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Review

Infective Endocarditis in Bicuspid Aortic Valve: A Contemporary Review of Clinical Characteristics, Structural Complications, and Surgical Outcomes

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Abstract

Bicuspid aortic valve-associated infective endocarditis (BAV-IE) is a unique and aggressive type of native valve infection. The combined effects of congenital valve malformation, altered hemodynamics, and genetic susceptibility promote endothelial injury and bacterial colonization, predisposing affected individuals to serious infections. Compared with endocarditis in the tricuspid aortic valve, BAV-IE affects young patients with few comorbidities and causes more severe tissue damage, periannular abscesses, and necessitates early surgery. Notably, streptococci and staphylococci remain the predominant pathogens causing the disease. Multimodal imaging, which integrates transthoracic and transesophageal echocardiography into cardiac computed tomography, is crucial for the early detection of structural complications and surgical planning. Prompt surgical interventions, including radical debridement, valve replacement, and appropriate aortic repair, ensure optimal infection control and long-term outcomes. Moreover, long-term survival is favorable, regardless of infection severity, when managed promptly and comprehensively. Lifelong surveillance and preventive strategies focusing on oral hygiene, infection control, and procedural asepsis are critical for reducing recurrence and improving prognoses in this high-risk population.

Keywords: bicuspid aortic valve; infective endocarditis; structural complication; diagnosis; surgical management; long-term outcome

1. Introduction

The bicuspid aortic valve (BAV) is the most common congenital cardiac malformation, affecting between 1% and 2% of the general population [1]. This structural abnormality predisposes affected individuals to a variety of complications, including aortic stenosis (AS), aortic regurgitation (AR), ascending aortic aneurysm, and infective endocarditis (IE) [2]. Although BAV may occur as an isolated finding, it is frequently associated with other congenital heart defects and genetic syndromes, such as aortic coarctation (50%–75%), Turner syndrome (30%), and ventricular septal defects (10%) [3].

Paget described BAV as a distinct pathological entity in 1844, and William Osler recognized its association with IE in 1886 [4]. Despite the considerable advances in diagnostic imaging and surgical techniques, IE remains a life-threatening condition, and in-hospital mortality rates reach up to 20% [5]. Epidemiological data indicate that individuals with BAV have a 2% lifetime risk of developing IE, which translates to an annual incidence of 0.3% [6]. The Mayo Clinic reported an incidence of BAV-associated IE (BAV-IE) of approximately 14 cases per 10,000 patient-years, which is 11 times that found in the general population [7].

Surgical intervention is required in nearly half of all cases of native-valve IE [8,9], but this proportion increases to approximately 75% in patients with BAV [10]. Such an increase emphasizes the disease's invasive and structurally destructive nature in this subgroup [10,11]. These findings confirm that BAV is a particularly vulnerable substrate for infective complications in native valve pathologies.

Given the distinct anatomical, hemodynamic, and pathological features of BAV-IE, a comprehensive understanding of its epidemiology, microbiology, imaging characteristics, structural complications, and management principles is essential for improving clinical outcomes. This review presents a comprehensive synthesis of current evidence on the clinical characteristics, pathological mechanisms, and therapeutic strategies unique to IE in the context of BAV.

2. BAV as the Predominant Substrate for IE

Individuals with BAV are considerably more susceptible to IE than those with normal tricuspid valve anatomy. According to current data, BAV is the leading predisposing substrate for IE, and epidemiological studies have consistently demonstrated a strong male predominance [12]. BAV affects only 2% of the general population, but it accounts for 24% of aortic valve endocarditis cases requiring surgery [13]. This vulnerability extends to high-risk populations because BAV is frequently affected in intravenous drug users due to its hemodynamic predisposition [2].

Hemodynamic changes remain central to this pathophysiology. Four-dimensional flow magnetic resonance imaging studies have demonstrated that even hemodynamically normal BAVs generate eccentric systolic jets and regions of elevated wall shear stress (WSS) in the ascending aorta, resulting in endothelial microtrauma that promotes bacterial colonization during transient bacteremia [14,15]. Additionally, aortic morphology influences flow asymmetry and WSS distribution, implying that inherited aortic geometry and disturbed hemodynamics interact to create a microenvironment conducive to infections [16].

The heightened susceptibility of individuals with BAV to IE is largely attributed to chronic shear stress across the abnormal valve, which causes endothelial injury and promotes bacterial adherence [13]. Increasing evidence points to a genetic contribution, and mutations in pathways, such as NOTCH1 and ACTA2, predispose these individuals to extracellular matrix disruption, aortic wall fragility, and abnormal endothelial responses, which increase infection risk [17,18].

Clinical data confirm the magnitude of this risk. A large multicenter cohort study found that the patients with BAV had a relative risk of contracting IE that is 23-fold that in patients with tricuspid aortic valves [19]. In individuals with BAV under the age of 65, the risk remains 15-fold that of individuals aged over 65, underscoring the inherent vulnerability of individuals with BAV regardless of comorbid factors [19]. Notably, these individuals have a cumulative lifetime incidence of 6% for IE by age 90 [20]. Patients with BAV-IE present nearly a decade earlier than those with tricuspid aortic valve (TAV)-associated IE, with mean ages of 50 years, and males are predominant (94%) [21]. Collectively, these findings establish BAV is a uniquely vulnerable substrate for IE and is driven by a complex interplay of genetic, structural, and hemodynamic factors.

3. Microbiological Spectrum: Causative Organisms in BAV-IE

The microbiological profile of IE in patients with BAV reflects the bicuspid valve's anatomical vulnerability and the epidemiology of bacteremia in specific populations. Contemporary studies have consistently demonstrated a predominance of streptococcal and staphylococcal species in BAV-IE, although pathogen distribution varies among regional factors, including intravenous drug use, dental hygiene, and diagnostic capacity [19–23].

Streptococci account for 30%–35% of BAV-IE cases, staphylococci for 29%–35%, and culture-negative endocarditis for 20%–24% [19–22]. Although the underlying anatomy influences disease aggressiveness and surgical outcomes, the overall microbiological spectrum is comparable to that of TAV endocarditis [19,21,22].

A large multicenter study combining U.S. and Italian cohorts [19] found that the incidence of *Staphylococcus aureus* infection is lower in BAV-IE than in TAV-IE. In the U.S. cohort, *S. aureus* caused 19.5% of BAV-IE cases and 46% of TAV-IE cases; in the Italian cohort, the figures were 8.3% and 16.7%, respectively. Streptococcal species, such as *Streptococcus viridans*, *Streptococcus mitis*, *Streptococcus mutans*, and *Streptococcus sanguinis*, were proportionally more frequently detected in BAV-IE. Culture-negative cases were more common in BAV-IE (17.1%) than in TAV-IE (10%), and no single organism was linked to complications, such as aortic root abscesses. In the present study, a species-specific breakdown was provided, and the relative frequencies of individual viridans-group streptococci were explored. This level of granularity, which is uncommon in most native-valve IE studies, emphasizes the predominance of streptococci in BAV-IE and the importance of species-level identification in guiding empiric and prophylactic therapy.

Enterococcus species appear less frequently in BAV-IE. However, enterococcal infections are more commonly associated with TAV-IE. This relationship can be explained by older age and high burden of comorbidities and incidence of urinary or colonic sources of infection in patients with TAV-IE [24]. These differences suggest that the underlying patient characteristics and infective sources considerably influence the microbiological profile of aortic valve endocarditis.

Overall, these findings show that although BAV-IE causes more structural damage and clinical severity than TAV-IE, its microbial spectrum is similar to native-valve IE, and minor differences are due to population and host factors [19–22]. This evidence supports current prophylactic and empiric antimicrobial strategies focusing on streptococcal and staphylococcal coverage in high-risk patients with BAV and on bacteremia-related procedures [2,22,25].

Table 1 (Ref. [6,13,21,24]) summarizes the distribution of causative organisms reported in major studies on BAV-IE.

4. Imaging Findings in BAV-IE

Transthoracic echocardiography (TTE) remains the first-line imaging modality for evaluating IE, particularly for patients with BAV. It usually reveals characteristic features, such as vegetations, valvular perforations, and perivalvular abscesses. However, in BAV-IE, routine parameters, including left atrial diameter, left ventricular end-diastolic diameter, and left ventricular end-systolic diameter, may not show considerable deviation, and the incidence rates of severe AR or AS consistently increase. Given the heightened risk of perivalvular abscess formation in BAV-IE, early application of TTE and transesophageal echocardiography (TEE) is strongly recommended because the prompt detection of such complications can critically influence clinical outcomes [6,26]. Although TTE is an essential screening tool, its sensitivity for detecting vegetations in BAV-IE ranges from 50% to 90%, necessitating additional evaluation with TEE in cases of inconclusive results or high clinical suspicion. TEE has a high sensitivity (approximately 90%–100%) for detecting vegetations and

Table 1. Prevalence of causative organisms in patients with BAV-IE and TAV-IE.

Study	Country	Study duration	Number of patients		Streptococcus		Staphylococcus		Enterococcus		Negative		Other causative organisms	
			BAV	TAV	BAV	TAV	BAV	TAV	BAV	TAV	BAV	TAV	BAV	TAV
Chen *et al*. (2017) [6]	China	2003–2012	51	120	21.6%	21.7%	13.7%	6.7%	2%	5%	60.8%	62.5%	2%	4.2%
Le *et al*. (2021) [13]	USA	1997–2017	51	159	51%	29%	27%	32%	3.9%	22%	7.8%	10%	9.8%*	6.9%*
Bohbot *et al*. (2023) [24]	Italy, France	2000–2019	123	605	30.9%	33.2%	17.1%	24%	3.3%	16.4%	23.6%	14.4%	25.2%	12.6%
Chatrath *et al*. (2024) [21]	UK	2015–2022	34	49	32%	47%	29%	27%	15%	10%	21%	16%	3%	0%

BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; BAV-IE, bicuspid aortic valve-associated infective endocarditis; TAV-IE, tricuspid aortic valve-associated infective endocarditis. * The "Other causative organisms" category represents the combined proportion of the "Fungal" and "Others" categories reported in the original study by Le et al. (2021) [13]. Percentages were recalculated by the authors based on the total number of BAV-IE and TAV-IE cases.

associated complications, such as abscesses and perforations [27].

Certain anatomical conditions, including extensive calcification, prosthetic valve endocarditis, or complex root infections, can reduce echocardiographic accuracy. In these scenarios, cardiac computed tomography (CCT), particularly multidetector computed tomography (MDCT), is a valuable tool. A meta-analysis comparing TEE and CCT found that CCT has a higher sensitivity for detecting perivalvular abscesses or pseudoaneurysms (78% vs. 69%), whereas TEE has a higher sensitivity for valvular vegetations (94% vs. 64%) [28]. A multimodality imaging approach integrating the anatomical detail of CCT for delineating paravalvular abscesses with the high-resolution functional assessment of TEE for identifying vegetations, fistulae, and perforations is pivotal for the comprehensive evaluation of BAV-IE, especially in anatomically complex presentations [29].

Multimodality imaging can be indispensable for surgical planning in complex BAV endocarditis. For instance, in a case involving a pseudoaneurysm of the mitral–aortic intervalvular fibrosa, echocardiography provides initial diagnosis, but cardiac MDCT is required to fully delineate the size, communications, and anatomical extent of the lesion, providing a surgical team with critical details [30]. In culture-negative cases, imaging results are crucial for guiding diagnosis and management [6,31].

In summary, although TTE remains the cornerstone of initial evaluation in BAV-IE, an early transition to TEE is essential for detailed structural assessment. When infection exceeds the diagnostic capabilities of echocardiography, CCT provides crucial anatomical insight. An integrated approach combining TTE, TEE, and advanced CCT is thus critical for accurate diagnosis, risk stratification, and surgical planning in patients with BAV-IE.

5. Clinical Characteristics of BAV-IE

BAV is a noncyanotic congenital cardiac anomaly that has distinct clinical characteristics when complicated by IE [2]. Patients with BAV-IE are typically 10 years younger than those with TAV-IE and have considerably fewer comorbidities, such as hypertension, atrial fibrillation, coronary artery disease, and diabetes mellitus. Despite their younger age and lower comorbidity burden, patients with BAV-IE have a more aggressive disease course, requiring early surgical intervention [13,32].

In some cases of BAV-IE, systemic inflammation and multiorgan involvement may occur, resulting in prolonged fever, diffuse purpura, anemia, thrombocytopenia, and acute renal dysfunction [26].

IE accounts for approximately 6% of all aortic valve surgeries performed on patients with BAV, and intraoperative findings revealed aortic root abscesses in up to 89% of BAV cases requiring concomitant aortic surgery, underscoring the infection's invasive and tissue-destructive nature [33].

Collectively, these data indicate that BAV-IE primarily affects young and otherwise healthy individuals but presents with a highly destructive phenotype characterized by rapid valvular deterioration, abscess formation, and the frequent need for urgent surgical intervention.

6. Complications of BAV-IE

IE involving a BAV is frequently accompanied by severe structural complications, reflecting the congenital valve morphology and altered hemodynamics inherent to this condition. These complications occur more frequently and progress more aggressively than those in TAV-IE, necessitating early surgical intervention.

The most common complications are valvular and myocardial abscesses, cusp perforation, and acute heart failure. Other side effects include embolic stroke, peripheral embolization, and intracardiac sequelae, such as fistulae and pseudoaneurysms [6,25,30]. Septic embolization from vegetations is the most common extracardiac manifestation, occurring in 30%–50% of cases, especially in left-sided IE [34,35].

Cusp perforation is a characteristic feature of BAV-IE, which frequently results in acute AR. Severe AR affects approximately 88% of patients with BAV-IE, versus 67% with TAV-IE [21]. Compared with TAV-IE, BAV-IE is associated with a considerably higher incidence of perivalvular abscess formation, thus frequently requiring early surgical intervention. Nevertheless, overall mortality rates remain comparable between the two conditions [36].

Periannular abscesses develop in 25%–40% of patients with BAV-IE, versus 4%–22% of TAV-IE patients [19,32]. Perivalvular extension of infection can cause complex structural lesions, such as sinus of Valsalva aneurysms, fistulous tracts, and conduction disturbances [2,37]. In severe cases, infection can spread into the left ventricular outflow tract (LVOT), causing pseudoaneurysm formation and intracardiac shunting. These cases are rare but life-threatening complications that require immediate surgical repair [38].

7. Management Strategies: Medical and Surgical Considerations

Acute surgical intervention is frequently needed in IE to manage severe valvular dysfunction and systemic complications [23]. Patients with BAV-IE have a considerably higher rate of valve replacement than those with TAV-IE (71% vs. 47%) [21]. Current evidence strongly supports that early surgery in BAV-IE controls infection and prevents progressive valvular and paravalvular destruction [5,9,12,32]. The frequent need for concomitant aortic surgery reflects the combined effects of congenital aortic wall abnormalities and chronic abnormal flow dynamics. BAV produces eccentric transvalvular jets that generate asymmetric WSS, leading to progressive aortic dilation and medial degeneration [6,12,18]. Moreover, elastin fragmentation, smooth muscle cell apoptosis, and matrix metalloproteinase overexpression weaken the aortic wall [12]. These changes increase the susceptibility of the aortic root to periannular infection and mycotic destruction, explaining the high rates of root abscess formation, pseudoaneurysm, and ascending aortic involvement observed in surgical series [6,32,33,39].

The percentage of patients with BAV-IE requiring concomitant ascending aortic replacement is higher than that in patients with TAV-IE (31% vs. 16%). This difference indicates the common presence of clinically significant aortopathy in BAV-IE [32]. Failure to address the infected or dilated aortic root during the index procedure may result in ongoing infection and the need for reoperation [2,6,9,23]. Therefore, comprehensive preoperative imaging of the aortic root and ascending aorta is required, and surgical planning should include root replacement or repair when necessary to ensure long-term infection control.

7.1 Valve Repair Versus Replacement

In BAV-IE, the surgical approach is determined by the extent of infection and the condition of valve tissue. Repair is preferred when the infection is localized and the cusp structure is preserved because it preserves native hemodynamics, avoids prosthetic material, and reduces the risk of reinfection. When performed in anatomically appropriate cases, repair yields excellent mid- to long-term results with low complication rates [40].

However, because active infection frequently causes extensive cusp or annular destruction, replacement is still the most common treatment option. Repair is rarely possible during the acute phase and is usually reserved for isolated regurgitation after infection has cleared [41]. Replacement ensures that the infection is completely eradicated. As a result, repair is only appropriate for limited, nondestructive disease, whereas replacement is necessary when tissue damage prevents a stable repair [13,40,41].

7.2 Choice of Prosthesis

Prosthesis selection in BAV-IE is primarily determined by age, comorbidities, and anticoagulant tolerance. When radical debridement is performed, mechanical and bioprosthetic valves provide comparable early survival and infection control. Mechanical valves are preferred in young patients because of their durability and low risk of reoperation, but they require lifelong anticoagulation, which increases the risk of bleeding. Bioprosthetic valves do not require anticoagulation but deteriorate more quickly, particularly in young people. Thus, mechanical prostheses are recommended for patients under the age of 60, whereas bioprostheses are appropriate for older adults or those who cannot tolerate anticoagulation [42].

7.3 Management of the Ascending Aorta

Given that BAV is frequently associated with aortopathy, the management of the ascending aorta is critical to a surgical strategy. Histopathological abnormalities, such as elastin fragmentation and medial degeneration, increase the risk of progressive dilation even after valve surgery [12,17]. When aortic valve replacement (AVR) is used to treat BAV-IE, the replacement of the ascending aorta should be considered if the diameter exceeds 45 mm or is small in cases of rapid growth, connective tissue disorder, or a family history of dissection [27].

7.4 Surgical AVR (SAVR) Versus Transcatheter AVR (TAVR) in BAV-IE

BAV anatomy is frequently observed in young patients and poses unique challenges for TAVR. The heterogeneous leaflet morphology and extensive calcification associated with BAV substantially increase procedural complexity and the risk of adverse events, such as paravalvular leak, valve embolization, and annular rupture. Although transcatheter approaches are evolving, their use in active IE remains contraindicated, and their role in previously infected bicuspid anatomy is limited to highly selected and post-healed cases with prohibitive surgical risk [1,2,12,43].

By contrast, SAVR allows for precise decalcification, tailored annular sizing, and anatomical correction, which are critical for achieving optimal valve function and durability [43,44]. SAVR enables complete debridement and excision of infected and necrotic tissues and the reconstruction of the annulus or aortic root. SAVR is more effective than TAVR in BAV-IE for infection control, structural repair, and long-term survival [43]. Thus, SAVR remains the preferred intervention for patients with BAV, especially in the presence of active infection or complex structural pathology [43,44].

7.5 Combined and Complex Surgical Approaches

Combined surgical procedures are often required in advanced or complex BAV-IE. Radical debridement, anatomical reconstruction with patch repair, and concurrent valve replacement result in optimal outcomes for LVOT pseudoaneurysms [38]. Similarly, the rupture of a sinus of Valsalva aneurysm into the right atrium necessitates valve replacement through bovine pericardial patch repair [37].

Early surgery, combined with targeted antimicrobial therapy, considerably improves survival, lowering mortality from 32.7% with medical therapy alone to 6.7% with surgery [31]. In *Brucella*-associated BAV-IE, starting doxycycline, rifampicin, and gentamicin enhances infection control [31].

Culture-negative endocarditis remains a particular challenge given that destructive valvular lesions can develop despite sterile blood cultures. Empirical therapy with vancomycin and gentamicin, followed by early AVR and surgical management of concomitant cardiac lesions when

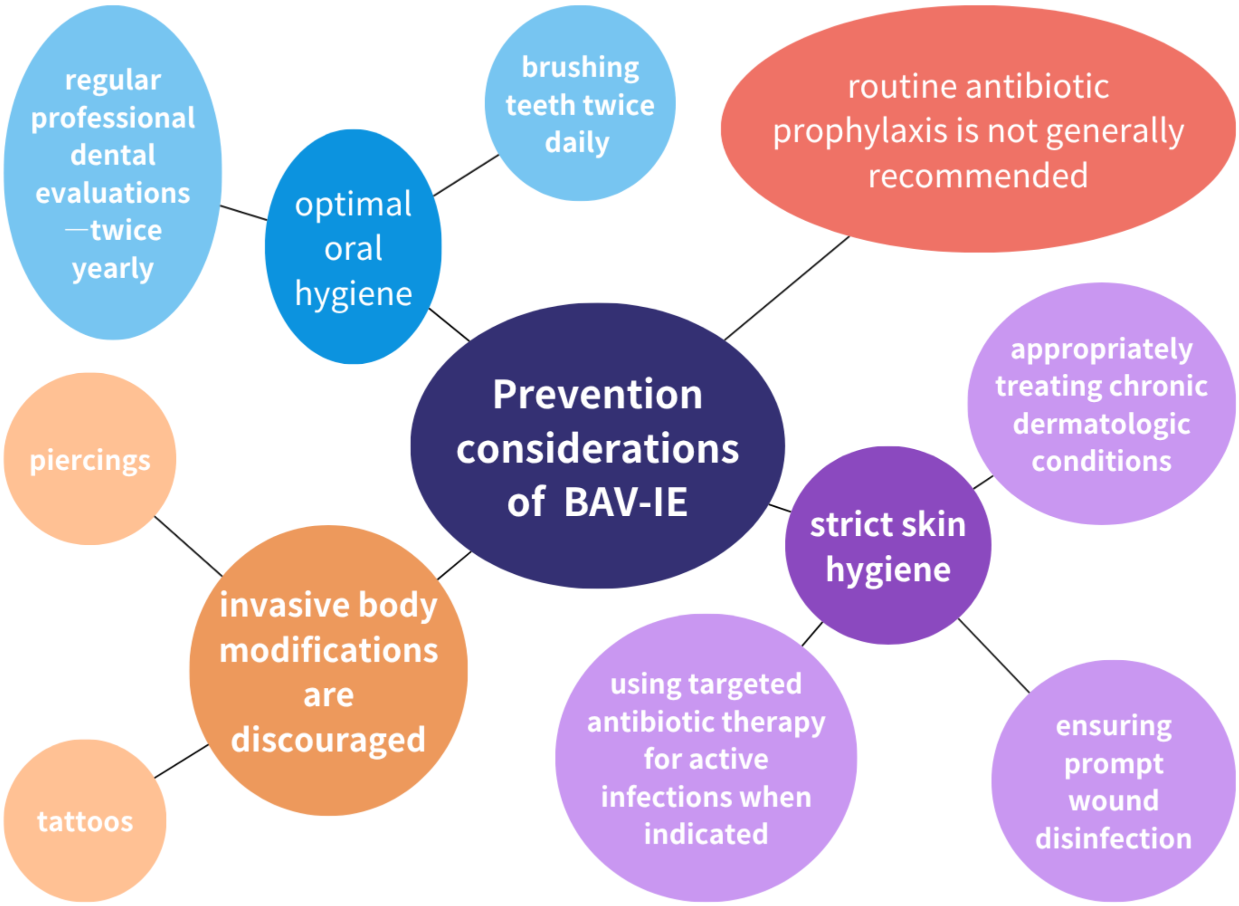

Fig. 1. According to the 2023 ESC Guidelines for the management of endocarditis, prevention considerations of BAV-IE. BAV-IE, Bicuspid aortic valve-associated infective endocarditis; ESC, European Society of Cardiology.

indicated, has been associated with favorable outcomes [26]. These cases demonstrate the importance of prompt antimicrobial treatment and surgical intervention in complex BAV-IE.

8. Prognosis and Outcomes

BAV-IE is a distinct clinical entity within the spectrum of native valve infections, distinguished from TAV-IE by patient demographics and disease course. Despite affecting younger individuals with fewer comorbidities, BAV-IE typically progresses more aggressively and is characterized by rapid tissue destruction, periannular abscesses, and pseudoaneurysm formation [2,5,6,19,20,38]. These characteristics reflect the combined influence of abnormal bicuspid valve hemodynamics, which is characterized by eccentric transvalvular flow and elevated WSS, and intrinsic aortic wall pathology, namely, elastin fragmentation and smooth muscle apoptosis, which enable infection to spread beyond the annulus [12,13,32].

Although advances in antimicrobial therapy and surgical techniques have improved early survival, BAV-IE is still associated with high morbidity and mortality [6]. Even after valve replacement, persistent aortopathy and altered aortic geometry may lead to late complications, such as prosthetic dehiscence and progressive dilation of the native aorta [45,46]. Surgical management is frequently more complex than that in TAV-IE, often requiring concomitant aortic root or ascending aortic replacement to address extensive infection and structural abnormalities [32]. Therefore, continued postoperative surveillance is essential for early detection of aortic and prosthetic complications.

Long-term results from surgical intervention are generally favorable. BAV-IE has a higher 10-year survival rate than TAV-IE (64% vs. 46%), but this is largely due to young age and a low comorbidity burden [13,19]. Patients with BAV have a higher one-year survival rate (94% vs. 69%), likely because of early surgical intervention and low baseline risk [47]. Reoperation rates are comparable between groups: approximately 15% of BAV and 13% of TAV patients requiring reintervention at follow-up [32].

Collectively, these findings indicate that although BAV-IE has a more aggressive pathological course, prompt and tailored surgical management can result in long-term outcomes comparable or even superior to those observed in TAV-IE.

9. Prevention Considerations

According to the *2023 European Society of Cardiology (ESC) Guidelines for the Management of Endocarditis*, patients with congenital valve abnormalities, such as BAV, have an intermediate risk of developing IE. Routine antibiotic prophylaxis is not generally recommended for this population, but it may be considered in certain individuals according to their clinical circumstances. Instead, the ESC guidelines emphasize the importance of comprehensive preventive measures, which are strongly recommended for intermediate- and high-risk populations [41].

Preventive strategies revolve primarily around maintaining good oral hygiene and skin care. Patients are advised to brush their teeth twice a day and have regular professional dental evaluations twice a year for those at high risk and once a year for those at intermediate risk. Additional recommendations include strict skin hygiene, appropriate treatment of chronic dermatologic conditions, prompt wound disinfection, and the use of targeted antibiotic therapy for active infections when indicated. Self-medication with antibiotics is not recommended, and invasive body modifications, such as piercings or tattoos, are discouraged because of the risk of bacteremia [41] (Fig. 1).

In the healthcare setting, following infection control protocols is critical. All invasive or intravascular procedures should be performed under strict aseptic conditions, and the use of indwelling infusion catheters should be limited to essential indications. Standardized care bundles for central and peripheral venous lines should be implemented to minimize procedure-related infections and the prevalence of healthcare-associated IE [41].

10. Conclusions

BAV-IE is a distinct and aggressive type of native valve infection caused by congenital structural abnormalities, altered hemodynamics, and a genetic predisposition. It typically affects young healthy individuals but progresses rapidly, often leading to severe valvular destruction, perianular abscesses, and early surgical intervention.

Multimodality imaging, including echocardiography and CCT, is essential for accurate diagnosis and surgical planning. Early surgery with radical debridement, valve replacement, and appropriate aortic repair offers the optimal outcomes and facilitates infection control. Regardless of severity, long-term survival in BAV-IE is favorable when managed promptly and comprehensively.

Ongoing surveillance for aortopathy and prosthetic complications is critical, in addition to preventive strategies emphasizing oral hygiene, infection control, and procedural asepsis. A multidisciplinary approach integrating cardiology, surgery, and infectious disease expertise remains the cornerstone for improving outcomes in this challenging clinical entity.

Author Contributions

BNA: Conceptualization, Methodology, Investigation, Writing – Original Draft, Visualization. BB: Investigation, Validation, Writing – Review & Editing. WZ: Supervision, Validation, Resources, Writing – Review & Editing, Project Administration. All authors approved the final version for publication and agreed to be accountable for all aspects of this work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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