ECHOCARDIOGRAPHIC PREDICTORS OF SUDDEN CARDIAC DEATH IN YOUNG PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

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Abstract: A combination of two echocardiographic parameters [reversed septal curvature and septum/left ventricular diastolic diameter (S/LVDd) index> 0,5] identifies a subgroup of adult hypertrophic cardiomyopathy (HCM) patients at increased risk of sudden death. The aim of the current study was to check these echocardiographic parameters as a risk factor for sudden death in HCM patients in whom the first echocardiogram was obtained at <20 years of age (in adolescence the septal thickness and left ventricular dimensions may dynamically change).

Methods: 15 (7 males, 8 females) HCM patients (mean age 15.3±4.9 years at initial evaluation) were retrospectively investigated. The end-points of follow-up were ventricular fibrillation (VF) or sustained ventricular tachycardia (sVT). One patient had VF as a first manifestation of HCM and the results of her first echocardiogram diagnosing HCM after successful resuscitation were defined as final (end-point) echocardiogram, thus follow-up data were not available in this case. In the remaining 14 patients echocardiographic follow-up data (from first to last echocardiogram) were collected [mean follow-up 6.5±4,9 years)]. The mean age at initial evaluation was 15.3±4.9 years versus 21.7±5.2 years at the latest examination (p<0.0004).

Results: Increase of S/LVDd index was significant (0,49±0,13 vs 0,64±0,31 p<0,04). Ten patients had reversed septal curvature whereas 5 patients presented with normal septal configuration with oval shape of left ventricle. Four patients had VF (successfully defibrillated) and 1 patient had sVT. Among these 5 patients 4 persons fulfilled both proposed echocardiographic criteria (at the end-point) indicating high risk of sudden death. Importantly, in all the 4 patients S/LVDd index increased markedly during follow-up. One patient with VF did not fulfil any criteria and this patient had WPW syndrome.

Conclusion: In young HCM patients increasing imbalance between thickening septum with reversed curvature and narrowing left ventricular cavity is associated with increased risk of sudden death.

INTRODUCTION:
Recent retrospective study revealed1 that a combination of two echocardiographic parameters [reversed septal curvature and septum/left ventricular diastolic diameter (S/LVDd) index> 0,5] identifies a subgroup of hypertrophic cardiomyopathy (HCM) patients at increased risk of sudden death. In that study only patients above 20 years of age were evaluated. The aim of the current study is to check these echocardiographic parameters as a risk factor for sudden death in HCM patients in whom the first echocardiogram was obtained below 20 years of age. Importantly, in this category of young patients the septal thickness and left ventricular dimensions may dynamically change2.

METHOD:
15 (7 males, 8 females) HCM patients (<20 years at initial evaluation) were included into the retrospective study. The end-points of follow-up were ventricular fibrillation (VF) or sustained ventricular tachycardia (sVT). One patient had VF as a first manifestation of HCM and the results of her first echocardiogram diagnosing HCM after successful resuscitation were defined as final (end-point) echocardiogram, thus follow-up data were not available in this case. In the remaining 14 patients echocardiographic follow-up data (from first to last echocardiogram) were collected [mean follow-up 6.5±4,9 years)]. The mean age at initial evaluation was 15.3±4.9 years versus 21.7±5.2 years at the latest examination (p<0.0004).

Patients were assessed on a 6-monthly interval basis or more frequently, as indicated. The echocardiographic findings in the 14 patients with follow-up were compared between the initial and the most recent examination (November 2004) or
echocardiograms after survived VF or sVT were used as the latest examination (the study end point). Each patient underwent M-mode and 2-dimensional echocardiographic study, followed by pulsed and continuous-wave Doppler ultrasound study. Standard views for M-mode and two-dimensional studies were obtained, and conventional techniques were used for sizing the left ventricle. The following parameters were measured from M-mode echocardiograms: left ventricular end diastolic diameter, left ventricular end systolic diameter, septal and posterior wall thickness. The S/LVDd index was calculated at end diastole. The left ventricular outflow tract gradient was measured using Doppler methods. According to the shape of septal contour assessed in the apical 4-chamber echocardiographic view patients were divided into two categories: with reversed septal curvature and with non-reversed curvature pattern as previously described\textsuperscript{1,3}. An abnormal convexity of the septum toward the left ventricular cavity (producing the crescent-shaped left ventricular cavity) was identified as reversed septal curvature\textsuperscript{1,3}.

**RESULTS.**

The left ventricular outflow tract gradient> 30 mmHg was present in 1 patient in initial echocardiograms and in 4 patients in the latest echocardiogram. The patient with VF as a first manifestation of HCM had septum thickness in diastole 28 mm, left ventricular end diastolic diameter 30 mm, S/LVDd index 0,94 and reversed septal curvature (see figure 1). In the remaining 14 patients, changes of echocardiographic parameters during follow-up are summarised in Table 1. The increase of septal thickness and decrease of left ventricular end diastolic diameter during follow-up were statistically insignificant, whereas increase of S/LVDd index was significant. The most thickened left ventricular segment was septum in all patients. Ten patients had reversed septal curvature whereas 5 patients presented with normal septal configuration with oval shape of left ventricle. The septal configuration remained unchanged during follow-up (patients were not reclassified - figure 1). Changes in S/LVDd index in individual patients during follow-up were depicted in figure 1. Four patients had VF episodes (successfully defibrillated) and 1 patient had sVT (figure 1). Among these 5 patients 4 persons fulfilled both proposed echocardiographic criteria indicating high risk of sudden death. Importantly, in all the 4 patients S/LVDd index increased markedly during follow-up (figure 1). One patient with VF did not fulfil any criteria and this patient had Wolff-Parkinson-White syndrome.

<table>
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<th>First echo</th>
<th>Final echo</th>
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<tr>
<td>Septum (mm)</td>
<td>19,6±3,2</td>
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<tr>
<td>LVDd (mm)</td>
<td>41,9±7,3</td>
<td>39,1±8,3</td>
<td>0,12</td>
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<tr>
<td>S/LVDd index</td>
<td>0,49±0,13</td>
<td>0,64±0,31</td>
<td>&lt;0,04</td>
</tr>
</tbody>
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Figure 1. Changes in S/LVDd index (labelled in OY axis) in individual patients. Open triangle-reversed septal curvature, closed triangle – single patient with ventricular fibrillation as first symptom of HCM, open circle- normal septal curvature.
DISCUSSION:
In adult patients, combination of echocardiographic parameters reflecting a significant morphological imbalance between hypertrophied septum with reversed curvature and narrowed left ventricular cavity allows for identification of a subgroup of HCM patients with increased risk of sudden death. Among HCM patients aged >65 years, reversed septal curvature is present in a minority of subjects (14%) and (5%)\(^3\). In contrast, in younger HCM patients the reversal pattern is more common 75%\(^3\) and 53%\(^4\). Premature sudden death in patients with reversed septal curvature may be a reason for a small number of these patients in the elderly population with HCM. In a pathomorphological study\(^5\) advanced abnormality in myocardial architecture (corresponding to reversed septal curvature) was common in patients who died at a mean age of 25 years. In contrast, most patients who died at >65 years of age had a normal, circular unit surrounding left ventricular cavity as a morphological marker of non-reversed septal configuration.

Especially in adolescent patients, left ventricular hypertrophy rapidly progresses which results in left ventricular cavity narrowing\(^2\). Children and adolescent patients despite a lack of malignant family history and usually without nonsustained ventricular tachycardia have a high annual mortality from sudden cardiac death.\(^6;7\) In such patients only syncopal episodes identify high-risk patients\(^6;7\). Accordingly, we hypothesised that rapidly decreasing left ventricular cavity size in adolescence may facilitate episodes of hypotension (manifested as presyncope/syncope) induced by tachycardia (supraventricular/ventricular or sinusual due to exercise/emotion). In these circumstances myocardial ischemia may develop (which was observed in young patients) and eventually tachycardia inducing profound hypotension may degenerate into VF\(^8;9\).

In the current study, episodes of VF occurred mainly in patients with dynamically increasing imbalance between thickening septum with reversed curvature and narrowing left ventricular cavity except one patient with normal septal curvature and stable S/LVDD index<0.5. However, this particular patient had Wolff-Parkinson-White syndrome and after genetic assessment verifying mutation of AMP-activated protein kinase gene (not yet available in our centre) this patient may be reclassified from HCM to another disease i.e. Wolff-Parkinson-White syndrome with myocardial hypertrophy recently defined as storage disease\(^10\).

CONCLUSIONS:
In young HCM patients increasing imbalance between thickening septum with reversed curvature and narrowing left ventricular cavity is associated with increased risk of sudden death.

REFERENCES:
5. Kuribayashi T, Roberts WC: Myocardial disarray at junction of ventricular septum and left and right ventricular free walls in hypertrophic cardiomyopathy. Am.J.Cardiol. 1992;70:1333-1340
