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ORIGINAL ARTICLE

Clinical Factors that Influence Response to Treatment Strategies in Recent Atrial Fibrillation

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Background The atrial hypocontractility caused by short episodes of atrial fibrillation has much faster onset and offset kinetics than the atrial contractile dysfunction caused after long periods of atrial fibrillation.

Purpose This is a prospective study aimed at detecting the most common predisposing factors for atrial fibrillation and how the clinical factors influence the response to cardioversion.

Patients & Methods The study included 62 consecutive patients (31 males and 31 females) with recent atrial fibrillation. They were subjected to: history taking, clinical examination, 12-leads ECG, laboratory investigations (C-reactive protein, complete blood picture, liver enzymes, total serum bilirubin, serum creatinine and blood Glucose level), two dimensional, M-mode transthoracic echocardiographic examination and color flow mapping were obtained to determine; ejection fraction, valvular lesion, and wall motion abnormalities.

The patients were divided into two groups: group 1 included 52 successfully cardioverted using pharmacological agents or electrically by DC. Group 2 included 10 patients who failed to be cardioverted. Both groups were studied and compared.

Results In the present study; Age of patients ranged from 22 to 80 years. 26 patients (50%) were hypertensive, 21 patients (40.4%) had valvular valve lesions, 18 patients (34.6%) were cigarette smokers, 12 patients (23.1%) had ischemic heart disease, 5 patients (9.6%) had heart failure and Cardiomyopathy, 3 patients (5.8%) had chronic obstructive pulmonary disease and one patient (1.9%) was thyrotoxic.

12 patients (23.1%) were cardioverted by propafenone, 26 patients (50%) were cardioverted by amiodarone, 9 patients (17.3%) were cardioverted by both, 3 patients (5.8%) were cardioverted by DC shock, one patient (1.9%) was cardioverted by verapamil IV and one patient (1.9%) was cardioverted by dogxin IV. 33 patients were given amiodarone, 26 of them have been cardioverted with a success rate of 78.8% and 15 patients were given propafenone 12 of them have been cardioverted with a success rate of 80%. C-reactive protein had a highly significant elevation in group 2 compared to group 1. Ejection fraction had a highly significant increase in group 2 compared to group 1. Left atrial diameter was significantly larger in group 2 than in group 1.

Conclusions The most important predisposing factors for development of atrial fibrillation were; hypertension (50%), valvular heart disease (42.8%), ischemic heart disease (23.5%), heart failure and cardiomyopathy (9.6%), chronic obstructive pulmonary disease (5.8%) and thyrotoxicosis (1.9%) of patients. The most important factors predicting persistence of atrial fibrillation and failure of cardioversion were; persistent high elevation of C-reactive protein, decreased ejection fraction and increased left atrial diameter.

Keywords Atrial fibrillation, age factors.
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INTRODUCTION

Atrial fibrillation (AF): is the most commonly sustained arrhythmia occurring in approximately 0.4% to 1% of the general population, the prevalence of AF increases with age affecting 4% of the population over age of 60 years and up to 10% of the population over age of 80 years (1,2).

Both sustained and paroxysmal AF have important implications for development of cerebrovascular accident (CVA) and other systemic emboli, it's estimated that 15-20% of CVA in non rheumatic patients are due to AF (3).

Brief episodes of AF may already cause a significant impairment of atrial contractility.

Chronic atrial fibrillation has been shown to lead to atrial dilatation not only in patients with organic heart disease (3), but also in patients with atrial fibrillation in the absence of any underlying disease (4).

The major issues in the management of patients with AF are related to the arrhythmia itself and to prevention of thromboembolism. In patients with persistent AF, there are fundamentally 2 ways to manage the dysrhythmia: to restore and maintain sinus rhythm or to allow AF to continue and ensure that the ventricular rate is controlled (5).

The aim of the present study is to detect the most common

Abbreviations and Acronyms

- CM = cardiomyopathy
- COPD = chronic obstructive airway disease
- CRP = C-reactive protein
- CVA = cerebrovascular accident
- DC = direct current
- IHD = ischemic heart disease

predisposing factors for atrial fibrillation and how the clinical factors influence the response to cardioversion.

PATIENTS AND METHODS

This study included 62 consecutive patients with recent atrial fibrillation, admitted to the cardiology department, C.C.U at Mansoura International Specialized Hospital from October 2005 to October 2006.

Inclusion Criteria:

Only patients admitted with recent acute AF during the first 48 hours from the beginning of the attack were included in this study.

Exclusion Criteria:

Patients with chronic AF.

Methods:

All patients were subjected to:

1. Full history taking and full clinical examination.
2. 12-lead electrocardiogram.
3. Laboratory investigations including; C-reactive protein (CRP) by qualitative and semi quantitative test, CBC, ALT, AST, total serum bilirubin, serum creatinine and blood glucose level.
4. Two dimensional and M-mode transthoracic echocardiographic examination and color flow mapping were obtained in the parasternal long axis, short axis and apical four chamber views; to determine left ventricular ejection fraction, valvular lesions, wall motion abnormalities and the left atrial diameter.

The choice of the method of cardioversion as well as the selection of the drug used for rate or rhythm control were both left to the discretion of the treating physician. The follow methods were utilized for cardioversion:

1. Amiodarone intravenous loading 1050 mg, over the remaining 24 hours, 150 mg, over 10-15 minutes then 360 mg, over next 6 hours, then 540 mg, over remaining 24 hours.
2. Propafenone oral loading 300 mg, tds with total dose of 900 mgs in the first 24 hours.
3. Combined loading by Amiodarone and Propafenone.
4. Electrical cardioversion by direct current (DC) shock was used in haemodynamically unstable patients.

The patients were divided into two groups:

Group I: Included 52 patients who successfully cardioverted to sinus rhythm by drugs or DC shock.

Group II: Included 10 patients who failed to be cardioverted.

Both groups were compared for the risk factors for AF,

laboratory findings and echocardiographic parameters.

RESULTS

Table (1) shows that the age of cardioverted patients ranged from 22 to 80 years, the mean age was 50.431±15.250 years. 18 patients (34.6%) were cigarette smokers, 26 patients (50%) were hypertensive, 21 patients (40.4%) had mitral valve lesions, 12 patients (23.1%) had IHD, 5 patients (9.6%) had HF and cardiomyopathy; (CM), 3 patients (5.8%) had COPD and one patient (1.9 %) was thyrotoxic (Figure 1).

Table 1. Characteristics of Group I.

Age	
Range	22.0 - 80.0
Mean ± SD	50.431 ± 15.250
Sex	
Male	26 (50.0 %)
Female	26 (50.0 %)
Smoking	18 (34.6 %)
Hypertension	26 (50.0 %)
Valvular heart lesions	21 (40.4 %)
IHD	12 (23.1 %)
COPD	3 (5.8 %)
Thyrotoxicosis	1 (1.9 %)
HF and Cardiomyopathy	5 (9.6 %)

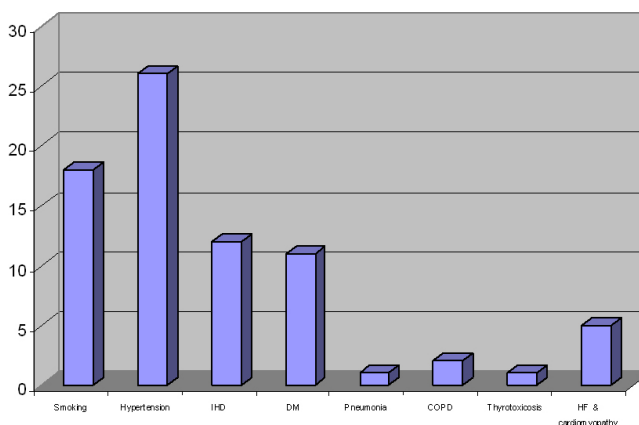


Figure 1. predisposing factors for AF.

Table (2) shows that 12 patients (23.1%) were cardioverted by propafenone, 26 patients (50%) were cardioverted by amiodarone, 9 patients (17.3%) were cardioverted by combined (propafenonee and amiodarone), 3 patients (5.8%) were cardioverted by DC shock, one patient (1.9%) was cardioverted by IV verapamil and one patient (1.9%) was cardioverted by IV digoxin.

Table 2. Sinus rhythm achievement in group 1.

	No	%
Propafenonee	12	23.1
Amiodarone	26	50.0
Propafenonee + Amiodarone	9	17.3
DC	3	5.8
Varapamil	1	1.9
Digoxin IV	1	1.9
Total	52	100.0

Table (3) shows that among the 33 cases treated with IV amiodarone 26 patients were cardioverted while 7 patients were not and persisted as AF, so success rate of cardioversion of amiodarone was 78.8%.

Among the 15 cases treated with propafenone, 12 patients were cardioverted while 3 patients were not and persisted as AF, So success rate of cardioversion of propafenone was 80%.

Table 3. Comparison between success rate of cardioversion of Amiodarone and Rythmonorm.

	Number of all cases Administrated With the drug	Number of cardioverted cases	Number of Cases failed to be cardioverted	Success rate of the drug
Amiodarone	33	26	7	78.8%
Propafenone	15	12	3	80%

Table (4) shows that the mean age in the cardioverted patients was 50.431±15.25 years while in patients not cardioverted it was 50.4 years±8.071 with P-value 0.99.

The mean CRP in the cardioverted patients was 14.823 mg/dl±15.195 while in patients not cardioverted it was 33.600 mg/dl±14.751 with P-value 0.001 (Figure 2).

Table 4. Comparison between group 1 and group 2.

	Group 1	Group 2	Student t test	
			t	p
Number	52 (83.9%)	10 (16.1%)		
Age	50.431 ± 15.250	50.400 ± 8.071	0.009	0.99
CRP	14.823 ± 15.195	33.600 ± 14.751	-3.58	0.001
S. creatinine	1.209 ± 0.829	1.608 ± 1.387	-1.22	0.22
Bilirubin	0.716 ± 0.440	1.688 ± 1.141	-0.65	0.25
ALT	33.451 ± 24.011	30.800 ± 14.942	.33	0.73
AST	34.082 ± 19.525	34.000 ± 10.176	.02	0.98
RBG	137.156 ± 99.624	122.200 ± 73.525	.45	0.65
EF	61.686 ± 8.281	51.600 ± 11.007	3.33	0.001
Lt atrium	3.821 ± 0.768	4.840 ± 0.488	-4.00	0.0001

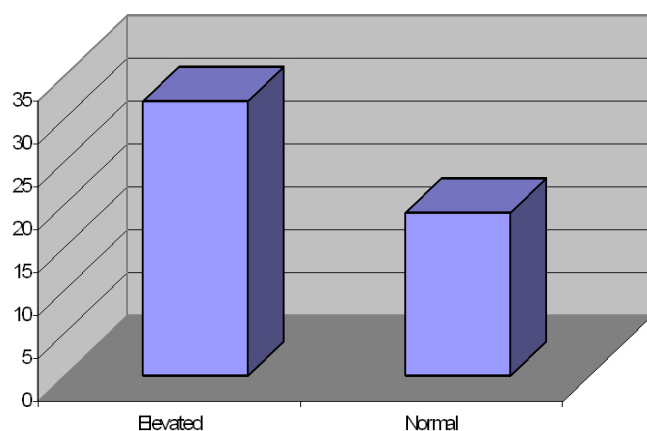


Figure 2. CRP in group 1.

The mean serum creatinine was 1.209±0.829 mg/dl in the cardioverted group versus 1.608±1.387 mg/dl in the noncardioverted group with P-value 0.22. The mean total S. bilirubin was 0.716±0.44 mg/dl in cardioverted patients

versus 1.688±1.141 mg/dl in patients not cardioverted with P-value 0.25. The mean ALT was 33.451±24.011 U/I in the cardioverted patients versus 30.800±14.942 U/I in the noncardioverted group with P-value 0.73. The main AST was 34.082±19.525 U/I in cardioverted patients versus 34.000±10.176 U/I in the noncardioverted patients with P-value 0.98. The mean RBG was 137.156±99.624 mg/dl in cardioverted patients versus 122.2±73.525 mg/dl in the noncardioverted group with P-value 0.65.

The mean EF was 61.686±8.28% in the cardioverted patients versus 51.600±11.007% in the noncardioverted patients with P-value 0.001 (Figure 3).

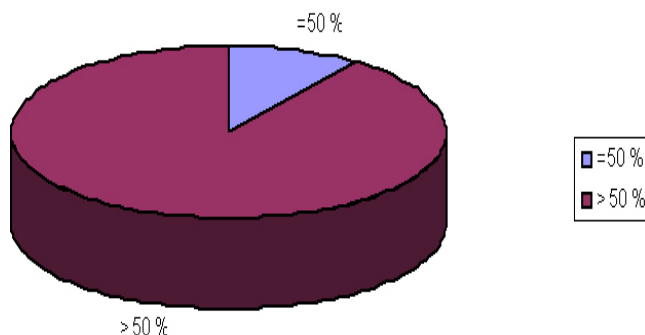


Figure 3. Ejection Fraction in group 1.

The mean left atrial diameter was 3.821±0.768cm in cardioverted patients versus 4.840±0.488cm in the noncardioverted group with P-value 0.0001 (Figure 4).

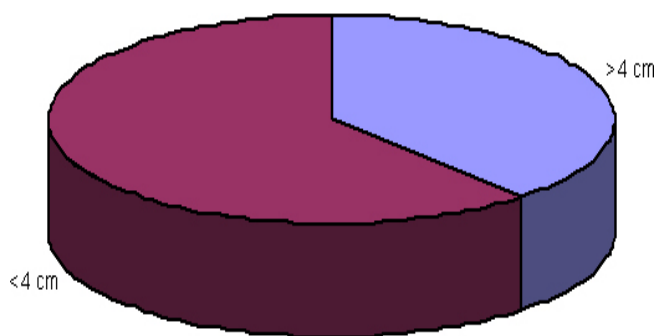


Figure 4. Left atrial diameter in group 1.

DISCUSSION

The aim of the present study is to detect the most common predisposing factors for atrial fibrillation in everyday clinical practice and how the clinical factors influence the response to cardioversion and to study the efficacy of electric cardioversion versus the most common drugs used for pharmacological cardioversion (amiodarone and propafenone) and finally trying to identify causes associated with persistent AF.

In the present study, we found that incidence of AF increases with aging. The mean age for patients with AF in the present study was 50.431 ± 15.25 years. Feinberg et al. found that the incidence of AF increases with aging. The prevalence approximately doubles with each advancing decade of age, from 0.5 per cent at age 50-59 years to almost 9 % at age 80-89 years, as aging cause cardiac dilatation, myocardial atrophy, decrease of conduction tissue and fibrosis of atria. These age related changes may be responsible for increase risk of AF (6).

In the present study, we identified many risk factors for development of AF. Hypertension was the most common risk factor for AF. In the present study, 26 patients (50%) were hypertensive. Ladva found that hypertension was shown to predict AF; this may be related to increased fibrosis and due to dispersion of atrial refractoriness (7).

Valvular heart diseases and lesions specially mitral valve diseases were found in 21 patients (40.4%). In the present study they were found to be a major risk factor for the development of AF either by causing cardiomyopathy or HF induced AF or by atrial dilatation and hypertrophy inducing atrial remodeling. In the present study 20 patients (42.5%) had a dilated left atrium (left atrial diameter >4 cm).

Ischemic heart disease was found in 12 patients (23.5%) in the present study.

In the present study, 5 patients (9.6%) had EF $<50\%$. An increased risk of AF due to HF depends on atrial remodeling as caused by ionic remodeling either at the atrial or at ventricular level by powerful neurohormonal changes. Hobai, et al. (8) stated that the study of atrial remodeling in HF was very difficult in human beings because of the structural changes caused by underlying myocardial pathology and the effect of drugs and antiarrhythmic agents. For this reason, most of the available data relies upon basic and experimental researches. Heavy alteration in calcium handling is prominent in ventricular myocytes, the sarcoplasmic carrier of calcium is down regulated in the failing myocytes, leading to increased cytosolic calcium as a maladaptive attempt to maintain contractility. The sodium calcium exchange current is instead upregulated in HF, acting to compensate the impaired calcium removal due to a sarcoplasmic carrier, to protect contractile function and cellular calcium homeostasis. Sodium calcium exchange. Is the exchange of one calcium for three sodium thus carrying a net current in the direction of sodium transport. The net current carried by sodium calcium exchange may cause delay after depolarization in certain electrophysiologic situation which proved to be arrhythmogenic in HF.

COPD, chronic lung diseases, pneumonia and smoking were found to be risk factors for AF, in the present study 3 patients (5.9%) with COPD and pneumonia had AF. Patients with COPD commonly have frequent premature atrial contractions, that may trigger AF. Also heavy smoking increases free radicals that increase calcium influx as in electrical remodeling of the atrium leading to AF (6).

In the present study, CRP (inflammatory marker) was elevated in 33 patients (63.5%) with AF especially with persistent AF (resistant to cardioversion). The mean CRP in the cardioverted patients was 14.823 mg/dl while it was 33.6 mg/dl in patients in whom AF persisted ($P < 0.001$). Persistent high elevation of CRP was a predictor of persistence of the presistence of AF and of being resistant to antiarrhythmic drug therapy for cardioversion. It is now believed that inflammation marked by elevated CRP is involved in structural atrial remodeling as reported by Psychari, 2005. He stated that increased left atrial diameter is associated with increased elevation of CRP and increased resistance (9).

In the present study, propafenone was used after clinical examination and exclusion of heart failure and IHD. All cases cardioverted by Propafenone had EF $>50\%$. The patients do not have major structural heart disease, (as propafenone has negative inotropic effect precipitating HF), Propafenone is contraindicated in SAN disease, Bundle Branch Block, severe bradycardia, marked hypotension and COPD (10).

In the present study, the success rate of Propafenone for cardioversion of AF was 80%. Boriani Giuseppe; 1995. found that maximum success of the conversion rate of oral loading dose of Propafenone was only 55% (11).

In the present study, amiodarone was used in 33 patients, 26 patients were cardioverted with a success rate of cardioversion at (78.8%). Boriani Giuseppe et al. reported a conversion rate of amiodarone ranging from 25-89% (11).

These results are not in agreement with those reported by Cotter 1999 who found that the success rate of I.V amiodarone in cardioversion was only 30-40% (12).

DC shock was used in the present study in 3 patients (5.8%) as they were hemodynamically unstable. DC is a procedure by which a synchronized electrical shock is delivered through the chest wall to the heart through special electrodes or paddles applied to the skin of chest to interrupt the abnormal electrical circuit(s) in the heart to restore sinus rhythm. In the present study DC shock was performed at 200 joules and all 3 patients were cardioverted from 1st. shock with cardioversion success rate 100%. Van Gelder et al. reported a success rate of 90% to cardiovert patients with AF into sinus rhythm (13).

In the present study, one patient (1.9%) was given 10 mg. Varapamil I.V to decrease the heart rate and another patient was given Digoxin I.V (0.5 mg) to decrease the heart rate, but both patients were cardioverted to sinus rhythm. Most properly both had been cardioverted spontaneously as reported by Dell'Orfano JT et al. (14).

In the present study, the mean CRP was highly significant in noncardioverted cases versus cardioverted cases. This suggests that inflammation plays an important role in persistence of AF. Calol et al. stated that inflammation marked by elevated CRP increases the risk of AF by

precipitating both atrial structural and electrical remodeling. They also stated that the use of vit. C and omega 3 FA (as anti-inflammatory) decreases this risk (15).

The main EF had a highly significant increase in cardioverted cases 61.686% compared to noncardioverted cases 51.6% explaining the significant P-value between the 2 groups as most of uncardioverted cases were cardiomyopathic or in HF.

The mean left atrial diameter was highly statistically significant in noncardioverted cases 4.840cm versus cardioverted cases 3.821cm. This confirms that increase in the left atrial diameter plays an important role in structural atrial remodeling increasing the risk for development and persistence of AF (11).

CONCLUSION

The most important risk factors for development of AF were; hypertension, valvular heart disease, ischemic heart disease, heart failure, Cardiomyopathy, chronic obstructive pulmonary disease and thyrotoxicosis.

Propafenonee has higher efficacy than Amiodarone in cardioversion of recent AF.

The most important factors predicting failure of cardioversion and persistence of AF were; Persistent high elevation of CRP, decreased EF and increased left atrial diameter.

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REFERENCES

1. Crawford MH, editor. Current diagnosis and treatment of cardiology. 2nd ed. New York: Lange Medical Books/McGraw Hill; 2003. p. 283,4.
2. Topol and Marso. Manual of cardiovascular medicine. Philadelphia: Lippincott Williams and Wilkins; 2000.
3. Allessie's MA, Konings KT, Kirchhof CJ, editors. Mapping of atrial fibrillation mechanisms and therapeutic strategies Armonk, NY: Futura Pub; 1994. p. 37.
4. Levy S. Classification system of atrial fibrillation. *Curr Opin Cardiol* 2000; 15(1):54-7.
5. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. *Eur Heart J* 2001; 22(20):1852-923.
6. Feinberg WM, Blackshear JL, Laupacis A, et al. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med* 1995; 155(5):469-73.
7. Ladva S. NICE and BHS launch updated hypertension guideline. National Institute for Health and Clinical Excellence; 2006 Jun 28.
8. Hobai, O'Rourke B. Enhanced Ca(2+)-activated Na(+)-Ca(2+) exchange activity in canine pacing -induced heart failure. *Circ Res* 2000; 87(8):690-8.
9. Psychari SN, Apostolou TS, Sinos L, et al. Relation of elevated C-reactive protein and interleukin-6 levels to left atrial size and duration of episodes in patients with atrial fibrillation. *Am J Cardiol* 2005; 95(6):764-7.
10. Diseases of cardiovascular system. 2001:1295.
11. Boriani G, Biffi M, Capucci A, et al. Conversion of recent-onset atrial fibrillation to sinus rhythm: Effects of different drug protocols. *Pacing Clin Electrophysiol* 1998; 21(11 Pt 2):2470-4.
12. Cotter G, Blatt A, Kaluski E, et al. Conversion of recent onset paroxysmal atrial fibrillation to normal sinus rhythm: The effect of no treatment and high-dose amiodarone. A randomized, placebo-controlled study. *Eur Heart J* 1999; 20(24):1833-42.
13. Van Gelder IC, Tuinenburg AE, Schoonderwoerd BS, et al. Pharmacologic versus direct-current electrical cardioversion of atrial flutter and fibrillation. *Am J Cardiol* 1999; 84(9A):147R-51R.
14. Dell'Orfano JT, Patel H, Wolbrette DL, et al. Acute treatment of atrial fibrillation: Spontaneous conversion rates and cost of care. *Am J Cardiol* 1999; 83(5):788,90, A10.
15. Calo L, Bianconi L, Colivicchi F, et al. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: A randomized, controlled trial. *J Am Coll Cardiol* 2005; 45(10):1723-8.
16. Di Marco JP, Gersh BJ, Opie LH. Antiarrhythmic drugs and strategies. In: Opie LH, editor. *Drugs for the heart*. 3rd ed.: WB Saunders Company; 1991. p. 218-74.