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Review

Visceral Adipose Tissue and Cardiac Arrhythmogenesis: Current Mechanistic Evidence and Clinical Implications

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Abstract

Visceral adiposity is increasingly recognized as a biologically relevant determinant of arrhythmic risk that is only partially captured by body mass index. The pathophysiological signal arises from both systemic adipose dysfunction and regional ectopic fat deposition, particularly epicardial adipose tissue, which lies in direct continuity with the atrial and ventricular myocardium. In contemporary literature, the association between adiposity and atrial fibrillation is no longer explained solely by chamber enlargement, hypertension, diabetes, or sleep apnea. Instead, obesity-related arrhythmogenesis appears to reflect, at least in part, an integrated atrial myopathy characterized by inflammatory activation, oxidative stress, fibrofatty remodeling, conduction heterogeneity, autonomic imbalance, and altered electromechanical coupling. Regional visceral and pericardial fat predict incident atrial fibrillation beyond general adiposity, while histological, imaging, and electroanatomical studies support a plausible contribution of epicardial adipose tissue to atrial fibrosis, low-voltage substrate, and post-ablation recurrence. Contemporary imaging studies also suggest that depot location and qualitative characteristics, such as tissue attenuation or density, may be as important as absolute fat volume. Therapeutically, durable weight loss and structured risk factor modification are associated with reverse remodeling of components of the arrhythmogenic substrate. In contrast, pharmacological strategies that reduce or modulate epicardial adipose tissue remain promising but require further prospective validation. Data for ventricular arrhythmias are emerging but remain substantially less mature, largely confined to observational studies and mechanistic inference. This review synthesizes current evidence on the relationship between visceral adiposity, epicardial fat, and cardiac arrhythmias.

Keywords: visceral obesity; visceral adipose tissue; epicardial adipose tissue; atrial fibrillation; ventricular arrhythmias; catheter ablation

1. Introduction

The relationship between adiposity and arrhythmia is no longer a niche topic within cardiometabolic medicine. It has become central to understanding why atrial fibrillation (AF) develops earlier, persists longer, and relapses more often in patients with obesity [1]. The modern literature supports a specific concept: the clinically relevant signal does not arise from excess body weight alone, but from the biological behavior and regional distribution of adipose tissue, especially visceral and ectopic fat depots [2,3,4,5].

This distinction matters because body mass index (BMI) is a crude marker. Two individuals with similar BMI may differ markedly in visceral fat burden, insulin resistance, inflammatory activation, hepatic steatosis, and ectopic lipid deposition. Those differences translate into different cardiovascular phenotypes and probably into different arrhythmic substrates [3,4,5]. Epicardial adipose tissue (EAT), the visceral fat depot enclosed by the visceral pericardium and directly apposed to the myocardium, has emerged as the most clinically accessible and pathobiologically relevant cardiac fat compartment [6,7]. Unlike paracardial fat, EAT has no fascial plane separating it from the underlying myocardium, shares aspects of the coronary microcirculation, and can therefore communicate with adjacent tissue by paracrine, vasocrine, and possibly direct infiltrative mechanisms [6,7].

At the population level, obesity clearly increases AF risk, and the association appears graded rather than threshold-based [8,9,10]. Yet the mechanistic pathway is not singular. Obesity amplifies blood volume, atrial pressure, sleep-disordered breathing, hypertension, diabetes, and ventricular diastolic dysfunction; all of these favor atrial enlargement and AF. At the same time, visceral adiposity creates a systemic inflammatory and neurohormonal milieu that promotes local structural and electrical remod-

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eling. These interacting pathways explain why abdominal obesity and metabolic syndrome often track AF risk even after adjustment for BMI alone [11,12]. Longitudinal studies have further shown that pericardial and visceral fat measures predict incident AF more specifically than generalized adiposity, reinforcing the view that regional fat depots provide information that BMI does not [13,14,15]. Emerging human genetic data also support the cardiovascular relevance of epicardial and pericardial adiposity as more than passive epiphenomena [16].

The contemporary field therefore asks a sharper question than earlier literature did. The issue is not simply whether obesity and arrhythmias coexist, but how visceral adiposity may contribute to myocardial remodeling, which cardiac fat features are clinically meaningful, and whether modifying those features is associated with improved outcomes. This review addresses those questions with an emphasis on mechanistic rigor, integrating anatomical, epidemiological, histological, imaging, electrophysiological, and therapeutic evidence. Because the evidence is most mature for AF, that condition occupies the center of the discussion. Ventricular arrhythmias are considered separately, where the signal is increasingly plausible but clearly less established.

Search Strategy and Scope of Review

A targeted search of PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar up to June 2026 was performed. Search terms included combinations of: visceral adiposity, visceral adipose tissue, epicardial adipose tissue, pericardial fat, atrial fibrillation, ventricular arrhythmias, premature ventricular complexes, ventricular tachycardia, sudden cardiac death, catheter ablation, low-voltage substrate, atrial fibrosis, adipokines, inflammation, oxidative stress, lipotoxicity, and autonomic remodeling. Priority was given to population studies, cardiac imaging studies, histological and mechanistic investigations, electroanatomical mapping studies, meta-analyses, and contemporary guidelines. No formal risk-of-bias assessment or systematic meta-analysis was performed. Article selection and interpretation were based on author judgment and were not intended to reproduce a systematic review or meta-analysis.

2. Visceral Adiposity, Cardiac Fat Depots, and Why Location Matters

Visceral adiposity refers to the accumulation of fat within the abdominal cavity and in ectopic sites such as the liver, pancreas, skeletal muscle, and heart. Relative to subcutaneous fat, visceral adipose tissue is more lipolytically active, more insulin resistant, and more likely to exhibit macrophage infiltration, oxidative stress, and a maladaptive adipokine profile [2,3,4]. In cardiovascular disease, these differences matter because they alter circulating cytokines, free fatty acid flux, endothelial function, sympathetic activity, and extracellular matrix biology [2,5].

Obesity, visceral adiposity, and EAT should therefore not be treated as interchangeable terms. Obesity is most often captured clinically by anthropometric measures such as BMI or waist circumference; visceral adiposity refers to a metabolically active body-fat distribution; and EAT represents the cardiac visceral fat depot through which part of this systemic adipose phenotype may be locally expressed at the myocardial surface. The rationale for discussing general adiposity in this review is that much of the epidemiological literature still uses BMI, waist measures, diabetes, or metabolic syndrome as upstream clinical surrogates, whereas the mechanistic focus increasingly shifts toward visceral and cardiac fat phenotypes.

Within the thorax, not all fat around the heart is biologically equivalent. EAT lies between the myocardium and the visceral pericardium and is therefore a true visceral fat depot. Pericardial or paracardial fat is external to the parietal pericardium and is anatomically more separated from the myocardium [6,7]. Under physiological conditions, EAT is not inherently pathological. It may provide mechanical cushioning, local thermogenesis, and a readily available source of fatty acids for the myocardium. It also contains adiponectin and other factors that may be cardioprotective in health [6,7]. The problem emerges when adipocyte hypertrophy, immune-cell recruitment, mitochondrial dysfunction, and hypoxia shift EAT toward an inflammatory secretory phenotype [5,7].

That transition is particularly relevant in AF because atrial myocardium lies immediately beneath substantial epicardial fat depots, especially along the posterior left atrium, interatrial groove, atrioventricular grooves, ligament of Marshall region, and around major autonomic ganglionated plexi [17,18,19]. The arrhythmic implications of this anatomy are straightforward. If a metabolically abnormal depot is physically contiguous with atrial myocardium, enriched in inflammatory mediators, and co-localized with autonomic neural structures, it may plausibly contribute to the substrate associated with AF initiation and maintenance [17,18,20]. This local-depot concept helps explain why left atrial or periatrial fat often performs better than total body adiposity in arrhythmic risk stratification.

The atrium may be especially susceptible for several reasons. Its wall is thin, its architecture is anisotropic, and the distance between epicardial adipose depots and endocardial conduction tissue is relatively short. Small increments in interstitial fibrosis or local fibro-fatty change can therefore produce clinically relevant conduction slowing long before gross chamber dysfunction becomes obvious [17,19,21]. In addition, atrial electrophysiology is unusually sensitive to autonomic shifts, stretch, and inflammation, all of which are intensified in cardiometabolic disease [20,22]. These features help explain why the evidence linking adiposity to AF is much stronger than the corresponding evidence for most ventricular arrhythmias.

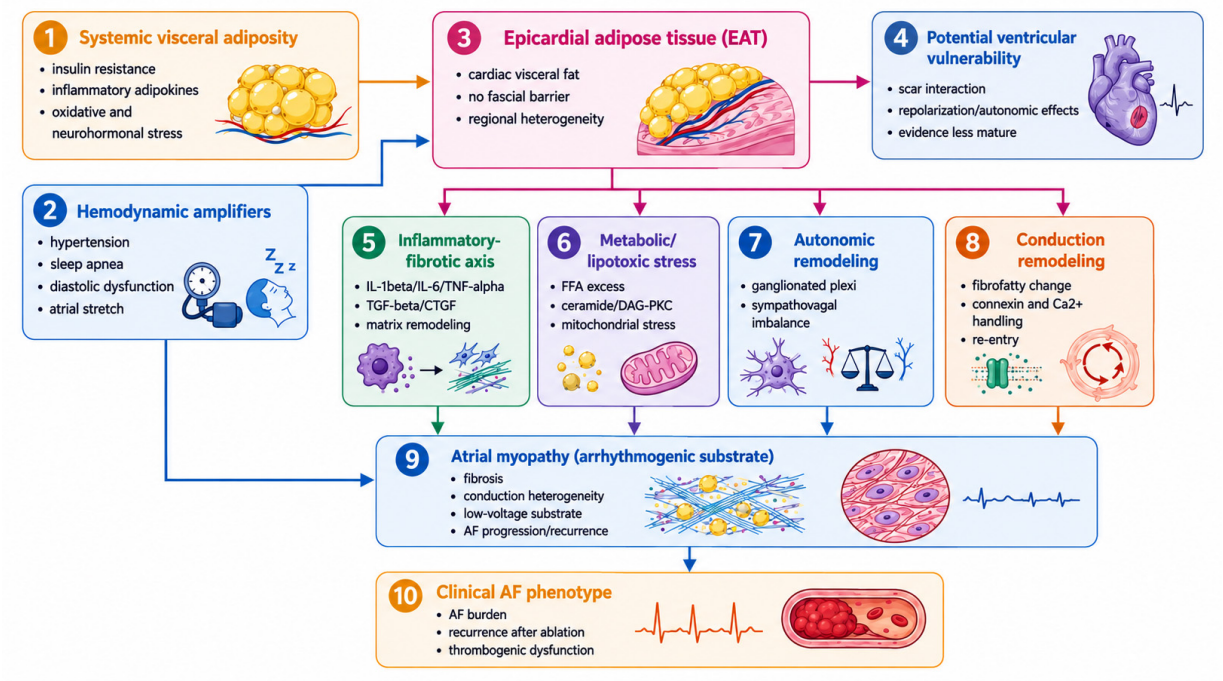


Fig. 1. Visceral adiposity-cardiac fat axis and mechanisms of arrhythmogenesis. Systemic visceral adiposity promotes adipocyte hypertrophy, insulin resistance, inflammatory adipokine signaling, and oxidative-neurohormonal stress. Within the heart, EAT localizes this adverse biology because it lies in direct contact with the myocardium and shares the coronary microcirculation. The resulting inflammatory-fibrotic signaling, cardio-lipotoxic stress, autonomic remodeling, and fibrofatty infiltration may converge on an atrial myopathy phenotype characterized by fibrosis, conduction heterogeneity, and low-voltage substrate, potentially facilitating AF initiation, persistence, and recurrence. A putative ventricular branch is shown separately to indicate that links between epicardial fat and ventricular arrhythmias are biologically plausible but supported by less mature evidence. Abbreviations: AF, atrial fibrillation; Ca^{2+}, calcium; CTGF, connective tissue growth factor; DAG, diacylglycerol; FFA, free fatty acids; IL-1β, interleukin-1 beta; IL-6, interleukin-6; PKC, protein kinase C; TGF-beta, transforming growth factor beta; TNF-alpha, tumor necrosis factor alpha.

Clinical phenotyping has gradually shifted in the same direction. Computed tomography (CT) and cardiac magnetic resonance imaging (CMR) can quantify total EAT volume, periatrial EAT, and, increasingly, qualitative features such as tissue attenuation or density. Echocardiography is more widely available but is limited to linear thickness measurements and is more operator dependent [7,20]. What matters clinically is not merely how much adipose tissue is present, but where it is located, whether it reflects metabolically active inflammation, and how it relates spatially to atrial scar, low-voltage zones, or ablation targets (Fig. 1).

3. Epidemiological and Clinical Evidence Linking Adiposity to Atrial Fibrillation

General adiposity and AF have been linked for years, but the most informative modern data involve regional fat distribution. In the Women's Health Study, increasing BMI was associated with a graded rise in incident AF risk [9]. Broader umbrella and meta-analytic work has since confirmed a positive association between adiposity and AF across observational and Mendelian-randomization frameworks [10]. Similarly, metabolic syndrome and its abdominal obesity component carry independent associations with AF incidence, suggesting that central adiposity captures a clinically meaningful component of risk beyond total body mass [11]. These population signals are biologically plausible but still nonspecific, because obesity also clusters with hypertension, diabetes, sleep apnea, and left-sided filling abnormalities. In Framingham, pericardial fat and abdominal visceral fat were associated with incident AF, and pericardial fat offered information not fully reproduced by generalized adiposity measures [13]. In the Multi-Ethnic Study of Atherosclerosis (MESA) and Jackson Heart cohorts, greater pericardial fat volume was likewise associated with incident AF [14]. More recent continuous-monitoring work using CMR-derived EAT suggests that atrial EAT may be linked not only to overt clinical AF but also to subclinical episodes detected by implantable monitoring, implying that adiposity may influence the earliest detectable stages of the arrhythmogenic process [15]. Rämö et al. [16] adds a further layer by linking these depots to cardiovascular outcomes and genetic architecture, supporting the view that cardiac fat phenotypes may capture stable biological traits relevant to disease development. The phenotype also extends to AF severity and treatment response.

Earlier work showed that left atrial epicardial adiposity distinguished AF patients from control subjects [23]. Importantly, not all obese patients behave similarly. Some have relatively little ectopic fat or less advanced metabolic dysfunction, whereas others show marked periatrial adiposity, diabetes, sleep apnea, or metabolic syndrome, features that likely place them farther along the atrial myopathy continuum [18,20]. This distinction has practical implications. Rhythm-control strategies, especially ablation, perform less well in patients with more advanced obesity-related remodeling unless weight and comorbidity management are addressed in parallel. In other words, obesity is not just a background characteristic; it is often part of the substrate that determines whether rhythm control is durable. That is one reason why the field has shifted from describing obesity as a comorbidity toward describing adiposity as an arrhythmogenic phenotype.

A related clinical nuance is that obesity-related arrhythmic risk is unlikely to be uniform across all patients with elevated BMI. Metabolically unhealthy obesity, central adiposity, diabetes, sleep apnea, hepatic steatosis, and reduced cardiorespiratory fitness probably identify a more adverse substrate than BMI alone, whereas so-called metabolically healthy obesity may carry a different risk profile. Similarly, obesity paradox observations in cardiovascular cohorts should be interpreted cautiously because they may reflect selection bias, reverse causality, age, fitness, or treatment differences rather than protection from adiposity itself [14,18,19].

4. Mechanistic Pathways From Visceral Adiposity to Atrial Arrhythmogenesis

To address the mechanistic evidence more systematically, the adiposity-arrhythmia link can be separated into four interacting levels: (1) inflammatory-secretory signaling from dysfunctional visceral and epicardial adipose tissue; (2) direct fibrofatty interaction between EAT and atrial myocardium; (3) electrical remodeling with conduction slowing, low-voltage substrate, and re-entry; and (4) autonomic and hemodynamic amplification (Figs. 2,3,4).

4.1 Inflammatory Remodeling and Adipose Tissue Dysfunction

The most coherent mechanistic model starts with adipose tissue dysfunction. Visceral obesity is characterized by adipocyte enlargement, altered mitochondrial handling, adipose hypoxia, extracellular matrix expansion, and infiltration by pro-inflammatory immune cells. These changes shift adipose secretory output away from protective adipokines and toward interleukin-6, tumor necrosis factor-alpha, monocyte chemoattractant protein-1, transforming growth factor-beta related signaling, oxidative stress mediators, and excess free fatty acid release [2,5,7]. EAT appears particularly prone to this switch in metabolically unhealthy states. Macrophage polarization within EAT has been linked to coronary disease and likely reflects a broader inflammatory transformation of the depot [24].

The inflammatory component may involve interleukin-1beta/nucleotide-binding oligomerization domain-like receptor pyrin domain-containing 3 (NLRP3) inflammasome signaling, interleukin-6/Janus kinase-signal transducer and activator of transcription 3 signaling, and tumor necrosis factor-alpha/nuclear factor-kappa B activation. Fibrotic remodeling can be conceptualized through transforming growth factor-beta/Smad signaling, connective tissue growth factor, matrix metalloproteinase/tissue inhibitor of metalloproteinase imbalance, and fibroblast-to-myofibroblast activation. Oxidative and mitochondrial stress may involve NADPH oxidase 2/4-derived reactive oxygen species, reactive oxygen species-dependent Ca^{2+}/calmodulin-dependent protein kinase II activation, and mitochondrial dysfunction. Electrical remodeling may include connexin 40/43 dysregulation, Nav1.5 sodium-channel impairment, L-type calcium-channel remodeling, and ryanodine receptor 2/sarcoplasmic-endoplasmic reticulum Ca^{2+}-ATPase 2a uncoupling. Lipotoxic signaling may include free fatty acid overload, ceramide accumulation, and diacylglycerol-protein kinase C activation, while neuro-adipose interaction may involve ganglionated plexi hyperactivity, sympathetic nerve sprouting, and parasympathetic modulation [19,25].

In AF, these inflammatory signals are clinically relevant because they have been associated with tissue remodeling. Human surgical studies have linked fibrotic remodeling of EAT and enrichment of cytokines or chemokines within that depot with atrial myocardial fibrosis [25]. Chitinase-3-like protein 1 (YKL-40) expression within EAT is increased in AF and correlates with atrial fibrosis [26]. Connective tissue growth factor expression in human EAT is independently associated with AF and closely linked to fibrotic remodeling [27].

At the molecular level, dysfunctional EAT may act as an inflammatory amplifier rather than as a passive fat depot. Adipocyte hypertrophy and relative hypoxia favor oxidative stress, mitochondrial dysfunction, endoplasmic-reticulum stress, and recruitment of macrophages with a more pro-inflammatory phenotype. This environment can activate NLRP3 inflammasome signaling and increase release of interleukin-1beta, interleukin-6, tumor necrosis factor-alpha, reactive oxygen species, and profibrotic mediators such as transforming growth factor-beta, connective-tissue growth factor, and YKL-40. These mediators provide a plausible bridge between local adipose inflammation and extracellular-matrix remodeling in adjacent atrial tissue [24,25,26,27,28,29,30,31,32,33].

The relevance of this pathway is not only biochemical. EAT is anatomically contiguous with the atrial epicardium and shares the coronary microcirculation; therefore, paracrine inflammatory signaling can be expressed locally in regions that are also important for AF maintenance,

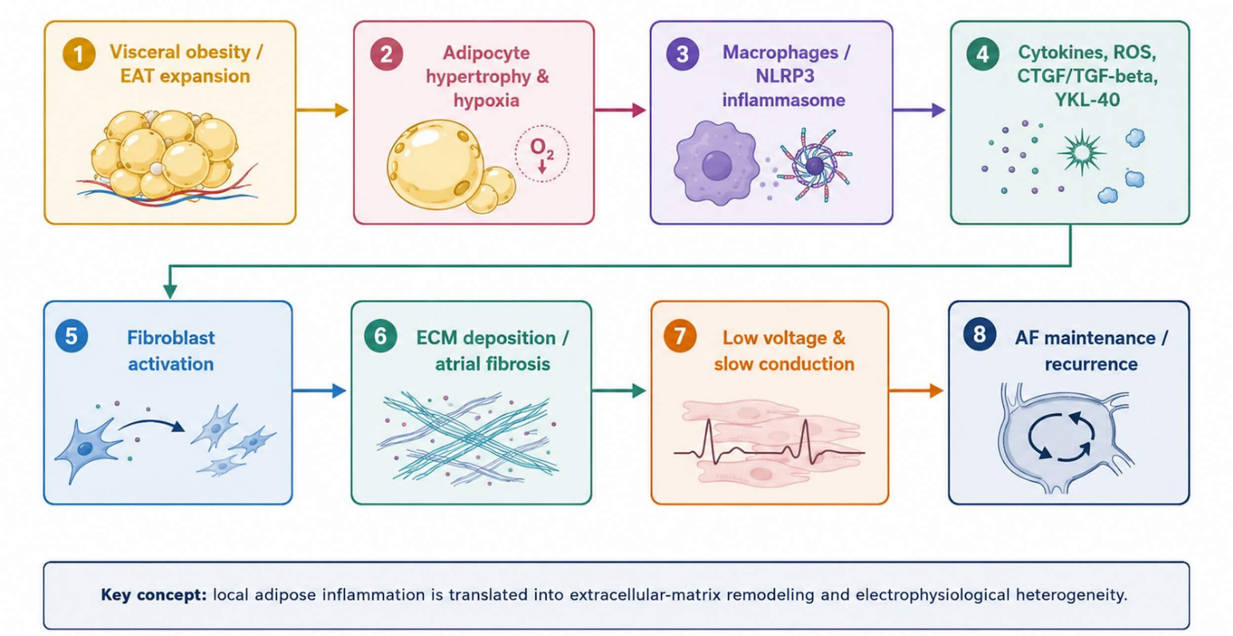


Fig. 2. Inflammatory-secretory pathway from dysfunctional EAT to atrial substrate. Adipocyte hypertrophy, hypoxia, macrophage infiltration, inflammasome activation, inflammatory cytokines, oxidative stress, and profibrotic signaling may converge on fibroblast activation, extracellular-matrix deposition, atrial fibrosis, low-voltage substrate, conduction heterogeneity, and AF maintenance or recurrence. Abbreviations: ECM, extracellular matrix; NLRP3, NOD-like receptor family pyrin domain-containing 3; ROS, reactive oxygen species; YKL-40, chitinase-3-like protein 1.

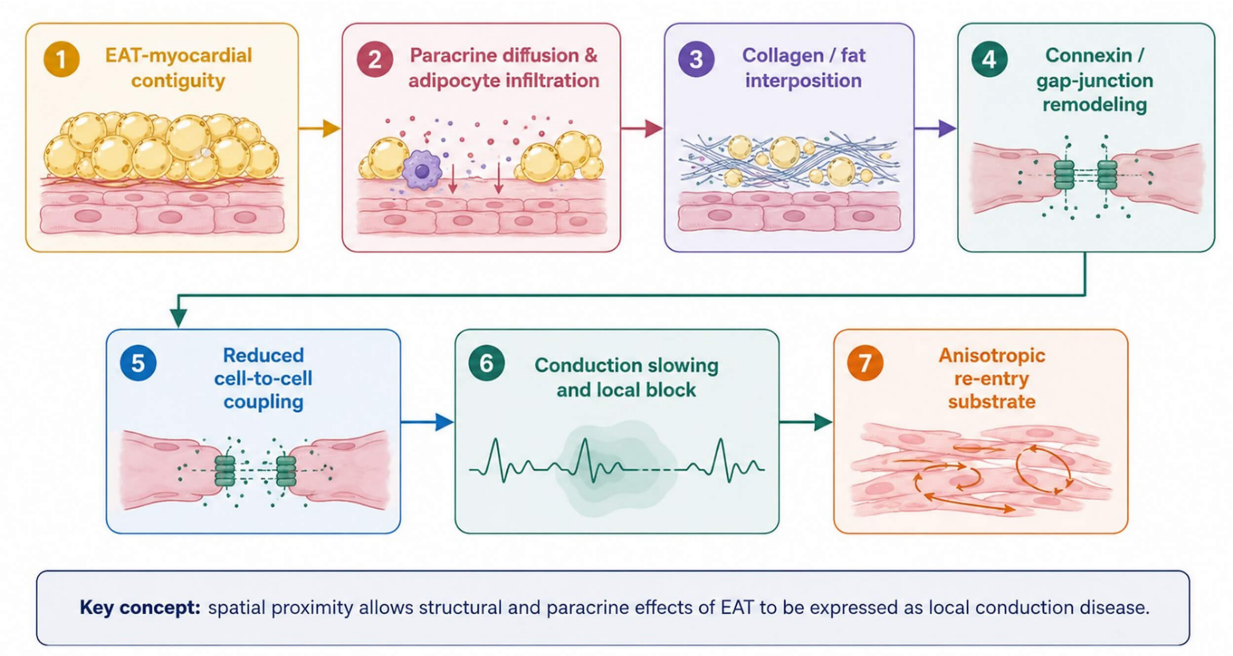


Fig. 3. Direct fibrofatty interaction and conduction-slowing pathway. Because EAT directly contacts the atrial epicardium, local adipose inflammation, adipocyte infiltration, collagen deposition, and gap-junction remodeling may reduce cell-to-cell coupling and produce conduction slowing, local block, anisotropy, and re-entry substrate.

including the posterior left atrium, interatrial groove, atrioventricular grooves, and areas close to ganglionated plexi. This spatial coupling helps explain why periatrial EAT and EAT attenuation may correlate more closely with atrial fibrosis, low-voltage areas, or ablation recurrence than BMI alone [28,29,30,31,32,33,34].

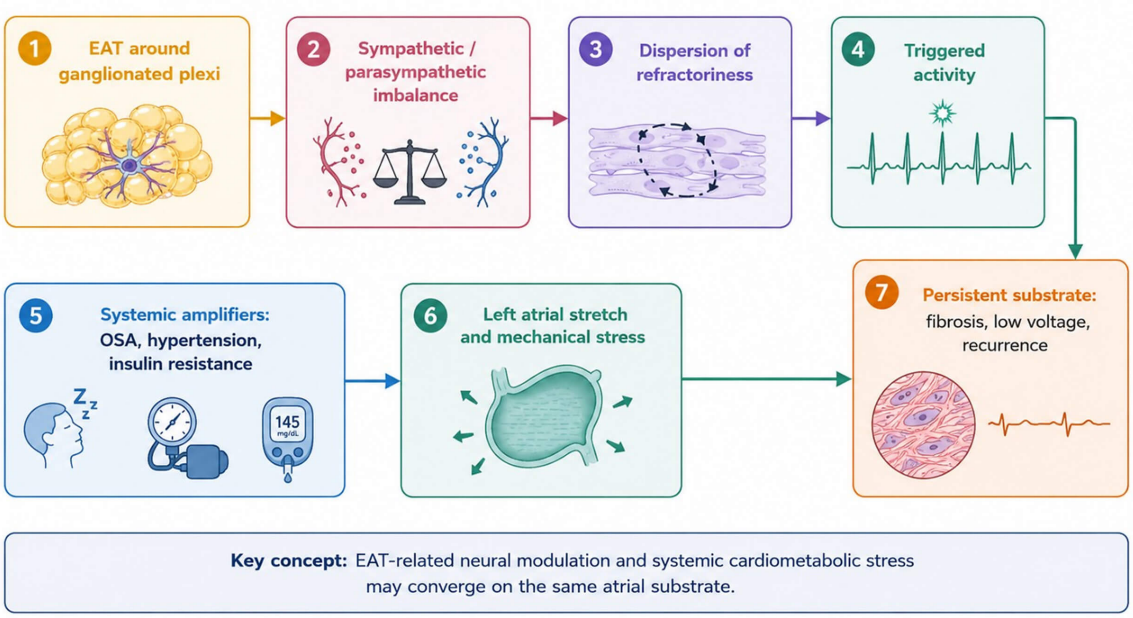


Fig. 4. Autonomic-electrical pathway and systemic mechanical amplification. EAT-associated autonomic remodeling may increase dispersion of refractoriness, action-potential heterogeneity, and triggered activity. Systemic obesity-related amplifiers such as obstructive sleep apnea, hypertension, insulin resistance, and left atrial stretch may then consolidate these triggers into a persistent arrhythmogenic substrate. OSA, obstructive sleep apnea.

4.2 Fibrofatty Atrial Myopathy and Direct Tissue Interaction

Structural remodeling is the key bridge between adiposity and sustained AF. The atrial substrate that maintains AF is characterized by interstitial fibrosis, myocyte hypertrophy, anisotropic conduction, chamber dilation, and loss of uniform electrical coupling. EAT may contribute to each of these processes. One mechanism is paracrine communication: inflammatory mediators, adipokines, and profibrotic factors diffuse from the adipose depot into adjacent myocardium. Another is direct cellular interaction. Reactivation of the epicardium has been implicated in fibrofatty infiltration during atrial cardiomyopathy, providing a developmental and histopathological framework for how adipose-related remodeling may extend into the atrial wall [28]. Reviews focusing on fibroblast-myocyte-EAT interaction have also highlighted the likelihood that EAT acts through multicellular crosstalk rather than through a single mediator [29].

The concept of cardio-lipotoxicity captures a broader set of mechanisms by which abnormal EAT can induce oxidative injury, mitochondrial dysfunction, altered substrate utilization, endoplasmic reticulum stress, and extracellular matrix remodeling in adjacent myocardium [30]. This framework is useful because it links traditional inflammatory models with metabolic stress, particularly in patients who have diabetes, obesity, heart failure with preserved ejection fraction, or mixed cardiometabolic disease.

A related point, often underemphasized, is that adipose dysfunction is not just about the presence of inflammatory cytokines; it is also about loss of normal adipose signaling. Protective adipokines decline, whereas leptin resistance, resistin-related pathways, and excess free fatty acid exposure may favor fibroblast activation, oxidative injury, and altered calcium handling [5,7,19]. The consequence is a depot that may behave less like a benign energy reserve and more like a metabolically active inflammatory organ applied directly to the atrial surface. Accordingly, EAT burden alone may not fully capture arrhythmic risk, because depots of similar size may differ substantially in inflammatory phenotype. Experimental evidence suggests that the secretome of atrial EAT can facilitate reentrant arrhythmias through myocardial remodeling, supporting the hypothesis that human atrial EAT may be capable of modifying arrhythmia vulnerability in selected settings rather than simply accompanying it [31]. In another mechanistic study, EAT-derived interleukin-1beta was implicated in postoperative AF, suggesting that inflammation within the adipose depot may help unmask AF in settings where operative stress provides the trigger and a vulnerable substrate already exists [32].

A second pathway is direct structural interaction. Unlike paracardial fat, EAT is not separated from the myocardium by a fascial plane. In an inflamed and expanded depot, this proximity may permit adipocyte infiltration, collagen deposition, fibroblast activation, and local interruption of myocyte bundles. The resulting architecture

is arrhythmogenic because strands of fibrosis and fat behave as electrically discontinuous tissue, creating source-sink mismatch, conduction slowing, conduction block, and anisotropic propagation. In this model, EAT does not need to be uniformly abnormal; patchy regional interaction with thin atrial myocardium may be sufficient to create localized low-voltage substrate and re-entry-prone conduction channels [17,18,19,28,29,30,31,33,34,35,36,37].

4.3 Electrical Remodeling, Conduction Heterogeneity, and Low-Voltage Substrate

The structural and secretory changes described above matter electrophysiologically because AF requires heterogeneity. Fibrosis disrupts cell-to-cell coupling, lengthens conduction pathways, promotes anisotropy, and creates the conditions for reentry. EAT may intensify these effects by altering ion-channel behavior, connexin expression, local calcium handling, and the microarchitecture of the atrial wall [17,18,19,21]. In experimental systems, adipose-derived mediators have been linked to slowed conduction, shorter wavelength, and greater vulnerability to reentrant activity, effects that are entirely consistent with the low-voltage phenotypes described in human AF cohorts [31,33]. Several studies now link higher periatrial or left atrial EAT burden to low-voltage zones, which serve as clinically relevant surrogates for atrial fibrosis. Chahine et al. [34] demonstrated an association between EAT, left atrial volume, and atrial fibrosis. Shao and colleagues [35] showed that left atrial EAT is associated with low-voltage zones in non-valvular AF. Similar observations were reported in a CT-based study relating EAT distribution to electroanatomical voltage mapping [36]. In normal-weight patients, increased left atrial EAT volume has also been associated with slower atrial conduction and longer P-wave duration, an important reminder that the local effect of EAT may persist even when global obesity is less prominent [37].

The potential link between EAT and atrial thrombogenicity or appendage dysfunction is also notable. Left atrial EAT has been associated with lower left atrial appendage flow velocity, which suggests that the impact of periatrial fat may extend beyond rhythm phenotype to the hemodynamic consequences of atrial remodeling [38]. While this observation does not establish causality, it fits the broader concept that EAT tracks with more advanced atrial disease.

4.4 Autonomic Remodeling

AF is not solely a structural disease. Triggering and perpetuation also depend on autonomic inputs. EAT contains ganglionated plexi and lies in close proximity to autonomic neural networks that influence atrial refractoriness, triggered activity, and spatial heterogeneity of conduction [17,18,21]. Obesity itself is associated with increased sympathetic tone, impaired vagal regulation, and sleep-disordered breathing, all of which may interact with local neuro-adipose signaling [19,20]. This is an area where direct human evidence remains less abundant than structural data, but the anatomical plausibility is high and the available electrophysiological observations are consistent with a meaningful role.

Mechanistically, autonomic remodeling may interact with the inflammatory and structural pathways rather than operate independently. EAT contains and surrounds autonomic ganglionated plexi, and adipose inflammation may alter local neural density, neurotransmitter release, and sympathetic-parasympathetic balance. Heterogeneous vagal activation can shorten atrial refractoriness, whereas sympathetic activation can promote calcium-handling abnormalities, delayed afterdepolarizations, and triggered activity. When these triggers occur in an atrium already remodeled by fibrosis or fibrofatty infiltration, the probability of AF initiation and maintenance increases.

This framework also clarifies why purely anatomical explanations are insufficient. The same EAT burden may carry different arrhythmic implications depending on systemic amplifiers such as insulin resistance, obstructive sleep apnea, hypertension, left atrial stretch, and diastolic dysfunction. These factors increase mechanical stress and neurohormonal activation, potentially converting a local adipose signal into a sustained atrial cardiomyopathy phenotype [4,12,19,20,21,22].

4.5 Hemodynamic and Mechanical Amplifiers

Any mechanistic account that focuses only on EAT would be incomplete. Visceral obesity also increases AF risk through indirect but potent hemodynamic pathways. Hypertension, volume expansion, diastolic dysfunction, obstructive sleep apnea, and ventricular remodeling all contribute to left atrial stretch, chamber enlargement, and adverse atrial geometry [4,12,22]. These pathways may amplify the local effect of EAT rather than compete with it. In practice, many patients likely experience both: systemic hemodynamic stress creates a permissive atrial environment, while periatrial adipose dysfunction adds inflammatory and electrophysiological instability. That combination may help explain why obesity-related AF often progresses from paroxysmal to persistent forms if the underlying metabolic state is not reversed (Table 1).

Visceral adiposity supplies the systemic inflammatory, metabolic, and hemodynamic background; EAT localizes part of this biology to the cardiac surface; atrial structural remodeling creates conduction heterogeneity; and autonomic-electrical instability supplies triggers. The clinical phenotype of obesity-related AF is therefore unlikely to be explained by a single mediator. It is more plausibly the result of cumulative interaction among adipose inflammation, fibrofatty myocardial remodeling, ion-channel and calcium-handling perturbation, autonomic imbalance, and mechanical atrial stretch.

Table 1. Visceral adiposity and cardiac arrhythmias: depot-specific mechanisms and clinical implications.

Axis	Principal biological features	Expected substrate consequences	Clinical interpretation	Evidence maturity
Systemic visceral adiposity	Adipocyte hypertrophy, insulin resistance, excess lipolysis, inflammatory adipokine shift, oxidative and neurohormonal stress	Creates a pro-fibrotic and pro-inflammatory milieu; amplifies hypertension, sleep apnea, diastolic dysfunction, and atrial stretch	Background arrhythmogenic state; not adequately captured by BMI alone	High epidemiological association
Epicardial adipose tissue (global)	Local cardiac ectopic fat in direct contact with myocardium; shared microcirculation; no fascial barrier	Paracrine/vasocrine signaling, altered depot phenotype, potential cardio-lipotoxicity	Tracks with more advanced AF phenotype and adverse cardiovascular risk	Moderate imaging evidence; causal role unproven
Periatrial/left atrial EAT	Regional inflammatory-fibrotic signaling, ganglionated plexi proximity, direct interaction with atrial wall	Atrial fibrosis, chamber enlargement, conduction slowing, low-voltage substrate, recurrence after ablation	Most clinically relevant local depot for AF phenotyping and recurrence risk	Relatively mature AF imaging/ mapping evidence
Autonomic remodeling	Neuro-adipose interaction within periatrial fat; sympathovagal imbalance; trigger facilitation	Shortened refractoriness, spatial heterogeneity, triggered activity	Likely important but less directly measurable than structural remodeling	Mechanistic plausibility; limited direct human validation
Ventricular fat-related substrate	Regional epicardial/periventricular fat, scar interaction, repolarization heterogeneity	Potential modulation of PVC/VT susceptibility and recurrence after ventricular ablation	Signal is plausible but evidence remains substantially less mature than for AF	Preliminary observational evidence; low maturity
Reversibility/ therapeutic leverage	Sustained weight loss, risk-factor control, exercise, bariatric surgery, selected cardiometabolic drugs	Reduction in visceral/EAT burden and partial reverse remodeling of arrhythmogenic substrate	Strongest evidence currently supports integrated lifestyle-based AF care	Moderate for AF care; EAT mediation unproven

Abbreviations: BMI, body mass index; PVC, premature ventricular complex; VT, ventricular tachycardia.

5. Imaging, Tissue Characterization, and Arrhythmic Substrate Mapping

A major advance of the last decade has been the shift from descriptive imaging of EAT toward research-based substrate-oriented phenotyping. The simplest quantitative parameter is total EAT volume, usually measured by CT or CMR. In many populations, higher EAT burden is associated with adverse cardiovascular outcomes [39]. For AF, however, regional measurements appear to matter more than global ones. Periatrial fat, posterior left atrial fat, and left atrial EAT proportions often show tighter relationships with AF phenotype and recurrence than total EAT volume alone [23,40,41].

Qualitative imaging metrics are increasingly important. CT attenuation or density, typically expressed in Hounsfield units, is thought to reflect a mixture of adipocyte size, fibrosis, water content, and inflammatory activity. Studies assessing periatrial attenuation have produced heterogeneous results, but they generally support the idea that tissue quality conveys information not captured by volume alone [40,41,42]. Nodera and colleagues [43] reported that EAT density predicted both the presence of AF and recurrence after ablation. Such data are attractive because they move the field toward a biologically richer imaging phenotype. The limitation is technical: attenuation is influenced by acquisition parameters, contrast use, scanner settings, and segmentation methodology, which currently complicates clinical standardization.

The connection to ablation outcomes is among the most clinically relevant, but not yet fully actionable, areas of the field. Patients with higher periatrial EAT burden, more abnormal attenuation, or both are more likely to demonstrate low-voltage substrate and to experience arrhythmia recurrence after apparently successful catheter ablation [35,36,40,41]. Two meta-analyses have shown that EAT is associated with recurrence risk after AF ablation, with peri-left-atrial measurements often outperforming crude total-volume measures [44,45]. This does not justify routine procedural decision-making based on EAT imaging alone, but it strongly suggests that the fat depot is integrated into the substrate clinicians are trying to modify. At the same time, one should be careful not to overstate the maturity of the imaging literature. Segmentation thresholds vary across studies, some analyses include total EAT whereas others isolate atrial EAT, and attenuation values are sensitive to technical factors such as tube voltage, contrast timing, reconstruction algorithms, and the exact anatomical region sampled [39,43]. CMR avoids ionizing radiation

Table 2. Current clinical applicability and limitations of imaging-based EAT assessment.

Modality	Main strengths	Main limitations	Current applicability
Echocardiography	Widely available, inexpensive, no ionizing radiation, useful for simple EAT thickness estimates.	Linear thickness only, operator dependence, limited regional and qualitative characterization.	Useful for preliminary phenotyping; not sufficient for procedural decision-making.
Cardiac CT	Most established for volumetric EAT quantification, regional periatrial assessment, and attenuation analysis.	Radiation exposure, protocol dependence, contrast/noncontrast variability, inter-scanner differences, and non-standardized segmentation thresholds.	Best suited for research phenotyping and selected clinical context; not a stand-alone determinant of ablation strategy.
Cardiac magnetic resonance	No ionizing radiation and potential for broader myocardial tissue characterization.	Lower standardization for EAT quantification, variable availability, and less routine use in arrhythmia workflows.	Promising for integrated substrate phenotyping, but prospective validation remains limited.
Integration with electroanatomical mapping	Allows spatial comparison between regional EAT and low-voltage or scar substrate.	Invasive mapping, selected cohorts, co-registration uncertainty, and limited prospective outcome validation.	Hypothesis-generating and useful in mechanistic studies; not ready for routine lesion-set selection.

Abbreviation: CT, computed tomography.

and may improve tissue characterization, but it is less standardized for EAT quantification in routine arrhythmia practice than CT. These limitations explain why EAT imaging is primarily useful for research and phenotyping and should not yet be considered a validated determinant of procedural strategy or daily decision making.

The current clinical usefulness and the main methodological limitations of imaging-based EAT assessment are summarized in Table 2.

6. Therapeutic Implications: Can Modifying Adiposity Influence Arrhythmic Substrate?

6.1 Weight Loss and Integrated Risk-Factor Management

The strongest therapeutic evidence still comes from weight reduction and comprehensive risk-factor management rather than from drugs targeted specifically at EAT. In the randomized study by Abed and colleagues [46], weight reduction coupled with cardiometabolic management reduced AF symptom burden and severity. The ARREST-AF cohort subsequently showed that aggressive risk-factor reduction improved post-ablation outcomes [47]. LEGACY demonstrated that sustained, goal-directed weight loss was associated with marked improvements in AF burden and arrhythmia-free survival [48]. CARDIO-FIT added the important observation that cardiorespiratory fitness independently modifies AF recurrence, supporting a broader lifestyle model rather than a purely weight-centric one [49]. REVERSE-AF further suggested that weight loss and risk-factor modification can alter the natural progression of AF itself [50]. In an ovine obesity model, weight reduction produced reverse remodeling of the atrial substrate, including structural and electrophysiological changes consistent with reduced AF vulnerability [51]. A dose-response meta-analysis has likewise reported an inverse association between weight loss and recurrent AF after ablation [52].

6.2 Effect on Epicardial Adipose Tissue

A key unresolved question is how much of the clinical benefit of weight loss is mediated by reduction in EAT specifically. A systematic review and meta-analysis found that exercise, diet, bariatric surgery, and pharmacological interventions can reduce EAT, although the magnitude and consistency of change vary by intervention type and population [53]. More recently, bariatric surgery has been associated with partial improvement in subclinical proarrhythmic structural, electrophysiological, and autonomic abnormalities in obesity, supporting the hypothesis that substantial metabolic improvement may influence the arrhythmogenic phenotype beyond simple changes in body weight [54].

The practical implication is that not all kilograms lost are equivalent. Durable loss of visceral and ectopic fat is likely more relevant than transient fluctuations in total weight. That distinction may explain why structured, sustained programs produce more reliable AF benefits than short-term or unstable weight loss.

6.3 Pharmacological Modulation of Adiposity and EAT

Pharmacological strategies are promising, but they are not yet definitive antiarrhythmic interventions. Conceptually, they may act through three partly overlapping mechanisms: reduction of total adiposity, preferential reduction of EAT, and improvement in the inflammatory phenotype of EAT. Packer et al. [55] proposed that some cardiometabolic drugs may derive part of their benefit from ameliorating EAT dysfunction, and Iacobellis and Baroni [56] later framed EAT as a plausible mediator of cardiovascular risk reduction with glucagon-like peptide-1 (GLP-1) receptor agonists and sodium/glucose cotransporter 2 (SGLT2) inhibitors.

Recent network meta-analytic evidence suggests that SGLT2 inhibitors may reduce EAT more than GLP-1 re-

ceptor agonists or exercise interventions in selected populations with diabetes and/or obesity [57]. Whether this tissue effect translates into clinically meaningful antiarrhythmic benefit remains less certain. Studies in patients undergoing AF ablation generally associate SGLT2 inhibitor use with lower arrhythmia recurrence, but many are retrospective or involve selected diabetic cohorts [58,59,60]. A 2025 report suggested that the association may persist across metabolic-syndrome strata [61]. The extent to which any apparent benefit depends on glycemic status, heart failure phenotype, background cardiometabolic risk, or baseline adiposity remains unclear.

Accordingly, reduced EAT volume should be considered an intermediate phenotype rather than direct evidence of antiarrhythmic efficacy. For SGLT2 inhibitors, available studies are influenced by indication bias because many cohorts include patients with diabetes, heart failure, or planned ablation. For GLP-1 receptor agonists, signals for new-onset AF and post-ablation recurrence remain inconsistent. In both drug classes, it is currently difficult to distinguish whether any observed arrhythmia benefit is mediated by EAT reduction, total weight loss, improved inflammation, improved heart failure status, better glycemic control, or broader cardiometabolic optimization.

For GLP-1 receptor agonists, the evidence is more mixed. A 2024 observational study found that preprocedural GLP-1 receptor agonist use was not associated with lower AF recurrence after ablation [62]. By contrast, a 2024 meta-analysis suggested a lower recurrence risk among patients receiving these agents [63]. Outside the ablation setting, a 2025 updated systematic review and meta-regression reported a reduction in new-onset AF with semaglutide across randomized trials [64]. The most honest interpretation is that GLP-1 receptor agonists are biologically plausible and clinically interesting, but the antiarrhythmic evidence remains inconsistent and far less mature than the weight-loss literature.

An additional translational issue is timing. It remains unclear whether these agents should be viewed primarily as long-term substrate modifiers, as short-term adjuncts before ablation, or as therapies whose apparent antiarrhythmic signal is simply a surrogate for broader cardiometabolic improvement. That distinction matters because the expected benefit would differ by AF phenotype. Patients with early obesity-related AF may still have a potentially modifiable adiposity-related component, whereas patients with advanced longstanding persistent AF may have more fixed fibrotic disease that is less responsive to metabolic intervention alone [19,20,65]. This is the type of mechanistic stratification future trials need to address.

6.4 Implications for Guidelines and Procedural Strategy

Contemporary guidelines already recognize obesity management as part of AF care. The 2024 European Society of Cardiology (ESC) guidelines place risk-factor control and weight management within modern AF treatment frameworks [65], and the 2024 European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) consensus similarly emphasizes patient optimization before and after ablation [66].

What guidelines do not yet endorse is routine EAT imaging to select patients for ablation, define lesion sets, or choose adjunctive drug therapy. The evidence is not mature enough for that step. Nevertheless, EAT may help explain why some patients recur despite technically successful pulmonary vein isolation. It may therefore evolve from a diagnostic curiosity into a substrate descriptor that informs timing, counseling, and expectations around rhythm-control strategies (Fig. 5).

7. Postoperative Atrial Fibrillation and the Problem of Mixed Evidence

The postoperative setting provides a useful stress test for the adiposity hypothesis because surgery imposes intense inflammatory and autonomic triggers over a short time period. If periatrial adiposity is truly part of the substrate, one would expect it to influence postoperative AF. The evidence is suggestive but not uniform. EAT-derived interleukin-1beta has been implicated mechanistically in postoperative AF [32], which is biologically compelling. Yet a CT-based study of atrial EAT and postoperative AF did not find indexed left atrial EAT measures to be independent predictors once age and left atrial volume were accounted for [67]. This mixed result is instructive rather than disappointing. It suggests that the role of EAT may vary by context. In some settings EAT may act as a dominant local amplifier; in others it may be one component of a broader substrate in which age, atrial enlargement, systemic inflammation, and operative factors outweigh local fat quantification. A practical way to frame postoperative AF is as an acute trigger superimposed on a susceptible adipose-inflammatory matrix. Cardiac surgery produces abrupt systemic and local inflammation, oxidative stress, pericardial irritation, fluid shifts, and autonomic fluctuation. In that context, EAT-derived interleukin-1beta may act as a local inflammatory amplifier, but EAT volume alone is unlikely to capture the full phenotype. Age, left atrial size, surgical type, cardiopulmonary bypass exposure, pericardial inflammation, and systemic inflammatory response may dominate risk in some cohorts [32,48,52,54].

8. Ventricular Arrhythmias: A Growing but Still Immature Field

Compared with AF, evidence linking visceral adiposity or EAT to ventricular arrhythmias is limited and less mechanistically resolved. The strongest current support comes from observational studies and pathophysiological reasoning rather than from integrated human histology-imaging-electrophysiology datasets. Reviews published in

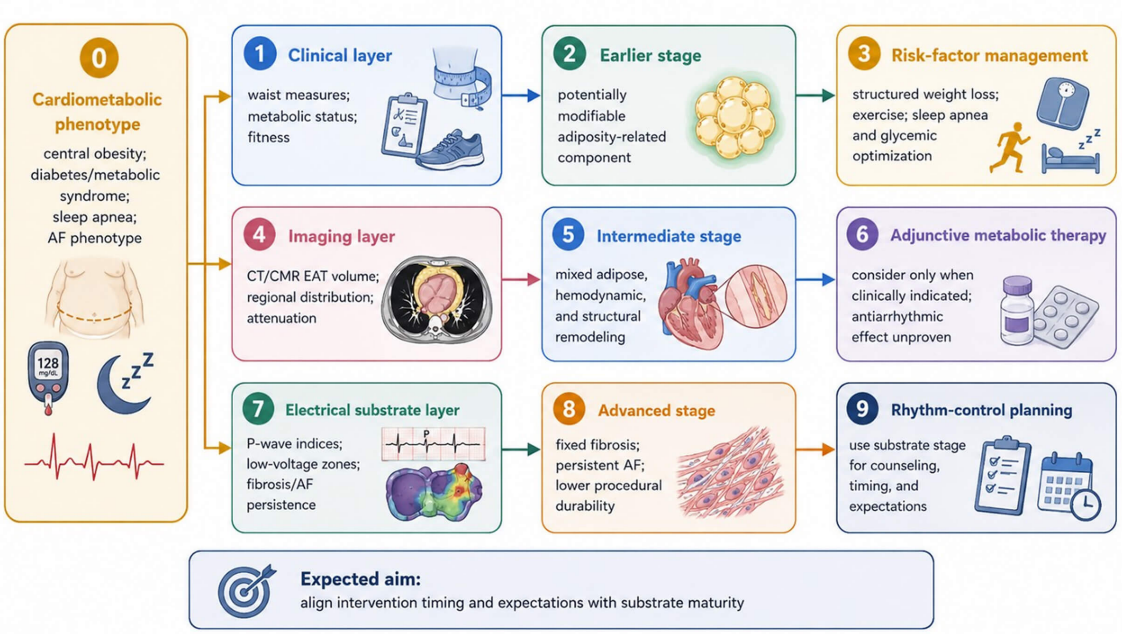


Fig. 5. Translational framework for adiposity-related arrhythmias. A practical clinical pathway is proposed in which the cardiometabolic phenotype is integrated with anthropometric, imaging, and electrical substrate data to estimate substrate stage. Earlier-stage disease may be more likely to include an adiposity-related and potentially modifiable component, whereas advanced disease may be dominated by fixed fibrosis and lower rhythm-control durability. The framework illustrates how structured weight loss, risk-factor management, selected cardiometabolic therapies when otherwise clinically indicated, and timing/counseling around ablation may be aligned to substrate stage rather than applied as isolated interventions. CMR, cardiac magnetic resonance imaging.

the past two years argue that epicardial fat may influence ventricular arrhythmogenesis through local inflammation, autonomic effects, repolarization heterogeneity, and interactions with subepicardial scar or structurally abnormal myocardium [33,68,69]. Clinical studies provide preliminary support. EAT thickness has been reported as an independent predictor of ventricular tachycardia recurrence after ablation [70]. In patients undergoing ablation for premature ventricular complexes, larger EAT volume has been associated with higher recurrence risk and with epicardial sites of origin [71]. In parallel, SGLT2 inhibitors have been associated with reductions in EAT volume/thickness, a mechanism that may be relevant to observed arrhythmia-related associations; consistent with this hypothesis, adjudicated randomized evidence suggests that SGLT2 inhibition may be associated with lower sudden cardiac death risk [72]. These findings are plausible because epicardial fat overlies regions where ventricular scar, autonomic innervation, and arrhythmogenic substrate often interact. However, the existing studies are mostly retrospective and procedurally selected. They do not yet establish whether EAT is a causal driver, a marker of adverse myocardial disease, or both. The ventricular field should resist borrowing too much certainty from AF. The anatomical and electrophysiological context is different, and the human evidence base is much thinner. At present, epicardial fat is a credible contributor to ventricular arrhythmogenic substrate, particularly in scar-related and epicardial phenotypes, but not yet a validated clinical target.

Ventricular endpoints are heterogeneous. Isolated premature ventricular complexes, scar-mediated ventricular tachycardia, sudden cardiac death, and autonomically triggered ventricular arrhythmias should not be treated as interchangeable phenotypes. In patients with ischemic or nonischemic cardiomyopathy, EAT may be most relevant when it co-localizes with subepicardial scar, border-zone tissue, or autonomic structures, but this remains a translational hypothesis rather than a validated clinical framework [73]. Similarly, in arrhythmogenic cardiomyopathy, fibro-fatty myocardial replacement is a distinct disease process and should not be equated with greater epicardial fat burden; potential interactions between epicardial fat, inflammation, and diseased subepicardial myocardium require dedicated study.

At present, the ventricular literature should be framed as a set of preliminary signals across different substrates rather than as a unified disease model. Future studies should separate premature ventricular complex (PVC) recurrence after ablation, scar-related ventricular tachycardia (VT) recurrence, sudden cardiac death risk, and autonomic triggers, and should integrate imaging with electroanatomical mapping, scar characterization, and cardiomyopathy phenotype.

9. Future Directions

First, phenotyping must improve. Studies still vary in how they define and segment EAT, whether they measure total or regional depots, how they handle CT voltage or contrast effects, and how they normalize values to body size. Without standardization, it is difficult to move from association to implementation. Second, intervention studies must disentangle whether benefit depends on total weight loss, visceral-fat reduction, EAT reduction, or changes in inflammatory phenotype. Third, future AF trials should consider embedding imaging and biomarker substudies so that mechanistic remodeling can be measured rather than inferred. A fourth priority is conceptual: arrhythmia studies need to move beyond BMI as the default obesity variable and should consider EAT within a broader cardiometabolic framework, including coronary microvascular disease and heart failure phenotypes [74]. BMI remains useful epidemiologically, but it is poorly suited to identifying the subgroup in whom local adipose biology is most relevant. Future studies should routinely integrate waist metrics, diabetes status, liver fat, sleep apnea burden, cardiorespiratory fitness, and direct cardiac fat phenotyping. Without this richer characterization, the field risks underestimating treatment effects in the very patients most likely to benefit. The most mature concept to emerge from the modern literature is that adiposity-related AF is not simply AF occurring in a person who happens to be obese. It is often the electrophysiological expression of a cardiometabolic atrial disease. That disease is shaped by visceral adiposity, transmitted in part through EAT, and modified by the hemodynamic, inflammatory, autonomic, and metabolic consequences of obesity. This framework is clinically useful because it unifies epidemiology, tissue biology, mapping studies, and treatment response.

Operationally, future studies should pre-specify EAT segmentation methods, contrast versus noncontrast CT protocols, attenuation thresholds, whether total or regional EAT is analyzed, AF phenotype, ventricular arrhythmia phenotype, monitoring duration, and clinically meaningful endpoints. They should also define a minimum confounder set including BMI or waist measures, diabetes, hypertension, sleep apnea, heart failure phenotype, renal function, medications, and inflammatory biomarkers. Interventional trials should ideally include imaging and biomarker substudies to test whether changes in EAT volume, attenuation, or inflammatory phenotype mediate arrhythmia outcomes rather than simply accompany broader cardiometabolic improvement.

10. Conclusions

Current evidence supports a substantial shift in how visceral adiposity is viewed in arrhythmia medicine. Visceral and epicardial fat should not be considered passive bystanders or crude correlates of BMI. In AF especially, they appear to be linked to the development of a vulnerable substrate characterized by inflammation, fibrosis, conduction heterogeneity, autonomic dysregulation, and adverse electromechanical remodeling. The strongest human data connect periatrial EAT with atrial fibrosis, low-voltage zones, and recurrence after catheter ablation. Equally important, weight reduction and integrated cardiometabolic management may be associated with partial reverse remodeling of this substrate, indicating that adiposity-related arrhythmogenesis is modifiable. What remains uncertain is how far the field is ready to move from mechanism to routine practice. EAT imaging is promising but not yet standardized enough to function as a stand-alone clinical decision tool. Pharmacological strategies that may modulate EAT are biologically attractive, but antiarrhythmic evidence remains preliminary and sometimes contradictory. Ventricular arrhythmia data are less mature than AF data. Future progress will depend on translating adipose biology into reproducible imaging phenotypes and prospective mechanistic and interventional trials able to distinguish association, substrate modulation, and causal therapeutic effects.

Author Contributions

AM designed the research study. GP performed the research. LS, MB, NP and MVM contributed to acquisition of data and provided help and advice on references and writing, AM, GP, SF and FN contributed also to acquisition of data and provided help and advice on references and wrote the manuscript. FC supervised the manuscript and contributed to the interpretation of data for the work. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of Interest

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