

## CONTROVERSIES AND RESEARCH IN ATRIAL FIBRILLATION

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**Keywords:** atrial fibrillation; sinus rhythm; stroke; mortality; quality of life

**Abstract:** The last years have been the witnesses of the significant changes in the management of patients with cardiac arrhythmias. Electrophysiology has evolved from a purely descriptive discipline to the international territory where the procedure finding the last fifteen years improved survival and quality of life in a large number of patients. Atrial fibrillation in the last years become a topic of major interest, presenting a series of controversies about the clinical, pathological and therapeutic issues. Sustained data show us that atrial fibrillation ranks as the second most common cause of cardiac arrhythmias. It is more common in men than in women, and its prevalence increases with age. Mortality in patients with atrial fibrillation is two times higher compared to people who have sinus rhythm. Several studies have investigated the relationship between the atrial fibrillation and diabetes, the link between this cardiac arrhythmias and Alzheimer disease. As a result of observations, although the efficacy of amiodarone compared with most other drugs were higher in arrhythmias treatment it was decided to develop a treatment algorithm for the maintenance of the sinus rhythm that tailored initial drug therapy to maximize safety. Both the loss of synchronous atrial activity and ventricular rate irregularity affects cardiac output. Uncommanded rapid ventricular frequency, usually > 130/min, may develop heart dilatation with global hypokinesia and ventricular dysfunction, a condition called tachycardiomyopathy. This form of cardiomyopathy is reversible to adequate control of ventricular frequency or to restore the sinus rhythm.

**Cuvinte cheie:** fibrilația atrială; ritm sinusal; atac vascular cerebral; mortalitate; calitatea vieții

**Rezumat:** Ultimii ani au fost martorii unei importante schimbări în managementul pacienților cu aritmii cardiace. Electrofiziologia a evoluat de la o disciplină pur descriptivă către un teritoriu internațional, în care procedurile descoperite în ultimii cincisprezece ani au îmbunătățit supraviețuirea și calitatea vieții la un număr mare de pacienți. În ultimii ani fibrilația atrială a devenit un subiect de interes major, prezentând o serie de controverse prin aspectele ei clinice, patologice și terapeutice. Date susținute ne arată că fibrilația atrială este a 2 – a ca frecvență dintre aritmiile cardiace. Ea este mai frecventă la bărbați decât la femei iar prevalența ei crește cu vârsta. Mortalitatea la pacienții cu fibrilație atrială este de 2 ori mai mare în comparație cu persoanele care prezintă un ritm sinusal. Mai multe studii au cercetat relația între fibrilația atrială și diabetul zaharat, legătura între această aritmie cardiacă și boala Alzheimer. În urma unor observații deși eficacitatea Amiodaronei era ridicată în comparație cu alte medicamente în tratarea aritmiilor cardiace, s-a hotărât găsirea unui algoritm prin care tratamentul efectuat pentru menținerea ritmului sinusal, să fie bine tolerat și să prezinte un maxim de siguranță. Pierderea activității sincronice atriale, cât și iregularitatea ritmului ventricular afectează debitul cardiac. O frecvență ventriculară rapidă necontrolată, de regulă, >130/min. poate dezvolta o dilatație cardiacă cu o hipochinezie globală și cu disfuncție ventriculară, condiție denumită tahicardiomiopatie. Această formă de cardiomiopatie este reversibilă la un control adecvat al frecvenței ventriculare sau la restabilirea ritmului sinusal

### SCIENTIFIC ARTICLE OF THEORETICALLY PREDOMINANCE

At the end of the twentieth century, atrial fibrillation were recognized as a separate rhythm, since the first decade of the twentieth century remains one of the biggest challenges about current medicine and also about the futures research in the medical field of this disease.

Last years have been the witnesses of the significant changes in the management of the patients with cardiac arrhythmias. Electrophysiology has evolved from a purely descriptive discipline to the international territory where the procedure finding the last fifteen years improved survival and quality of life in a large number of patients.

Atrial fibrillation is an arrhythmia caused by electrical dysfunction of the heart activity. It represents an arrhythmia with fast ventricular rhythm, irregular and variable. Diseases that affect the myocardium or overload the heart (mitral stenosis, ischemic heart disease, hyperthyroidism), frequently cause atrial fibrillation, in which the atria are free of normal contractions and the ectopic center emitting fueled with a frequency of 400-600/min.

Atrial fibrillation in the last years become a topic of major interest, presenting a series of controversies about the clinical, pathological and therapeutic issues. Sustained data show us that atrial fibrillation ranks as the second most common of cardiac arrhythmias. It is more common in men than in

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women, and its prevalence increases with age. Mortality in patients with atrial fibrillation is two times higher compared to people who have sinus rhythm.

Dr. Gerald Naccarelli said that atrial fibrillation is the most frequent disease of the cardiac arrhythmias, the number of person diagnosed with this disease is growing, annually numbers rising to 500.000 cases which are hospitalized in USA. All this involve substantial cost for care of these patients. In addition to this, atrial fibrillation have an increased risk for mortality, for the occurrence of cardiovascular disease, for occurrence of fatal or nonfatal stroke, for occurrence of heart failure.

Atrial fibrillation is the most common arrhythmia, about 1/3 patients with arrhythmias presents this disease. This disease is relatively rare under 50 years, but the peoples over 65 years become progressively more frequent and after 80 years occurred in 10% of subjects.

There has been an increase of 66% of hospitalization for atrial fibrillation in the last 20 years due to factors including: age population, increasing prevalence of chronic disease of the heart and more frequent diagnosis through the use of ambulatory monitoring devices.

Several studies have investigated the relationship between the atrial fibrillation and diabetes. According to a trial published in October 2009, Dr. Gregory A. Nichols (Kaiser permanente Center for Health Research, Portland), atrial fibrillation was more frequently found in diabetic patients than in those who did not have this disease and it seems that the prevalence was higher in women than in man. Dr. Gregory said: "this association between diabetes and atrial fibrillation has been reported before, but to my knowledge this is the first time that diabetes has been shown to be an independent risk factor for atrial fibrillation. Our study showed an elevated risk of atrial fibrillation in man with diabetes. But in women we found a highly statistically significant association, diabetes being a stronger risk factor for atrial fibrillation than obesity or raised blood pressure. This stronger association between diabetes and atrial fibrillation in women than in man is a new observation and is somewhat of a mystery".

Atrial fibrillation is one of those conditions that often go undiagnosed. The results of this study should tell clinicians to look a little harder for atrial fibrillation in patients with diabetes and to investigate more closely the possibility of the existence or occurrence of atrial fibrillation in these patients. Most times there is a tend to look for atrial fibrillation more in man than in women, but the results of this study suggest that if a women has diabetes, her risk of having atrial fibrillation is just as high as that of a man.

Many patients with atrial fibrillation do not show any symptoms. The most common symptoms of this disease are palpitations. In 57,8% cases patients were not able to show a definite cause of developing atrial fibrillation. In a study conducted on patients with atrial fibrillation found that in 13,1% of patients the arrhythmia appeared during physical effort, in 5,2% of patients pre-existing condition of the disease was alcohol. Hypertensive crisis have also contributed to the onset in 4,2% cases and psycho-emotional stress in 2,8% cases. According to this study in 38% of cases, the patients reported previous episode of atrial fibrillation. Symptoms may progress from palpitation to pulmonary edema. A small fraction of patients who have this disease reported other symptoms including: fatigue, dyspnea, angina, syncope, pre-syncope.

In the FRACTAL study (Fibrillation Registry Assessing Cost) just first onset atrial fibrillation patients hospitalization during 2 years of follow-up were associated with reduced quality of life and higher patients reported symptoms. Basically, the more symptoms they had the more likely they

were to have a recurrence, the more likely they are hospitalize, and patients really just don't like being in hospital.

Another study of atrial fibrillation focused on the link between this cardiac arrhythmias and Alzheimer's disease. Treating atrial fibrillation with radiofrequency catheter ablation, significantly reduces the risk of Alzheimer disease and reduces the risk of developing all form of dementia, according to the results of a new study lead by Dr John Day (Heart Institute of Intermountain Medical Center, Salt Lake City) which also show that in addition to these finding, the catheter ablation reduced the risk of mortality and stroke at 3 years. The good news from this study is that if you can potentially get rid of atrial fibrillation, not only does it make patients feel better, but it might also have a significant benefit as far as the long term rates of stroke, helping to prevent premature death, as well as to reduce the risk of dementia and Alzheimer disease. The researchers presented the results of the study which included 37908 patients from the Intermountain Medical Center Salt Lake City. In a previously study the researchers established a link between Alzheimer's disease, dementia and atrial fibrillation, and the results show that atrial fibrillation is a powerful predictor of subsequent Alzheimer's disease. They explained that among patients who develop both atrial fibrillation and Alzheimer's disease, the rate of cognitive decline is rapid and mortality rates are very high.

The concept of safety over efficacy is described in the ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. So, as a result of these observations although the efficacy of amiodarone compared with most other drugs were higher in arrhythmias treatment it was decided to developed a treatment algorithm for maintenance of sinus rhythm that tailored initial drug therapy to maximize safety. Studies were included in several antiarrhythmic drugs which satisfying these algorithm, one of this were Dronedarone. Other studies conducted with other antiarrhythmic drugs such as propafenone, sotalol had no better results. Before seeing what position algorithm includes Dronedarone, must answer two questions:

- which patients are best suited for a rhythm-control compared with rate-control strategy
- what is the best metric to define therapeutic success

The AFFIRM trial demonstrated equivalency in major outcomes for both, the rhythm-control and rate-control strategies. The selection of a rate-control or rhythm-control strategy remains an important first decision for the clinician. If a patient stays in atrial fibrillation for years, anatomical and electrophysiological atrial remodeling may preclude the ability to restore and maintain sinus rhythm in these patients. The AFFIRM trial include patients (older than 65 years) enrolled in randomized controlled trials of rate-control versus rhythm-control, who present increased risk factors for stroke, whereas younger patients with paroxysmal atrial fibrillation were not well represented in these trials.

Atrial fibrillation prognosis is determined for the emergence or worsening of existing hemodynamic disturbances (especially heart failure), thromboembolic accidents and increased mortality as possible.

Characteristic likeness of atrial fibrillation such as loss of synchronous atrial mechanical activity, irregular ventricular rhythm and rapid ventricular rate (uncontrolled), are three factors that lead to the development of hemodynamic disorders. An immediate consequence of atrial fibrillation is lower on average by 20-25% in cardiac output, especially when there is a ventricular hypertrophy and diastolic dysfunction and less in the case of systolic dysfunction. These disorders are more pronounced when atrial systole to ventricular filling contribution

not exceeding 40%. Irregularity of RR intervals in atrial fibrillation causes changes in diastolic filling. This fluctuation of the duration of ventricular filling is followed by a large variation of stroke volume and increased pressure in the left atrium, the flow decrease and the appearance of symptoms of heart failure.

In conclusion, both the loss of synchronous atrial activity and ventricular rate irregularity affects cardiac output. Uncommanded rapid ventricular frequency, usually > 130/min, may develop hear dilatation with global hypokinesia and ventricular dysfunction, a condition called tachycardiomyopathy.

Tachycardiomyopathy development mechanism means:

1. fast heart rate
2. decreased cardiac output and renal blood flow
3. neurohormone activation (rennin-angiotensin system activation, decreased natriuretic hormones)
4. decrease in  $\beta$  receptor expression heart remodeling – fibrosis with dilatation and finally heart failure. This form of cardiomyopathy is reversible to adequate control of ventricular frequency or to restore sinus rhythm.

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