Letters to the Editor

Are some of the last advances in cardiovascular therapeutics fighting against the historic evolution of the heart and the cardiovascular system?

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Human race as we know it nowadays has been favored by progressive evolutionary changes aimed to make us more resistant to the environment. The heart and cardiovascular system play an important role in this process and comparative analysis has yielded some relevant evolutionary adaptations in comparison to reptiles, amphibians and, even, other mammals [1]. Nonetheless, the progressive increase of life expectancy and the relevant changes in lifestyle and dietary patterns adopted by humankind in the last 6 decades have exposed us to hazards against which we might not be biologically prepared. Most of these threats are directly involved in the incidence of cardiovascular disease, which has emerged as the leading cause of death in humans [2]. We aim to review, with four examples, how some advances in cardiovascular therapeutics seem to run against human evolution or, even, lead to regress to previous stages.

First, by the development of monoclonal antibodies against the proprotein convertase subtilisin/kevin type 9 (PCSK-9), a protease involved in the degradation of the hepatic receptor for low-density lipoprotein (LDL), PCSK-9 binds such receptor and induces its degradation which reduces the hepatic LDL uptake and increases serum LDL [3]. PCSK-9 seems to be a gerontologic remnant, developed to maintain serum LDL levels during the long periods of fasting of primitive humans.

Nonetheless, it has a deleterious effect on lipid profile and several contemporary studies have demonstrated that subjects with lower PCSK-9 activity, mainly due to nonsense mutations, have 12% lower serum LDL-cholesterol levels and around 28% lower risk of cardiovascular mortality or coronary heart disease incidence [4]. These findings have encouraged the development of selective antibodies but the clinical benefit of this therapy will be clarified by the clinical trials that are about to start in 2013.

A second example could be the exclusion of the left atrial appendage (LAA) for stroke prevention in patients with atrial fibrillation. LAA could emerge during human evolution as a structure not only to collect blood in prevention of severe bleeding but also to secret atrial natriuretic hormone in cases of sodium overload [5]. The long-term effect of LAA exclusions on hemodynamic and hormonal balance might challenge some many protective systems.

The third example is based on neurohormonal treatments. The renin–angiotensin–aldosterone system (RAAS) is the most important volume regulator in vertebrates and appeared through the Precambrian and Paleozoic eras as the result of the long evolutionary specialization of an ancient protease [6]. An abnormal activation of the RAAS and the sympathetic nervous system are the main compensatory mechanisms started up to maintain homeostasis when myocardial injury and remodeling are produced; but chronic exposure to RAAS produces tissue fibrosis, vasoconstriction, and sodium retention, a “vicious cycle” which eventually leads to end-stage heart failure and death. Agents that block the RAAS have been developed to counteract those detrimental effects and clinical trials have shown their large protective effect on vascular organs and cardiovascular prognosis [2]. As consequence, a mechanism was developed to allow out-of-water living turns to be first-line target to block after overt cardiovascular injury [7].

This leads us to the last example: renal denervation. The sympathetic nervous system is crucial in the initiation and maintenance of hypertension, considered the background of a complex interaction between multiple other mechanisms (that are beyond the scope of this manuscript). Recent advances have developed catheter-based renal denervation as a minimally invasive strategy to treat resistant hypertension and have shown encouraging intermediate-term results with minimal complications [8]; we now need to clarify its long-term effect because the abolishment of such an important mechanism for survival such in case of massive bleeding, severe congestive heart failure or sleep apnea is unknown.

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In conclusion, we believe that these four examples reflect how cardiovascular investigation might be seeking regression to previous stages of the human species. Current situation of humans is past centuries in our history: larger longevity, more sedentary and more prone to atherosclerosis. Adapting the lifestyle of the humans in past centuries to current habitat and habits is a great challenge for public health and encouraging healthy lifestyle could be crucial [9]. Furthermore, present and future cardiovascular therapeutics also face the challenge of developing strategies to provide health and the best quality of life to a human race not adapted to its contemporary habitat. Some of the medical advances in cardiovascular therapeutics seem to look for anti-evolution effects and we raise the question of whether they are reasonable for reversion of evolutionary advances of homankind or should we focus on re-adopting past habits.

References

Effects of bariatric surgery on cardiac remodeling: Clinical and pathophysiologic implications

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Obesity produces a variety of cardiac structural changes and hemodynamic alterations that can lead to the obesity cardiomyopathy [1]; moreover, each unit increase of body mass index (BMI) is associated with a 2-fold increased risk of heart failure [2]. Several studies report beneficial effects of weight loss on cardiac function [3,4] but systematic studies on the effects of surgically-induced weight loss as compared to the effects of persistent morbid obesity are lacking.

To this aim we conducted a prospective, longitudinal, echocardiographic study including 100 morbidly obese patients (BMI 47.7 ± 7 kg/m2; 43 males) referred for bariatric surgery (BS). All patients prospectively underwent an echocardiogram. Sixty-five patients underwent BS, 35 patients did not and were used as controls. Fifty-one operated and 29 non-operated patients underwent repeat imaging after 2 years. Exclusion criteria were: clinical, electrocardiographic or echocardiographic features of any cardiomyopathy secondary to a specific disease, primary pulmonary disease, technically poor echocardiograms.

Transthoracic echocardiograms were performed according to the recommendations of the European Society of Echocardiography [5] using a Toshiba Artida echocardiograph with a 2.25-MHz probe. All echocardiograms were digitized and re-analyzed off-line by a second blinded experienced operator. This study complies with the Declaration of Helsinki, the local ethics committee approved the research protocol and informed consent was obtained from all subjects.

Normal distribution was tested by the D’Agostino–Pearson’s test. Continuous variables were compared by t-test and ANOVA as appropriate. Correlations were evaluated by Pearson’s r tests. Categorical variables were compared with the use of Fischer’s exact test. Differences of p < 0.05 were considered significant. Statistical analyses were divided into 2 sets. In the first set we compared the measurements in patients who had undergone BS with the measurements in the control group. In particular, we analyzed the effect of BS on anthropometric and echocardiographic features performing a two-way ANOVA for repeated measures in operated patients and in controls. Then, we analyzed each group separately by paired t-tests. Finally, we compared the changes of anthropometric and echocardiographic features (variable at follow-up–variable at baseline) in operated patients vs controls using an unpaired t-test. For the second set of analyses we pooled the data from the entire