Heart Failure in β-thalassemia: A Local or Universal health problem?

Demetris Kremastinos
Professor of Cardiology Athens University, Attikon University Hospital , Athens Greece.

B-thalassemia belongs to the group of Hemoglobinopathies which are the most common monogenic disorders in the world population, and they were the first diseases to be analyzed by recombinant DNA technology.
Homozygous β-thalassemia is characterized by severe hemolytic anemia associated with chronic organ damage and high incidence of infections. It is well expanded beyond the borders of Mediterranean Sea extending in a line to countries of Middle and Far East. However, in our days, β-thalassemia seems to become a universal health problem since thousands of people have emigrated from these countries to the EU and USA
Despite progress in chelation therapy, heart failure is still the main cause of death in patients with β-thalassemia major since approximately 70-80% of β-thalassemic patients die of heart failure. (1,2)
Iron deposition is considered the fundamental aetiologic factor of organs dysfunction and failure in this disease. However, in the pathogenesis of heart failure immunogenetic abnormalities and myopericarditis undoubtedly contribute. The severity of iron toxicity in β-thalassemia major seems to be related to the magnitude of the body iron burden. The exact mechanism of iron overload toxicity has been uncertain for many years. Via the iron-driven Fenton and Haber-Weiss reactions, the nontransferrin plasma iron, in its bivalent or trivalent form, has a high toxicity through the formation of hydroxyl radicals (OH). This leads to peroxidative damage of membrane lipids and proteins. Imbalance between production of oxygen free radicals and antioxidant defense mechanisms can result in odixative stress and human disease. In the heart, the imbalance between free radicals and antioxidant mechanisms is manifested as impaired function of the mitochondrial inner-membrane respiratory chain resulting in abnormal energy metabolism expressed clinically with fatal cardiomyopathy. Apart from iron overload, it has been recently shown by our group that myocarditis appears to be involved in the pathogenesis of left ventricular failure in approximately 4% of patients with heart failure. As shown in animal models, oxygen free radicals may also contribute to the pathogenesis of infectious myocarditis.(3,4,5,6,7)
The clinical presentation of heart failure is mainly expressed as left ventricular systolic or diastolic dysfunction. Diastolic dysfunction appears early in the patients life, progresses slowly, and leads to left ventricular restrictive abnormalities, pulmonary hypertension, right ventricular dilatation and failure. (8)
Systolic dysfunction is presented as dilated type of cardiomyopathy leading to death within one year since the onset of heart failure symptoms. (9)
However, by increasing the total number of blood transfusions and intensification of iron chelation therapy we reported a five-year survival 48%, approximately similar to the survival observed in the general population with heart failure.(9)

Myocardial iron deposition does not affect LV relaxation but directly causes LV myocardial diastolic dysfunction, which is expressed as echo-Doppler restrictive pattern. (10)
Meanwhile it was also reported recently that echo-Doppler indices do not detect mild diastolic dysfunction which is characterized by increased filling pressures at exertion. (11,12)
In this respect we found that the increased level of NT - pro BNP biomarker expresses LV early diastolic dysfunction before the conventional echo-Doppler indices become apparently abnormal in patients with β-thalassemia major. (13)
Therefore, this biomarker may be used in clinical practice, since a progressive increase in NT-pro BNP for an individual patient could be a signal for intensification of chelation therapy and improvement in hemoglobin levels before the heart failure symptoms become apparent. This strategy is expected to further improve the life expectancy of β-thalassemic population.

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