

Pathogenesis of atrial fibrillation

Mechanism of atrial fibrillation

The mechanism of atrial fibrillation (AF) is still debatable. Several mechanisms have been proposed and seen in a variety of animal models. A traditional mechanism theory has suggested that AF is maintained by multiple migrating wavelets of re-entrant atrial activation. During AF, the atria contract at a rate of 350–900 beats/min, conducting to the ventricles at a rate of 90–170 beats/min. The wavelet collisions cause chaotic re-excitation and re-excite the multiple propagating wavelets [1,2].

It has been shown that AF is probably triggered by a rapidly firing focal source (usually in the superior pulmonary veins, but it can be in other pulmonary veins, the ligament of Marshall, the atrial septum, the superior vena cava, or right atrium). The rapidly firing foci may stimulate multiple wavelet re-entry within the atrial substrate or engage a spiral or rotor for re-entry [3–5]. Moreover, atrial interstitial fibrosis has also been shown to increase AF vulnerability by creating a substrate for intra-atrial re-entry circuit (intracellular scar) that promotes AF [6]. Atrial interstitial fibrosis is increased with age in humans and in congestive heart failure (CHF).

Autonomic influences in atrial fibrillation

The balance between sympathetic and vagal influences plays an important role in the initiation and prediction of AF. Vagal predominance has been observed in the minutes preceding the onset of AF in some patients with structurally normal hearts, while in others there is a shift toward sympathetic predominance [7,8]. Although certain patients can be characterized in terms of a vagal or an adrenergic form of AF, these cases likely represent the extremes of either influence [9]. In general, vagally mediated AF occurs at night or after meals, while adrenergically induced AF typically occurs during the daytime [10]. In patients with vagally mediated AF (the more common

form), adrenergic-blocking drugs, or digitalis, sometimes worsen symptoms. For AF of the adrenergic type, β -blockers are the initial treatment of choice.

Risk factors and causes of atrial fibrillation

The risk factors and causes of AF can be broadly divided into several categories: reversible causes, cardiac, non-cardiac, autonomic, and familial [11].

Reversible causes of atrial fibrillation

AF may be related to acute temporary causes, such as an alcohol binge (holiday heart syndrome), thyrotoxicosis, surgery (cardiac or non-cardiac), electrocution, acute myocardial infarction, pericarditis, myocarditis, pulmonary embolism or other pulmonary diseases (eg, pneumonia), hyperthyroidism, and pheochromocytoma. In such cases, successful treatment of the underlying condition often eliminates AF. AF is also very common after surgery, including cardiac, pulmonary, or esophageal surgery.

Obesity, sleep apnea, and metabolic syndrome has also been linked to the development of AF, probably as a result of left atrial dilation associated with increased body mass index. Weight loss has been linked to regression of left atrial enlargement [12,13].

If atrial fibrillation is provoked by a so-called transient cause, it is more likely that these patients will have subsequent recurrences of the arrhythmias, provoked by similar or other factors.

Atrial fibrillation associated with heart disease

Mitral valve disease (including mitral stenosis and regurgitation and mitral valve prolapse), tricuspid valve disease, coronary artery disease, heart failure, and hypertension, particularly when left ventricular hypertrophy (LVH) is present, are associated with AF. In addition, AF may be associated with hypertrophic cardiomyopathy, dilated cardiomyopathy, or atrial septal defect in adults. Other cardiac causes include:

- infiltrative restrictive cardiomyopathies (eg, amyloidosis, hemochromatosis, and endomyocardial fibrosis);
- cardiac tumors; and
- constrictive pericarditis (from tuberculosis).

Other conditions that have been associated with a high incidence of AF include cor pulmonale.

In the setting of acute myocardial infarction, the development of AF carries a worse prognosis compared with pre-infarct AF or sinus rhythm [14,15]. When AF is associated with atrial flutter, Wolff–Parkinson–White syndrome,

or atrioventricular nodal re-entrant tachycardia, treatment of the underlying primary arrhythmia reduces or eliminates the incidence of recurrent AF [16].

Atrial fibrillation without associated heart disease

Approximately 30–45% of cases of paroxysmal AF and 20–25% of cases of persistent AF occur in young patients without identifiable underlying disease (lone AF) [17,18]. AF can present as an isolated or familial arrhythmia, although a causal underlying disease may appear over time [19]. AF may also occur in the elderly without underlying heart disease as a result of the changes in cardiac structure and function that accompany aging, such as increased myocardial stiffness.

Familial atrial fibrillation

Familial AF, defined as lone AF running in a family, is more common than previously recognized. The likelihood of developing AF is increased among the children of patients with AF, suggesting a familial susceptibility to the arrhythmia. However, the mechanisms associated with genetic transmission are not necessarily electrical, because the relationship has also been seen in patients with a family history of hypertension, diabetes, or heart failure [20]. The molecular defects responsible for familial AF are largely unknown. Specific chromosomal loci associated with AF in some families suggest distinct genetic mutations [21,22]. AF is more common in some channelopathies such as Brugada syndrome, short and long QT syndromes.

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Yap, Y.G.; Camm, J.

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