Atrial Cardiomyopathy: evolution of the concept, pathophysiology, multimodality Assessment, and clinical Implications

Cardiomyopathie atriale : évolution du concept, physiopathologie, évaluation multimodale et implications cliniques

Oussama Haddar [1], Amine Bahloul [1], Nadia Bouattour [2], Islem Kharrat[1], Mariem Dammak [2], Selma Charfeddine [1], Leila Abid [1],

1. *Hedi Chaker University Hospital, Cardiology Department, Sfax, Tunisia*
2. *Habib Bourguiba University Hospital, Neurology department, Sfax, Tunisia*

Summary

Atrial cardiomyopathy (AtCM) has emerged as a distinct clinical entity characterized by structural, electrical, mechanical, and biological abnormalities of the atria. Initially defined through histopathological findings, the concept has evolved into a multidimensional syndrome encompassing progressive atrial remodeling and dysfunction. Multiple mechanisms, including fibrosis, fibro-fatty infiltration, inflammation, and electrical remodeling, contribute to its development and are promoted by common cardiovascular risk factors such as aging, hypertension, obesity, diabetes, and heart failure. Because no single modality can fully characterize the atrial substrate, the diagnosis of AtCM relies on an integrated approach combining electrocardiography, echocardiography, cardiac magnetic resonance imaging, rhythm monitoring, and circulating biomarkers. Beyond its association with atrial fibrillation, AtCM has been increasingly linked to stroke, heart failure, and adverse cardiovascular outcomes. This review summarizes the evolution of the AtCM concept, its underlying pathophysiological mechanisms, current multimodality assessment strategies, and its growing clinical implications.

Keywords

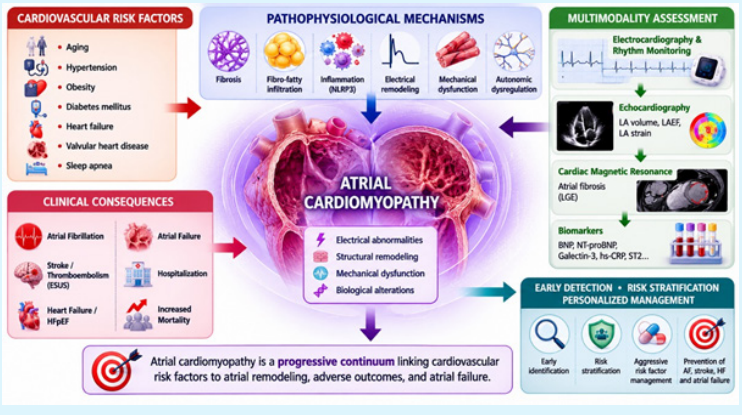
Atrial cardiomyopathy; atrial remodeling; atrial fibrosis; atrial fibrillation; left atrial strain; stroke.

Résumé

La cardiomyopathie atriale (AtCM) s'est imposée comme une entité clinique distincte, caractérisée par des anomalies structurelles, électriques, mécaniques et biologiques des oreillettes. Initialement définie sur la base de constatations histopathologiques, cette notion a évolué vers un syndrome multidimensionnel englobant le remodelage et la dysfonction atriale progressifs. Plusieurs mécanismes, notamment la fibrose, l'infiltration fibro-graisseuse, l'inflammation et le remodelage électrique, contribuent à son développement et sont favorisés par des facteurs de risque cardiovasculaires fréquents tels que le vieillissement, l'hypertension artérielle, l'obésité, le diabète et l'insuffisance cardiaque. En raison de l'absence d'une méthode unique capable de caractériser pleinement le substrat atrial, le diagnostic de l'AtCM repose sur une approche intégrée associant l'électrocardiogramme, l'échocardiographie, l'imagerie par résonance magnétique cardiaque, la surveillance du rythme cardiaque et les biomarqueurs circulants. Au-delà de son association avec la fibrillation atriale, l'AtCM est de plus en plus reconnue comme un facteur impliqué dans la survenue des accidents vasculaires cérébraux, de l'insuffisance cardiaque et d'autres événements cardiovasculaires défavorables. Cette revue présente l'évolution du concept de cardiomyopathie atriale, ses principaux mécanismes physiopathologiques, les stratégies actuelles d'évaluation multimodale ainsi que ses implications cliniques croissantes..

Mots-clés

Cardiomyopathie atriale ; remodelage atrial ; fibrose atriale ; fibrillation atriale ; strain atrial gauche ; accident vasculaire cérébral



Correspondance

Oussama Haddar

INTRODUCTION

Over the past decades, atrial fibrillation (AF) has been considered the predominant manifestation of atrial disease and the principal determinant of atrial-related thromboembolic complications. Consequently, both clinical practice and research have largely focused on detecting and managing AF as the primary therapeutic target. However, accumulating evidence has challenged this traditional paradigm by demonstrating that the atrial substrate itself may represent a distinct pathological entity capable of promoting adverse cardiovascular outcomes independently of documented arrhythmia. (1) (2)

In response to these observations, the concept of atrial cardiomyopathy (AtCM) has emerged as a comprehensive framework for understanding atrial disease. In 2016, an expert consensus statement from the European Heart Rhythm Association (EHRA) defined atrial cardiomyopathy as "any complex of structural, architectural, contractile, or electrophysiological changes affecting the atria with the potential to produce clinically relevant manifestations." (3)

Atrial cardiomyopathy is now recognized as a dynamic and progressive process involving multiple interconnected mechanisms, including structural remodeling, electrical abnormalities, mechanical dysfunction, autonomic imbalance, and inflammatory activation. These alterations may develop gradually in response to aging, hypertension, obesity, diabetes mellitus, heart failure, valvular heart disease, or infiltrative disorders, ultimately creating a vulnerable atrial substrate. While AF may arise as a consequence of this remodeling process, increasing evidence suggests that atrial cardiomyopathy can itself contribute directly to thromboembolic events, heart failure progression, and mortality, even in patients who remain in sinus rhythm. (4) (5) (6)

The diagnosis of atrial cardiomyopathy requires a multimodality approach, as no single technique can fully characterize the atrial substrate. Electrocardiography and echocardiography remain the cornerstone of evaluation, while left atrial strain has emerged as a sensitive marker of early atrial dysfunction. Cardiac magnetic resonance imaging provides a valuable assessment of atrial fibrosis, and rhythm monitoring and circulating biomarkers may further improve risk stratification. (7)

In this review, we provide a comprehensive overview of the current understanding of atrial cardiomyopathy, focusing on its pathophysiological mechanisms, multimodality diagnostic assessment, and clinical implications.

EVOLUTION OF THE CONCEPT: FROM HISTOPATHOLOGICAL CLASSIFICATION TO THE CONTINUUM OF ATRIAL DISEASE

The concept of atrial cardiomyopathy has evolved considerably over the last decade, reflecting a progressive shift from a purely histopathological perspective toward a comprehensive clinical and pathophysiological framework.

The first major step in conceptualizing atrial cardiomyopathy was achieved with the 2016 EHRA/HRS/APHRS/SOLAECE consensus document, which provided a standardized definition and introduced the EHRA classification. This histopathological classification categorizes atrial cardiomyopathies into 4 stages based on predominant tissue alterations, including cardiomyocyte abnormalities, fibrotic remodeling, mixed cardiomyocyte-fibrotic changes, and non-collagenous infiltrative processes such as amyloid deposition, fatty infiltration, or inflammatory cell accumulation. (3) Although this framework significantly improved the understanding of the structural substrates underlying atrial disease, its direct clinical applicability remained limited because histological characterization is rarely available in routine practice.

As knowledge of atrial remodeling expanded, it became increasingly evident that atrial cardiomyopathy represents a progressive disease process involving electrical, structural, and mechanical dysfunction. Consequently, the updated 2024 EHRA clinical consensus proposed a staging system based on disease severity rather than solely on histopathological findings. This framework distinguishes mild, moderate, and severe atrial cardiomyopathy based on the extent of electrical abnormalities, structural remodeling, mechanical dysfunction, biomarker elevations, and clinical manifestations. (8)

More recently (2025), the Heart Failure Association of the European Society of Cardiology introduced a broader disease continuum extending from healthy atria to overt atrial failure. Within this model, atrial cardiomyopathy is no longer viewed as a static entity but as a dynamic process characterized by progressive atrial dysfunction. The earliest stage corresponds to individuals at risk of developing atrial cardiomyopathy. As remodeling progresses, the diagnosis of atrial cardiomyopathy is established by the presence of electrical atrial dysfunction together with evidence of mechanical dysfunction, atrial enlargement, or excessive atrial fibrosis. Ultimately, advanced disease culminates in atrial failure, characterized by persistent atrial arrhythmias, severe mechanical impairment, marked structural remodeling, and the development of symptoms or heart failure. (4)

A summary of the key developments in the understanding of atrial cardiomyopathy is provided in Table I.

This contemporary vision highlights atrial cardiomyopathy as a continuum rather than a discrete condition. Importantly, it identifies a potential window of opportunity during the early stages of atrial remodeling, where aggressive management of cardiovascular risk factors and comorbidities may prevent or delay progression toward overt atrial cardiomyopathy, atrial fibrillation, and atrial failure. Such a paradigm shift has profound implications for early diagnosis, risk stratification, and the development of preventive therapeutic strategies.

Table 1. Evolution of Atrial Cardiomyopathy: From Histopathological Classification to the Atrial Failure Paradigm

Year	Key Publication / Consensus	Major Advancement	Clinical Significance
2016	EHRA/HRS/ APHRS/SOLAECE Expert Consensus	First formal definition of Atrial Cardiomyopathy (AtCM) and introduction of the EHRAS histopathological classification	Established a common framework for research and clinical characterization of atrial disease
2024	EHRA Clinical Consensus Statement	Introduction of a multidimensional clinical staging system integrating electrical, structural, mechanical, and biomarker abnormalities	Facilitated earlier diagnosis, risk stratification, and personalized management
2025	HFA–ESC Clinical Consensus	Conceptualization of a continuum from healthy atria to atrial failure	Highlighted disease progression and emphasized opportunities for prevention and early intervention

PATHOPHYSIOLOGY OF ATRIAL CARDIOMYOPATHY

Structural Remodeling: Fibro-Fatty Infiltration and Fibrosis

Structural remodeling represents a hallmark of atrial cardiomyopathy and encompasses a broad spectrum of histopathological alterations affecting the atrial myocardium. Among these changes, fibro-fatty infiltration and atrial fibrosis are considered major contributors to disease progression and arrhythmogenesis.

Fibro-fatty infiltration refers to the replacement of normal atrial myocardium by fibrotic tissue and adipocytes, predominantly within the subepicardial layers. This process has been frequently observed in patients with atrial fibrillation, heart failure, aging-related atrial remodeling, and valvular heart disease. Expansion of epicardial adipose tissue plays a pivotal role by releasing inflammatory mediators, adipokines, and profibrotic cytokines that promote extracellular matrix remodeling and collagen deposition. (9) (10)

The accumulation of fibrotic tissue disrupts normal myocardial architecture, resulting in increased conduction heterogeneity and electrical uncoupling between adjacent cardiomyocytes. Consequently, fibro-fatty remodeling promotes conduction slowing, conduction block, epicardial-endocardial dissociation, and the formation of re-entrant circuits. These electrophysiological disturbances create a favorable substrate for atrial arrhythmias and contribute to the maintenance of atrial fibrillation. (11) (12)

Beyond its arrhythmogenic effects, the extent of fibro-fatty infiltration has been associated with impaired atrial contractile performance, reduced compliance, and progressive atrial dysfunction. Therefore, structural remodeling constitutes a fundamental mechanism linking atrial cardiomyopathy to both electrical instability and mechanical impairment. (8)

Inflammatory Remodeling: The Central Role of Inflammasome Signaling

Growing evidence indicates that inflammation is a key driver of atrial cardiomyopathy development and progression. Among the inflammatory pathways involved, activation of the NLRP3 inflammasome has emerged as one of the most extensively studied mechanisms linking systemic cardiovascular risk factors to atrial disease.

The NLRP3 inflammasome is a multiprotein intracellular complex that regulates innate immune responses through activation of caspase-1 and subsequent release of pro-inflammatory cytokines, particularly interleukin-1β (IL-1β) and interleukin-18 (IL-18). Activation of the inflammasome initiates a cascade of pathological events involving abnormal calcium handling, oxidative stress, electrical remodeling, cardiomyocyte hypertrophy, and progressive fibrosis. These alterations collectively promote atrial dysfunction and increase susceptibility to atrial fibrillation. (13) (14)

In addition to NLRP3, recent investigations have identified the AIM2 inflammasome as another important mediator of inflammatory atrial remodeling. Furthermore, cardiac macrophages actively participate in the remodeling process through cytokine secretion and modulation of fibroblast activity. (15)

These findings have positioned inflammasome signaling as a potential therapeutic target for preventing atrial remodeling and interrupting the progression of atrial cardiomyopathy.

CLINICAL RISK FACTORS AND CONDITIONS ASSOCIATED WITH ATRIAL CARDIOMYOPATHY

Atrial cardiomyopathy is a multifactorial disorder resulting from the complex interaction between cardiovascular risk factors, systemic diseases, genetic predisposition, and aging-related processes. These factors contribute to progressive atrial remodeling through various mechanisms, including pressure and volume overload, metabolic dysfunction, neurohormonal activation, inflammation, oxidative stress, and fibrosis. The cumulative effect of these alterations ultimately leads to structural, electrical, and mechanical atrial dysfunction. (16)

Cardiovascular diseases were considered important contributors to atrial remodeling. Hypertension promotes chronic atrial pressure overload, leading to left atrial enlargement, fibrosis, and conduction abnormalities. Similarly, heart failure and valvular heart diseases increase atrial wall stress and accelerate structural remodeling. (17)

Obesity is associated with expansion of epicardial adipose tissue, chronic low-grade inflammation, and increased atrial fibrosis. Diabetes mellitus contributes to microvascular dysfunction, oxidative stress, and activation of profibrotic pathways. Non-alcoholic fatty liver disease has recently been recognized as an additional marker of systemic metabolic dysfunction associated with atrial remodeling. (18)

Aging remains one of the strongest risk factors for atrial cardiomyopathy. Progressive accumulation of fibrotic tissue, cardiomyocyte loss, impaired cellular repair mechanisms, and increased oxidative stress contribute to age-related atrial dysfunction. Importantly, these changes may occur even in the absence of overt cardiovascular disease. (17) (19)

Lifestyle-related factors further influence the development of atrial cardiomyopathy. Excessive alcohol consumption has been consistently associated with atrial structural remodeling. Obstructive sleep apnea promotes intermittent hypoxia, sympathetic activation, inflammation, and atrial stretch, thereby accelerating atrial remodeling. Psychological stress and anxiety disorders may also contribute through autonomic nervous system dysregulation and neurohormonal activation. (16)

Genetic susceptibility represents another important component of atrial disease. Several genetic variants involved in ion-channel function, myocardial structure, and extracellular matrix regulation have been associated with increased vulnerability to atrial remodeling and atrial fibrillation. Although the precise contribution of genetic factors remains incompletely understood, inherited predisposition may modulate the response to environmental and cardiovascular stressors. (16) (20)

Importantly, these risk factors do not act independently but interact synergistically throughout the disease process. Regardless of the initial trigger, they converge toward common pathophysiological pathways characterized by inflammation, fibrosis, endothelial dysfunction, electrical remodeling, mechanical impairment, and a prothrombotic state.

MULTIMODALITY ASSESSMENT OF ATRIAL CARDIOMYOPATHY

Overview of the Multimodal Approach

Atrial cardiomyopathy is characterized by the coexistence of electrical, structural, mechanical, and biological abnormalities. Because these alterations may develop at different stages of the disease process, no single diagnostic modality can comprehensively characterize the atrial substrate. Consequently, contemporary assessment of atrial cardiomyopathy relies on a multimodality approach integrating electrocardiographic, imaging, rhythm-monitoring, and biomarker-based information.

While electrocardiography primarily reflects electrical dysfunction, echocardiography evaluates atrial structure and function, cardiac magnetic resonance imaging provides tissue characterization, and biomarkers offer insights into the biological processes underlying atrial remodeling. Together, these modalities provide a comprehensive assessment of atrial disease and facilitate risk stratification.

Electrocardiographic and Rhythm Assessment

Electrocardiography is the cornerstone of electrical substrate evaluation and often provides the earliest evidence of atrial dysfunction. Several electrocardiographic markers of atrial remodeling have been linked to atrial cardiomyopathy, including prolonged P-wave duration, interatrial block, abnormal P-wave axis, increased P-wave terminal force in lead V1, and increased P-wave dispersion. These abnormalities reflect impaired atrial conduction and activation and may precede overt structural remodeling. (21) (22) (23) Beyond conventional ECG analysis, prolonged rhythm monitoring plays an important role in detecting subclinical atrial arrhythmias and excessive supraventricular ectopic activity, both of which have been linked to atrial remodeling and adverse cardiovascular outcomes. (24) (25)

Echocardiographic Assessment

Echocardiography remains the first-line imaging modality for the evaluation of atrial cardiomyopathy because of its wide availability and ability to simultaneously assess atrial structure and function. Conventional echocardiographic parameters provide valuable information regarding atrial size and remodeling, whereas advanced techniques have significantly improved the characterization of atrial mechanics. (26) (27)

Particular attention has recently focused on atrial functional assessment, as mechanical dysfunction may develop before overt atrial enlargement becomes apparent. In this context, left atrial strain analysis has emerged as a promising tool for detecting early atrial dysfunction and estimating the severity of atrial remodeling. (28) (29) Furthermore, three-dimensional echocardiography offers improved volumetric assessment. In addition, left atrial ejection fraction (LAEF) was considered a valuable indicator of global atrial mechanical performance. (30)

Cardiac Magnetic Resonance Imaging

Cardiac magnetic resonance imaging has become an increasingly important modality in the assessment of atrial cardiomyopathy owing to its unique ability to characterize myocardial tissue. In particular, late gadolinium enhancement imaging enables the detection and quantification of atrial fibrosis, which represents a central component of atrial fibrosis.

Beyond fibrosis assessment, cardiac magnetic resonance provides comprehensive information regarding atrial anatomy, chamber remodeling, and functional impairment. However, technical challenges remain due to the thin atrial wall. (31)

Biomarkers and Emerging Diagnostic Tools

Circulating biomarkers provide complementary information regarding atrial remodeling and may assist in risk stratification. Among them, B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) reflect myocardial stretch and have been associated with atrial dysfunction and incident atrial fibrillation. Other biomarkers related to fibrosis and inflammation, such as galectin-3 and C-reactive protein (CRP), may provide additional insights into the underlying remodeling process. Although no biomarker is currently specific for atrial cardiomyopathy, their integration with imaging and electrophysiological data may contribute to a more comprehensive assessment of the atrial substrate. (32) (33)

Emerging technologies, including electroanatomical mapping and artificial intelligence-based algorithms, are expected to further refine the characterization of atrial remodeling and facilitate earlier detection of atrial disease.

Toward an Integrated Diagnostic Framework

The diagnosis of atrial cardiomyopathy should not rely on isolated abnormalities but rather on the integration of electrical, mechanical, structural, and biological information. Such a multidimensional approach reflects the complex nature of atrial remodeling and allows a more accurate characterization of disease severity.

Future diagnostic algorithms will likely combine electrocardiographic markers, advanced echocardiographic parameters, cardiac magnetic resonance findings, rhythm-monitoring data, and circulating biomarkers to establish a comprehensive assessment of atrial health and to identify patients at increased risk of atrial fibrillation, stroke, heart failure, and atrial failure.

CLINICAL IMPLICATIONS OF ATRIAL CARDIOMYOPATHY

The clinical significance of atrial cardiomyopathy extends far beyond the development of atrial fibrillation. Growing evidence indicates that atrial remodeling itself may contribute to a wide spectrum of adverse cardiovascular outcomes, including thromboembolic events, progression of heart failure, and increased mortality. As a result, atrial cardiomyopathy is now recognized not only as an arrhythmogenic substrate but also as a clinically relevant disease entity with important diagnostic, prognostic, and therapeutic implications.

Atrial Fibrillation: Cause, Consequence, or Both?

Atrial fibrillation represents the most common clinical manifestation of atrial cardiomyopathy. Structural remodeling, fibrosis, fibro-fatty infiltration, and electrical conduction abnormalities create a vulnerable substrate that promotes AF initiation and maintenance. Conversely, AF itself contributes to progressive atrial remodeling through electrical, structural, and mechanical alterations, giving rise to the well-established concept that "AF begets AF".

This bidirectional relationship makes it difficult to determine whether atrial fibrillation is the cause or the consequence of atrial disease. Current evidence suggests that AF should be viewed as one manifestation of an underlying atrial cardiomyopathic process rather than an isolated arrhythmia. Consequently, the identification of atrial cardiomyopathy may allow earlier recognition of patients at risk of developing

AF before the occurrence of clinically overt arrhythmias.

Stroke and Thromboembolism

One of the most significant advances in the understanding of atrial cardiomyopathy has been the recognition of its direct association with thromboembolic events, independent of documented atrial fibrillation. Traditionally, atrial fibrillation was considered the primary mechanism responsible for cardioembolic stroke. However, accumulating evidence suggests that the underlying atrial substrate may itself contribute to thrombus formation and systemic embolism, even in patients who remain in sinus rhythm.

This concept emerged from several observations. First, many patients experience ischemic stroke without prior documentation of atrial fibrillation despite prolonged rhythm monitoring. Second, markers of atrial remodeling, including left atrial enlargement, atrial fibrosis, impaired atrial function, and abnormal electrocardiographic parameters, have consistently been associated with an increased risk of stroke independently of AF. These findings suggest that atrial cardiomyopathy may represent the true pathological substrate linking atrial dysfunction to thromboembolic events. (34) (35)

The mechanisms underlying this association are multifactorial and can be interpreted through the framework of Virchow's triad. Mechanical dysfunction of the left atrium and left atrial appendage promotes blood stasis, particularly in advanced stages of atrial remodeling. Structural alterations, including fibrosis and endothelial injury, contribute to local thrombogenicity, while systemic inflammation and neurohormonal activation may favor a procoagulant state. Together, these abnormalities create a prothrombotic atrial environment capable of promoting thrombus formation independently of overt arrhythmia. (5)

The concept of atrial cardiopathy has further reinforced this paradigm. Originally introduced in the field of stroke medicine, atrial cardiopathy refers to the presence of structural, functional, or electrophysiological atrial abnormalities associated with thromboembolic risk in the absence of documented atrial fibrillation. This concept provides a potential explanation for a proportion of embolic strokes of undetermined source (ESUS), in which an abnormal atrial substrate may represent the underlying mechanism despite the absence of detectable AF. (36) (37)

These observations have important clinical implications. They challenge the traditional AF-centered model of stroke prevention and suggest that assessment of atrial health may be as important as arrhythmia detection. Consequently, multimodality evaluation of atrial remodeling has emerged as a promising strategy for identifying patients at increased thromboembolic risk and refining future approaches to stroke prevention.

Heart Failure and Atrial Failure

The relationship between atrial cardiomyopathy and heart failure is complex and bidirectional. While chronic pressure and volume overload associated with heart failure promote atrial remodeling, increasing evidence suggests that atrial dysfunction itself may contribute to the development and progression of heart failure.

The left atrium plays a crucial role in maintaining cardiovascular performance through its reservoir, conduit, and booster-pump functions. Progressive atrial remodeling impairs these physiological functions, leading to reduced ventricular filling, increased filling pressures, pulmonary congestion, and exercise intolerance. (38) (39)

This interaction appears particularly relevant in patients with heart failure with preserved ejection fraction (HFpEF), in whom left atrial dysfunction is frequently observed even before the onset of overt atrial fibrillation. Structural remodeling, fibrosis, and impaired atrial compliance contribute to elevated left ventricular filling pressures and worsening symptoms. In this setting, atrial dysfunction has emerged as an important determinant of exercise capacity, hospitalization risk, and prognosis. (6)

ATRIAL CARDIOMYOPATHY IN SPECIFIC CARDIOMYOPATHIES

Cardiac Amyloidosis

Cardiac amyloidosis represents a paradigmatic model of atrial cardiomyopathy, as amyloid infiltration directly affects the atrial myocardium, leading to severe structural and mechanical dysfunction. Atrial impairment may occur even in the absence of atrial fibrillation and has been associated with an increased risk of thromboembolic events. In this setting, left atrial strain has emerged as a valuable marker of atrial involvement and prognosis, being associated with atrial fibrillation, stroke, heart failure progression, and mortality. (40)

Hypertrophic Cardiomyopathy

In hypertrophic cardiomyopathy, chronic diastolic dysfunction and elevated filling pressures promote progressive atrial remodeling characterized by atrial enlargement, fibrosis, and mechanical dysfunction. These alterations contribute to the development of atrial fibrillation and adverse cardiovascular outcomes. Importantly, impaired atrial function, particularly

reduced left atrial strain, may be detected before the onset of overt arrhythmias and severe cardio-embolic events (41)

CONCLUSION

Atrial cardiomyopathy has evolved from a largely histopathological concept to a clinically relevant syndrome encompassing electrical, structural, mechanical, and biological abnormalities of the atria. Increasing evidence indicates that atrial remodeling is not merely a consequence of atrial fibrillation but rather a distinct disease process that may precede arrhythmia onset and independently contribute to stroke, heart failure, and adverse cardiovascular outcomes. The growing recognition of atrial cardiomyopathy has led to a paradigm shift from an arrhythmia-centered approach toward a substrate-based understanding of atrial disease. In this context, multimodality assessment integrating electrocardiography, cardiac imaging, rhythm monitoring, and biomarkers has become essential for the comprehensive evaluation of the atrial substrate and for identifying patients at risk of disease progression and complications

REFERENCES

1. Kamel H, Okin PM, Longstreth WT, Elkind MSV, Soliman EZ. Atrial cardiopathy: a broadened concept of left atrial thromboembolism beyond atrial fibrillation. Future Cardiol. 2015 May;11(3):323–31. doi:10.2217/fca.15.22 PubMed PMID: 26021638; PubMed Central PMCID: PMC4868349.
2. Kottkamp H. Fibrotic Atrial Cardiomyopathy: A Specific Disease/Syndrome Supplying Substrates for Atrial Fibrillation, Atrial Tachycardia, Sinus Node Disease, AV Node Disease, and Thromboembolic Complications. J Cardiovasc Electrophysiol. 2012;23(7):797–9. doi:10.1111/j.1540-8167.2012.02341.x
3. Goette A, Kalman JM, Aguinaga L, Akar J, Cabrera JA, Chen SA, et al. EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol. 2016 Oct;18(10):1455–90. doi:10.1093/europace/euw161 PubMed PMID: 27402624; PubMed Central PMCID: PMC6392440.
4. Weerts J, Țica O, Aranyo J, Basile C, Borizanova-Petkova A, Borovac JA, et al. Atrial Cardiomyopathy: From Healthy Atria to Atrial Failure. A Clinical Consensus Statement of the Heart Failure Association of the ESC. Eur J Heart Fail. 2025 Nov 1;27(11):2173–94. doi:10.1002/ejhf.3782
5. Darlington A, McCauley MD. Atrial Cardiomyopathy: An Unexplored Limb of Virchow's Triad for AF Stroke Prophylaxis. Front Cardiovasc Med. 2020 Feb 18;7. doi:10.3389/fcvm.2020.00011
6. Vad OB. Atrial cardiomyopathy: markers and outcomes.
7. Kreimer F, Gotzmann M. Left Atrial Cardiomyopathy – A Challenging Diagnosis. Front Cardiovasc Med. 2022 Jun 30;9. doi:10.3389/fcvm.2022.942385
8. Goette A, Corradi D, Dobrev D, Aguinaga L, Cabrera JA, Chugh SS, et al. Atrial cardiomyopathy revisited—evolution of a concept: a clinical consensus statement of the European Heart Rhythm Association (EHRA) of the ESC, the Heart Rhythm Society (HRS), the Asian Pacific Heart Rhythm Society (APHRS), and the Latin American Heart Rhythm Society (LAHRS). Europace. 2024 Aug 30;26(9):euae204. doi:10.1093/europace/euae204
9. Abe I, Teshima Y, Kondo H, Kaku H, Kira S, Ikebe Y, et al. Association of fibrotic remodeling and cytokines/chemokines content in epicardial adipose tissue with atrial myocardial fibrosis in patients with atrial fibrillation. Heart Rhythm. 2018 Nov 1;15(11):1717–27. doi:10.1016/j.hrthm.2018.06.025 PubMed PMID: 29908372.
10. Mazurek T, Zhang L, Zalewski A, Mannion JD, Diehl JT, Arafat H, et al. Human Epicardial Adipose Tissue Is a Source of Inflammatory Mediators. Circulation. 2003 Nov 18;108(20):2460–6. doi:10.1161/01.CIR.0000099542.57313.C5
11. Ravelli F, Masè M, Cristoforetti A, Avogaro L, D'Amato E, Tessarolo F, et al. Quantitative assessment of transmural fibrosis profile in the human atrium: evidence for a three-dimensional arrhythmic substrate by slice-to-slice histology. EP Eur. 2023 Feb 16;25(2):739–47. doi:10.1093/europace/euac187
12. Nalliah CJ, Bell JR, Raaijmakers AJA, Waddell HM, Wells SP, Bernasochi GB, et al. Epicardial Adipose Tissue Accumulation Confers Atrial Conduction Abnormality. J Am Coll Cardiol. 2020 Sep;76(10):1197–211. doi:10.1016/j.jacc.2020.07.017
13. Yao C, Veleva T, Scott L, Cao S, Li L, Chen G, et al. Enhanced Cardiomyocyte NLRP3 Inflammasome Signaling Promotes Atrial Fibrillation. Circulation. 2018 Nov 13;138(20):2227–42. doi:10.1161/CIRCULATIONAHA.118.035202
14. Poppenborg T, Saljic A, Bruns F, Abu-Taha I, Dobrev D, Fender AC. A short history of the atrial NLRP3 inflammasome and its distinct role in atrial fibrillation. J Mol Cell Cardiol. 2025 May;202:13–23. doi:10.1016/j.yjmcc.2025.02.011
15. Karakasis P, Pamporis K, Theofilis P, Milaras N, Vlachakis PK, Grigoriou K, et al. Inflammasome Signaling in Cardiac Arrhythmias: Linking Inflammation, Fibrosis, and Electrical Remodeling. Int J Mol Sci. 2025 Jun 20;26(13):5954. doi:10.3390/ijms26135954
16. Liu Z, Liu T, Wu G. Atrial Cardiomyopathy: From Diagnosis to

Treatment. Rev Cardiovasc Med. 2025 Jan 20;26(1):25124. doi:10.31083/RCM25124

17. Allan V, Honarbakhsh S, Casas JP, Wallace J, Hunter R, Schilling R, et al. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. Thromb Haemost. 2017 May 3;117(5):837–50. doi:10.1160/TH16-11-0825
18. Rashid AM, Khan MS, Alenezi F, Anker SD, Knebel F. Obesity and left atrial function: state of the art. Glob Cardiol. 2026 Mar 31;4(1). doi:10.4081/cardio.2026.96
19. Wang MF, Hou C, Jia F, Zhong CH, Xue C, Li JJ. Aging-associated atrial fibrillation: A comprehensive review focusing on the potential mechanisms. Aging Cell. n/a(n/a):e14309. doi:10.1111/acel.14309
20. Atrial cardiomyopathy: from cell to bedside - Li - 2022 - ESC Heart Failure - Wiley Online Library
21. Chen LY, Ribeiro ALP, Platonov PG, Cygankiewicz I, Soliman EZ, Gorenek B, et al. P Wave Parameters and Indices: A Critical Appraisal of Clinical Utility, Challenges, and Future Research—A Consensus Document Endorsed by the International Society of Electrocardiology and the International Society for Holter and Noninvasive Electrocardiology.
22. He J, Tse G, Korantzopoulos P, Letsas KP, Ali-Hasan-Al-Saegh S, Kamel H, et al. P-Wave Indices and Risk of Ischemic Stroke.
23. Kamel H, Soliman EZ, Heckbert SR, Kronmal RA, Longstreth WT, Nazarian S, et al. P-Wave Morphology and the Risk of Incident Ischemic Stroke in the Multi-Ethnic Study of Atherosclerosis. Stroke. 2014 Sep;45(9):2786–8. doi:10.1161/STROKEAHA.114.006364
24. Meng L, Tsiaousis G, He J, Tse G, Antoniadis AP, Korantzopoulos P, et al. Excessive Supraventricular Ectopic Activity and Adverse Cardiovascular Outcomes: a Systematic Review and Meta-analysis. Curr Atheroscler Rep. 2020 Apr;22(4):14. doi:10.1007/s11883-020-0832-4
25. Guichard JB, Guasch E, Roche F, Da Costa A, Mont L. Premature atrial contractions: A predictor of atrial fibrillation and a relevant marker of atrial cardiomyopathy. Front Physiol. 2022 Oct 24;13:971691. doi:10.3389/fphys.2022.971691
26. Kizer JR, Bella JN, Palmieri V, Liu JE, Best LG, Lee ET, et al. Left atrial diameter as an independent predictor of first clinical cardiovascular events in middle-aged and elderly adults: The Strong Heart Study (SHS). Am Heart J. 2006 Feb 1;151(2):412–8. doi:10.1016/j.ahj.2005.04.031
27. Kim J, Yum B, Palumbo MC, Sultana R, Wright N, Das M, et al. Left Atrial Strain Impairment Precedes Geometric Remodeling as a Marker of Post-Myocardial Infarction Diastolic Dysfunction. JACC Cardiovasc Imaging. 2020 Oct;13(10):2099–113. doi:10.1016/j.jcmg.2020.05.041 PubMed PMID: 32828776; PubMed Central PMCID: PMC7554167.
28. Thomas JD, Edvardsen T, Abraham T, Appadurai V, Badano L, Banchs J, et al. Clinical Applications of Strain Echocardiography: A Clinical Consensus Statement From the American Society of Echocardiography Developed in Collaboration With the European Association of Cardiovascular Imaging of the European Society of Cardiology. J Am Soc Echocardiogr. 2025 Nov;38(11):985–1020. doi:10.1016/j.echo.2025.07.007
29. Hauser R, Nielsen AB, Skaarup KG, Lassen MCH, Duus LS, Johansen ND, et al. Left atrial strain predicts incident atrial fibrillation in the general population: the Copenhagen City Heart Study. Eur Heart J - Cardiovasc Imaging. 2021 Dec 18;23(1):52–60. doi:10.1093/ehjci/jeab202
30. Li L, Li M, Ran H, Fang LL, Ding QS, Zhang PY. Left Atrial Volume and Phasic Function Assessed by 4D Auto LAQ Echocardiography in Treatment-Naive, Newly Diagnosed Type 2 Diabetes Mellitus Patients Without Hypertension or Obesity. J Cardiovasc Dev Dis. 2026 Mar 10;13(3):131. doi:10.3390/jcdd13030131
31. Jabbour JP, Palombi M, Bonanni M, Matteucci A, Arcari L, Pierucci N, et al. The Role of Cardiac Magnetic Resonance in Characterizing Atrial Cardiomyopathy and Guiding Substrate Ablation in Atrial Fibrillation: A Narrative Review. J Cardiovasc Dev Dis. 2025 Mar 25;12(4):114. doi:10.3390/jcdd12040114
32. Wasser K, Weber-Krüger M, Gröschel S, Uphaus T, Liman J, Hamann GF, et al. Brain Natriuretic Peptide and Discovery of Atrial Fibrillation After Stroke: A Subanalysis of the Find-AFRANDOMISED Trial. Stroke. 2020 Feb;51(2):395–401. doi:10.1161/STROKEAHA.119.026496
33. Bai J, Sun H, Xie L, Zhu Y, Feng Y. Detection of cardioembolic stroke with B-type natriuretic peptide or N-terminal pro-BNP: a comparative diagnostic meta-analysis. Int J Neurosci. 2018 Nov 2;128(11):1100–8. doi:10.1080/00207454.2017.1408612 PubMed PMID: 29874952.
34. Sposato LA, Chaturvedi S, Hsieh CY, Morillo CA, Kamel H. Atrial Fibrillation Detected After Stroke and Transient Ischemic Attack: A Novel Clinical Concept Challenging Current Views. Stroke. 2022 Mar;53(3). doi:10.1161/STROKEAHA.121.034777
35. Bhat A, Khanna S, Chen HH, Lee L, Gan GCH, Negishi K, et al. Impairment of left atrial function and cryptogenic stroke: Potential insights in the pathophysiology of stroke in the young. Int J Cardiol Heart Vasc. 2019 Dec 26;26:100454. doi:10.1016/j.ijcha.2019.100454
36. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB,

O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. Lancet Neurol. 2014 Apr 1;13(4):429–38. doi:10.1016/S1474-4422(13)70310-7

37. Ntaios G, Baumgartner H, Doehner W, Donal E, Edvardsen T, Healey JS, et al. Embolic strokes of undetermined source: a clinical consensus statement of the ESC Council on Stroke, the European Association of Cardiovascular Imaging and the European Heart Rhythm Association of the ESC. Eur Heart J. 2024 May 21;45(19):1701–15. doi:10.1093/eurheartj/ehae150
38. Rosenberg MA, Gottdiener JS, Heckbert SR, Mukamal KJ. Echocardiographic diastolic parameters and risk of atrial fibrillation: the Cardiovascular Health Study. Eur Heart J. 2012 Apr;33(7):904–12. doi:10.1093/eurheartj/ehr378
39. Thomas L, Marwick TH, Popescu BA, Donal E, Badano LP. Left Atrial Structure and Function, and Left Ventricular Diastolic Dysfunction: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019 Apr 23;73(15):1961–77. doi:10.1016/j.jacc.2019.01.059 PubMed PMID: 31000000.
40. Akintoye E, Majid M, Klein AL, Hanna M. Prognostic Utility of Left Atrial Strain to Predict Thrombotic Events and Mortality in Amyloid Cardiomyopathy. JACC Cardiovasc Imaging. 2023 Nov;16(11):1371–83. doi:10.1016/j.jcmg.2023.01.015
41. Hussain K, Nso N, Tsourdinis G, Haider S, Mian R, Sanagala T, et al. A systematic review and meta-analysis of left atrial strain in hypertrophic cardiomyopathy and its prognostic utility. Curr Probl Cardiol. 2024 Jan 1;49(1, Part C):102146. doi:10.1016/j.cpcardiol.2023.102146;