Understanding Pediatric Hypertrophic Cardiomyopathy (HCM) by Age of Presentation: ECHO Measurements

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Hypertrophic Cardiomyopathy (HCM) Background

- Presence of hypertrophied, nondilated ventricle without hemodynamic causes
- Most common genetic heart disease: 1 in every 500 individuals
- 35% of SCD cases → 1~8% annual mortality in adolescents & young adults
- *Symptoms:* Chest pain, dizziness, syncope, palpitations, shortness of breath, reduced exercise tolerance, heart murmur
- *Clinical Outcomes:* Sudden cardiac arrest (SCA), non-sustained arrhythmias (ventricular tachycardia [NSVT]), devices (implantable cardioverter defibrillator [ICD]), heart failure, death

Methods

- Subjects diagnosed with HCM w/ ECHO records:
  - <12 years cohort
  - ≥12 years cohort
- Stata 17: Descriptive statistics, t-test analysis of IVSd, LVPWd, LV mass, LVIDd, LVIDs, ejection fraction mean and Z score Differences between cohorts in patient characteristics (clinical presentation & outcomes) marking HCM progression
- ECHO measurements stratified by subject demographics
- Data presented by mean (SD), frequency (%)
- IRB approved

Objectives

1) To develop a more complete understanding associated with age of presentation of HCM and to determine the effects of age, sex, race, and ethnicity on clinical course and outcomes between the two cohorts.
2) To determine the progression of HCM in pediatric subjects by age of presentation.

Aims

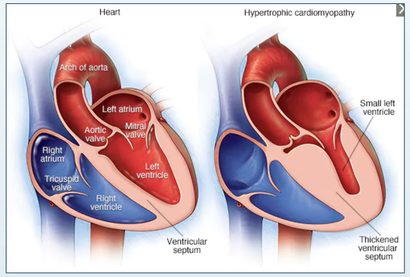
Aim 1: To determine the population characteristics, clinical presentations, symptoms, family history, and outcome differences between the two cohorts.
Aim 2: To determine differences in ECHO measurements for both cohorts by age of presentation.
Aim 3: To determine the progression of ECHO changes by age of presentation. (in progress)

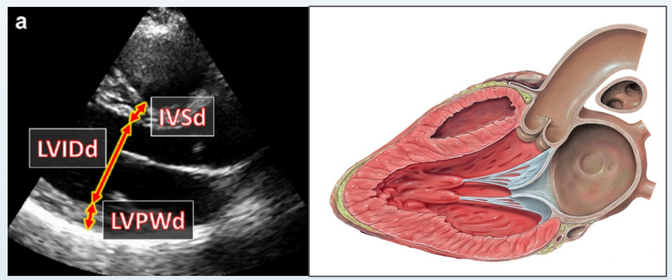
Results

- Age Difference: A majority of HCM subjects presented in the first year of life for the <12 years cohort. In the ≥12 years cohort most presented at 18 years.
- Family History: 23% of the <12 years cohort and 31% of the ≥12 years cohort had positive parent history of HCM (Pr = 0.39). 1.4% of the <12 years cohort and 8.3% of the ≥12 years cohort had positive parent history of sudden cardiac death (SCD) (Pr = 0.066).

Significance

- Symptom/event as reason for diagnosis was a significant clinical presentation for the ≥12 years cohort (Pr = 0.030).
- Palpitations were a statistically significant symptom between the two cohorts (Pr = 0.021).
- There is a significant difference in presentation by abnormal ECG with the older cohort more likely to present with an abnormal reading (Pr = 0.021).
- A trend was observed for SCA as a symptom more prevalent in the ≥12 years cohort (Pr = 0.066) however no significance was determined.
- History of a myomectomy was a significant outcome (Pr = 0.002) in addition to heart failure (Pr = 0.009); <12 years cohort more likely to present with these outcomes than the ≥12 years cohort.
- No subject deaths were observed in the cohort populations.





Results

Figure 1: Box and Whisker plot of *age at presentation*

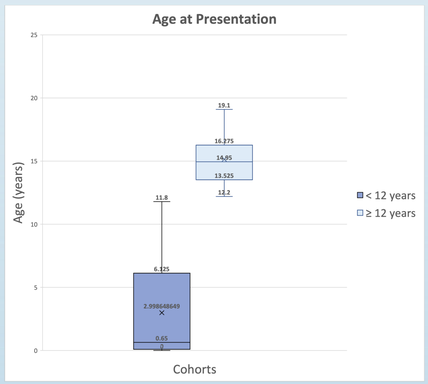


Figure 3: Table of ECHO Measurements (Mean, Z score) & P values

	Mean ± SD		P values	Z score ± SD		P values
Characteristic	**< 12 years**	**≥ 12 years**		**< 12 years**	**≥ 12 years**	
IVSd (cm)	1.4 ± 0.8	1.7 ± 0.7	NS	6.5 ± 5.3	4.6 ± 4.4	<0.006 (S)
LVPWd (cm)	0.9 ± 0.4	1.1 ± 0.3	NS	2.5 ± 2.9	1.5 ± 2.5	0.004 (S)
LV Mass (g)	153.6 ± 145.3	249.6 ± 123.3	NS	2.4 ± 2.4	1.3 ± 2.0	0.002 (S)
LVIDd (cm)	3.2 ± 1.1	4.4 ± 0.6	NS	-1.5 ± 2.1	-1.6 ± 1.3	NS
LVIDs (cm)	1.8 ± 0.8	2.5 ± 0.5	NS	-2.4 ± 2.4	-1.9 ± 1.3	NS
Ejection Fraction (%)	68.8 ± 7.5	67.0 ± 6.4	NS <0.056 (trend)			

Z scores are used in pediatrics to standardize values and account for differences related to growth/size of subjects.

Figure 2: Chart of the *racial composition* by cohort

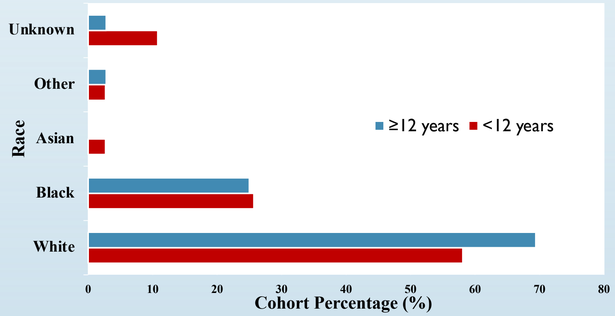
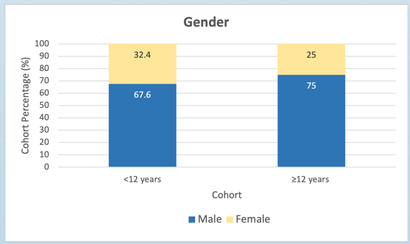
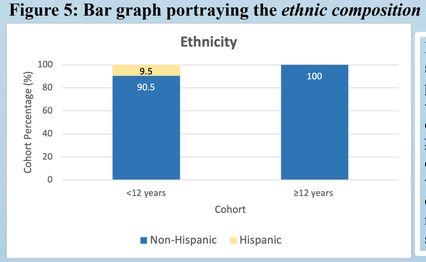


Figure 4: Bar graph portraying the *gender composition* of each cohort



There were more male subjects and less female subjects in the ≥12 years cohort than the <12 years cohort.

Figure 5: Bar graph portraying the *ethnic composition* of each cohort



More Hispanic subjects were present in the < 12 years cohort than the ≥ 12 years cohort, which was entirely composed of non-Hispanic subjects.

Figure 5: Frequencies of *clinical presentation* by cohort

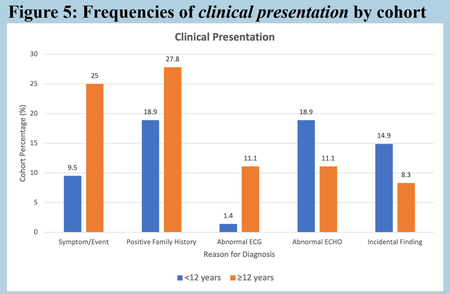
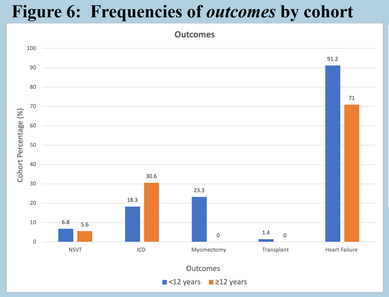


Figure 6: Frequencies of *outcomes* by cohort



Symptom/event & Abnormal ECG are statistically significant for <12 cohort

Myomectomy & Heart Failure are statistically significant

ECHO Measurements

- IVSd = interventricular septum thickness in diastole
- LVPWd = left ventricular posterior wall thickness in diastole
- LV Mass = left ventricular mass
- LVIDd = left ventricular internal diameter in *diastole*
- LVIDs = left ventricular internal diameter in *systole*
- Ejection Fraction (EF) = volume of blood LV pumps out to body with each contraction (stroke volume [SV]) divided by total volume of blood in ventricle (end-diastolic volume [EDV]) – indicator of efficiency of heart pumping function

These ECHO measurements, especially IVSd values, are used to diagnose or confirm diagnosis of HCM.

Limitations

- Retrospective chart study design: some information is incomplete and is limited to the data available
- Small sample size: the cohorts do not fully represent the true population and its characteristics

Conclusion

1) There are statistically significant differences in patient characteristics in clinical presentation attributed to symptoms/events (0.03), abnormal ECG (0.02), palpitation (0.02), and myomectomy (0.002) and heart failure (0.009) outcomes.

2) There are no significant differences between the two cohorts for the *absolute* measured values of all the ECHO measurements observed. There are statistically significant differences in the Z scores of IVSd (0.0056), LVPWd (0.0041), and LV mass (0.0015) supporting the observation of younger HCM subjects having more extreme echocardiographic signs and further poorer outcomes compared to older HCM subjects.

3) The analysis of Aim 3 is still in progress.

Seeing the significance of the greater prevalence of abnormal ECGs in the ≥12 years cohort and the implication that older children are more likely to undergo ECG screening and receive a HCM diagnosis confirming result, we speculate that with more younger children receiving screening they can similarly be diagnosed and treated earlier. We will explore the ECG findings with future research and learn more effective ways to diagnose children with HCM faster to improve their outcome.

Significance/Implications

- Improved understanding of HCM progression that varies within the pediatric population with age, especially as seen on ECHO → earlier diagnosis & modification of treatment plans

References:

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- Losi, M. A., Nistri, S., Galderisi, M., Betocchi, S., Cecchi, F., Olivotto, I., Agricola, E., Ballo, P., Buralli, S., D'Andrea, A., D'Errico, A., Mele, D., Sciomer, S., Mondillo, S., & Working Group of Echocardiography of the Italian Society of Cardiology (2010). Echocardiography in patients with hypertrophic cardiomyopathy: usefulness of old and new techniques in the diagnosis and pathophysiological assessment. *Cardiovascular ultrasound*, 8, 7. https://doi.org/10.1186/1476-7120-8-7

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