What Do Patients With Hypertrophic Cardiomyopathy Die from?

Barry J. Maron, MD[a,*], Ethan J. Rowin, MD[b], Susan A. Casey, RN[a], Ross F. Garberich, MSc[a], and Martin S. Maron, MD[b]

Hypertrophic cardiomyopathy (HC) has become a contemporary and treatable genetic heart disease, now with disease-related mortality reduced to as low as 0.5% per year, based largely on more effective risk stratification and the use of the implantable cardioverter-defibrillator for primary prevention of sudden death. This paradigm change in the natural history of HC has caused us to reconsider the overall mortality risk in this disease. We interrogated the databases of 2 HC referral centers, Minneapolis Heart Institute and Tufts Medical Center. Of 1,902 consecutive patients evaluated between 1992 and 2013, 1,653 patients (87%) have survived to the end of follow-up and 249 patients (13%) have died. Most deaths (178 of 249; 72%) were unrelated to HC, commonly because of cancer and predominantly in older patients. Non-HC mortality was significantly more common in adults presenting ≥60 years and least common in the youngest patients aged <30 years (p <0.001). Notably, deaths from non-HC causes substantially exceeded HC-related causes by 2.6-fold (p <0.001). In conclusion, only about 25% of patients with HC ultimately died of their disease, including predominantly those who were <30 years of age. These data allow patients with HC to develop a more realistic and reassured perception of their disease. **(Am J Cardiol 2016;117:434–435)**

Long regarded as a grim and unrelenting disease with generally poor prognosis and inadequate treatment options,[1] hypertrophic cardiomyopathy (HC) has now become a contemporary treatable disease with reasonable expectation for extended or normal longevity in many patients.[2–6] HC-related mortality has decreased significantly due principally to penetration of implantable cardioverter-defibrillators into disease management for prevention of sudden death (SD).[2] Patients with HC are, of course, still subjected to all-cause and noncardiac mortality because of a variety of other organ system diseases.[2–6]

To determine the causes of mortality in a contemporary HC population, which may require redefinition in the rapidly evolving treatment environment for this complex genetic heart disease,[2–6] we studied natural history and outcome of 1,902 consecutive patients. These patients were evaluated between 1992 and 2013 (27% obstructive at rest with outflow gradient, ≥30 mm Hg) at 2 HC referral institutions: Minneapolis Heart Institute Foundation and Tufts Medical Center (Boston) with complete follow-up over 6.6 ± 5.3 years.[2–4]

Of 1,902 patients, 1653 patients (87%) survived to the end of follow-up, whereas 249 patients (13%) have died (Figure 1). Most deaths (n = 178 of 249; 72%) were due to causes unrelated to HC, predominantly in patients aged ≥60 years: cancer (n = 37), other noncardiac (n = 16), coronary artery disease (n = 15), postoperative, including surgical myectomy (n = 9), advanced age associated with multiple cardiovascular and other organ system involvement, and co-morbidities largely independent of HC (n = 71; including nursing home deaths in patients aged >90 years [n = 20]; lost to follow-up [n = 10]).

The other 71 of the 249 deaths (28%) were due to causes directly related to HC: SD (n = 31); heart failure (n = 17); embolic stroke (n = 8); postoperative (n = 7); and transplant complications (n = 8). *Notably, deaths due to non-HC causes substantially exceeded HC-related causes by 2.6-fold (p <0.001;* Table 1).

When mortality was analyzed with respect to age at presentation, distinct differences were evident (Table 1). Non-HC mortality was most common in adults presenting ≥60 years and least common in youngest patients aged <30 years (p <0.001). For HC deaths, an inverse relation was present with mortality greatest in the youngest patients and least common in older patients (p <0.001). Patients with non-HC death were significantly older than patients with HC-related mortality (74 ± 14 vs 48 ± 18 years; p <0.001).

A new diagnosis of HC represents a landmark for many patients, usually unprepared for a disease often presented in the context of potentially profound clinical consequences, (particularly SD).[6] Indeed, a HC diagnosis often dominates the patient perception of their overall clinical profile, even in the presence of other non-HC conditions with more profound implications. Therefore, we find many patients come to believe that with aging, HC will become a relentlessly progressive disease process ultimately leading to their demise.

[a]Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, Minneapolis, Minnesota; and [b]Hypertrophic Cardiomyopathy Center, Division of Cardiology, Tufts Medical Center, Boston, Massachusetts. Manuscript received August 14, 2015; revised manuscript received and accepted November 3, 2015.

See page 435 for disclosure information.

*Corresponding author: Tel: (612) 863-3996; fax: (612) 863-3875.
E-mail address: hcm.maron@mhif.org (B.J. Maron).

0002-9149/15/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2015.11.013

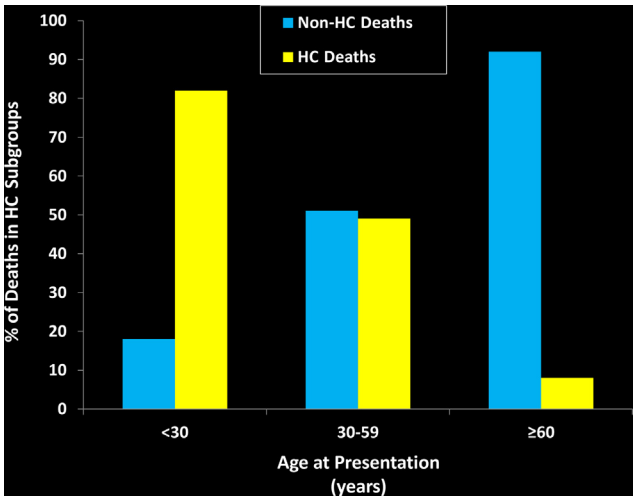

Figure 1. Outcome with causes of mortality in 1,902 consecutive patients with HC, stratified according to age at presentation ($p < 0.001$).

be anticipated and accompanied by effective treatment options.[1,4–6]

In conclusion, although HC has been cited as a highly visible cause of SD in the young, paradoxically it is uncommonly responsible for mortality in established HC patient cohorts. Only about 25% of patients with HC ultimately die of their disease, and indeed, mortality in adult patients with HC is more frequently due to other organ system diseases. These insights empower many patients to adopt a more realistic and reassured perception of their disease and promote the importance of surveillance and preventive strategies for non-HC conditions which may harbor greater potential for morbidity and mortality.

Disclosures

The authors have no conflicts of interest to disclose.

Table 1
Survival and mortality outcome in 1,902 patients with HC, stratified according to age at presentation

Age at Presentation (years)	No. Patients	Survived	Mortality			
			All Deaths	Died Non-HC	Died HC	Ratio[†]
<30	474	452 (95%)	22 (5%)	4/22 (18%)	18/22 (82%)	4.6
30-59	1000	918 (92%)	82 (8%)	42/82 (51%)	40/82 (49%)	1.04
≥60	428	283 (66%)	145 (34%)	132/145 (92%)	13/145 (8%)	11.5
Totals	1902	1653 (87%)*	249 (13%)	178/249 (72%)	71/249 (28%)	2.6

* Includes aborted SD and heart failure deaths: by implantable defibrillators (n = 68); heart transplant (n = 31); and out-of-hospital defibrillation/therapeutic hypothermia (n = 29).

† Comparison of HC and non-HC deaths.

The present data, however, clearly dispute such patient intuitions by showing that risk for death in adult patients with HC is significantly greater due to diseases *other than HC*. Indeed, it is very possible for adult patients in low HC-related risk groups to become distracted by HC and neglect preventive measures for other potentially lethal conditions such as cancer or coronary artery disease. In contrast, not unexpectedly, in children, adolescents, and young adults aged <30 years with HC, mortality is predominantly due to HC, given that deaths from other disorders are rare in this age group.

All-cause mortality in HC exceeds that in the general population[4–6] likely because deaths due to HC are part of the calculated total mortality. However, adverse interaction between HC and other disease processes that potentially increase lifetime risk cannot be absolutely excluded.

An important message often lost to patients with HC is that their disease is not ultimately lethal, but rather consistent with extended (if not normal) longevity, given that adverse clinical consequences and complications can now

1. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, Hagege AA, Lafont A, Limongelli G, Mahrhold H, McKenna WJ, Mogensen J, Nihoyannopoulos P, Nistri S, Pieper PG, Pieske B, Rapessi C, Rutten FH, Tillmanns C, Watkins H. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J* 2014;35:2733–2779.
2. Maron BJ, Rowin EJ, Casey SA, Link MS, Lesser JR, Chan RH, Garberich RF, Udelson JE, Maron MS. Hypertrophic cardiomyopathy in adulthood associated with low cardiovascular mortality with contemporary management strategies. *J Am Coll Cardiol* 2015;65:1915–1928.
3. Maron BJ, Rowin EJ, Casey SA, Haas TS, Chan RH, Udelson JE, Garberich RF, Lesser JR, Appelbaum E, Manning WJ, Maron MS. Risk stratification and outcome of patients with hypertrophic cardiomyopathy ≥60 years of age. *Circulation* 2013;127:585–593.
4. Maron BJ, Rowin EJ, Casey SA, Lesser JR, Garberich RF, McGriff DM, Maron MS. Hypertrophic Cardiomyopathy in Children, Adolescents and young adults associated with low cardiovascular mortality with contemporary management strategies. *Circulation* 2015; Epub ahead of print.
5. Spirito P. The dawn of a better day for patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2015;65:1929–1930.
6. Maron BJ, Ommen SR, Semsarian C, Spirito P, Olivotto I, Maron MS. Hypertrophic cardiomyopathy: present and future, with translation into contemporary cardiovascular medicine. *J Am Coll Cardiol* 2014;64:83–99.