



Scientific Comment

Haemoglobinopathies from the cardiac point of view



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ARTICLE INFO

Article history:

Received 9 May 2019

Accepted 9 May 2019

Available online 23 July 2019

Heart disease is a leading cause of mortality and the main determinant of prognosis in haemoglobinopathies as beta-thalassaemia (β T) and sickle cell disease (SCD). Cardiac involvement is affected not only by the molecular defect causing chronic haemolysis, but also by the therapeutic requirements involving transfusion and chelation therapy.¹ Chronic haemolysis causes anemia and then a high cardiac output state.² Repetitive haemotransfusions, on the other hand, leads to myocardial iron deposition, which can evolve to a pattern of Restrictive Cardiomyopathy.

Two geometric patterns of left ventricle (LV) remodeling can be observed although they are not exclusive. High output Cardiomyopathy is characterized by a kind of Dilated Cardiomyopathy (CMP), with left chamber dilatation secondary to overload, eccentric LV hypertrophy, and in general, a preserved LV ejection fraction. Diastolic function of LV can be severely altered in a proportion of patients even before systolic dysfunction.³ Myocardial ischemia can happen in a subset of patients with this physiopathology and can contribute to further LV systolic dysfunction.

Restrictive Cardiomyopathy secondary to iron overload is associated to chronic transfusions. It is characterized by LV thickness and concentric pattern of hypertrophy, also

associated to diastolic LV dysfunction and left atria (LA) enlargement. LV ejection fraction is also usually preserved until a late phase of disease. Two variables can be of particular importance in iron deposition and cardiac alterations: the necessity of transfusion and the combined iron chelation therapy.^{1,4,5} These variables can be very difficult to control in scientific studies. Although iron overload CMP is more prevalent in β T patients, an incidence of 2–5% is described in SCD patients.⁶

Detection of CMP in this heterogeneous group of patients can be a challenge. Echocardiography is a very useful image method able to identify geometric and functional changes in all cardiac chambers. However, LV ejection fraction, although being a so robust measurement of systolic LV function, is not a sensitive parameter of incipient myocardial damage. LA volume and LV diastolic parameters as mitral annulus Tissue Doppler are usually early compromised in β T patients.^{7,8} LV diastolic dysfunction is also very prevalent in SCD patients, as high as 30%.⁸ Right ventricle involvement can also be detected by echocardiography associated or not to pulmonary hypertension.^{9–11} Myocardial deformation analysis from bidimensional speckle tracking echocardiography is a very sensitive tool able to detect incipient myocardial

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<https://doi.org/10.1016/j.htct.2019.05.002>

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damage in several CMP. The technique is based on tracking of bidimensional speckles and is relatively independent of load conditions. Although it is not really a measurement of myocardial contractility it is very close to it. Few studies have tested global longitudinal strain (GLS) in patients with haemoglobinopathies. Whipple et al. in 2018 studied a large number of children with SCD evaluating myocardial deformation of both ventricles. Although there was no significant difference in LV GLS from controls, RV GLS of SCD patients (and not of controls) decreased with aging and it was associated with LA enlargement and LV volume increase.¹² In another study of strain echocardiography, applied to patients with β T, Odoardo et al. compared LV global indexes of deformation with the cardiac magnetic resonance (CMR) index T2*, a marker of myocardial iron deposit. Significant reductions of strain indexes were found in β T patients compared to controls. However, no correlation of strain parameters and T2* was demonstrated, reinforcing the concept that iron deposition is not the only determinant of myocardial damage.¹³

CMR has been established as the only non-invasive method of detection of myocardium iron deposit. T2* technique, which is based on heterogeneity of magnetic field imposed by iron deposition on tissues, was validated to myocardium decades ago. It was also demonstrated as a strong predictor of myocardial dysfunction at evolution of patients with haemoglobinopathies.¹⁴ The CMR ability to measure both cardiac function and iron deposition and further to evaluate liver deposition in the same scan has revolutionized the understanding of iron storage disease. Introduction of routinely CMR evaluation for patients with haemoglobinopathy, specially those with β T, has changed prognosis of this group of patients.¹⁵

Regardless of this complex diagnosis scenario, there is a group of patients with a double heterozygosity of SCD and β T, which leads to the clinical expression of a variant of SCD. This condition has a considerable prevalence in Brazil and cardiac alterations of a sample of these patients were studied by Benites et al.¹⁶ and presented at this journal. There were no cardiac geometry alterations neither differences in LV systolic function between SCD variant patients and controls when evaluated by conventional echocardiographic indexes. Results probably reflect what was pointed before about the difficulties to demonstrate early myocardial damage in this group of patients with conventional echocardiographic measurements. New techniques able to detect myocardial damage as strain echocardiography may play an important role in this so special disease.

Conflicts of interest

The author declares no conflicts of interest.

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