatheter implantation of a balloon expandable bioprosthesis for a failing surgically implanted aortic bioprosthesis. Additionally, this was the first study in which echocardiographic follow-up was assessed at a core laboratory. Thirty-day all-cause mortality was ~3% vs. an STS score predicted mortality of ~9%. While one-year all-cause mortality was ~12% (vs. 17% in the international V-i-V registry[12]). At 1-year follow-up decrease in aortic valve mean gradient and effective orifice area were durable. Patient prosthesis mismatch criteria were fulfilled in more than half of the patients at 1-year, but no correlation with mortality was observed in this study. Moreover, patient functional status and self-assessed quality of life was significantly improved at 1-year follow up. It is interesting that a higher mortality was observed in the first ~100 patients who were included in the study (30 days: 8% vs. 0.7%, $p < 0.0001$; 1 year: 20% vs. 10%; $p=0.006$). The authors attributed it to the existence of a learning curve. Still, these patients were also reported to be frailer and have higher logistic EuroSCORE levels.

More recently, the results of the Swiss-TAVI Registry were also published.[15] Ferrari E. et al studied 1-month and 1-year outcomes of patients undergoing V-i-V TAVI procedures for failing surgically implanted bioprostheses.[15] These registry data from 15 centers in Switzerland included 157 V-i-V cases (age 78 years; logistic EuroSCORE 28%; 106 patients due to bioprosthesis stenosis and 51 patients due to bioprosthesis regurgitation) vs. 4599 patients undergoing native TAVI. All-cause and cardiovascular mortality at 1-month was ~2%, and at 1-year follow up was ~7%.[15]

3. Reintervention after S-AVR: Comparison of V-i-V versus Redo S-AVR

In 2018, five meta-analyses comparing transcatheter aortic valve-in-valve implantation to conventional redo-aortic valve replacement for the treatment of a failed bioprosthesis were published.[16–20] All five meta-analyses incorporated data from retrospective studies.[21–26] Safety and efficacy at the follow-up ranging from 6 to 36 months were reported. Key findings of the aforementioned studies are presented in Tables 1 and 2.

In the enrolled studies[21–26] all recruited patients demonstrated comparable baseline characteristics (sex, diabetes mellitus, coronary artery disease, baseline NYHA class ≥ III and baseline ejection fraction). In the V-i-V group, however patients were older (from 2.8[16] years to 5 years[17]) with a higher CAD, CABG, and CKD prevalence. Furthermore, they had higher predicted surgical risk (23% higher predicted mortality risk-[16]). Additionally, it should be noted that more patients with smaller valve profiles (≤21 mm) were included in the redo-SAVR groups.[16]

Available meta-analyses provide consistent data (as more or less expected since they -at large - analyzed the same raw studies). Mortality (in-hospital; 30-day; 1-year) is the outcome of interest for all the meta-analyses and was shown to be comparable in the two groups despite the higher baseline operative risk of V-i-V patients.[16–20]

Comparing the 30-day mortality of V-i-V patients presented in the meta-analyses[16–20] to this reported by the Valve-in Valve International Data (VIVID) Registry,[12] arise similarities, with a non-significant tendency for higher 30-day mortality in VIVID Registry (7,6 vs 4,4%, $p > 0.05$[16]). This may be attributed to the higher mortality risk of the enrolled patients. With regard to long-term survival, only Gozdek M. et al reported better survival rate for re-SAVR patients at 18 months (H.R. 1.91, 95% C.I. 1.03-3.57: $p=0.039$[17]).

Data regarding other clinical outcomes are available in 4 of 5 metanalyses,[16–20] because Takagi H. et al focused mainly on mortality and on baseline group characteristics, providing only a summary-statistics from the individual studies.[19] Stroke, MI, and AKI without the need of dialysis were similar between V-i-V and re-SAVR patients, whereas V-i-V TAVI was associated with a significantly lower rate of permanent pacemaker implantation according

Table 1
Metanalyses of studies comparing V-i-V and re-SAVR after SAVR

Year, First Author	Studies Included, n	Patients, n	RS, %	V-i-V, %	V-i-V Type	Follow up, months
2018, Tam D.Y. et al[16]	6 [21–26]	498	49	51	54% BE	6-36
2018, Gozdek M. et al[17]	5 [21,22,24–26]	342	49	51	60% BE	12-36
2018, Nalluri N. et al[18]	6 [21–26]	594	57	43	54% BE	≤ 12
2018, Takagi H. et al[19]	6 [21–26]	498	49	51	54% BE	6-36
2018, Neupane S. at al.[20]	4 [21,22,25,26]	489	54	46	51% BE	≤ 12

BE: Balloon- Expandable (vs. Self-Expandable), RS: Redo Surgery.

Table 2
Basic outcomes of metanalyses comparing V-i-V and re-SAVR after SAVR

	Tam D.Y. et al[16]		Gozdek M. et al[17]		Nalluri N. et al[18]		Takagi H. et al[19]		Neupane S. et al[20]	
	V-i-V, %	RS, %	V-i-V, %	RS, %	V-i-V, %	RS, %	V-i-V, %	RS, %	V-i-V, %	RS, %
Procedural mortality	4	6	2	4	2	4	**	**	**	**
30-day mortality	4	6	5	4	5	5	**	**	5	4
1 year mortality	**	**	*	*	14	10	**	**	n/r	n/r
MI	2	<1	3	1	2	<1	n/r	n/r	2	1
Stroke	2	3	2	4	1	2	n/r	n/r	2	2
New pacemaker	8*	15*	7*	19*	9*	16*	n/r	n/r	9*	15*
Atrial fibrillation	16*	44*	n/r	n/r	n/r	n/r	n/r	n/r	n/r	n/r
Vascular Compl.	7	2	12*	3*	12*	2*	n/r	n/r	n/r	n/r
Major bleeding	12	27	10*	28*	12	27	n/r	n/r	n/r	n/r
Dialysis	3*	10*	**	**	n/r	n/r	n/r	n/r	7	10
AKI	8	12	8	12	7	12	n/r	n/r	n/r	n/r
PVL	21*	6*	21*	6*	20	5	n/r	n/r	n/r	n/r
Severe PPM	14*	3*	16*	4*	n/r	n/r	n/r	n/r	n/r	n/r
Post procedural aortic valve gradients	**	**	28*	5*	29	8	n/r	n/r	n/r	n/r
ICU stay, days		Δ+2*		Δ+3*	n/r	n/r	n/r	n/r	n/r	n/r
Hospital stay, days		Δ+5*		Δ+4*	n/r	n/r	n/r	n/r	n/r	n/r
Hospital readmission	n/r	n/r	**	**	17	11	n/r	n/r	n/r	n/r

AKI: Acute Kidney Injury, ICU: Intensive Care Unit, PVL: Paravalvular Regurgitation, MI: Myocardial Infarction, n/r: Not Reported, PPM: Patient Prosthesis Mismatch.
Δ: RS − V-i-V.
*statistically significant difference between the two groups.
**comparable findings between the two groups.

to the aforementioned metanalyses. In addition, more vascular complications and fewer bleeding events were recorded for V-i-V patients by Nalluri N. et al and Gozdek M. et al.[17,18]

Regarding valve hemodynamics and total hospitalization, comparable data are provided only by 3 out of 5 meta-analyses.[16–18] Yam et al found a higher incidence of severe patient-prosthesis mismatch and greater paravalvular leak was reported in V-i-V patients, without significant changes in postoperative aortic valve gradients.[16] Nalluri et al agreed with Tam D.Y. et al regarding postoperative aortic valve gradient, without, however, recording any significant difference in PVL.[18] According to Tam D.Y. et al, these worse hemodynamic parameters were not translated into a mortality benefit for the redo-SAVR group. This could potentially be explained by the fact that re-SAVR patients suffered more frequently from atrial fibrillation, permanent pacemaker implantation, and new onset of dialysis (shown after the inclusion of the propensity score match study). Additionally, the effects of patient-prosthesis mismatch on short- and long-term survival remained controversial with conflicting studies in the surgical literature.[16]

In contrast, Gozdek M. et al reported an increase in post-operative prosthesis gradients in the V-i-V group after the exclusion of the study by Grutzbich H. et al.[17] In this study, only patients with surgically implanted degenerated stentless bioprostheses were enrolled, leading to lower postoperative prostheses' gradients after V-i-V TAVI.[21] After excluding this patient subset, the risk of higher postoperative AV gradient (>20 mmHg) was nearly 10-fold greater in the V-i-V TAVI patients (R.R. 9.74, 95% C.I. 3.62-26.19; $p < 0.001$). However, there is currently no evidence supporting that lower postprocedural gradients are associated with improved clinical outcomes.[18]

Finally, both intensive care unit and total hospitalization were significantly lower for the V-i-V group according to the aforementioned metanalyses,[16,17] whereas hospital readmissions remained comparable between the two groups.[17,18]

The small sample size, the large heterogeneity especially of V-i-V group, and the lack of randomization characterize all the above metanalyses. Therefore, the risk of bias and underpowering the true clinical effects of the measured outcomes are increased. Yet, there is convergence that the V-i-V approach can serve as a safe and feasible alternative to re-SAVR technique, offering an effective and less invasive treatment for high surgical risk patients with failed aortic valve bioprosthesis. Re-SAVR should remain the standard of care, particularly in low-risk population as it offers superior hemodynamic outcomes with similar mortality rates. One should be aware that frequently these patient subsets feature specific anatomical and clinical characteristics that do not fit in the common rules and need to be evaluated by cardiac teams on a one-by-one basis.[16,17]

4. Reintervention after TAVI: TAVI-in-TAVI

As already mentioned, the first published case of TAVI-in-TAVI is attributed to Ruiz C. et al.[10] Since then, a series of cases have been reported. Indeed, issues regarding proper terminology occurred with "valve-in-valve", "Russian doll concept" and "TAV(I)-in-TAV(I)" alternatively appearing in the literature.[5]

Data from the two major available randomized controlled trials will be summarized here. In the PARTNER ("Placement of AoRTic TraNscathetER Valve Trial
Edwards SAPIEN Transcatheter Heart Valve") trial multiple valve implantation was required in 1-2% (Cohort B: 1.1% - 2 of 179 patients[27]; Cohort A: 2% - 7 out of 348 patients[28]). In the CoreValve U.S. Pivotal Trial multiple valves were implanted in 3.5 - 4.5% (Extreme Risk Cohort: 3.5% - 17 out of 486 patients[29]; High Risk Cohort: 4.1% - 16 out of 389 patients - data provided in study's supplementary appendix[30]).

In a comprehensive review, Witkowsky A. et al,[31] summarized the available published cases up to May 2013. According to them, a total of 149 cases (39 with CoreValve; 110 with SAPIEN) had been reported at that time. TAVI-in-TAVI has mostly been used as a means of acute management of suboptimal function of the bioprosthesis during a TAVI procedure. Aortic regurgitation (of paravalvular or transvalvular etiology) was the main reason for implantation of a second bioprosthesis within the first.

In the same year, Makkar R.R. et al[32] analyzed a large dataset of patients who underwent TAVI with a SAPIEN bioprosthesis comprising patients from the PARTNER trial and patients from

accompanying non-randomized registries. In a total of 2,554 consecutive patients, TAVI-in-TAVI was required for ~2.5% of the population. In most cases, TAVI-in-TAVI was required intra-procedurally (89%), while the rest were required up to 4 months post procedurally (1 patient at 2 months; 1 patient at 4 months; the rest earlier). Regarding etiology, almost 50% of the cases were attributed to technical factors, 15% to anatomical factors, 8% to the need for cardiopulmonary resuscitation, while no cause was identified in 27%. Aortic regurgitation was practically the only indication for TAVI-in-TAVI accounting for 97% of the cases (the only other indication was "unstable prosthesis positioning"). Interestingly, 50% of these referred to trans-valvular, 36% para-valvular and 13% mixed aortic regurgitation. The authors attributed this high incidence of post-TAVI trans-valvular insufficiency to technical characteristics of the (older) SAPIEN bioprosthesis model that was used at that time and that was tackled in the subsequent models.

The authors did not observe any relationship between TAVI-in-TAVI utilization and operators' learning curve; indeed, they comment that an experienced operator might be more confident in utilizing such techniques, if deemed so.[32] Finally, TAVI-in-TAVI was related to higher cardiovascular mortality despite no difference in intermediate term valve functioning. However, these early results, which are largely derived from, rescue TAVI-in-TAVI procedures shall not be extrapolated to future patient populations. One should note that the pathophysiological substrate will be different in future indications. It may refer to elective TAVI-in-TAVI for degenerated bioprostheses', which will have completed their life cycle.

Currently, published case reports literally depict the great variation in clinical scenarios that structuralists will be required to confront. For example, Kaneko H. et al conducted TAVI-in-TAVI as the first valve was implanted for off-label treatment of native aortic regurgitation.[33] Further, Eftychiou C. et al have recently described a TAVI-in-TAVI procedure for device failure (~8 years post initial implantation) with both procedures conducted under a transapical approach.[34] Additionally, TAVI-in-TAVI-in-SAVR either in the acute setting[35,36] or in an elective basis (new TAVI procedure up to 4 years after TAVI-in-SAVR)[37,38] has also been reported.

5. Technical Issues

Major considerations regarding V-i-V approaches involve the following three issues: bioprosthesis malpositioning and deformation, critical coronary flow obstruction, and residual elevated transvalvular gradients.[39]

In a computational study by Martin C. and Sun W.,[40] regarding issues for bioprosthesis' (transcatheter) within bioprosthesis (surgical) deformation, they suggest that leaflet configuration and function are affected by valve underexpansion and consequently the expected device durability may decline. The authors also illustrate the need for bioprostheses primarily designed for V-i-V utilization, so that deformation concerns are addressed. Until then, screening in view of valve profile selection and plan for positioning meticulous pre-procedural should be meticulously conducted. The effects of a balloon valvuloplasty on the degenerated bioprosthesis prior to TAVI have not been studied. However, such an approach is considered high risk for creating acute aortic insufficiency of the bioprosthetic valve or creating systemic emboli.[41] Undeniably, newer TAVI systems with smaller crossing profiles and repositioning capabilities may minimize the potential negative effects of such procedures. Further, available data on performance post V-i-V show that - whilst potentially less favorable than those after native TAVI or after redo-SAVR – hemodynamics are acceptable and do not imply any mortality differences.[15–18,42,43]

With regard to coronary artery ostia protection during V-i-V procedures, except for meticulous choice of the TAVI system, that it best fits the given patient anatomy, different strategies have been reported. The technical characteristics and the anatomical dimensions (inner diameter, height of leaflets, etc.) of the pre-existing prosthesis are of paramount importance in order to select the appropriate TAVI valve and safely perform the procedure. The best preventive strategy, according to our opinion, seems to be the insertion, but not deployed unless required, of a stent into the coronary artery at risk. This can be easily deployed for abrupt ostial obstruction.[44]

With regard to patient prosthesis mismatch (too small effective orifice area in relation to patient body size[45]), V-i-V in such cases may almost be considered as futile (or even harmful). The resulted gradient after V-i-V cannot be less than the initially obtained after surgery. However, special procedural maneuvers (e.g., small transcatheter heart valve selection and/or supra-valvular implantation; note a high dislodgment risk) may lead to acceptable results.[39,46] The heart valve team shall make final decision bearing in mind that a surgical redo -if feasible-would potentially be the most appropriate approach. Last but not least, one should remember that high but stable gradients of a surgically replaced aortic valve may indicate prosthesis with patient prosthesis mismatch and not bioprosthesis degeneration (i.e., this residual gradient may be present from the first post-surgical day).[47]

Another patient group that needs to carefully be identified is those who present with aortic regurgitation attributed to a significant paravalvular leak. In the multinational V-i-V registry significantly more residual paravalvular leaks were observed in such patients.[12] A potential explanation for this is an erroneous choice of treatment.[12] Thorough pre-procedural screening, guided by multimodal imaging, including multislice CT and trans-esophageal echocardiography plays a pivotal role.[48] Indeed, transcatheter paravalvular leak closure with special devices is feasible, yet technically demanding, for prosthesis implanted through a surgical or a transcatheter procedure.[49–51]

Special care should also be taken for cases of a co-existing mitral prosthesis. This special population had been excluded from the major randomized controlled trials; therefore, such data are sparse. In a literature review by our team, published in 2014, a total of 27 TAVI procedures in such a case have been reported at that time.[52] Indeed, 2 of these cases were V-i-V cases (i.e., TAVI in SAVR in a patient with co-existent mitral prosthesis). The rule of V-i-V here remains the same—individualization and comprehensive pre-procedural screening and planning in order to avoid interference of the lower part of the inserted aortic valve with the pre-existing mitral prosthesis.

Moreover, optimal antiplatelet and/or anticoagulation treatment in TAVI patients has been a point of discussion.[53–55] Consequently, such a unique -and heterogeneous-patient population like V-i-V patients would intensify the debate. Indeed, relative blood stasis within the final complex multiple bioprosthetic structure could be anticipated[46]; therefore, the need for anticoagulation could probably be reasonable. Further, in an MRI study by Eitan A. et al, it has been shown that subclinical asymptomatic micro-embolisms that has been observed in native TAVI procedures are also present in V-i-V procedures, but with a lower incidence.[56] Indeed, in view of the recent (2017), ACC/AHA focused update in the guidelines for the management of patients with valvular heart disease, which suggests anticoagulation in the first post (single) TAVI trimester (Class: IIb; LoE: NR[57]), the answer for V-i-V patients could be more straightforward. The duration of treatment would be another Gordian knot.

6. Future considerations

Greason KL in a recent editorial commentary underlines that V-i-V therapeutics were officially approved by Food and Drug Administration (FDA) prior to adequate documentation from in vitro and/or in vivo trials, demonstrating a clear paucity of translational research in the field.[58] This issue has been discussed in a Food and Drug Administration viewpoint article for medical device clinical trials, published in the New England Journal of Medicine.[59] Interestingly, transcatheter valve therapeutics are presented as a landmark example of rapid expansion of official indications based on real-word data, prior to the results of formal trials.[59]

It is remarkable that the case of V-i-V evolution delineates a field where clinical needs (and in some instances, even patient preference) not only push the limits of the available technology but actively interact with the future. As presented in the current review article, there is much that is currently redefined in a real-life lesson fashion, while there is also need for long-term follow up of V-i-V patients. Even though, a clear trend for surgical implantation of biological (vs. mechanical) valves in younger ages (in whom aging valve deterioration should be considered) is preferred.[60] This indicates a sound claim - and a certainty - that bioengineering may and will provide the community with the needed solutions. As Albert Einstein would note “I never think of the future - it comes soon enough”.

Conflicts of interest

Manolis Vavuranakis is a proctor for CoreValve; Medtronic Inc.

REFERENCES

1. Vavuranakis M, Vrachatis DA, Tousoulis D. Bioengineering, Clinical and Therapeutical Trends in Transcatheter Aortic Valve Implantation. *Curr Pharmaceut Des*. 2016;22(13):1851–1852.
2. Vavuranakis M, Voudris V, Vrachatis DA, et al. Transcatheter aortic valve implantation, patient selection process and procedure: two centres' experience of the intervention without general anaesthesia. Hellenic J Cardiol. 51(6):492-500.
3. Kanakakis I. Is TAVR going to be our default choice for treating aortic valve stenosis? *Hellenic J Cardiol*. July 2019. https://doi.org/10.1016/j.hjc.2019.03.009.
4. Corrigan FE, Zhou X, Lisko JC, et al. Mean Aortic pressure gradient and global longitudinal strain recovery after transcatheter aortic valve replacement – A retrospective analysis. *Hellenic J Cardiol*. 2018;59(5):268–271. https://doi.org/10.1016/j.hjc.2018.01.006.
5. Vavuranakis M, Vrachatis DA, Siasos G, et al. Managing complications in transcatheter aortic valve implantation. *Hellenic J Cardiol*. 2015;56(Suppl A):20–30.
6. Vavouranakis M, Vrachatis DA, Toutouzas KP, Chrysohoou C, Stefanadis C. “Bail out” procedures for malpositioning of aortic valve prosthesis (CoreValve). *Int J Cardiol*. 2010;145(1):154–155. https://doi.org/10.1016/j.ijcard.2009.07.040.
7. Vavuranakis M, Vrachatis D, Stefanadis C. CoreValve Aortic Bioprosthesis. *JACC Cardiovasc Interv*. 2010;3(5):565. https://doi.org/10.1016/j.jcin.2010.03.004.
8. Vavuranakis M, Kariori M, Vrachatis D, et al. "Balloon withdrawal technique" to correct prosthesis malposition and treat paravalvular aortic regurgitation during TAVI. *J Invasive Cardiol*. 2013;25(4):196–197.
9. Wenaweser P, Buellesfeld L, Gerckens U, Grube E. Percutaneous aortic valve replacement for severe aortic regurgitation in degenerated bioprosthesis: the first valve in valve procedure using the Corevalve Revalving system. *Cathet Cardiovasc Interv*. 2007;70(5):760–764. https://doi.org/10.1002/ccd.21300.
10. Ruiz CE, Laborde JC, Condado JF, Chiam PTL, Condado JA. First percutaneous transcatheter aortic valve-in-valve implant with three year follow-up. *Cathet Cardiovasc Interv*. 2008;72(2):143–148. https://doi.org/10.1002/ccd.21597.
11. Landes U, Barsheshet A, Finkelstein A, et al. Temporal trends in transcatheter aortic valve implantation, 2008-2014: patient characteristics, procedural issues, and clinical outcome. *Clin Cardiol*. 2017;40(2):82–88. https://doi.org/10.1002/clc.22632.
12. Dvir D, Webb JG, Bleiziffer S, et al. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA*. 2014;312(2):162–170. https://doi.org/10.1001/jama.2014.7246.
13. Chen H-L, Liu K. Clinical outcomes for transcatheter valve-in-valve in treating surgical bioprosthetic dysfunction: A meta-analysis. *Int J Cardiol*. 2016;212:138–141. https://doi.org/10.1016/j.ijcard.2016.03.024.
14. Webb JG, Mack MJ, White JM, et al. Transcatheter Aortic Valve Implantation Within Degenerated Aortic Surgical Bioprostheses. *J Am Coll Cardiol*. 2017;69(18):2253–2262. https://doi.org/10.1016/j.jacc.2017.02.057.
15. Ferrari E, Stortecky S, Heg D, et al. The hospital results and 1-year outcomes of transcatheter aortic valve-in-valve procedures and transcatheter aortic valve implantations in the native valves: the results from the Swiss-TAVI Registry. *Eur J Cardiothorac Surg*. 2019;56(1):55–63. https://doi.org/10.1093/ejcts/ezy471.
16. Tam DY, Vo TX, Wijeysundera HC, Dvir D, Friedrich JO, Fremes SE. Transcatheter valve-in-valve versus redo surgical aortic valve replacement for the treatment of degenerated bioprosthetic aortic valve: A systematic review and meta-analysis. *Cathet Cardiovasc Interv*. 2018;92(7):1404–1411. https://doi.org/10.1002/ccd.27686.
17. Gozdek M, Raffa GM, Suwalski P, et al. Comparative performance of transcatheter aortic valve-in-valve implantation versus conventional surgical redo aortic valve replacement in patients with degenerated aortic valve bioprostheses: systematic review and meta-analysis. *Eur J Cardiothorac Surg*. 2018;53(3):495–504. https://doi.org/10.1093/ejcts/ezx347.
18. Nalluri N, Atti V, Munir AB, et al. Valve in valve transcatheter aortic valve implantation (ViV-TAVI) versus redo-Surgical aortic valve replacement (redo-SAVR): A systematic review and meta-analysis. *J Interv Cardiol*. 2018;31(5):661–671. https://doi.org/10.1111/joic.12520.
19. Takagi H, Mitta S, Ando T. Meta-analysis of Valve-in-Valve Transcatheter versus Redo Surgical Aortic Valve Replacement. *Thorac Cardiovasc Surg*. August 2018. https://doi.org/10.1055/s-0038-1668135.
20. Neupane S, Singh H, Lämmer J, et al. Meta-Analysis of Transcatheter Valve-in-Valve Implantation Versus Redo Aortic Valve Surgery for Bioprosthetic Aortic Valve Dysfunction. *Am J Cardiol*. 2018;121(12):1593–1600. https://doi.org/10.1016/j.amjcard.2018.02.054.
21. Grubitzsch H, Zobel S, Christ T, et al. Redo procedures for degenerated stentless aortic xenografts and the role of valve-in-valve transcatheter techniques†. *Eur J Cardiothorac Surg*. 2017;51(4), ezw397. https://doi.org/10.1093/ejcts/ezw397.
22. Silaschi M, Wendler O, Seiffert M, et al. Transcatheter valve-in-valve implantation versus redo surgical aortic valve replacement in patients with failed aortic bioprostheses. *Interact Cardiovasc Thorac Surg*. 2017;24(1):63–70. https://doi.org/10.1093/icvts/ivw300.
23. Spaziano M, Mylotte D, Thériault-Lauzier P, et al. Transcatheter aortic valve implantation versus redo surgery for failing surgical aortic bioprostheses: a multicentre propensity score analysis. *EuroIntervention*. 2017;13(10):1149–1156. https://doi.org/10.4244/EIJ-D-16-00303.
24. Ejiofor JI, Yammine M, Harloff MT, et al. Reoperative Surgical Aortic Valve Replacement Versus Transcatheter Valve-in-Valve Replacement for Degenerated Bioprosthetic Aortic Valves. *Ann Thorac Surg*. 2016;102(5):1452–1458. https://doi.org/10.1016/j.athoracsur.2016.05.086.
25. Santarpino G, Pietsch LE, Jessl J, et al. Transcatheter aortic valve-in-valve implantation and sutureless aortic valve replacement: two strategies for one goal in redo patients. *Minerva Cardioangiol*. 2016;64(6):581–585.
26. Erlebach M, Wottke M, Deutsch M-A, et al. Redo aortic valve surgery versus transcatheter valve-in-valve implantation for failing surgical bioprosthetic valves: consecutive patients in a single-center setting. *J Thorac Dis*. 2015;7(9):1494–1500. https://doi.org/10.3978/j.issn.2072-1439.2015.09.24.
27. 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(17):1597–1607. https://doi.org/10.1056/NEJMoa1008232.
28. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients. *N Engl J Med*. 2011;364(23):2187–2198. https://doi.org/10.1056/NEJMoa1103510.
29. Popma JJ, Adams DH, Reardon MJ, et al. Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery. *J Am Coll Cardiol*. 2014;63(19):1972–1981. https://doi.org/10.1016/j.jacc.2014.02.556.
30. Adams DH, Popma JJ, Reardon MJ. Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis. *N Engl J Med*. 2014;371(10):967–968. https://doi.org/10.1056/NEJMc1408396.
31. Witkowski A, Jastrzebski J, Dabrowski M, Chmielak Z. Second transcatheter aortic valve implantation for treatment of suboptimal function of previously implanted prosthesis: review of the literature. *J Interv Cardiol*. 2014;27(3):300–307. https://doi.org/10.1111/joic.12120.
32. Makkar RR, Jilaihawi H, Chakravarty T, et al. Determinants and outcomes of acute transcatheter valve-in-valve therapy or embolization: a study of multiple valve implants in the U.S. PARTNER trial (Placement of AoRTic TraNscathetER Valve Trial Edwards SAPIEN Transcatheter Heart Valve). *J Am Coll Cardiol*. 2013;62(5):418–430. https://doi.org/10.1016/j.jacc.2013.04.037.
33. Kaneko H, Hoelschermann F, Tambor G, Neuss M, Butter C. Rescue Valve-in-Valve Transcatheter Aortic Valve Replacement for Pure Aortic Regurgitation. *JACC Cardiovasc Interv*. 2017;10(3):e23–e24. https://doi.org/10.1016/j.jcin.2016.11.031.
34. Eftychiou C, Kokkinos C, Evangelakis E, et al. Repeated transapical TAVI for the treatment of a degenerated bioprosthetic valve. *Hellenic J Cardiol*. 2018;59(1):40–42. https://doi.org/10.1016/j.hjc.2017.06.004.
35. Bagur R, Dumont É, Doyle D, De Larochellière R, Rodés-Cabau J. Transcatheter aortic valve-in-valve-in-valve implantation for a failed xenograft. *Ann Thorac Surg*. 2012;93(2):647–650. https://doi.org/10.1016/j.athoracsur.2011.07.020.
36. Nuis R-J, Benitez LM, Nader CA, Perez S, de Marchena EJ, Dager AE. Valve-in-valve-in-valve transcatheter aortic valve implantation to treat a degenerated

surgical bioprosthesis in a subaortic position. *Texas Hear Inst J*. 2013;40(3):323–325.
37. Hollander KN, Montealegre-Gallegos M, Mahmood F. Valve-in-valve-in homograft: A case of a repeat transcatheter aortic valve replacement in a patient with an aortic homograft. *Ann Card Anaesth*. 2016;19(4):737–739. https://doi.org/10.4103/0971-9784.191575.
38. Leung Wai Sang S, Giri J, Vallabhajosyula P. Transfemoral transcatheter valve-in-valve-in-valve replacement. *J Thorac Cardiovasc Surg*. 2016;152(2):622–623. https://doi.org/10.1016/j.jtcvs.2016.03.047.
39. Dvir D. Treatment of Small Surgical Valves: Clinical Considerations for Achieving Optimal Results in Valve-in-Valve Procedures. *JACC Cardiovasc Interv*. 2015;8(15):2034–2036. https://doi.org/10.1016/j.jcin.2015.10.012.
40. Martin C, Sun W. Transcatheter Valve Underexpansion Limits Leaflet Durability: Implications for Valve-in-Valve Procedures. *Ann Biomed Eng*. 2017;45(2):394–404. https://doi.org/10.1007/s10439-016-1738-8.
41. Vavuranakis M, Lavda M, Vrachatis D, et al. Impact of balloon aortic valvuloplasty on transcatheter aortic valve implantation with self-expandable valve. *J Cardiol*. May 2016. https://doi.org/10.1016/j.jjcc.2016.03.016.
42. Akodad M, Meilhac A, Lefèvre T, et al. Hemodynamic Performances and Clinical Outcomes in Patients Undergoing Valve-in-Valve Versus Native Transcatheter Aortic Valve Implantation. *Am J Cardiol*. 2019;124(1):90–97. https://doi.org/10.1016/j.amjcard.2019.04.009.
43. Sedeek AF, Greason KL, Sandhu GS, Dearani JA, Holmes DR, Schaff HV. Transcatheter Valve-in-Valve Vs Surgical Replacement of Failing Stented Aortic Biological Valves. *Ann Thorac Surg*. 2019;108(2):424–430. https://doi.org/10.1016/j.athoracsur.2019.03.084.
44. Maggio S, Gambaro A, Scarsini R, Ribichini F. Preventive left main and right coronary artery stenting to avoid coronary ostia occlusion in high-risk stentless valve-in-valve transcatheter aortic valve implantation. *Interact Cardiovasc Thorac Surg*. 2017;25(1):147–149. https://doi.org/10.1093/icvts/ivx068.
45. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: definition, clinical impact, and prevention. *Heart*. 2006;92(8):1022–1029. https://doi.org/10.1136/hrt.2005.067363.
46. Tseng EE. When valve-in-valve implantation is not sufficient: Bioprosthetic Russian dolls. *J Thorac Cardiovasc Surg*. 2016;152(2):624–625. https://doi.org/10.1016/j.jtcvs.2016.04.018.
47. Webb JG, Dvir D. Transcatheter aortic valve replacement for bioprosthetic aortic valve failure: the valve-in-valve procedure. *Circulation*. 2013;127(25):2542–2550. https://doi.org/10.1161/CIRCULATIONAHA.113.000631.
48. Latsios G, Spyridopoulos TN, Toutouzas K, et al. Multi-slice CT (MSCT) imaging in pretrans-catheter aortic valve implantation (TAVI) screening. How to perform and how to interpret. *Hellenic J Cardiol*. 2018;59(1):3–7. https://doi.org/10.1016/j.hjc.2017.09.013.
49. Cruz-Gonzalez I, Rama-Merchan JC, Rodríguez-Collado J, et al. Transcatheter closure of paravalvular leaks: state of the art. *Neth Heart J*. 2017;25(2):116–124. https://doi.org/10.1007/s12471-016-0918-3.
50. Vavuranakis M, Vrachatis DA, Tousoulis D. Percutaneous paravalvular leak closure after TAVI: a demanding approach. *Cathet Cardiovasc Interv*. 2015;85(6):1104–1105. https://doi.org/10.1002/ccd.25669.
51. Rihal CS, Sorajja P, Booker JD, Hagler DJ, Cabalka AK. Principles of percutaneous paravalvular leak closure. *JACC Cardiovasc Interv*. 2012;5(2):121–130. https://doi.org/10.1016/j.jcin.2011.11.007.
52. Vavuranakis M, Vrachatis DA, Kariori MG, et al. TAVI in the case of preexisting mitral prosthesis: tips & tricks and literature review. *J Invasive Cardiol*. 2014;26(11):609–613.
53. Vavuranakis M, Siasos G, Zografos T, et al. Dual or Single Antiplatelet Therapy After Transcatheter Aortic Valve Implantation? A Systematic Review and Meta-Analysis. *Curr Pharmaceut Des*. 2016;22(29):4596–4603.
54. Magkoutis NA, Fradi S, Azmoun A, et al. Antiplatelet Therapy in TAVI: Current Clinical Practice and Recommendations. *Curr Pharmaceut Des*. 2016;22(13):1888–1895.
55. Vavuranakis M, Kolokathis A-M, Vrachatis DA, et al. Atrial Fibrillation During or After TAVI: Incidence, Implications and Therapeutical Considerations. *Curr Pharmaceut Des*. 2016;22(13):1896–1903.
56. Eitan A, Brinkmann C, Haselbach T, Witt J, Schofer J. Does valve in valve TAVR carry a higher risk for thromboembolic events compared to native valve TAVR? *Catheter Cardiovasc Interv*. July 2019:28391. https://doi.org/10.1002/ccd.28391. ccd.
57. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 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 Clinical Practice Guidelines. *J Am Coll Cardiol*. 2017;70(2):252–289. https://doi.org/10.1016/j.jacc.2017.03.011.
58. Greason KL. Transcatheter aortic valve-in-valve insertion: That train has sailed. *J Thorac Cardiovasc Surg*. 2017;153(2):264–265. https://doi.org/10.1016/j.jtcvs.2016.10.032.
59. Faris O, Shuren J. An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials. *N Engl J Med*. 2017;376(14):1350–1357. https://doi.org/10.1056/NEJMra1512592.
60. Isaacs AJ, Shuhaiber J, Salemi A, Isom OW, Sedrakyan A. National trends in utilization and in-hospital outcomes of mechanical versus bioprosthetic aortic valve replacements. *J Thorac Cardiovasc Surg*. 2015;149(5):1262–1269. https://doi.org/10.1016/j.jtcvs.2015.01.052. e3.