Natural history of left ventricular hypertrophy in infants of diabetic mothers

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Background: Left ventricular hypertrophy (LVH) in infants of diabetic mothers (IDMs) has been generally considered a benign condition, which usually regresses as the stimulus for the insulin production disappears, resulting in normalized left ventricular wall thickness in the 6 months of life. However, these conclusions have been based on small, mostly outdated cohort studies. Indeed, it has been recently shown that increased left ventricular mass persists in late infancy (6 to 12 months), long after the intrauterine exposure has been removed, suggesting that other factors may potentially contribute.

Purpose: This study sought to describe the characteristics and the natural course of LVH in a wellcharacterized consecutive cohort of IDMs.

Methods: Sixty consecutive IDMs with LVH have been retrospectively identified and enrolled in the study. All IDMs were evaluated at baseline and every 6 months until LV wall thickness regression, defined as the decrease of wall thickness measurement into the normal reference range for cardiac parameters (z-score >-2 and <2). A comprehensive assessment was performed in those patients with diagnostic markers suggestive of a different cause and/or without significant reduction of the LVH during follow-up.

Results: At 1-year follow-up, all IDMs showed a significant reduction of maximal wall thickness (MWT) (MWT-mm: 6.67±2.37 vs. 5.83±1.70, p-value<0.001; MWT-z-score: 6.67±4.71 vs. 2.39±2.55, p-value<0.001) and left ventricular outflow tract (LVOT) gradient (15.35±15.58 vs. 11.22±8.14, p-value<0.004), compared to baseline, and all patients showed LV wall thickness regression or residual mild or moderate LVH (57%, 28%, and 12%, respectively) (Figure 1), except 2 patients with persistent severe LVH, that after a comprehensive clinical-genetic assessment were diagnosed as Noonan syndrome with multiple lentigines.

At multivariate analysis, MWT was significantly associated with LV wall thickness regression at 1-year follow-up (MWT-mm: OR 0.48[0.29-0.79], p-value=0.004; MWT-z-score: OR 0.71[0.56-0.90], p-value=0.004) in an inversely proportional fashion.

Overall, 59%, 72% and 79% of IDMs with LVH showed a complete LV wall thickness regression at 1-year, 2-year and 3-year follow-up, respectively (Figure 2). Excluding the two patients with a different cause of LVH, all IDMs showed a LV wall thickness regression in the first 6 years of life.

Conclusions: LVH in IDMs represents a benign condition with complete regression during the first years of life. In those patients without LV wall thickness regression, combined with clinical markers suggesting a specific disease, a complete work-up is required for a definite diagnosis.

Figure 1. Left ventricular hypertrophy degree at baseline and at 1-year follow-up according to the baseline maximal wall thickness *z*-score.





Figure 2. Percentages of IDMs with left ventricular wall thickness regression during follow-up.