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EDITORIAL

Hypertrophic Cardiomyopathy in Elderly Individuals: Is It a Rose by Another Name?

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Hypertrophic cardiomyopathy (HCM) is a familial heart muscle disease characterized by a diverse clinical and phenotypic spectrum that is usually identified in the second through fifth decades of life.[1,2] Since its early descriptions in 1957,[3,4] HCM has been increasingly recognized in older patients. However, studies suggest that the condition takes a different form when first diagnosed in this age group and may ultimately represent a disease entity that is distinct from that which predominates in the young.[2,5–10]

See Article by Alashi et al.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Alashi et al[11] describe the clinical characteristics and outcomes of 1100 consecutively studied elderly (aged >75 years) patients with HCM at the Cleveland Clinic over a 16.5-year period. They found a higher prevalence of traditional cardiovascular risk factors, such as hypertension, hyperlipidemia, and atrial arrhythmia, as opposed to HCM-related sudden cardiac death risk factors. Half of the study cohort had obstructive physiological features, of which a third underwent symptom-guided septal reduction therapy with myectomy (79%) or alcohol septal ablation (21%) with low in-hospital mortality and similar longer-term outcomes to that of a normal age-sex matched US population. This study provides an insight into the clinical profile and outcomes of a large elderly population with "HCM," managed in a specialist tertiary referral center.

The biggest limitation of this study relates to the fundamental issue of whether HCM in elderly individuals, and thus the cohort studied by the authors, truly represents the same disease as that in young and middle-aged individuals or in most, is a phenocopy related to aging and hypertension. It is recognized that many elderly patients with HCM have distinct echocardiographic features and clinical characteristics, including a higher prevalence of hypertension, exaggerated basal septal hypertrophy, small left ventricular (LV) cavity size, and marked distortion of LV outflow tract morphological features.[6,9,10,12] In addition, unlike HCM in younger patients, most are women and only ≈10% have a recognized pathogenic mutation. There is often dynamic LV outflow tract obstruction, with only a modest increase in LV wall thickness and a different septal shape compared with the younger patients with the more typical phenotypic expression.[6,9] Although dynamic LV outflow obstruction is common, the mechanism may differ, with an angulated aorta and mitral annular calcification contributing to narrowing the LV outflow tract. Furthermore, there appears to be a later onset of symptoms in elderly patients and an inverse relationship between advanced age and disease-related risk, which further supports the theory that a different disease process may be involved.[5,6]

The authors importantly demonstrate that in an HCM surgical center of excellence, myectomy can be performed at a relatively low risk and well below the predicted Society of Thoracic Surgeons' risk score. The overall hospital mortality with septal reduction therapy

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was only 2.5%. It is surprising that so many patients were offered myectomy rather than alcohol septal ablation, the therapy more commonly used in an elderly cohort. Such a distinction is important because their surgical data cannot be extrapolated to most centers,[13] and as they indicate, low-volume centers can have an alarming mortality, even in younger patients. It is likely that in most experienced centers, alcohol septal ablation will be the more common intervention. However, alcohol septal ablation, as noted, should also be performed in experienced centers shown to have low rates of mortality and morbidity. Ultimately, an adequately powered prospective study would be needed to truly understand outcomes in septal reduction therapy and to avoid "cherry-picking" of lower-risk patients, but the inherent challenges of undertaking a randomized control trial in this setting are significant, as previously highlighted.[14]

The authors focused on all-cause mortality rather than cardiovascular mortality. Most of the mortality documented was attributable to patient age and comorbidity rather than that seen in traditional HCM, with sudden death and progression to systolic or diastolic heart failure. This again highlights the distinction of this cohort with younger patients. Traditional HCM risk factors for sudden cardiac death were also not prevalent, as would be expected. Quantitative contrast-enhanced cardiovascular magnetic resonance imaging with late gadolinium enhancement is recognized as an important imaging marker for myocardial fibrosis and has a linear relationship to increased risk of sudden cardiac death.[15] Cardiovascular magnetic resonance imaging was performed in just 10% of the study cohort of Alashi et al, reporting only presence or absence of late gadolinium enhancement without formal late gadolinium enhancement quantification. The 52% who had evidence of late gadolinium enhancement could potentially include patients with enhancement isolated to right ventricular insertion areas, which has been shown to represent gadolinium pooling rather than replacement scarring.[16] Cardiovascular magnetic resonance imaging and genetic testing have significantly advanced our understanding and evaluation of HCM over time. Both are powerful strategies for diagnosis and differentiation of this complex inherited condition from its phenocopies.[17] Only 3% of the study population underwent genetic testing, again raising the question as to whether this group represents a genuine cohort with HCM who would frequently have a familial pattern of inheritance.

Another important limitation is the unavoidable degree of selection bias that inherently exists in many studies undertaken in dedicated HCM units.[18] It is likely that such institutions represent the most symptomatic patients or those with the most significant morphological characteristics and may not necessarily capture undiagnosed HCM or the milder spectrum of disease managed in the community.

Applying information from this study and other HCM studies of elderly patients to clinical practice requires awareness of the potential ambiguities surrounding the diagnosis of this condition in elderly patients and difficulties of generalizing outcome data from a single center. Does this cohort really have what we would traditionally consider true sarcomeric HCM, or rather do most have an acquired form of septal hypertrophy, often associated with dynamic LV outflow tract obstruction and potentially mixed or perhaps even alternative causes, such as hypertension and amyloidosis? It is likely that patients diagnosed earlier in life who progress to older age are different than patients first diagnosed when aged >65 years.

This distinction is important as these patients have a different phenotype, different clinical characteristics, different risk, and, ultimately what some might argue, a different disease process. As William Shakespeare has Juliette tell Romeo, "What's in a name? That which we call a rose by any other name would smell as sweet." Although the strength of their relationship does not depend on their names, she is a Capulet and he is a Montague, and this distinction makes them different.[19] In patients with HCM, it is important to correctly separate true HCM from phenocopies. Although HCM in elderly patients may be a misnomer, the authors provide important insights into the characteristics, management, and outcomes of this large, unique population.

ARTICLE INFORMATION

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Disclosures

None.

REFERENCES

1. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA*. 2002;287:1308–1320.DOI: 10.1001/jama.287.10.1308.
2. Lewis JF, Maron BJ. Clinical and morphologic expression of hypertrophic cardiomyopathy in patients ≥ 65 years of age. *Am J Cardiol*. 1994;73:1105–1111.DOI: 10.1016/0002-9149(94)90291-7.
3. Brock R. Functional obstruction of the left ventricle: acquired aortic subvalvar stenosis. *Guys Hosp Rep*. 1957;106:221–238.
4. Teare D. Asymmetrical hypertrophy of the heart in young adults. *Heart*. 1958;20:1–8.DOI: 10.1136/hrt.20.1.1.
5. Lever HM, Karam RF, Currie PJ, Healy BP. Hypertrophic cardiomyopathy in the elderly: distinctions from the young based on cardiac shape. *Circulation*. 1989;79:580–589.DOI: 10.1161/01.CIR.79.3.580.
6. Maron BJ, Casey SA, Hauser RG, Aeppli DM. Clinical course of hypertrophic cardiomyopathy with survival to advanced age. *J Am Coll Cardiol*. 2003;42:882–888.DOI: 10.1016/S0735-1097(03)00855-6.
7. Shapiro LM. Hypertrophic cardiomyopathy in the elderly. *Br Heart J*. 1990;63:265–266.DOI: 10.1136/hrt.63.5.265.
8. Fay William P, Taliercio Charles P, Ilstrup Duane M, Jamil Tajik A, Gersh BJ. Natural history of hypertrophic cardiomyopathy in the

elderly. *J Am Coll Cardiol*. 1990;16:821–826.DOI: 10.1016/S0735-1097(10)80328-6.
9. Lewis JF, Maron BJ. Elderly patients with hypertrophic cardiomyopathy: a subset with distinctive left ventricular morphology and progressive clinical course late in life. *J Am Coll Cardiol*. 1989;13:36–45.DOI: 10.1016/0735-1097(89)90545-7.
10. Topol EJ, Traill TA, Fortuin NJ. Hypertensive hypertrophic cardiomyopathy of the elderly. *N Engl J Med*. 1985;312:277–283.DOI: 10.1056/NEJM198501313120504.
11. Alashi A, Smedira NG, Popovic ZB, Fava A, Thamilarasan M, Kapadia SR, Wierup P, Lever HM, Desai MY. Characteristics and outcomes of elderly patients with hypertrophic cardiomyopathy. *J Am Heart Assoc*. 2020;9:e018527. DOI: 10.1161/JAHA.120.018527.
12. Canepa M, Pozios I, Vianello PF, Ameri P, Brunelli C, Ferrucci L, Abraham TP. Distinguishing ventricular septal bulge versus hypertrophic cardiomyopathy in the elderly. *Heart*. 2016;102:1087–1094.DOI: 10.1136/heartjnl-2015-308764.
13. Kim LK, Swaminathan RV, Looser P, Minutello RM, Wong SC, Bergman G, Naidu SS, Gade CLF, Charitakis K, Singh HS, et al. Hospital volume outcomes after septal myectomy and alcohol septal ablation for treatment of obstructive hypertrophic cardiomyopathy: US Nationwide Inpatient Database, 2003–2011. *JAMA Cardiol*. 2016;1:324–332.DOI: 10.1001/jamacardio.2016.0252.
14. Iacopo O, Ommen Steve R, Maron Martin S, Franco C, Maron BJ. Surgical myectomy versus alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2007;50:831–834.DOI: 10.1016/j.jacc.2007.05.018.
15. Chan RH, Maron BJ, Olivotto I, Pencina MJ, Assenza GE, Haas T, Lesser JR, Gruner C, Crean AM, Rakowski H, et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation*. 2014;130:484–495.
16. Chan RH, Maron BJ, Olivotto I, Assenza GE, Haas TS, Lesser JR, Gruner C, Crean AM, Rakowski H, Rowin E, et al. Significance of late gadolinium enhancement at right ventricular attachment to ventricular septum in patients with hypertrophic cardiomyopathy. *Am J Cardiol*. 2015;116:436–441.DOI: 10.1016/j.amjcard.2015.04.060.
17. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, Naidu SS, Nishimura RA, Ommen SR, Rakowski H, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;124:2761–2796.DOI: 10.1161/CIR.0b013e318223e230.
18. Maron BJ, Spirito P. Impact of patient selection biases on the perception of hypertrophic cardiomyopathy and its natural history. *Am J Cardiol*. 1993;72:970–972.DOI: 10.1016/0002-9149(93)91117-Z.
19. Shakespeare W. *Romeo and Juliet, 1957*. Oxford: published for the Malone Society by Oxford University Press, 2000; 1564–1616.