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Editorial

The many applications of stress echocardiography in heart transplantation

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In the current issue of the Journal, dual imaging vasodilator stress echocardiography (SE) with combined assessment of regional wall motion abnormalities and coronary flow velocity reserve shows excellent feasibility and negative predictive value for excluding significant cardiac allograft vasculopathy (CAV) in patients evaluated after heart transplantation (HT) [1]. These results add further evidence to previous similar experiences showing that SE can offer several opportunities in HT setting for acute and chronic rejection surveillance and heart recruitment from marginal donors.

Since first HT performed in South Africa in 1967, and particularly after introduction of cyclosporine-based immunosuppression in 1970s, HT has spread worldwide, becoming the standard treatment for end-stage heart failure. In the last decade, amount of HTs has stabilized because of the limited number of donors. Nowadays, about 5500 HT are performed every year worldwide [2].

In HT patients, pharmacological SE is chosen instead of exercise SE because of the cardiac denervation leading to blunted chronotropic response to physical exercise [3]. Different conditions can be identified with different markers during SE. Antibody-mediated rejection targets the endothelium of small coronary vessels. Acute rejection is characterized by an acute impairment of coronary microcirculatory function which can be best detected as a reduction in coronary flow velocity reserve. SE information is added to resting transthoracic echocardiography, which may show increased wall thickness and wall echogenicity, pericardial effusion, left ventricular diastolic dysfunction, and regional or global diastolic dysfunction.

The target of chronic rejection is CAV which is a major limiting factor for long-term prognosis. The epicardial vessel involvement can cause ischemia and regional wall motion abnormalities and/or a reduction in coronary flow velocity reserve also due to concomitant increase in microvascular resistances [4].

Early stages of CAV can be identified through the evaluation of the coronary flow reserve, which may result impaired before any abnormalities of epicardial vessels become detectable [5]. Furthermore, a negative coronary angiography (CA) does not exclude a functionally relevant CAV, which may conversely be mirrored by wall motion abnormalities during SE. If SE shows abnormalities, CA is performed, and if this test does not yield evidence of CAV, an additional intravascular ultrasound study may be warranted [6], also due to its ability to identify intimal thickening in two thirds of patients with normal CA.

This approach helps to avoid repeat cardiac catheterization in some patients and leads to closer surveillance of patients with functionally relevant and/or progressive CAV. This aspect of radiation-free surveillance of HT patients is especially important in pediatric patients, who are 4-times more sensitive to oncogenic effects of radiation exposure [7]. Also adults receive high cumulative radiation exposure from cardiac diagnostic and therapeutic procedures after HT and show an increased risk of cancer possibly for the combined effects of immunosuppression and radiation exposure. Therefore a radiation-sparing diagnostic policy is welcome in these patients, when it leads to no loss in accuracy. Dual imaging vasodilator SE can replace scintigraphy and may reduce the need of CA, considering the highly negative prognostic value of the combined evaluation of coronary flow reserve and wall motion abnormalities.

A third aspect of SE is its potential role in the recruitment of donor hearts to minimize the problem of organ donation. If a patient aged >55 years or with coronary risk factors has a negative SE, without rest or stress-induced regional wall motion abnormalities, and with preserved global left ventricular contractile reserve, it can be safely used for donation. In Italy, at present 50 hearts have been used for HT with this SE-driven approach in the last 10 years [8].

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1. Stress echo in clinical guidelines

The International Society of Heart and Lung Transplantation Guidelines for the care of HT recipient recognize that SE "*may be useful for the detection of cardiac allograft vasculopathy in heart transplant recipients unable to undergo invasive evaluations*" [9]. SE has been included in national recommendations of the Italian Transplant Center to encourage the selection of marginal (age > 55 years) donors to limit the current shortage of hearts for cardiac transplantation. The recent recommendations of the European Association of Cardiovascular Imaging and Brazilian Society of Cardiology for the use of cardiac imaging in patients after HT suggest that pharmacological SE might be a suitable alternative to routine CA to assess CAV at centers with adequate experience with the methodology, and coronary flow velocity reserve might be combined with SE to improve the accuracy of the test [10] – which can otherwise remain unsatisfactory if based only on wall motion abnormalities.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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