Cardiac Resynchronization and Myocardial Oxidative Metabolism

To the Editor:

We read with great interest the recently published paper by Ukkonen et al. We authors concluded that cardiac resynchronization therapy (CRT) did not have any effect on global left or right ventricular oxidative metabolism (OM), suggesting that metabolic demand does not increase with CRT. Nevertheless, some concerns arise based on our experience and from careful review of the literature.

The new finding of the study by Ukkonen et al was that regional myocardial OM increases in the intraventricular septum as a result of CRT, although global OM was unaffected. However, the main question regarding this particular study is whether it represents acute or chronic effects of CRT. Although the patients of the study were receiving chronic CRT, the authors studied the effect of acute changes in pacing mode (2 hours of pacing in each mode). Consequently, they studied the acute effect on a chronic substrate, not the chronic effect of CRT.

Thus, the increase in OM of the intraventricular septum could be explained by the abolishment of left bundle branch block (LBBB) with atrioventricular pacing, since this was the conduction abnormality noticed in all patients and it is known to impair early diastolic coronary blood flow in the left anterior descending coronary artery. Additionally, in any chronic functional and structural changes that affect myocardial OM and coronary blood flow, at least in patients with permanent ventricular pacing, could not be assessed by the design of this study. Nevertheless, the relatively high OM of the right ventricle in comparison to that of the left ventricle supports the relative normality noticed in all patients and it is known to impair early diastolic coronary blood flow in the left anterior descending coronary artery.

In addition, any chronic functional and structural changes that affect myocardial OM and coronary blood flow, at least in patients with permanent ventricular pacing, could not be assessed by the design of this study. Nevertheless, the relatively high OM of the right ventricle in comparison to that of the left ventricle supports the relative normality noticed in all patients and it is known to impair early diastolic coronary blood flow in the left anterior descending coronary artery.

As they point out, the study was designed to evaluate the acute effect of cardiac resynchronization therapy (CRT) in patients already receiving it. Reverse remodeling after CRT may have explained the relatively smaller observed effect of CRT found in previous studies. Furthermore, the individual variation in stroke volume and systolic blood pressure values—rather than oxidative metabolism—likely accounts for the wide range of Work Metabolic Index observed.

As noted in our discussion, we share their opinion that the abolishment of left bundle branch block (LBBB) due to successful CRT is likely to explain the increase in oxidative metabolism in the intraventricular septum. Skalidis and Vardas note that blood flow may also be altered in LBBB. However, myocardial blood flow—rest or stress—was not assessed in this study. Further studies may be warranted in this area.

Skalidis and Vardas suggest that the increased right ventricular (RV) oxidative metabolism may be due to RV pacing. However, relatively increased RV oxidative metabolism has been previously reported in patients with congestive heart failure without pacing. Chronic RV pacing alone causes LBBB-like activation pattern and is known to have deleterious effects on LV perfusion and function. CRT improves this conduction abnormality and improves LV systolic and diastolic performance, congestive heart failure symptoms, and morbidity. Therefore, RV pacing data cannot be applied to evaluate the effects of CRT.

Recent data from Baller et al showed that long-term CRT decreases LV oxidative metabolism and increases LV efficiency. In conclusion, all the current data, including those from our study, show that CRT improves cardiac function without increasing cardiac oxidative metabolism.

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Response

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