Cross-sectional Study of Treatment Strategies on Atrial Fibrillation

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Abstract

Background: Despite the high prevalence and clinical importance of atrial fibrillation (AF), there is no Brazilian study about the clinical profile of patients with AF and the most used treatment strategy (heart rhythm control vs. heart rate control) for them.

Objective: To assess the most used treatment strategy for AF in an outpatient clinic specialized in the management of that disease. In addition, the clinical profile of the population studied was provided.

Methods: Cross-sectional study assessing sequentially, in 167 patients with AF, the most used treatment strategy, as well as their clinical profile. A standardized form was used for data collection. The statistical analysis was performed by using the SPSS® software, version 13.0.

Results: In that population at high risk for thromboembolic events (61% had CHADS² ≥ 2), 54% of the patients had paroxysmal or persistent AF, 96.6% used vitamin K antagonists or acetylsalicylic acid, and 76.6% used beta-blocker (heart rate, 81.2% x heart rhythm, 58.8%; p < 0.05). Heart rate control was the most used treatment strategy (79.5% x 20.5%; p < 0.001). A statistical tendency towards more patients with ventricular dysfunction (15.2% x 2.9%; p = 0.06), CHADS² ≥ 2 (60.5% x 39.5%; p = 0.07) and heart valve diseases (25.8% x 11.8%; p = 0.08) was observed in the heart rate control group.

Conclusion: In that population at high risk for thromboembolic events, the heart rate control strategy was the most used.

Keywords: Heart rate/drug effects; atrial fibrillation/epidemiology; anti-arrhythmia agents.

Introduction

Atrial fibrillation (AF) is the most common sustained heart arrhythmia in clinical practice. Its prevalence in the general population ranges from 0.4% to 1%, and proportionally increases with age, thus, 8% of individuals aged 80 years have AF. Population aging has caused a significant increase in the incidence and prevalence of AF worldwide. Approximately one third of all admissions due to heart rhythm disorders are caused by AF. Considering only the United States and the European Union, there are 2.2 million and 4.5 million individuals affected by that disorder, respectively. Projections for 2050 estimate that 16 million North Americans will be affected by AF, if the AF incidence maintains its current rates. In Brazil, AF is the fifth major cause of hospitalization in the Brazilian Unified Health System (SUS).

The way heart rhythm should be treated is still controversial, and several studies have shown no difference in the survival of patients with AF between the treatment strategy of controlling heart rate and that of controlling heart rhythm. Cross-sectional studies and registries provide tools for establishing health policies and allow assessing the adherence to the recommendations proposed in guidelines. To our knowledge, there is no Brazilian registry quantifying the most used clinical treatment strategy for AF.

Objectives

This study aimed at assessing the most used treatment strategy for controlling AF in a specialized outpatient clinic. In addition, the epidemiological profile of the population assessed was provided.

Methods

This is a cross-sectional study that assessed sequentially all patients cared for by cardiologists at the AF outpatient clinic of a tertiary hospital for two months. Concomitantly with the assessment of the patients, data of their medical records were analyzed, and a standardized form was completed.
All patients aged 18 years or older who had no contraindications to the use of antiarrhythmic or negative dromotrophic drugs, and who accepted to participate in the study were selected. Patients with either AF occurring in the 30 days following heart surgery or AF of reversible cause were excluded.

Of the 178 forms completed, 167 were considered adequate for analysis. Eleven were ruled out due to inadequate data collection: eight duplicated and three incomplete forms. Forms with up to two blank fields were included. Such fields were ignored and the remaining data were considered in the analysis.

The study’s project was approved by the Ethics Committee of the institution, according to the recommendation of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed with the SPSS® software, version 13.0 (IBM®), and the categorical variables were expressed as percentages, and the continuous variables as means and standard deviations. The categorical variables were compared by use of the chi-square test. The means of the continuous variables with normal distribution were treated by use of the Student t test, while the means of the continuous variables without normal distribution were compared by use of the Mann Whitney non-parametric test. Statistical significance was considered for p values < 0.05.

Results

The mean age of the patients studied was 65.9 ± 13.1 years, and 52.4% of them were men. The prevalences of systemic arterial hypertension, diabetes mellitus, and heart valve diseases (mitral and/or aortic) were elevated and estimated as 75.4%, 20.5%, and 22.9%, respectively (tab. 1). Moderate and significant left ventricular dysfunction was found in 12.7% of the patients (tab. 1). Approximately one third of the population studied had paroxysmal AF, mean CHADS

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was 1.89, and 60.4% of the population studied had either CHADS

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or heart valve disease (tab. 3). Polypharmacy, defined as the concomitant use of five or more drugs

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was found in 53.9% of the patients assessed (tab. 2). The mean number of medications used was 5 ± 2.3 (tab. 2). Of the patients with no heart valve disease and with indication for oral anticoagulation (CHADS

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, 85% were on vitamin K antagonists. All the others were on acetylsalicylic acid. The prevalence of patients using vitamin K antagonists and antiplatelet drugs was 3%.

Heart rate control was the most common treatment strategy for AF (79% vs. 21%; p < 0.001 - fig. 1). Regarding the paroxysmal type of AF, the strategies were equally used (heart rate control, 53%, vs. heart rhythm control, 47%; p = 0.69). In that group, 27 patients were on the following antiarrhythmic drugs: amiodarone (16 patients); sotalol (six patients); and propafenone (five patients). Regarding the persistent type of AF, a significant difference favoring heart rate control was observed (96% vs. 4%, p < 0.001). When the paroxysmal and persistent types of AF were grouped, heart rate control was also the most often used treatment strategy (66% vs. 34%; p = 0.003 - fig. 1).

The prevalences of systemic arterial hypertension and diabetes mellitus were similar in the heart rate and heart rhythm control groups (81% vs. 70.6%; p = 0.46%, and 22.7% vs. 11.8%; p = 0.16 respectively - tab. 1). Regarding ventricular dysfunction [considered as ejection fraction (EF) ≤ 40%] and heart valve diseases, a statistical tendency towards a greater number of patients in the heart rate control strategy was observed (15.3% vs. 2.9%; p = 0.055, and 25.8% vs. 11.8%; p = 0.08, respectively - tab. 1).

The mean number of medications used per patient was similar in the heart rate control and heart rhythm control groups, as were the prevalences of polypharmacy in those groups (4.9 vs. 5.2 agents; p = 0.65, and 53.4% vs. 55.9%; p = 0.8, respectively - tab. 1 and 2). Beta-blockers were more commonly used by the heart rate control group patients (81.2% vs. 58.8%; p = 0.008 – tab. 2), and angiotensin-converting-enzyme inhibitors (ACEI) were used in both groups similarly (heart rate, 61.7%, vs. heart rhythm, 58.8%; p = 0.76 – tab. 2).

Although mean CHADS

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2

did not differ between the heart rate control and heart rhythm control groups (1.97 ± 1.46; p = 0.76, respectively), a statistical tendency towards a greater prevalence of patients with either CHADS

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or heart valve diseases was observed in the first group (63.9% vs. 47.1%; p

0.055).

Table 1 – Prevalence of comorbidities related to the treatment strategy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Heart rate control</th>
<th>Heart rhythm control</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.1 (±13.1)</td>
<td>63.9 (±13.5)</td>
<td>65.9 (±13.1)</td>
<td>0.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>69/132 (50%)</td>
<td>21/34 (61.8%)</td>
<td>87/166 (52.4%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Female</td>
<td>68/132 (50%)</td>
<td>13/34 (38.2%)</td>
<td>79/166 (47.6%)</td>
<td></td>
</tr>
<tr>
<td>Ventricular dysfunction (EF &lt; 40%)</td>
<td>20/131 (15.3%)</td>
<td>1/34 (2.9%)</td>
<td>21/165 (12.7%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Hypertension</td>
<td>102/133 (81%)</td>
<td>24/34 (70.8%)</td>
<td>126/167 (75.4%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30/132 (22.7%)</td>
<td>4/34 (11.8%)</td>
<td>34/166 (20.5%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Heart valve disease</td>
<td>34/132 (25.8%)</td>
<td>4/34 (11.8%)</td>
<td>38/166 (22.9%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Medications</td>
<td>4.9 (±2.3)</td>
<td>5.2 (±2.5)</td>
<td>5.0 (±2.3)</td>
<td>0.65</td>
</tr>
</tbody>
</table>
Oliveira e cols.
Estratégias de tratamento na FA

Patients undergoing heart rate control used vitamin K antagonists more often (74.4% vs. 52.9%; p = 0.015) and for longer periods (68.7 ± 57.4 vs. 37.2 ± 31.9 months; p = 0.014 – tab. 2).

Discussion

To our knowledge, this is the first Brazilian study to assess the epidemiological profile of patients with AF and their most commonly used treatment strategy. In the population studied, more patients were undergoing heart rate control than heart rhythm control.

The multicenter registry Euro Heart Survey on Atrial Fibrillation has assessed the treatment strategy in 5,333 patients of different European centers and has observed that heart rhythm control was used in as much as 77% of the cases. Similarly, the German registry AFNET, analyzing similar parameters in 9,582 patients from 194 centers in Germany, has concluded that heart rhythm control was the strategy used in 53.4% of the individuals. The RecordAF study has assessed 5,064 patients of 532 centers in 21 countries (including the Brazilian contribution with 1.6% of the sample) and has reported that heart rhythm control was the strategy used in 63.1% of the individuals. When assessing the patients with paroxysmal or persistent AF, heart rhythm control was used in 54% of them (fig. 3).

The AFIB Geneva study has reported that the heart rhythm control strategy was used in 53% of the 622 patients assessed in an initial consultation with 23 cardiologists in the city of Geneva. The ALFA study has assessed the treatment strategy used by French cardiologists in 550 patients, and has found heart rhythm control to be used in approximately 72.7% of the sample. Attempts to restore sinus rhythm at the time the patients entered those studies might be an explanation for the different results found. The heart rhythm each patient had before entering those studies has not been informed by the authors.

The percentage of individuals using vitamin K antagonists and their mean use in months can be a

<table>
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<th>Table 2 - Medications, catheter ablation, duration of oral anticoagulation related to the treatment strategy</th>
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<tr>
<td></td>
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<tr>
<td>Beta-blocker</td>
</tr>
<tr>
<td>ACEI</td>
</tr>
<tr>
<td>Diuretic</td>
</tr>
<tr>
<td>Vitamin K antagonists</td>
</tr>
<tr>
<td>OAC (months)</td>
</tr>
<tr>
<td>Antiplatelet drug</td>
</tr>
<tr>
<td>Polypharmacy</td>
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<tr>
<td>AF ablation</td>
</tr>
</tbody>
</table>

ACEI - Angiotensin-converting-enzyme inhibitors; OAC - Oral anticoagulation; AF - Atrial fibrillation.

<table>
<thead>
<tr>
<th>Table 3 – Tipos de fibrilação atrial e estratificação de risco tromboembolico conforme estratégia de tratamento</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>AF type ≠</td>
</tr>
<tr>
<td>Paroxysmal</td>
</tr>
<tr>
<td>Persistent</td>
</tr>
<tr>
<td>Permanent</td>
</tr>
<tr>
<td>SR after CVE</td>
</tr>
<tr>
<td>Mean CHADS₂</td>
</tr>
<tr>
<td>CHADS₂ 0 or 1</td>
</tr>
<tr>
<td>CHADS₂ 2 or more heart valve disease</td>
</tr>
<tr>
<td>CHADS₂ 2 or more*† on OAC</td>
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</tbody>
</table>

(*) Only 3% of the total population (5/166) used a vitamin K antagonist associated with an antiplatelet drug. Of those five patients, four were in the heart rate control group (three with CHADS₂ < 2 and another with CHADS₂ ≥ 2), and only one patient of the heart rhythm control group used both medications (CHADS₂ ≥ 2). No patient of the heart rhythm control group with CHADS₂ < 2 used both medications; (†) Of all patients with CHADS₂ ≥ 2 who were not on vitamin K antagonists, regardless of the treatment strategy for AF, used an antiplatelet drug; (‡) At the time of consultation, of the eight patients on heart rhythm control strategy, seven underwent cardioversion and had sinus rhythm at the time of consultation. Of those, four were on an antiarrhythmic drug. Patients with permanent AF assigned to the heart rhythm control group might represent individuals using amiodarone as an adjuvant to control ventricular response; SR - sinus rhythm; CVE – cardioversion; OAC - oral anticoagulation.
parameter to estimate the time for diagnosing AF. Assuming that 70.1% of the population in our study used vitamin K antagonists for a mean period of 63.4 months (tab. 2), our population is believed to have a long history of AF, which might have contributed to the preference in choosing the heart rate control strategy.

Although prospective, some of the data published regarding the treatment strategy in the large international registries have been obtained at the beginning of the studies. Thus, they might not reflect the clinical practice in patients followed up in the long run and at the same service or with the same physician.

In a recent analysis of the Canadian Registry of Atrial Fibrillation (CARAF I and II), Andrade et al\textsuperscript{14} have reported that the prevalence of the treatment strategies for AF varied over time. CARAF I\textsuperscript{15} has involved seven centers in six
Canadian cities, and, assessing 967 patients diagnosed with their first episode of AF, has concluded that 56% of the patients used no antiarrhythmic drug (heart rate control). With the publication of the AFFIRM and RACE studies, a progressive reduction in the use of those agents has been observed. By the end of the first year of follow-up, 49% of the patients were on antiarrhythmic drugs in the CARAF I. That prevalence dropped to 39% by the end of the fifth year of follow-up. In the CARAF II, that prevalence was 42% and 22% for the same time intervals considered. The large clinical trials showing equivalence between the treatment strategies regarding patients’ survival, along with the natural history of AF, have been considered to explain the results obtained in those studies. We believe that our population is very similar to that assessed by the end of the fifth year of follow-up in the CARAF II, in which either the likelihood of maintaining sinus rhythm by using antiarrhythmic drugs was considered small or the disadvantages related to their use exceeded the benefits. The results obtained in our study and in the analysis by Andrade et al14 of the Canadian registries might be a closer reproduction of the reality.

Differences in the prevalence of factors associated with the development of AF, such as arterial hypertension, diabetes mellitus, ventricular dysfunction7,14,17 and heart valve diseases (fig. 2), might have contributed to the differences in results related to the use of treatment strategies for AF. Failure in controlling those diseases is known to make the maintenance of sinus rhythm difficult. Only the RecordAF and AFIB Geneva studies have quantified the prevalence of moderate to significant ventricular dysfunction (EF < 40%) in isolation (10% and 9%, respectively), while the AFNET study and the Euro Heart Survey on Atrial Fibrillation have quantified the combination of EF < 35% and heart failure (29.8% and 37.6%, respectively). Although that prevalence has not been disclosed in the ALFA study, the mean EF was 58.7 ± 12.9.

The higher prevalence of patients with ventricular dysfunction (EF £ 40%) in the heart rate control strategy (95%) was a finding similar to that of the RecordAF study15 (59.5%). The difference in the magnitude of the findings might be attributed to the smaller sample assessed in the present study. The analysis of the CARAF I and CARAF II9 has shown that, although initially a higher prevalence of the heart rate control strategy was observed in patients with heart failure, as time went by, no difference between both treatment strategies was seen. Subanalyses have shown that, even among symptomatic patients with EF £ 40%, no preference of one treatment strategy over the other has been evidenced.

Considering that the treatment strategy does not influence survival4-6, that the atrial electrical and anatomical remodeling makes the maintenance of sinus rhythm difficult, and that heart rate control is cost-effective in the treatment of persistent AF18,19, many might consider the limitation of ventricular response a more practical option easier to be obtained.

One of the indications for AF reversal is the presence of symptoms1,7 in patients undergoing the heart rate control strategy. Maintaining asymptomatic or mildly symptomatic individuals only with a reduction in ventricular response...
might justify the prevalence of that strategy in this study. Because that variable has not been assessed, a conclusion cannot be obtained.

Considering that amiodarone is the only drug with properties to control heart rhythm in AF provided by the SUS and that there are costs involved in assessing the appearance of its adverse effects, many might hesitate to prescribe it. In the literature, there are recommendations for systematic laboratory assessment before and during the treatment with amiodarone\textsuperscript{20,21}. That is a relevant aspect in using a drug that does not aggregate survival and increases costs to a health system that needs to optimize its resources.

In this study, it is worth noting the high prevalence of the use of beta-blockers and vitamin K antagonists. The use of the former by 75% of the population studied might be associated with the high prevalence of ventricular dysfunction and arterial hypertension. The attempt to control symptoms with those drugs might also be justified (fig. 4). The greater use of vitamin K antagonists by patients undergoing heart rate control might be attributed to the high prevalence of patients with heart valve diseases or with \textup{CHA}_2\textup{DS}_2\geq 2 in that population.

There are several hypotheses to explain the high number of individuals with \textup{CHA}_2\textup{DS}_2 0 or 1 using vitamin K antagonists, which might be used due to reasons other than prevention of thromboembolic events due to AF. The magnitude of such influence, and even if it really exists, cannot be confirmed or refuted with the data obtained. Lee et al\textsuperscript{22}, however, after a mean follow-up of 22 months, have shown in a population of 422 patients with AF and \textup{CHA}_2\textup{DS}_2 1 that anticoagulation with vitamin K antagonists reduced the incidence of stroke as compared with that of the use of antiplatelet drugs (4.2\% vs. 12.9\%, respectively; \( p = 0.008 \)). The bleeding rate was similar in both groups.

The concomitant use of an antiplatelet drug and a vitamin K antagonist was lower in this study (3\%) as compared with that of all the studies considered (fig. 5). Such results are compatible with the careful use of that association, because of the high risk of bleeding and the lack of incontestable improvement in survival.

**Limitations**

The cross-sectional design of this study and the reduced size of its sample as compared with those of other registries are limitations, although they do not nullify the expressivity of the data presented. Data collection from medical records might have caused some bias.

Because it is a single-center study and carried out at a tertiary outpatient clinic specialized in treating AF, the population assessed is worth noting. It is formed by patients with a high prevalence of comorbidities, referred from other outpatient clinics and services, who, thus, might have a more complex clinical profile. Although neither the duration of AF nor the attempts to revert to sinus rhythm have been assessed, most patients might have a long history of disease (as already commented). That profile might not represent the population of primary health care services.

The duration of the AF progression, the left atrial dimensions, the previous treatment strategies, the recording of attempts to sinus rhythm reversal, and the follow-up of such parameters over time are data that could provide a better understanding of the results obtained. Considering that this is an assessment regarding clinical practice, however, the results are useful for the establishment of public health policies.

![Figure 4](image-url) - Comparison of the prevalence of the use of beta-blockers in the different studies: (*) In the CARAF I, the prevalence of the beta-blocker use was expressed along with sotalol.
Conclusion

In this study, heart rate control was the most commonly used treatment strategy for AF. Those results should be carefully interpreted, because this study was conducted in a tertiary center, and a population with a greater prevalence of atrial remodeling might have been selected. A Brazilian registry involving primary and tertiary centers could improve the understanding of the way AF has been managed in Brazil.

References


