

UNIVERSITATEA DE MEDICINĂ, FARMACIE, ȘTIINȚE ȘI TEHNOLOGIE
„GEORGE EMIL PALADE” DIN TÎRGU MUREȘ

ȘCOALA DE STUDII DOCTORALE

REZUMATUL TEZEI DE DOCTORAT

**Corelații clinice, paraclinice și
imagistice în managementul
pacienților cu cardiomiopatie
dilatativă în populația
pediatrică**

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INTRODUCTION: Pediatric dilated cardiomyopathy (DCM) is a rare and severe myocardial disorder characterised by left ventricular (LV) dilatation and progressive systolic dysfunction, and is one of the most important causes of heart failure (HF) and heart transplantation in children. The distinct pathophysiology of the paediatric population, including adaptive compensatory mechanisms, growth-related dynamics, and etiological heterogeneity, underpins important clinical variability and limits the direct applicability of prognostic models developed in adults. Early identification of patients at increased risk of rapid progression to advanced HF or major cardiovascular events remains a major clinical challenge. Conventional echocardiographic parameters and routine biomarkers provide an incomplete characterisation of myocardial remodelling and fail to adequately capture subclinical dysfunction due to their dependence on loading conditions.

AIM OF THE RESEARCH: This doctoral thesis was based on the hypothesis that myocardial deformation assessment using speckle-tracking echocardiography (STE) allows a more sensitive evaluation of the functional severity and disease progression risk in pediatric DCM compared with conventional parameters of global systolic function. Therefore, the general objective of the thesis was to develop an integrated perspective on cardiac remodelling in pediatric DCM through the simultaneous analysis of LV, right ventricular (RV) and left atrial (LA) mechanics, and by correlating advanced imaging parameters with relevant biological and metabolic biomarkers.

METHODOLOGY: The thesis comprises a structured review of the literature and a series of five prospective observational clinical studies conducted in a tertiary pediatric cardiology center. The clinical cohort included 29 pediatric patients diagnosed with idiopathic DCM, while the control group consisted of healthy children matched for demographic and anthropometric characteristics. The evaluation protocol included clinical assessment, laboratory testing (age- and sex- adjusted NT-proBNP and 25-hydroxyvitamin D) and standardised transthoracic echocardiography with two-dimensional STE analysis.

STUDY 1- Vitamin D and heart failure- A structured literature review: The objective of this study was to critically evaluate the available evidence regarding the relationship between vitamin D status and HF, following PRISMA guidelines. The review demonstrated that, in adult population, vitamin D deficiency is frequently associated with HF severity, myocardial stress biomarkers and adverse outcomes. However, interventional studies have reported heterogeneous findings, and a direct causal effect on myocardial function remains inconclusive. Pediatric data are scarce, supporting the need for dedicated clinical investigations. This first study provided the conceptual framework for exploring vitamin D as a potential adjuvant metabolic marker in pediatric DCM.

STUDY 2- Vitamin D status in pediatric DCM and its relationship with conventional echocardiographic parameters: This case-control study included 29 pediatric patients with DCM and 31 healthy controls, aiming to assess vitamin D status and its association with conventional echocardiographic indices. The results revealed a significantly higher prevalence of vitamin D deficiency among DCM patients compared to controls. Hypovitaminosis D correlated with LV dimensions, suggesting an association with structural remodelling, but showed no significant relationship with LV ejection fraction. These findings support the concept that vitamin D primarily reflects structural and metabolic aspects rather than global contractile performance.

STUDY 3- Left ventricular global longitudinal deformation: This study evaluated LV global longitudinal strain (LVGLS) as a marker of systolic dysfunction. The cohort included 29 DCM patients and 27 controls. LVGLS was significantly reduced in DCM compared to controls and demonstrated stronger associations with clinical severity and NT-proBNP compared with LV ejection fraction. The

results indicate that longitudinal deformation imaging identifies early and diffuse myocardial impairment preceding alterations in conventional systolic parameters.

STUDY 4- Right ventricular longitudinal deformation (RVFWSL). This study investigated RV free wall longitudinal strain in pediatric DCM. Compared with controls, DCM patients exhibited significantly reduced RV deformation parameters, even in the absence of consistent abnormalities in conventional RV indices. Right-ventricular dysfunction appeared predominantly in more advanced disease stages, supporting the concept of progressive biventricular involvement and highlighting the clinical relevance of RV mechanical assessment.

STUDY 5- Left atrial deformation analysis. The fifth study of the thesis was dedicated to the evaluation of LA phasic mechanics, particularly LA reservoir strain (LASr) in pediatric patients with DCM (n=29), hypertrophic cardiomyopathy (HCM, n=29) and healthy controls. Left-atrial strain parameters provided a sensitive assessment of diastolic dysfunction and LV filling pressures, independent of conventional atrial size measurements. Distinct atrial deformation patterns between DCM and HCM suggest disease-specific remodelling mechanisms and support the role of LA mechanics as an integrative marker of atrioventricular interaction and hemodynamic burden.

STUDY 6- Imaging and biological predictors of 12-month cardiovascular events in pediatric DCM. The final study of the thesis adopted a prognostic design integrating multicomponent STE parameters and biological biomarkers for predicting major cardiovascular events at 12 months. Therefore, LVGLS, LASr and age-adjusted NT-proBNP demonstrated superior predictive performance compared with conventional echocardiographic indices. Right-ventricular dysfunction contributed complementary prognostic information, identifying advanced stages of global cardiac impairment. The absence of significant associations between vitamin D and STE parameters suggests that vitamin D reflects metabolic and structural dimensions, rather than direct myocardial mechanical dysfunction.

In conclusion, this thesis demonstrates that pediatric DCM is a multicomponent disease characterised by diffuse LV longitudinal dysfunction, significant atrial mechanical alterations and progressive RV involvement. Speckle-tracking derived parameters provide superior functional and prognostic information compared with conventional indices, while biomarker integration enhances risk stratification. Vitamin D status appears predominantly associated with structural remodelling and neurohormonal activation, supporting its role as a complementary metabolic marker.

The originality of this work resides in the integrated imaging-biological approach applied to a rare pediatric cohort, with simultaneous LV, RV and LA deformation analysis, systematic adjustment of biomarkers for age, and the exploration of vitamin D within a functional and prognostic framework.