AMP ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Antithrombotic Treatment After Valve-in-Valve, Valve-in-Ring, and Valve-in-MAC Procedures: A Systematic Review and Meta-Analysis

Tratamento Antitrombótico Após Procedimentos *Valve-in-Valve*, *Valve-in-Ring* e *Valve-in-MAC*: Uma Revisão Sistemática e Meta-Análise

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Acta Med Port 2025 Sep;38(9):528-537 ▪ https://doi.org/10.20344/amp.22905

ABSTRACT

Introduction: While antithrombotic therapy following transcatheter valve implantation has been extensively studied in various clinical trials, there remains a notable gap in evidence regarding the optimal approach following valve-in-valve (ViV), valve-in-ring (ViR) and valve-in-mitral annular calcification (ViMAC) procedures, warranting further assessment. This gap is particularly concerning due to the apparent increased risk of thrombosis associated with ViV interventions. The aim of this systematic review was to explore the potential benefits of anticoagulation in ViV, ViR, and ViMAC procedures.

Methods: We searched PubMed, Embase, and the Cochrane Central Register of Controlled Trials, as well as the grey literature, for observational and interventional studies published until December 2023. Trials were included if a comparative analysis between the two antithrombotic strategies was feasible and excluded if patients under 18 years old were analysed. The primary efficacy endpoints were incidence of clinical and total valve thrombosis (VT), major bleeding was the sole safety primary endpoint. Additional analyses were performed regarding valves in the mitral position and valve type. The risk of bias was evaluated using the Newcastle-Ottawa scale. Data was assessed using the Review Manager 5.4 software.

Results: A total of five observational and one case series were included (n = 614 on anticoagulation and n = 468 on antiplatelets), comprising a total of 1082 participants. Clinical VT rates were 4.2% for all procedures, and patients on anticoagulants were associated with a a lower risk of clinical VT (1.1% *vs* 8.3%; OR: 0.18; 95% CI: 0.07 - 0.42, I^2: 0%) and total VT (1.3% *vs* 8.5%; OR: 0.16; 95% CI: 0.07 - 0.37, I^2: 0%). Regarding bleeding events, the existing literature did not provide adequate information to enable a thorough analysis.

Conclusion: Our study suggests a potential benefit of anticoagulation regimens to decrease the high rates of VT following valve-in-valve, valve-in-ring and valve-in-mitral annular calcification procedures. However, the lack of randomized controlled trials and data on bleeding and mortality emphasises the necessity for further research.

Keywords: Anticoagulants/administration & dosage; Bioprosthesis; Cardiac Catheterization; Heart Valve Prosthesis; Heart Valve Prosthesis Implantation; Thrombosis/prevention & control

RESUMO

Introdução: Embora a terapêutica antitrombótica após a implantação de válvulas percutâneas tenha sido amplamente estudada em diversos ensaios clínicos, persiste uma lacuna significativa quanto à abordagem ideal após os procedimentos *valve-in-valve* (ViV), *valve-in-ring* (ViR) e *valve-in-mitral annular calcification* (ViMAC). Essa lacuna é particularmente relevante devido ao aparente aumento do risco trombótico associado aos procedimentos ViV. O objectivo desta revisão sistemática foi explorar os potenciais benefícios da anticoagulação em procedimentos ViV, ViR e ViMAC

Métodos: Foi feita uma pesquisa na PubMed, Embase, Cochrane Central Register of Controlled Trials, bem como da literatura cinzenta, para estudos observacionais e intervencionais publicados até dezembro de 2023. Foram incluídos estudos que realizaram uma análise comparativa entre uma estratégia anticoagulante e uma estratégia antiagregante, sendo excluídos aqueles que incluíram doentes com menos de 18 anos. O *outcome* primário de eficácia foi definido como a incidência de trombose valvular (TV) clínica e total. O *outcome* primário de segurança foi hemorragia *major*. Foram feitas análises adicionais relativamente à posição mitral e de acordo com o tipo de válvula utilizada. O risco de viés foi avaliado utilizando a escala de Newcastle-Ottawa. Os dados foram analisados com o *software* Review Manager 5.4.

Resultados: Foram incluídos cinco estudos observacionais e uma *case-series* (n = 614 sob anticoagulação e n = 468 sob antiagregantes), num total de 1082 participantes. A taxa de TV clínica foi de 4,2% para todos os procedimentos, e os doentes sob anticoagulação apresentaram uma redução significativa da TV clínica (1,1% *vs* 8,3%; OR: 0,18; IC 95%: 0,07 - 0,42; I^2: 0%) e da TV total (1,3% *vs* 8,5%; OR: 0,16; IC 95%: 0,07 - 0,37; I^2: 0%). Em relação aos eventos hemorrágicos, os dados disponíveis na literatura não permitiram uma análise adequada.

Conclusão: O nosso estudo sugere um potencial benefício potencial dos regimes anticoagulantes na redução das elevadas taxas de TV após os procedimentos *valve-in-valve*, *valve-in-ring* e *valve-in-mitral annular calcification*. No entanto, a ausência de ensaios clínicos randomizados e de dados sobre hemorragias e mortalidade reforça a necessidade de mais investigação.

Palavras-chave: Anticoagulantes/administração e dosagem; Bioprótese; Cateterismo Cardíaco; Implante de Prótese de Válvula Cardíaca; Trombose/prevenção e controlo

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Recebido/*Received*: 20/01/2025 - **Aceite/*Accepted*:** 20/05/2025 - **Publicado *Online*/*Published Online*:** 21/07/2025 - **Publicado/*Published*:** 01/09/2025

KEY MESSAGES

- Anticoagulation was associated with significantly lower rates of clinical and total valve thrombosis after ViV, ViR, and ViMAC procedures, suggesting potential clinical benefit in this population.
- The findings were robust in the sensitivity analyses and showed no evidence of publication bias.
- Data on post-discharge bleeding and mortality are lacking, hindering assessment of net clinical benefit.
- Randomized controlled trials are urgently needed to establish the optimal antithrombotic strategy in this high-risk population.

INTRODUCTION

Annually, approximately 280 000 valve prostheses are implanted worldwide.[1,2] The majority are biological prostheses, which are mostly selected as they do not require antivitamin K anticoagulation, despite a shorter lifespan and susceptibility to degenerative damage.[3,4] The necessity of reintervention is a known surgical risk factor for open-heart surgery,[4-6] which led to the emergence of valve-in-valve (ViV) and valve-in-ring (ViR) procedures as alternatives for this subset of patients. While ViV involves implanting a bioprosthetic valve within the existing surgical prosthesis, benefiting from a defined and stable seating surface, ViR places the transcatheter valve inside a previously implanted annuloplasty ring (a device used to reshape and reinforce the mitral annulus), a procedure that is more technically challenging due to variability in ring design and rigidity and carries a higher risk of complications such as residual regurgitation and left ventricular outflow tract obstruction.These percutaneous procedures have shown better short- and mid-term outcomes than redo surgical valve replacements.[5,7-9] Nevertheless, the optimal antithrombotic management of these patients is unclear.

Several large-scale randomised controlled trials have evaluated antithrombotic therapies following transcatheter aortic valve implantation (TAVI), favouring antiplatelet therapy over anticoagulation in patients without an indication for anticoagulation.[10,11] Current guidelines reflect these findings.[12] However, for ViV, ViR, and valve-in-mitral annular calcification (ViMAC) procedures - the latter involving deployment of a balloon-expandable valve directly into a severely and variably calcified mitral annulus - the evidence remains limited. This is particularly relevant because patients undergoing aortic ViV appear to face a higher risk of clinical leaflet thrombosis and structural valve deterioration (SVD) than those undergoing conventional TAVI.I.[13,14] Moreover, there is a notable accumulation of reports of valve thrombosis (VT) following ViV procedures,[15-17] leading not merely to valve dysfunction and the need for reintervention,[15,16] but also posing a heightened risk of transient ischemic attacks and stroke,[18] sometimes resulting in death.[15,17]

Against this background we performed a systematic review and meta-analysis to further elucidate the potential role of anticoagulation in reducing the thrombotic risk associated with ViV, ViR, and ViMAC procedures.

METHODS

Protocol

This study was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The systematic review and meta-analysis were registered in the PROSPERO database (CRD42023443581). No amendments to the protocol were deemed necessary.

Literature search

A systematic search was conducted in PubMed, Embase and the Cochrane Central Register of Controlled Trials from their inception to December 2023 for observational and interventional studies comparing individuals on anticoagulants and those not on anticoagulants following ViV, ViR, and ViMAC procedures. A similar search was conducted in the grey literature. No publication date limits were imposed on this latter search. The search was restricted by subject type (human), but not by language. The details of study selection are illustrated in Fig. 1.

Eligibility and exclusion criteria

We included observational studies comparing patients on anticoagulants and those not on anticoagulants at discharge, following ViV, ViR, and ViMAC procedures. Studies were excluded if no comparison between groups were conducted or not possible with available data or if patients under the age of 18 years were included.
Ethics committee approval was obtained in the context of each study.

Primary and secondary outcomes

The study's primary endpoints encompassed major bleeding, as per the criteria defined by the Bleeding Academic Research Consortium (BARC).[19] Major bleeding was defined as BARC 5, 3c, 3b or 3a. The other primary endpoint involved the assessment of clinical and total VT. Given the absence of a universally agreed-upon definition, the

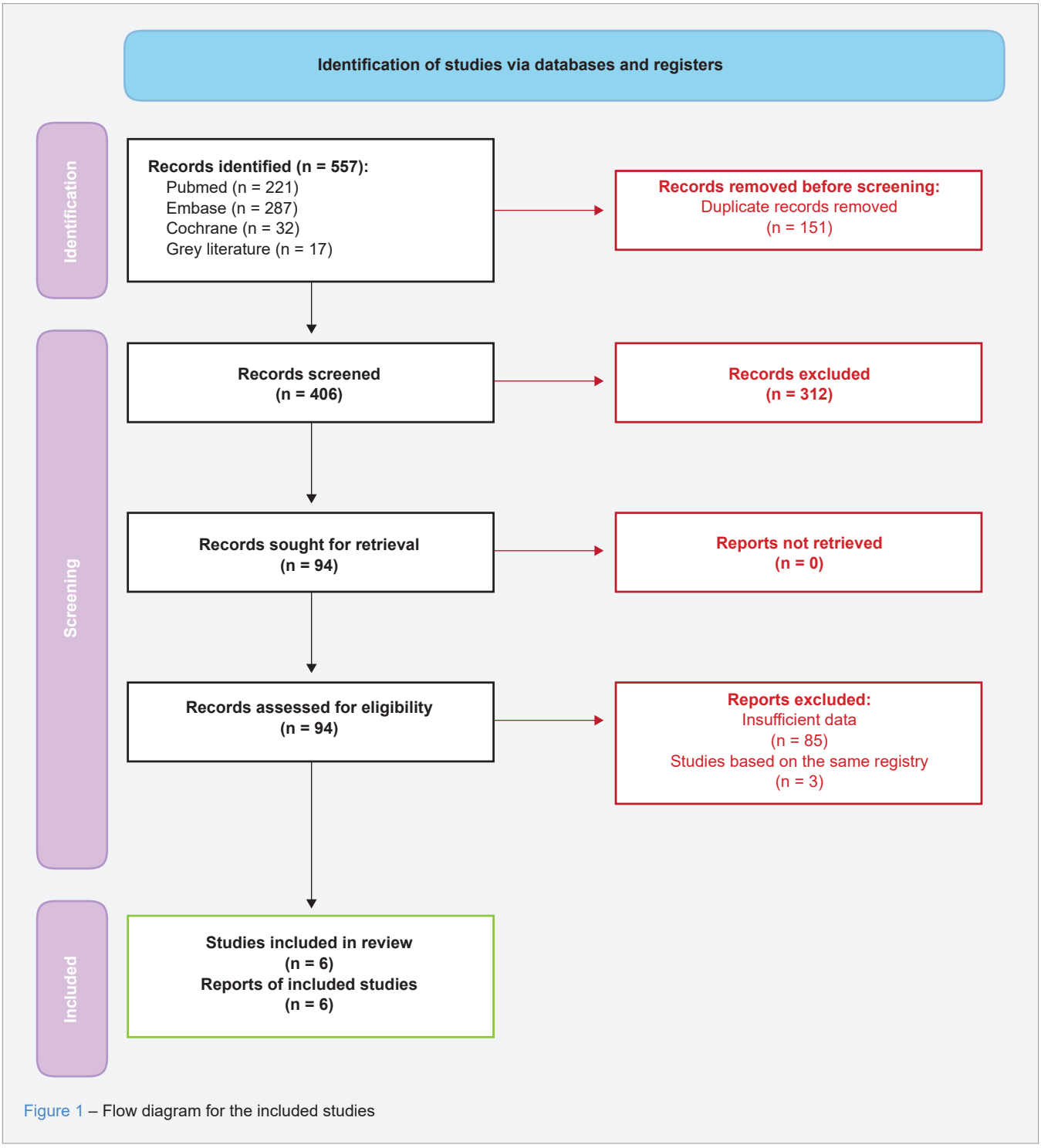


Figure 1 – Flow diagram for the included studies

study relied on the individual definitions provided by each participating study. In cases where only clinical history was described, clinical VT was determined if any of the following criteria were met: (1) manifestation of symptoms, (2) necessity of reintervention due to significant valve dysfunction or (3) documentation of notable increases in valve gradients. Cases of VT that did not meet any of these criteria, or situations where insufficient data was available, were categorized as subclinical valve thrombosis.

Additionally, the study considered all-cause mortality as

a secondary endpoint.

Secondary analysis regarding valve type was performed. Namely, comparisons between porcine and pericardial valves and porcine and other valve types were performed. A separate analysis regarding only valves in the mitral position was performed as well.

Results are presented as odds ratios (OR) with 95% confidence intervals.

Data collection and management

For each study, the following data were independently extracted: (i) general data (study design, year of publication), (ii) characteristics of trial participants [number, mean age, sex, coronary artery disease (CAD), peripheral artery disease, diabetes *mellitus*, hypertension, previous MI and previous stroke], (iii) type of valve, and (iv) number of patients with study outcomes in each treatment arm.

Risk of bias assessment

To explore the validity of eligible trials, the authors independently determined the appropriate generation of random allocation sequence, allocation concealment, blinding of patients and personnel, blinding of outcomes assessment, incomplete outcome data, selective reporting, and other bias. Risk of bias was defined as 'high', 'medium' or 'low'. We resolved disagreements by discussion. The risk of bias was assessed by using the Newcastle-Ottawa scale. The quality assessment for each study is presented in the Risk of Bias Summary [Appendix 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22905/15700)].

To assess the robustness of the results, sensitivity analyses were conducted by excluding studies with a high risk of bias, applying alternative analytical models, and using different effect size measures. Egger's test was also performed to improve the analysis.

Statistical analysis

The statistical analysis was performed from January 25th, 2024, to February 12th, 2024, using the Mantel-Haenszel procedure in a random-effects model to calculate pooled OR with dichotomous non-adjusted data. Due to potential heterogeneity related to procedural aspects, the type of valve implanted, and the characteristics of the previously degenerated valve, a random-effects model was selected. The relatively small number of studies included in each analysis also contributed to the choice of this model. Study heterogeneity was evaluated by funnel plots. The mean effect was considered significant if its 95% confidence interval (CI) did not include one. Heterogeneity was assessed using the I^2 statistic and assumed to be relevant if it exceeded 50%.

RESULTS

Search results

A comprehensive search initially yielded a total of 557 articles for consideration. After eliminating duplicates, we were left with 406 publications for further evaluation, involving scrutiny of titles, abstracts, study types, and study populations. After screening, we identified six observational studies and one case series comparing antithrombotic strategies in ViV, ViR, and ViMAC patients. Upon closer examination, we identified two studies as updates of previously included research. In one instance, the updated version lacked discrimination between clinical and subclinical VT, limiting its inclusion to the analysis of clinical VT, for which only data from the initial publication was considered. In the other case, only the updated paper was included, resulting in a total of five observational studies and one case series included, involving 1082 patients.

It is noteworthy that, unfortunately, no published randomized controlled trials on this topic were available.

Detailed study characteristics are summarized in Table 1, while Fig. 1 represents study selection.

Table 1 – Baseline characteristics of the patients in each included study

Study	Patients (n)	Anticoagulated patients (%)	Age[a] (years)	Male (%)	PAD (%)	Diabetes (%)	HTN (%)	Previous MI (%)	Previous stroke (%)	STS score (%)
Eng 2021[29]	88	83[+]	76	43	12.0	26.0	NR	18.0	21.0	8.2
Yoon 2019[4]	521	72[#]	73	46	11.3	23.8	70.6	15.7	15.7	9.0
McElhinney 2019[30]	306	53[†]	40	NR	NR	NR	NR	NR	NR	NR
Abdel-Wahab 2018[31]	300	33*	80	59	24.4	25.8	NR	NR	18.8	7.8
Eng 2017[32]	13	77	75	38	15.0	38.0	NR	36.0	15.0	10.9
Whisenant 2015[33]	11	27	NR	NR	NR	NR	NR	NR	NR	NR

HTN: hypertension; MI: myocardial infarction; n: number; NR: not reported; PAD: peripheral artery disease; STS: Society of Thoracic Surgeons
a: Age is reported as mean for Eng[31] and Yoon,[4] and as median for the remaining studies.
+: A total of seven patients died before discharge and were excluded from our analysis
#: A total of 110 patients were excluded as antithrombotic strategy was unknown.
†: A total of 19 patients were excluded (9 because no therapy was initiated and 10 for lack of data available)
*: A total of eight patients were excluded (four because antithrombotic strategy was unknown and four as data regarding them was not provided).

Primary outcomes

In the pooled analysis, the incidence of clinical VT was 4.2% for all procedures (ViV, ViR, ViMAC) with significant differences between both groups. In fact, anticoagulation was associated with a lower risk of thrombosis in both clinical VT (1.1% *vs* 8.3%; OR: 0.18; 95% CI: 0.07 - 0.42; I^2 = 0%; p = 0.0001) and total VT (1.3% *vs* 8.5%; OR: 0.16; 95% CI: 0.07 - 0.37; I^2 = 0%; p < 0.0001).

This effect was accentuated when only considering ViV and ViR procedures, with clinical VT rates reaching 5.8% and slightly more pronounced differences between both groups (1.1% *vs* 9.4%; OR: 0.15; 95% CI: 0.05 - 0.46; I^2 = 0%; p = 0.0009).

Unfortunately, no analysis regarding post-discharge bleeding complications was feasible since each study reported only procedure-related bleeding or total bleeding, encompassing procedure-related events.

Forest plots of each analysis are represented in Figs. 2 and 3 and heterogeneity funnel plots are available in Appendix2(Appendix2:https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22905/15701).

To ensure the robustness of the findings, a sensitivity analysis was performed. No significant differences were observed when excluding studies with a higher risk of bias, nor when applying alternative analytical models or effect size measures. Egger's test was conducted for each analysis, with no statistically significant evidence of small-study effects or publication bias detected for clinical VT (p = 0.81), total VT (p = 0.52), and for ViV and ViR (p = 0.99).

The certainty of the evidence was assessed using the GRADE approach. All included studies were observational, which implies a starting rating of low certainty. However, the consistency of results (I^2 = 0%), the magnitude and statistical significance of the effect (OR 0.18; 95% CI: 0.07 - 0.42; OR: 0.16; 95% CI: 0.07 - 0.37), and the precision of estimates support an upgrade in confidence. Risk of bias was deemed serious due to the lack of adequate control for confounding in several studies, with Newcastle-Ottawa scores ranging from 5 to 7. Therefore, the overall certainty of the evidence was rated as moderate for the outcome of clinical valve thrombosis.

Secondary analysis

An additional analysis focused on mitral valves was performed. In this subset of patients, even though clinical VT rates only reached 2.8%, 71% of patients were on anticoagulants. Nonetheless, anticoagulation was also associated with a lower risk of VT (7.1% *vs* 1%; OR: 0.19; CI 95% CI: 0.06 -0.66, I^2: 0%) (Fig. 4).

Regarding valve type, our analysis found a non-significant association between previously implanted porcine valves and an increased risk of valve thrombosis in comparison to pericardial valves (OR: 1.72; CI: 0.66 - 4.48, CI 95%, I2: 0%) or to any other valve type (OR: 1.56; CI: 0.67 - 3.64, CI 95%, I2: 0%). Forest plots are available in Appendix 2 (Appendix 2: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22905/15701).

Regrettably, the available published data did not provide sufficient information to conduct analyses related to all-cause mortality or cardiovascular mortality.

DISCUSSION

Given the potential complications related to VT following TVI, extensive research on antithrombotic strategies for its prevention has been conducted, ultimately culminating in the development of randomized controlled trials (RCT). Specifically, two major RCTs compared an anticoagulant regimen with an antiplatelet regimen in TAVI patients: the ATLANTIS trial (apixaban *versus* single or dual antiplatelet strategy)[10] and the GALILEO trial (rivaroxaban and aspirin *versus* clopidogrel and aspirin).[11] In the GALILEO trial, patients on rivaroxaban faced, not only a higher risk of bleeding, but also a heightened risk of death or thromboembolic complications compared to those on an antiplatelet-based strategy. In an ATLANTIS substudy focused on VT,[20] patients receiving apixaban experienced an increase in non-cardiovascular deaths. Neither trial observed discernible clinical benefit in the anticoagulation arms.

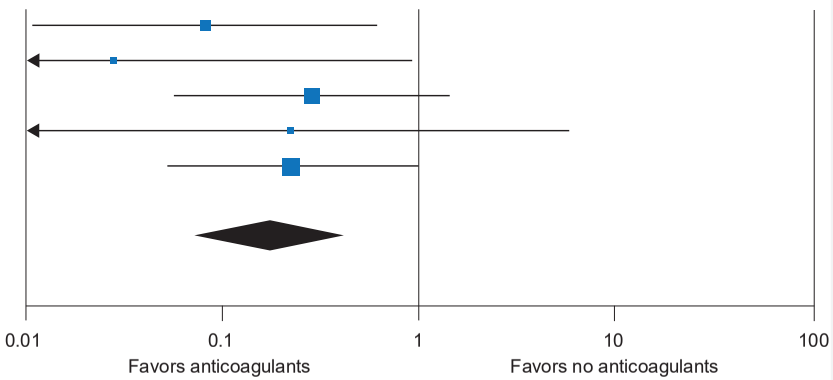
Based on this randomized controlled data, upon the release of the European Society of Cardiology (ESC) guidelines on valvular disease, recommendations for lifelong single antiplatelet therapy (SAPT) after TAVI and against anticoagulation in patients without other indication for its use, were published. As for transcatheter mitral valve implantation (TVMI), three months of VKA is suggested, but no formal recommendation was possible due to lack of data. Moreover, no specific recommendations were made for ViV, ViR or ViMAC procedures[21] as no substantial comparative data on the ideal antithrombotic treatment after discharge is available, creating a substantial evidence gap in this field.

In fact, the issue of VT following these procedures is of paramount importance given the apparent increased risk of thrombosis[13] and remarkably high VT rates in comparison to TAVI patients, as demonstrated in a previous observational study (11.6% *vs* 2.2%).[22]

Despite persistent research efforts, the exact factors contributing to this heightened risk remain elusive.[23-26] Nevertheless, some researchers have offered insightful perspectives on possible contributing factors. It has been suggested that the geometric constraints resulting from the encirclement of the valve's stent by a degenerated bioprosthesis may increase blood stagnation on the leaflets, potentially contributing to thrombosis.[23] Additionally, factors such as proximal valve implantation, under-expansion, and

Study or subgroup	Anticoagulant use Events	Total	No anticoagulant use Events	Total	Weight	Odds ratio M-H, Random, 95% CI
Abdel-Wahab 2018[31]	1	97	22	195	19.1%	0.08 [0.01, 0.62]
Eng 2017[32]	0	10	2	3	6.4%	0.03 [0.00, 0.93]
McElhinney 2019[30]	2	152	6	135	29.8%	0.29 [0.06, 1.44]
Whisenant 2015[33]	0	3	3	8	7.4%	0.22 [0.01, 5.80]
Yoon 2019[4]	3	295	5	116	37.2%	0.23 [0.05, 0.97]
Total (95% CI)		557		457	100.0%	0.08 [0.01, 0.62]
Total events	6		38			

Heterogenelty: Tau² = 0.00; χ^2 = 2.17, df = 4 (p = 0.70); I² = 0%
Test for overall effect: Z = 3.86 (p = 0.0001)



Study or subgroup	Anticoagulant use Events	Total	No anticoagulant use Events	Total	Weight	Odds ratio M-H, Random, 95% CI
Abdel-Wahab 2018[31]	1	97	22	195	16.3%	0.08 [0.01, 0.62]
Eng 2017[32]	2	67	4	14	20.1%	0.08 [0.01, 0.48]
McElhinney 2019[30]	2	152	6	135	25.5%	0.29 [0.06, 1.44]
Whisenant 2015[33]	0	3	3	8	63%	0.22 [0.01, 5.80]
Yoon 2019[4]	3	295	5	116	31.8%	0.23 [0.05, 0.97]
Total (95% CI)		614		468	100.0%	0.16 [0.07, 0.37]
Total events	8		40			

Heterogenelty: Tau² = 0.00; χ^2 = 1.84, df = 4 (p = 0.77); I² = 0%
Test for overall effect: Z = 4.34 (p < 0.0001)

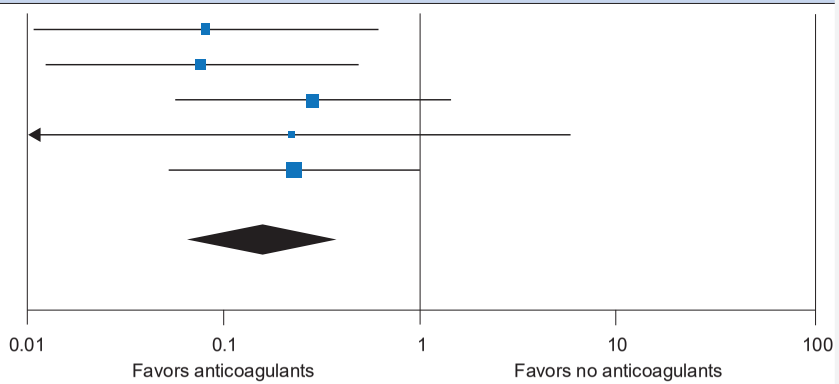


Figure 2 – Forest plot of meta-analysis for clinical VT (top) and total VT (bottom) following ViV, ViR and ViMAC
CI: confidence interval; M-H: Mantel–Haenszel

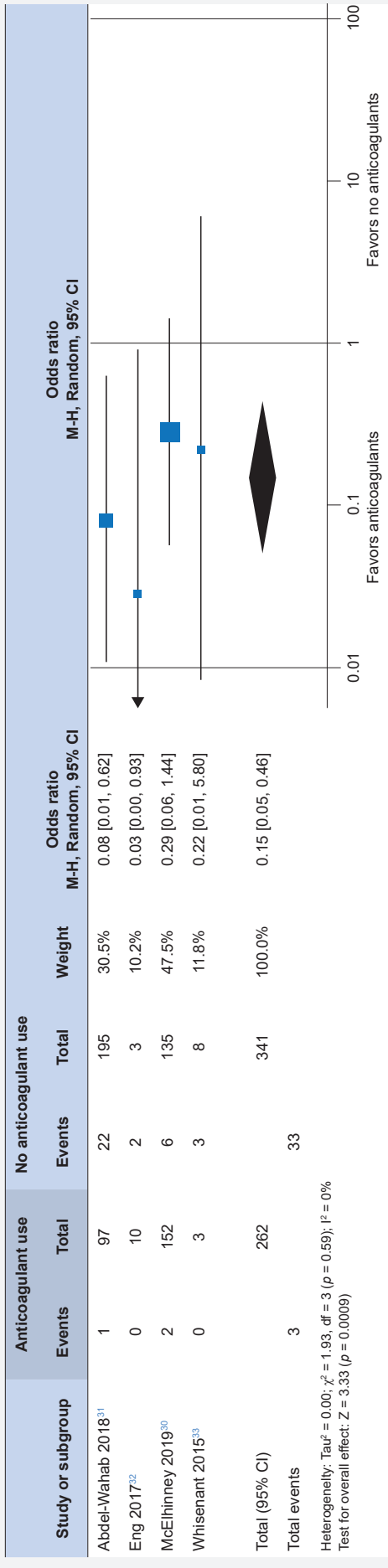


Figure 3 – Forest plot of metanalysis for clinical VT following ViV and ViR
CI: confidence interval; M-H: Mantel–Haenszel

device asymmetry have also been identified as possible contributors.[24]

Moreover, the potential severe complications of VT should not be undervalued.[15-17]

The influence of valve type on VT risk

There is no robust evidence on the relationship between valve type and VT in surgical cohorts, possibly due to the low incidence of events. In fact, in a large retrospective analysis of more than 4500 patients with surgically implanted bioprosthetic valves, early VT rates requiring reoperation in less than two years following implantation only reached 1.3%; however, every case occurred in porcine valves.[27] Whether porcine valves have increased thrombotic risk and, if so, the exact mechanisms for this risk remain to be explored.

Similar questions regarding the potential influence of valve type on VT risk arise in ViV patients. In fact, our study found that patients with previously implanted porcine stented valves tended to have higher VT rates compared to those with other valve types. However, this difference did not reach statistical significance. Notably, two additional studies were not included in our analysis due to insufficient data; nevertheless, these studies seem to align with that tendency. In one instance, five cases of ViV VT were reported, all of them in patients with porcine valves (Mosaic or Hancock II),[22] and in the other instance, ten cases of ViV VT were observed, with nine occurring in patients with previously implanted stented porcine valves.[28]

Further research to support or refute this tendency is needed.

Bleeding risk and death

Data regarding bleeding and death is severely lacking in this population. No published study reports such a comparison between anticoagulated and non-anticoagulated patients. This gap makes a net clinical gain analysis impossible, which would significantly increase the strength of our findings. Data regarding these two endpoints needs to be addressed by future research as it plays a pivotal role in the decision for the optimal antithrombotic strategy.

Exploring the role of anticoagulation after VIV, VIR and VIMAC procedures

Much like the historical debate surrounding antithrombotic treatment after TAVI, there is a contentious discourse concerning the role of anticoagulation following ViV, ViR and ViMAC. The challenge lies in evaluating the potential benefits of reducing thrombotic events in comparison to the associated risk of bleeding – a balance that has traditionally been unfavourable for TAVI patients.[10,11] However, for ViV patients, no such conclusion is possible.

Quantifying the bleeding risk remains unfeasible, given the absence of data. However, considering the significantly

increased thrombotic risk, the potential benefits of anticoagulation appear to be greater, especially given the remarkable efficacy of anticoagulation in decreasing clinical VT cases, which could yield substantial benefits for this population.

If the potential benefits outweigh the associated risks is still questionable and further studies are needed to address these unanswered questions.

Future approach: the BASILICA procedure

The BASILICA procedure is a technique designed to lacerate aortic valve leaflets, whether native or bioprosthetic, to prevent coronary artery occlusion in high-risk TAVI patients.[29] While initially developed for this specific high-risk situation, this procedure may assume a pivotal role in managing high-thrombotic risk patients, considering recent publications on the hemodynamic benefits of the procedure. Using computational simulations for two types of bioprosthetic transcatheter valves (SAPIEN 3 and Evolut Pro), BASILICA significantly decreased high-risk thrombotic areas, with laceration of two leaflets as the superior technique when compared to the laceration of one or three leaflets. This two-leaflet approach led to a significant reduction in thrombotic risk areas, decreasing from 27.06% to 15.42% with the SAPIEN valve and experiencing a remarkable decline from 22.31% to a 0.57% with the Evolut device.[30]

While real-world data on the BASILICA procedure remains scarce, despite its increasing popularity, these findings suggest the potential utility of this procedure in managing high-thrombotic risk patients.

Limitations

We identified several limitations in this study. Firstly, the absence of data comparing mortality and bleeding events between anticoagulated and non-anticoagulated groups hinders our ability to perform a comprehensive net clinical benefit analysis, which could have significantly enriched the depth of our research. Furthermore, the lack of randomized controlled trials within the selected studies decreases the robustness of our findings.

Moreover, due to the limited available body of evidence, no analysis divided by procedure (ViV, ViR, and ViMAC) or by valve position (aortic, mitral or tricuspid) was possible.

Additionally, the analysis conducted on the different valve types was constrained by the inclusion of only two studies. Expanding this aspect with more publications would undoubtedly strengthen the overall analysis.

As the field continues to evolve, we anticipate that future research will contribute with more evidence, potentially mitigating these limitations and allowing for a more comprehensive understanding of anticoagulation strategies in ViV, ViR, and ViMAC procedures.

CONCLUSION

While our understanding of anticoagulation in post-discharge

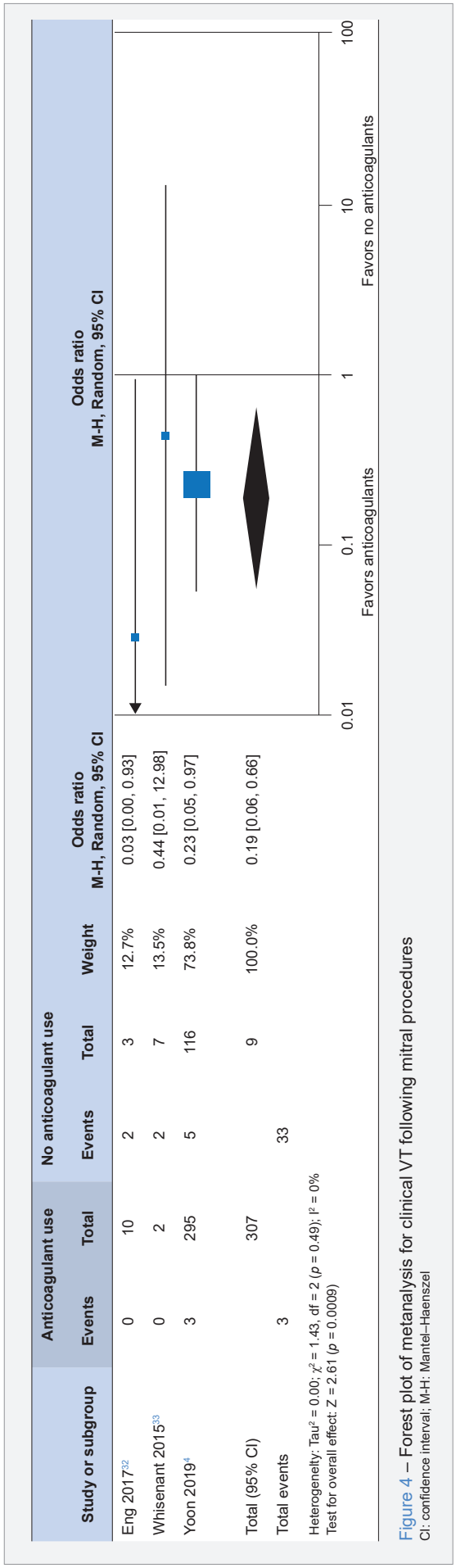


Figure 4 – Forest plot of metanalysis for clinical VT following mitral procedures
CI: confidence interval; M-H: Mantel–Haenszel

ViV, ViR, and ViMAC patients remains a work in progress, the thrombotic risk in these patients is higher and might benefit from a different antithrombotic strategy. Whether there is a significant benefit for any patients, or specifically for those at low bleeding risk and/or high thrombotic risk, remains to be explored.

Our work highlights the urgent need for further research to bridge the knowledge gaps in this area.

AUTHOR CONTRIBUTIONS

GTB, GFC: Literature search, writing of the manuscript.
JDS, LG: Critical review of the manuscript.
All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Kiyose AT, Suzumura EA, Laranjeira L, Buehler AM, Santo JA, Berwanger O, et al. Comparison of biological and mechanical prostheses for heart valve surgery: a systematic review of randomized controlled trials. Arq Bras Cardiol. 2019;112:292-301.
2. Bartus K, Sadowski J, Litwinowicz R, Filip G, Jasinski M, Deja M, et al. Changing trends in aortic valve procedures over the past ten years—from mechanical prosthesis via stented bioprosthesis to TAVI procedures—analysis of 50,846 aortic valve cases based on a Polish National Cardiac Surgery Database. J Thorac Dis. 2019;11:2340-9.
3. Rodriguez-Gabella T, Voisine P, Puri R, Pibarot P, Rodés-Cabau J. Aortic bioprosthetic valve durability. J Am Coll Cardiol. 2017;70:1013-28.
4. Yoon SH, Whisenant BK, Bleiziffer S, Delgado V, Dhoble A, Schofer N, et al. Outcomes of transcatheter mitral valve replacement for degenerated bioprostheses, failed annuloplasty rings, and mitral annular calcification. Eur Heart J. 2019;40:441-51.
5. Bruno F, Elia E, D'Ascenzo F, Marengo G, Deharo P, Kaneko T, et al. Valve-in-valve transcatheter aortic valve replacement or re-surgical aortic valve replacement in degenerated bioprostheses: a systematic review and meta-analysis of short and midterm results. Catheter Cardiovasc Interv. 2022;100:122-30.
6. Kilic A, Acker MA, Gleason TG, Sultan I, Vemulapalli S, Thibault D, et al. Clinical outcomes of mitral valve reoperations in the United States: an analysis of the society of thoracic surgeons national database. Ann Thorac Surg. 2019;107:754-9.
7. Xu X, Liu H, Gu J, Li M, Shao Y. Valve-in-valve/valve-in-ring transcatheter mitral valve implantation vs. redo surgical mitral valve replacement for patients with failed bioprosthetic valves or annuloplasty rings: a systematic review and meta-analysis. Heliyon. 2023;9:e16078.
8. Sá MP, Eynde J Van den, Simonato M, Cavalcanti LR, Doulamis IP, Weixler V, et al. Valve-in-valve transcatheter aortic valve replacement versus redo surgical aortic valve replacement. JACC Cardiovasc Interv. 2021;14:211-20.
9. Ahmad D, Yousef S, Kliner D, Brown JA, Serna-Gallegos D, Toma C, et al. Outcomes of valve-in-valve transcatheter aortic valve replacement. Am J Cardiol. 2024;215:1-7.
10. Collet JP, Belle EV, Thiele H, Berti S, Lhermusier T, Manigold T, et al. Apixaban vs. standard of care after transcatheter aortic valve implantation: the ATLANTIS trial. Eur Heart J. 2022;43:2783-97.
11. Dangas GD, Tijssen JG, Wöhrle J, Søndergaard L, Gilard M, Möllmann H, et al. A controlled trial of rivaroxaban after transcatheter aortic-valve replacement. N Engl J Med. 2020;382:120-9.
12. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2022;43:561-632.
13. Mehilli J, Giannini C. Transcatheter valve-in-valve implantation for failed surgical bioprostheses – some answers and many unanswered questions. EuroIntervention. 2020;16:529-31.
14. Rheude T, Pellegrini C, Cassese S, Wiebe J, Wagner S, Trenkwalder T, et al. Predictors of haemodynamic structural valve deterioration following transcatheter aortic valve implantation with latest-generation balloon-expandable valves. EuroIntervention. 2020;15:1233-9.
15. Aktuerk D, Mirsadraee S, Quarto C, Davies S, Duncan A. Leaflet thrombosis after valve-in-valve transcatheter aortic valve implantation: a case series. Eur Heart J Case Rep. 2020;4:1-6.
16. Notaristefano F, Reccia MR, Notaristefano S, Annunziata R, Sclafani R, Ambrosio G, et al. Bailout surgical explantation of a transcatheter valve-in-valve for subacute thrombosis: when there is no time for anticoagulation. Cardiovasc Revasc Med. 2018;19:536-9.
17. Chu J, Nath N, Attanasio S. Thrombolysis for cardiogenic shock secondary to aortic bioprosthetic valve-in-valve thrombosis. Cureus. 2022;14:e33141.
18. Rosseel L, Backer OD, Søndergaard L. Clinical valve thrombosis and subclinical leaflet thrombosis following transcatheter aortic valve replacement: is there a need for a patient-tailored antithrombotic therapy? Front Cardiovasc Med. 2019;6:44.
19. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials. Circulation. 2011;123:2736-47.
20. Montalescot G, Redheuil A, Vincent F, Desch S, Benedictis M De, Eltchaninoff H, et al. Apixaban and valve thrombosis after transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2022;15:1794-804.
21. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2022;43:561-632.
22. Jose J, Sulimov DS, El-Mawardy M, Sato T, Allali A, Holy EW, et al. Clinical bioprosthetic heart valve thrombosis after transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2017;10:686-97.
23. Vahidkhah K, Javani S, Abbasi M, Azadani PN, Tandar A, Dvir D, et al. Blood stasis on transcatheter valve leaflets and implications for valve-in-valve leaflet thrombosis. Ann Thorac Surg. 2017;104:751-9.
24. Mangione FM, Jatene T, Gonçalves A, Fishbein GA, Mitchell RN, Pelletier MP, et al. Leaflet thrombosis in surgically explanted or post-mortem TAVR valves. JACC Cardiovasc Imaging. 2017;10:82-5.
25. Dangas GD, Weitz JI, Giustino G, Makkar R, Mehran R. Prosthetic heart valve thrombosis. J Am Coll Cardiol. 2016;68:2670-89.
26. Brown ML, Park SJ, Sundt TM, Schaff HV. Early thrombosis risk in patients with biologic valves in the aortic position. J Thorac Cardiovasc Surg 2012;144:108-111.

27. Khan JM, Dvir D, Greenbaum AB, Babaliaros VC, Rogers T, Aldea G, et al. Transcatheter laceration of aortic leaflets to prevent coronary obstruction during transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2018;11:677-89.
28. Plitman Mayo R, Yaakobovich H, Finkelstein A, Shadden SC, Marom G. Impact of BASILICA on the thrombogenicity potential of valve-in-valve implantations. J Biomech. 2021;118:110309.
29. Eng MH, Kargoli F, Wang DD, Frisoli TM, Lee JC, Villablanca PS, et al. Short- and mid-term outcomes in percutaneous mitral valve replacement using balloon expandable valves. Catheter Cardiovasc Interv. 2021;98:1193-203.
30. McElhinney DB, Aboulhosn JA, Dvir D, Whisenant B, Zhang Y, Eicken A, et al. Mid-term valve-related outcomes after transcatheter tricuspid valve-in-valve or valve-in-ring replacement. J Am Coll Cardiol. 2019;73:148-57.
31. Abdel-Wahab M, Simonato M, Latib A, Goleski PJ, Allali A, Kaur J, et al. Clinical valve thrombosis after transcatheter aortic valve-in-valve implantation. Circ Cardiovasc Interv. 2018;11:e006730.
32. Eng MH, Greenbaum A, Wang DD, Wyman JD, Arjomand H, Yadav P, et al. Thrombotic valvular dysfunction with transcatheter mitral interventions for postsurgical failures. Catheter Cardiovasc Interv. 2017;90:321-8.
33. Whisenant B, Jones K, Miller D, Horton S, Miner E. Thrombosis following mitral and tricuspid valve-in-valve replacement. J Thorac Cardiovasc Surg. 2015;149:e269.