Myocardial contrast echocardiography: another discriminator of physiological and pathological left ventricular hypertrophy?

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This editorial refers to 'The relative myocardial blood volume differentiates between hypertensive heart disease and athlete’s heart in humans'† by A. Indermühl et al., on page 1571

Left ventricular (LV) hypertrophy is a structural and functional adaption to increased wall stress. For years, there has been an attempt to distinguish physiological hypertrophy, such as occurs in athletes, from pathological hypertrophy, such as occurs in patients with hypertension and hypertrophic cardiomyopathy. Physiological hypertrophy is characterized by normal systolic and diastolic cardiac function and metabolism, and a supranormal coronary vasodilator reserve. Pathological hypertrophy due to pressure overload arises from hypertrophy of myocytes and extracellular collagen deposition, which stiffens the left ventricle, impairs diastolic filling, and leads to reduced coronary vasodilator reserve. In the past, imaging modalities like cardiovascular magnetic resonance and magnetic resonance spectroscopy have assisted in the distinction of physiological vs. pathological hypertrophy. A potential new method in unravelling these different forms of LV hypertrophy may consist of myocardial contrast echocardiography.

The appropriate method to quantify myocardial blood flow in ml/min/g by contrast echocardiography in humans has been published for the first time in 2005 by Vogel et al. The method is based on the assessment of refill curves of ultrasound contrast agent after the ultrasound-induced microsphere destruction during continuous infusion of ultrasound contrast agent. The density of subsequently acquired images shows a refill curve that can be fitted by $y(t) = A * (1 - e^{-t/\beta})$ in which $y(t)$ is the time-dependent density, $A$ is the myocardial plateau signal intensity, and $\beta$ is the rate constant of the density rise. The value of $A$ represents microvascular cross-sectional area, and depends on the concentration of ultrasound contrast agent, scanner settings, and acoustic tissue properties. The value of $\beta$ represents microsphere velocity. Earlier, it has been shown that, in the dog heart, $\beta$ and the product $A*\beta$ are semiquantitative estimates of myocardial blood flow. Vogel et al. proposed a volumetric model and the equation myocardial blood flow $= (rBV*$ $\beta$ $)/P_T$, in which $rBV$ is the relative blood volume and $P_T$ is the tissue density ($= 1.05$ g/mL). The value of relative blood volume is approximated by $A/A_{LV}$ which is the myocardial plateau signal intensity $A$ divided by the signal intensity of an adjacent region of the left ventricle $A_{LV}$. In a phantom model mimicking microcirculation and macrocirculation, volumetric pump flow could be estimated on the basis of $(rBV*$ $\beta$) quite well. In the protocol with normal individuals, myocardial blood flow values were collected using $^{13}$-ammonia positron emission tomography studies, under resting conditions and during maximal coronary hyperemia by intravenously administered adenosine. Under resting conditions and hyperaemia, myocardial blood flow by myocardial contrast angiography and myocardial blood flow by positron emission tomography showed good agreement. Patients underwent coronary angiography to localize ischaemic areas. By calculating myocardial blood flow by myocardial contrast angiography at rest and during maximal hyperaemia, myocardial perfusion reserve was calculated which correlated well with coronary flow velocity reserve determined by intracoronary Doppler wire measurements ($r = 0.85$). Vogel et al. concluded from their validation study results that quantification of myocardial blood flow in humans using myocardial contrast echocardiography is feasible and accurate.

Indermühl et al. measured relative blood volume, exchange frequency ($\beta$) and regional myocardial blood flow using myocardial contrast echocardiography in hypertensive patients, triathletes, football players, and sedentary individuals. This study was set up to clarify the postulated differences of the microvascular response in hypertensive and athletic LV hypertrophy. Compared with sedentary individuals, hypertensives had lower relative blood volume and higher $\beta$, whereas well-trained athletes had higher relative blood volume and lower $\beta$ than sedentary individuals. Although myocardial blood flow was equal in all four groups at rest, myocardial blood flow during adenosine-induced hyperaemia was generally lower in hypertensives and generally higher in triathletes than in sedentary individuals. The highest LV mass was found in the hypertensive group. However, LV mass was lower in the triathletes, lower...
in the football players, and lowest in the sedentary individuals. Thus, LV hypertrophy per se does not explain the findings of Indermühl et al.\textsuperscript{1,4} In the pressure-overloaded hypertrophied heart, myocardial capillary density is subnormal and myocardial arterioles exhibit medial hypertrophy, leading to subnormal coronary reserve particularly in the subendocardium.\textsuperscript{5-8} However, hypertrophic hearts of exercise-trained experimental animals demonstrate myocardial capillary density that has adapted to cardiomyocyte hypertrophy.\textsuperscript{9} Pluim et al.\textsuperscript{1} have investigated the response of myocardial high-energy phosphate metabolism to high work loads induced by atropine–dobutamine stress in elite cyclists having a mean LV mass index of 102 g/m\textsuperscript{2} and sedentary individuals having a mean LV mass index of 69 g/m\textsuperscript{2}. They showed that the myocardial phosphocreatine (PCr) to adenosine triphosphate (ATP) ratio measured with \textsuperscript{1}HPhosphorus magnetic resonance spectroscopy during atropine–dobutamine stress (1.41) did not differ between elite cyclists and sedentary individuals, nor did this ratio differ at rest between the two groups (1.21 and 1.16, respectively).\textsuperscript{1} However, if this test protocol was applied to patients with hypertensive heart disease having a mean LV mass index of 98 g/m\textsuperscript{2}, myocardial PCr/ATP ratio during stress was significantly lower than that of sedentary individuals having a mean LV mass index of 73 g/m\textsuperscript{2} (0.95 vs. 1.16, respectively); this difference was even evident at rest (1.20 vs. 1.39, respectively).\textsuperscript{10} These results clearly demonstrate a difference in myocardial high-energy phosphate metabolism independent from the severity of LV hypertrophy. The study by Indermühl et al.\textsuperscript{4} provides information about the pathophysiological alterations of myocardial perfusion in stressed hypertrophic myocardium of hypertensive patients which was compared with physiological alterations of myocardial perfusion in stressed hypertrophic myocardium of well-trained athletes. A subnormal regional blood volume found in hypertensives vs. a normal regional blood volume in triathletes, compared with regional blood volume of sedentary individuals—all determined under adenosine-induced stress—indicated reduced blood volume in the microcirculation of hypertension-induced LV hypertrophy. However, the exchange frequency $\beta$ determined during stress did not differ between hypertensives and sedentary individuals, but was significantly increased in triathletes probably due to an increase of arterial blood supply compensating for training-induced LV hypertrophy. These mechanisms lead to subnormal myocardial perfusion during stress in hypertensives and supranormal myocardial perfusion during stress in triathletes compared with sedentary individuals.

The advantages of the presented technique to measure regional myocardial blood flow by myocardial contrast echocardiography are its quantification in absolute units and the non-invasive acquisition of data. As to application in patients with coronary artery disease, the consequences of angiography-assessed coronary artery stenoses can be quantified to obtain a measure of regional myocardial ischaemia.

As a result, the study by Indermühl et al.\textsuperscript{4} has clearly shown that myocardial contrast echocardiography is quite capable of distinguishing physiological hypertrophy in athletes from pathological hypertropy in hypertensive patients. Further studies in this field seem warranted as this imaging modality might also be used for the distinction between hypertensive patients and patients with hypertrophic cardiomyopathy, because vasodilator reserve is more reduced in hypertrophic cardiomyopathy than in hypertensive patients. Myocardial contrast echocardiography can therefore be considered as an additional valuable discriminator of physiological vs. pathological LV hypertrophy.

Conflict of interest: none declared.

References