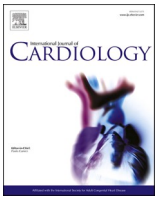
International Journal of Cardiology 402 (2024) 131854

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Review Article

Concomitant transthyretin cardiac amyloidosis in patients undergoing TAVR for aortic stenosis: A systemic review and meta-analysis

Kaneez Fatima [a,1], Qazi Shurjeel Uddin [a,1], Zoaib Habib Tharwani [a,1], Muhammad Arham Bin Kashif [a,*,1], Syed Sarmad Javaid [c,1], Prince Kumar [a,1], Muhammad Twaha Zia [a,1], Maarij Javed [a,1], Malaika Saeed Butt [a,1], Zoraiz Asim [b,1]

[a] Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
[b] Department of Medicine, Karachi Medical and Dental College, Karachi, Pakistan
[c] Department of Medicine, Jinnah Sindh Medical University, Karachi, Pakistan

ARTICLE INFO

Keywords:
Amyloidosis
Transthyretin amyloidosis
Transthyretin-related
Aortic stenosis
Transcatheter aortic valve replacement

ABSTRACT

Objective: Transcatheter aortic valve replacement (TAVR) is a successful treatment for aortic stenosis (AS) patients, and previous studies indicate favorable outcomes for those with concomitant aortic stenosis and transthyretin-associated cardiac amyloidosis (TTRCA-AS). However, the impact of TAVR on more adverse outcomes in TTRCA-AS patients compared to those with AS alone is still uncertain, with conflicting findings reported in the literature.

Methods: PubMed and Scopus were extensively searched from inception till August 2021. Studies were included if they reported data for prevalence and outcomes including mortality and cardiovascular-related hospitalization events in TTRCA-AS patients referred for TAVR. The data for these outcomes were pooled using a random effects model and forest plots were created.

Results: After initially screening 146 articles, 6 were shortlisted for inclusion in our analysis. Pooled analysis demonstrated a 13.3% [95% CI: 10.9–16.5; $p = 0.307$] prevalence of TTRCA in patients with AS undergoing TAVR. The incidence of mortality and cardiovascular (CV) hospitalization in patients with TTRCA-AS undergoing TAVR were 28.3% [95% CI: 18.7–39.0, $p = 0.478$] and 21.1% [95% CI: 10.2–34.5, $p = 0.211$], respectively.

Conclusion: The overall pooled TTRCA-AS prevalence was reported to be 13.3% in AS patients who underwent TAVR. Furthermore, transthyretin-associated CA was found to be associated with an increased risk of mortality and hospitalization. Large patient population studies are required to assess the safety and efficacy of TAVR in TTRCA-AS patients, as current research report data from small patient cohorts.

1. Introduction

Myocardium and other cardiac tissues can develop cardiac amyloidosis (CA), which is characterized by extracellular deposition of amyloid fibrils. [1,2] Transthyretin (TTR) amyloidosis and immunoglobulin-derived light chain (AL) amyloidosis are the two most prevalent forms of CA. [2] Age-related increases in the prevalence of myocardial amyloid after endomyocardial biopsy or autopsy are observed in the general population: 25% over 85 years, 32% over 95 years, and 63% over 100 years. [3,4] Patients with aortic stenosis (AS) frequently develop CA, with transthyretin-associated cardiac amyloidosis (TTRCA) being the most common form. Previous research has demonstrated the coexistence of these concomitant pathologies. [5,6,7] In one study, 16% of patients with wild-type TTRCA were also identified with AS. [8] Patients with these coexisting diseases show advanced cardiac remodeling and poor heart function, suggesting an increased likelihood of experiencing all-cause mortality, hospitalization, and readmissions. [9,10]. Thus, the combination of AS and TTRCA complicates the diagnosis and management of the patients.

Transcatheter aortic valve replacement (TAVR) is an effective treatment option for AS patients [11]. Although several studies have shown that TAVR is a safe option for patients with AS including those at high risk for surgical complications [12,13], the impact of TTRCA on outcomes in AS patients undergoing TAVR procedure is still unclear due

* Corresponding author at: Department of Medicine, Dow University of Health Sciences, A-6, United Square, Block 14. Gulistan-e-Johar, Karachi 75290, Pakistan.
E-mail address: arhamkashif2000@gmail.com (M.A.B. Kashif).

[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

https://doi.org/10.1016/j.ijcard.2024.131854
Received 1 September 2023; Received in revised form 15 January 2024; Accepted 10 February 2024
Available online 15 February 2024

to the conflicting results reported in the literature. According to studies, patients with concomitant aortic stenosis and transthyretin-associated cardiac amyloidosis (TTRCA-AS) may have worse mortality outcomes and a similar risk of peri-procedural complications, such as hemorrhage and cardiac arrhythmias as those with AS only. [7,14] Conversely, other studies have shown a reduction in adverse outcomes after TAVR compared to supportive medical therapy. [9,10] Challenges in studying the safety of TAVR in this population may also stem from the small sample sizes, differences in methodology, and varying patient populations of these studies, which creates difficulty in concluding. Consequently, this lack of agreement complicates the formulation of universally acceptable guidelines for the use of this procedure, as careful consideration of the risk-to-benefit ratio is required in TTRCA-AS patients. Therefore, this review aims to address this gap in the literature by pooling the prevalence and severe outcomes such as mortality and hospitalization, to provide a holistic assessment of the impact of TAVR on patients with these concomitant pathologies, enabling us to understand the safety of the procedure.

2. Methodology

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards [15,16]. Since this study involves a review of data that is readily available to the public, it was exempt from Institutional Board Review approval.

2.1. Data sources and search strategy

The databases PubMed and Scopus were extensively searched from inception till August 2021. The keywords and MeSH terms used for performing the search were: "(transcatheter aortic valve replacement OR TAVR OR aortic valve replacement) AND (aortic stenosis OR aortic valve narrowing) AND (amyloidosis OR transthyretin amyloidosis OR cardiac amyloidosis OR TTR-CA). Selected articles were transferred to Endnote X7 (Clarivate Analytics, PA) to check and remove duplicates. Two reviewers (M.A.K *and* Q.S·U) independently reviewed the relevant articles. Any discrepancies were rectified by a senior author (S.S.J). The initial search was completed by reading titles and abstracts, after which the shortlisted articles were assessed for full text.

2.2. Study selection and eligibility criteria

Studies were considered for the meta-analysis if they met all of the following inclusion criteria: (a) report patients with concomitant aortic stenosis and transthyretin-associated cardiac amyloidosis (TTRCA-AS) [confirmed by [99mTc]-3,3-Diphosphono-1,2-Propanodicarboxylic Acid (DPD) bone scintigraphy] (b) report AS patients including those with TTRCA-AS referred for TAVR. The studies were excluded if (a) they only reported patients with lone AS (i.e. AS patients without TTRCA); (b) if they only reported AS patients with concomitant immunoglobulin-derived light chain-associated cardiac amyloidosis (AL-CA) (c) if they did not include information regarding prevalence or mortality or cardiovascular hospitalization (CV); (d) case reports or studies in which the essential patient data were missing; and (e) the recruited amyloidosis patients were not diagnosed with AS.

2.3. Data extraction, and quality assessment

The data for the included studies were extracted onto a spreadsheet by the two investigators (Z. H. T. and P. K.), and the third investigator double-checked the accuracy (M. S. B.). The following information was extracted: baseline characteristics (patient demographics, clinical parameters, and follow-up data), outcomes of interest including (1) prevalence of TTRCA in AS patients who underwent TAVR and (2) incidence of mortality and CV hospitalization in these patients after undergoing TAVR procedure. Due to the single-arm nature of all the included studies, no quality assessment was performed.

2.4. Statistical analysis

The statistical analysis was performed using OpenMetaAnalyst. The prevalence of TTRCA in aortic stenosis patients was calculated by dividing the total number of patients with TTRCA by the total number of patients with aortic stenosis undergoing TAVR. Then for all other outcomes, the percentage was obtained by dividing the incidence of a particular outcome by the total number of TTRCA-AS patients undergoing TAVR. A meta-analysis was conducted on the calculated frequencies of the outcomes of interest and an average incidence was obtained for each outcome, along with confidence intervals (CI). The I^2 test was performed to examine the heterogeneity in the study outcomes. An I^2 score of 50% was assumed to indicate a high amount of heterogeneity [17,18].

3. Results

3.1. Literature search results

Initial searches of the databases yielded 146 potential studies. Out of these, 66 studies remained after duplicates were removed. 14 articles remained for full-text assessment after the title and abstract screening. A comprehensive search strategy and the search results obtained from the databases used are provided in **Supplementary Data**. From these 14 articles, one was a case report, two did not report findings of interest for the current analysis, two studies were not included as their patient pool was utilized by Nitsche et al. [9], and three studies had fewer than 5 patients. The inclusion of studies with <5 patients would have introduced selection bias or publication bias due to their low statistical power, hence we were unable to include them so that our findings can be more robust [10]. Finally, a total of six studies met the eligibility criteria that were used in our analysis. [5,6,9,11,19,20]. The literature search results have been summarized in a PRISMA flowchart (Fig. 1), and the demographics, laboratory, and clinical findings of the included patients are provided in Table 1.

4. Results of meta-analysis

4.1. Prevalence

Out of 6 selected studies, all reported patients with TTRCA-AS. A combined total of 839 randomly selected patients with AS underwent TAVR, of whom 112 were also diagnosed with concomitant transthyretin-associated cardiac amyloidosis disease (TTRCA). The overall pooled prevalence of TTRCA-AS was 13.3% (95% CI: 10.9–16.5; $p = 0.307$, Fig. 2).

4.2. Mortality

Out of 6 selected studies, 2 reported mortality. The findings showed that 28.3% of TTRCA-AS patients died after undergoing the TAVR operation (95% CI: 18.7–39.0, $p = 0.478$, Fig. 3).

4.3. CV hospitalization

Out of 6 selected studies, 2 reported CV hospitalizations. About 21.1% of the patients with TTRCA-AS (95% CI: 10.2–34.5, $p = 0.211$; Fig. 4) experienced hospitalizations due to cardiovascular causes after undergoing TAVR. No heterogeneity was observed.

5. Discussion

To reduce the risk of numerous pre- and post-operative problems

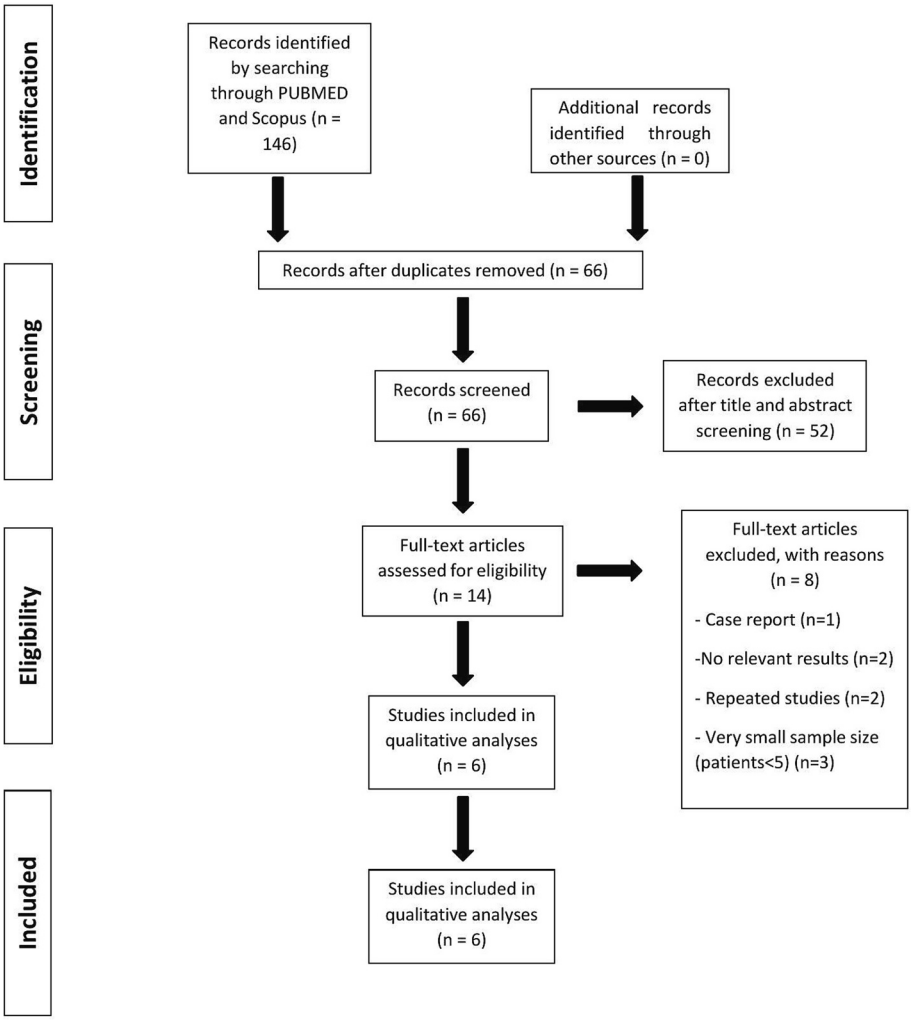


Fig. 1. PRISMA flow diagram.

such as progressive heart failure and myocardial infarction, a diagnosis of TTRCA is required for patients with AS who are undergoing aortic valve replacement. [5,21] Due to the diversity in the study sample and diagnostic techniques, the prevalence of TTRCA in AS patients undergoing TAVR in the literature ranges from 8% to 16%. [5,11]. Our estimated pooled prevalence of TTRCA-AS was reported to be 13%. A slightly higher rate of 14.4% was observed by Ying Ho et al., while a lower rate of 9% was observed by Ricci et al. [22,23]. In our analysis, we exclusively considered patients diagnosed with TTRCA-AS who underwent TAVR. This deliberate inclusion criterion was chosen to align with the specific objectives of our study, focusing solely on the outcomes and implications of TAVR in the context of concomitant TTRCA-AS. We intentionally excluded patients opting for alternative therapeutic interventions, such as surgical aortic valve replacement (SAVR) or medical management, to maintain the clarity and relevance of our investigation. This may account for the variation in prevalence rates observed in our study when compared to those mentioned above. The low overall prevalence may be attributed to the comparable clinical and pathophysiological features between AS and TTRCA (such as left ventricular hypertrophy, diastolic dysfunction, and increased risk of arrhythmias). This is because the initiation and progression of the two pathologies are interlinked resulting in similar downstream complications creating difficulty in diagnosis and allowing TTRCA to proceed unnoticed for many years [24]. This could explain why extensive studies have revealed the occurrence of dual pathology in the elderly, as evidenced by the findings of Castano et al., Nitsche et al., and Calvacante et al. [5,9,11]. However, Triebel et al. reported the presence of TTRCA in the younger population and Myasoedova et al. also found that the younger population was more vulnerable to the detrimental effects of cardiac amyloidosis [25,26]. This emphasizes the significance of standardizing TTRCA testing in young AS patients and conducting extensive research to ascertain the connection and cause of TTRCA in young AS patients.

One of the concerns shown by cardiologists is whether TAVR is safe to perform in patients with dual pathology. Is it associated with adverse effects in the presence of concomitant amyloidosis? Various pre- and post-procedural problems, including myocardial injury, cardiac conduction defects, and left ventricular rupture, have been linked to a higher risk for TAVR in certain studies. [19,27,28–29] We computed the mortality and hospitalization rates in concomitant TTRCA-AS patients undergoing TAVR. We observed a mortality rate of 28.3%, which contrasts with the 14.9% mortality rate observed in AS patients without concomitant TTRCA who underwent TAVR [30]. Furthermore, Quintana et al. observed a mortality rate of 15% in AS patients without CA. [31] According to Ricci et al., people with concurrent TTRCA-AS had twice as high risk of developing the condition. [23] This demonstrates that amyloidosis heralds a higher mortality risk in AS patients undergoing TAVR, perhaps by raising the possibility of post-procedural ventricular instability brought on by extensive amyloid deposits. [29] However, Nitsche et al. found that TAVR patients with TTRCA-AS had better mortality results than those receiving conventional therapy.

It is crucial to note that the prevalence rates we noted among patients with TTRCA-AS who underwent TAVR were distinct from those reported

Table 1
Study Characteristics: The baseline characteristics are given as follows:

Study	Participants (n)	Age, years (SD)	Sex, n (%)		BMI in kg/m2 (SD)	BP, mmHg (SD)		Atrial fibrillation, n (%)	LVEF, % (SD)	AVA, n (SD)	AV mean gradient, n (SD)	QRS Interval, n (SD)	Average IV septal thickness (cm)	Follow up (months)
			Male	Female		Systole	Diastole							
Nietlispach (2012)	17	77.5 (10.5)	10 (58.8)	7(41.2)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	14
Longhi (2017)														
AS*	43	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
TTRCA-AS	5	84(3.5)	4(80)	1(20)	N/A	N/A	N/A	N/A	N/A	0.6	N/A	N/A	18	
Castano (2017)														
TTRCA-AS	24	86.3(5.7)	22 (91.7)	2(8.3)	25.5(2.7)	125.3 (21.5)	61.1 (10.6)	10(41.7)	47.6 (17.6)	0.8 (0.16)	35.2(13.9)	127.4(29.8)	1.3	24
AS	127	83.3(6.3)	80 (60.3)	47(37)	27(5.3)	143.6 (25.1)	65.1 (14.3)	54(42.5)	56.1 (14.1)	0.77 (0.19)	41.1(13.8)	110.7(30.7)	1.1	
Cavalcante (2017)														
AS	104	70(14)	58(56)	46(44)	N/A	N/A	N/A	21(20.2)	52(18)	0.5(0.2)	31(15)	N/A	1.3	36
TTRCA-AS	9	88(6)	8(89)	1(11)	N/A	N/A	N/A	6(67)	43(17)	0.4(0.2)	30(14)	N/A	1.8	
Rosenblum (2020)														
AS	27	86(5)	26(93)	1(7)	98(18)	126(18)	69(10)	10(37)	48(17)	0.8 (0.15)	35(13)	125(30)	1.4	24
TTRCA-AS	177	82(10)	107 (60.4)	70(40)	108(25)	128(18)	69(12)	73(41)	55(15)	0.76 (0.23)	41(14)	113(31)	1.2	
Nitsche (2021)														
DPD+ 0	359	84(3.8)	173 (48.2)	186 (51.8)	26.4(1.5)	134(7)	69(4.8)	130(36.3)	58(5)	0.7 (0.05)	44(4.5)	96(8)	1.4	23
DPD1	16	85.4(2.2)	8(50)	8(50)	27.6(1.4)	138(11)	80(8.2)	8(50)	55(6.5)	0.7 (0.05)	39(5.5)	128(8.75)	1.3	
DPD2/3	32	86.6(4)	21 (65.6)	11 (34.4)	25.7(1.5)	126(10)	68(3.5)	16(50)	51(11)	0.7(0.1)	36(5.8)	107(11.2)	1.6	

AS: aortic stenosis only, TTRCA: Transthyretin-Associated Cardiac Amyloidosis, DPD: ^{99m}technetium-labeled 3,3-diphosphono-1,2-propanodicarboxylic acid bone scintigraphy, BMI: Body Mass Index, BP Blood pressure, LVEF: left ventricular ejection fraction, AVA: aortic valve area **(in cm^2/m^2)**, IV: interventricular AV: Aortic valve.

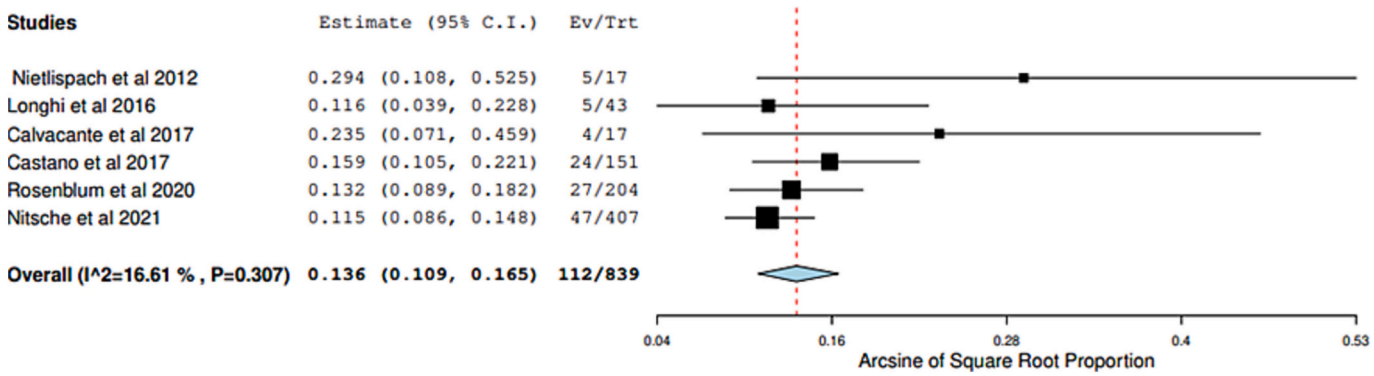


Fig. 2. Forest plot for prevalence of TTRCA-AS patients undergoing TAVR.

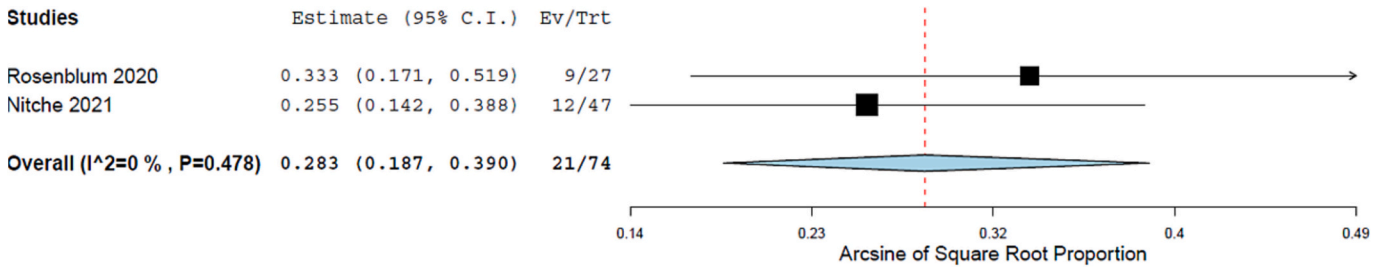


Fig. 3. Forest plot for mortality for TTRCA-AS patients undergoing TAVR.

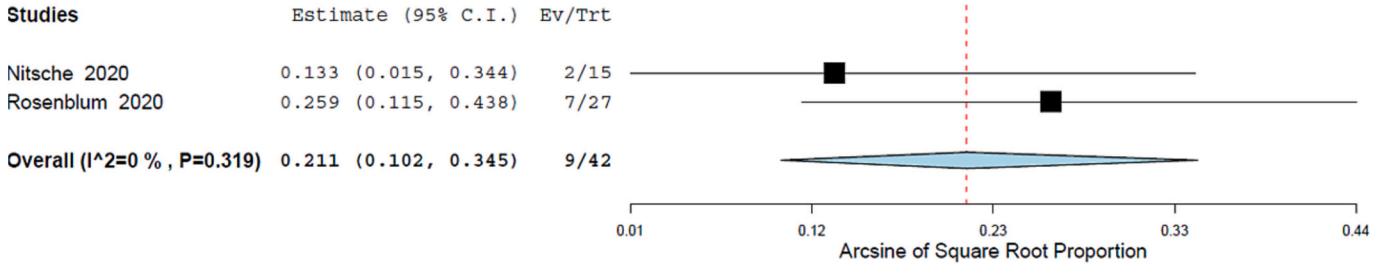


Fig. 4. Forest plot for CV hospitalizations in TTRCA-AS patients undergoing TAVR.

in studies that involved patients undergoing SAVR instead (TAVR: 13% vs SAVR: 6%) [25]. This disparity can be attributed to the higher mortality rates, delayed hospital discharge, and increased risk of complications like acute renal injury and permanent pacemaker placement associated with the latter [32]. This is also corroborated by Treibel et al.'s finding of a 50% mortality rate among TTRCA-AS patients who underwent SAVR, in contrast to our own rate of 28.3% [25]. However, contradictory evidence exists regarding the likelihood of mortality in TTRCA-AS patients undergoing TAVR or SAVR. [26]. Future research with large sample sizes is needed to compare the postoperative problems of the two procedures and gain a better understanding of their efficacy.

A small proportion of the patient population experienced CV hospitalizations. In the pooled population, 21.1% of TTRCA-AS patients required hospitalization, which contrasts with the study by Elmariah et al., which reported a hospitalization rate of 12.8% in AS patients. [33] These findings indicate that amyloidosis may contribute to complications during TAVR, as it poses a risk of senile calcific deposits being dislodged during valve fracture and post-procedural balloon dilatation. [34,35] According to preliminary findings of The Transthyretin Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT), the combined risk of mortality and hospitalization is decreased with tafamidis post-TAVR treatment compared to a placebo. [36] Although being a minimally invasive procedure, our findings suggest that the presence of TTRCA may complicate the procedure making its effectiveness questionable in such cases. As the prevalence of TAVR-related problems, including vascular injuries and stroke, rises with age, they may exceed the surgical advantages of the procedure in a considerable portion of these cases, which primarily involve the elderly. [37,20] Thus, future studies are needed to assess the possible relevance and timing of interventional and pharmacologic management techniques for AS patients with concomitant TTRCA to reduce mortality and morbidity associated with concurrent illness. Moreover, future research with a large sample size is warranted to further examine the mortality and hospitalization rate in TTRCA-AS patients undergoing TAVR.

Studying adverse outcomes in patients with both TTRCA and AS undergoing TAVR is crucial. Patients with TTRCA-AS present a complex clinical profile due to underlying systemic amyloidosis, increasing their vulnerability. Understanding the specific risks and outcomes associated with TAVR in this cohort is essential for informed decision-making in clinical practice. Additionally, comparing outcomes in TTRCA-AS patients to those with AS alone undergoing TAVR serves as a benchmark to evaluate the procedure's efficacy and safety. This has been previously done in a meta-analysis by Cannata et al. which addressed the safety of TAVR in CA-AS patients (TTR and AL type combined) by comparing clinical outcomes and complications with those undergoing TAVR for AS alone [38]. In contrast, our study focused specifically on severe

outcomes like mortality and cardiovascular-related hospitalization in patients with TTRCA-AS. While procedural complications are vital to assess, adverse events like mortality and hospitalization provide much clearer ground for the treatment's overall safety and efficacy, which are deemed more important for healthcare providers and policymakers.

5.1. Limitations

It is important to consider the study's limitations when evaluating its strengths. A certain amount of bias may have been incorporated into the study due to the prevalence of retrospective research and the limited sample size in some studies. Only TTRCA patients who were referred for TAVR rather than SAVR or conservative treatment were taken into consideration. Nitsche et al. did not specify the precise number of patients who crossed over to SAVR or medicinal therapy, which may have led to an overestimation of the pooled population. The stage of amyloidosis diagnosis may have influenced the results of the mortality analysis in AS patients. Subsequent investigations into the mortality and hospitalization rates among TTRCA-AS patients undergoing TAVR should encompass additional trials with larger sample sizes.

6. Conclusion

The overall pooled prevalence of TTRCA-AS was reported to be 13.3%. Furthermore, TTRCA was found to be associated with an increased risk of mortality and hospitalization in patients with AS undergoing TAVR. Large patient population studies are needed to determine the efficacy of TAVR in TTRCA-AS patients, as current studies report data based on small patient cohorts. In addition, comparative studies are required that compare the adverse outcome rates with other treatment options such as SAVR or medical therapy to yield the true dominance of the efficacy of TAVR in TTRCA-AS patients.

CRediT authorship contribution statement

Kaneez Fatima: Conceptualization, Validation, Visualization. **Qazi Shurjeel Uddin:** Formal analysis, Supervision, Writing – original draft, Data curation, Validation. **Zoaib Habib Tharwani:** Data curation, Investigation, Methodology, Validation, Writing – original draft. **Muhammad Arham Bin Kashif:** Data curation, Formal analysis, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Syed Sarmad Javaid:** Validation, Project administration, Supervision, Visualization, Writing – review & editing. **Prince Kumar:** Investigation, Methodology, Validation, Writing – original draft. **Muhammad Twaha Zia:** Validation, Writing – original draft. **Maarij Javed:** Validation, Writing – original draft. **Malaika Saeed Butt:** Methodology, Validation, Writing – original draft. **Zoraiz Asim:** Validation, Writing – original draft.

Declaration of competing interest

None to declare.

Acknowledgments

The authors would like to acknowledge the Research Council of Pakistan (RCOP) for their support along all aspects of conducting this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2024.131854.

References

[1] J. Ternacle, L. Krapf, D. Mohty, J. Magne, A. Nguyen, A. Galat, R. Gallet, E. Teiger, N. Côté, M.A. Clavel, F. Tournoux, P. Pibarot, T. Damy, Aortic stenosis and cardiac amyloidosis: JACC review topic of the week, J. Am. Coll. Cardiol. 74 (21) (2019 Nov 26) 2638–2651, https://doi.org/10.1016/j.jacc.2019.09.056 (PMID: 31753206).

[2] S. Ash, E. Shorer, D. Ramgobin, M. Vo, J. Gibbons, R. Golamari, R. Jain, R. Jain, Cardiac amyloidosis-a review of current literature for the practicing physician, Clin. Cardiol. 44 (3) (2021 Mar) 322–331, https://doi.org/10.1002/clc.23572 (Epub 2021 Feb 17. PMID: 33595871; PMCID: PMC7943900).

[3] G.G. Cornwell 3rd, W.L. Murdoch, R.A. Kyle, P. Westermark, P. Pitkänen, Frequency and distribution of senile cardiovascular amyloid. A clinicopathologic correlation, Am J Med 75 (4) (1983) 618–623, https://doi.org/10.1016/0002-9343(83)90443-6.

[4] M. Tanskanen, T. Peuralinna, T. Polvikoski, et al., Senile systemic amyloidosis affects 25% of the very aged and associates with genetic variation in alpha2-macroglobulin and tau: a population-based autopsy study, Ann. Med. 40 (2008) 232–239.

[5] A. Castaño, D.L. Narotsky, N. Hamid, et al., Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement, Eur. Heart J. 38 (2017) 2879.

[6] S. Longhi, M. Lorenzini, C. Gagliardi, et al., Coexistence of degenerative aortic stenosis and wild-type transthyretin-related cardiac amyloidosis, J. Am. Coll. Cardiol. Img. 9 (2016) 325.

[7] T.A. Treibel, M. Fontana, J.A. Gilbertson, et al., Occult transthyretin cardiac amyloid in severe calcific aortic stenosis: prevalence and prognosis in patients undergoing surgical aortic valve replacement, Circ. Cardiovasc. Imag. 9 (2016) e005066.

[8] P.R. Scully, J.C. Moon, T.A. Treibel, Cardiac amyloidosis in aortic stenosis: the tip of the iceberg, J. Thorac. Cardiovasc. Surg. 156 (3) (2018 Sep 1) 965–966.

[9] C. Nitsche, P.R. Scully, K.P. Patel, A.A. Kammerlander, M. Koschutnik, C. Dona, T. Wollenweber, N. Ahmed, G.D. Thornton, A.D. Kelion, N. Sabharwal, J. D. Newton, M. Ozkor, S. Kennon, M. Mullen, G. Lloyd, M. Fontana, P.N. Hawkins, F. Pugliese, T.A. Treibel, Prevalence and outcomes of concomitant aortic stenosis and cardiac amyloidosis, J. Am. Coll. Cardiol. 77 (2) (2021) 128–139, https://doi.org/10.1016/j.jacc.2020.11.006.

[10] J.A. Sterne, D. Gavaghan, M. Egger, Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature, J. Clin. Epidemiol. 53 (11) (2000) 1119–1129, https://doi.org/10.1016/s0895-4356(00)00242-0.

[11] J.L. Cavalcante, S. Rijal, I. Abdelkarim, A.D. Althouse, M.S. Sharbaugh, Y. Fridman, P. Soman, D.E. Forman, J.T. Schindler, T.G. Gleason, J.S. Lee, E.B. Schelbert, Cardiac amyloidosis is prevalent in older patients with aortic stenosis and carries worse prognosis, J. Cardiovasc. Magnet. Reson. : Off. J. Soc. Cardiovasc. Magnet. Resonan. 19 (1) (2017) 98, https://doi.org/10.1186/s12968-017-0415-x.

[12] Jenna Spears, Yousif Al-Saiegh, David Goldberg, Sina Manthey, Sheldon Goldberg, TAVR: A Review of Current Practices and Considerations in Low-Risk Patients, J. Interv. Cardiol. 2020 (2020) 13, https://doi.org/10.1155/2020/2582938. Article ID 2582938.

[13] M.J. Mack, M.B. Leon, C.R. Smith, D.C. Miller, J.W. Moses, E.M. Tuzcu, J.G. Webb, P.S. Douglas, W.N. Anderson, E.H. Blackstone, S.K. Kodali, 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial, Lancet 385 (9986) (2015 Jun 20) 2477–2484.

[14] Y. Sammour, A. Krishnaswamy, A. Kumar, R. Puri, K.G. Tarakji, N. Bazarbashi, S. Harb, B. Griffin, L. Svensson, O. Wazni, S.R. Kapadia, Incidence, predictors, and implications of permanent pacemaker requirement after transcatheter aortic valve replacement, Cardiovasc. Interv. Ther. 14 (2) (2021 Jan 25) 115–134.

[15] P. Scully, K. Patel, T. Treibel, G. Thornton, R. Hughes, S. Chadalavada, et al., Prevalence and outcome of dual aortic stenosis and cardiac amyloid pathology in patients referred for transcatheter aortic valve implantation, Eur. Heart J. 41 (29) (2020) 2759–2767.

[16] G. Rao, F. Lopez-Jimenez, J. Boyd, F. D'Amico, N.H. Durant, M.A. Hlatky, G. Howard, K. Kirley, C. Masi, T.M. Powell-Wiley, A.E. Solomonides, Methodological standards for meta-analyses and qualitative systematic reviews of cardiac prevention and treatment studies: a scientific statement from the American Heart Association, Circulation. 136 (10) (2017 Sep 5) e172–e194.

[17] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P. Ioannidis, M. Clarke, P.J. Devereaux, J. Kleijnen, D. Moher, The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, J. Clin. Epidemiol. 62 (10) (2009 Oct 1) e1–e34.

[18] J.P. Higgins, S.G. Thompson, J.J. Deeks, et al., Measuring inconsistency in meta-analyses, Bmj 327 (7414) (2003) 557–560.

[19] F. Nietlispach, J.G. Webb, J. Ye, A. Cheung, S.V. Lichtenstein, R.G. Carere, R. Gurvitch, C.R. Thompson, A.J. Ostry, L. Matzke, M.F. Allard, Pathology of transcatheter valve therapy, J. Am. Coll. Cardiol. Intv. 5 (5) (2012) 582–590, https://doi.org/10.1016/j.jcin.2012.03.012.

[20] H. Rosenblum, A. Masri, D.L. Narotsky, J. Goldsmith, N. Hamid, R.T. Hahn, S. Kodali, T. Vahl, T. Nazif, O.K. Khalique, S. Bokhari, P. Soman, J.L. Cavalcante, M.S. Maurer, A. Castaño, Unveiling outcomes in coexisting severe aortic stenosis and transthyretin cardiac amyloidosis, Eur. J. Heart Fail. 23 (2) (2021) 250–258, https://doi.org/10.1002/ejhf.1974.

[21] N. Kotani, H. Hashimoto, M. Muraoka, S. Kabara, H. Okawa, A. Matsuki, Fatal perioperative myocardial infarction in four patients with cardiac amyloidosis, Anesthesiology 92 (2000) 873–875.

[22] J. Ho, Q. Kor, W. Kong, Y. Lim, M. Chan, N. Syn, et al., Prevalence and outcomes of concomitant cardiac amyloidosis and aortic stenosis: a systematic review and meta-analysis, Hell. J. Cardiol. 64 (2022) 67–76.
[23] F. Ricci, L. Ceriello, M. Khanji, G. Dangas, C. Bucciarelli-Ducci, M. Di Mauro, et al., Prognostic significance of cardiac amyloidosis in patients with aortic stenosis, JACC Cardiovasc. Imaging 14 (1) (2021) 293–295.
[24] J. Ternacle, L. Krapf, D. Mohty, J. Magne, A. Nguyen, A. Galat, R. Gallet, E. Teiger, N. Côté, M.A. Clavel, F. Tournoux, P. Pibarot, T. Damy, Aortic stenosis and cardiac amyloidosis: JACC review topic of the week, J. Am. Coll. Cardiol. 74 (21) (2019 Nov 26) 2638–2651, https://doi.org/10.1016/j.jacc.2019.09.056 (PMID: 31753206).
[25] T.A. Treibel, M. Fontana, J.A. Gilbertson, K.A. Boniface, S.K. White, A. Abdel-Gadir, S. Rosmini, D.F. Hutt, C.J. Whelan, J.D. Gillmore, A. Wechalekar, M. P. Hayward, M.A. Ashworth, P.N. Hawkins, J.C. Moon, Occult senile cardiac amyloid in severe calcific aortic stenosis is not rare and has a poor prognosis: a 146 patient CMR biopsy study, J. Cardiovasc. Magn. Reson. 18 (Suppl. 1) (2016) O40, https://doi.org/10.1186/1532-429x-18-s1-o40.
[26] V. Myasoedova, M. Conte, V. Valerio, D. Moschetta, I. Massaiu, L. Petraglia, et al., Red flags, prognostic impact, and Management of Patients with Cardiac Amyloidosis and Aortic Valve Stenosis: a systematic review and Meta-analysis, Front. Med. (2022) 9.
[27] A. Castaño, S. Bokhari, M.S. Maurer, Could late enhancement and need for permanent pacemaker implantation in patients undergoing TAVR be explained by undiagnosed transthyretin cardiac amyloidosis? J. Am. Coll. Cardiol. 65 (2015) 311–312.
[28] A. Mangieri, C. Montalto, M. Pagnesi, G. Lanzillo, O. Demir, L. Testa, et al., TAVI and Post procedural cardiac conduction abnormalities, Front. Cardiovasc. Med. (2018) 5.
[29] F.C. Monticelli, S.N. Kunz, T. Keller, S. Bleiziffer, Cardiac amyloidosis as a potential risk factor for transapical transcatheter aortic valve implantation, J. Card. Surg. 29 (2014) 623–624.
[30] Y. Saito, E. Lewis, A. Raval, G. Gimelli, K. Jacobson, S. Osaki, The prognosis of elderly patients with aortic stenosis after Transcatheter aortic valve replacement, Intern. Med. 60 (4) (2021) 517–523.
[31] R. Quintana, D. Monlezun, A. DaSilva-DeAbreu, U. Sandhu, D. Okwan-Duodu, J. Ramírez, et al., One-year mortality in patients undergoing Transcatheter aortic valve replacement for stenotic bicuspid versus tricuspid aortic valves: a Meta-analysis and Meta-regression, J. Interv. Cardiol. 2019 (2019) 1–12.
[32] Muhammad Zubair Khan, Yevgeniy Brailovsky, Oleg Alec Vishnevsky, Abdul Baqi, Kirten Kumar Patel, J. Rene, Alvarez, Clinical outcome of TAVR vs. SAVR in patients with Cardiac Amyloidosis, Cardiovas. Revascularizat. Med. 43 (2022) 20–25. ISSN 1553-8389, https://doi.org/10.1016/j.carrev.2022.04.027.
[33] S. Elmariah, I. Palacios, T. McAndrew, I. Hueter, I. Inglessis, J. Baker, et al., Outcomes of Transcatheter and surgical aortic valve replacement in high-risk patients with aortic stenosis and left ventricular dysfunction, Circ. Cardiovasc. Interv. 6 (6) (2013) 604–614.
[34] J.J. Bax, V. Delgado, V. Bapat, H. Baumgartner, J.P. Collet, R. Erbel, C. Hamm, A. P. Kappetein, J. Leipsic, M.B. Leon, P. MacCarthy, N. Piazza, P. Pibarot, W. C. Roberts, J. Rodes-Cabau, P.W. Serruys, M. Thomas, A. Vahanian, J. Webb, J. L. Zamorano, S. Windecker, Open issues in transcatheter aortic valve implantation. Part 2: procedural issues and outcomes after transcatheter aortic valve implantation, Eur. Heart J. 35 (2014) 2639–2654.
[35] M. Arnold, S. Schulz-Heise, S. Achenbach, S. Ott, A. Dorfler, D. Ropers, R. ϵ Feyrer, F. Einhaus, S. Loders, F. Mahmoud, O. Roerick, W.G. Daniel, M. Weyand, S. M. Ensminger, J. Ludwig, Embolic cerebral insults after transapical aortic valve implantation detected by magnetic resonance imaging, JACC Cardiovasc. Interv. 3 (2010) 1126–1132.
[36] M.S. Maurer, J.H. Schwartz, B. Gundapaneni, P.M. Elliott, G. Merlini, M. Waddington-Cruz, A.V. Kristen, M. Grogan, R. Witteles, T. Damy, B. M. Drachman, S.J. Shah, M. Hanna, D.P. Judge, A.I. Barsdorf, P. Huber, T. A. Patterson, S. Riley, J. Schumacher, M. Stewart, M.B. Sultan, C. Rapezzi, Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy, N. Engl. J. Med. 379 (2018) 1007–1016.
[37] O. Alsara, A. Alsarah, H. Laird-Fick, Advanced age and the clinical outcomes of transcatheter aortic valve implantation, J. Geriatr. Cardiol. : JGC 11 (2) (2014) 163–170, https://doi.org/10.3969/j.issn.1671-5411.2014.02.004.
[38] F. Cannata, M. Chiarito, G. Pinto, A. Villaschi, J. Sanz-Sánchez, F. Fazzari, D. Regazzoli, A. Mangieri, R.M. Bragato, A. Colombo, B. Reimers, G. Condorelli, G. G. Stefanini, Transcatheter aortic valve replacement in aortic stenosis and cardiac amyloidosis: a systematic review and meta-analysis, ESC Heart Fail. 9 (5) (2022) 3188–3197, https://doi.org/10.1002/ehf2.13876.