Correspondence

Letter by Fragasso et al Regarding Article by Tuunanen et al, "Free Fatty Acid Depletion Acutely Decreases Cardiac Work and Efficiency in Cardiomyopathic Heart Failure"

To the Editor:

We read with interest the study by Tuunanen et al,[1] which showed that acutely decreased serum free fatty acids (FFA) in patients with failing hearts further depress cardiac work. The authors, although considering these findings as unexpected, conclude that their results "argue against the important hypothesis that switching substrate metabolism acutely from FFA to glucose may be beneficial for the failing heart." We think that such a "hard" conclusion cannot be drawn from their results.

A situation similar to that observed in the study of Tuunanen et al can be mimicked by meal administration, which induces insulin release with prompt inhibition of lipolysis (insulin is the most potent inhibitor of lipolysis) and consequent drop of plasma FFA. In a previous study employing stress echocardiography, we showed that patients with stable coronary disease had a lower ischemic threshold and greater stress-induced left ventricular dysfunction after a meal with high carbohydrate content (ie, when the lowest FFA levels were observed). These adverse effects were improved by the partial fatty acid inhibitor trimetazidine. Conversely, a meal with high fat content (inducing a minor decrease of plasma FFA) did not yield significant adverse effects compared with the fasting state.[2]

We believe that the study by Tuunanen et al did not take into account that during their experimental procedure, acipimox could also have induced a marked decline in plasma insulin concentrations,[3] which were measured only in the basal state. As shown in Table 2 of their work, the drop in the plasma FFA concentration was also paralleled by a significant drop of plasma glucose. We believe that the simultaneous reduction of insulin and glucose concentration may work against an increase in cardiac glucose oxidation, as assumed but not measured by the authors.

Therefore, reduced FFA availability, without a concomitant induction of glycolysis, may not be enough to yield a positive effect. In fact, despite the fact that an increased supply of FFA will diminish the rate of glucose oxidation to a minimum, the opposite has not been proven. Therefore, we agree that just reducing FFA availability by acipimox may not be sufficient to optimize cardiac metabolism and, as a consequence, contractile function. Conversely, direct cellular FFA oxidation inhibitors may be the answer, as has been shown in recent studies.[4,5] Therefore, switching metabolic preferences, rather than starving, may be a better therapeutic strategy.

Disclosures

Dr Fragasso has given remunerated lectures on behalf of Servier International, the manufacturer of trimetazidine. Drs Perseghin and Palloshi report no conflicts.

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