

## Current Situation of the Treatment of Heart Failure in Brazil

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Heart failure has been addressed with increasingly frequency in symposia, congresses and researches because of its very high incidence, morbidity and mortality. The number of individuals with heart failure is about 23 million worldwide, with two million new cases each year. In Brazil, according to the IBGE (*Instituto Brasileiro de Geografia e Estatística* – Brazilian Institute of Geography and Statistics), the population in 2007 will be of almost 190 million, seven million of which with this syndrome<sup>1</sup>. The number of new patients has been growing despite the increasingly greater advances in treatment. And what would be the causes to explain this fact? There are attempts to explain it by the increase in population survival, as well as by the increase in industrialization and urbanization of countries in constant development. As a consequence, there is a deterioration of eating habits and an increase in the incidence of sedentary lifestyle, stress and smoking, thus leading to an increased incidence of artery diseases, diabetes mellitus and hypertension, which are potential causes of heart failure. To make this situation even worse, high rates of individuals with Chagas disease and rheumatic disease are still seen in our country. In parallel, there is a decrease in the number of hospital admissions and an increase in in-hospital deaths, facts that are explained by a decrease in hospital bed supply and increased severity of cases hospitalized<sup>2-4</sup>.

For decades, researchers have struggled to diminish morbidity, mortality and costs of this syndrome. New agents, surgical therapeutic approaches, devices, and multiprofessional clinics have been introduced in the clinical practice. What are the results of this huge endeavor, and what is the cost-benefit ratio for society?

When the impact of the use of medications on mortality is analyzed, the conclusion is not favorable. The new agents available in the market had positive results on death rates, albeit modest. This was predictable. For instance, the analysis of the original graphs of the CONSENSUS study (Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study<sup>5</sup>), published two decades ago, shows an evident drop in mortality in the group treated; however, when we pay attention to the values and compare the treatment group with the placebo group, the numerical difference is small.

### Key words

Cardiac output, low; Brazil; data analysis.

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The use of angiotensin converting enzyme inhibitors brought an unquestionable benefit, but unfortunately the cost-benefit ratio was not as favorable.

We addressed this issue at that time in several symposia and lectures, and the discussions were always heated; there was great resistance to accept this argument. It was the beginning of a new stage in the treatment of heart failure, in which the neurohormonal axis was being directly approached. Studies conducted later corroborated these results. The RALES<sup>6</sup> study, which showed a drop in mortality of patients with heart failure receiving spironolactone, was also questioned. We participated in this project and 60 of the patients studied had chagasic cardiomyopathy, 30 of whom received spironolactone and 30 received placebo. No difference in mortality was observed between the two groups. This fact encouraged us to develop a project in an animal model to test the same hypothesis, and more favorable results were obtained<sup>7</sup>. These results cannot be extrapolated to humans, and a similar protocol is afoot, still with few patients studied.

These uncertainties were useful to question information on drug treatments for this syndrome that do not take into consideration the etiopathogenesis of the cardiomyopathy causing the dysfunction. Would the agents available have the same effect regardless of the different causes of the disease? Even today we have doubts on the use of beta-blockers in chagasic cardiomyopathy, for instance. Recent studies show different progression, actuarial curves, and histopathological findings in similar patients with different etiologies<sup>8-10</sup>.

Would the treatments proposed have different effects on the different cardiomyopathies? The answer is almost certainly affirmative. The day will come when the treatment of myocardial aggressions will be individualized, and not collective, the way we treat patients with heart failure today. To accomplish this purpose, the clinical tests developed should have more subsidies from research laboratories. How many of these projects, some of them exceedingly expensive, do not reach satisfactory results because of these shortcomings? Are we perhaps carrying out research in the direction opposite to that recommended by academic methods? Ongoing projects, as well as those lately presented in congresses and in the medical literature make us believe so. The pattern is always the same: “is drug A better than drug B, or than placebo?”

In relation to invasive treatments, we can say that the same criticisms apply. As an example, when the idea of ventriculectomy emerged, a reduction of the ventricular cavity was the single argument in favor of it, and we questioned the idea by stating that the quality of the wall was much more important than the volumes. Before being introduced into medical practice, this procedure should have been

## Point of View

tested in different laboratory models of cardiomyopathy. Not unexpectedly, the results of this technique in chagasic cardiomyopathy, as would have been in any other inflammatory cardiomyopathy, were the worst. The ventricular wall, in these cases, is more damaged<sup>11</sup>. However, we only “discovered” this fact, and its prohibitive mortality rates, after the method had been tested in humans.

We recall that, on that occasion, the ethics committees were engaged in prohibiting the use of endomyocardial biopsy<sup>12</sup> as a diagnostic procedure, but approved this surgical technique in which not only fragments of muscle were removed via puncture, but a “steak” was removed via sternotomy. The Cardiology community applauded this technique and even said that we were before one of the greatest breakthroughs of the century. The media, with its an extremely professional marketing, can be more powerful than the ethical principles that should guide medical research.

The different consequences of different types of myocardial aggression made us consider that morphological as well as functional indexes would be necessary to surgically treat any patient with ventricular dilatation. They are also useful to explain why individuals with aortic regurgitation, with volume increases similar to those seen in chagasic patients, have a more favorable prognosis. And what would be the optimal time for surgical correction of aortic regurgitation? This is a subject of enormous interest, for which morphological indexes would be very useful<sup>13,14</sup>.

When the impact of ventricular assist devices, transplantation, cardioverters and pacemakers on the population with severe heart failure is analyzed, the results are modest. In some situations, mistakes keep being repeated. To date, we still do not know what patients have the best indications to receive a pacemaker, although pacemakers have been routinely used. The cost of these devices is very high even for developed countries, and this is not our case. As for transplantations, they are undoubtedly a major advance in the treatment of this syndrome. Nevertheless, the cost-benefit ratio is far from satisfactory.

Multiprofessional heart failure clinics are a most welcome addition to these developments. Advice and information to patients and their respective families has shown that a good talk with clinicians, nurses, nutritionists, physical therapists, occupational therapists and other health professionals has diminished morbidity and mortality from this syndrome. For a country like ours, and even for the developed ones, it is good and cheaper. We have to revert to the thought that clinical picture is of paramount importance.

What should be the future perspectives for drug therapy in light of the situation presented? First, clinicians should always keep the word prevention in mind. When the level of impact of antihypertensive, lipid-lowering and hypoglycemic agents, as well as of weight reduction, on the reduction of heart failure incidence is analyzed, the results are moderate to good<sup>2</sup>. Therefore, heart failure can and must be prevented. Other diseases that affect the heart insidiously should be closely watched. As an example, I mentioned scleroderma<sup>15</sup>, among many others, that affect the myocardium before the onset of any symptom or sign of dysfunction.

The same is observed in asymptomatic chagasic individuals<sup>16</sup> who have abnormal electrocardiogram and normal cardiothoracic ratio, systolic function, volumes and wall thickness on echocardiogram. If these individuals undergo stress testing, subclinical dysfunctions will be detected. Even today, only one drug is available to specifically treat this disease, and even so its positive results have not yet been duly proven, in addition, it causes a high incidence of side effects<sup>17</sup>. Efforts have been driven toward the search of new parasiticides<sup>18</sup>. Also, how many of us consider the diagnosis of myocarditis for recent-onset cardiac dysfunctions<sup>19,20</sup>?

The discovery of new drugs that inhibit collagen deposition, and even reabsorb it, as well as other fiber protectors that have the potential to protect and/or increase intramyocardial circulation should be pursued. Lately, only agents with a preferential peripheral action in the neurohormonal axes have been launched or are being studied. However, the key problem is the “core”, the heart, which is more difficult to be studied. Our poverty, in this sense, is illustrated by digitalis compounds, the only positive inotropic agents approved for chronic use in the past 200 years<sup>21</sup>.

It is up to us to change this situation. We need better results, at lower costs. Our duty is to seek, and not only to disseminate. This is the duty of a true scholar.

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

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### Study Association

This study is not associated with any graduation program.

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