Comparisons in Cardiovascular Outcomes and Mortality in Patients Diagnosed with Hypertrophic Cardiomyopathy

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INTRODUCTION

- Prior studies evaluating CV outcomes in patients with hypertrophic cardiomyopathy (HCM), including obstructive HCM (oHCM) and non-obstructive HCM (nHCM), have been limited in size.[1]
- We investigated these associations in a large, US national cohort of patients with HCM.

METHODS

Study Design

- Retrospective cohort study of adult patients with HCM in Optum's Market Clarity database from Jan 1, 2013 through Dec 31, 2021 (index date = first HCM diagnosis).
  - Patients with ≥2 medical claims with International Classification of Diseases codes 9 and 10 (ICD-9: 425.1, 425.11, or 425.18; ICD-10: I42.1 or I42.2) for HCM in any position on different dates of service ≥30 days apart were included.
  - 6 months of baseline and ≥6 months of follow-up continuous enrollment, and no evidence of Fabry disease or amyloidosis during the study period.

Study Outcomes

- Clinical characteristics, CV outcomes (AF, stroke, HF, VAT, stress CM, SCA, and heart transplant), and mortality.

Statistical Methods

- Event rates per 100,000 PT years to estimate risk of CV outcomes.
- KM analysis to evaluate risk of mortality.
- Comparison of outcomes between oHCM and nHCM; all tests were 2-sided α=0.05

RESULTS

Study Population (Table 1)

- Among 24,586 patients with HCM, 14,744 (60.0%) had oHCM.
- The proportion of females was greater among patients with oHCM (50.9%) vs nHCM (46.2%; *P*<0.001).
- Other demographics were similar across both oHCM and nHCM: mean age, 61.8 ± 14.0 vs 60.6 ± 16.2 years, *P*<0.001; mean follow-up, 43.1 ± 28.4 vs 45 ± 28.6 months, *P*<0.001; non-Hispanic White 73.8% vs 74.2%, non-Hispanic Black/African American 19.7% vs 19.5%, *P*=not significant.
- Comorbidities were greater in patients with oHCM vs nHCM (*P*<0.001), including hypertension (65.9% vs 54.2%), coronary artery disease (27.8% vs 23.1%), type 2 diabetes (25.3% vs 22.6%), obesity (20.0% vs 16.9%), and chronic kidney disease (13.7% vs 12.0%).

CV Treatment Outcomes

- Patients with oHCM had greater rates of AF, stroke, HF, VF, SVT, and stress CM compared with those with nHCM (**Table 2**).
- Furthermore, patients with oHCM experienced greater rates of SCA (*P*=0.019), but there was no significant difference in all-cause mortality (*P*=0.464) (**Figures 1 and 2**).

RESULTS

Table 1. Baseline demographic and clinical characteristics

n (%)[a]	Total N=24,586	oHCM n=14,744	nHCM n=9842	*P* value
Age, mean (SD) years	61.3 (14.9)	61.8 (14.0)	60.6 (16.2)	<0.001
Age group, y				<0.001
18–39	2176 (8.9)	1027 (7.0)	1149 (11.7)	<0.001
40–54	4964 (20.2)	3006 (20.4)	1958 (19.9)	0.345
55–64	6696 (27.2)	4316 (29.3)	2380 (24.2)	<0.001
65–74	5509 (22.4)	3333 (22.6)	2176 (22.1)	0.36
75+	5241 (21.3)	3062 (20.8)	2179 (22.1)	0.01
Sex				<0.001
Female	12,049 (49.0)	7504 (50.9)	4545 (46.2)	<0.001
Male	12,537 (51.0)	7240 (49.1)	5297 (53.8)	<0.001
Insurance type				<0.001
Commercial	11,173 (45.4)	6251 (42.4)	4922 (50.0)	<0.001
Medicare	7737 (31.5)	4947 (33.6)	2790 (28.4)	<0.001
Medicaid	2207 (9.0)	1453 (9.9)	754 (7.7)	<0.001
Other	113 (0.5)	77 (0.5)	36 (0.4)	0.076
Unknown/missing	3356 (13.7)	2016 (13.7)	1340 (13.6)	0.896
US region				0.045
Northeast	6668 (27.1)	3905 (26.5)	2763 (28.1)	0.006
Midwest	10,502 (42.7)	6350 (43.1)	4152 (42.2)	0.171
South	5504 (22.4)	3345 (22.7)	2159 (21.9)	0.167
West	1912 (7.8)	1144 (7.8)	768 (7.8)	0.899
Plan type[b]				<0.001
HMO	5878 (23.9)	3897 (26.4)	1981 (20.1)	<0.001
IND	109 (0.4)	68 (0.5)	41 (0.4)	0.606
POS	1725 (7.0)	1102 (7.5)	623 (6.3)	<0.001
PPO	4034 (16.4)	2526 (17.1)	1508 (15.3)	<0.001
EPO	358 (1.5)	212 (1.4)	146 (1.5)	0.77
SPN	2 (0.0)	2 (0.0)	0 (0.0)	0.248
Other	2951 (12.0)	1902 (12.9)	1049 (10.7)	<0.001
Unknown/missing	9529 (38.8)	5035 (34.2)	4494 (45.7)	<0.001

n (%)[a]	Total N=24,586	oHCM n=14,744	nHCM n=9842	*P* value
Race/ethnicity				0.357
White, non-Hispanic	18,181 (74.0)	10,875 (73.8)	7306 (74.2)	0.407
Black/African American, non-Hispanic	4814 (19.6)	2898 (19.7)	1916 (19.5)	0.716
Asian, non-Hispanic	559 (2.3)	355 (2.4)	204 (2.1)	0.084
Hispanic	1032 (4.2)	616 (4.2)	416 (4.2)	0.852
Clinical characteristics				
Baseline CCS (continuous)				
Mean (SD)	1.40 (1.8)	1.43 (1.8)	1.36 (1.8)	0.006
Median (IQR)	1 (0 to 2)	1 (0 to 2)	1 (0 to 2)	
Other baseline comorbidities				
Coronary artery disease	6370 (25.9)	4101 (27.8)	2269 (23.1)	<0.001
Pulmonary hypertension	1058 (4.3)	677 (4.6)	381 (3.9)	0.006
Hyperthyroidism	220 (0.9)	147 (1.0)	73 (0.7)	0.037
Hypothyroidism	3056 12.4	1886 12.8	1170 11.9	0.035
Bradyarrhythmia	1545 (6.3)	950 (6.4)	595 (6.1)	0.208
HF	4206 (17.1)	2526 (17.1)	1680 (17.1)	0.898
Chronic kidney disease	3204 (13.0)	2023 (13.7)	1181 (12.0)	<0.001
AF	3833 (15.6)	2424 (16.4)	1409 (14.3)	<0.001
Hypertension	15,047 (61.2)	9709 (65.9)	5338 (54.2)	<0.001
≥2 diagnosis codes 30 days apart, 1 diagnosis date at baseline[c]	14,832 (98.6)	9607 (99.0)	5225 (97.9)	<0.001
≥2 diagnosis codes 60 days apart, 1 diagnosis date at baseline[c]	14,769 (98.2)	9571 (98.6)	5198 (97.4)	<0.001
Obstructive sleep apnea	3140 (12.8)	2032 (13.8)	1108 (11.3)	<0.001
Diabetes type 2	5953 (24.2)	3731 (25.3)	2222 (22.6)	<0.001
Obesity	4607 (18.7)	2949 (20.0)	1658 (16.9)	<0.001
Myocardial fibrosis	775 (3.2)	514 (3.5)	261 (2.7)	<0.001

[a] Unless otherwise indicated.
[b] No patients had GPO as their plan type.
[c] Presented among patients with ≥1 diagnosis of hypertension.
Two-sample *t*-test was used for continuous measures. Pearson chi-square test was used for binary measures.
CCS, Charlson comorbidity score; EPO, Exclusive Provider Organization; GPO, Group Purchasing Organization; HMO, Health Maintenance Organization; IND, Indemnity Health Plan; IQR, interquartile range; POS, Point of Service; PPO, Preferred Provider Organization; SPN, State Policy Network.

Table 2. Incidence rate of CV treatment and outcomes during follow-up

	Incident rate						IRR	
	oHCM n=14,744			nHCM n=9842			oHCM vs nHCM	
	Events	PT, y	Rate	Events	PT, y	Rate	Ratio	*P* value
Pharmacotherapy								
Beta-blocker	12,185	11,486	106,082	2478	30,438	8141	13.03	<0.001
Calcium channel blocker	8343	26,368	31,641	1792	32,417	5528	5.72	<0.001
Disopyramide	482	51,289	940	58	36,661	158	5.94	<0.001
Antiarrhythmic	4517	39,748	11,364	2241	30,573	7330	1.55	<0.001
Procedures								
Septal myectomy	1125	49,527	2271	-	-	-	-	-
Alcohol septal ablation	526	50,935	1033	-	-	-	-	-
ICD[a]	2549	44,831	5686	1587	31,650	5014	1.13	<0.001
Pacemaker	3544	41,764	8486	2053	30,269	6782	1.25	<0.001
Heart transplantation	144	52,556	274	80	36,648	218	1.26	0.102
Clinical outcomes								
AF	5739	35,471	16,179	3120	27,034	11,541	1.40	<0.001
Stroke	2653	45,767	5797	1553	32,451	4786	1.21	<0.001
HF	7182	32,351	22,200	4073	24,761	16,449	1.35	<0.001
VT	3029	9495	31,900	1653	5353	30,877	1.03	0.287
VF	429	17,105	2508	203	9832	2065	1.21	0.021
SVT	2317	11,964	19,366	1125	7236	15,546	1.25	<0.001
Stress CM	133	52,617	253	63	36,698	172	1.47	0.010

[a] Implantable cardioverter defibrillator.

Figure 1. KM analysis of SCA during variable follow-up period

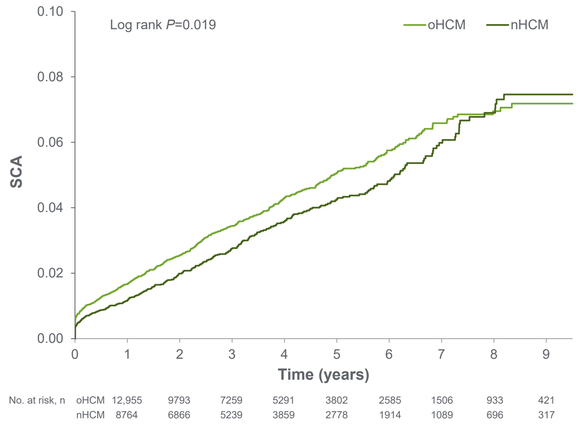
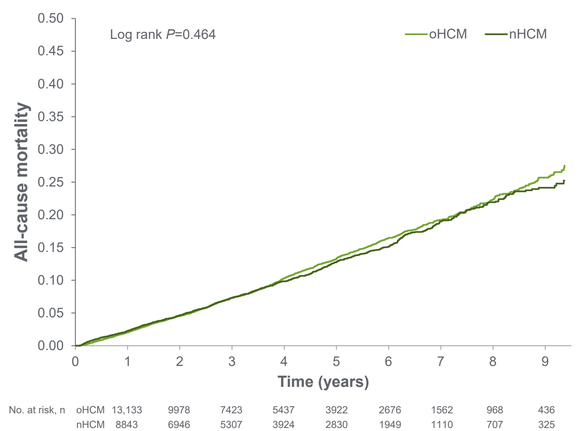


Figure 2. KM analysis of all-cause mortality during variable follow-up period



LIMITATIONS

- Real-world data in this study utilized ICD-9 and-10 coding for disease identification, patient demographics, and CV outcomes, and may be subject to inconsistencies without patient-level genetic and anatomical confirmation.

CONCLUSIONS

- In a large cohort of patients with HCM, those with oHCM experienced higher rates of adverse CV outcomes. Additionally, this group of patients utilized more drugs and procedures.
- Nevertheless, HF, AF, VT, and stroke were common in patients with nHCM, highlighting the necessity for specific treatments to reduce disease burden for this unique clinical population.

References

1. Lu DY, et al. *J Am Heart Assoc* 2018;7(5):e006657.

Disclosures

MB and SS: Employees of and own stock in Cytokinetics, Incorporated; **KB, AA, QA, and AB:** Employees of Optum/UHG, consultants for Cytokinetics, Incorporated for this study. **QA, AB, and AA:** Shareholders of UHG stock. **NR:** Consulting/speaking honoraria from Roche Diagnostics and Zoll, and supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) under Award Number K23HL166961 (content is solely the responsibility of the author and does not necessarily represent the official views of the NIH). **AO:** Consultant/advisor fees from Cytokinetics, Incorporated, Bristol Myers Squibb/MyoKardia, and Pfizer.

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Abbreviations

AF, atrial fibrillation; CV, cardiovascular; HCM, hypertrophic cardiomyopathy; HF, heart failure; IRR, incidence risk ratio; KM, Kaplan–Meier; nHCM, non-obstructive HCM; oHCM, obstructive HCM; SCA, sudden cardiac arrest; stress CM, stress cardiomyopathy; PT, person-time; SVT, superventricular tachycardia; VAT, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.

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