

President's Page

 β -Thalassemia Heart Disease: Is It Time for Its Recognition as a Distinct Cardiomyopathy?

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The Hellenic Cardiology Society took the initiative to organize a special workshop on β -thalassemia cardiomyopathy within the context of the Pan-Hellenic Congress of Cardiology and under the auspices of the European Society of Cardiology (ESC). A panel of world-wide experts in the field of β -thalassemia attended the workshop, along with the former president of the ESC Working Group on Cardiomyopathies.

Beta (β)-thalassemia is a genetically inherited hemoglobin disorder characterized by severe chronic hemolytic anemia, which is caused by the impaired synthesis of the β globin chains.¹ It belongs to the group of hemoglobinopathies, which are the most common monogenic disorders in the world population. Although the disease was traditionally prevalent in the Mediterranean basin (the word "thalassemia" comes from the Greek word "thalassa", which means sea), Middle East, North India, Southeast Asia and the Indochina Peninsula, immigration of those populations to the USA, Canada and Western European countries has led to a universal distribution of the disease.²⁻⁴

Thalassemia major is the most prevalent clinical form of the disease and is characterized by severe hemolytic anemia from the first year of life, which requires blood transfusion therapy for the patient's survival. This is followed by multiple chronic organ damage, growth retardation and a considerably reduced life expectancy. However, modern therapy, which has developed over the past four decades and consists of regular blood transfusions combined with iron chelation agents to overcome the transfusional iron overload, has led to a remarkable improvement in patients' prognosis, and survival has now been expanded beyond the fourth decade of life.^{3,5,6} Moreover, it has

been shown that the combination of intensified blood transfusions and iron chelation with the regular heart failure treatment led to a 5-year survival rate of 48% in thalassemia major patients with heart failure, which is similar to that of the general heart failure population.⁷

Heart failure always was and still remains the leading cause of mortality, accounting for approximately two thirds of deaths in β -thalassemia.⁸⁻¹¹ However, heart failure in these patients represents a unique entity, characterized by a particular clinical presentation and pathophysiology. It is mainly expressed as two different phenotypes: a dilated cardiomyopathy phenotype, characterized by left ventricular dilatation and reduced contractility, leading to congestive heart failure; and a restrictive cardiomyopathy phenotype, characterized by restrictive left ventricular filling with subsequent pulmonary hypertension, right ventricular dilatation and heart failure.^{7,12,13}

Myocardial iron overload is traditionally considered the fundamental pathogenetic mechanism of heart failure. However, over the last few years it became clear that the pathogenesis of heart failure in β -thalassemia is much more complex, and it is now believed that viral infections and immunogenetic factors contribute significantly to the development of heart disease in these patients.¹⁴⁻¹⁶ Overall, it seems that the pathophysiology of left ventricular failure of the dilated type is multifactorial, with a significant contribution from immuno-inflammatory and inherited components. On the other hand, myocardial iron deposition does not affect left ventricular relaxation but directly causes left ventricular myocardial diastolic dysfunction, which is expressed as an echo-Doppler restrictive pattern.¹³ However, it has been reported that the echo-Doppler indices do not detect mild dia-

stolic dysfunction characterized by increased filling pressures on exertion.^{17,18} In this context, it has recently been shown that the increased levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) may be used as an early index of left ventricular diastolic dysfunction in β -thalassemia patients, before the conventional echo-Doppler indices become apparently abnormal.² Thus, in the individual patient's assessment, a progressive increase of NT-proBNP may serve as an early sign for intensification of transfusion and chelation therapy, in order to prevent the development of overt heart failure.

The outcome of the workshop will be a position paper on β -thalassemia cardiomyopathy, which will soon find its way to publication in one of the ESC journals. It is our belief that the particular pathogenetic and phenotypic characteristics of thalassemia heart disease, along with its unique therapeutic requirements and its world-wide distribution, require its recognition as a distinct cardiomyopathy.¹⁹

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