After 60 Years Hypertrophic Cardiomyopathy is Finally Recognized as a Contemporary Treatable Disease With Low Mortality and Morbidity, But is This Paradigm Under-Recognized in the Literature?

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The evolving nature of a cardiovascular disease is defined for the clinician and patient communities by its portrayal in the peer-reviewed medical-scientific literature. This is a particularly relevant principle for those less common chronic diseases such as hypertrophic cardiomyopathy for which individual practitioners with limited direct clinical experience acquire their understanding largely from the published observations of other more experienced clinicians and authors.

However, misunderstandings can arise in the literature, sometimes attributable to the methodologies employed in analyzing clinical data. Such factors can even create differing clinical profiles for the same disease entity, and a dilemma for the readership in judging which data or publications are the most current and credible sources of important clinical information.

Historically, hypertrophic cardiomyopathy, as a heterogeneous disease with relatively low event rate associated with an overwhelming disease-specific literature (now with 1,000 papers/year in PubMed),[1] has been uniquely susceptible to an environment of uncertainty and skepticism.[2,3] Therefore, we wish to take this opportunity to directly address such issues, underscoring the maturation of HCM with respect to clinical course, management and outcome[3-8] i.e., from a uniformly grim, unrelenting and even malignant condition to its much different and more favorable profile today.

Indeed, innovative initiatives utilizing aggressive and targeted contemporary management strategies have revised the now obsolete perceptions of earlier eras, casting hypertrophic cardiomyopathy into a more positive light.[1,3,5,7] Large outcome studies have shown the way forward for predicting future events, preventing adverse disease consequences, and substantially altering natural history.[1–9]

Specifically, this progress relies on a matured risk stratification algorithm to identify patients for primary prevention ICDs and prevention of sudden death; treatments to reverse heart failure symptoms such as surgical myectomy (and selectively percutaneous alcohol septal ablation); anticoagulation prophylaxis to protect against embolic stroke; and advance more effective heart failure therapies for end-stage nonobstructive disease with systolic dysfunction (Figure).

Consequently, HCM-related mortality has been substantially reduced from 6%/year (in eras >20 years ago) to only 0.5%/year currently (Figure). This new clinical paradigm offering low mortality and morbidity (largely independent of age) has led to the reasonable expectation of most patients for achieving normal longevity with good quality of life.[1,3,7] Furthermore, a sizeable proportion of HCM patients experience benign clinical course without requiring major (or often any) treatment interventions (Figure).[1]

Indeed, hypertrophic cardiomyopathy is now one of the least common disease-related causes of death among those conditions which constitute the overall risks of living.[9] Notably, this progress has transpired without independent insights from molecular science and laboratory studies in animal models.[10]

Nevertheless, some concern remains that these highly positive messages for the HCM population may not yet be sufficiently appreciated by many clinicians in practices comprised largely of patients with ischemic heart disease or other conditions. Indeed, some recent reports in the hypertrophic cardiomyopathy literature from Europe and an international database appear to characterize a much different clinical experience with this disease,[11-14] encumbered by excess mortality and disease burden,[12] but in part bypassing contemporary treatments supported by the aforementioned body of evidence.[1,3] Consequently, the literature may appear to describe multiple disease entities residing under the umbrella of hypertrophic cardiomyopathy, for example, hopeful and treatable versus seemingly mired in the past and foreboding.

We believe that such differences in the portrayal of hypertrophic cardiomyopathy in the literature can be explained as publication bias in a number of ways, including variability in the demographics and clinical features of different patient cohorts, and alternatively by the strategies used in assembling clinical data. For example, mortality rates can be inflated when life-threatening events which are reversed by major targeted treatment interventions are instead tabulated as surrogate end-points equivalent to death, for example, when prophylactic ICD therapy terminates ventricular fibrillation,[5] or when progressive heart failure is reversed by advanced treatments such as heart transplant.[14,15] Also, large collaborative studies that span old (and new) treatment eras ultimately combine variable outcome data without giving disproportionate weight to more recent and more effective management strategies. Also, there have been situations in which representatives of industry have enthusiastically promoted new potential therapies, by ignoring established competitive strategies.[16-18]

In conclusion, patients with hypertrophic cardiomyopathy have waited literally a half-Century to reach this crossroads in which aggressive therapeutic interventions have

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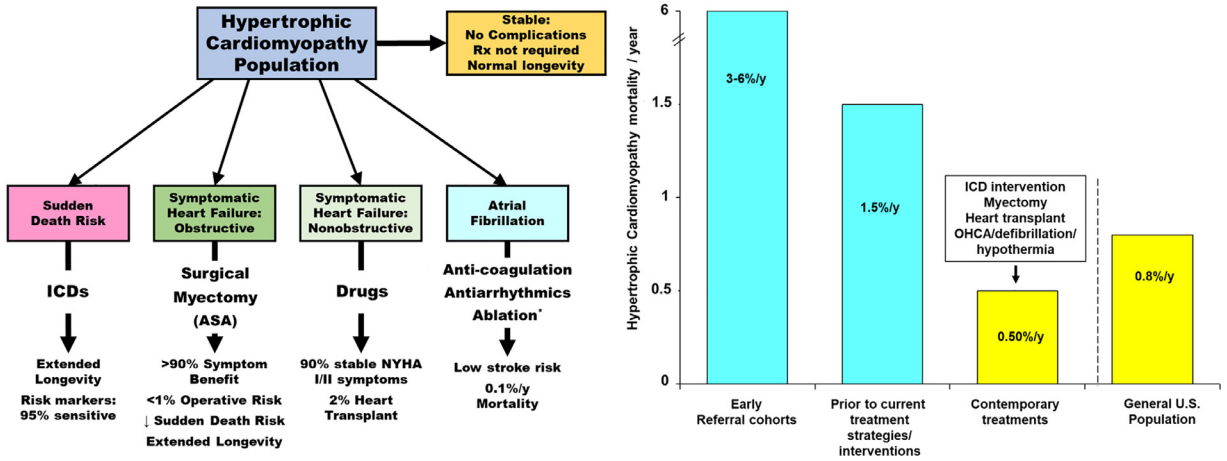

Figure. Contemporary management strategies associated with clinical benefit for patients with hypertrophic cardiomyopathy. Left. Treatment pathways and outcome. Right. Reduction in hypertrophic cardiomyopathy-related mortality over 40 years, now 0.5%/year with current treatment options. ASA = alcohol septal ablation; ICDs = implantable cardioverter-defibrillator; NYHA = New York Heart Association; OHCA = out-of-hospital cardiac arrest; Rx = treatment.

measurably altered the landscape of hypertrophic cardiomyopathy, by substantially reducing mortality and providing realistic aspirations for good quality of life and extended longevity in most patients.

Therefore, although misunderstanding has periodically plagued the hypertrophic cardiomyopathy historical record, this moment represents an opportune time to extinguish the old and now obsolete reputation of this disease, by avoiding unnecessarily contradictory messages that can obscure the substantial progress and opportunities now available to patients.

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