Implantable defibrillators in hypertrophic cardiomyopathy

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The implantable defibrillator (ICD) is one of the transformational technologies defining contemporary procedural cardiology. Advances in all aspects of device design have facilitated implantation and the detection, discrimination and correction of rhythms that otherwise can result in death.[1 2] However, as with most advanced technologies, initial enthusiasm is tempered by experience, which in the case of ICDs has highlighted the leads as a major source of mischief.[3] As emphasised in numerous articles, these highly engineered components, while generally withstanding the battering of the intravascular environment, can on occasion fail.[4] Lead design has evolved, but failure with potential consequences of inappropriate shocks, the need for revision and possible death have softened the enthusiasm of referrers. The upside is that ICDs are extremely effective and provide almost complete protection against sudden cardiac death (SCD). The difficulties remain in balancing the benefits weighed in relation to the largely technical but very real potential risks of devices. Of course, the longer the device is in place, the greater both the potential benefit and the incremental risks,[4] so in the younger patient the heavier the burden when deciding between options.

One disease that highlights the difficulty of these decisions is hypertrophic cardiomyopathy (HCM). This is by almost an order of magnitude more common than other diseases associated with SCD in the young and is likely to be seen in general cardiology practice. The literature is large, expanding rapidly and difficult to synthesise with the well-documented genetic and phenotypic heterogeneity complicating summary statements that concern all aspects of its management.[5] The critical issues are to identify those patients who will gain net benefit from an ICD while minimising the numbers of devices implanted that will not be needed.

Non-specialist cardiologists are almost universally aware of the current limitations of the non-invasive risk assessment of patients with HCM.[6] Intuitively they feel uneasy that critical decisions have to be made based on retrospective, observational, registry-based studies of patients that may be unrepresentative of those seen in their practices.[7–10] Of course what we ideally need are tests of high positive predictive value (PPV) to increase our confidence in ICD prescription that also have a high negative predictive value.[11 12] The availability of such tests would be anticipated to increase the numbers of patients being referred for assessment leading to more ICD implantations.

Many of the key issues surrounding the use of ICDs in this condition are highlighted in the paper in the current issue of *Heart* (***see page 709***).[13] It describes the Mayo Clinic experience in the years 1988 through 2005. This is the largest, single centre experience of ICDs in HCM to be published and reinforces messages from previous multicentre, registry-based reports.[10] The life-saving capabilities (16% received appropriate shocks) and the contrasting negative aspects of ICD therapy (23% received inappropriate shocks) are both fully observed. The fact that the young are especially susceptible to device complications is again highlighted.[2] Accordingly, device complications and inappropriate ICD activity are seen to occur frequently (in 36%), and although there is no detailed documentation of the psychological consequences the substantial impact that shocks have on the mental equilibrium of the young is clear.[2]

Two major issues have to be resolved to manage these patients better: we need to identify with greater certitude those that will benefit from an ICD, and working with industry we have to develop better devices. To move towards these desirable goals, the design and implementation of large-scale and most probably global, prospective studies will be critical.[14] The further trawling of retrospective, non-representative registries in an attempt to obtain value from non-invasive markers universally shown to be of low predictive accuracy (eg, syncope, family history, outflow tract obstruction, etc)[14] has largely run its course.[8] Approaches in which risk determination with all its implied downstream consequences will depend on "… the experience and clinical judgement of the individual physician evaluating the patient's overall risk profile …"[10] may be all we have, but they will not withstand scrutiny as a worthwhile and robust approach to patient management as we go forward.

The only way out of our current impasse will be to quantify potential parameters defining risk and seeing how these perform in predicting natural history.[12 14 15] Study designs will need to be inclusive, with large cohorts and long follow-up, not based on ICD randomisation, which is clearly not an option, and include new approaches to risk assessment. The feasibility of such studies has been demonstrated in the assessment of Paced Electrogram Fractionation Analysis (PEFA).[16] This carefully designed study[11] many years in its planning and execution and based on several previous retrospective studies[17 18] recruited patients at a number of centres throughout Europe, recorded their non-invasive risk profile and conducted PEFA. The 179 patients were then followed for over 4 years with the results demonstrating that the electrophysiological approach predicted outcome with a high PPV (0.38), whereas the use of two or more markers from a conventional non-invasive assessment yielded a PPV of little clinical use (0.106). The invasive, albeit demonstrably safe, dynamic interrogation of the myocardium may not be appealing to all asymptomatic relatives[14] but many will seek out such a test if it will provide them with a greater understanding of the risk of their disease. For the moment non-invasive electrophysiological measures, while disappointing,[11] will doubtless improve. Imaging studies that are currently adding greatly to our understanding of the pathophysiology of HCM[19 20] should also be tested along with previously reprieved genetic approaches[21] in such prospective evaluations.

New thinking and approaches are also being applied to devices. Subcutaneous implantable defibrillators (SICDs) which have long been anticipated for this patient group[22] are in clinical trials and are likely to provide advantages to those needing protection with mitigated long-term risk. Such devices may also be useful as a research tool, as one would anticipate an absence of intracardiac leads would reduce the possibility of device-associated proarrhythmia[16 23] making data interpretation from prospective trials more straightforward.

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In summary, the optimal use of ICDs in those with HCM and indeed other genetically determined causes of SCD has not been determined. Part of this difficulty relates to the inability of currently available risk stratifiers to provide surety in risk assessment and part relates to difficulties with ICDs mainly related to rhythm discrimination[13] and transvenous leads.[3 4] In the 50 years or so since its first description, HCM has been the focus of attention of some outstanding clinical investigators[5 10 14] who have thoroughly documented its clinical heterogeneity, but despite their efforts we are still unable accurately to predict risk.[8 14 16] We need to move to the next stage of description that will be based on properly powered, prospective studies of risk management allowing in turn the formulation of clear, evidence-based guidelines.[14]

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