Associations Between Sex and Cardiovascular Outcomes in Patients with Hypertrophic Cardiomyopathy

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BACKGROUND

- Prior studies on the associations of sex with CV outcomes and mortality in patients with hypertrophic cardiomyopathy (HCM) have been limited in size.[1,2]
- The objective of this study was to investigate 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 Disease 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.
- 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 by sex; all tests were 2-sided α=0.05.

RESULTS

- Among 24,586 patients with HCM, median age was 61.3 ± 14.9 years, 12,049 (49.0%) were female, and 73.9% were non-Hispanic White, 19.6% non-Hispanic Black/African American, 4.2% Hispanic, and 2.3% non-Hispanic Asian (**Table 1**).
- 14,744 (60.0%) patients had obstructive HCM (oHCM).
- Compared with males, females were more likely to receive beta-blockers, calcium channel blockers, and disopyramide (IRR: 1.15, 1.27, 1.50, respectively; all $P<0.001$).
- Female patients were at increased risk of stroke, HF, and stress CM ($P<0.001$) but were less likely to receive pacemaker and implantable cardioverter-defibrillator (IRR: 0.80 and 0.62, respectively; $P<0.001$) (**Table 2**).
- Compared with males, female patients were less likely to have AF (IRR: 0.83, $P<0.001$), VT (IRR: 0.68, $P<0.001$), and VF (IRR: 0.68, $P<0.001$).
- Males with HCM and oHCM were also more likely to receive a heart transplant (IRR: 0.59 and 0.54, respectively; $P<0.001$).
- For patients with oHCM, there were no sex differences in receipt of septal reduction therapy.
- All-cause mortality was significantly greater in female patients with HCM compared with males, including the oHCM and nHCM subgroups ($P<0.001$) (**Figure 1**).
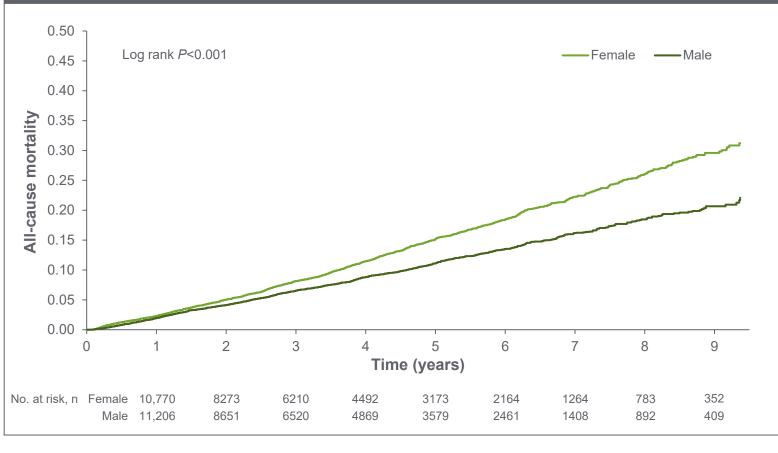
RESULTS

Table 1. Baseline patient demographics

Demographics, n (%)[a]	Total N=24,586	Female n=12,049	Male n=12,537
Age, continuous, mean (SD), y	61.3 (14.9)	64.4 (14.6)	58.4 (14.7)
Age group, y			
18–39	2176 (8.9)	813 (6.7)	1363 (10.9)
40–54	4964 (20.2)	1869 (15.5)	3095 (24.7)
55–64	6696 (27.2)	2871 (23.8)	3825 (30.5)
65–74	5509 (22.4)	3027 (25.1)	2482 (19.8)
75+	5241 (21.3)	3469 (28.8)	1772 (14.1)
Insurance type			
Commercial	11,173 (45.4)	4557 (37.8)	6616 (52.8)
Medicare	7737 (31.5)	4783 (39.7)	2954 (23.6)
Medicaid	2207 (9.0)	1133 (9.4)	1074 (8.6)
Other	113 (0.5)	54 (0.4)	59 (0.5)
Unknown/missing	3356 (13.7)	1522 (12.6)	1834 (14.6)
US Region			
Northeast	6668 (27.1)	2986 (24.8)	3682 (29.4)
Midwest	10,502 (42.7)	5302 (44.0)	5200 (41.5)
South	5504 (22.4)	2799 (23.2)	2705 (21.6)
West	1912 (7.8)	962 (8.0)	950 (7.6)
Plan type[b]			
HMO	5878 (23.9)	3122 (25.9)	2756 (22.0)
IND	109 (0.4)	65 (0.5)	44 (0.4)
POS	1725 (7.0)	629 (5.2)	1096 (8.7)
PPO	4034 (16.4)	1742 (14.5)	2292 (18.3)
EPO	358 (1.5)	149 (1.2)	209 (1.7)
SPN	2 (0.0)	1 (0.0)	1 (0.0)
Other	2951 (12.0)	1730 (14.4)	1221 (9.7)
Unknown/missing	9529 (38.8)	4611 (38.3)	4918 (39.2)
Race/ethnicity			
White, non-Hispanic	18,181 (73.9)	8607 (71.4)	9574 (76.4)
Black / African American, non-Hispanic	4814 (19.6)	2689 (22.3)	2125 (16.9)
Asian, non-Hispanic	559 (2.3)	229 (1.9)	330 (2.6)
Hispanic	1032 (4.2)	524 (4.3)	508 (4.1)
Baseline CCS continuous, mean (SD)	1.40 (1.80)	1.49 (1.42)	1.32 (1.77)

[a] Unless otherwise indicated.
[b] No patients had GPO as their plan type.
CCS, Charlson comorbidity score; EPO, Exclusive Provider Organization; GPO, Group Purchasing Plain; HMO, Health Maintenance Organization; IND, Indemnity Health Plan; 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	
	Female (n=12,049)			Male (n=12,537)				
Clinical outcomes	Events	PT, y	Rate/100,000	Events	PT, y	Rate/100,000	Ratio	P value
HCM (n=24,586)								
AF	4075	31,594	12,898	4784	30,911	15,477	0.83	<0.001
Stroke	2347	37,044	6336	1859	41,174	4515	1.40	<0.001
HF	5953	26,340	22,600	5302	30,773	17,230	1.31	<0.001
VT	1919	7508	25,559	2763	7341	37,639	0.68	<0.001
VF	232	12,380	1874	400	14,558	2748	0.68	<0.001
Stress CM	159	43,111	369	37	46,204	80	4.61	<0.001
SCA	408	42,888	951	486	45,447	1069	0.89	0.081
ICD[a]	1594	38,533	4137	2542	37,949	6699	0.62	<0.001
Pacemaker	2464	35,777	6887	3133	36,256	8641	0.80	<0.001
Heart transplant	80	43,334	185	144	45,871	314	0.59	<0.001
oHCM (n=14,744)	Female (n=7504)			Male (n=7240)				
AF	2735	18,699	14,626	3004	16,772	17,910	0.82	<0.001
Stroke	1539	22,425	6863	1114	23,341	4773	1.44	<0.001
HF	3936	15,317	25,697	3246	17,034	19,056	1.35	<0.001
VT	1277	4936	25,871	1752	4559	38,426	0.67	<0.001
VF	157	8092	1940	272	9013	3018	0.64	<0.001
Stress CM	106	26,319	403	27	26,298	103	3.92	<0.001
SCA	254	26,148	971	308	25,761	1196	0.81	0.014
ICD[a]	1018	23,424	4346	1531	21,407	7152	0.61	<0.001
Pacemaker	1622	21,505	7542	1922	20,259	9487	0.79	<0.001
Heart transplant	51	26,471	193	93	26,085	357	0.54	<0.001
nHCM (n=9842)	Female (n=4545)			Male (n=5297)				
AF	1340	12,895	10,391	1780	14,139	12,589	0.83	<0.001
Stroke	808	14,619	5527	745	17,832	4178	1.32	<0.001
HF	2017	11,023	18,298	2056	13,738	14,965	1.22	<0.001
VT	642	2572	24,960	1011	2781	36,350	0.69	<0.001
VF	75	4288	1749	128	5545	2309	0.76	0.055
Stress CM	53	16,792	316	10	19,906	50	6.28	<0.001
SCA	154	16,739	920	178	19,687	904	1.02	0.874
ICD[a]	576	15,109	3812	1011	16,541	6112	0.62	<0.001
Pacemaker	842	14,272	5900	1211	15,998	7570	0.78	<0.001
Heart transplant	29	16,863	172	51	19,785	258	0.67	0.080

[a] Implantable cardioverter defibrillator.

Figure 1. KM all-cause mortality in HCM population by sex

Log rank $P<0.001$

No. at risk, n									
Female	10,770	8273	6210	4492	3173	2164	1264	783	352
Male	11,206	8651	6520	4869	3579	2461	1408	892	409

CONCLUSIONS

- In this large cohort of patients with HCM, females were at increased risk of stroke, HF, stress CM and all-cause mortality, whereas males were more likely to have cardiac arrhythmias.

- These findings underscore the unique challenges in morbidity and survival experienced by females, emphasizing the imperative for novel treatments to alleviate the clinical burden for both males and females living with HCM.

References

1. Rowin EJ, et al. *J Am Heart Assoc* 2019;8:e012041. 2. Meghji Z, et al. *JAMA Cardiol* 2019;4:237-45.

Abbreviations

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

Presented at the European Society of Cardiology Heart Failure (ESC-HF) Congress | Lisbon, Portugal | May 11–14, 2024

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