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 describing the clinical profile of patients with AF and the most used treatment strategy (rhythm control vs. rate control).

Objective: Assess the most common treatment on AF in an outpatient specialized clinic for management of AF. In addition, the clinical profile of the population studied was provided.

Methods: Cross-sectional study assessing the most used strategy for atrial fibrillation control in 167 patients. The clinical profile was also described. A standardized form was used for data collection and statistical analysis was performed by SPSS 13.0 software.

Results: In this high risk population for thromboembolic events (61% had CHADS\textsuperscript{2} ≥ 2), 54% of patients had paroxysmal or persistent AF, 96.6% were on vitamin K antagonists or acetylsalicylic acid, and 76.6% on beta-blocker (rate control 81.2% x rhythm control 58.8%; \( p < 0.05 \)). Heart rate control was the most used strategy (79.5% x 20.5%; \( p < 0.001 \)). A statistical tendency towards more patients with ventricular dysfunction (15.2% x 2.9%; \( p = 0.06 \)), \( \text{CHADS}^2 \geq 2 \) (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 this high risk population for thromboembolic events, the rate control strategy was the most used.

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

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice\(^1\). Its prevalence in general population ranges from 0.4% to 1%, and proportionally increases with age, in such a manner that, 8% of individuals aged 80 years have AF\(^1\). Population aging significantly increases the incidence and prevalence of AF worldwide\(^2\). Approximately one third of all admissions due to heart rhythm disorders are caused by AF. Only in the United States and in the European Union, there are 2.2 million and 4.5 million individuals affected by that disorder, respectively\(^1\). Projections for 2050 estimate that 16 million North Americans will be affected by AF, if the AF incidence maintains its current rates\(^1\). In Brazil, AF is the fifth major cause of hospitalization in the Brazilian Public Health System (SUS).

Rhythm management is still controversial, and several studies have shown no difference in survival between rate and rhythm control strategies\(^4-6\). Cross-sectional studies and registries provide tools for establishing health policies and allow assessing the adherence to the recommendations proposed in guidelines\(^7\). To our knowledge, there is no Brazilian registry quantifying the most used clinical treatment strategy on 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, data of their medical records were analyzed, and a standardized form was fulfilled.

All patients aged 18 years or older who had neither contraindications of antiarrhythmic nor negative dromotropic
drugs and accepted to participate were selected. Patients with either AF occurring in the 30 days following heart surgery or AF of reversible cause were excluded.

Among 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 project was approved by the Ethics Committee of the institution, according to Helsinki Declaration.

Statistical analysis

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

Results

The mean age was 65.9 ± 13.1 years, and 52.4% of them were male. 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 patients (tab. 1). Approximately one third of population had paroxysmal AF, mean CHADS2, was 1.89, and 60.4% had either CHADS2 ≥ 2 or heart valve disease (tab. 3). Polypharmacy, defined as the concomitant use of five or more drugs, was found in 53.9% of patients (tab. 2). The mean number of medications used was 5 ± 2.3 (tab. 1). Among patients with no heart valve disease and with indication for oral anticoagulation (CHADS2 ≥ 2), 85% were on vitamin K antagonists. The remaining were on acetylsalicylic acid. The prevalence of patients using vitamin K antagonists and antiplatelet drugs was 3%.

Rate control was the most common treatment strategy on AF (79% vs. 21%; p < 0.001 - fig. 1). Regarding paroxysmal type of AF, the strategies were equally used (rate control, 53%, vs. rhythm control, 47%; p = 0.69). In the latter, 27 patients were on the following antiarrhythmic drugs: amiodarone (16 patients); sotalol (six patients); and propafenone (five patients). Regarding persistent AF, a significant difference favoring rate control was observed (96% vs. 4%, p < 0.001). When the paroxysmal and persistent types of AF were grouped, 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 rate and 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 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 was similar in the rate and 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 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 (rate, 61.7% vs. rhythm, 58.8%; p = 0.76 – tab. 2).

Although mean CHADS2 did not differ between rate control and rhythm control groups (1.97 x 1.46; p = 0.7, respectively), a statistical tendency towards a greater prevalence of patients with either CHADS2 ≥ 2 or heart valve diseases was observed in the first one (63.9% vs. 47.1%; p = 0.07, respectively). Patients undergoing 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).

Table 1 – Prevalence of comorbidities related to the treatment strategy

<table>
<thead>
<tr>
<th></th>
<th>Heart rate control</th>
<th>Heart rhythm control</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</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>69/132 (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 (70.6%)</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>
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 rate control than 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 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 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 rhythm control as the strategy used in 63.1% of the individuals. When assessing the patients with paroxysmal or persistent AF, rhythm control was used in 54% of them (fig. 3).

Table 2 - Medications, catheter ablation, duration of oral anticoagulation related to the treatment strategy

<table>
<thead>
<tr>
<th></th>
<th>Heart rate control</th>
<th>Heart rhythm control</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>108/133 (81.2%)</td>
<td>20/34 (58.8%)</td>
<td>128/167 (76.6%)</td>
<td>0.006</td>
</tr>
<tr>
<td>ACEI</td>
<td>82/133 (61.7%)</td>
<td>20/34 (58.8%)</td>
<td>102/167 (61.1%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Diuretic</td>
<td>83/126 (66%)</td>
<td>18/34 (52.9%)</td>
<td>101/160 (63.1%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Vitamin K antagonists</td>
<td>99/133 (74.4%)</td>
<td>18/34 (52.9%)</td>
<td>117/167 (70.1%)</td>
<td>0.015</td>
</tr>
<tr>
<td>OAC (months)</td>
<td>68.7 (DP:57.4)</td>
<td>37.2 (DP:31.9)</td>
<td>63.4 (55.1)</td>
<td>0.014</td>
</tr>
<tr>
<td>Antiplatelet drug</td>
<td>33/131 (25.2%)</td>
<td>17/34 (50%)</td>
<td>50/165 (30.3%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>70/89 (53.4%)</td>
<td>19/34 (55.9%)</td>
<td>89/165 (53.9%)</td>
<td>0.8</td>
</tr>
<tr>
<td>AF ablation</td>
<td></td>
<td></td>
<td>11/167 (6.6%)</td>
<td></td>
</tr>
</tbody>
</table>

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

Table 3 – Tipos de fibrilação atrial e estratificação de risco tromboembólico conforme estratégia de tratamento

<table>
<thead>
<tr>
<th>AF type ≠</th>
<th>Heart rate control</th>
<th>Heart rhythm control</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal</td>
<td>27/37 (73%)</td>
<td>25/37 (68%)</td>
<td>52/74 (70%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Persistent</td>
<td>25/37 (68%)</td>
<td>30/37 (81%)</td>
<td>55/72 (75%)</td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>18/37 (49%)</td>
<td>6/37 (16%)</td>
<td>24/74 (32%)</td>
<td></td>
</tr>
</tbody>
</table>

Mean CHADS2 1.97 1.46 1.89 0.7

CHADS2, 0 or 1 48/133 (36.1%) 18/34 (52.9%) 66/167 (39.5%) 0.07

CHADS2, 2 or more heart valve disease 85/133 (63.9%) 16/34 (47.1%) 101/167 (60.4%) 0.005

CHADS2, 2 or more*† on OAC 74/85 (87.1%) 12/16 (75%) 86/101 (85.1) 0.7

(*) 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 control rate group (three with CHADS2 < 2 and another with CHADS2 ≥ 2), and only one patient of the rhythm control group used both medications (CHADS2 ≥ 2). No patient of the 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 AF, used an antiplatelet drug; (‡) At the time of consultation, of the eight patients on 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 rhythm control group might represent individuals using amiodarone as an adjuvant to control ventricular response; SR - sinus rhythm; CVE – cardioversion; OAC - oral anticoagulation.

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 rate control than rhythm control.

The multicenter registry Eureo Heart Survey on Atrial Fibrillation has assessed the treatment strategy in 5,333 patients of different European centers and has observed that 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 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 rhythm control as the strategy used in 63.1% of the individuals. When assessing the patients with paroxysmal or persistent AF, rhythm control was used in 54% of them (fig. 3).

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

The percentage of individuals using vitamin K antagonists and the length they were taking it might be a parameter to estimate duration of AF. Assuming that 70.1% of population in our study used vitamin K antagonists for a mean period of 63.4 months (tab. 2), we suppose they might have a long history of AF, which might have led preference in choosing the 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. have reported that prevalence of the treatment strategies for AF varied over time. CARAF I involved seven centers in six Canadian cities, and, assessing 967 individuals with their first episode on AF, has concluded that 56% of patients used no antiarrhythmic drug (rate control). With publication of AFFIRM and RACE studies, a progressive reduction in use of those agents has been observed. By the end of the first year of follow-up, 49% of patients were on antiarrhythmic drugs in 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. 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 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 al.\textsuperscript{14} of the Canadian registries might be a closer reproduction of clinical practice.

Differences in prevalence of factors associated with development of AF, such as arterial hypertension, diabetes mellitus, ventricular dysfunction\textsuperscript{7,16,17} and heart valve diseases (fig. 2), might have contributed to the differences in results related to the use of treatment strategies on 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 AFNET study and 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 rate control strategy (95%) was a finding similar to that of RecordAF\textsuperscript{15} (95%). The difference in the magnitude of the findings might be attributed to the smaller sample assessed in the present study. Analysis of CARAF I and CARAF II\textsuperscript{15} has shown that, although initially a higher prevalence of 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 asymptomatic patients with EF ≤ 40%, no preference of one treatment strategy over the other has been evidenced.

Considering that treatment strategy does not influence survival\textsuperscript{4-6}, that atrial electrical and anatomical remodeling makes maintenance of sinus rhythm difficult, and that rate control is cost-effective in the treatment of persistent AF\textsuperscript{18,19}, many might consider the limitation of ventricular response a more practical and easier option to be obtained.

One indication for AF reversal is the presence of symptoms\textsuperscript{1,7} in patients undergoing 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 made.

Considering that amiodarone is the only drug capable of controlling rhythm in AF available in Brazilian public health system and costs are involved in assessing adverse effects, many might hesitate to prescribe it. There are recommendations for systematic laboratory assessment before and during 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 care system that needs to optimize its resources.

It is worth noting the high prevalence of use of beta-blockers and vitamin K antagonists. Seventy five percent of individuals were on beta-blocker treatment which might be associated with high prevalence of ventricular dysfunction.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Prevalence of the treatment strategies in the different studies; Prevalence of the treatment strategy used in the present study for patients with the paroxysmal and persistent AF types; (†) Prevalence of the treatment strategy in the EUROHEART registry regarding the paroxysmal and persistent AF types; 5% of the patients either used no medication or the information was not available; (#) In the AFIB study, the results express the prevalence of the most used treatment strategy for the total of patients with no distinction of the AF type; (§) The AFNET study assessed the prevalence of the treatment strategy for patients with persistent AF. Patients undergoing ablation were considered to be on the heart rhythm control strategy; (‖) In the express ALFA study, the treatment strategy for the total of patients regardless of the AF type; (¶) The RECORDAF study shows the prevalence of the treatment strategy used in individuals with paroxysmal and persistent AF types. When assessed separately, the prevalences of the heart rhythm and heart rate treatment strategies were 29.5% and 70.5% in paroxysmal AF; and 63.1% and 39.9% in the persistent type, respectively; (†) Data of the CARAF II after five years of follow-up. On the occasion of the analysis, 25% of the patients were on neither antiarrhythmic drugs nor negative dromotropic drugs.}
\end{figure}
and arterial hypertension. The attempt to control symptoms with those drugs might also justify this findings (fig. 4). The greater use of vitamin K antagonists by patients undergoing rate control might be attributed to the high prevalence of patients with heart valve diseases or with CHADS
2 ≥ 2.

Several hypotheses might explain the high number of individuals with CHADS
0 or 1 on vitamin K antagonists. One of them might be other reasons for oral anticoagulation 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 these data. Lee et al
22, however, after a mean follow-up of 22 months, have shown in a population of 422 patients with AF and CHADS
2 1 that anticoagulation with vitamin K antagonists reduced the incidence of stroke as compared with that on 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 others (fig. 5). Such results are compatible with judicious use of drugs that increase the risk of bleeding without improvement in survival rates.

**Limitations**

The cross-sectional design and reduced sample size as compared with 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 carried out at a tertiary specialized outpatient clinic on AF, attention must be payed on population. It is formed by patients with a high prevalence of comorbidities, referred from other outpatient clinics and services who 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.

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

**Conclusion**

Rate control was the most commonly strategy used on AF treatment. Those results should be carefully interpreted, since 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 AF has been managed in Brazil.

**Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**Sources of Funding**

There were no external funding sources for this study.

**Study Association**

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**Figure 4** - 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.
References


