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ORIGINAL RESEARCH

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Subclinical leaflet thrombosis and anticoagulation strategy following trans-catheter aortic valve replacement: A systematic review

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Abstract

Objective: Subclinical leaflet thrombosis (SLT) develops in 15% of patients undergoing trans-catheter aortic valve replacement (TAVR). TAVR is a procedure in which a faulty aortic valve is replaced with a mechanical one. An aortic valve replacement can be done with open-heart surgery; this is called surgical aortic valve replacement (SAVR). A significant problem is defining the best course of treatment for asymptomatic individuals with SLT post-TAVR, including the use of oral anticoagulation (OAC) in it.

Study design: Systematic review.

Method: The most pertinent published research (original papers and reviews) in the scientific literature were searched for and critically assessed using the online, internationally indexed databases PubMed, Medline, and Cochrane Reviews. Keywords like "Transcatheter valve replacement" and "Subclinical leaflet thrombosis" were used to search the papers. Selected studies were critically assessed for inclusion based on predefined criteria.

Results: The review examined the prevalence and characteristics of SLT after TAVR. To note, the incidence of SLT is seen to be higher in TAVR compared SAVR. Dual antiplatelet therapy, which is utilized in antithrombotic regimens post-TAVR, can possibly hasten SLT progression which could result in the impaired mobility of leaflets and the worsening of pressure gradients.

Conclusion: The use of dual antiplatelet drugs in routine antithrombotic therapy tends to accelerate initial subclinical leaflet thrombosis after TAVI, which results in a developing restriction of leaflet mobility and an increase in pressure differences.

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KEYWORDS
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1 | INTRODUCTION

In bioprosthetic aortic valves after TAVR, computed tomography (CT) was employed to identify asymptomatic leaflet thrombosis.[1] Two different entities are recognized, namely, "hypoattenuated leaflet thickening (HALT)" and "restricted leaflet motion (RELM)." HALT is the thickening of valve leaflets as a result of abnormal thrombosis. RELM, a secondary consequence of HALT, leads to the dysfunction of valve. The conjunction of low attenuation and restricted motion (LARM) is a sign of "Hypoattenuation affecting motion (HAM)."

"4DCT (four-dimensional CT)" has now become the standard to determine which patients are at risk of HALT and RELM and is comparable to transesophageal echocardiography (TEE). The hypodense leaflet lesions seen on CT in diastole are used to assess HALT, which requires visualization of leaflet coaptation. The RELM is assessed in systole and maximal leaflet opening. The leaflet is classified as mildly (<50%), moderately (50%–69%) or severely (70%–99%) restricted or immobile. HALT and 50% or more restriction means HAM.

The use of TAVR has been demonstrated to be a successful therapy option for those with evident, severe cardiovascular valve stenoses at greater risk of requiring surgery (Figure 1). The "NOTION trial (Nordic Aortic Valve Intervention)" also demonstrated that TAVR can be a smart choice for those with a moderate risk level. Following TAVR, antithrombotic therapy is to prevent transcatheter heart valve (THV) thrombosis.[2]

Although it is far less common with "bioprosthetic heart valves (BHVs)," valve thrombosis is a well-known problem with "mechanical heart valves (MHVs)." MHVS are quite thrombogenic, but they are more wear-resistant. These valves have gone from the early caged ball (e.g., Starr-Edwards valve) and tilting disc design (e.g., Bjork-Shiley valve) to the current bileaflet valve mounted on a Teflon- or Dacron-covered sewing ring. BHVs have lower thrombogenicity than MHV and better hemodynamic characteristics, but they are less durable.[3] Throughout the remaining period of their lifespans, individuals receiving mechanical heart prostheses must take oral anticoagulant therapy. In contrast, individuals who undergo a transcatheter or surgical bioprosthetic heart valve seem to benefit from long-term antiplatelet medication (6 months to 1 year). Even though bioprosthetic heart valves are not as thrombogenic, recent studies have shown that several surgical aortic transcatheter bioprostheses can develop valve/leaflet thrombosis.[4] Therefore, the difference between symptomatic valve thrombosis and asymptomatic leaflet thrombosis must be made. Clinical valve thrombosis is distinguished by thrombosis on the mechanical heart valve on echo or multidetector computed tomography (MDCT), medical synthetic valve dysfunction, and the distinctive appearance of a moving mass.[5] The inability of the prosthetic valve to operate properly due to diminished leaflet motion or reduced leaflet coaptation must be distinguished from other factors, such as valve degradation or the formation of fibrous pannus. Cardiovascular symptoms or a left-sided thrombo-embolic occurrence are examples of clinical signs of this illness.[6,7]

1.1 | Transcatheter aortic valve replacement (TAVR)

Aortic valve stenosis, or thickening of the valve, prevents the aortic valve from opening fully. TAVR is a less invasive replacement of the

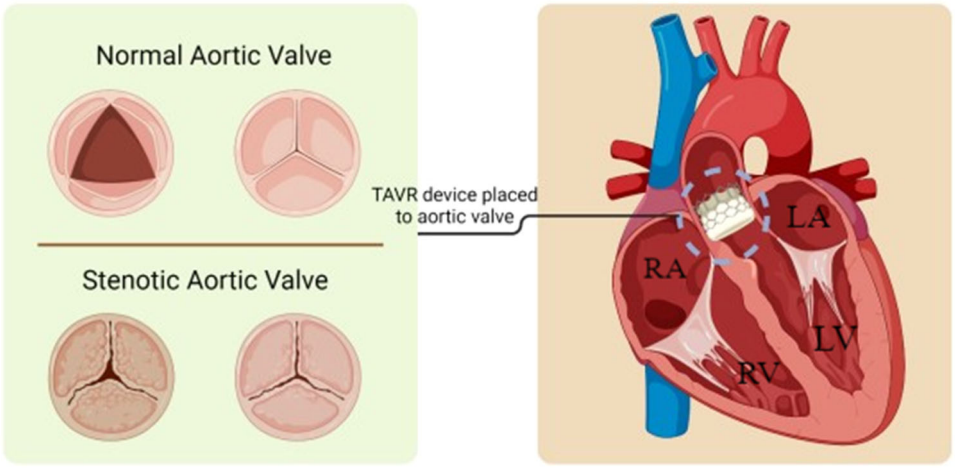

FIGURE 1 Transcatheter aortic valve procedure (original figure, created using Biorender). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

aortic valve method. The aortic valve is one of four heart valves and is the final one encountered by oxygenated blood as it leaves the heart. It is also called aortic semilunar due to its semilunar shape. It is between the left ventricle and the aorta to ensure that oxygen-rich blood does not flow back into the left ventricle. Inadequate valve opening results in reduced efficacy of the circulatory system in propelling blood throughout the body.[8]

Replacement of the aortic valve via catheter can help those with clinically severe aortic stenosis at exceedingly dangerous or extremely high risk for surgery. Although the most recent study has shown that it is no less successful than SAVR in this circumstance, aortic valve replacement (TAVR) has also been utilized to treat patients with moderate risk for surgery.[8]

Before TAVR, MDCT had established itself as the standard of excellence for determining prosthetic sizing. Research from the years,[7,8] and more recently[5,9] has clarified its application in evaluating the shape and integrity of leaflets following surgery. Compared to transesophageal echocardiography (TEE), MDCT delivers great spatial image resolution, has lower intraoperator variation, and is often noninvasive. These factors make MDCT a viable imaging tool for assessing leaflet shape. However, TEE is more often than not considered to be more cost-effective in some clinical circumstances. TEE is cheaper to provide and in some cases can be done at the patient's bedside, eliminating the need for patient transfer to radiology departments. Though TEE may be cost-effective, it is contraindicated in patients with esophageal disease such as esophageal strictures, esophageal varices, esophageal tumors, recent esophageal surgery, or severe esophagitis, due to the risk of complications, limiting its applicability in these cases.

Subclinical leaflet thrombosis (SLT), which was discovered using MDCT in the setting of TAVR and, to a lesser extent, following bioprosthetic SAVR, has been shown in recent investigations.[7,10] SLT is a type of leaflet thrombosis (LT). Transvalvular gradient measures in SLT patients are within the normal range. Yet, MDCT has detected HALT, and the patients are asymptomatic, unlike explicit clinical leaflet thrombosis, which can result in overt valve failure and symptoms of cardiovascular disease.[11] In observational investigations, most individuals with MDCT-defined LT were categorized as SLT and asymptomatic at diagnosis.[10]

When the use of TAVR is expanded to populations with lower surgical risk, knowing the process of SLT and its curative properties will grow even more crucial. There are legitimate worries regarding the impact of SLT on prosthetic durability and integrity, even though younger patients may get TAVR in the not-too-distant future and remain alive longer with these implants.[12]

1.1.1 | Transcatheter aortic valve implantation (TAVI)

TAVI has emerged as a widely accepted treatment option for people with symptomatic aortic stenosis who are not eligible for surgery or have a very high risk.[13] Surgical aortic valve replacement was once among the most prevalent forms of therapy for serious aortic stenosis. The most frequent or only option for treating severe symptomatic aortic stenosis is no more surgical repair due to advancements in transcatheter device development during the past 10 years. TAVI has emerged as a significant alternative to surgery to replace the aortic valve for patients with stenosis of the aorta who are at moderate or severe risk for surgery.

Considering the technological maturity of TAVI, the best approach has not been evaluated in many guidelines for postprocedural antithrombotic therapy. Extrapolation from surgical bioprosthetic valves for the aorta has limitations due to the declining quality of the data supporting the implementation of various bioprosthetic valves and the medical care of individuals.[6]

1.1.2 | Surgical aortic valve replacement (SAVR)

Patients with serious aortic stenosis or cardiac valve shrinkage may benefit from (SAVR). Depending on the surgeon's operating method, the incision's length and position may change.[14]

Unlike any significant procedure, SAVR may have risks and disadvantages. Blood clots, bleeding, infections, arrhythmia, and stroke are among them. Therefore, TAVR may offer a superior and less hazardous treatment option for frail, malnourished elderly patients.[14]

Subclinical leaflet thrombosis, an uncommon phenomenon, has just been discovered despite the unresolved durability issue. Recent research has shown that SLT can occur in many individuals getting bioprostheses for aortic stenosis, whether or not there is reduced leaflet movement.[5] Hypoattenuated leaflet thrombosis, or HALT, is the term used to describe localized leaflet thrombosis on MDCT. Reduced leaflet mobility/motion (RELM), also known (as HAM), is a more severe type of leaflet illness if HALT is present. Retrospective electrocardiographically controlled CT, also known as 4-dimensional MDCT, is required to assess the valve for RELM and HAM. These events have been described[15] with regard to several surgical bioprostheses and TAVR valves.

1.2 | Antithrombotic strategy

Without any other OAC indication, the American and European recommendations advise routinely administering dual antiplatelet therapy (DAPT) for the initial three to 6 months following TAVR. In addition, the US standards advise patients with low bleeding risks to think about OAC therapy for the initial 3 months after installing bioprosthetic valves.[16] Although the US guidelines offer no specific recommendations, the European Union supports the combination of vitamin K-antagonist (VKA) with aspirin or thienopyridine for people with atrial fibrillation. This is so that EU regulations can account for each patient's unique bleeding risk. Treatment with OAC, as opposed to antiplatelet therapy (APT), has been proven to halt the progression of clinical and subclinical valve thrombosis. As a result, OAC treatment seems to, at least temporarily, enhance leaflet mobility in HAM patients.[4,5,17]

Anyone at low risk of bleeding should consider taking oral anticoagulant medication with an antagonist to vitamin K as a viable therapeutic option for a minimum of a 3-month following TAVI, according to the 2017 AHA/ACC targeted update.[7] Aspirin or clopidogrel are frequently administered alongside oral anticoagulation medicine for TAVI individuals who possess additional indications for oral anticoagulation. Oral anticoagulation medication was originally advised for the initial 3 months following surgery for bioprosthetic aortic valves while the sutured ring is endothelializing.[13]

However, the notion that antiplatelet medicine alone might provide a superior risk-benefit analysis was refuted by a research investigation. Recent European and American guidelines[16] state that low-dose aspirin use should be considered because it is connected to a greater likelihood of bleeding during the initial 3 months following the installation of a bioprosthetic aortic valve.

Both new intravenous anticoagulants and vitamin-K antagonists appear to stop this from occurring.[2] Because this condition may have a temporal dynamic pattern of advancement, it is not yet known whether it will require only a short period of therapy or lifetime treatment with these anticoagulants taken by mouth.[11] This demonstrates that in some cases, without a change in antithrombotic medication, subclinical leaflet thrombosis can occur or reverse at any time after the valve replacement. Consequently, it's possible that short thrombosis (anticoagulant or antiplatelet for just a few days postprocedure) won't always work to stop early leaflet thrombosis.

Initial research on subclinical leaflet thrombosis found that it occurred 10%–15% more often in transcatheter bio-prosthetic valves than in surgical ones in patients who underwent aortic valve replacement via a catheter (TAVR). Due to the aortic valve's gradients appearing to be normal on transthoracic echocardiograms, the finding was frequently overlooked. A few research investigations have found a connection between neurologic disorders (such as stroke or transient ischemic attacks) and asymptomatic leaflet thrombosis.[18] Anticoagulation therapy is effective in both treating and postponing the development of asymptomatic leaflet thrombosis throughout both randomized studies and databases. To comprehend the natural course of asymptomatic leaflets thrombosis, the US Food and Drug Administration, or FDA, ordered the inclusion of CT substudies within the largely risk-free TAVR research. Numerous industry-sponsored randomized studies were conducted concurrently[19] to examine the effects of continued anticoagulation after TAVR on clinical outcomes and asymptomatic leaflet thrombosis.

1.3 | Objectives

- To examine the prevalence, physical effects, and potential causes of asymptomatic leaflet thrombosis (SLT) after a transcatheter replacement of the aortic valve (TAVR).
- Assessing the efficacy of existing treatment options for patients experiencing SLT post-TAVR.

2 | METHODOLOGY

2.1 | Design

The study followed the recommendations made by the Centre of Reviews and Dissemination (CRD, 2009) and employed a thorough and well-founded design that included comprehensive statistical evaluation and grand narrative analysis. The research process involved several essential steps, starting with carefully selecting an appropriate search technique. In executing the search strategy, strict criteria for inclusion and exclusion were meticulously considered. Subsequently, data extraction and synthesis were conducted based on the results obtained from the search process. These exacting methods ensured that the pertinent research on asymptomatic leaflet clotting after a transcatheter replacement of the aortic valve was assessed systematically and objectively.

2.2 | Search method

PRISMA was used to conduct the current systematic review (Figure 2). The research team gathered pertinent data from numerous websites and internet search engines using logical and systematic procedures. In the Cochrane Database and PubMed, search phrases “subclinical leaflet thrombosis” and “transcatheter aortic valve replacement” were used with various modifications and abbreviations, such as “SLT OR hypoattenuating leaflet thickening” (as shown in Table 1). Upon meeting the inclusion criteria, the entire text of selected publications was thoroughly examined while looking through the references of pertinent evaluations to find further qualified studies (Table 2).

2.3 | Inclusion criteria

The following were included in the study selection criteria to ensure a thorough examination of SLT after a TAVR:

1. Inclusion of case reports, meta-analysis, systematic reviews, research investigations, observational studies, and randomized controlled trials that specifically focus on subclinical leaflet thrombosis and anticoagulation after TAVR.
2. Including research on patient outcomes and the medical importance of asymptomatic leaflet thrombosis following TAVR. This review's primary goals are to describe the efficacy of therapies for individuals having SLT as well as to determine whether the presence of SLT affects the likelihood of dangerous thrombotic episodes.

2.4 | Exclusion criteria

The articles included in the review were carefully chosen based on specific criteria. Only studies directly addressing subclinical leaflet thrombosis and anticoagulation were considered eligible for

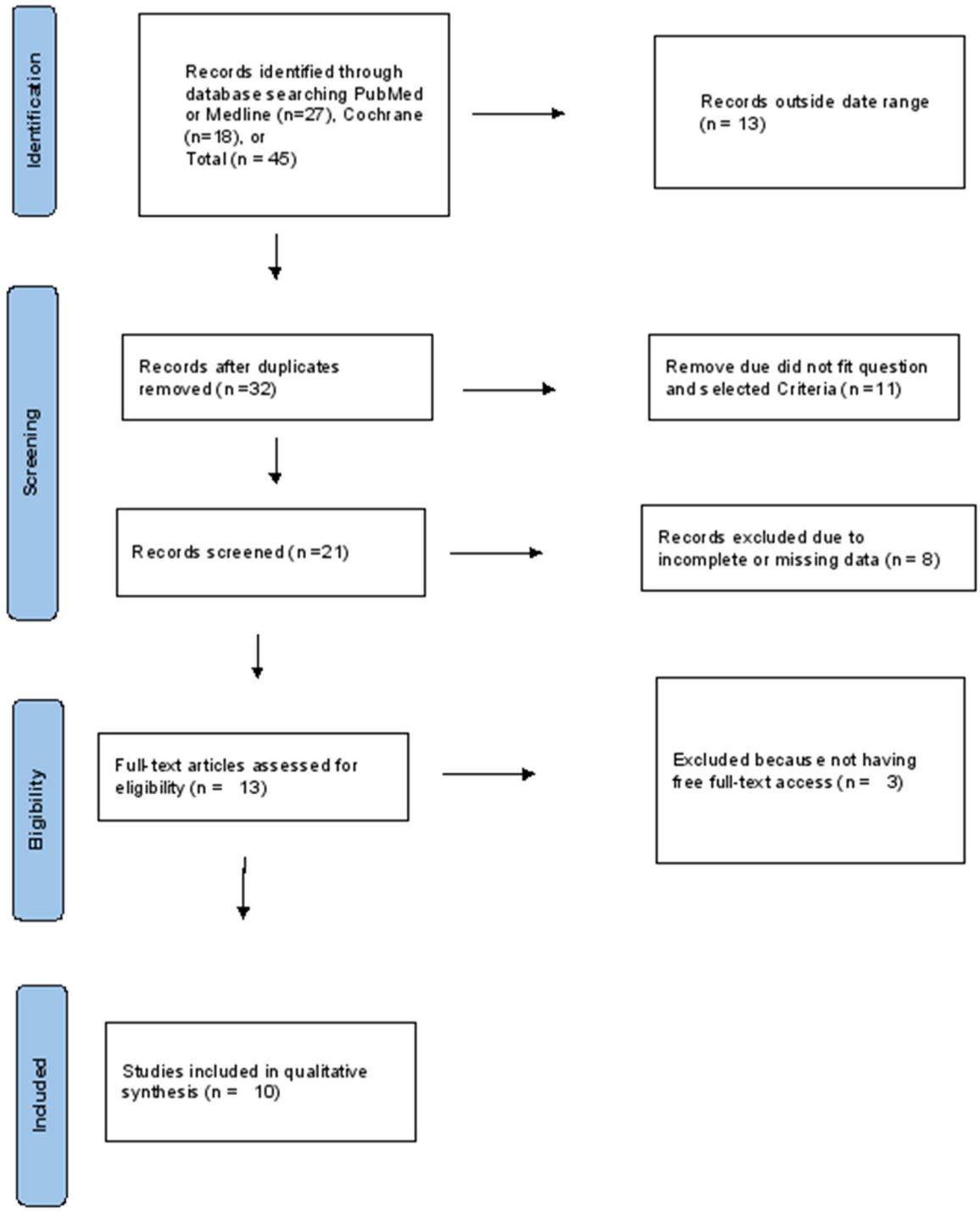

FIGURE 2 Showing the PRISMA flowchart.

TABLE 1 Search strategy used to find relevant articles.

Search no.	Search terms	Results
#1	(Subclinical Leaflet Thrombosis) AND (Transcatheter Aortic Valve Replacement)	23
#2	(Subclinical Leaflet Thrombosis SLT [Title/Abstract]) OR (Hypoattenuating Leaflet Thickening [Title/Abstract])	4
#3	(Subclinical Leaflet Thrombosis) AND (Transcatheter Aortic Valve Replacement) [Title/Abstract]	18

TABLE 2 Synthesis of data from the included studies in this review.

No	References	Study type	Objective	Conclusion
1	Chakravarty et al.[5]	Review	Learn the prevalence of subclinical leaflet thrombosis in transcatheter and surgical aortic valves and how new oral anticoagulants affect this issue	Subclinical leaflet thrombosis occurs more commonly in transcatheter valves than in surgical valves in bioprosthetic aortic valves. Anticoagulation, but not dual antiplatelet therapy, prevented or treated subclinical leaflet thrombosis more successfully.
2	Ruile et al.[13]	Clinical trial	To look into how the antithrombotic therapy affects the progression of leaflet thickening	Depending on whether anticoagulation was present or not, the evolution of leaflet constriction took a fundamentally different progress, with constant regression under phenprocoumon but predominantly progression under antiplatelet treatment alone. Transvalvular pressure gradient alterations were correlated with changes in leaflet restriction.
3	Holy et al.[20]	A retrospective study	The goal of this study was to evaluate safety and efficacy outcomes in relation to the type of antithrombotic medication utilized following TAVR	Without statistically significant increases in bleeding problems, OAC after TAVR appears to lower the incidence of clinical valve thrombosis
4	Jilaihawi et al.[21]	Review	To analyze the scientific approach to evaluating leaflet thrombosis in aortic bioprostheses shown on CT	With a high correlation to transesophageal echocardiography findings, subclinical leaflet thrombosis is easily diagnosed noninvasively by technically acceptable CT. The hypoattenuated leaflet thickness and reduced leaflet motion were recognized as the CT characteristics.
5	Rashid et al.[12]	Review	This paper discusses current treatment options and future trials that may clarify the optimal antithrombotic. Strategies of subclinical leaflet thrombosis.	Patients with symptomatic severe aortic stenosis at high or extremely high surgical risk can benefit from transcatheter aortic valve replacement. Recent research has shown that TAVR is at least as effective as surgical aortic valve replacement (SAVR) when used to treat patients at intermediate surgical risk.
6	Kanjanauthai et al.[22]	Review	The current review article addresses leaflet thrombosis primarily after TAVR and describes the range of this disease process, its diagnostics, available treatments, and the field's future directions	Subclinical leaflet thrombosis in THVs is a novel entity that needs to be better understood. The disease process has the potential to worsen, leading to eventual structural valve failure and clinical symptoms.
7	Rosseel et al.[16]	Review	Reviewing most current knowledge of clinical valve thrombosis and subclinical leaflet thrombosis in transcatheter aortic bioprosthesis, focusing on antithrombotic treatment	Results indicated that oral anticoagulant therapy protects against and resolves clinical valve thrombosis and subclinical leaflet thrombosis
8	Sannino et al.[23]	A meta-analysis	This article aimed to assess and describe the incidence of leaflet thrombosis and determine risk factors for THV thrombosis	Although patients on anticoagulants appear to be at lower risk of LT, the available evidence does not allow formulation of recommendations for prophylactical anticoagulation nor routine computed tomography after transcatheter aortic valve replacement
9	Bogyi et al.[24]	A meta-analysis and systematic review	Assessing the clinical significance of subclinical leaflet thrombosis (SLT) after a transcatheter replacement of the aortic valve	Moving to OAC seems to work for SLT resolution. Because SLT increases the risk of stroke or severe ischemic incidents in the included population, more study is needed to evaluate whether screening procedures for SLT and appropriate antithrombotic therapy improve valve performance and clinical prognosis
10	Cahill et al.[15]	Review	To assess the impact of OAC on patients who have had transcatheter aortic valve replacement	The findings demonstrated that OAC is useful in preventing asymptomatic leaflet thrombosis. However, OAC did not result in a therapeutic benefit over the study period and may even be harmful to some individuals due to the risk of bleeding.

inclusion, ensuring relevance to the topic. Non-English papers were excluded. Additionally, articles without the full text of the source were removed. The review focused solely on articles discussing SLT and TAVR, therapeutic interventions, and associated benefits.

2.5 | Data collection method

The systematic review included in this study involved a comprehensive search of relevant articles from multiple databases using the Zotero plugin for Microsoft Edge. Titles and abstracts were imported into the Zotero desktop application for efficient data organization. The findings from the various investigations were then consolidated into tables within a Word document, facilitating further analysis. The review provided an in-depth analysis of the relevant literature focusing on the results for patients and SLT after TAVR.

2.6 | Information sources

1. PubMed or Medline (2007–2022).
2. Cochrane Reviews (2007–2022).

3 | RESULT

Our systematic review identified a significant body of literature addressing SLT following TAVR. Analysis of the selected studies revealed key findings regarding the incidence, characteristics, and clinical implications of SLT in this patient population.

Several studies have noticed a higher rate of SLT in TAVR patients than in those who underwent SAVR. Significantly, SLT was noted in about 10%–15% of the patients undergoing transcatheter bioprosthetic valves. This implies that SLT is a probable consequence after TAVR.

Additionally, the evaluation showed the possible influence of antithrombotic therapy on the rate of SLT progress. Dual antiplatelet therapy, commonly used in the antithrombotic regimens after TAVR, may have a potential effect of quickening the process of SLT. The speeding-up process might cause the leaflets to lose mobility and result in high-pressure gradients that finally would affect the valve function.

Overall, the results of our systematic review underscore the importance of further research to better understand the mechanisms and clinical significance of SLT post-TAVR. Improved knowledge in this area will inform the development of optimal management strategies aimed at optimizing patient outcomes and maximizing the longevity of bioprosthetic valves.

4 | DISCUSSION

According to the valvular heart condition regulations from the American College of Cardiology/American Heart Association in 2017 and the European Society of Cardiology for the year 2020,[25] patients are advised to undergo TAVR rather than SAVR if they are thought to be at a higher risk for perioperative complications. Additionally, individuals at moderate risk for perioperative morbidity are thought to benefit from TAVR.[26] In particular, new research indicates that the indications for TAVR may be expanded, given its superior results to SAVR in low-risk groups of individuals suffering from serious aortic stenosis.[5,27]

4.1 | Bioprosthetic aortic heart valves

Over time, there has been a gradual shift in the choice of valve replacements for individuals with severe, symptomatic aortic stenosis, moving from mechanical to bioprosthetic valves.

This shift can be linked to several things, including the desire to avoid oral anticoagulant medication (OAC) and the conviction that transcatheter valves for the heart (THV) can successfully repair surgical artificial valves that have degraded over time. In addition, a transcatheter replacement of the aortic valve is becoming more popular, particularly among elderly patients with aortic stenosis, according to randomized clinical trials. It is important to remember that compared to mechanical heart valves, bioprosthetic heart valves have some drawbacks, most notably decreased longevity and greater susceptibility to structural valve degeneration (SVD), which can lead to valve thrombosis.[28]

4.2 | Bioprosthetic aortic heart valve thrombosis

In contrast to mechanical valves, artificial ones are typically less prone to forming blood clots. However, valve thrombosis continues to be a major worry. Clinical valve thrombosis, often referred to as prosthetic valve failure, is characterized by a blood clot on the valve, a sizable pressure difference across the valve, and signs and symptoms resembling coronary artery disease or left-sided bleeding clotting-related incidents. Clinical valve thrombosis has been shown to happen in 0.6%–2.8% of TAVR patients. OAC therapy has demonstrated promise in controlling the sudden increase in pressures above the heart valve and lowering clinical thrombotic symptoms.[11,29]

Both transcatheter and surgical bioprosthetic aortic valves are susceptible to SLT, which appears as a fine film covering a few leaflets with blood clots and is known as “HALT” when seen on a 4DCT scan.[30] HALT[28] may occasionally impair the leaflets' ability to move effectively.

Studies have shown that postdilated self-expanding transcatheter valves for the heart have a reduced likelihood of SLT, but stent frames that are not sufficiently expanded have a greater risk of this condition. There is some evidence of success in non-self-expanding valves too.[31] The causes of subclinical leaflet thrombosis are still not entirely understood, though. It is unclear exactly how subclinical leaflet thrombosis affects thromboembolic incidents and structural valve degeneration (SVD). Despite this, a previous observational study did discover a connection between subclinical leaflet thrombosis and

cerebrovascular accidents.[5,32] The study's main flaw was the significant time gap between the clinical episode and 4DCT imaging.

Subclinical leaflet thrombosis can be treated with OAC, however, this disease is unpredictable and can voluntarily advance from a normal leaflet via HALT to more significant HALT with a rise in mass (HAM), while it can additionally reverse at various points.[32] This fluctuating nature makes it difficult to draw a firm link between asymptomatic leaflet thrombosis and brain events.[32]

4.3 | Impact of antithrombotic therapy on subclinical leaflet thrombosis

In comparison with single or double antiplatelet medicines, direct oral anticoagulants (DOACs) have demonstrated promising efficiency in avoiding and curing asymptomatic leaflet thrombosis.[5,30]

However, the fact that TAVR or SAVR is a lifelong treatment makes choosing the best antithrombotic medicine difficult. Patients who are elderly, in particular, have a higher risk of bleeding when taking OAC medications. Randomized research investigations are now used to help prescribe TAVR, whereas expert advice has primarily been used to help prescribe post-TAVR antithrombotic medication. Yet, the Galileo study has offered valuable insights into picking the best antithrombotic medication following TAVR. In this research, participants were randomly assigned to one of two treatment groups, every single one of which received rivaroxaban 10 mg on a daily basis coupled with aspirin 75–100 mg for 3 months, then rivaroxaban 10 mg monotherapy. The other group received clopidogrel 75 mg once a day together with aspirin 75–100 mg regularly for 3 months, after which they received aspirin 75–100 mg monotherapy. The trial's primary endpoint was a composite endpoint consisting of significant, incapacitating, or severe bleeding or death. According to Galileo's trial, DOAC was associated with a greater likelihood of hemorrhage death or thromboembolic events in the older patient population.[33]

Furthermore, 3 months following randomization, researchers taking part in the GALILEO-4D substudy assessed 231 patients who underwent TAVR using 4DCT.[34] According to the study, asymptomatic leaflet thrombosis occurred less frequently (12.4%) in the rivaroxaban category than in the antiplatelet category (32.4%). Similar to the predominance of HAM, the rivaroxaban-based strategy was highly effective in preventing subclinical microvascular blood clots even while being in the drug-controlled group was associated with a higher risk of hemorrhaging and mortality (2.1% vs. 10.9%).

4.4 | Subclinical versus clinical

Subclinical and symptomatic types of transcatheter heart valve thrombosis, additionally referred to as leaflets coagulation, may be distinguished based on symptoms and medical documentation. Despite the rarity of clinical valve or leaflet thrombosis following TAVR, ignoring its existence can result in symptoms and unfavorable outcomes. On the other side, it increased subclinical leaflet thrombosis identification after TAVR results from better diagnosis imaging performance and use. This kind of thrombosis is more common, frequently asymptomatic, or is being reported in the scientific literature more regularly.[29,35]

4.5 | Clinical leaflet thrombosis

Less than 1% of patients who receive a TAVR experience leaflet thrombosis, which is a rare complication.[36,37] However, it can result in serious effects such as cardiac arrest, stroke, a transient ischemic attack (TIA), and fatality.[38] The most common thrombosis symptom is dyspnea, which worsens over time.[38]

According to a study by Jose et al.[11] clinical leaflet thrombosis was more common (2.8%), with balloon-expandable TAVR along with valve-in-valve (ViV) surgeries showing a higher chance of doing so. There was a noticeably greater risk for leaflet thrombosis (11.6%) following SAVR or a TAVR, which was connected to a 3.4:1 ratio of unfavorable cerebrovascular events.[12]

4.6 | Current recommendations regarding subclinical leaflet thrombosis

Although TAVR with DOAC therapy has proven efficiency in lowering asymptomatic leaflet thrombosis, it is not recommended to suggest anticoagulation as a regular therapy for those who have never shown symptoms of thrombosis. This is because such treatment could increase the likelihood of fatality or create major problems without benefiting the patients. Future trials should look at possible connections among asymptomatic leaflet thrombosis, cerebrovascular incidents, or premature SVD to fully assess this risk.

Routine 4DCT should not be used outside clinical investigations to identify asymptomatic leaflet thrombosis. This is because it is not appropriate to expose sufferers to radiotherapy and compare results without definite proof that a positive impact justifies anticoagulant treatment. Those who have had TAVR or SAVR and later experience another cerebral infarction or TIA or have a high transvalvular gradient may be advised to use a 4DCT scan and anticoagulant medication in the event of valve thrombosis.

5 | CONCLUSION

Our article highlights the importance of subclinical leaflet thrombosis (SLT) after the TAVR. Despite being a clinically challenging condition with still obscure biological mechanisms, our analysis indicates the relatively high frequency of SLT, especially in patients who undergo TAVR procedures. Notably, the role of dual antiplatelet therapy in SLT progression warrants further investigation, as it may have implications for optimizing post-TAVR management strategies.

In the future, the role of SLT has to be further investigated to understand the mechanisms and clinical implications of this condition to optimize the management of asymptomatic people who have undergone TAVR. Increased awareness of this domain will not only lead to the betterment of patient outcomes but will also contribute to the optimization of bioprosthetic valve durability and performance.

Finally, our systematic review calls for further investigation on SLT post-TAVR to unravel the mysteries behind it and develop guidelines based on evidence. Through this, we could work toward the goal of optimizing the safety and effectiveness of TAVR procedures, and thus ensuring better care for patients with aortic valve disease. Through the resolution of these issues, we can proceed with the safety and efficacy of TAVR procedures and the betterment of patients with aortic valve diseases.

AUTHOR CONTRIBUTIONS

Singam Shashank: Conceptualization; data curation; formal analysis; investigation; visualization; writing—original draft; writing—review and editing. **Lalitha Devi Balireddi**: Conceptualization; data curation; formal analysis; investigation; visualization; writing—original draft; writing—review and editing. **Pugazhendi Inban**: Formal analysis; investigation; visualization; writing—original draft; writing—review and editing. **Saud Muthanna Shakir Al-ezzi**: Formal analysis; investigation; visualization; writing—original draft; writing—review and editing. **Nalla Jaipal Reddy**: Visualization; writing—original draft; writing—review and editing. **Yarub Alalousi**: Writing—original draft; writing—review and editing. **Priyadarshi Prajjwal**: Validation; writing—original draft; writing—review and editing. **Jobby John**: Writing—original draft; writing—review and editing. **Mohammed Abulgaith Ali Shajeri**: Writing—original draft; writing—review and editing. **Mohammed Khaleel I. K. H. Almadhoun**: Writing—original draft; writing—review and editing. **Mukhamed Sulaimanov**: Validation, writing—original draft; Writing—review and editing. **Bita Amiri**: Validation; writing—original draft; writing—review and editing. **Mohammed Dheyaa Marsool Marsool**: Validation; writing—original draft; writing—review and editing. **Omniat Amir Hussin**: Validation; writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable as no new data were generated or analyzed in this study.

TRANSPARENCY STATEMENT

The lead author Omniat Amir Hussin affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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