Comparisons in Clinical Outcomes for Pediatric Patients Diagnosed with Hypertrophic Cardiomyopathy

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BACKGROUND

- Pediatric hypertrophic cardiomyopathy (HCM) is associated with substantial morbidity and mortality.[1]
- Phenotype-specific differences in outcomes between obstructive HCM (oHCM) and non-obstructive HCM (nHCM) remain incompletely characterized for children and adolescents.
- **Objective:** We evaluated these associations in a real-world cohort of pediatric patients with HCM in the United States.

METHODS

Study Design

- Retrospective cohort study used patient-level administrative claims to identify pediatric patients with HCM in the United States from 2016 through 2024 (Index date = first HCM diagnosis), and followed them from index diagnosis until death, health plan disenrollment, or end of study.

Database

- Symphony Health's Integrated Dataverse (IDV) includes longitudinal US claims data (Jan 2016–Mar 2024) spanning prescription, medical, and hospital records across all payer types, and captured >10 billion deidentified prescription claims from >280 million patients (average ~5 years of history).

Inclusion Criteria

- Evidence of HCM: Patients with HCM met the following selection criteria:
  - ≥2 medical claims with a diagnosis code for HCM (ICD-10: I42.1 or I42.2) ≥30 days apart.
- Age <18 years at index diagnosis date.
- Continuous enrollment with medical and pharmacy benefits for 12 months prior to and ≥12 months after (and including) the index date.
- oHCM was defined as ≥2 ICD-10 I42.1 diagnoses, evidence of septal reduction therapy (SRT), or a higher frequency of I42.1 vs I42.2 codes; confirmed nHCM was defined as ≥2 I42.2 diagnoses without SRT or a higher frequency of I42.2 vs I42.1 codes.

Exclusion Criteria

- Patients with evidence of Pompe disease, Danon disease (LAMP2 deficiency), Noonan syndrome, mitochondrial myopathy/disease, amyloidosis, or Fabry disease during the study period were excluded.

Study Outcomes

- The primary outcome was cardiovascular composite endpoint, which included atrial fibrillation/flutter, supraventricular or ventricular tachyarrhythmia, ventricular fibrillation, ventricular tachycardia, sudden cardiac arrest, heart failure, heart transplant, implantable cardioverter defibrillator, pacemaker, implantable loop recorder, wearable cardioverter defibrillator, ventricular assist device, or septal myectomy.

Statistical Analysis

- Analyses were conducted using Kaplan–Meier methods, with between-group comparisons assessed using the log-rank test.
- Time-to-event outcomes were analyzed using Kaplan–Meier estimates, with between-group comparisons conducted using the log-rank test.

RESULTS

Patient Population

- Among 6093 children with HCM (**Table 1**), 4641 (76%) had nHCM: mean age 10.5 ± 5.3 years; 64.3% were male; mean length of follow-up 56.5 ± 29.7 months.
- 1378 (95%) patients with oHCM and 4341 (94%) patients with nHCM had no prior record of a cardiac event (6-months prior to index diagnosis).

Study Endpoints

- During follow-up (**Figure 1**), 529 (38.4%) patients with oHCM and 750 (17.3%) with nHCM experienced a cardiovascular composite event (*P*<0.0001).
- Patients with oHCM experienced higher rates of individual cardiovascular complications compared with those with nHCM (**Figure 2**).
- Septal myectomy occurred in 93 (6.4%) patients with oHCM over the follow-up period.

Limitations

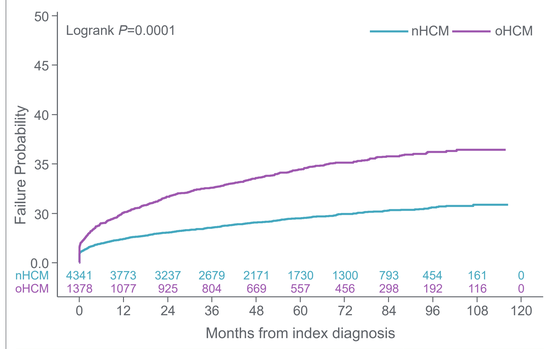
- Real-world data in this study utilized ICD-10 coding for disease identification, study outcomes, and may be subject to inconsistencies without patient-level genetic and anatomical confirmation.
- Due to the descriptive nature of this study, these results only include unadjusted analyses.

Table 1: Baseline patient demographics

	oHCM (n=1452; 24%)	nHCM (n=4641; 76%)	*P* value
Age at index diagnosis			
Mean (SD)	11.0 (5.07)	10.5 (5.33)	0.0012
Median (Q1, Q3)	12 (8, 15)	12 (6, 15)	
Min, max	(1, 17)	(1, 17)	
Year of index diagnosis, n (%)			
2015	148 (10.2)	232 (5.0)	<0.0001
2016	252 (17.4)	514 (11.1)	
2017	219 (15.1)	508 (10.9)	
2018	236 (16.3)	637 (13.7)	
2019	159 (11.0)	518 (11.2)	
2020	104 (7.2)	435 (9.4)	
2021	115 (7.9)	580 (12.5)	
2022	105 (7.2)	577 (12.4)	
2023	86 (5.9)	466 (10.0)	
2024	28 (1.9)	174 (3.7)	
Gender, n (%)			
Male	971 (66.9)	2982 (64.3)	0.0680
Female	481 (33.1)	1659 (35.7)	
Region, n (%)			
Northeast	287 (19.8)	895 (19.3)	<0.0001
Midwest	291 (20.0)	1271 (27.4)	
South	572 (39.4)	1518 (32.7)	
West	266 (18.3)	794 (17.1)	
Unknown	36 (2.5)	163 (3.5)	
Insurance plan type, n (%)			
Commercial	1,130 (77.8)	3501 (75.4)	0.0081
Medicare	2 (0.1)	8 (0.2)	
Medicaid	245 (16.9)	940 (20.3)	
Cash	5 (0.3%)	28 (0.6)	
Unknown/missing	70 (4.8%)	164 (3.5)	
Follow-up from index diagnosis to end of maximum activity date, months			
Mean (SD)	69.1 (30.4)	56.5 (29.66)	<0.0001
Median (Q1, Q3)	74 (43, 95)	54 (32, 80)	
Min, max	(6, 116)	(6, 116)	

Max, maximum; min, minimum; nHCM, non-obstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy; Q, quartile.

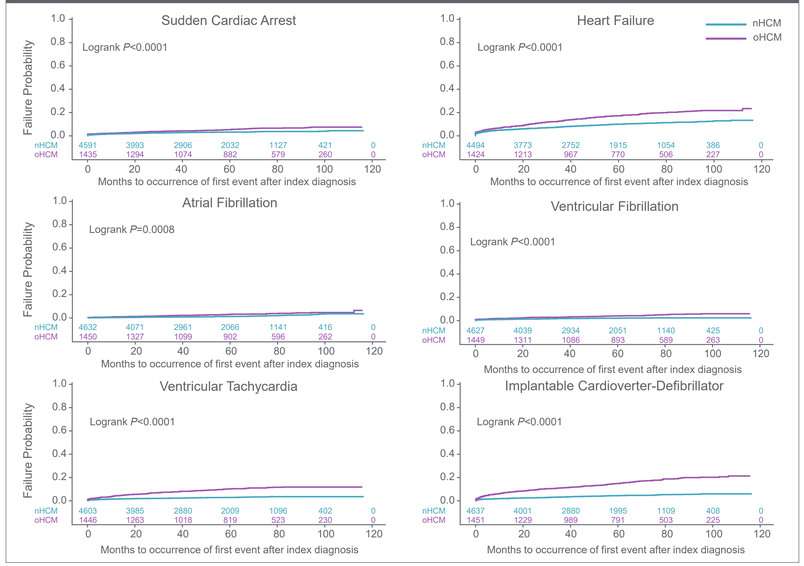
Figure 1: KM analysis of primary outcome for cardiovascular composite



	oHCM	nHCM
At risk patients, n	1378	4341
Events, n (%)	529 (38.4)	750 (17.3)
Mean survival (SE), months	68.3 (1.18)	89.4 (0.58)
P value	<.0001	
Event rate (%)		
0 months	0	0
12 months	20.2	9.7
24 months	26.74	12.23
48 months	34.33	16.36
72 months	40.47	19.74
96 months	44.86	22.41

Values inside graph are number of patients at risk.
CE, cardiac event; KM, Kaplan–Meier; nHCM, non-obstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

Figure 2: KM analysis of time to cardiovascular outcomes



Values inside graph are number of patients at risk.
KM, Kaplan–Meier; nHCM, non-obstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

CONCLUSIONS

- Pediatric patients with HCM experience substantial clinical burden.
- oHCM was associated with a higher cumulative risk of cardiovascular events compared with nHCM.
- These findings demonstrate clinically relevant heterogeneity in pediatric HCM and may inform risk mitigation strategies, including treating with novel therapies.

Reference

1. Bogle C, et al. *Circulation* 2023;148(2):174-95. doi:10.1161/CIR.0000000000001151.

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