Hemodynamic Follow-Up after Valve-in-Valve TAVR for Failed Aortic Bioprosthesis

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Abstract

Background VIV-TAVR is established and provides good initial clinical and hemodynamic outcomes. Lacking long-term durability data baffle the expand to lower risk patients. For those purposes, the present study adds a hemodynamic 3-years follow-up. *Methods* A total of 77 patients underwent VIV-TAVR for failing aortic bioprosthesis during a 7-years period. Predominant mode of failure was stenosis in 87.0%. Patients had a mean age of 79.4±5.8 years and a mean logistic EuroSCORE of 30.8±15.7%. The STS-PROM averaged 5.79±2.63%. Clinical results and hemodynamic outcomes are reported for 30-days, 1-, 2- and 3-years. Completeness of follow-up was 100% with 44 patients at risk after 3-years. Follow-up ranged up to 7.1 years. *Results* Majority of the surgical valves were stented (94.8%) with a mean labeled size of 23.1±2.3mm and true-ID of 20.4±2.6mm. A true-ID [?]21mm had 58.4% of the patients. Self-expanding valves were implanted in 68.8% (mean labeled size 24.1+-1.8mm) and balloon-expanded in 31.2% (mean size 24.1+-1.8mm). No patient died intraoperatively. Hospital mortality was 1.3% and three-years survival 57.1%. All patients experienced an initial significant dPmean-reduction to 16.8+-7.1mmHg. After 3-years mean dPmean raised to 26.0+-12.2mmHg. This observation was independent from true-ID or type of TAVR-prosthesis. Patients with a true-ID [?]21mm had a higher initial (18.3+-5.3mmHg vs. 14.9+-7.1mmHg; p=0.005) and dPmean after 1-year (29.2+-8.2mmHg vs. 13.0+-6.7mmHg; p=0.004). There were no significant differences in survival. *Conclusions* VIV-TAVR is safe and effective in the early period. In surgical valves with a true-ID[?]21mm inferior hemodynamic and survival outcomes must be expected. Nonetheless, also patients with larger true-ID's showed steadily increasing transvalvular gradients. This raises concern about durability.

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Methods

A total of 77 patients underwent VIV-TAVR for failing aortic bioprosthesis during a 7-years period. Predominant mode of failure was stenosis in 87.0%. Patients had a mean age of 79.4±5.8 years and a mean logistic EuroSCORE of 30.8±15.7%. The STS-PROM averaged 5.79±2.63%. Clinical results and hemodynamic outcomes are reported for 30-days, 1-, 2- and 3-years. Completeness of follow-up was 100% with 44 patients at risk after 3-years. Follow-up ranged up to 7.1 years.

Results

Majority of the surgical valves were stented (94.8%) with a mean labeled size of 23.1±2.3mm and true-ID of 20.4±2.6mm. A true-ID [?]21mm had 58.4% of the patients. Self-expanding valves were implanted in 68.8% (mean labeled size 24.1+-1.8mm) and balloon-expanded in 31.2% (mean size 24.1+-1.8mm). No patient died intraoperatively. Hospital mortality was 1.3% and three-years survival 57.1%. All patients experienced an initial significant dPmean-reduction to 16.8+-7.1mmHg. After 3-years mean dPmean raised to 26.0+-12.2mmHg. This observation was independent from true-ID or type of TAVR-prosthesis. Patients with a true-ID [?]21mm had a higher initial (18.3+-5.3mmHg vs. 14.9+-7.1mmHg; p=0.005) and dPmean after 1-year (29.2+-8.2mmHg vs. 13.0+-6.7mmHg; p=0.004). There were no significant differences in survival.

Conclusions

VIV-TAVR is safe and effective in the early period. In surgical valves with a true-ID[?]21mm inferior hemodynamic and survival outcomes must be expected. Nonetheless, also patients with larger true-ID's showed steadily increasing transvalvular gradients. This raises concern about durability.

Introduction

The clinical implementation of transcatheter aortic valve replacement (TAVR) induced profound and ongoing changes in treatment of valvular heart disease [1-3]. Since the first successful TAVR, as reported by Alain Cribier in 2002, TAVR has advanced to an essential part in contemporary heart valve therapy [4].

At the same time, surgical aortic valve replacement (AVR) experienced significant changes too [2]. Today, bioprosthetic valves are preferred over mechanical valves by physicians and patients. Recently, more than 80% of all surgically implanted valves are biologic substitutes [2, 5-7]. Even industry adopted this trend and brought "valve-in-valve-TAVR-ready"-implants into the market [8]. Despite reported long-term results for more than 20 years, the basically limited durability of bioprosthetic valves still is an important issue [9].

For those reasons, a significant number of patients presenting with a failed aortic bioprosthesis will be upcoming in the near future. Most of those patients are suitable for conventional redo-surgery at nearly normal risk. But for some higher risk subgroups, undoubted a significantly increased risk for mortality or morbidity up to 20% is reported [2, 5, 10, 11].

An alternative to surgical redo AVR, is "valve-in-valve" TAVR (VIV-TAVR) for failed aortic bioprostheses, as firstly described by Walther et al. in 2007 [2, 3, 12]. Since then, VIV-TAVR continuously spread into the TAVR-centers and today is an established treatment option.

Already in 2014 Dvir et al. reported the initial outcomes of VIV-TAVR in the largest multicenter valve-in-valve registry, including 459 patients and 55 centers worldwide [13]. In this work, Dvir demonstrated the feasibility and safety of the VIV-procedure in a large multicentric cohort [13]. The initial results confirmed good immediate and one-year outcomes [13]. But already this early study described inferior results for patients with small prosthesis and predominant valve stenosis [13].

Up today, there exists only little information concerning mid-term, and no information about long-term durability of VIV-TAVR. The presently available studies contain only limited data, mostly reporting a follow-up limited to one year ([13-16]. Recently, a sub-analysis of the PARTNER 2-registry reported 3-year outcomes, but under exclusion of bioprosthetic valves with a labeled diameter less than 21mm [17]. The longest follow-up is provided by Bleiziffer et al., reporting 5-years clinical data of the VIVI-registry, but lacking echocardiographic data [18].

To address this lack of knowledge in present literature, this study adds a 3-years echocardiographic follow-up after VIV-TAVR.

Methods

Patients and study design

Between January 2010 and December 2017 a total of 2.224 patients underwent TAVR at our institution. Out of these, 77 patients presented with a failed aortic bioprosthesis and were eligible for VIV-TAVR. Predominant mode of failure was stenosis (88.3%). Mean patient's age was 79.4 +- 5.8 years. The established risk calculators by means of STS PROM (5.79 +- 2.63%) and logistic EuroSCORE (30.8 +- 15.7%) proofed the patients to be at high surgical risk.

The present study is a retrospective data analysis out of the hospital's database. We recorded and analyzed pre-, intra- and postoperative data. All hospital survivors were supposed to undergo echocardiographic control after 1, 2 and 3 years during regular follow-up care. Corresponding completeness of follow up was 100% within the follow-up survivors. Follow-up time ranged up to 2.600 days. The study was reviewed and approved by the institutional review board at University Heart Center Dresden, Medical Faculty "Carl Gustav Carus" at Technical University of Dresden (Dresden, Germany).

Statistical analysis

Statistical analysis was performed with JMP 12.0.1(c) Software (SAS institute, Cary NC, USA). Numeric variables are expressed in means with standard error of means (means +- SEM) and categorial data as absolute numbers and percentages. Continuous data were tested using T-Test, categorial variables with the Fisher-exact test. Time-to-event analysis were performed using Kaplan-Meier method and a logrank-test. A p-value <0.05 was considered statistically significant.

Screening protocol for TAVR- candidates

All patients being admitted with aortic valve disease or failed bioprosthesis are discussed in a multidisciplinary "heart valve board", consisting of cardiac surgeons, cardiac anesthesiologists and cardiologists. For risk estimation, the Society of Thoracic Surgeons (STS)-Score and the EuroSCORE were used. Subsequently, patients were determined for a catheter-based procedure according to the Heart team's decision. Informed consent was obtained from all patients.

Valve sizing and implantation technique

Standard transcatheter devices used for valve-in-valve procedures were Edwards SAPIEN, SAPIEN XT and SAPIEN 3 (Edwards Lifesciences Inc., Irvine, CA. USA) as well as Medtronic CoreValve Evolut R (Medtronic, Minneapolis, MN, USA) and Symetis Accurate (Boston Scientific, Nattick, MA, USA). Choice of the valve depended on the individual surgeon's preference and morphologic patterns of the failed bioprosthetic valve, e.g. the internal diameter.

Prior to the procedure, the internal diameter of the failed bioprostheses was determined from the manufacturer's data. This represented the key parameter for sizing of the transcatheter devices. The internal diameter was intraoperatively additionally assessed by transesophageal echocardiography as well as measured prior in the CT-scan. The size choice of best transcatheter heart valve then based on the manufacturer's recommendations, supported by the "ViV Aortic" App (supported by Minneapolis Heart institute Foundation and the Joseph F. and mary M. Fleischhacker Family Foundation; developed by Dr. Vinayak Bapat).

The procedure itself was performed like described previously [2, 3, 12]. For achieving an optimal hemodynamic result, a pronounced high position of the TAVR-prosthesis was aimed for [19].

Hemodynamics were evaluated by transthoracic echocardiography (TTE). Predischarge was defined as 6^{th} postoperative day. Diagnostics during follow-up likewise were performed using TTE.

Results

Clinical Baselines and Patient Characteristics

The patient population was characterized by a broad spectrum of relevant comorbidities, as depicted in **Table 1** . Most common comorbidities were chronic kidney disease (n=33/77; 42.9%), diabetes on insulin (n=17/77; 22.1%), presence of concomitant coronary artery disease (n=24/77; 31.2%) and atrial fibrillation (n=21/77; 27.3%). Most of the patients suffered from poor mobility or relevant frailty (n=58/77; 75.3%).

Procedural Characteristics

First surgery dated back in mean 7.9 +- 4.3 years. Per definition, all patients had prior aortic valve replacement. Concomitant procedures during first surgery were CABG (n=32/77; 41.6%) and surgery for aortic disease (n=5/77; 6.5%). Further details are summarized in **Table 2** .

Type of degenerated surgical valve was predominantly stented with 94.8% (n=73/77). Out of these 37.0% (n=27/73) had externally mounted leaflets. Mean labeled size of the surgical valves was 23.1 +- 2.3mm with a mean true-ID of 20.4 +- 2.6mm. A proportion of 58.4% (n=45/77) had a true-ID less or equal 21mm.

Chosen access route was transfemoral in 72.7% (n=56/77) and transapical in the remaining cases (n=21/77; 27.3%). Used TAVR-valves were Edwards SAPIEN (n= 8/77; 27.7%), SAPIEN XT (n= 10/77; 29.8%) and SAPIEN 3 (n= 6/77; 12.8%) as balloon-expandable devices and the Medtronic Evolut R (n= 44/77; 29.8%)

and Symetis Accurate (n=9/77; 11.7%) as self-expanding prostheses. The overall-ratio of self-expandable valves was 68.8% (n=53/77). The TAVR procedures themselves were uneventful. There were neither intraoperative deaths nor procedure related complications. Particularly device malposition, embolization or conversion to surgery did not occur. Mean procedure time was 45.3 +- 12.7 minutes. **Table 2** summarizes the procedural data.

Clinical Results

The postoperative course mainly was uneventful. Majority of the patients (n=54/77; 70.1%) had an ICU-stay less than 24 hours. Neither low cardiac output nor postoperative myocardial infarction or stroke were observed. One patient suffered from postoperative bleeding, needing re-exploration (n=1/77; 1.3%). Three patients had postoperative respiratory failure needing reintubation (n=3/77; 3.9%). Main postoperative morbidity consisted of delirium in 9.1% (n=7/77) of the patients. Mean hospital averaged 12.8 +- 6.6 days. One patient (n=1/77; 1.3%) died during primary hospital stay in consequence of pneumonia. Further clinical results are summarized in **Table 1** .

Long-Term Clinical Follow-up

Thirty-days mortality was 1.3% (n=1/77). Overall survival during further follow-up was 70.1% (n=54/77). Observed survival rates for 1-, 2- and 3-years were 90.9%, 68.8% and 57.1%, respectively. Further follow-up ranged to 7.1 years. Estimated 7-years survival was 20.6 +- 16.1%. **Figure 1A** depicts the Kaplan-Meier survival curve for the entire cohort and **Figure 1B** shows the corresponding Kaplan-Meier curve grouped by the true-ID without any significant difference..

Three-years freedom from rehospitalization was 72.7% (n=56/77). Main cause for rehospitalization were cardiac (n=16/21; 76.2%) and pulmonary (n=3/21; 14.3%) reasons. During the same period, freedom from (indication for) reintervention was 93.2% (n=41/44). Herein two patients presented with a new high grade aortic valve stenosis and one patient with leaflet thrombosis. All three patients refused the formally indicated reintervention.

Immediate and Long-term Echocardiographic Outcomes

The mean preoperative pressure gradients were significantly elevated (dP_{mean} 41.3 +- 15.3 mmHg) as consequence of stenosis as predominant mode of failure (n=68/77; 88.3%).

All patients with preoperative stenotic bioprosthesis experienced a significant reduction of their transvalvular pressure gradients after successful TAVR, as confirmed by predischarge transthoracic echocardiography (dP_{mean} 16.8 +- 7.1 mmHg; $p<0.01$; **Figure 2A**). This was independent from the inner diameter of the degenerated valve (**Figure 2B**).

Median postprocedural mean transvalvular pressure gradient was 18.0 mmHg with an interquartile range from 12.0 to 23.5 mmHg. None of the patients had a mean postprocedural pressure gradient above 40 mmHg postoperatively. Initial device success according to VARC-2 criteria was achieved in 62.3% (n=48/77) of the cases (**Figure 3**). The overall low success-rate was driven by mean transvalvular pressure gradients, exceeding 20mmHg in 37.7% (n=29/77) of the patients. Hereby, patients with a true-ID equal or less 21mm had significant less primary device success compared to patients with a larger true-ID (48.9% [n=22/45] vs. 81.3% [n=26/32] p=0.0299). Residual paravalvular leakage was infrequent (n=6/77;7.8%). None of the residual PVL were larger than trace.

During further follow-up transvalvular pressure gradients steadily increased and correspondingly the device success rate decreased (**Figure 2 and 3)** . After 3-years, only 28.6% (n=22/77) of the patients had persisting device success according to VARC-2 criteria. Mean V_{max} was 317 +- 76 cm/sec (Median 280 cm/sec) with a dP_{mean} averaging 26.0 +- 12.2 mmHg (Median 24 mmHg) after three years of follow-up (**Table 3; Figure 2A**). This observation was particularly true for internal diameters less or equal 21mm – after an initial significant reduction, the mean transvalvular gradients remained significantly increased (**Figure 2B**).

Additionally, the trend of steadily deteriorating hemodynamic performance during follow-up was independently from the type of prosthesis. Despite self-expandable prostheses having a significant higher rate of initial device success compared to balloon-expandable valves (69.2% vs. 56.3%; p=0.047), this observation turned after 3 years with balloon-expandable THV now having a significantly higher rate of persisting device success (36.3% vs. 21.4%, p=0.041) (**Figure 3**).

Discussion

Valve-in-valve TAVR is a seductive option in case of degenerated bioprostheses. Apparently the advantages are obvious: the procedure is safe, easy and convenient to perform, positioning of the valve is simplified due to radiopaque markers and paravalvular leakages as a risk factor for mortality are not an relevant issue [1-3, 12, 13]. Furthermore, waiving surgery is a striking and convenient point for the patient. Therefore, the crucial point remains durability. If the initially unargued excellent results proof to be stable over time, VIV-TAVR is ready for the many. If not, it must remain a bailout-option for risky patients. The presently available literature does not allow to answer this crucial question conclusively [13-18].

The primary clinical efficacy of VIV-TAVR is unargued. Regarding this point, the present study continuous excellent early results of our group and is in line with the data given by the VIVID-registry [3, 13]. The present patient cohort represents a typical TAVR patient population. Likewise, procedural data and hospital outcome are comparable with VIVID [13]. The procedure itself is convenient and technically less demanding - radiopaque markers of the bioprosthesis clearly indicate the perfect landing zone and facilitate an easy and orthograde positioning of the valve. Additionally, the sealing is much more effective compared to "native"-TAVR and though, paravalvular leakages are no matter of greater concern in VIV-TAVR as the present study and the VIVID-registry could demonstrate [20]. Nonetheless, one point has to be taken into account: coronary obstruction. Despite rare with an overall incidence of 0.7%, coronary obstruction is an issue being associated with a high mortality up to 42% [21]. To prevent from this fatal course, some considerations should be taken into account during procedure planning. There exist some predicting variables like female gender, low coronary ostial height (<10mm), Sinus Valsalva width <30mm and presence of biological valves with externally mounted leaflets or even worse, stentless valves [22]. For those conditions the BASILICA procedure or alternatively the OPEN-BASILICA-procedure were described before [22-24]. Anyhow, in the present series coronary obstruction played no role.

Generally, the procedural and hospital outcomes observed in this study confirmed the safety of VIV-TAVR. Indeed, the hospital survival as well as stroke rate were better than the results reported in the VIVID (1.3% vs. 7.6% for mortality and 0.0% vs. 1.7% for major stroke).

During the implantation, particularly with self-expanding prostheses it is aimed to release the valve in a pronounced high position to ensure supra-annular positioning and to allow a good hemodynamic result. According to this supra-annular concept, the immediate hemodynamic outcomes are superior with self-expandable prostheses compared to intra-annularly implanted balloon-expandable valves. This fact could be confirmed by the present study demonstrating a significantly higher rate of early device success according to the VARC-2 criteria for balloon-expandable devices. These observations made are mainly in line with those reported by the Dvir and colleagues [13, 18].

Concluding procedural aspects and initial outcomes, it seems to be evident, that VIV-TAVR as a heterogeneous group consisting of different procedures (by means of combinations of surgical and TAVR valves) - with respect to some special cases - basically is safe and provides good or at least acceptable initial hemodynamic results [3, 13, 16]. Furthermore, it is evident, that VIV-TAVR in small surgical valves as well as stented valves is associated with higher postprocedural gradients [16].

As far as good – but Dvir and colleagues identified a sore spot already in the VIVID [13]. Patients presenting with an internal diameter equal or less 20mm of the surgical valve showed to have an inferior 1-year survival [13]. Accordingly, the PARTNER 2 Valve-in-Valve Study at 3-years priorly defined a labeled size <21mm as a key exclusion criterion [17]. The present study confirms these findings. Despite experiencing an initial sufficient reduction of transvalvular pressure gradients in true-ID's equal or less 21mm, gradients continuously

were significantly higher up to 1-year of follow-up, compared to larger valve. After 2 and 3-years the gradients stayed to be high, but not anymore being significantly higher compared to larger valves. This development could be explained by two facts. First, the larger valves likewise experienced a fundamental increase in transvalvular pressure gradients and second, a potential bias within the small-ID group due to patients with assumably higher gradients dying earlier. This explanation fits into the observed higher mortality of the small-ID group during follow-up. Bleiziffer et al. reported in the 5-years outcome of the VIVID likewise a significantly increased mortality in small-ID patients [18]. Hence, the presently available results allow to conclude, that VIV-TAVR in patients with a small ID ([?]21mm or [?]20mm depending on the definition) are likely to have inferior outcomes after their primary hospital stay.

A quite more unclear situation applies to larger valves with an ID [?] 21mm. For example, Webb and colleagues reported in the 3-Year outcomes of 365 patient in the PARTNER 2-registry sustained hemodynamic status with at least only minimal changes in mean transvalvular pressure gradients [17]. The observation we made in the present series are contradictory: the predischarge hemodynamic outcomes were quite comparable to those reported by Webb and colleagues (16.8 +- 7.1 mmHg vs. 17.4 mmHg) [17] - despite 100% use of balloon-expandable valves in the PARTNER 2-registry and the large portion (68.8%) of self-expanding devices in the present series.

In the present series the mean gradients steadily increased over the following 3-years (**Figure 2A**), which happened independently from the true-ID of the surgical valve (**Figure 2B**) or the type of implanted transcatheter valve (**Figure 3**). This could not be explained by size of the surgical valves: the ratio of patients with a true-ID less or equal 21mm was even higher in the PARTNER 2-registry compared to our data (76.7% vs. 58.4%).

Up to date, there exist no further long-term hemodynamic data in the present literature for further comparison. Most studies dealing with hemodynamic results, end after 1-year of outpatient follow-up [14-16]. Accordingly, hemodynamic long-term-follow-up has much more to be elaborated in further studies.

A particular matter of concern beside hemodynamics is survival. All presently available essential long-term-trials describe mainly comparable survival outcomes [17, 18, 25, 26]. In the PARTNER 2-registry Webb and colleagues reported an estimated all-cause mortality of 32.7% after 3-years of follow-up, which fits to 27.7% mortality after 3-years described in the CoreValve US Expanded Use Study [17, 25]. The data given by the present study is with an estimated mortality of 42.9% after 3-years mainly in range, but being somewhat higher.

Further long-term-outcomes are provided by a small multicenter study with 116 patients reporting 5-years mortality of 32.1% as well as by the long-term data of the VIVID with 62.0% mortality after 8-years [18, 26]. In the present series a poor estimated 7-years survival of 20.6 +- 16.1% was found. Interpreting these poor survival data should respect the average age ranging between 76.0 +- 11.0 and 79.4 +- 5.8 years [17, 18, 25, 26].

Meanwhile the large VIVID-registry identified smaller true-IDs as a risk factor for mortality beginning from 1-year of follow-up, the smaller PARTNER 2-registry as well as the present study could not confirm that observation findings [13, 17, 18]. Potentially, the overall high mortality rate in the study population conceals possible significant differences.

Conclusion

Concluding the data given by this study and the presently available literature, it seems to be evident that the initial clinical and hemodynamic results are satisfying. The procedure is safe and effective. Nonetheless, small true-ID's equal or less 21mm are associated with inferior hemodynamic outcomes. Due to the high overall-mortality in the study population, a potential significant difference in long-term survival potentially is concealed. In contrast to only one available long-term-study on hemodynamic outcomes, the present study showed steadily increasing pressure gradients over time, independently from true-ID of the surgical valve or type of transcatheter prosthesis. After 3-years more than 70% of the patients did not meet the VARC-2-

device success criteria anymore. This finding is a matter of concern and needs to be evaluated by further studies prior bringing VIV-TAVR into younger and lower risk patients.

Limitations

VIV-TAVR is heterogeneous group of procedures with various combinations of types and sizes of surgical and transcatheter valves. This must result in a strong bias for studies dealing with this topic. Furthermore, the present study is a single-center consecutive cohort with a limited number of patients.

References

1. Wilbring, M., et al., *Transapical transcatheter valve-in-valve implantation for deteriorated mitral valve bioprostheses.* Ann Thorac Surg, 2013. **95** (1): p. 111-7.

2. Wilbring, M., et al., *Transcatheter valve-in-valve therapies: patient selection, prosthesis assessment and selection, results, and future directions.* Curr Cardiol Rep, 2013. **15** (3): p. 341.

3. Wilbring, M., et al., *Transcatheter valve-in-valve implantation for deteriorated aortic bioprosthesis: initial clinical results and follow-up in a series of high-risk patients.* Ann Thorac Surg, 2012.**93** (3): p. 734-41.

4. Cribier, A., et al., *Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description.* Circulation, 2002. **106** (24): p. 3006-8.

5. Seiffert, M., et al., *Transcatheter mitral valve-in-valve implantation in patients with degenerated bioprostheses.* JACC Cardiovasc Interv, 2012. **5** (3): p. 341-9.

6. Piazza, N., et al., *Transcatheter aortic valve implantation for failing surgical aortic bioprosthetic valve: from concept to clinical application and evaluation (part 1).* JACC Cardiovasc Interv, 2011.**4** (7): p. 721-32.

7. Piazza, N., et al., *Transcatheter aortic valve implantation for failing surgical aortic bioprosthetic valve: from concept to clinical application and evaluation (part 2).* JACC Cardiovasc Interv, 2011.**4** (7): p. 733-42.

8. Tamagnini, G., et al., *Device profile of the Inspiris Resilia valve for aortic valve replacement: overview of its safety and efficacy.* Expert Rev Med Devices, 2021. **18** (3): p. 239-244.

9. Borger, M.A., et al., *Twenty-year results of the Hancock II bioprosthesis.* J Heart Valve Dis, 2006. **15** (1): p. 49-55; discussion 55-6.

10. Jones, J.M., et al., *Repeat heart valve surgery: risk factors for operative mortality.* J Thorac Cardiovasc Surg, 2001.**122** (5): p. 913-8.

11. Maganti, M., et al., *Redo valvular surgery in elderly patients.* Ann Thorac Surg, 2009. **87** (2): p. 521-5.

12. Walther, T., et al., *Valve-in-a-valve concept for transcatheter minimally invasive repeat xenograft implantation.* J Am Coll Cardiol, 2007. **50** (1): p. 56-60.

13. Dvir, D., et al., *Transcatheter aortic valve implantation in failed bioprosthetic surgical valves.* JAMA, 2014. **312** (2): p. 162-70.

14. Landes, U., et al., *Transcatheter Replacement of Transcatheter Versus Surgically Implanted Aortic Valve Bioprostheses.* J Am Coll Cardiol, 2021. **77** (1): p. 1-14.

15. Raschpichler, M.C., et al., *Valve-in-Valve for Degenerated Transcatheter Aortic Valve Replacement Versus Valve-in-Valve for Degenerated Surgical Aortic Bioprostheses: A 3-Center Comparison of Hemodynamic and 1-Year Outcome.* J Am Heart Assoc, 2020. **9** (14): p. e013973.

16. Kherallah, R.Y., et al., *Hemodynamic outcomes after valve-in-valve transcatheter aortic valve replacement: a single-center experience.* Ann Cardiothorac Surg, 2021. **10** (5): p. 630-640.

17. Webb, J.G., et al., *3-Year Outcomes After Valve-in-Valve Transcatheter Aortic Valve Replacement for Degenerated Bioprostheses: The PARTNER 2 Registry.* J Am Coll Cardiol, 2019. **73** (21): p. 2647-2655.

18. Bleiziffer, S., et al., *Long-term outcomes after transcatheter aortic valve implantation in failed bioprosthetic valves.* Eur Heart J, 2020. **41** (29): p. 2731-2742.

19. Simonato, M., et al., *In vitro evaluation of implantation depth in valve-in-valve using different transcatheter heart valves.*EuroIntervention, 2016. **12** (7): p. 909-17.

20. Azadani, A.N., et al., *Effect of transcatheter aortic valve size and position on valve-in-valve hemodynamics: An in vitro study.* J Thorac Cardiovasc Surg, 2017. **153** (6): p. 1303-1315 e1.

21. Ribeiro, H.B., et al., *Predictive factors, management, and clinical outcomes of coronary obstruction following transcatheter aortic valve implantation: insights from a large multicenter registry.* J Am Coll Cardiol, 2013. **62** (17): p. 1552-62.

22. Khan, J.M., et al., *The BASILICA Trial: Prospective Multicenter Investigation of Intentional Leaflet Laceration to Prevent TAVR Coronary Obstruction.* JACC Cardiovasc Interv, 2019.**12** (13): p. 1240-1252.

23. Wilbring, M., et al., *The OPEN-BASILICA Procedure for Failed Bioprosthetic Valves.* JACC Cardiovasc Interv, 2021. **14** (18): p. 2075-2076.

24. Khan, J.M., et al., *Preventing Coronary Obstruction During Transcatheter Aortic Valve Replacement: Results From the Multicenter International BASILICA Registry.* JACC Cardiovasc Interv, 2021.**14** (9): p. 941-948.

25. Dauerman, H.L., et al., *Durability and Clinical Outcomes of Transcatheter Aortic Valve Replacement for Failed Surgical Bioprostheses.* Circ Cardiovasc Interv, 2019. **12** (10): p. e008155.

26. de Freitas Campos Guimaraes, L., et al., *Long-Term Outcomes After Transcatheter Aortic Valve-in-Valve Replacement.* Circ Cardiovasc Interv, 2018. **11** (9): p. e007038.

Tables

Table 1 Baselines and clinical outcomes

Preoperative Data

Age	79.4 ± 5.8 years	79.4 ± 5.8 years
STS Prom	5.79 ± 2.63%	5.79 ± 2.63%
log. EuroSCORE	30.8 ± 15.7%	30.8 ± 15.7%
Body-Mass-Index	*27.2* ± 3.7 kg/m^2	*27.2* ± 3.7 kg/m^2
Male gender	*n=41/77*	*53.2%*
Atrial fibrillation	*n=21/77*	*27.3%*
CAD	*n=24/77*	*31.2%*
COPD	*n=10/77*	*13.0%*
Extracardiac arteriopathy	*n=22/77*	*28.6%*
Diabetes on insulin	*n=17/77*	*22.1%*
Chronic kidney disease	*n=33/77*	*42.9%*
Poor mobility / frail	*n=58/77*	*75.3%*
h/o Stroke	*n=5/77*	*6.5%*
Hospital Mortality & Morbidity	Hospital Mortality & Morbidity	Hospital Mortality & Morbidity
Hospital Stay	*12.8* ± 6.6 days	*12.8* ± 6.6 days
Hospital Death	*n=1/77*	*1.3%*
ICU-stay < 24 hours	*n=54/77*	*70.1%*
Respiratory failure	*n=3/77*	*3.9%*
Stroke (Rankin >2)	*n=0/77*	*0.0%*
Delirium	*n=7/77*	*9.1%*
Renal failure (CVVH)	*n=5/77*	*6.5%*
Re-exploration (TA only)	*n=1/77*	*1.3%*

Table 2 Procedural Characteristics

Index procedure

Time to first surgery	7.9 ± 4.3 years	7.9 ± 4.3 years	7.9 ± 4.3 years
Concomitant CABG	*n=32/77*	*n=32/77*	*41.6%*
Concomitant Aortic Surgery	*n=5/77*	*n=5/77*	*6.5%*
Stenosis as predominant mode of failure	*n=68/77*	*n=68/77*	*88.3%*
Procedural Data	Procedural Data	Procedural Data	Procedural Data
Transfemoral access	*n=56/77*	*n=56/77*	*72.7%*
Transapical access	*n=21/77*	*n=21/77*	*27.3%*
Procedure time (min)	*45.3* ± 12.7	*45.3* ± 12.7	*45.3* ± 12.7
Procedural Death	*n=0/77*	*n=0/77*	*0.0%*
Degenerated Surgical valves	Degenerated Surgical valves	Degenerated Surgical valves	Degenerated Surgical valves
Stented	*Stented*	*n=73/77*	*94.8%*
Externally mounted leaflets	*Externally mounted leaflets*	*n=27/73*	*37.0%*
Stentless	*Stentless*	*n=4/77*	*5.2%*
Mean Labeled Size	*Mean Labeled Size*	*23.1* ± 2.3mm	*23.1* ± 2.3mm
Mean True-ID	*Mean True-ID*	*20.4* ± 2.6mm	*20.4* ± 2.6mm
True-ID [?] 21mm	*True-ID [?] 21mm*	*n=45/77*	*58.4%*
Implanted Balloon-expandable valves	Implanted Balloon-expandable valves	Implanted Balloon-expandable valves	Implanted Balloon-expandable valves
Account of balloon-expandables	*Account of balloon-expandables*	*n=24/77*	*31.2%*
Edwards SAPIEN	*Edwards SAPIEN*	*n=8/77*	*10.4%*
Edwards SAPIEN XT	*Edwards SAPIEN XT*	*n=10/77*	*13.0%*
Edwards SAPIEN 3	*Edwards SAPIEN 3*	*n=6/77*	*7.7%*
Mean labeled size	*Mean labeled size*	*24.1* ± 1.8mm	*24.1* ± 1.8mm
Implanted Self-expanding Valves	Implanted Self-expanding Valves	Implanted Self-expanding Valves	Implanted Self-expanding Valves
Account of self-expandables	*Account of self-expandables*	*n=53/77*	*68.8%*
Medtronic Evolute R	*Medtronic Evolute R*	*n=44/77*	*57.1%*
Symetis Accurate	*Symetis Accurate*	*n=9/77*	*11.7%*
Mean labeled size (if applicable)	*Mean labeled size (if applicable)*	*24.8* ± 2.3mm	*24.8* ± 2.3mm

Table 3 Follow-Up Data and hemodynamic endpoints

Major Outcomes

Hospital survival	*n=76/77*	*98.7%%*
1-year survival	*n=70/77*	*90.9%*
2-years survival	*n=53/77*	*68.8%*
3-years survival	*n=44/77*	*57.1%*
Rehospitalization	*n=23/77*	*29.9%*

Freedom from reintervention @ 3 years	*n=41/44*	*93.2%*
Freedom from Death, stroke, rehospitalization @ 3 years	*n=44/77*	*57.1%*
Completeness of Follow-Up	Completeness of Follow-Up	Completeness of Follow-Up
- 1 year	*70 out of 70 pts. at risk*	*100.0%*
- 2 years	*53 out of 53 pts. at risk*	*100.0%*
- 3 -years	*44 out of 44 pts. at risk*	*100.0%*
Hemodynamics @ discharge	Hemodynamics @ discharge	Hemodynamics @ discharge
Vmax	*283* ± 53 cm/sec (Median 282 cm/sec)	*283* ± 53 cm/sec (Median 282 cm/sec)
dPmean	*16.8* ± 7.1 mmHg (Median 13 mmHg)	*16.8* ± 7.1 mmHg (Median 13 mmHg)
VARC-2 device success	*n=48/77*	*62.3%*
Hemodynamics @ 1-year	Hemodynamics @ 1-year	Hemodynamics @ 1-year
Vmax	*254* ± 82 cm/sec (Median 240 cm/sec)	*254* ± 82 cm/sec (Median 240 cm/sec)
dPmean	*19.9* ± 14.2 mmHg (Median 18 mmHg)	*19.9* ± 14.2 mmHg (Median 18 mmHg)
VARC-2 device success	*n=51/77*	*66.2%*
Hemodynamics @ 2-years	Hemodynamics @ 2-years	Hemodynamics @ 2-years
Vmax	*276* ± 62 cm/sec (Median 275 cm/sec)	*276* ± 62 cm/sec (Median 275 cm/sec)
dPmean	*22.0* ± 13.1 mmHg (Median 21 mmHg)	*22.0* ± 13.1 mmHg (Median 21 mmHg)
VARC-2 device success	*n=36/77*	*46.8*
Hemodynamics @ 3-years	Hemodynamics @ 3-years	Hemodynamics @ 3-years
Vmax	*317* ± 76 cm/sec (Median 280 cm/sec)	*317* ± 76 cm/sec (Median 280 cm/sec)
dPmean	*26.0* ± 12.2 mmHg (Median 24 mmHg)	*26.0* ± 12.2 mmHg (Median 24 mmHg)
VARC-2 device success	*n=22/77*	*28.6%*

Figures

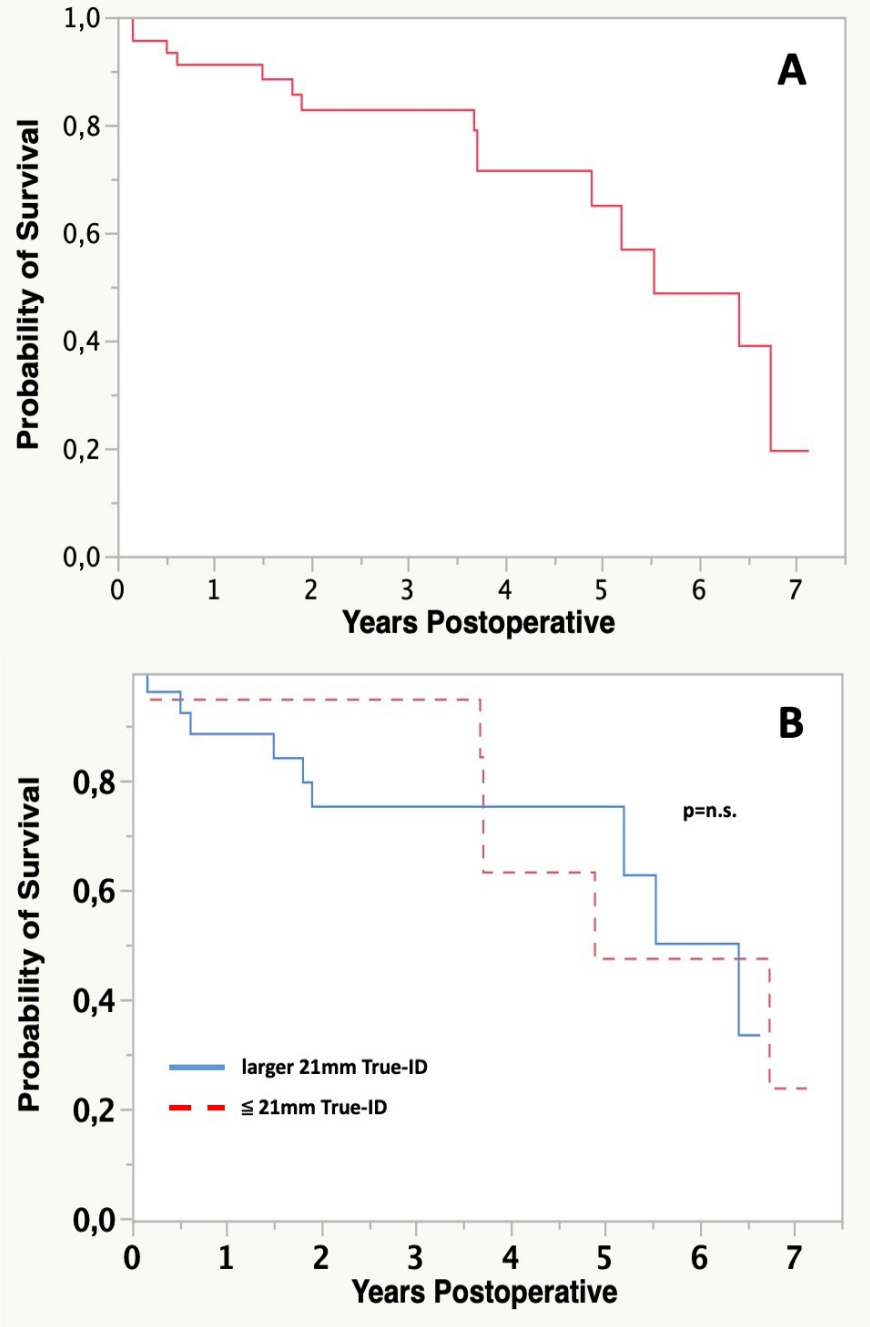

Figure 1 Kaplan-Meier Survival curves. **A** ... for all patients **B** ... by true-ID-groups

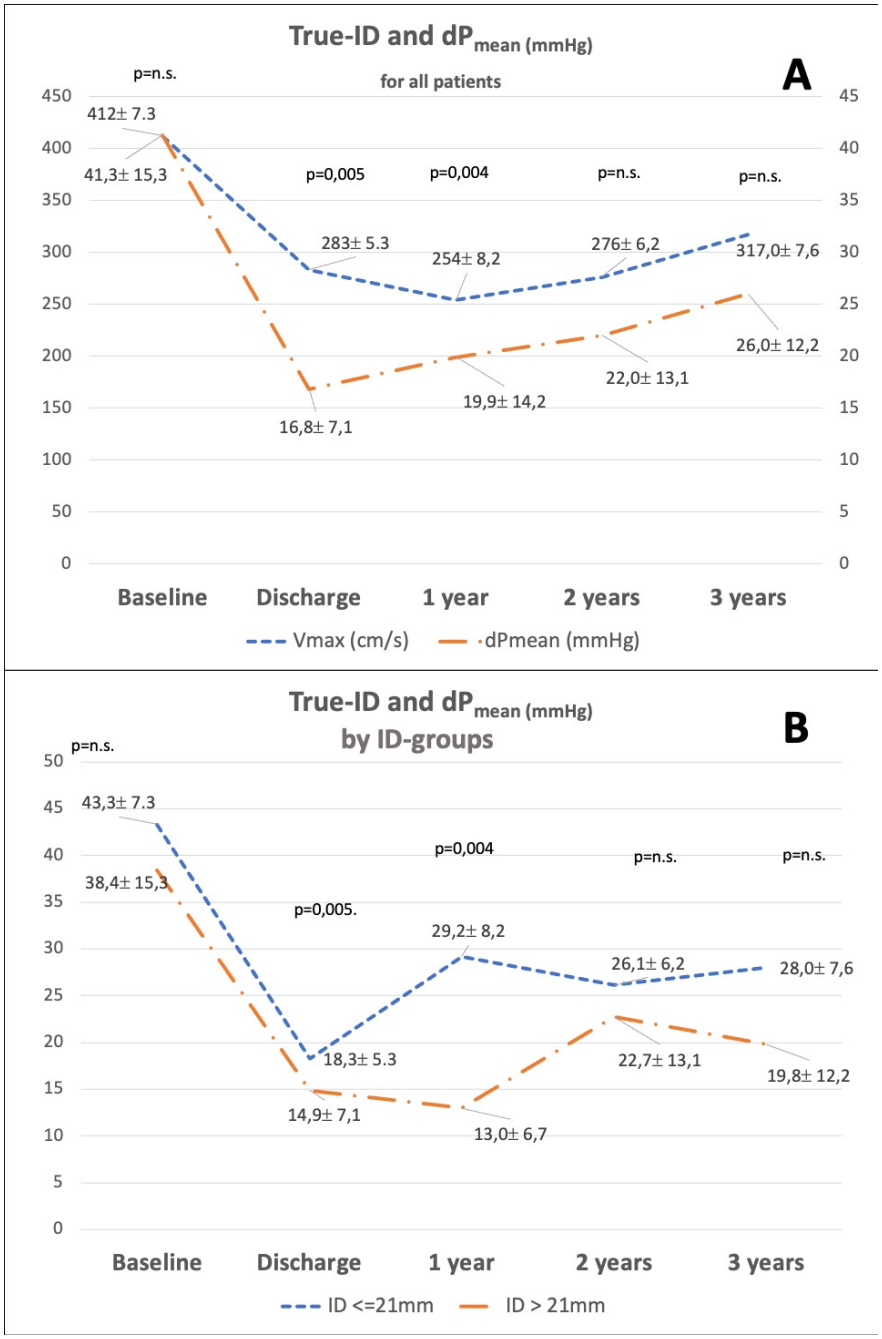

Figure 2 A ... Changes over time in $V_{max}$and dP_{mean} for all patients. **B** ... True-ID and dP_{mean} over time by ID-groups

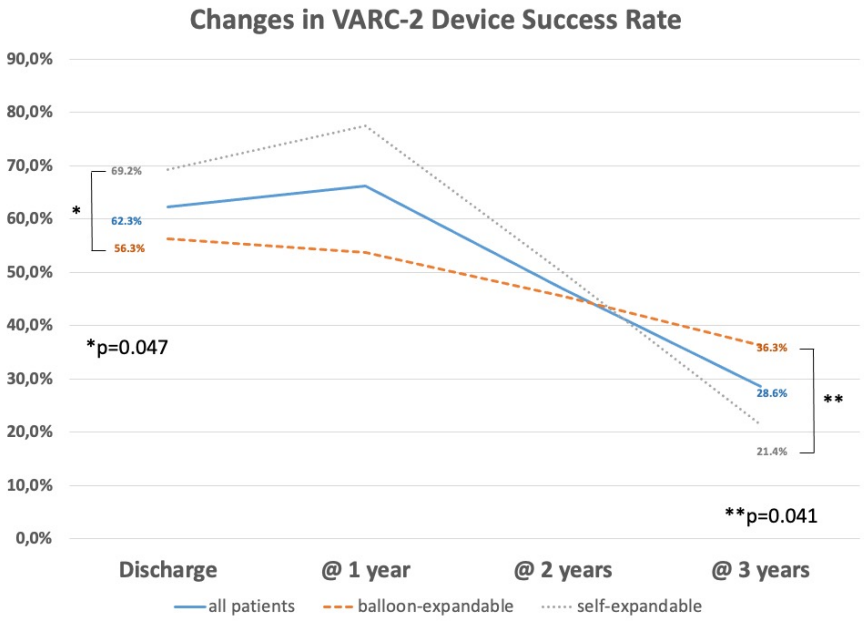

Figure 3 VARC-2 device success during follow-up