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Long-Term Incidence and Risk Factors of Subaortic Pannus Overgrowth After Bileaflet Mechanical Aortic Valve Replacement

Hung Dung Van[1,2]; Minh Chau Van Nguyen[3]; Dang Huu Danh[1]; Nguyen Lam Vuong[*,4]

[1]Cardiac Surgery Department, Heart Institution of Ho Chi Minh City, 4 Duong Quang Trung Street, Ward Hoa Hung, Ho Chi Minh City 700000, Vietnam
[2]Department of Thoracic and Cardiovascular Surgery, Pham Ngoc Thach University of Medicine, 2 Duong Quang Trung Street, Ward Hoa Hung, Ho Chi Minh City 700000, Vietnam
[3]Analyst and Strategic Insights Department, Open Polytechnic, 3 Cleary Street, Lower Hutt 5011, New Zealand
[4]Department of Medical Statistics and Informatics, Faculty of Public Health, University of Medicine and Pharmacy at Ho Chi Minh City, 217 Hong Bang Street, Ward Cho Lon, Ho Chi Minh City 700000, Vietnam

*Corresponding author. Department of Medical Statistics and Informatics, Faculty of Public Health, University of Medicine and Pharmacy at Ho Chi Minh City, 217 Hong Bang Street, Ward Cho Lon, Ho Chi Minh City 700000, Vietnam (nguyenlamvuong@ump.edu.vn).

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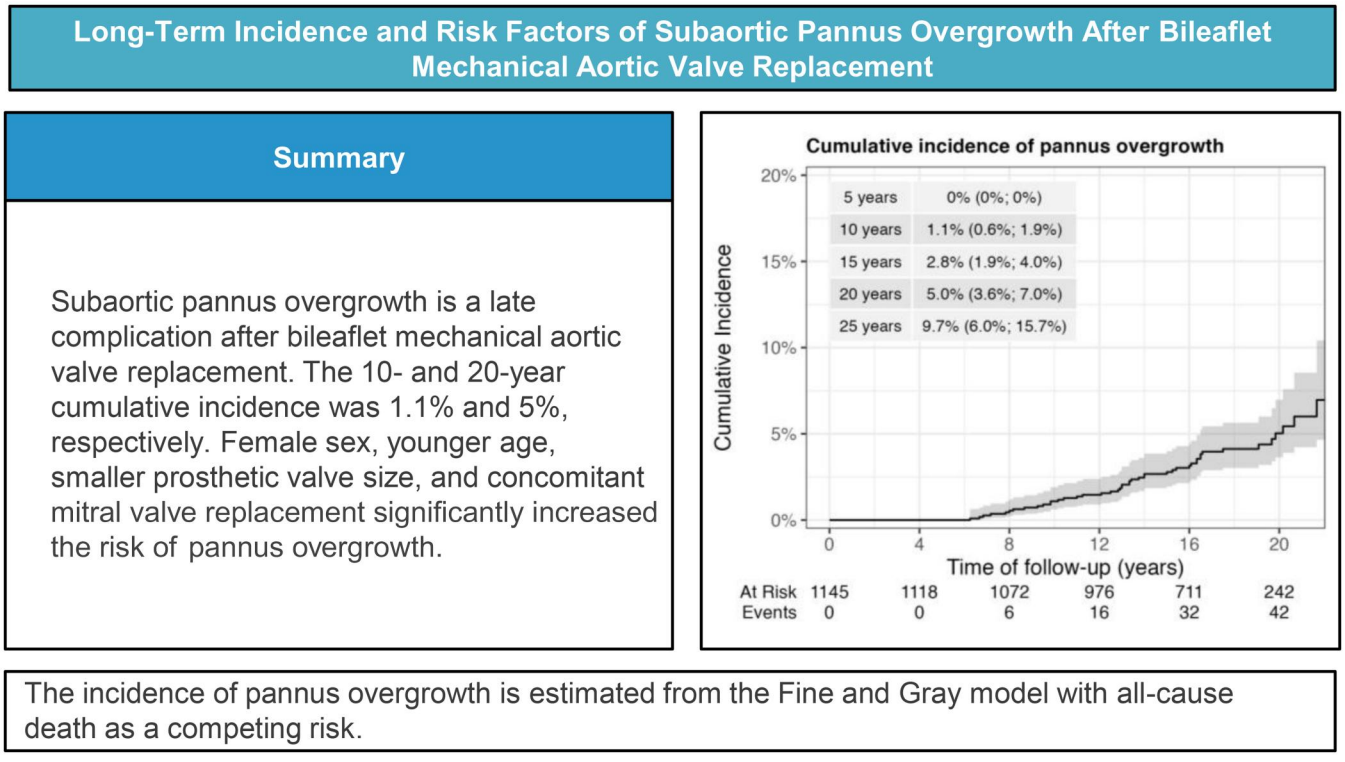
Graphical abstract



Abstract

Objectives: Subaortic pannus overgrowth is a recognized complication following aortic valve replacement (AVR) with mechanical prostheses, potentially requiring reoperation. Since data on its incidence and risk factors remain scarce, this study aimed to determine the incidence and risk factors for subaortic pannus overgrowth after AVR with bileaflet mechanical valves.

Methods: We retrospectively analysed 1145 patients who underwent AVR with bileaflet mechanical valves between 1995 and 2010 at a cardiac referral centre. Subaortic pannus overgrowth was defined by imaging evidence causing clinical stenosis and confirmed

intraoperatively. Cumulative incidence was estimated using competing risks analysis, and risk factors were identified using Fine and Gray models.

Results: During a mean follow-up of 16.5 years, 47 patients (4.1%) developed subaortic pannus overgrowth requiring reoperation (mean interval 13.6 years). The 10- and 20-year cumulative incidence was 1.1% and 5.0%, respectively. Multivariable analysis identified female sex (hazard ratio [HR]: 2.18), smaller prosthetic valve size (21 mm vs ≥23 mm, HR: 8.62, and ≤19 mm vs ≥23 mm, HR: 12.02), and concomitant mitral valve replacement (HR: 2.63) as independent risk factors. Older age at AVR was protective (HR: 0.69 per 10-year increase). Recurrence occurred in 1 patient after isolated pannus resection.

Conclusions: Subaortic pannus overgrowth is a late complication after bileaflet mechanical AVR, with a gradually increasing incidence. Female sex, smaller prosthesis size, younger age, and concomitant mitral valve replacement are significant risk factors. Complete pannus removal and valve replacement should be considered during reoperation. Further research into the underlying mechanisms is warranted for prevention strategies.

Keywords: aortic valve; mechanical prosthesis; pannus.

INTRODUCTION

Aortic valve disease stands as a prevalent valvular heart condition frequently necessitating surgical or interventional treatment.[1,2] The advent of mechanical prosthetic heart valves has transformed the treatment of severe valve dysfunction, offering life-saving solutions. Nevertheless, the long-term function and durability of these artificial valves can be jeopardized by complications, notably mechanical valve obstruction. Among the causes of such obstruction, pannus formation, defined by the excessive proliferation of fibroelastic tissue around the prosthetic valve, has become a significant concern.[3] This subvalvular, fibrotic soft-tissue growth within the prosthetic heart valve, known as pannus, is a recognized postoperative complication. With an ageing demographic leading to increased longevity post-valve surgery, pannus formation has become an increasingly frequent issue requiring reintervention.[4,5]

Subaortic pannus is believed to arise from a non-immunological inflammatory response within the periannular neointima of the left ventricular outflow tract.[6] Proposed pathophysiological mechanisms include: (1) the impact of turbulent blood flow across the valve, (2) a non-immune inflammatory reaction to the prosthesis within the periannular neointima on the left ventricular septum, and (3) elevated shear stress near the valve's pivot guard.[6,7] Despite its recognition as a non-structural valve dysfunction, comprehensive data regarding the incidence and associated risk factors of subaortic pannus overgrowth remain scarce. Consequently, this study aimed to evaluate the occurrence rate of subaortic pannus overgrowth and to analyse factors associated with its development following aortic valve replacement (AVR) using bileaflet mechanical valves.

METHODS

Study design and patients

This retrospective study included all patients who underwent AVR with bileaflet mechanical valves between 1995 and 2010 at a specialized cardiac referral centre in Ho Chi Minh City, Vietnam. The patient inclusion period was closed in 2010 to ensure a sufficiently long follow-up duration for the detection of pannus overgrowth. The study was approved by the institutional Ethics Committee (No. 29/VT-HDDD, dated September 24, 2021). The requirement for individual written informed consent was waived due to the study's minimal-risk retrospective nature. All procedures adhered to the principles outlined in the Helsinki Declaration as revised in 2008. Patients undergoing concomitant complex heart defects, those lost to follow-up immediately after the surgery, or those with missing medical records were excluded. All patient information was collected from standardized paper medical records.

Initial aortic valve replacement procedure

All surgical procedures were performed via a median sternotomy under aortic and bicaval cannulation, moderate hypothermia, and cold cardioplegic arrest. Aortic valve prostheses were implanted using non-everting mattress sutures reinforced with pledgets. Two types of bileaflet mechanical valves were utilized: Sorin Bicarbon (LivaNova, Saluggia, Italy) and St Jude HP (St Jude Medical, Minnesota, United States). Depending on individual patient conditions, several concomitant procedures were performed, including mitral valve replacement or repair, tricuspid valve repair, coronary artery bypass grafting, or thrombus removal.

Postoperative assessment and follow-up

Early mortality was defined as death occurring within 30 days post-surgery or during the same hospital admission. Following discharge, patients were scheduled for regular outpatient follow-up visits every 3 to 6 months during the first year, then every year, involving clinical examination and transthoracic echocardiography. In instances where subaortic pannus overgrowth was suspected (indicated by an increase in aortic valve mean pressure gradient or peak velocity without leaflet motion restriction), transoesophageal echocardiography and cinefluoroscopy were performed to investigate the underlying cause of the dysfunction. Since 2005, computed tomography (CT) scans were routinely performed in all suspected cases. Prothrombin time was monitored every 1 to 3 months. Oral anticoagulation therapy was prescribed to maintain a target international normalized ratio of 2.0 to 2.5 for patients with a mechanical aortic valve and 2.5 to 3.0 for those with a mechanical mitral valve or atrial fibrillation. Clinical follow-up concluded in December 2024. Patients whose last clinic visit was not within the scheduled timeframe were contacted by telephone to ascertain their current status.

Evaluation of subaortic pannus overgrowth

Subaortic pannus overgrowth is a gradual process of tissue ingrowth around the prosthetic valve. For the purpose of this study, it was

diagnosed by the presence of at least 2 of the following criteria: (1) a gradual increase in the mean pressure gradient across the mechanical aortic valve without echocardiographic evidence of leaflet motion restriction, (2) an aortic valve mean pressure gradient exceeding 40 mmHg or an aortic valve peak velocity surpassing 4 m/s on echocardiography, and (3) any visible subaortic tissue ingrowth beneath the mechanical aortic valve observed on echocardiography or CT. Patients diagnosed with subaortic pannus overgrowth exhibiting clinical signs and symptoms of aortic valve stenosis were indicated for surgical intervention.

Surgical procedure for subaortic pannus overgrowth

All reoperative procedures were performed via a median sternotomy under moderate hypothermia and cold cardioplegic arrest (**Figure 1**). Arterial cannulation was achieved through the ascending aorta or, in emergency cases, the femoral artery. Venous cannulation was performed via the vena cava. Three surgical approaches were employed based on the condition of the existing prosthetic valve. Subaortic pannus resection alone, leaving the original prosthetic valve in place, was performed when the valve's function remained satisfactory. Subaortic pannus resection combined with prosthetic valve replacement was undertaken in cases when the aortic annulus cannot be expanded. Finally, subaortic pannus resection combined with prosthetic valve replacement and aortic annular enlargement using either the Nick-Nunez[8] or Konno-Rastan[9] techniques was performed when the aortic annulus was stenotic and incompatible with the patient's body surface area (BSA). Postoperative follow-up for these patients was conducted in a manner similar to that described for the initial AVR.

Statistical analysis

Statistical analyses were conducted using R Statistical Software version 4.2.3. Continuous variables were presented as mean ± standard deviation, while categorical variables were summarized by frequency and percentage. Long-term outcomes included overall survival and the incidence of pannus overgrowth. In the analysis for these outcomes, all cases without the respective outcome event were censored as the last time of follow-up. The rate of all-cause mortality was estimated using the Kaplan-Meier method. Risk factors for all-cause mortality were analysed using Cox proportional hazards models. The cumulative incidence of subaortic pannus overgrowth was estimated, with all-cause death treated as a competing risk. Clinical risk factors for subaortic pannus overgrowth were identified using the Fine and Gray model, which explicitly accounted for competing risks and provided a subdistribution hazard ratio (HR).[10] Results from these statistical models were reported as HRs with their corresponding 95% CIs and *P*-values. For both the all-cause mortality and pannus overgrowth analyses, all variables exhibiting a *P*-value less than .2 in the univariable analysis were included in the multivariable models. The proportional hazards assumption was assessed using scaled Schoenfeld residuals—results showed that the assumption was well-supported for all variables in the models (**Figure S1**). A *P*-value less than .05 was considered statistically significant.

RESULTS

Between January 1995 and December 2010, a total of 1232 patients underwent AVR with bileaflet mechanical valves at our institution. Of these, 87 patients were excluded from the analysis due to the following reasons: 32 were lost to follow-up immediately after the index surgery, 23 had concomitant complex congenital heart defects, 29 had incomplete medical records, and 3 experienced recurrent infective endocarditis within 1 year of initial endocarditis treatment (**Figure 2**). The final analysis included 1145 patients. A majority of patients (84%) were from nearby areas, including the Southeast, Mekong Delta, and South Central Coast regions of Vietnam. The proximity of a patient's

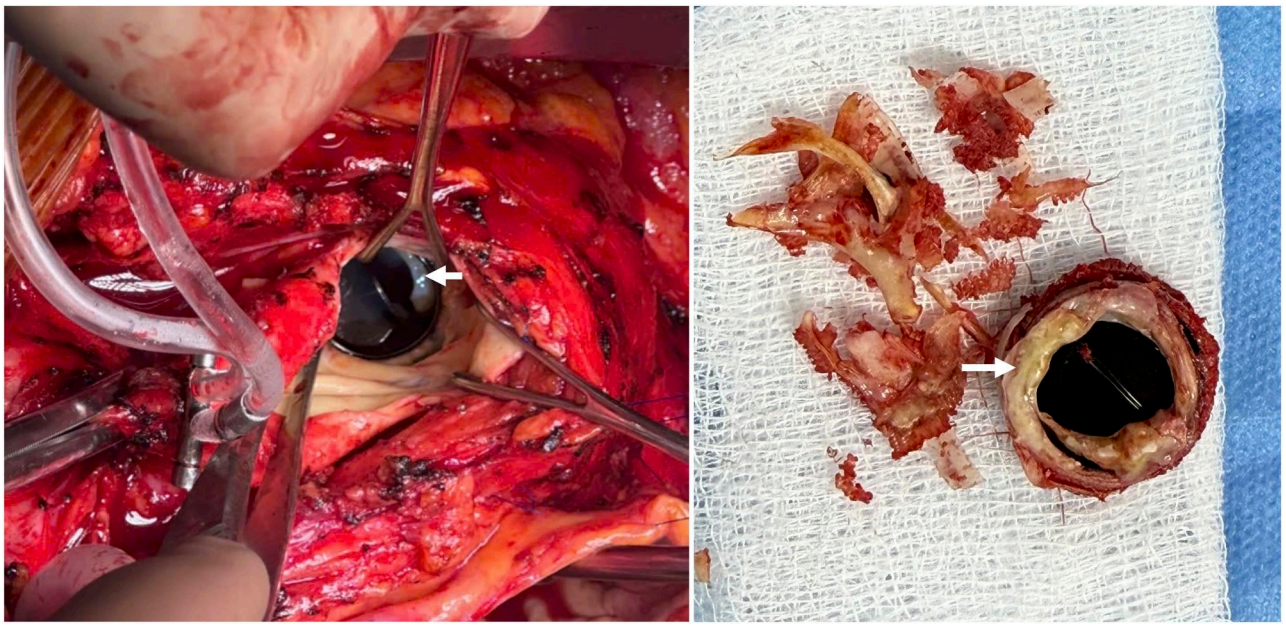


Figure 1. Intraoperative Images of Subaortic Pannus Overgrowth. White arrows indicate subaortic pannus overgrowth

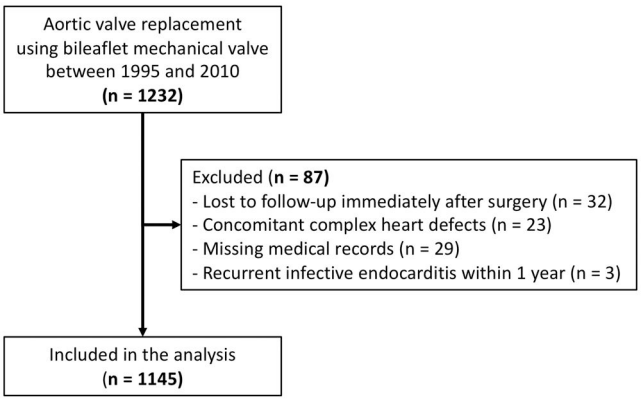


Figure 2. Study Flowchart of Patient Selection

residence was associated with a longer length of follow-up (**Table S1**).

Patient characteristics

The mean age at the time of the initial AVR was 40.3 ± 13.4 years, and 617 patients (53.9%) were male (**Table 1**). The primary cause of aortic valve disease was rheumatic heart disease, affecting 957 patients (83.6%). Other aetiologies included bicuspid aortic valve in 72 patients (6.3%), cardiac endocarditis in 58 patients (5.1%), and other miscellaneous causes in 58 patients (5.1%). Preoperatively, moderate-to-severe aortic valve regurgitation was present in 917 patients (80.1%).

The bileaflet mechanical valves implanted were predominantly Sorin Bicarbon in 1135 patients (99.1%), with St Jude valves used in the remaining 10 patients (0.9%). The most frequently implanted prosthetic valve sizes were 19 mm (285 patients, 24.9%), 21 mm (430 patients, 37.6%), and 23 mm (275 patients, 24.0%). Smaller proportions of patients received 17-, 25-, or 27-mm mechanical valves. Concomitant surgical procedures were performed in 756 patients (66.0%), including mitral valve replacement or repair in 709 patients (62%), tricuspid valve repair in 223 patients (19.5%), coronary artery bypass grafting in 34 patients (3%), and thrombus removal in 29 patients (2.5%) (**Table 2**).

Early and long-term clinical outcomes

The early mortality rate was 0.9%, with 10 deaths occurring out of 1145 patients. Postoperative complications were observed in 39 patients (3.4%), including heart failure in 9 patients (0.8%), bleeding requiring reoperation in 7 patients (0.6%), sepsis in 7 patients (0.6%), and pneumonia in 6 patients (0.5%). Other less frequent complications (<0.5%) included acute renal failure, sternal wound infection, multi-organ failure, and myocardial infarction (**Table 2**).

During a mean follow-up period of 16.5 years, 82 all-cause deaths occurred, including 28 deaths suspected to be cardiac-related and 32 deaths with unknown causes (**Table S2**). The overall survival rates at 10 and 20 years were 96.4% (95% CI: 95.4%-97.5%) and 91.2% (95% CI: 89.3%-93.2%), respectively (**Figure 3**A). Multivariable Cox regression analysis identified older age (HR [95% CI]: 1.98 [1.65-2.39] per 10-year increase),

Table 1. Clinical Characteristics of the Initial Aortic Valve Replacement

	Total (*N* = 1145)
Age (years)	40.3 ± 13.4
Sex (male)	617 (53.9)
BSA (m^2)	1.59 ± 0.08
Hypertension	90 (7.9)
Coronary diseases	34 (3.0)
Diabetes	24 (2.1)
Dyslipidemia	10 (0.9)
NYHA classification	
Class I	5 (0.4)
Class II	818 (71.4)
Class III	288 (25.2)
Class IV	34 (3.0)
Atrial fibrillation	428 (37.4)
Etiology of aortic valve disease	
Rheumatic disease	957 (83.6)
Bicuspid aortic valve	72 (6.3)
Cardiac endocarditis	58 (5.1)
Others	58 (5.1)
Ejection fraction (%)	62.9 ± 8.2
Left ventricular end diastolic dimension (mm)	55.0 ± 9.6
Systolic pulmonary artery pressure (mmHg)	51.4 ± 15.8
Moderate-to-severe aortic valve regurgitation	917 (80.1)

Summary statistics are mean ± standard deviation and *n* (%).
Abbreviations: BSA, body surface area; NYHA, New York Heart Association.

cardiac endocarditis as the aetiology of aortic valve disease (HR [95% CI]: 2.69 [1.21-5.98] compared to rheumatic disease), and mechanical valve size (≥23 mm or ≤19 mm compared to 21 mm, HR [95% CI]: 2.10 [1.12-3.95] and 2.23 [1.19-4.17], respectively) as independent risk factors for all-cause mortality (**Table S3**).

Subaortic pannus overgrowth

During the follow-up period, 47 patients (4.1%) were diagnosed with subaortic pannus overgrowth and subsequently underwent surgical intervention (**Table S2**). The mean interval between the initial AVR and the first diagnosis of pannus overgrowth was 13.6 ± 4.5 years, with the earliest occurrence at 6.3 years. Notably, 12 patients were diagnosed with pannus overgrowth within 10 years following their initial surgery. The cumulative incidence of subaortic pannus overgrowth at 10 and 20 years was estimated to be 1.1% (95% CI: 0.6%-1.9%) and 5.0% (95% CI: 3.6%-7.0%), respectively (**Figure 3**B).

In univariable analyses, age, sex, BSA, ejection fraction, left ventricular end-diastolic dimension, size of the aortic valve prosthesis, concomitant mitral valve replacement, and concomitant tricuspid valve repair were identified as significant factors associated with pannus overgrowth (**Table 3**). The multivariable analysis revealed that female sex (HR [95% CI]: 2.18 [1.08-4.42]), smaller prosthetic valve size (HR [95% CI] for 21-mm valve was 8.62 [1.09-68.1], and for ≤19-mm valve was 12.02 [1.49-97.3], when compared with ≥23-mm valves), and concomitant mitral valve replacement (HR [95% CI]: 2.63 [1.02-6.79]) were significant risk factors for pannus overgrowth. Conversely, older age (HR [95% CI]: 0.69 [0.55-0.86] per 10-year increase) appeared to be a protective factor (**Table 3**).

Table 2. Operative Characteristics of the Initial Aortic Valve Replacement

	Total (*N* = 1145)
Size of aortic valve prosthesis	
17 mm	47 (4.1)
19 mm	285 (24.9)
21 mm	430 (37.6)
23 mm	275 (24.0)
25 mm	83 (7.2)
27 mm	25 (2.2)
Annular enlargement procedure	1 (0.1)
Concomitant surgery	756 (66.0)
Mitral valve replacement	643 (56.2)
Tricuspid valve repair	223 (19.5)
Mitral valve repair	66 (5.8)
Coronary artery bypass	34 (3.0)
Removal of thrombus	29 (2.5)
Ascending aortic replacement	13 (1.1)
Any complication	39 (3.4)
Heart failure	9 (0.8)
Bleeding requiring reoperation	7 (0.6)
Sepsis or septic shock	7 (0.6)
Pneumonia	6 (0.5)
Acute renal failure requiring hemodialysis	4 (0.4)
Sternal wound infection	3 (0.3)
Multi-organ failure	1 (0.1)
Heart failure and acute renal failure	1 (0.1)
Myocardial infarction	1 (0.1)
Early mortality	10 (0.9)

Summary statistics are mean ± standard deviation and *n* (%).

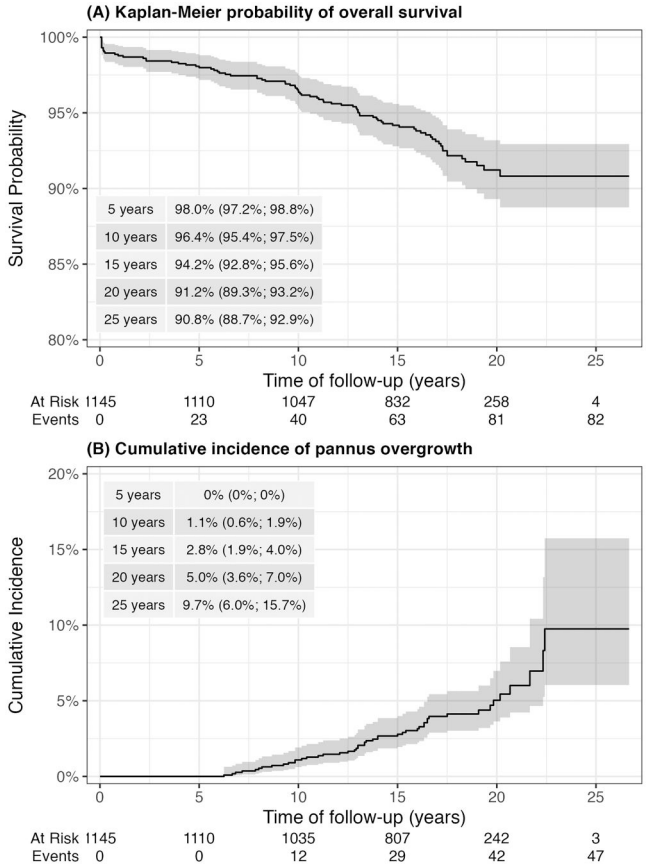


Figure 3. Kaplan-Meier Probability of Overall Survival and Cumulative Incidence of Pannus Overgrowth. The black line in each plot illustrates the Kaplan-Meier estimate for overall survival (Panel A) and the cumulative incidence of pannus overgrowth (Panel B). The shaded grey area represents the 95% CI for the respective estimate. The inset table within each plot provides the estimated probability or cumulative incidence, along with its 95% CI, at specific time points

The mean systolic pulmonary artery pressure in patients diagnosed with pannus overgrowth was 34.8 ± 8.6 mmHg. All these patients exhibited clinical signs and symptoms consistent with aortic valve stenosis, and CT imaging detected pannus overgrowth in 35 patients (74.5%) (**Table S4**). The presence of subaortic pannus overgrowth was confirmed intraoperatively in all 47 patients. The most frequently employed surgical technique for pannus management was pannus resection combined with prosthetic valve replacement and aortic annular enlargement (26 patients, 55.3%), followed by pannus resection combined with prosthetic valve replacement alone (18 patients, 38.3%). The remaining 3 patients (6.4%) underwent pannus resection through the existing prosthetic valve only. Postoperative complications following reoperation occurred in 3 patients (6.4%), including bleeding requiring reoperation and heart failure. Early mortality occurred in 1 patient. One patient (33%) experienced a recurrence of pannus overgrowth 75 months after undergoing pannus resection alone.

DISCUSSION

Our study highlights subaortic pannus overgrowth as a notable long-term complication following AVR with bileaflet mechanical valves. While no cases of pannus overgrowth were observed within the first 5 years post-implantation, the incidence gradually increased thereafter, reaching 1.1% at 10 years and 5.0% at 20 years. Furthermore, we identified several independent risk factors significantly associated with the development of subaortic pannus overgrowth, including younger age at initial surgery, female sex, smaller prosthetic valve size, and concomitant mitral valve replacement.

Although subaortic pannus overgrowth is a recognized non-structural dysfunction following AVR, limited research has specifically evaluated its occurrence in this setting.[11-14] Earlier studies from the 2000s reported a lower incidence of subaortic pannus formation, approximately 2% over a 20-year follow-up period,[6,12] in contrast to the higher rates observed in our study. However, a recent study conducted in Korea reported a similar incidence of pannus overgrowth to our findings, around 5% at 20 years post-index surgery. This discrepancy in incidence rates across studies may be attributed to variations in the definition of pannus formation and the statistical methodologies employed. The diagnosis of pannus formation can involve various imaging modalities, including cinefluoroscopy, transthoracic echocardiography, transoesophageal echocardiography, and CT.[3,6,15,16] However, definitive confirmation of pannus formation typically requires operative findings. Consequently, many studies investigating pannus formation have enrolled patients who underwent reoperation and whose subaortic pannus was confirmed intraoperatively.[4,5,17] This approach, however, may underestimate the true incidence of pannus formation, as some patients may decline reoperation or be lost to follow-up before surgical confirmation. In the present study, our focus was on pannus overgrowth, defined as pannus formation identified via imaging

Table 3. Factors Associated with Subaortic Pannus Overgrowth

	Univariable analysis			Multivariable analysis		
	HR	**95% CI**	***P*-value**	**HR**	**95% CI**	***P*-value**
Age (per 10-year increase)	0.83	0.69, 0.99	**.041**	0.69	0.55, 0.86	**.001**
Sex (female vs male)	4.70	2.34, 9.41	**<.001**	2.18	1.08, 4.42	**.031**
BSA (per 0.1-m^2 increase)	0.60	0.45, 0.81	**<.001**	0.65	0.41, 1.06	.082
Etiology of aortic valve disease						
Rheumatic disease	1	Ref				
Bicuspid aortic valve	1.16	0.36, 3.73	.801			
Cardiac endocarditis	-	-	-			
Others	–	–	–			
Ejection fraction (every 10% increase)	1.50	1.05, 2.15	**.027**	1.30	0.88, 1.93	.191
Left ventricular end diastolic dimension (mm)	0.93	0.90, 0.97	**<.001**	0.97	0.92, 1.01	.122
Systolic pulmonary artery pressure (mmHg)	1.01	0.99, 1.02	.390			
Moderate-to-severe aortic valve regurgitation	0.99	0.48, 2.03	.975			
Size of aortic valve prosthesis						
≥23 mm	1	Ref				
21 mm	19.32	2.57, 145	**.004**	8.62	1.09, 68.1	**.041**
≤19 mm	39.21	5.21, 295	**<.001**	12.02	1.49, 97.3	**.020**
Mitral valve replacement	4.85	2.06, 11.4	**<.001**	2.63	1.02, 6.79	**.045**
Tricuspid valve repair	1.87	1.02, 3.43	**.042**	1.42	0.76, 2.63	.270

Bold face p-values indicate statistical significance.

Abbreviations: BSA, body surface area; HR, hazard ratio.

that resulted in clinical signs and symptoms necessitating reoperation and subsequently confirmed intraoperatively.

In prior research, the time interval between the initial surgery and reoperation for pannus was typically reported as 10 to 13 years.[4,12] However, the more recent study from Korea documented a longer mean interval exceeding 18 years,[14] with only 2 patients diagnosed with pannus formation within the first decade post-surgery. In our cohort, 12 patients were diagnosed with subaortic pannus overgrowth within 10 years of AVR, and the mean interval to reoperation was over 13.5 years. This variation might be attributable to the different types of prosthetic valves utilized across studies, as certain designs could potentially promote turbulent transvalvular blood flow, thereby increasing the risk of subaortic pannus development.[12]

Earlier studies identified several factors potentially associated with subaortic pannus formation, including elevated plasma transforming growth factor-β1 levels, prosthesis design, surgical techniques, a low cardiac output state, turbulent blood flow, endocarditis, pregnancy, inadequate anticoagulation, and female patients with a small BSA.[5,11,12,18] However, it is important to note that these risk factors were often derived from analyses considering a composite endpoint of both valve thrombosis and pannus formation. Our findings largely align with the recent Korean study,[14] which identified younger age, smaller prosthesis size, and concomitant mitral valve replacement as significant independent risk factors for pannus overgrowth. Our study also corroborated female sex in patients with a small BSA as a risk factor. While the precise underlying mechanisms remain to be fully elucidated, several potential explanations exist. In smaller prosthetic valves, even a limited amount of pannus can exert a more substantial haemodynamic impact compared to larger valves, as the same tissue growth occupies a greater proportion of the valve orifice area. Furthermore, in smaller valves, pannus formation may have a relatively higher likelihood of encroaching upon critical components such as the pivot guard, thereby affecting leaflet movement. This vulnerability is compounded by the fact that smaller valves are also associated with a higher incidence of prosthesis-patient mismatch (PPM).[19] Our findings support this, as our estimated PPM incidence, derived from mean effective orifice areas reported in the literature,[20,21] was concentrated almost entirely in our smallest valve cohort (**Table S5**). It is important to note, however, that due to a lack of routinely collected data, we were unable to calculate the exact PPM incidence for our entire cohort. Younger age emerged as a risk factor, potentially due to a more pronounced inflammatory response compared to older individuals. The association between concomitant mitral valve replacement and subaortic pannus formation could be explained by: (1) the close proximity of the 2 prosthetic valves when implanted simultaneously, potentially leading to a more intense local inflammatory reaction; and (2) the potential for the prosthetic mitral valve to alter haemodynamics in the subaortic region, thereby creating an environment conducive to pannus growth. Previous research supports this hypothesis by demonstrating higher transaortic pressure gradients in patients undergoing concomitant mitral valve replacement compared to those with isolated AVR.[22,23]

Surgical management of subaortic pannus overgrowth is generally technically feasible. However, the optimal strategy regarding preservation versus replacement of the existing prosthetic valve remains a subject of debate. Some authors advocate for isolated pannus resection through the mechanical aortic valve, without valve replacement, provided the original valve exhibits satisfactory function.[24,25] Preserving the existing valve also simplifies the surgical procedure. Conversely, others favour concomitant prosthetic valve replacement.[4,26,27] Recurrence of aortic pannus overgrowth has been reported in several instances.[4] In our series, 1 patient experienced recurrent pannus, having initially undergone pannus resection alone without valve replacement. Our experience suggests that complete removal of subvalvular pannus, particularly in the area below the hinge area, is challenging without explanting the original valve. Therefore, we recommend complete pannus excision and prosthetic valve replacement in patients requiring

reoperation for subaortic pannus overgrowth. Aortic annulus enlargement should also be considered to accommodate a larger prosthesis necessitated by the patient's increase in BSA over the long follow-up period.

The present study has several limitations. First, its retrospective observational design and the fact that it was conducted at a single cardiac centre restrict the generalizability of our findings. The exclusion of a subset of patients with incomplete medical records or those lost to follow-up may have also introduced selection bias, potentially influencing the observed outcomes. Second, our definition of pannus overgrowth required both imaging evidence and associated clinical signs and symptoms with intraoperative confirmation. Data from longitudinal echocardiogram follow-ups were not available, meaning patients with asymptomatic subaortic pannus formation were not included, which likely underestimates the true incidence of pannus formation in our cohort. Third, while the predominant aetiology of aortic valve disease in our study population was rheumatic heart disease (84.5%), it did not emerge as a significant risk factor for pannus formation in our analyses. Nevertheless, caution should be exercised when extrapolating our findings to patients with other underlying aortic valve pathologies. Fourth, our study relied almost exclusively on a single type of valve (Sorin Bicarbon), and therefore our results might not be directly applicable to other mechanical or biological prostheses. Finally, biomarkers related to pannus formation, such as TGF-β1 and inflammatory markers, were not measured in this study, which prevented us from exploring the underlying molecular mechanisms of pannus formation.

In conclusion, subaortic pannus overgrowth is a long-term complication following AVR with bileaflet mechanical valves, with cumulative incidences of 1.1% and 5.0% at 10 and 20 years, respectively. Younger age at the initial valve replacement, female sex, smaller prosthetic valve size, and concomitant mitral valve replacement were identified as independent risk factors for its development. We suggest prioritizing the selection of larger prosthetic valve sizes in younger patients, particularly those requiring concomitant mitral valve replacement. For patients undergoing reoperation for pannus overgrowth, complete pannus excision and prosthetic valve replacement are recommended. Future research focusing on the molecular mechanisms underlying pannus formation is warranted to identify optimal strategies for its prevention in patients undergoing AVR.

AUTHOR CONTRIBUTIONS

H.D.V.: conceptualization, data curation, methodology, writing—original draft. M.C.V.N.: data curation, methodology, writing—review & editing. D.H.D.: conceptualization, methodology, writing—review & editing. N.L.V.: conceptualization, formal analysis, methodology, writing—review & editing.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

FUNDING

None declared.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, NLV, upon reasonable request.

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