Impact of Basic Research on Advances in Cardiology

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The impact of basic research on advances in cardiology is undisputable. Didactically and simplistically speaking, we can identify four different levels of work in this field. Firstly, it enables the development of new treatments related to cardiology; in addition, basic research provides tools for studying various aspects of cardiovascular diseases; thirdly, new concepts can be created on topics already studied, and, finally we can use basic research to study the pathophysiological mechanisms involved in different pathologies.

In Brazil, the Brazilian Archives of Cardiology (ABC) play a prominent role on publications involving basic research in cardiology. Importantly, as discussed below, the journal has been contributing with expertise covering the four levels of work, as previously cited.

Taking into account the development of new treatments, several recent publications have addressed this issue. Interestingly, we can identify several research areas emphasizing new treatments for cardiovascular disease. For example, the dietary manipulation was one of the main areas within the journal. Indeed, a study with animals that underwent hypercaloric diet revealed that obesity induced a decreased vascular reactivity associated to changes in the L-arginine/nitric oxide pathway. Conversely, it was shown that a slight caloric restriction was accompanied by changes in gene expression of different proteins related to the calcium handling. Specifically, the authors have found increased mRNA of SERCA2a, phospholamban and the Na/Ca exchanger, suggesting beneficial adaptations with food restriction. Another group showed that supplementation of vitamin C at a daily dose of 500 mg induced lower levels of blood pressure and restored the peripheral vasodilator response in obese children. A further example of dietary manipulation can be seen in the study by Soares Filho et al., in which spontaneously hypertensive rats subjected to physical exercise and supplementation with red wine showed a reduction in blood pressure levels and increased HDL, compared to control animals or those undergoing individual treatments. These examples show that cardiology and nutrition have an important interaction in the journal, as it has been occurring in high-impact journals across the world.

However, the study of new treatment options was not restricted to the area of nutrition. Thus, another research area on basic issues with a significant number of publications in recent years in the ABC was the physical training. For example, the effects of different rest intervals between sets of resistance exercise on post-exercise blood pressure were studied in non-hypertensive sedentary young males. The recovery interval did not influence the reduction of systolic blood pressure, but there was a decrease in diastolic pressure lasting up to 30 minutes. Also during resistance exercise, the influence of the number of maximum repetitions and rest intervals between sets in twenty healthy individuals was investigated. Cardiovascular responses were affected by the load and the interval between sets. Another study showed that a swimming training program attenuated the contractile dysfunction in diabetic rat cardiomyocytes. A model of heart failure induced by sympathetic hyperactivity studied the combined effects of two interventions commonly used in the treatment of ventricular dysfunction: physical exercise and beta-blockers. The combination of these two interventions resulted in functional improvement and attenuation of cardiac remodeling. We should consider that the fact that the issue of exercise is extensively discussed in the journal is in agreement with what occurs in other publications, while emphasizing the importance of the theme.

As mentioned earlier, another important level of work refers to the fact that basic research provides new concepts on topics exhaustively studied. Accordingly, the ABC has been playing their role, particularly on two different areas of research.

The first area refers to the effects of smoking on the heart. Thus, although the effect of smoking on blood vessels is universally accepted, until recently, little was known about the morphological and functional cardiac changes induced by exposure to cigarette smoke. Castardeli et al. studied the effects of smoking on several cardiac variables. After four months of exposure, smoking animals presented increased mass index and left ventricular end systolic and diastolic diameters associated with worsening of fractional shortening and ejection fraction. These results have occurred in addition to the well-known effects of smoking on the vascular system. Importantly, this work became the reference article on the subject, while it introduced a new area of research in the journal. For example, it was later shown that propranolol attenuated the remodeling induced by smoking, suggesting the involvement of the sympathetic system in this process.

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In another experiment, it was found that smoking animals had four different left ventricular geometric patterns, considering the index of mass and the relative wall thickness: normal pattern (51%), eccentric hypertrophy (32%), concentric hypertrophy (13%), and concentric remodeling (4%). These findings reveal that animals with the same characteristics respond differently when subjected to the same aggressor. In a recent study, exposure to cigarette smoke for three weeks did not alter the baroreflex sensitivity in normotensive rats.

The second research area that is present in the journal deals with new concepts using echocardiography. This equipment is one of the methods of choice for cardiac morphological and functional analysis in rats because it is reliable, practical and noninvasive, which enables time-based analyses. This instrument has also been used consistently in the ABC for monitoring the process of cardiac remodeling secondary to various stimuli, particularly after experimental acute myocardial infarction. Initially, the Doppler echocardiogram presented high sensitivity and specificity for the detection of large infarcts in the chronic phase and identified signs of increased ventricular cavity and pulmonary artery pressure. Subsequently, it was shown that animals subjected to myocardial infarction presented two patterns of left ventricular geometry which were not factors predictive of ventricular dysfunction. In the same vein, the sphericity index was associated, but it was not a predictor of ventricular dysfunction in infarcted rats. Additionally, it was found that the rate of left ventricular wall stress was an independent predictor of ventricular dysfunction in infarcted rats. In another model, echocardiography was used in the temporal characterization of morphological and functional cardiac abnormalities associated with supravalvar aortic stenosis. Therefore, a robust area of research is characterized in the field of echocardiography in rodents, with significant contributions from the ABC.

The journal has also addressed the ability of basic research in providing tools for the study of cardiovascular disease. Clearly enough, the main tool addressed in the publications of the ABC was molecular biology, particularly for the study of mutations and polymorphisms. Thus, in two families with long QT syndrome, a strategy was developed to identify variants of genes KCNQ1, KCNH2, and SCN5A, linked to ionic channels. Evaluating the influence of polymorphisms in lipid metabolism, variations in genes APOA1, SCARB1 and CETB influenced HDL levels in people from the Southern portion of Brazil. Analyzing the relevance of genetic variants and insulin resistance in patients with diabetes, we found no association between the polymorphism K121Q of gene ENPP1 and the presence of ischemic heart disease. Concerning ischemic heart disease, the absence of the allele *235T of angiotensinogen decreased the risk of cardiac dysfunction after acute coronary syndromes. Finally, in patients from the state of Espírito Santo with hypertrophic cardiomyopathy, the relevance of mutations related to the muscle was evidenced by the association of the mutation p.E441K in exon 16 of gene MYBPC3 with a less severe phenotype. Moreover, the mutation p.R92W in exon 9 of gene TNNT2 was associated with severe forms of hypertrophy.

Finally, another area in which basic research has been widely addressed in the journal is the study of the pathophysiological mechanisms involved in several pathologies. We can mention three examples in this area. An issue that has been studied extensively in recent years relates to the effects of obesity on functional and morphological cardiac variables. Thus, the mechanism of cardiac dysfunction was studied in obesity. It was found that functional worsening in research studies involving obese rats was associated with changes in the activation of Serca2a through activation of calmodulin kinase. In another area, in evaluating the hemodynamic effects of right ventricular overload promoted by the selective obstruction of the pulmonary vasculature in pigs, the authors found that, despite the intense right ventricular overload promoted by the obstruction of 82.0% of the pulmonary vasculature and the significant increase in pulmonary artery pressure, no severe cardiovascular dysfunction and/or circulatory shock was found during the period studied. Finally, we studied the effects of angiotensin-I and ischemia in the functional recovery in isolated hearts. The data suggested that angiotensin-II participates directly or indirectly in post-ischemic damage and the ability of an angiotensin-converting enzyme inhibitor in mitigating this damage depends on the time of ischemia.

For these reasons, the analysis of some of the latest works in the basic/experimental area in the ABC delivers three conclusions. Firstly, it is evident that there is a strong association between clinical and basic research, and that this interaction occurs in both directions, because in some situations, the clinical observations lead to the study of the mechanisms involved through basic research. Additionally, it is evident that some preferred research areas are published in the journal, especially nutrition, the study of polymorphisms, the effects of smoking in the process of cardiac remodeling, echocardiography in rodents and study of the pathophysiological mechanisms involved in several pathologies. Finally, we are pleased to find that on the four potential levels of work of basic research, the high quality of publications resulted in important contributions to this field of knowledge.
References


