

Atrial Fibrillation, the Arrhythmia of the Elderly, Causes And Associated Conditions

Samuel Levy, MD

University of Marseille, School of Medicine Chief Cardiology Division Hôpital Nord, Marseille, France

Abstract: Atrial fibrillation (AF) is a common clinical problem, particularly in the elderly, and in patients with organic heart disease. A small percentage of patients, have a potentially reversible cause. Atrial fibrillation is in most patients (approximately 70%) associated with chronic organic heart disease including valvular heart disease, coronary artery disease, hypertension, particularly if left ventricular hypertrophy is present, hypertrophic cardiomyopathy, dilated cardiomyopathy and congenital heart disease and most commonly in adults, atrial septal defect. As in many chronic conditions, determining whether AF is the result or is unrelated to the underlying heart disease, remains unclear. The list of possible etiologies also include cardiac amyloidosis, hemochromatosis and endomyocardial fibrosis. Other heart diseases, such as mitral valve prolapse (with or without mitral regurgitation), calcification of the mitral annulus, atrial myxoma, pheochromocytoma and idiopathic dilated right atrium, present a higher incidence of AF. The relationship between these findings and the arrhythmia are still unclear. Atrial fibrillation may occur in the absence of detectable organic heart disease, the so-called "lone AF", in about 30% of cases. The term "lone AF" or "idiopathic AF" implies the absence of any detectable etiology including hyperthyroidism, chronic obstructive lung disease, overt sinus node dysfunction, and overt or concealed preexcitation (Wolf-Parkinson-White syndrome), only to mention a few of other rare causes of AF. In every instance of recently discovered AF, thyrotoxicosis should be ruled out. The autonomous nervous system may contribute to the occurrence of AF in some patients. Atrial fibrillation occurs commonly in patients with valvular heart disease, particularly when it involves the mitral valve. The occurrence of AF is unrelated to the severity of mitral stenosis but is more common in patients with enlarged left atrium and congestive heart failure. In patients with coronary artery disease, AF occurs predominantly in older patients, males and patients with left ventricular dysfunction. Important predictive factors of AF include hypertension, left ventricular hypertrophy and diabetes. However, the relation between AF and hypertension remains unclear. The risk of the development of AF, in an individual patient, is often difficult to assess but increasing age, presence of valvular heart disease and congestive heart failure, increase the risk of AF. (*Ana Kar Der, 2002; 55-60*)

Key words: Atrial fibrillation, elderly, organic heart diseases

Introduction

Atrial fibrillation (AF) is an arrhythmia commonly associated with organic heart disease but in a significant proportion of patients (10-30 %), detectable heart disease is not found (1). According to epidemiological studies (2-4), the prevalence of AF was 0.4% of the general population. However, the prevalence increases with age, and was estimated to range between 2 to 4 % of the population over 60 years of age. The presence of heart disease increases the prevalence of AF.

Atrial fibrillation may be associated with he-

modynamic impairment, symptoms occasionally disabling and a decrease in life expectancy. The most important concern with AF relates to the frightening embolic complications, which in 3/4 of cases are represented by cerebro-vascular accidents (5).

Recently, an international group of experts from both sides of the Atlantic Ocean got together in order to achieve a consensus of definitions based on the clinical presentation of the arrhythmia (6). They distinguished 3 clinical subsets of AF: first episode of AF, paroxysmal AF and persistent AF. Self-terminating episode of AF was defined as paroxysmal AF and non-self terminating episode of AF as persistent AF. The first episode of AF either self-terminating or not, was isolated as it serves as a reference point and requires proper management as we

do not know if recurrence will happen and when. The permanent form of AF is the accepted AF either because cardioversion is not indicated or failed. The 3 forms of AF may evolve eventually to permanent AF. The first episode of AF may be self-terminating or require pharmacological or electrical cardioversion. The persistent form of AF by definition requires electrical or pharmacological cardioversion. This presentation will be focused on paroxysmal and persistent AF. Paroxysmal AF will be defined as attacks of arrhythmia lasting less than 7 days and most often less than 48 hours. Persistent AF will be defined to describe an episode of AF not self-terminating lasting within 7 days.

Acute causes of atrial fibrillation

Atrial fibrillation may be related to acute causes and may not recur should the cause disappear or be cured. The acute causes of AF include acute alcoholism ("holiday heart syndrome"), electrocution, acute heart disease such as, acute myocardial infarction, acute pericarditis, acute myocarditis, acute pulmonary embolus, hyperthyroidism and acute pulmonary disease (6). Atrial fibrillation is a common complication of cardiac surgery (e.g. coronary bypass surgery) or non-cardiac surgery. The treatment of the underlying condition and/or of the acute episode may result in the disappearance of the arrhythmia and in the absence of recurrence.

Conditions associated with atrial fibrillation

The prevalence of various conditions associated with AF varies according to the age group and the population considered. The presence of heart disease,

of atrial inflammation, atrial enlargement, elevated atrial pressures or heart failure increase the incidence of AF. Of the patients admitted to our Cardiology Division over 1 year, a history of AF was present in 245 patients (15 %) and included the paroxysmal form in 53.8 % and the persistent or permanent form in 46.6 %. The age ranged from 19 to 96 years with a mean age of 69 years, and 58 % of the patients were male. Valvular heart disease was present in 56 patients (22.8 %) of whom 41 patients had mitral valve disease. This is in keeping with the results of Davidson et al (7) who found valvular heart disease to be present in 22.8 % of their patients but much lower than the incidence found in less recent studies such as those reported by Radford et al. (8), Delahaye et al. (9) and others (10,11) (Table 1). Hurst et al (12), found valvular heart disease in 20 % of their patients. Congestive heart failure is a predictive factor of the occurrence of AF in patients with valvular heart disease. Other valvular heart diseases, which may be associated with AF, include mitral valve prolapse and calcifications of the mitral annulus.

Hypertension is the most common affection found in AF patients. In the Framingham Study (2), hypertension was found in half of the AF population and one third of the control population. In the ALFA study, hypertension was present in 39.4% of patients in clinical practice in France and hypertensive disease defined as hypertension with significant left ventricular hypertrophy or/and heart failure as the leading cause AF (1). Hypertension was followed by coronary artery disease (16.6%) and myocardial diseases (15.3%) as the most common disorders. The relationship between coronary artery disease and AF is not clear. In patients with hypertrophic cardiomyopathy and dilated cardiomyopathy, AF often leads to significant functional deterioration. Others causes of

Table 1: Conditions associated with AF

Authors	N ^o Of Pts	Valvular (%)	CAD HTA	Myocardial	Hyperthyreoid	Misc	Id
Maurice 1956	313	57	18		2	1	20
Hurst 1964	230	20	57	5	4	5	
Radford 1968	219	53	11			5	15
Bossel 1981	207	68	4	5	3	2	18
Delahaye 1984	585	64	8	9	2	8	7
Davidson 1989	704	22	55		2		4
our series 1990	245	22	15	16	3	6	20

CAD: Coronary Artery Disease, HTA: Hypertension, Id: Idiopathic, Misc: Miscellaneous, Pts: Patients

AF include chronic obstructive pulmonary disease, pericarditis, congenital heart disease such as left atrial myxoma and atrial septal defect. In the latter condition, AF develops in adulthood and is often the first presentation of the condition. Other rarer causes of AF include cardiac amyloidosis, hemochromatosis, pheochromocytoma and endomyocardial fibrosis. Routine screening for hyperthyroidism is performed in recently discovered AF, and the condition was found in 2% of our patients. The Wolff-Parkinson-White syndrome, the Lown-Ganong-Levine syndrome and sick sinus node disease are also recognized causes of AF.

Among the predisposing factors to AF, diabetes in women and left ventricular hypertrophy in both sexes should be emphasized (2).

Coumel et al. (13) emphasized a clinical aspect of AF in which the autonomic nervous system seems to play a role in the genesis of AF. Vagal activity by its effect on the atrial refractory periods may predispose to AF (13). Vagally-induced AF occurs at rest in situations with high vagal tone such as during sleep or after meals. This type of AF was found predominantly in young individuals predominantly men. Situations associated with high adrenergic tone such as exercise or emotion can also be shown to be in some patients, precipitating factors to AF. Shortening and inhomogeneity in refractory periods in response to the predominance of one or the other autonomic tone are electrophysiological changes which may explain facilitation of the onset of AF in some patients.

Predisposing factors to atrial fibrillation

The probability of developing AF is difficult to assess in an individual patient. Combining factors such as age, presence of valvular heart disease, congestive heart failure, hypertension and diabetes, may make

Table 2: Underlying heart disease in the ALFA study.

Heart Disease	Total (%)	Paroxysmal (%)	Chronic (%)	Recent (%)
Hypertension	39	35	38	45
Hypertensive heart disease	21	10	21	25
CAD	16	11	17	18
Valvular (R)	15	16	19	11
Dilated CMP	9	2	12*	8

Modified from Lévy et al. *Circulation* 1999, 99: 3028 with permission.

an estimate of the medium to long-term risk. Other well-known anatomic predisposing factors to AF include atrial hypertrophy and atrial dilatation

In most patients with underlying heart disease, the relationship between AF and the underlying heart disease is difficult to ascertain (14). For example, in a patient with mitral valve disease, it is difficult to assess the role played by the atrial lesions (rheumatic in origin), and the hemodynamic consequences of the valvular lesions in the genesis of AF. Similarly, in patients with coronary artery disease, the role of ischemia in the genesis of AF is unknown.

In a significant number of patients, AF is idiopathic (15). Although the prognosis of patients with idiopathic AF is better than that of patients with heart disease, it is not known whether the lesions in this group are any different from those of patients with an underlying heart disease.

The risk of developing AF is higher in patients with a ventricular pacemaker than in those with an atrial or a double chamber pacemaker.

Some authors have proposed signal averaged ECG as a mean to predict recurrence of AF in patients with paroxysmal AF, or of persistent AF following cardioversion. In the Framingham Study (16), the echocardiogram was found to provide useful markers to predict non-rheumatic AF. Left atrial enlargement, increased left ventricular wall thickness and reduced left ventricular wall shortening, were found good predictors of the future occurrence of AF in patients which age ranged from 59 to 90 years (16).

Intra and inter atrial conduction have been found to be also present in patients with AF and the P wave is broad in a substantial proportion of patients with paroxysmal AF. Attuel et al. (19, 20) have demonstrated that in patients with paroxysmal AF, the atrial effective refractory period is short and fails to adapt to the pacing cycle length. They suggested that such abnormalities could be useful to detect those patients with suspected but not documented AF such as those patients with cerebral embolism of unknown cause. However such hypothesis remains to be validated.

Characteristics of atrial fibrillation in selected conditions

The risk of the development of AF may vary in various conditions and this review will focus on selected underlying disorders.

The Wolff-Parkinson-White Syndrome

The Wolff-Parkinson-White syndrome is a rare but interesting cause of AF. Preexcitation should always be suspected in patients with AF and rapid ventricular response. As the majority of patients with the Wolff-Parkinson-White syndrome do not have detectable organic heart disease, a role for the accessory pathway is suspected in the genesis of AF. Spontaneous conversion of atrioventricular reentrant tachycardias to AF has been documented in numerous instances. It is therefore not unreasonable to expect that radiofrequency ablation of the accessory pathway may result not only in the cure of the reciprocating tachycardias but of the AF as well. This is supported by the study of Sharma et al. (19) in which AF was found in patients with an accessory pathway conducting only in the antegrade direction and in 5 of 166 patients during the follow-up of successful surgical ablation, suggesting that additional mechanisms beside the occurrence of paroxysmal reciprocating tachycardias, may contribute to the occurrence of AF.

Valvular Heart Disease

Despite the decline of rheumatic fever in western countries, rheumatic heart disease remains a common underlying disorder in patients with AF. Conversely, AF is a common complication in patients with mitral valve disease. Mitral stenosis, mitral regurgitation and tricuspid regurgitation account for 70 % of AF related to valvular heart disease. About 50 % of patients with mitral valve disease will have AF. In mitral stenosis, the onset of AF is associated with deterioration in the functional status of the patient. Interestingly, AF appears to be unrelated to the severity of the mitral stenosis and may occur in patients with minimal mitral valve obstruction. However, AF is more common in patients with enlarged left atrium (16). In patients with mitral regurgitation the prevalence of AF does not seem to be related to the severity of mitral regurgitation. However, AF is more likely to occur at the end stage of the disease and in disabled patients. Following the onset of AF, congestive heart failure often occurs within 5 years, but heart failure is also a predictive factor of the occurrence of AF. So, the causal role of each on the other remains unclear (20).

Coronary Artery Disease

Coronary artery disease is not commonly associated with AF except in the context of myocardial infarction and congestive heart failure. In acute myocardial infarction, the incidence of AF averages 10 % (21). Whether AF is an independent predictor of increased mortality in the post-infarction period, remains controversial. In the CASS study, AF was found in only 0.6 % of the 18 843 patients with documented coronary artery disease (22). Similarly, a relationship between AF and coronary artery disease was not found in the Reykjavik study (23). Atrial fibrillation occurs more commonly in older patients, patients with congestive heart failure and those with ventricular arrhythmias, factors which are also associated with an increased mortality. Failure to fully control for these factors, might explain why in some studies AF was found to be a marker of increased mortality (23, 24). In patients with stable coronary artery disease, AF is again associated with older age and left ventricular dysfunction but also occurs more commonly in males (1, 2, 23, 24).

Dilated Cardiomyopathy

Atrial fibrillation was found in 27% of 236 patients with dilated cardiomyopathy from the series reported by Haissaguerre et al.(25) and was the cause of the presenting symptom in 5.5% of patients. The patients with AF were older, had a higher incidence of mitral valve prolapse and of congestive heart failure. Surprisingly, the left ventricular ejection fraction was higher and the left ventricular end-diastolic pressure was significantly lower in patients with AF than those in sinus rhythm. However, as expected, the size of the left atrium at mode M echocardiogram was significantly larger in the AF group. The prognostic significance of AF in patients with dilated cardiomyopathy is determined by the presence and the severity of associated heart failure (22-26).

Hypertrophic cardiomyopathy

Atrial fibrillation was observed in 10-28% (26-28) of patients with hypertrophic cardiomyopathy. This arrhythmia is often poorly tolerated hemodynamically since in these patients, atrial contraction is critical for filling the non-compliant left ventricle. In a number of patients, emergency cardioversion of AF

may be required. Why a minority of patients develop AF and others do not is not known, is unclear.

Congestive heart failure and atrial fibrillation

Atrial fibrillation is present in a large proportion of patients with heart failure. It appears often after increased degree of heart failure. Middlekauf et al (20) found AF in 75 of 390 patients (19%) with severe heart failure. We reviewed the ECG's of 69 consecutive patients with pulmonary oedema occurring in patients with left ventricular dysfunction (unpublished data). Atrial fibrillation was present in 24 (34%). Whether AF is facilitated by heart failure or heart failure is precipitated by AF is not always easy to determine in an individual patient (the chicken and egg dilemma). In Middlekauf et al. study (20), left ventricular ejection fraction was significantly higher ($p < 0.04$) in the AF group (0.21 ± 0.04) than in the group of patients in sinus rhythm (0.19 ± 0.08). Thus, left ventricular ejection fraction does not seem to be the sole determinant of the development of AF. The prognostic significance of AF in patients with heart failure is still subject of debate.

Conclusions

Long-standing AF is associated, in the majority of patients, with organic heart disease. A small percentage of patients have a potentially reversible cause. In about 30%, of cases AF occurs in individuals with apparently normal hearts, a clinical scenario referred to as "lone AF". Atrial fibrillation is often associated with hypertension but the relation between AF and hypertension remains unclear. Atrial fibrillation occurs commonly in patients with valvular heart disease, particularly when it involves the mitral valve. In patients with coronary artery disease, AF occurs predominantly in older patients, males and patients with left ventricular dysfunction. The autonomous nervous system may contribute to the occurrence of AF in some patients. Predictive factors of AF include diabetes, hypertension, increasing age, presence of valvular heart disease, enlarged left atrium, left ventricular hypertrophy and congestive heart failure.

References

1. Lévy S, Maarek M, Coumel P, et al. Characterization of different subsets of atrial fibrillation in general practice in France: The Alfa Study. *Circulation* 1999; 99: 3028-35.
2. Kannel WB, Abbot RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. *N Engl J Med* 1982; 306: 1018-22.
3. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *Am J Cardiol* 1994; 74: 236-41.
4. Psaty BM, Manolio TA, Kuller LH et al. Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997; 96: 2455-61.
5. Cabin HS, Clubb KS, Hall C, Perlmutter RA, Feinstein AR. Risk for systemic embolization of atrial fibrillation without mitral stenosis. *Am J Cardiol* 1990; 61: 714-717.
6. Fuster V, Ryden L, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation *Eur Heart J* 2001;22: 1852-923.
7. Davidson E, Weinbeger I, Rotenberg Z, Fusch SJ, Agmon J. Causes and time of onset of atrial fibrillation. *Arch Intern Med* 1989; 149: 457-9.
8. Radford D, Evans DW Long term results of DC reversal of atrial fibrillation. *Brit Heart J* 1968; 30: 91.
9. Delahaye JP, Milon H, Boissonat P. La fibrillation auriculaire: quelques problèmes pratiques actuels. *Ann Cardiol Angeiol* 1986; 35: 597-606.
10. Boissel JP, Wolf E, Gilet J, et al. Controlled trial of a long acting quinidine for maintenance of sinus rhythm after conversion of sustained atrial fibrillation. *Eur Heart J* 1981;2: 49-55.
11. Maurice P, Acar J, Rullière R, Lenégre J Traitement par la quinidine de 390 cas de fibrillation auriculaire. *Arch Mal Coeur* 1956 ; 49: 615-36.
12. Hurst JW, Paulk EA, Proctor HD et al. Management of patients with atrial fibrillation. *Amer J Med* 1964; 37: 728-41.
13. Coumel P, Leclercq JF. Cardiac arrhythmias and the autonomous nervous system In Lévy S, Scheinman M, editors. *Cardiac arrhythmias from diagnosis to therapy*. Mount Kisco: Futura Publishing Co; 1984. p37.
14. Rawles J. *Atrial fibrillation*. London: Springer-Verlag; 1992. p. 181-97.
15. Evans W, Swann P. Lone auricular fibrillation. *Br Heart J* 1954; 16: 194.
16. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of non rheumatic atrial fibrillation. *Circulation* 1994; 89: 724-30.
17. Attuel P, Childers R, Cauchemez B et al. Failure in the rate adaptation of the atrial refractory periods: its relationship to vulnerability. *Int J Cardiol* 1982; 2 : 179-97.

18. Attuel P, Pellerin D, Gaston J et al. Latent atrial vulnerability: new means of electrophysiologic investigations in paroxysmal atrial arrhythmias. In Attuel P, Coumel P, Janse MJ, editors. The atrium in health and disease. Mount Kisco: Futura Publishing Co; 1989. p.159-200.
19. Sharma AD, KleinGJ, Guiraudon GM, Milstein S. Atrial fibrillation in patients with the Wolff-Parinson-White Syndrome: incidence after surgical ablation of the accessory pathway. *Circulation* 1985; 72: 161-9.
20. Middlekauff HR, Stevenson WG, Stevenson LW. Prognostic significance of atrial fibrillation in advanced heart failure. *Circulation* 1991; 84: 40-8.
21. Liberthson RR, Salisbury KW, Hutter AM Jr, De Sanctis RW. Atrial tachyarrhythmias in acute myocardial infarction. *Am J Med* 1976; 60: 956.
22. Cameron A, Schwartz MJ, Kronmal RA, Kosinski AS. Prevalence and significance of atrial fibrillation in coronary artery disease (CASS Registry). *Am J Cardiol* 1988; 61: 714-7.
23. Onundarson PT, Thorgeirsson G, Jonmundsson E, Sigfusson N, Hardarson T. Chronic atrial fibrillation. Epidemiologic features and 14 year follow-up: a case control study. *Eur Heart J* 1987; 8: 521-7.
24. Kannel WB, Abbot RD, Savage DD, McNamara PM. Coronary heart disease and atrial fibrillation: The Framingham Study. *Am Heart J* 1983; 106: 389-96.
25. Haissagu re M, Bonnet J, Billes MA et al. Prevalence, signification et pronostic des arythmies auriculaires dans les myocardopathies dilat es. A propos de 236 cas. *Arch Mal C eur* 1985; 4: 536-41.
26. Convert G, Delaye J, Beaune J, Biron A, Gonin A. Etude pronostique des myocardopathies primitives non obstructives. *Arch Mal Coeur* 1980; 73: 227.
27. Glancy DL, O'Brien KP, Gold HK, Epstein SE. Atrial fibrillation in patients with idiopathic hypertrophic subaortic stenosis. *Br Heart J* 1970; 32: 652.
28. Robinson K, Frenneaux MP, Stockins B et al. Atrial fibrillation in hypertrophic cardiomyopathy: a longitudinal study. *J Am Coll Cardiol* 1990; 15: 1279-85.



Dr.G lseren Engin'in bir  alıřması.