Improvement of myocardial efficiency in a patient with hypertrophic obstructive cardiomyopathy after alcohol septal ablation

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Abstract

A 70-year-old female patient presented with symptomatic hypertrophic obstructive cardiomyopathy (HOCM). Reduction of the left ventricular outflow tract obstruction by alcohol septal ablation is an established treatment strategy in patients with HOCM who remain symptomatic despite optimal medical treatment. Forward left ventricular stroke work, myocardial oxygen consumption, and myocardial efficiency were measured using cardiac magnetic resonance and positron emission tomography. Myocardial oxygen consumption was unchanged after reduction of the left ventricular outflow tract obstruction, but forward left ventricular stroke work per gram of myocardium was greater after the procedure. Alcohol septal ablation therefore improved the myocardial efficiency in this patient with HOCM.

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Case report

A 70-year-old female experienced dyspnea whilst cycling in 2001. At first, this exertional dyspnea was attributed to her moderate obesity (90kg, 1.70 m), but despite weight reduction, her symptoms slowly progressed. In 2006, she was unable to walk two flights of stairs without resting, because of severe shortness of breath. An electrocardiogram showed signs of left ventricular hypertrophy, so she was referred to a cardiologist for further evaluation. With cardiac magnetic resonance (CMR), hypertrophy of, mainly, the basal anteroseptal segment of the left ventricle was found, together with moderate-to-severe
eccentric mitral regurgitation (Figure 1). In addition, a gradient over the left ventricular outflow tract (LVOT) of 30 mm Hg at rest increased to 80 mm Hg after 10 knee bends. The patient was diagnosed with hypertrophic obstructive cardiomyopathy (HOCM), and was initially treated with diltiazem SR 200 mg. However, her symptoms did not improve, and she was therefore referred for alcohol septal ablation (ASA), for relief of her symptoms.

Hypertrophic cardiomyopathy (HCM) is an inheritable disease that is caused by mutations in genes that mainly encode for sarcomeric proteins. It is characterized macroscopically by left ventricular hypertrophy in the absence of any disease likely to cause this hypertrophy, such as systemic hypertension or aortic stenosis. At the cellular level, the HCM mutations are believed to cause an increased calcium sensitivity of the sarcomeres. Although calcium homeostasis can be considered the driving force behind the contraction–relaxation cycle, the increased calcium sensitivity of sarcomeres is suggested to cause ‘‘hypercontractility’’ and impaired relaxation, whereas actin and myosin myofilaments may remain able to interact even at very low diastolic concentrations of calcium [1]. This metabolically inefficient functioning of the sarcomere may cause the myocyte to be less adaptive to altered loading conditions, which is an important trigger for the development of hypertrophy [2].

When hypertrophy develops, increased extracellular collagen depositions are found (interstitial fibrosis) in the myocardium of carriers of the HCM mutation, together with disorganization of the myocardial architecture (myocyte disarray), and microvascular dysfunction [3]. These processes may further compromise myocardial function, and in turn might trigger more hypertrophy. Overall, the HCM mutations initiate a vicious cycle of molecular perturbations that, ultimately, lead to the clinical manifestation of disease.

The hypertrophy in HCM typically involves the interventricular septum and, when progressive, causes dynamic LVOT obstruction. The LVOT obstruction results in greater intracavitary wall stress and increased blood flow velocities within the LVOT tract during systole, through the Venturi effect, which subsequently causes systolic anterior motion of the anterior mitral valve leaflet towards the septum and eccentric mitral valve regurgitation (Figure 1). The

Figure 1. Cardiac magnetic resonance three-chamber cine image in end-diastole (left) and end-systole (right) of a patient with hypertrophic obstructive cardiomyopathy before alcohol septal ablation. Note that the obstruction of the left outflow tract (red arrow) causes severe eccentric mitral regurgitation (yellow arrow).

Figure 2. Cardiac magnetic resonance three-chamber cine image of a patient with hypertrophic obstructive cardiomyopathy after alcohol septal ablation. In the left panel, the induced infarct is clearly visible (blue arrow). Subsequently, left ventricular outflow tract obstruction is substantially reduced (middle panel, red arrow), and mitral regurgitation is almost completely resolved (right panel, yellow arrow).
increased external work, or stroke work, may further impair myocardial efficiency. Although no definitive treatment of the disease is yet available, symptomatic relief of HCM may be provided by reduction of the LVOT obstruction, by either surgery or ASA [4]. The latter involves the percutaneous injection of a small amount of alcohol (1–5 ml) into one of the most proximal septal branches of the left coronary artery, causing a localized myocardial infarction and subsequent scarring at the level of the LVOT obstruction. This procedure has proven to be effective in reducing the LVOT obstruction and concomitant mitral regurgitation, which, importantly, results in relief of symptoms.

To monitor the effect of treatment on myocardial efficiency, CMR was performed before and 6 months after the procedure for measurement of mass, and to quantify flow in the aorta to determine forward left ventricular stroke volume. Stroke volume was measured in the aorta to avoid overestimation of effective volume through mitral regurgitation. In addition, scar tissue can be visualized with CMR by using late gadolinium enhancement imaging. Directly before the CMR acquisition, dynamic carbon-11-labeled acetate ([11C]acetate) positron emission tomography (PET) was performed. The transfer of [11C] activity from [11C]acetate to [11C]carbon dioxide is strongly related to oxidative metabolism, and the rate of clearance of [11C]acetate is regarded as an adequate index of oxygen consumption and is expressed as $k_{\text{mono}}$ [5]. Myocardial efficiency can be estimated from the ratio of forward left ventricular (LV) stroke work (systolic blood pressure × forward LV stroke volume × heart rate) and the rate of clearance of [11C]acetate per gram [6].

Six months after the procedure, the patient’s symptoms improved, and she was able to walk two flights of stairs again without taking a rest (“...and even do it again directly afterwards to get my keys if I have to...”). A significant reduction of the LVOT obstruction was observed on the CMR images, and a residual resting gradient of 7 mm Hg was measured (Figure 2). In addition, mitral regurgitation was almost completely resolved. On late gadolinium enhancement image, the localized iatrogenic infarct in the anteroseptal segment of the left ventricle was clearly visible.

Before the ASA, left ventricular mass index was 96 g m$^{-2}$, forward left ventricular stroke work was 6.45 mm Hg L g$^{-1}$ min$^{-1}$ and $k_{\text{mono}}$ was 0.054 units min$^{-1}$. After ASA, left ventricular mass index was reduced to 57 g m$^{-2}$, forward left ventricular stroke work was increased to 7.85 mm Hg L g$^{-1}$ min$^{-1}$, and $k_{\text{mono}}$ was reduced to 0.047 units min$^{-1}$. Consequently, myocardial efficiency was improved from 119 mm Hg L g$^{-1}$ min$^{-1}$ to 167 mm Hg L g$^{-1}$. Merged dynamic [11C]acetate activity and late gadolinium enhancement CMR images obtained before and after ASA showed mildly reduced oxygen consumption in the lateral wall in the presence of the scar (Figure 3).

In the patient reported here, we expected to observe an increased level of oxygen consumption before ASA, as a result of the increased left ventricular intracavitary wall stress caused by the LVOT obstruction. However, myocardial oxygen consumption before and after ASA were relatively comparable. We observed that the “pseudonormalization” of oxygen consumption before ASA occurred at the expense of a further increase in left ventricular hypertrophy, and subsequent normalization of wall stress. However, this mechanism of compensation decreases myocardial efficiency. Therefore, we can postulate from the data obtained from this patient that LVOT obstruction in patients with HCM reduces myocardial efficiency, and is restored after ASA.

REFERENCES

Case report
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