Historical Perspectives on the Implantable Cardioverter–Defibrillator and Prevention of Sudden Death in Hypertrophic Cardiomyopathy

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KEYWORDS

• Implantable defibrillators • Sudden death • Hypertrophic cardiomyopathy

KEY POINTS

- The implantable defibrillator has had a proven life-saving capability in coronary artery disease for 35 years.
- The defibrillator has been translated to hypertrophic cardiomyopathy (HCM) and has been effective in primary prevention of sudden death over the last 15 years in a range of patients.
- Risk stratification and selection of HCM patients for defibrillators has matured but is not yet complete.

THE EARLY YEARS

Hypertrophic cardiomyopathy (HCM) is an important, if not the most common cause of unexpected and unanticipated nontraumatic sudden death (SD) in the young (including competitive athletes).[1–5] The often cited and remarkable paper of Donald Teare, coroner of London, reported 8 young people (15 to 45 years of age; mean 27) with SDs that he attributed to asymmetric left ventricular hypertrophy mimicking a cardiac tumor.[6] In addition to its focus on sudden and apparently arrhythmic death, Teare's detailed morphologic observations included the now acknowledged key features of HCM such as a disorganized arrangement of myocytes, extensive fibrosis, and familial occurrence, as well as the recognition that syncope and exercise can be risk factors.

Although SDs are now known to be relatively uncommon among the expansive disease spectrum of HCM (about 5% of patients), such events remain the most devastating potential disease complication, dominating the discourse on HCM both among patients and in the practicing cardiovascular community.[1–5] Indeed, for more than 3 decades following the initial recognition of HCM as a disease state, no effective treatment or intervention was available to prevent SD occurring predominantly in young people without symptoms or warning signs. Cardioactive drugs such as amiodarone, beta-blockers, verapamil, and antiarrhythmic medications (eg, procainamide or quinidine) had previously been administered to HCM patients as a means of preventing SD, but ultimately with no evidence of efficacy.[7]

MIROWSKI, MOWER, AND THE IMPLANTABLE CARDIOVERTER–DEFIBRILLATOR

The impetus for creating an implantable defibrillator to abort impending sudden cardiac death was

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fundamentally the vision of Michel Mirowski, and its development ultimately the work of Mirowski and Morton Mower at Sinai Hospital (Baltimore, Maryland) (Fig. 1).[8,9] Initially, they were working in a self-funded animal laboratory[8] and against multiple economic and other impediments including antagonism from the cardiology establishment.[10,11] After 10 years of investigation, the implantable cardioverter—defibrillator (ICD) was eventually placed into clinical trials. A major obstacle to overcome for Mirowski in the early development of the ICD came from Bernard Lown at Harvard Medical School, who regarded the defibrillator as a "gadget" and an "imperfect solution in search of a plausible and practical application," created only "because it was possible," and also taking the view that ventricular fibrillation does not recur.[10]

The initial ICD patient trial was conducted in 1980 at Johns Hopkins Hospital on 3 patients in the laboratory setting for whom ventricular fibrillation was reliably terminated and sinus rhythm immediately restored spontaneously by the defibrillator.[9] Notably, US Food and Drug Administration (FDA) approval required recruitment of patients who had survived 2 or more cardiac arrests, and 2 of the first 3 patients to receive ICDs were patients with HCM.

Fig. 1. Dr Michel Mirowski. (*From* Nisam S, Barold S. Historical evolution of the automatic implantable cardioverter defibrillator in the treatment of malignant ventricular tachyarrhythmias. In: Alt E, Klein H, Griffin JC, editors. The implantable cardioverter/defibrillator. Springer-Verlag Berlin Heidelberg: 1992. p. 3; with permission.)

LINKING THE IMPLANTABLE CARDIOVERTER–DEFIBRILLATOR TO HYPERTROPHIC CARDIOMYOPATHY

Clinical development and introduction of the ICD to the cardiology community began with the vast population of at-risk patients with atherosclerotic coronary artery disease following resuscitated cardiac arrest (ventricular fibrillation) or myocardial infarction (Fig. 2). With the development of transvenous lead systems in 1992, a number of large prospective and randomized secondary and primary prevention trials showed a survival benefit attributable to the ICD in patients with coronary artery disease (or nonischemic cardiomyopathy, eg, Antiarrthythmics versus Implantable Defibrillator Study [AVID], Multicenter Unsustained Tachycardia Trial [MUSTT], and Multicenter Automatic Defibrillator Implant Studies [MADIT I/II]).[12–16]

While this early evolutionary period for the ICD focused on prevention of SD due to ischemic heart disease, genetic heart diseases (including HCM) were largely ignored. Furthermore, at the onset, it was not at all certain that the standard ICD would be appropriate for a genetic disease such as HCM, being so different pathophysiologically from coronary artery disease (ie, with marked [if not extreme] increase in mass, left ventricular [LV] outflow obstruction and mitral regurgitation, diastolic dysfunction, and microvascular ischemia.[1–3]

The landmark clinical study that demonstrated for the first time the efficacy of the ICD specifically for patients with HCM was published in the New England Journal of Medicine in 2000 (see Fig. 2).[17] Translating the ICD to HCM represented a paradigm change in disease management by altering the natural course of the disease for many patients, including children implanted younger than 20 years of age with aggressive forms of HCM.[17–20]

Subsequently, a series of retrospective studies comprising hundreds of HCM patients judged to be at increased risk by the generally accepted stratification algorithm[1–3,21–25] proved the ICD to be highly effective in terminating potentially lethal ventricular tachyarrhythmias. A primary prevention appropriate intervention rate of 4% per year has been reported consistently (about 10% per year for secondary prevention),[18–20,26–28] with about 20% of devices intervening for ventricular tachycardia/ventricular fibrillation (VT/VF) about 4 years after implant (Fig. 3).[18] Indeed, in adult HCM patients, the ICD has been largely responsible for a reduction in HCM-related mortality to 0.5% per year, less than that expected for all-cause