

New Perspectives in the Treatment of Cardiac Arrhythmias and Their Application in Brazil

Mauricio Scanavacca

Instituto do Coração - HC - FMUSP, São Paulo, SP - Brazil

Cardiac arrhythmias are common in the general population, especially in patients with heart disease. Patients can spend life without any specific clinical manifestations or have their quality of life significantly adversely affected and, in extreme cases, be susceptible to sudden death. This broad spectrum of presentation and risk makes the management of patients with cardiac arrhythmias a constant challenge for emergency medical units, general practitioners, cardiologists and even specialists. Moreover, the constant advancement of knowledge and its quick translation into clinical practice calls for the continuous updating of knowledge in this field. The Brazilian Society of Cardiology regularly reassesses the recommendations for treatment of cardiac arrhythmias in our country in order to adjust the cost/effectiveness of these treatments and adapt them to the reality of our population. The Brazilian Archives of Cardiology (ABC) represent the main vehicle of transmission of clinical experience of Brazilian cardiologists involved or not in research to their peers, becoming an important channel for disseminating the Brazilian experience. The purpose of this article is to review the characteristics of publications on the treatment of cardiac arrhythmias in the last three years in ABC and evaluate the profile of the journal in this area.

From 2010 to 2012, 28 articles were published focusing on cardiac arrhythmias, representing 3.6% of the ABC publications in this period. This publication rate reflects the gradual reduction in the proportion of papers on arrhythmia in total papers published by the ABC over the last decade: 8.9% in 2002, 6.5% in 2007, 2.7% in 2010, with a slight increase in 2011 (4.1%) and 2012 (4.8%). This low rate of publications on topics related to cardiac arrhythmias contrasts with that of other journals that are similar to the ABC, as the main representative of the cardiology specialty in Brazil. In 2011, the Spanish Journal of Cardiology published 47 (12.8%) papers on cardiac arrhythmias and the Portuguese Journal of Cardiology published 12 (10.1%) articles on cardiac arrhythmias in the same year. The reasons for the reduction of cardiac arrhythmias papers in the ABC are unclear, but

it may be motivated by factors such as the reduction in the submission of papers due to the preference of paper-writing groups from international journals with high impact factors, internal competition with other journals of regional or specialty societies or due to differences in criteria used in the selection of papers to be published. On the other hand, it may also reflect a proportional increase in the scientific production of other cardiology areas. Accordingly, the review of submissions by the executive department of the ABC indicates that the rate of approval by the editorial staff has remained around 25% (one out of every four papers), which is similar to other areas of the journal. The ratio of submissions from other areas increased significantly during this period, probably due to the higher volume of theses presented by graduate students in various subspecialties of cardiology. Therefore, the main reason for the reduction is the reduced rate of submissions by the groups that write papers on arrhythmias, contrasting with the progressive increase in submissions from other areas, particularly those related to epidemiology.

Out of the 28 papers published between 2010 and 2012, 10 (38.4%) involved clinical aspects, seven (25%) involved interventional treatment, five (17.8%) addressed the issue of noninvasive assessment, four (14.2%) dealt with cardiac pacing and two (7.1), basic science. Of these papers, 18 (64.2%) were original papers; six (21.4%) were case reports; three (10.7%) were clinical updates and editorial articles (3.8%). This distribution reflects the new ABC policy in favor of original papers and towards restricting review papers, adding a stronger scientific profile to the journal.

All of the six case reports selected are very interesting and are worth being highlighted. Sarabanda et al¹ described a well illustrated case of a patient who underwent persistent ablation of atrial fibrillation (AF), which resulted in stenosis of the left superior pulmonary vein, effectively treated with stenting angioplasty. The paper reviews the incidence of this complication in the contemporary phase of AF ablation and the importance of clinically following up these patients. Almeida et al² report an unusual case of pacemaker electrode mistakenly implanted in the left ventricle through the foramen ovale. The importance of early diagnosis is stressed to reposition the electrode avoiding the risk of systemic embolism or the need for chronic anticoagulation. Tavares et al³ reported three cases of amiodarone-induced thyrotoxicosis. They discuss the clinical and laboratory aspects and different approaches to properly control clinical cases. Chemello et al⁴ also report an unusual case of a patient with non-Hodgkin lymphoma with cardiac involvement that resulted in sustained ventricular tachycardia. They reviewed the literature, described the aspects of diagnosis and the satisfactory outcome

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Mailing Address: Mauricio Scanavacca •

Av. Joaquim C. A. Marques, 1205, Morumbi. Postal Code 05688-021, São Paulo, SP - Brazil
E-mail: mibrahim@cardiol.br, mauricio.scanavacca@gmail.com
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after chemotherapy. Garcia-Diaz et al⁵ described a case of fetal non-paroxysmal junctional tachycardia not evolving with hydrops. Echocardiography was very interesting and showed ventricular tachycardia rhythm decoupled from the atria. They discuss the differential diagnosis of ventricular tachycardia and clinical management of this unusual situation. Benvenuti et al⁶ also reported a rare case of cardiomyopathy due to deposit of desmin which evolved to restrictive heart failure, atrioventricular block, cardiogenic shock and death. They showed that the cause of the block was fibrosis of the conduction system located in the branching portion of the His bundle and in the initial portions of the right and left branch bundles. The pathophysiology of the disease is not yet well known, but it also promotes extensive fibrosis in the contractile myocardium.

Among the original papers dealing with clinical issues, five stand out: two of them deal with the use of vitamin K antagonists in the prevention of embolic events, one is on strategies for clinical treatment of AF and two deal with the use of drugs without primary antiarrhythmic effect for the prevention of cardiac arrhythmias. Leiria et al⁷ reported the outpatient experience of anticoagulation with the use of vitamin K antagonists for the prevention of embolism in 127 patients. They observed that phenprocoumon was the most commonly used anticoagulant (60% of patients) and patients on this medication remained at a higher therapeutic level compared to those who were taking warfarin (60% versus 45% respectively). Patients on warfarin also had a higher rate of bleeding than patients on phenprocoumon (18.8 vs. 5.5/100 patients/year). They noted that patients on warfarin remained longer outside the therapeutic range and that patients under phenprocoumon were younger, with prolonged use of anticoagulation and had fewer adverse drug effects. Lavitola et al⁸ present the results of a clinical study conducted on 229 patients with rheumatic AF, 110 of which were randomized to take aspirin and 129 to take warfarin. They noted great difficulty faced by the patients in the warfarin group, which led to a substantial number of patients outside the therapeutic range and high rate of embolic events. However, patients with adjustment in the use of oral anticoagulants showed significant reduction in events compared to those who took aspirin. Another interesting observation was reported by Oliveira et al⁹ who studied the profile of patients with AF and the strategies applied at an outpatient level. They observed that 54% of the study population had paroxysmal or persistent AF, and 46%, permanent AF. Most had a high risk of embolic events (60% with CHADS2 \geq 2) and 96% received vitamin K inhibitors or aspirin. The most used treatment strategy was HR control in 80% of patients, who had higher left ventricular dysfunction, higher CHADS2 and valvulopathy.

Alves et al¹⁰ studied the occurrence of postoperative AF after cardiac surgery in patients using statins or not. They documented 39% occurrence of FA, higher (45%) in those who did not use statin compared to 23% in those who used statin for at least 6 months prior to surgery. They did not observe any differences in the classic predictors of AF between the groups. Falco et al¹¹ also submitted a compelling paper about the effect of magnesium pidolate in the reduction of the frequency of extrasystoles in individuals without heart disease. The study

was randomized and double-blind, involving 60 patients taking 3.0 g magnesium pidolate per day or placebo. The criterion for success was a 70% reduction in the number of extrasystoles on Holter after 30 days. They observed a significant reduction in the number of extrasystoles (70% achieved success criteria) and symptoms (93.3%) in patients with active treatment compared to a reduction of 30% and 16.7%, respectively, in patients who received placebo. The study results suggest that supplementation with magnesium pidolate may be useful in treating patients with symptomatic extrasystoles, at least in a short period of observation. A study with a larger number of patients and long-term observation is needed to confirm this interesting preliminary observation.

In the field of interventional treatment of arrhythmias, six works stood out. Ribeiro et al¹² evaluated the cost/effectiveness of implantable cardioverter defibrillator (ICD) in patients with heart failure in Brazil. Similar studies have already been conducted in other countries, but they do not apply to Brazil due to different economic conditions. They observed that, in the public scenario, the cost of ICD is around R\$ 68,000 adjusted for the length and quality of life, and in the private sector, it is R\$ 90,000, with cost/effectiveness incompatible for its application, because these amounts are much higher than the cutoff value suggested by the World Health Organization, i.e., three times the country's per capita (in Brazil, this would be R\$ 40,000.) However, if the patient profile is set to the profile of patients enrolled in the MADIT I¹³ study (clinical and invasive stratification), the adjusted cost/effectiveness would fall to R\$ 23,000 in public service and R\$ 33,000 in the private service, hence more acceptable to the national reality.

Saad et al¹⁴ evaluated a practical aspect of anticoagulation in patients undergoing AF ablation. They compared two strategies. In the conventional strategy, patients under oral anticoagulation with vitamin K antagonist undergo intervention with enoxaparin, then returns to the oral anticoagulant. The tested strategy consisted in carrying out the intervention with therapeutic INR, without discontinuation of oral anticoagulants. They confirmed a previous observation¹⁵ that the procedure can be performed safely in patients with therapeutic INR, because there were no significant differences in the rate of hemorrhagic or embolic events in the two strategies evaluated.

Silva et al¹⁶ evaluated the role of epicardial and endocardial simultaneous mapping with multiple catheters in patients with recurrent sustained ventricular tachycardia with nonischemic cardiomyopathy (85% of Chagas' disease). They observed that, of the 20 tachycardias that could be induced and mapped, 11 had epicardial origin, and nine were endocardial, confirming that the epicardial circuits are common in sustained ventricular tachycardias of chronic Chagas heart disease and that the simultaneous epicardial and endocardial mapping increases probability of identifying the site of origin of tachycardia.^{17, 18}

Melo et al¹⁹ described the experience of ablation in children aged 44 days and 15 years, conducted from 1991 to 2010. The results of 125 children were evaluated and confirmed that ablation is a safe and effective treatment in children of different ages, with tachycardia refractory to medical treatment. The expected results are the better in tachycardias involving

accessory pathways of atrioventricular conduction or through nodal reentrant; however, 20% required further intervention, mostly due to recurrence of tachycardias. At mean follow-up of 5 years, 88% of children remained without clinical recurrences or serious complications.

It is also worth citing two articles evaluating a new approach for prevention of embolic events in patients with AF. The percutaneous closure of the atrial appendage has been considered in patients at high risk of embolic events, but unable to maintain adequate oral anticoagulation. A preliminary comparative study showed that a type of atrial occluder (Watchman) is as effective as oral anticoagulation with vitamin K antagonists, but with a high number of complications in the training phase²⁰. Guérios et al²¹ reported the experience of the University Hospital of Bern, Switzerland, including 86 patients with contraindications to the use of oral anticoagulants. The patients had an average 2.6 CHADS2 and the prosthesis used was AmplatzerCardiacPlug (ACP). There were five severe events related to the implant (two hemopericardial accidents, two embolic events and a displacement of prosthesis removed percutaneously), but no deaths related to the procedure. Six patients had thrombus on the prosthesis, which disappeared after introduction of oral anticoagulants for three months. No new events were detected during outpatient follow-up. Montenegro et al²² reported the first national experiment involving five patients with nonvalvular AF who underwent implantation of ACP with contraindications for the chronic use of oral anticoagulation without immediate complications. Nevertheless, they conclude that comparative prospective clinical studies are needed involving a large number of patients before these prostheses are used as alternatives to oral anticoagulants.

In the field of non-invasive assessment, the work of Mello et al²³ is noteworthy. They studied 41 patients with chronic Chagas heart disease (26 patients with sustained ventricular tachycardia and 15 with non-sustained ventricular tachycardia). All patients underwent magnetic resonance imaging of the heart with the infusion of gadolinium and delayed enhancement detailing the areas of myocardial fibrosis. They observed that, although all groups presented

some degree of delayed enhancement at different ventricular sites, patients with SVT had areas of more extensive transmural fibrosis. The presence of two or more segments with transmural fibrosis was highly associated with clinical occurrence of sustained ventricular tachycardia.

Only two studies were published in the area of basic research of arrhythmia. Curty et al²⁴ conducted molecular research with sequencing of the coding regions of genes KCNQ1, KCNH2, and SCN5A of two families with clinical features of long QT syndrome. They found two gene variants previously associated with LQTS and developed a strategy to identify variants of genes KCNQ1, KCNH2, and SCN5A, an important method for the training of technical personnel for future application in routine practice. Nascimento et al²⁵ studied the association between two polymorphisms of gene ADBR1 of beta₁-adrenergic receptor, Ser49Gly and Arg 389Gly, with the presence of atrial fibrillation in 144 patients with heart failure (24 with AF and 120 without AF). The research was based on previous observations that associate genotype Arg389Arg to exacerbation of adrenergic response in physiological states or not and with a higher incidence of ventricular tachycardia. The genotype Ser49Ser is associated with a lower down-regulation of beta₁-adrenergic receptors with high levels of expression agonist under high adrenergic activity. In this study, they found a significant association of the two genes with AF even after adjustment for age and size of the left atrium. The clinical implication of this observation is that if this finding is confirmed in future studies, it may contribute to risk stratification and prevention of the development of AF in patients with heart failure.

Thus, the analysis of articles published in the ABC over the last few years shows a relative disproportion of papers on cardiac arrhythmias compared to the total number of publications. The papers deal predominantly with different forms of treatment. Clinical works and original papers predominate among the publications. The papers focused on arrhythmias are practical and current, in accordance with the technological development in the area in question and point to the progressive incorporation of these new technologies by the various Brazilian services, without losing the scale of the risks, benefits and costs/effectiveness.

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