Etiology-Specific Outcome in Pediatric Hypertrophic Cardiomyopathy

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Background: Hypertrophic Cardiomyopathy (HCM) in children is an etiologically diver disease with outcomes that depend on the underlying disorder. The relative frequency of the various causes and etiology-specific survival rates have not been established. Existing data, based on small groups of children, suggest annual mortality rates of 4-6% in older children and 10-50% in infants.
Methods: Longitudinal data from 855 patients diagnosed with HCM in the NHLBI Pediatric Cardiomyopathy Registry (PCMR) from 1990 to 2003 were analyzed with regard to etiology and outcome. Etiologies were grouped as: inborn errors of metabolism (IEM); malformation syndromes (MS, predominantly Noonan's Syndrome); neuromuscular disorders (ND, predominantly Friedreich's ataxia); and sarcomeric HCM (SHCM). Because of an inability to genotype all cases of SHCM, older patients with idiopathic HCM are clinically assumed to have SHCM. We followed this clinical paradigm and for purposes of analysis we defined SHCM as all patients 1) with genotyped SHCM, 2) patients ≥ 1 year old idiopathic HCM, or 3) patients < 1 year old with a family history of SHCM. The remaining children < 1 year old with idiopathic HCM were categorized as IIHCM (infantile idiopathic HCM).
Results: IEM comprised of 8.7% of cases, MS 9.0%, ND 7.5%, SHCM 67.3%, and IIHCM 7.6%. The Kaplan Meier survival estimates after diagnosis of HCM (95% CI) by group (log rank p<.0001) were:

Time Post-HCM Diagnosis	IEM (N=74)	MS (N=77)	ND (N=64)	SHCM (N=575)	IIHCM (N=65)
1-year	54% (41%, 66%)	82% (73%, 92%)	98% (95%, 100%)	98% (96%, 99%)	47% (28%, 67%)
2-years	45% (32%, 58%)	76% (66%, 87%)	98% (95%, 100%)	96% (94%, 97%)	47% (28%, 67%)
5-years	42% (28%, 55%)	74% (63%, 86%)	98% (95%, 100%)	93% (90%, 96%)	N/A*
Overall	21% (0%, 50%)	74% (63%, 86%)	92% (79%, 100%)	88% (80%, 96%)	47% (28%, 67%)

*Maximum length of observation in IIHCM was 3 years post-HCM diagnosis.
Only ND vs. HCM and IEM vs. IIHCM (both p>.01) had similar rates of survival.

Conclusions: At least 1 in 3 children with HCM have causes other than SHCM. Annual mortality in children with SHCM is <2%, similar to unselected adult cohorts, and better than has been previously reported. In contrast, HCM due to IEM and MS carries a considerably higher risk.