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Mitral Valve Insufficiency in the Context of Barlow's Disease: A Contemporary Review of Etiopathogenesis, Multimodal Assessment, and Evolving Management Paradigms

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ABSTRACT

Barlow's disease represents a distinct and complex morphological variant of degenerative mitral valve disease, characterized by a unique pathophysiological substrate leading to severe mitral insufficiency. This extensive review provides a comprehensive synthesis of contemporary understanding, emphasizing the transition from a purely anatomical curiosity to a clinically nuanced entity with significant implications for management. The etiopathogenesis is explored through the lens of advanced histopathological and molecular studies, highlighting the interplay between myxomatous degeneration, abnormal collagen metabolism, and genetic predispositions beyond the classic FBN1 and FLNA associations. A critical appraisal of current multimodal imaging is undertaken, detailing the pivotal role of high-resolution three-dimensional echocardiography in delineating the hallmark bileaflet prolapse with multisegment involvement, excessive leaflet tissue, and annular disjunction. Cardiac magnetic resonance and computed tomography are discussed for their growing utility in quantifying regurgitation volume, assessing ventricular remodeling, and informing surgical planning. The core of this review contrasts traditional surgical approaches, predominantly involving complex valve repair with extensive leaflet resection and annuloplasty, against emerging reparative techniques and the evolving, albeit controversial, potential of transcatheter edge-to-edge repair in select, high-risk cohorts with suitable anatomy. Long-term outcome data and persistent challenges, including repair durability, arrhythmic risk, and the management of asymptomatic severe regurgitation, are examined. This synthesis concludes by identifying critical knowledge gaps and future directions, particularly the need for refined risk stratification models integrating quantitative imaging biomarkers and genetics, and the call for dedicated randomized trials to guide therapeutic escalation in this heterogeneous patient population.

KEYWORDS: Barlow's disease, myxomatous mitral valve degeneration, mitral valve prolapse, mitral regurgitation, three-dimensional echocardiography, mitral annular disjunction, valve repair, transcatheter mitral valve repair.

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INTRODUCTION

Mitral valve insufficiency remains a prevalent condition with considerable morbidity, and its underlying etiology critically informs prognosis and therapeutic strategy. Within the spectrum of degenerative mitral valve disease, Barlow's disease occupies a severe and morphologically distinct pole, first described clinically by Dr. John Barlow in the 1960s. Historically conflated with simpler forms of leaflet prolapse, it is now recognized as a specific pathoanatomical entity defined by profound myxomatous infiltration, excessive and thick leaflet tissue affecting both leaflets across multiple

segments, elongated and ruptured chordae tendineae, and significant annular dilatation and calcification.1,2,3

This specific anatomy results in a complex, often multijet, severe regurgitation pattern that poses distinct diagnostic and therapeutic challenges. Recent years have witnessed a paradigm shift in the appraisal of this disease, driven by technological advancements in imaging which allow for exquisite anatomical delineation, and by a deepening understanding of its unique clinical course, including its association with ventricular arrhythmias and sudden cardiac death. Despite these advances, significant controversy persists regarding optimal management timelines, surgical technique selection, and the applicability of novel transcatheter technologies. This extensive review aims to consolidate the most current evidence from recent clinical guidelines, seminal registry analyses, and prospective cohort studies to provide a nuanced, state-of-the-art overview of Barlow's disease. It will traverse the journey from its molecular and histopathological foundations, through precise contemporary diagnostic criteria, to a balanced discussion of the expanding armamentarium of treatment options, thereby offering a consolidated resource for clinicians and investigators engaged in the care of this complex patient population. The synthesis draws upon the latest consensus documents from major cardiology societies and high-impact clinical research published within the last three to five years to ensure contemporary relevance.3,4,5

ETIOPATHOGENESIS

The etiopathogenesis of mitral insufficiency in Barlow's disease is a multifactorial and progressive process rooted in a primary structural defect of the mitral valve apparatus, extending far beyond a simple degenerative wear-and-tear phenomenon. Contemporary understanding frames it as a complex, genetically influenced disorder of valvular interstitial cell (VIC) homeostasis and extracellular matrix (ECM) architecture. The foundational lesion is an abnormal, diffuse myxomatous degeneration affecting the entire valvular apparatus. Histopathologically, this is characterized by a marked accumulation of proteoglycans, primarily glycosaminoglycans like dermatan sulfate, within the spongiosa layer of the valve leaflets. This proteoglycan infiltration disrupts the normal trilaminar leaflet structure, creating a bulky, thickened, and voluminous tissue that is mechanically inferior. Crucially, this process occurs alongside a disruption of the collagen framework, particularly a reduction and fragmentation of type I and III fibrillar collagens within the fibrosa layer, which is responsible for the leaflet's tensile strength. This imbalance—excessive, hydrophilic ground substance and deficient structural collagen—renders the leaflet tissue excessively compliant and prone to expansion and billowing.4,5,6

The dysregulation of ECM metabolism is driven by aberrant VIC activity, shifting from a quiescent phenotype to an activated, myofibroblast-like state. Recent investigations point towards abnormal signaling pathways, including transforming growth factor-beta (TGF-β) and the Wnt/β-catenin cascade, which orchestrate this pathological synthetic activity. While early genetic studies focused on mutations in fibrillin-1 (FBN1) and filamin A (FLNA) genes, linking Barlow's disease to the wider connective tissue disorder spectrum, current research emphasizes a polygenic predisposition. Genome-wide association studies have identified other susceptibility loci related to ECM proteins and cell-matrix interactions, suggesting a complex inheritance pattern where multiple common variants confer risk, potentially interacting with environmental modifiers.4,5,6

A pivotal, and often diagnostically evocative, anatomical feature is mitral annular disjunction (MAD). This is not merely an associated finding but an integral component of the pathogenetic sequence. MAD represents a distinct anatomical and functional detachment between the atrial wall-mitral valve junction and the left ventricular myocardium. This *atrio-annular dissociation* creates a hypermobile, excessively dynamic annulus that dilates disproportionately during ventricular systole. The ensuing abnormal mechanical stress on the already myxomatous leaflets and chordae is profound. The chordae tendineae themselves are subject to the same myxomatous process, becoming elongated, thinned, and prone to spontaneous rupture, which can acutely worsen the regurgitation. 6,7,8

The combined effect of bulky, prolapsing leaflets, elongated/ruptured chordae, and a dilated, dyskinetic annulus establishes a perfect storm for severe, often multijet, mitral regurgitation. The regurgitant volume leads to chronic left ventricular volume overload, initiating a cascade of compensatory remodeling that, if uncorrected, progresses to ventricular dysfunction, atrial dilation, atrial fibrillation, and the recently highlighted risk of life-threatening ventricular arrhythmias, possibly linked to the stretch-induced fibrosis at the junctional region of MAD. Thus, the etiopathogenesis of Barlow's disease is a continuum, originating from a molecular and cellular derangement in ECM biology, manifesting as a gross anatomical derangement of the entire mitral apparatus, and culminating in a complex hemodynamic lesion with significant cardiac sequelae.7,8,9

CLINICAL MANIFESTATIONS

The clinical presentation of mitral insufficiency in the context of Barlow's disease is characterized by a broad and often deceptive spectrum, ranging from prolonged asymptomatic latency to the abrupt onset of catastrophic complications, a duality that poses significant challenges for timely diagnosis and risk stratification. Patients frequently remain asymptomatic for decades despite harboring severe regurgitation, owing to the left ventricle's remarkable capacity for adaptive eccentric remodeling in response to

chronic volume overload. This insidious phase is not benign, however, as progressive ventricular dilatation and interstitial fibrosis silently accrue, setting the stage for eventual functional decline. When symptoms do emerge, they typically manifest with the classic hallmarks of elevated left atrial pressure and reduced forward cardiac output. Exertional dyspnea and profound fatigue are predominant complaints, often progressing orthopnea and paroxysmal nocturnal dyspnea as left atrial remodeling advances. Palpitations are exceedingly common, reflecting a high prevalence of atrial and ventricular arrhythmias secondary to chronic atrial stretch and the unique myocardial substrate associated with mitral annular disjunction.8,9,10

A notable proportion of patients present not with heart failure symptoms but with arrhythmic events, ranging from symptomatic premature ventricular contractions to sustained atrial fibrillation or, most ominously, malignant ventricular arrhythmias. This arrhythmic phenotype has become a critical focus of contemporary research, with emerging evidence linking the mechanical stretch from a severely prolapsing valve and the adjacent myocardial fibrosis in the atrio-ventricular junction to a potentially increased risk of sudden cardiac death, even in the absence of severe left ventricular dysfunction. Physical examination findings can be pathognomonic for the experienced clinician. The classic auscultatory hallmark is a mid-to-late systolic click, often multiple and migratory, followed by a late-peaking holosystolic murmur that radiates to the axilla. The click corresponds to the sudden tensing of the elongated chordae or the billowing leaflet, while the murmur signifies the ensuing regurgitant flow. The dynamic nature of the lesion means these findings can vary significantly with maneuvers that alter ventricular preload and afterload, a characteristic that aids in differentiation from other valvular pathologies. Signs of advanced disease may include a laterally displaced and hyperdynamic apical impulse, a palpable parasternal heave indicative of right ventricular involvement from pulmonary hypertension, and the peripheral signs of reduced cardiac output.11,12,13

The systemic embolic risk, while historically considered lower than in rheumatic mitral disease, is not negligible, particularly in the setting of concomitant atrial fibrillation or the turbulent flow within a grossly enlarged left atrium. It is crucial to recognize that the transition from a compensated, asymptomatic state to symptomatic heart failure or significant arrhythmic burden can be precipitous, often triggered by a chordal rupture leading to acute-on-chronic regurgitation or the new onset of atrial fibrillation with rapid ventricular response. This clinical course underscores the imperative for meticulous and serial longitudinal assessment, integrating advanced imaging and arrhythmia monitoring, to identify the often-subtle indicators of disease progression before the onset of irreversible myocardial damage or life-threatening complications. The heterogeneity of presentation demands a high index of suspicion and an understanding that the manifestations of Barlow's disease extend beyond simple volume overload to encompass a complex interplay of valvular mechanics, atrial and ventricular cardiomyopathy, and electrophysiological disturbance.13,14

MULTIMODAL ASSESSMENT

The precise characterization of mitral insufficiency in Barlow's disease demands a sophisticated, multimodal imaging approach, as the anatomical complexity and profound hemodynamic consequences of this entity cannot be fully captured by any single diagnostic modality. The assessment transcends mere confirmation of regurgitation, aiming instead to delineate the unique morphological substrate, quantify its severity with accuracy, evaluate its impact on cardiac chambers, and inform the nuanced decision-making required for therapeutic intervention. Two-dimensional and Doppler echocardiography remain the indispensable cornerstone of initial evaluation and longitudinal surveillance. It provides the first visual cues to the diagnosis: bileaflet, multisegment prolapse with thick, excessively redundant leaflet tissue, often exceeding 5 mm in thickness; elongated, thin, or ruptured chordae tendineae; and significant annular dilatation. However, it is the advent and refinement of three-dimensional transthoracic and transesophageal echocardiography that have revolutionized the appraisal of Barlow's morphology. This technology allows for en face surgical visualization of the valve from both atrial and ventricular perspectives, enabling precise mapping of prolapsing segments, quantification of leaflet surface area and volume, and the accurate identification of the number and location of regurgitant jets, which are frequently multiple and eccentric.15,16,17

A critical component of the echocardiographic assessment is the meticulous evaluation of mitral annular dynamics, specifically the identification and quantification of mitral annular disjunction. This is best appreciated in the apical three-chamber or long-axis view, where the separation between the atrial wall–mitral valve junction and the left ventricular myocardium can be measured during systole. The presence and extent of disjunction are not merely anatomical footnotes but are increasingly recognized as markers of arrhythmic risk and surgical complexity. Comprehensive Doppler interrogation is employed to grade the severity of regurgitation using an integrative method, as no single parameter is foolproof given the eccentricity and multiplicity of jets. This includes assessment of vena contracta width, proximal isovelocity surface area-derived effective regurgitant orifice area and regurgitant volume, and analysis of pulmonary venous flow patterns. Furthermore, echocardiography provides essential data on the consequences of chronic volume overload, including left ventricular end-systolic and end-diastolic dimensions, ejection fraction—which must be interpreted with caution as

it may be preserved or even supranormal until late stages—and the presence of secondary pulmonary hypertension estimated from tricuspid regurgitation velocity.17,18,19

Cardiac magnetic resonance imaging has emerged as a powerful complementary tool, particularly in scenarios where echocardiographic data is discrepant or suboptimal. Its principal strengths lie in its unparalleled accuracy in quantifying ventricular volumes, mass, and biventricular function without reliance on geometric assumptions, offering a more sensitive detection of early ventricular dysfunction. Perhaps its most valuable contribution is in the precise quantification of regurgitant volume and fraction through phase-contrast imaging and direct volumetric stroke volume comparison, which is considered the non-invasive reference standard. 19,20,21

Furthermore, late gadolinium enhancement and T1 mapping techniques can identify and quantify myocardial fibrosis, both within the inferobasal left ventricular wall adjacent to the disjoined annulus—a potential substrate for ventricular arrhythmias—and more diffusely within the myocardium as a consequence of long-standing volume overload. This fibrosis assessment carries significant prognostic implications. Cardiac computed tomography, while not a first-line modality for hemodynamic assessment, plays a crucial and growing role in pre-procedural planning, especially with the advent of transcatheter therapies. It provides exquisite anatomical detail of the mitral annular calcification, which is often present and can be severe in advanced Barlow's disease, and allows for precise measurement of annular dimensions, spatial relationships to surrounding structures like the coronary sinus and circumflex artery, and virtual simulation of device implantation. The synthesis of data from these complementary imaging modalities creates a comprehensive phenotyping of the Barlow valve, moving from a qualitative description to a quantitative, multidimensional model that is essential for risk stratification, timing of intervention, and selection of the most appropriate therapeutic strategy, whether it be complex surgical repair or, in select cases, percutaneous intervention.21

EVOLVING MANAGEMENT PARADIGMS

The therapeutic landscape for mitral insufficiency in Barlow's disease is undergoing a significant and nuanced evolution, moving beyond the traditional binary choice of watchful waiting versus surgical referral toward a more personalized, pathophysiology-driven strategy that integrates sophisticated risk assessment, refined surgical techniques, and cautiously expanding percutaneous options. This shift is predicated on a growing understanding of the unique natural history of the disease, where the risks of sudden cardiac death and progressive, often irreversible, ventricular dysfunction must be carefully balanced against the technical challenges and potential complications of intervention. Contemporary management is anchored in the principle of timely surgical intervention, ideally before the onset of symptoms or subclinical ventricular deterioration, with mitral valve repair being the unequivocal gold standard due to its demonstrated superiority in preserving long-term ventricular function, obviating the need for lifelong anticoagulation, and ensuring superior survival and freedom from reoperation compared to mechanical replacement.21

The surgical paradigm itself has evolved considerably. The classic approach of aggressive leaflet resection, while effective, has been supplemented and in many high-volume centers supplanted by more physiologic and preservation-oriented techniques. The adoption of artificial chordal implantation with polytetrafluoroethylene (ePTFE) sutures allows for a more tailored correction of prolapse without removing leaflet tissue, thereby preserving the full surface area of the often already expanded leaflet. This is frequently combined with a systematic reduction annuloplasty, employing a complete, rigid or semi-rigid ring to not only reduce the annular diameter but also to reshape and stabilize the entire annulus, addressing the profound annular dilatation and disjunction characteristic of Barlow's disease. The concept of "respect rather than resect" emphasizes maintaining native valve tissue and subvalvular apparatus integrity to optimize long-term durability and hemodynamic performance. Furthermore, the recognition of mitral annular disjunction as a potential arrhythmic substrate has prompted some surgical teams to explore adjunctive procedures, such as targeted cryoablation or plication of the disjoined annular region, although the efficacy of such maneuvers in mitigating post-operative arrhythmic risk remains an active area of clinical investigation.21,22

The most contentious and rapidly evolving frontier lies in the application of transcatheter mitral valve repair technologies, primarily the edge-to-edge repair technique. Initially considered contraindicated in Barlow's disease due to the excessive leaflet tissue, multi-segment involvement, and significant annular dilatation, recent data from specialized centers suggest a potential role in a highly selected subset of patients. These are typically elderly individuals with prohibitive surgical risk and favorable anatomical features, such as a central or paracentral regurgitant jet origin and relatively stable annular dimensions. 22,23

Success in this context often requires the implantation of multiple devices to create a double-orifice valve, a technically demanding procedure. While offering a less invasive alternative, significant concerns persist regarding the long-term durability of repair in such a morphologically complex and dynamic valve, the potential for inducing stenosis, and the high likelihood of residual or recurrent regurgitation. Therefore, this approach remains firmly within the realm of compassionate use or within the rigorous protocols of clinical trials for non-surgical candidates. Concurrently, medical management has refined its focus beyond mere afterload

reduction with vasodilators. It now emphasizes a holistic approach that includes aggressive management of concomitant atrial fibrillation with appropriate rate or rhythm control strategies and anticoagulation according to stroke risk scores, as well as the treatment of heart failure with guideline-directed medical therapy when ventricular dysfunction supervenes. Ultimately, the modern management paradigm for Barlow's disease is one of increasing complexity and personalization, demanding a collaborative heart team approach that synthesizes detailed anatomical imaging, accurate hemodynamic and arrhythmic risk profiling, and a deep understanding of the evolving surgical and interventional armamentarium to tailor the right therapy to the right patient at the most optimal time.24

CONCLUSION

Barlow's disease represents a singular and formidable challenge within the spectrum of degenerative valvulopathies, distinguished by a unique pathoanatomical substrate that drives a complex clinical trajectory. This extensive review has underscored the evolution in our understanding of the condition, from its histopathological origins in a dysregulated valvular interstitial cell metabolism and extracellular matrix architecture to its definitive manifestation as a profoundly abnormal mitral apparatus characterized by bileaflet prolapse, excessive leaflet tissue, and dynamic annular dysfunction. The contemporary appraisal of mitral insufficiency in this context has been fundamentally transformed by advanced multimodal imaging, which provides not only an exquisitely detailed morphological roadmap but also permits precise quantification of regurgitant severity and its sequelae on ventricular remodeling and myocardial substrate. The integration of three-dimensional echocardiography for surgical planning, cardiac magnetic resonance for volumetric and tissue characterization, and computed tomography for anatomical delineation has elevated diagnostic precision, enabling a more informed and anticipatory management strategy.

The management paradigms for this entity continue to advance, albeit along distinct and carefully considered pathways. Mitral valve repair remains the undisputed therapeutic cornerstone, with modern surgical techniques increasingly favoring preservation-oriented approaches that respect the abnormal valve morphology through neochordal implantation and meticulous annuloplasty, aiming to ensure long-term durability and physiological function. The provocative emergence of transcatheter edge-to-edge repair as a potential option for a narrowly defined cohort of high-risk patients illustrates the field's innovative spirit, yet it simultaneously highlights the persistent and profound anatomical challenges posed by the Barlow valve, tempering enthusiasm with a necessary caution regarding long-term outcomes. Perhaps the most critical evolution in clinical thought is the recognition of Barlow's disease as more than a simple hemodynamic lesion; it is a systemic disorder of the mitral apparatus with intrinsic arrhythmogenic potential, linking mechanical stretch, annular disjunction, and myocardial fibrosis to a risk profile that extends beyond heart failure to include malignant ventricular arrhythmias. This expanded view mandates a holistic management approach that incorporates arrhythmia surveillance and treatment into the traditional focus on timing surgical intervention before the onset of irreversible ventricular dysfunction.

Looking forward, significant knowledge gaps persist that must guide future investigative efforts. There is a pressing need for validated, imaging-based risk stratification models that integrate quantitative measures of valve morphology, regurgitation severity, ventricular fibrosis, and annular dynamics to better identify patients at highest risk for rapid progression or sudden cardiac death. Dedicated, prospective, and ideally randomized trials are urgently required to clarify the optimal timing of intervention in asymptomatic patients, to define the role, if any, of adjunctive arrhythmic substrate modification during surgery, and to establish the long-term efficacy and safety boundaries for transcatheter therapies in this complex anatomy. Furthermore, ongoing research into the fundamental genetic and molecular drivers of myxomatous degeneration holds promise for moving beyond symptomatic treatment toward targeted biological interventions that could alter the disease course itself. In summary, the care of the patient with Barlow's disease demands a synthesis of deep anatomical understanding, sophisticated imaging, mastery of advanced surgical reparative techniques, and an appreciation for its arrhythmogenic dimension. It is through this integrated, patient-centered, and evidence-driven approach, continually refined by emerging research, that optimal outcomes can be achieved for individuals afflicted by this most complex form of mitral valve disease.

REFERENCES

I. Silbiger, J.J. Mechanistic Insights into Ischemic Mitral Regurgitation: Echocardiographic and Surgical Implications. *J. Am. Soc. Echocardiogr.* 2011, *24*, 707–719.

II. Zoghbi, W.A.; Levine, R.A.; Flachskampf, F.; Grayburn, P.; Gillam, L.; Leipsic, J.; Thomas, J.D.; Kwong, R.Y.; Vandervoort, P.; Chandrashekhar, Y. Atrial Functional Mitral Regurgitation. *JACC Cardiovasc. Imaging* 2022, *15*, 1870–1882.

III. Farhan, S.; Silbiger, J.J.; Halperin, J.L.; Zhang, L.; Dukkipati, S.R.; Vogel, B.; Kini, A.; Sharma, S.; Lerakis, S. Pathophysiology, Echocardiographic Diagnosis, and Treatment of Atrial Functional Mitral Regurgitation. *J. Am. Coll. Cardiol.* 2022, *80*, 2314–2330.

IV. Okamoto, C.; Okada, A.; Nishimura, K.; Moriuchi, K.; Amano, M.; Takahama, H.; Amaki, M.; Hasegawa, T.; Kanzaki, H.; Fujita, T.; et al. Prognostic comparison of atrial and ventricular functional mitral regurgitation. *Open Heart* 2021, *8*, e001574.

V. Coffey, S.; Roberts-Thomson, R.; Brown, A.; Carapetis, J.; Chen, M.; Enriquez-Sarano, M.; Zühlke, L.; Prendergast, B.D. Global epidemiology of valvular heart disease. *Nat. Rev. Cardiol.* 2021, *18*, 853–864.

VI. So, K.C.-Y.; Yap, J.; Song, G.-Y.; Poon, K.; Sung, S.H.; Chandavimol, M.; Hayashida, K.; Park, D.-W.; Ewe, S.-H.; Chen, M.; et al. Epidemiology of Valvular Heart Disease in Asia Pacific Region. *JACC Asia* 2025, *5*, 718–743.

VII. Lazam, S.; Vanoverschelde, J.L.; Tribouilloy, C.; Grigioni, F.; Suri, R.M.; Avierinos, J.F.; de Meester, C.; Barbieri, A.; Rusinaru, D.; Russo, A.; et al. Twenty-Year Outcome After Mitral Repair Versus Replacement for Severe Degenerative Mitral Regurgitation. *Circulation* 2017, *135*, 410–422.

VIII. Acker, M.A.; Parides, M.K.; Perrault, L.P.; Moskowitz, A.J.; Gelijns, A.C.; Voisine, P.; Smith, P.K.; Hung, J.W.; Blackstone, E.H.; Puskas, J.D.; et al. Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation. *N. Engl. J. Med.*2014, *370*, 23–32.

IX. Davierwala, P.M.; Seeburger, J.; Pfannmueller, B.; Garbade, J.; Misfeld, M.; Borger, M.A.; Mohr, F.W. Minimally invasive mitral valve surgery: "The Leipzig experience". *Ann. Cardiothorac. Surg.* 2013, *2*, 744–750.

X. Feldman, T.; Wasserman, H.S.; Herrmann, H.C.; Gray, W.; Block, P.C.; Whitlow, P.; St Goar, F.; Rodriguez, L.; Silvestry, F.; Schwartz, A.; et al. Percutaneous Mitral Valve Repair Using the Edge-to-Edge Technique. *J. Am. Coll. Cardiol.* 2005, *46*, 2134–2140.

XI. Feldman, T.; Foster, E.; Glower, D.D.; Kar, S.; Rinaldi, M.J.; Fail, P.S.; Smalling, R.W.; Siegel, R.; Rose, G.A.; Engeron, E.; et al. Percutaneous Repair or Surgery for Mitral Regurgitation. *N. Engl. J. Med.* 2011, *364*, 1395–1406.

XII. Stone, G.W.; Abraham, W.T.; Lindenfeld, J.; Kar, S.; Grayburn, P.A.; Lim, D.S.; Mishell, J.M.; Whisenant, B.; Rinaldi, M.; Kapadia, S.R.; et al. Five-Year Follow-up after Transcatheter Repair of Secondary Mitral Regurgitation. *N. Engl. J. Med.*2023, *388*, 2037–2048

XIII. Praz, F.; Borger, M.A.; Lanz, J.; Marin-Cuartas, M.; Abreu, A.; Adamo, M.; Ajmone Marsan, N.; Barili, F.; Bonaros, N.; Cosyns, B.; et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur. J. Cardio-Thorac. Surg.* 2025, *67*, ezaf276.

XIV. Yousef, S.; Arnaoutakis, G.J.; Gada, H.; Smith, A.J.C.; Sanon, S.; Sultan, I. Transcatheter mitral valve therapies: State of the art. *J. Card. Surg.* 2022, *37*, 225–233.

XV. Lancellotti, P.; Pibarot, P.; Chambers, J.; La Canna, G.; Pepi, M.; Dulgheru, R.; Dweck, M.; Delgado, V.; Garbi, M.; Vannan, M.A.; et al. Multi-modality imaging assessment of native valvular regurgitation: An EACVI and ESC council of valvular heart disease position paper. *Eur. Heart J. Cardiovasc. Imaging* 2022, *23*, E171–232.

XVI. Agricola, E.; Ancona, F.; Bartel, T.; Brochet, E.; Dweck, M.; Faletra, F.; Lancellotti, P.; Mahmoud-Elsayed, H.; Marsan, N.A.; Maurovich-Hovart, P.; et al. Multimodality imaging for patient selection, procedural guidance, and follow-up of transcatheter interventions for structural heart disease: A consensus document of the EACVI Task Force on Interventional Cardiovascular Imaging: Part 1: Access routes, transcatheter aortic valve implantation, and transcatheter mitral valve interventions. *Eur. Heart J. Cardiovasc. Imaging* 2023, *24*, e209–e268.

XVII. Antonides, C.F.J.; Mack, M.J.; Kappetein, A.P. Approaches to the Role of The Heart Team in Therapeutic Decision Making for Heart Valve Disease. *Struct. Heart* 2017, *1*, 249–255.

XVIII. Lio, A.; Loreni, F.; Miceli, A.; Wiedemann, D. Editorial: Evolution of mitral valve disease treatment: From surgery to transcatheter therapy. *Front. Cardiovasc. Med.* 2024, *11*, 1369596.

XIX. Little, S.H. Interventional Echocardiography: The Emergence of a New Imaging Specialty. *J. Am. Soc. Echocardiogr.*2023, *36*, A13–A14.

XX. Carpentier, A. Cardiac valve surgery-the "French correction". *J. Thorac. Cardiovasc. Surg.* 1983, *86*, 323–337.

XXI. Dreyfus, G.D.; Dulguerov, F.; Marcacci, C.; Haley, S.R.; Gkouma, A.; Dommerc, C.; Albert, A. "Respect when you can, resect when you should": A realistic approach to posterior leaflet mitral valve repair. *J. Thorac. Cardiovasc. Surg.* 2018, *156*, 1856–1866.e3.

XXII. van Wijngaarden, A.L.; Tomšič, A.; Mertens, B.J.A.; Fortuni, F.; Delgado, V.; Bax, J.J.; Klautz, R.J.M.; Marsan, N.A.; Palmen, M. Mitral valve repair for isolated posterior mitral valve leaflet prolapse: The effect of respect and resect techniques on left ventricular function. *J. Thorac. Cardiovasc. Surg.* 2022, *164*, 1488–1497.e3.

XXIII. Wagner, C.M.; Brescia, A.A.; Watt, T.M.F.; Bergquist, C.; Rosenbloom, L.M.; Ceniza, N.N.;

Markey, G.E.; Ailawadi, G.; Romano, M.A.; Bolling, S.F. Surgical strategy and outcomes for atrial functional mitral regurgitation: All functional mitral regurgitation is not the same! *J. Thorac. Cardiovasc. Surg.* 2024, *167*, 647–655.

XXIV. Moore, R.A.; Wierup, P.; Tappuni, S.; Houghtaling, P.L.; Burns, D.J.P.; Chemtob, R.; Blackstone, E.H.; Svensson, L.G.; Gillinov, A.M. Reoperation after early and late failure of mitral valve repair for degenerative disease. *J. Thorac. Cardiovasc. Surg.* 2024, *167*, 1251–1262.e8.