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CARDIOMAG NEWSLETTER

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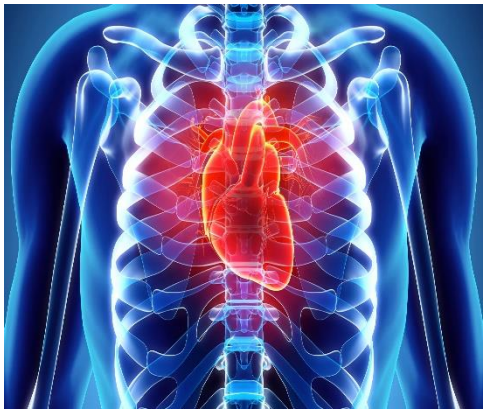
Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "Cardio Mag" which contains latest and interesting news in the field of Cardiology

Estimation of the treatment effect of intensive blood pressure lowering on stroke prevention



Cardiovascular Disease

INTRODUCTION- High blood pressure (BP) remains the leading risk factor for cardiovascular disease and death worldwide. Over the past 50 years, there has been a significant decrease in the incidence of cardiovascular disease, notably stroke, due to a reduction in raised blood pressure levels among the population.[1] It was estimated that high BP accounts for nearly half of the global stroke burden. Consequently, managing BP effectively is a crucial strategy for stroke prevention. Previous randomized trials, such as the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD-BP) and Systolic Blood Pressure Intervention Trial (SPRINT) studies, have explored the effects of intensive BP lowering, aiming to reduce systolic blood pressure (SBP) to below 120 mmHg compared to standard control (below 140 mmHg). While the ACCORD-BP trial, which focused on patients with diabetes, demonstrated a significant reduction in stroke risk with intensive BP lowering, the SPRINT trial did not find a statistically significant benefit. The discrepancy in findings may be due to differences in the study populations and competing risks such as mortality. However, no research has been done on the heterogeneity of treatment effect (HTE) of intense blood pressure reduction based on individual stroke risk. This study sought to evaluate the impact of intensive BP control on stroke-free survival (SFS) by pooling data from both trials and to investigate whether baseline stroke risk influences the treatment effect.[2]

METHODS- This post-hoc analysis combined data from two large clinical trials, SPRINT and ACCORD. The SPRINT trial enrolled 9,361 participants without diabetes but at high cardiovascular risk, aiming to compare the effects of intensive SBP lowering (<120 mmHg) with standard control (<140 mmHg). In contrast, the ACCORD-BP study included 4,733 diabetic patients at high cardiovascular risk, also randomized to the same BP targets. Participants with a history of stroke were excluded to maintain consistency between the cohorts. The primary outcome was stroke-free survival (SFS), a composite endpoint defined as the time until the first occurrence of stroke or death. Kaplan-Meier survival analysis was used to estimate the cumulative incidence of SFS in both treatment arms, and log-rank tests assessed statistical differences.

RESULTS- The analysis included 14,094 patients, with an average age of 66 years and a female proportion of 39.66%. Most participants (89.65%) were receiving antihypertensive treatment, and 22.39% had a history of clinical cardiovascular disease. The baseline systolic BP averaged 139.5 mmHg across the pooled population, and stroke risk varied among individuals, with an average Framingham Stroke Risk Score of 9.29%. After a median follow-up period of 3.68 years, 834 patients (5.92%) experienced SFS events, with an incidence rate of 1.51 per 100 person-years in the intensive BP group and 1.79 per 100 person-years in the standard BP group (Figure 1). The intensive BP group exhibited a 24% lower risk of SFS events compared to the standard group (HR: 0.76, 95% CI: 0.65–0.89, p = 0.001), corresponding to a risk difference of 0.98% and a number needed to treat (NNT) of 102. The benefit of intensive BP control was more pronounced in participants at higher stroke risk. For the highest risk tertile, intensive treatment reduced the SFS hazard by 31% (HR: 0.69, 95% CI: 0.56–0.86), with a risk difference of 2.00% and an NNT of 50. In contrast, there was no statistically significant benefit in the lowest risk tertile (HR: 0.76, 95% CI: 0.52–1.11). These findings suggest that intensive BP lowering may be particularly beneficial for patients with a higher baseline risk of stroke.

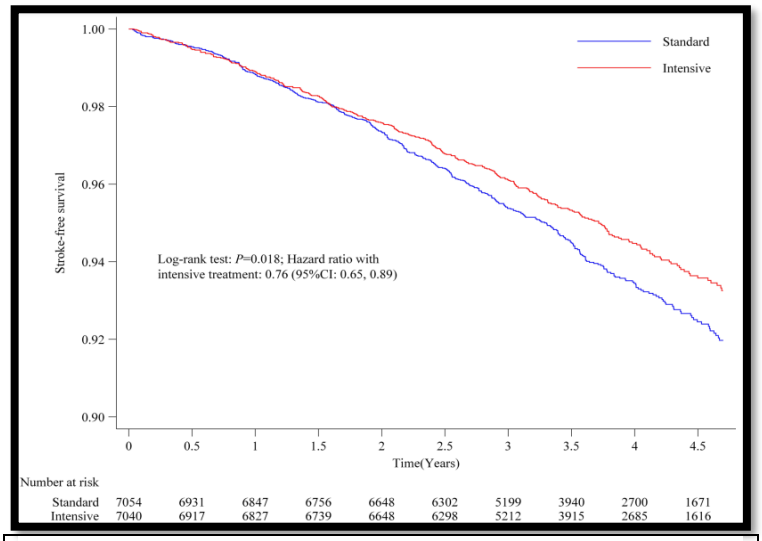


Figure 1. Kaplan–Meier Curve comparing intensive BP Versus Standard BP on stroke-free survival.

DISCUSSION- This pooled analysis of the SPRINT and ACCORD-BP trials demonstrated that intensive blood pressure control significantly improves SFS, particularly in individuals at higher stroke risk. The observed 24% reduction in SFS events aligns with findings from other major studies demonstrating the benefits of more aggressive BP management for cardiovascular disease prevention.[2] A meta-analysis by Ettehad et al. found that each 10 mmHg reduction in systolic BP was associated with a 27% reduction in stroke risk, consistent across different patient populations, including those with and without diabetes.[3] The results of the current study corroborate these findings, as lowering systolic BP to below 120 mmHg led to a significant reduction in the risk of stroke or death compared to a target of 140 mmHg.[2]

CONCLUSION- This study concluded that intensive BP lowering improves stroke-free survival, with the most pronounced effects in high-risk patients. These supports target intensive BP management for primary stroke prevention in individuals with elevated stroke risk scores.

Intensive blood pressure lowering enhances stroke-free survival, with the most noticeable effects in high-risk patients.

REFERENCES

1. Reboldi G, Angeli F, Gentile G, Verdecchia P. Benefits of more intensive versus less intensive blood pressure control. Updated trial sequential analysis. Eur J Intern Med. 2022 Jul;101:49-55.
2. Zhang Z et al. Association between intensive blood pressure lowering and stroke-free survival among patients with and without Diabetes. Sci Rep. 2024 Sep 16;14(1):21551.
3. Ettehad D et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016 Mar 5;387(10022):957-967.

Impact of Obesity and Depressive Symptoms on Chest Pain in Patients with Nonobstructive Coronary Artery Disease

INTRODUCTION- Nonobstructive coronary artery disease (NOCAD) is a common condition that presents with chest pain (CP) despite the absence of significant blockages.[1] Also, it accounts for less than 50% of stenosis in coronary arteries. Understanding the risk factors for CP in NOCAD is crucial for developing targeted interventions to alleviate symptoms and improve outcomes. Obesity and depressive symptoms are two potential risk factors that may influence the prevalence and severity of CP in NOCAD. Obesity is a well-documented risk factor for cardiovascular disease, and studies have linked it to an increased risk of angina in the general population. However, its role in patients with NOCAD is not fully understood. Similarly, depression has been associated with more frequent and severe CP in various cardiac conditions. Obesity with angina in individuals with established NOCAD on angiography is unclear. So, this study aimed to investigate the relationships between obesity, depressive symptoms, and CP in patients with NOCAD, hypothesizing that both factors would be associated with a higher prevalence and frequency of CP.[2]

METHODS- This was a prospective study involving 814 participants from the Emory Cardiovascular Biobank, aged 20-90, who underwent left heart catheterization between 2003 and 2022. Eligible participants were aged 20-90 years and had angiographically confirmed NOCAD. Individuals with obstructive coronary artery disease (≥50% stenosis), heart failure, valvular disease, or other significant comorbidities were excluded. Data collection included demographic and clinical information, such as age, sex, race, medical history, and social determinants of health. Obesity was defined using a body mass index (BMI) of 30 or higher, with further classification into obesity classes based on BMI ranges. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9), a validated tool for screening depression, with scores indicating symptom severity. CP frequency was measured using the Seattle Angina Questionnaire (SAQ), a self-administered questionnaire that includes items on physical limitations, angina frequency, treatment satisfaction, and quality of life. The angina frequency domain score (AFCS), calculated from responses about the frequency of CP and nitro-glycerine use, was used as the primary measure of CP. Statistical analyses involved logistic regression to determine factors associated with CP prevalence and linear regression to assess CP frequency. A mediation analysis was conducted to explore the role of depressive symptoms in the association between obesity and CP.

RESULTS- The average age of the study population was 58.8 years, with 52.6% of participants being female. Obesity was present in 42.7% of the sample, and CP was reported by 71.5%. The mean AFCS was 76.4, indicating varying degrees of angina frequency across the cohort. Compared to individuals without obesity, those with obesity had a higher prevalence of CP (77.6% vs. 67%, p<0.001) and reported more frequent CP (lower AFCS, p=0.02) (Figure 1). Multivariable analyses showed that obesity was independently associated with a 1.7 times higher likelihood of experiencing CP, even after adjusting for demographics, cardiovascular risk factors, and social determinants. Additionally, depressive symptoms, as indicated by higher PHQ-9 scores, were independently correlated with CP prevalence (OR 1.07, p=0.03). Interaction analyses revealed that the association between obesity and CP was more pronounced in men and individuals without depression, while women and those with depression showed higher baseline CP regardless of obesity status. Mediation analysis indicated that depressive symptoms partially mediated the association between obesity and CP, accounting for approximately 12.6% of the relationship. This suggests that addressing depressive symptoms may help alleviate CP in patients with NOCAD who are also obese.

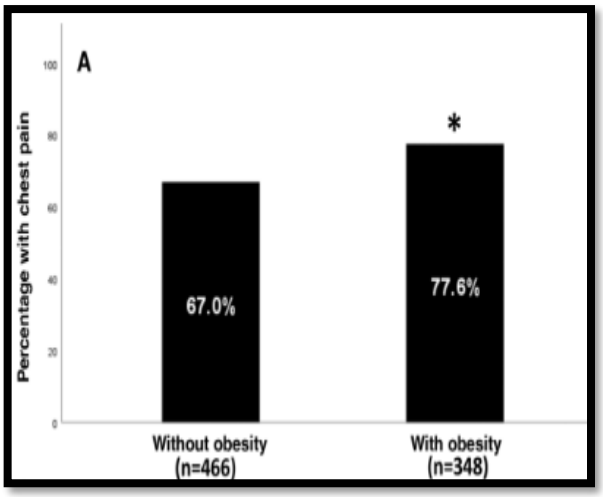


Figure 1. Prevalence of self-reported chest pain by obesity status

DISCUSSION- The association between depressive symptoms and CP observed in this study was also consistent with previous findings in cardiac populations.[2] A systematic review by Mommersteeg P et al. highlighted the higher prevalence of CP in individuals with NOCAD who also experienced anxiety and depression. Like the current results, they found that depressive symptoms were associated with a greater burden of CP. These findings suggest that the psychological state of patients plays a crucial role in the perception and severity of chest pain, potentially mediated by neurohormonal pathways and inflammatory processes that are affected by both depression and obesity.[3]

CONCLUSION- This study concluded that for individuals with NOCAD, obesity was linked to both the prevalence and frequency of self-reported chest pain, and this relationship was unaffected by demographics, medications, depressive symptoms, social determinants of health, or risk factors for CVD. Men and those without depression have a stronger correlation between self-reported chest pain and fat. In patients with NOCAD, the relationship between obesity and self-reported chest pain was partially mediated by depressive symptoms, and more severe depressive symptoms were independently linked to self-reported chest pain prevalence and burden.

In patients with nonobstructive coronary artery disease, obesity and depressive symptoms were independently linked to CP; in men, in particular, this association was partially mediated by depressive symptoms.

REFERENCES

1. Maddox TM, Stanislawski MA, Grunwald GK, Bradley SM, Ho PM, Tsai TT, Patel MR, Sandhu A, Valle J, Magid DJ, Leon B, Bhatt DL, Fihn SD, Rumsfeld JS. Nonobstructive coronary artery disease and risk of myocardial infarction. JAMA. 2014 Nov 5;312(17):1754-63.
2. Vatsa N et al. Patients With Nonobstructive Coronary Artery Disease and Chest Pain: Impact of Obesity and Depressive Symptoms. J Am Heart Assoc. 2024 Oct;13(19):e031429.
3. Mommersteeg P, Widdershoven J, Aarnoudse W, Denollet J. Personality subtypes and chest pain in patients with nonobstructive coronary artery disease from the TweeSteden Mild Stenosis study: mediating effect of anxiety and depression. Eur J Pain. 2016;20:427–437.

Relationship between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio and major adverse cardiovascular and cerebrovascular events in coronary artery disease

INTRODUCTION- Dyslipidemia is a significant contributor to adverse outcomes in patients with coronary artery disease (CAD), which remains a leading cause of mortality worldwide. Managing dyslipidemia traditionally focuses on reducing low-density lipoprotein cholesterol (LDL-C). However, residual cardiovascular risks persist even with aggressive LDL-C lowering, necessitating the identification of novel lipid indices that better predict adverse events.[1] The total cholesterol content of lipoproteins containing apolipoprotein B is known as non-high-density lipoprotein cholesterol (non-HDL-C). This comprises low-density lipoproteins (LDL), lipoprotein (a), intermediate-density lipoproteins (IDL), and very low-density lipoproteins (VLDL) and their metabolic remnants.[2] The non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) integrates both atherogenic and anti-atherogenic lipid parameters and has emerged as a potential risk marker. Nevertheless, there was a dearth of data regarding the association between the NHHR and the chance of adverse outcomes for CAD patients. So, this study aimed to evaluate the association between NHHR and the risk of major adverse cardiovascular and cerebrovascular events (MACCEs) in CAD patients undergoing percutaneous coronary intervention (PCI).[1]

METHODS- A retrospective analysis was conducted using data from 2251 patients who underwent PCI. Patients were included if they had complete data on total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) levels. The primary outcome was the incidence of MACCEs, which included cardiac mortality, acute myocardial infarction (AMI), stroke, and repeat revascularization. Patients were categorized into quintiles based on NHHR values: quintile 1 (<2.15), quintile 2 (2.15–2.77), quintile 3 (2.78–3.39), quintile 4 (3.40–4.22), and quintile 5 (>4.22). Data on demographics, clinical presentation, comorbidities, and treatment were collected. Logistic regression models were used to assess the relationship between NHHR and MACCEs, adjusting for confounders such as age, sex, smoking status, comorbidities (heart failure, atrial fibrillation, diabetes, hypertension), and medication use.

RESULTS- This study showed that over a median follow-up of 29.8 months, 270 patients experienced MACCEs. Patients in quintile 3 (NHHR 2.78–3.39) had the lowest adjusted odds of experiencing MACCEs (OR 0.64, 95% CI 0.42–0.99), while those in quintile 5 (>4.22) had an elevated risk (OR 1.17, 95% CI 0.74–1.64). Specifically, quintile 5 patients were more likely to be smokers and exhibited elevated levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C). Furthermore, they had a higher prevalence of ST-segment elevation myocardial infarction (STEMI) and a greater history of diabetes. In contrast, patients in quintile 1 were typically older, more likely to be male, and presented with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). They also had higher high-density lipoprotein cholesterol (HDL-C) levels and a greater percentage of bifurcation lesions. RCS analysis revealed a U-shaped association between NHHR and MACCEs, with the lowest risk observed at an NHHR of approximately 3.119 (Figure 1). Below this value, higher NHHR was associated with a decreased risk of MACCEs, while above this threshold, the risk increased significantly. Subgroup analysis demonstrated consistent U-shaped relationships across different patient demographics, except for younger patients (<65 years), where a linear association was observed.

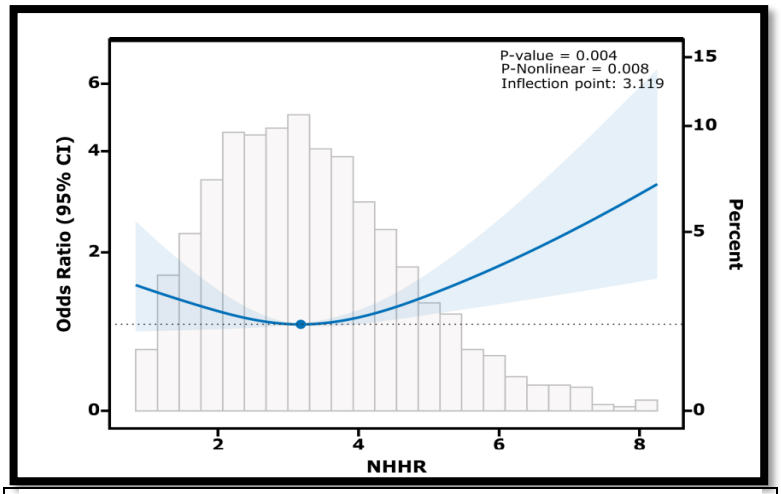


Figure 1. Association between NHHR and MACCEs in CAD patients with PCI

DISCUSSION- This study confirmed a U-shaped association between NHHR and the risk of MACCEs in CAD patients undergoing PCI, indicating that both very high and very low NHHR values were linked to increased adverse event risk. The findings suggested that NHHR was a more comprehensive lipid measure than individual lipid parameters like LDL-C, as it encompasses a balance of pro- and anti-atherogenic lipoproteins.[1] You J et al. reported similar associations between NHHR and adverse outcomes but did not completely explore non-linear relationships or adjust for confounders. This study extends those findings by employing RCS analysis to better delineate the dose-response relationship and identify an optimal NHHR range for minimizing risk.[3]

CONCLUSION- This study concluded that the clinical utility of NHHR as a predictor of MACCEs in patients undergoing PCI, with an optimal range around 3.119 associated with the lowest risk. These findings suggested that NHHR could guide more personalized lipid management strategies in CAD patients.

In patients with CAD having PCI, this study shows a U-shaped relationship between the baseline NHHR and the incidence of MACCE.

REFERENCES

1. Liu J et al. Association between the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) and cardiovascular outcomes in patients undergoing percutaneous coronary intervention: a retrospective study. Lipids Health Dis. 2024 Oct 1;23(1):324.
2. Zeng RX et al. U-Shaped Relationship of Non-HDL Cholesterol With All-Cause and Cardiovascular Mortality in Men Without Statin Therapy. Front Cardiovasc Med. 2022 Jul 7;9:903481.
3. You J, Wang Z, Lu G, Chen Z. Association between the Non-high-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol Ratio and the Risk of Coronary Artery Disease. Biomed Res Int. 2020; 2020:7146028.

Case Report on Successful Transcatheter Aortic Valve Replacement for Bicuspid Aortic Valve with Aortic Dissection

INTRODUCTION- Transcatheter aortic valve replacement (TAVR) was first developed as a novel treatment option for patients with symptomatic severe aortic stenosis (AS) who were unable to undergo surgery. Over 15 years, various randomized controlled trials (RCTs) have verified the effectiveness of TAVR.[1] However, performing TAVR in patients with bicuspid aortic valve (AV) stenosis complicated by previous type A aortic dissection presents unique challenges. The presence of a dissected aorta increases the risk of procedural complications, including embolism. This case report details a successful transfemoral TAVR performed in a patient with a history of type A aortic dissection, highlighting the procedural considerations and the need for novel cerebral embolic protection strategies.[2]

CASE PRESENTATION- A 69-year-old male presented with progressive dyspnea over several months. His medical history included a type A aortic dissection 19 years ago, treated with surgical replacement of the ascending aorta. Transthoracic echocardiography revealed severe bicuspid AV stenosis, characterized by a peak transvalvular flow velocity of 4.9 m/s, a mean pressure gradient of 61 mmHg, an aortic valve area of 0.5 cm², and a left ventricular ejection fraction of 46%. A three-dimensional computed tomography (CT) scan confirmed a type 0 bicuspid aortic valve with significant leaflet calcification, a patent coronary artery, and a supra-coronary graft in the ascending aorta. There was a patent false lumen in the left carotid, subclavian arteries, and suprarenal descending aorta. Given his previous aortic surgery, the high surgical risk scores (Society of Thoracic Surgeons risk score of 7.01 and EuroSCORE II of 7.77), and anatomical constraints, the patient was considered unsuitable for SAVR. Furthermore, the dissection involved the

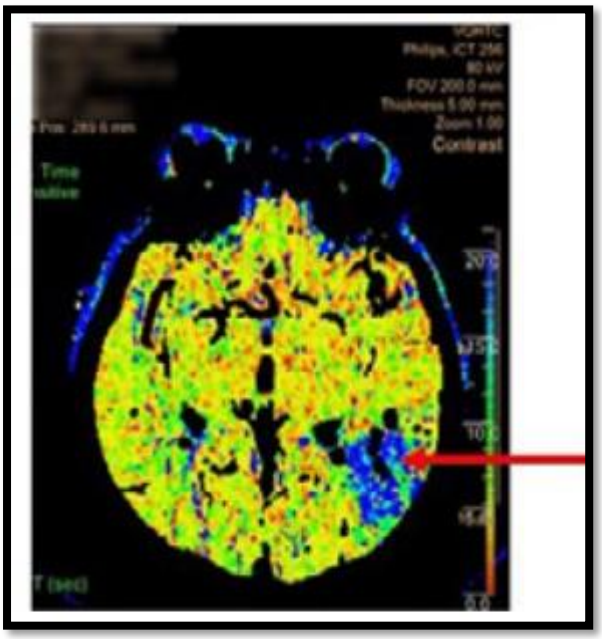


Figure 1. Brain CT tomography and perfusion scans on day 1 after TAVR, showing acute left temporoparietal infarction (arrows).

innominate, left subclavian, and carotid arteries, precluding the use of conventional cerebral embolic protection devices. The Cardiology team opted for transfemoral TAVR as the only viable therapeutic option. Under general anesthesia, the right femoral artery was accessed using angiographic guidance. A 20 Fr × 65 cm hydrophilic long sheath was advanced to the ascending aorta to bypass the dissected segment. A 25 mm Portico™ transcatheter aortic valve was deployed, followed by pre- and post-implantation balloon dilatation to reduce paravalvular leak. Although the patient was extubated without incident, he developed a minor left temporoparietal cerebral infarction postoperatively (Figure 1), which led to partial sensory aphasia but no motor deficits. Imaging confirmed no significant stenosis in major cerebral arteries, suggesting embolization from the valve as the infarction source. The patient was discharged on day seven with improved neurological function.

DISCUSSION- This case illustrated the feasibility and challenges of performing TAVR in patients with a history of type A aortic dissection and bicuspid aortic valve stenosis. In this patient, the use of an extended sheath allowed safe navigation and device deployment, avoiding contact with the dissected aortic segments.[2] Similarly, Konami Y et al. reported a TAVR procedure guided by three-dimensional CT/fluoroscopy fusion imaging in a patient with a right-sided aortic arch and chronic aortic dissection. The outcome was favorable, and the report highlighted the role of advanced imaging techniques in navigating complex aortic anatomies, which helped mitigate procedural risks.[3]

CONCLUSION- This study concluded that transfemoral TAVR is a feasible treatment option for patients with severe bicuspid aortic valve stenosis and previous type A aortic dissection, particularly when conventional surgical approaches are contraindicated. Successful outcomes require meticulous procedural planning, including the use of specialized sheaths and careful navigation to mitigate the risks associated with residual aortic dissection.

Transfemoral TAVR is a feasible treatment option for patients with severe bicuspid aortic valve stenosis and previous type A aortic dissection, particularly when conventional surgical approaches are contraindicated.

REFERENCES

1. Vincent F et al. Transcatheter aortic valve replacement in bicuspid aortic valve stenosis. Circulation. 2021 Mar 9;143(10):1043-61.
2. Liu CN et al. Successful TAVR for a Patient with Bicuspid Aortic Valve Stenosis and Previous Type A Aortic Dissection. Int Heart J. 2024;65(5):960-962.
3. Konami Y et al. Transfemoral Transcatheter Aortic Valve Implantation by Three-Dimensional Computed Tomography/Fluoroscopy Fusion Imaging Guidance in a Patient with Right-Sided Aortic Arch and Chronic Aortic Dissection. Cardiovasc Revasc Med 2022;40S:179-81.