# Implantable Cardioverter-Defibrillators for Hypertrophic Cardiomyopathy

## *The Times They Are a-Changin'*

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**Abstract**

The implantable cardioverter-defibrillator (ICD) is a life-saving therapy in patients with hypertrophic cardiomyopathy (HCM) at high risk of sudden cardiac death (SCD). The heterogeneity of clinical scenarios in HCM and the availability of ICDs with distinct characteristics emphasizes the need for selecting the right device for the right patient. There is growing awareness that unnecessarily complex devices can lead to short- and long-term complications without adding significant clinical benefits. Young patients have the greatest potential years of life gained from the ICD but are also most exposed to device-related complications. This increases the complexity of decision-making of ICD prescription in these often otherwise well patients in whom device selection should be tailored to preserve survival benefit without introducing morbidity.

In the light of the multiple clinical phenotypes characterizing HCM, the present article offers evidence-based perspectives helpful in predicting the individual impact of the ICD and choosing the most appropriate device.

**Keywords:** hypertrophic cardiomyopathy, implantable cardioverter-defibrillator, sudden cardiac death.

The implantable cardioverter-defibrillator (ICD) is an established life-saving therapy in patients with hypertrophic cardiomyopathy (HCM) at high risk from sudden cardiac death (SCD) [1, 2]. Contemporary ICDs have complex arrhythmia discrimination algorithms, high-energy output, bradycardia-pacing, anti-tachycardia pacing (ATP) and resynchronization capabilities. With increasing awareness that these more complex devices may lead to long-term complications without necessarily adding significant clinical benefits, the paradigm is currently shifting away from the need for an "all-purpose" ICD towards a strategy based on selecting the right device for the right patient. The clinical heterogeneity and unique clinical profile of HCM – when compared to "classic" ICD candidates, e.g. primary prevention post-myocardial infarction - add complexities to the device prescription decision [3].

This article offers evidence-based information for determining the impact of the ICD in HCM according to a spectrum of clinical scenarios to inform appropriate personalised device selection, especially timely given recent publications of landmark trials in Subcutaneous ICD (S-ICD) [4, 5] and the latest AHA/ACC guidelines in HCM sudden death prevention [6].

## CANDIDACY FOR PRIMARY PREVENTION ICD IN HYPERTROPHIC CARDIOMYOPATHY PATIENTS

Risk assessment for SCD in HCM is one of the most paradigmatic models of controversy in cardiovascular medicine. Individual risk markers of SCD were introduced late in the '90s [7] early in the 2000s and consisted of recent unexplained

syncope, family history of juvenile SCD, episodes of non-sustained ventricular tachycardia (NSVT), massive left ventricular hypertrophy, and exercise-induced hypotension. ICD decision-making was traditionally driven by the assumption that even a single risk factor for SCD is sufficient for primary prevention ICD candidacy [8]. On the contrary, Europeans promoted a strategy based on counting risk factors: a minimum of 2 non-invasive markers justified an ICD in at risk patients [9]. This approach has been questioned, as prospective analyses did not show that adding risk factors multiplies the risk or predicts ICD interventions [10]. Current American guidelines [11] endorse a single risk factor-based decision model that has been improved with the addition of recently introduced markers of SCD: extensive late gadolinium-enhancement on cardiac magnetic resonance (CMR), heart failure, and LV apical aneurysm. Also, the risk profile takes into account age, as in adults over 60 years event rates are so low [12] that ICD implantation should be considered on an individual basis. On the contrary, Europeans abandoned risk assessment strategies based on counting or weighting single risk factors and endorsed a scoring system that combines 4 continuous (age, max LV wall thickness, left atrial size, LV outflow gradient) and 3 binary variables (NSVT, family history of SCD and unexplained syncope) to predict the risk of SCD over 5 years [13]. High risk patients (≥6%/5 years) deserve protection with an ICD, while low-risk patients (<4%/5 years and no other clinical characteristics of proven significance) do not [14]. For patients with an estimated 5-year risk of SCD between 4% and <6%, an ICD may be considered and, in common clinical practice, is often adopted. Besides, this individualized risk model is envisioned to help in establishing proactive patient interaction in ICD decision-making.

The American and European approaches differ in terms of sensitivity and specificity. Particularly, American authors claim that the single-factor approach is superior in terms of sensitivity, as only a very small proportion of HCM patients without established risk factors die suddenly [15]. On the contrary, the European model displays higher specificity and could prevent ICD overtreatment [16]. Aside from debates on validation cohorts that retrospectively corroborated the models [17, 18], a recent study that assessed ICD adoption in US an non-US countries [19] brings findings that deserve consideration. While primary prevention ICD implantation rates in US are two-fold higher that in non-US countries, non-recipients of ICDs in US vs non-US sites have similar incidence of SCD/cardiac arrest. In this view, more “liberal” ICD indications would expose to long-term complications a substantial proportion of young ICD recipients who will probably never benefit from a defibrillator.

ICD adoption is a major determinant of the decline in HCM mortality in the modern era. Moreover, advancing technologies that focus on reducing ICD-related morbidity will lead to reconsider the risk/benefit ratio of ICDs in HCM and extend ICD therapy to patients for whom ICD decision is currently uncertain. However, as ICD therapy has clinical and healthcare costs, lack of specificity of any risk assessment strategy should promote prediction model refinement and does not justify tout-court ICD overtreatment.

**ICD-related hazards: are HCM patients different?**

As most HCM patients at risk for SCD have a low competitive risk of dying from non-arrhythmic causes, the ICD can be considered a life-saving rather than life-prolonging therapy in this disease [20]. However, ICD therapy is not without risks: complications may occur during implantation (e.g. pneumothorax, cardiac tamponade, haemothorax) or result from permanent indwelling intracardiac leads (venous thrombosis, infections, lead failures). Young patients, while benefitting most from the ICD, are also most exposed to long-term complications, particularly lead failure [21], due to their prolonged life expectancy and greater mechanical stress arising from an active life-style. With specific reference to HCM, high annual rates of lead malfunction (1.4%) or displacement (1.3%) and infection (1.1%) have been reported in ICD recipients [22]. Even excluding inappropriate shocks, the rate of ICD-related complications is as high as 3.4% per year [23]. Notably, in a cohort of children and adolescents with HCM, ICD-related complications, particularly inappropriate shocks and lead malfunction, occurred in 91 patients (41%) with a mean age of 17±5 years (9.5% per year) [24]. These very high complication rates add complexity to ICD implant decisions, particularly in young patients at intermediate risk of SCD in whom the therapy needs to be highly individualized.

The recently introduced subcutaneous ICD (S-ICD), by eliminating the need for permanent leads in the heart, would be expected to reduce complication rates considerably by removing the impact of intravascular lead sequelae. In the EFFORTLESS cohort [25], the rate of infections requiring device removal (2.4% over

3.1 years) was comparable to that of transvenous ICDs (TV-ICDs) [26]. However, the risk of bloodstream dissemination of device infections is substantial with transvenous and negligible with subcutaneous ICDs [25, 27]. Furthermore, until recently subcutaneous lead failure has been described anecdotally [28], although a 0.2%/41month lead fracture rate has just been reported (Model 3501 Electrode) due to manufacturing issue which is being addressed. Longer follow-up is required to ascertain the true incidence of lead-related events in S-ICD recipients.

In HCM patients implanted with an S-ICD and followed in the EFFORTLESS registry [29], the 2 year Kaplan-Meier freedom from complications estimate was 92.7%. Event rates for most common procedural complications were between 0.1 and 0.5%. There were no device erosions. Suspected device malfunction, sub-optimal electrode or generator position, each accounted for less than 1% of events. Although in this specific study no premature battery depletions were reported among HCM patients, a large subset of S-ICDs (Models A209 and A219) is currently demonstrating an elevated likelihood for accelerated battery depletion (the current projected occurrence rate is 3.7% at 5 years) that triggered a specific Medical Device Advisory. Concerning infections, 2% of the HCM patients required device explantation with no documented endocarditis or lead extraction-related complications [29].

According to both the US and European guidelines for prevention of sudden cardiac death [30, 31], if bradycardia or anti-tachycardia pacing, or CRT is neither needed nor anticipated, ICD candidates equally benefit from a transvenous or a subcutaneous ICD (class IIa indication). The findings from the recent randomized PRAETORIAN trial [4] show that in contemporary ICD candidates the S-ICD is noninferior to the TV-

ICD with respect to device-related complications and inappropriate shocks, corroborating these guidelines. Overall, current data suggest that the lower rate of lead-related complications and the generally good prognosis of device infections favour S-ICD in HCM patients with long-life expectancy and no need for pacing. Indeed, the recent advance of SMART Pass high pass filter sensing in Gen3 S-ICDs has reduced inappropriate shock rates due to oversensing to 2.4% in primary prevention reduced ejection fraction patients, lower than transvenous ICDs [5]. This is combined with setting high rate therapy cut-offs as outlined in MADIT-RIT [32]. The impact of SMART Pass on T wave oversensing specifically in HCM is yet to be fully assessed but given the fact that this was the commonest cause of inappropriate shocks in the combined IDE & EFFORTLESS S-ICD HCM substudy (10.4% of patients were, versus 7.2% T-wave oversensing in the non-HCM patients) in the era before SMART Pass, a benefit would be expected as has been reported in non-HCM cases [4,16].

**S-ICD eligibility**

With S-ICDs, ventricular sensing is achieved through three subcutaneous electrograms recorded between two sensing electrodes and the pulse generator. When subcutaneous electrograms display abnormal QRS or T-wave morphology leading to oversensing, inappropriate shocks may occur. Therefore, pre-implantation screening is routinely performed to determine S-ICD eligibility [33, 34]. Patients with HCM, who frequently have high amplitude R waves and large discordant T-waves on surface ECG, may pose specific difficulties. Eligibility for S-ICD based on pre-implant ECG screening has been reported in the range of 85% to 90% [35, 36] in HCM patients,

although recent studies reported much more prudent estimates, mainly based on dynamic ECG changes occurring during exercise [37, 38]. In most studies, high R wave amplitude is the most common factor affecting S-ICD eligibility. A new automated screening tool has recently been introduced that mimics the S-ICD sensing scheme and applies the improved signal-processing filters currently used by the device to analyse the ECG [39] (**Figure 1**). This new screening tool is more tolerant to high T-wave and R wave amplitudes and has been reported to increase eligibility in HCM patients up to 97% [40]. Interestingly, a substantial fraction of S-ICD recipients in whom the screening predicted non-eligibility have flawlessly working S-ICD systems [39]. This finding suggests that the false-positive prediction of ineligibility may be a weakness of current screening tools potentially denying S-ICD therapy.

Despite conflicting evidence, screening failure in HCM seems to be moderately low, provided that patients with severe hypertrophy and high R waves on surface ECG are carefully evaluated both at rest and during exercise. It is prudent to screen such patients on exercise to assess for dynamic T wave morphological changes and utilise the left, right and mid-sternal positions to ensure the maximum number of vectors are identified pre-implantation, hence enabling more versatility in programming optimal sensing or facilitate alternative sensing if inappropriate shocks occur due to oversensing.

**Does appropriate equal life-saving? The case of ATP**

Appropriate ICD interventions have been reported at a rate of 3-5% per year in primary and 11% per year in secondary prevention HCM patients [10, 20, 41]. In non-HCM patients, however, ICD shocks are a poor surrogate for SCD. In the DEFINITE

trial [42], non-ischemic primary prevention patients who received an ICD experienced twice as many shocks as the number of fatal events in the control medical therapy group. In the MADIT-RIT trial [32], patients assigned to a more conservative programming had significantly fewer appropriate and inappropriate ICD interventions (mainly ATP), improved survival, and no evidence of increased rate of syncope [43]. This finding has been further confirmed by a retrospective analysis of the MADIT-RIT cohort with appropriate therapies ≥200 bpm [44], which demonstrated that increasing therapy delays results in marked reductions in ATP interventions. Indeed, the incidence of appropriate ATP in patients with prolonged ICD therapy delay (i.e. 12 seconds) was as low as 2%, suggesting a limited value of ATP for treating VTs ≥200 bpm in primary prevention patients with appropriately programmed ICDs. Thus, interventions for monomorphic VTs may represent a limitation of ICD programming rather than a therapeutic success. A similar story seems to unfold in HCM patients. Independent studies reported monomorphic VT to be the most common arrhythmia triggering ICD interventions in HCM [24, 45-48], potentially representing a dominant cause of cardiac arrest among high-risk patients. Similar results have been reported in a recent non-randomized prospective study that assessed HCM patients implanted with either a subcutaneous or a transvenous ICD [49]. Such findings would seem to corroborate the need for ATP therapy and challenge the role of the S-ICD, which does not deliver pacing. However, as a result of ICD programming, time to first ATP was short in some series, and many HCM monomorphic VTs for which ATP was ineffective self-terminated within few seconds [46-48]. Therefore, there is growing evidence showing that aggressively programmed ICDs often treat what would otherwise be self-terminating monomorphic VTs, overestimating the incidence of

potentially lethal arrhythmias and of truly necessary ICD interventions [27, 50] (**Figure 2**). The importance of this concept is two-fold. First, lack of ATP might not represent a major limitation in a setting of primary prevention. Indeed, the average time to therapy for S-ICD is 15 sec, creating a safe and potentially beneficial window for self-termination. Second, ICD programming in HCM patients should follow the general rules that apply to common ICD patients [51]. Therefore, pending any compelling evidence that prolonged VTs may trigger disease-specific hemodynamic instability, ischemia, and/or early VT desynchronization into VF, long therapy delays and high-rate cut-offs should be preferred in primary prevention.

**Atrial fibrillation and inappropriate therapies**

Atrial fibrillation (AF) affects about 20% of patients with HCM [52, 53] and is a common cause of inappropriate ICD interventions [54, 55]. The dual-chamber ICD has been reported to discriminate AF from ventricular arrhythmias more reliably than the single-chamber ICD [56]. However, a decrease in inappropriate shocks has never been convincingly demonstrated [56-58]. This also applies to HCM patients, in whom single and dual-chamber ICDs have similar rates of inappropriate interventions [59]. The START (Subcutaneous versus Transvenous Arrhythmia Recognition Testing) trial [60], which compared discrimination algorithms of S-ICDs and TV-ICDs, reported that specificity for supraventricular arrhythmia discrimination was significantly better for the former. In HCM patients enrolled in the EFFORTLESS registry [29], the rate of inappropriate shocks was higher (6.9%/year) as compared to that of a previous study focusing on HCM TV-ICD patients (4.6%/year) [23]. However, inappropriate shocks

were mainly due to T-wave oversensing in S-ICD patients and “misinterpreted” AF in TV-ICD patients, respectively. The finding that cardiac and non-cardiac oversensing is the dominant cause of inappropriate shocks and that rapid AF is effectively discriminated in S-ICD recipients has been recently confirmed in the large prospective UNTOUCHED trial [5]. Therefore, with specific reference to the need of avoiding AF-related shocks, current data do not support the adoption of a transvenous rather than a subcutaneous system. Moreover, there is no evidence that dual-chamber ICDs offer advantages over single-chamber or S-ICDs in avoiding AF-related inappropriate shocks in HCM patients.

Irrespective of whether transvenous or non-transvenous technologies are considered, the rate of inappropriate ICD therapies in HCM patients is of concern. Altough ICD therapy does not substantially impair physical or psychological well-being *per se* [20], inappropriate shocks negatively affect quality of life and mental health [61], as they inevitably convey anxiety in expectation of future shocks. From a technological standpoint, there is considerable large room for improvement so in the meantime high rate programming and antiarrhythmic and rate slowing medications should be utilised with consideration of AF ablation when appropriate (e.g., paroxysmal AF).

**Defibrillation threshold in HCM patients**

High defibrillation threshold (DFT) in HCM patients has been reported in some [62] but not all [63] studies. More recently, DFT in HCM patients has been shown to be at least 10J lower than the maximal ICD output, independent of the magnitude of LV hypertrophy, and did not predict shock efficacy for spontaneous VT/VF episodes [64].

An initial experience [65] has shown that the S-ICD is effective in recognizing and terminating VF with a wide safety margin in HCM patients. Of note, patients with greatest maximum LV wall thickness had a DFT between 35 and 50 J, well below the maximal 80J output [65]. A recent report From the National Cardiovascular Data Registry [66] confirmed that there is no association between inadequate ICD energy safety margin and HCM. Moreover, two independent studies have shown that S-ICD defibrillation success rate is high and comparable to that of transvenous ICDs [29, 67]. Indeed inter/submuscular implantation with posterior generator positioning plus ensuring minimal subcutaneous fat under the sternal coil to achieve a low PRAETORIAN score maximise the chances of optimal DFT [68-70].Taken together, these studies support the concept that all contemporary ICDs are safe and effective in HCM patients, and that there are no disease-specific or left ventricular mass-related concerns regarding S-ICD defibrillation efficacy.

## SPECIFIC CLINICAL SCENARIOS

### Left ventricular outflow tract obstruction

Among HCM patients who are candidates for ICD implantation, those presenting with LVOT obstruction deserve special consideration. Surgical myectomy (SM) and alcohol septal ablation (ASA) relieve left ventricular outflow tract obstruction by removing or ablating myocardial tissue in the ventricular septum. As both SM and ASA can cause damage to the adjacent bundles, conduction system defects are common complications. Indeed, SM results in left bundle branch block

(LBBB) in 30-40% and complete heart block (CHB) requiring pacemaker implantation in 2-10%[71-73], mostly in patients with pre-existing RBBB. On the other hand, approximately 30% of patients undergoing ASA develop right bundle branch block (RBBB), and 8-14% CHB [72, 74-76]. Therefore, there is a non-negligible risk that SM or ASA could result in conduction defects requiring permanent pacing, a condition contraindicating S-ICD implantation. Moreover, changes in QRS-T morphology following septal reduction may prompt inappropriate S-ICD shocks due to T-wave oversensing and/or failure to recognize the stored QRS-T template [77]. Therefore, there is a risk that S-ICD eligibility might not be preserved after SM or ASA which should be taken into consideration when selecting a device for obstructive HCM patients.

Based on these considerations, obstructive HCM patients who are candidates for an ICD and have no compelling indication to SM or ASA could reasonably benefit more from a trans-venous rather than a subcutaneous ICD. Notably, a trans-venous system provides the additional bonus of allowing atrial-synchronized ventricular pacing with short AV delay, an approach known to reduce the outflow gradient and improve symptoms in selected, generally older, patients, in whom invasive interventions may be avoided or postponed [78]. If surgery cannot be deferred, it is reasonable to delay ICD implantation and reassess S-ICD eligibility (as well as SCD risk) after septal reduction.

**CRT for end-stage disease**

HCM patients fulfilling standard criteria for CRT are exceedingly rare. However, 5-7% develop the so-called end-stage or “burnt-out” phase of the disease,

arbitrarily defined by the presence of LV systolic dysfunction with ejection fraction less than 50%, usually in severely symptomatic patients [79]. End-stage HCM is a predictor of life-threatening arrhythmias with an annual event-rate of approximately 10% [80], and represents an indication for ICD implantation in primary prevention and as a bridge to transplantation [6]. As LBBB is common in such settings, cardiac resynchronization therapy with defibrillation backup (CRT-D) has been attempted to improve LV function and symptoms. CRT was moderately effective in one study [81], while it failed to improve LV function or outcome in a more recent experience [82]. At present, specific indications for biventricular pacing are lacking in HCM patients and standard criteria for candidate selection are recommended [83]. CRT failure in the end-stage phase is likely due to the extensive myocardial fibrosis present (exceeding 35% of the whole LV), poorly amenable to reverse remodeling. Whether CRT may be beneficial in earlier phases of HCM (e.g. to mitigate LBBB-related dysfunction following myectomy or in patients with permanent ventricular pacing) remains to be established.

In younger patients, and mostly in the few who are potential candidates to a left ventricular assist device as a bridge to heart transplantation, an S-ICD could be favoured as part of a strategy to reduce the risk of bloodstream infections [84]. Nevertheless, S-ICD vectors should be carefully re-assessed after surgery because assist device electromagnetic fields have been anecdotally reported to interfere with S-ICD sensing [85].

Furthermore, although not yet specifically addressed in published HCM series, there is reasonable concern that progressive myocardial fibrosis may involve the cardiac conduction system and cause AV block in patients with end-stage phenotype.

Therefore, when cardiac MR reveals massive fibrosis of the interventricular septum, particularly in the presence of first-degree AV block and bundle branch block, caution should be adopted in selecting a subcutaneous ICD.

**LV apical aneurysms**

The prognosis of HCM patients with LV apical aneurysms is generally unfavourable, with an overall rate of life-threatening complications between 6 and 10% per year, mostly consisting of arrhythmic SD and thromboembolic events [86]. The scarred rim and the surrounding areas of myocardial fibrosis offer the substrate for re-entrant ventricular tachycardia (VT), the dominant arrhythmia in patients with LV aneurysm [45, 87]. Accordingly, it has been suggested that these patients should receive trans-venous ICDs with ATP capability [45]. As studies that systematically distinguished the rate of monomorphic VTs from that of VF episodes in ICD recipients are lacking, it is difficult to anticipate whether the benefits of having ATP exceed the long-term risks of permanent intracardiac leads in primary prevention. In young patients, an alternative strategy involving radiofrequency ablation appears reasonable in cases of post S-ICD implant monomorphic VTs [86, 88], albeit never systematically assessed. Indeed, apical aneurysm patients represent the only subgroup within the broad spectrum of HCM for which catheter ablation has been reported as an effective treatment for refractory sustained monomorphic ventricular arrhythmia [86]. As ATP may suppress monomorphic VTs and be a useful programming feature for patients with apical aneurysms, the forthcoming modular combination of a leadless pacemaker and an S-ICD may be considered in this clinical setting when it is approved for clinical use [89].

**Children**

From 1997 to 2016, a series of paediatric population-based studies reported a 3- to 4-fold increase in ICD implantation [90, 91], likely because of improved understanding of the risk of SCD in children with heart diseases and enhanced survival of those who later become ICD candidates.

HCM is the second most common cardiomyopathy occurring during childhood [92]. Recent population-based and registry studies have reported annual mortality rates between 1% and 2.5% [93], SCD being the most common cause of death. In a recent analysis on 3.461 patients aged <21 years implanted with an ICD (17% with HCM) [90], 2.6% had intra- or post-operative complications and 3% had early need for re-intervention, mainly because of device infection, relocation, or failure. Notably, information on lead-only revision procedures was incomplete and therefore not reported in this study**.** In children with HCM, ICDs have been shown to be effective in treating VT/VF at the price of a higher rate of complications as compared to adults [24, 92-94]. Indeed, although techniques have been developed to address the problem of lead stretching during body growth, the rate of long-term failure and infections remains high (**Figure 3**). In a broader perspective, when facing the issue of protecting children from SCD, the widespread view is that the anticipated cumulative life-long risk of transvenous ICD-related complications is unacceptably high. Thus, the S-ICD seems to represent an ideal option and has indeed been successfully used in children [95], despite a substantial risk of complications in patients with low BMI. To date, a major limitation of the S-ICD remains device size, which is more than two-fold that of a traditional TV-ICD due to the need of delivering higher energies. Studies are

ongoing to test whether a lower output S-ICD can provide an adequate safety margin to terminate VF in clinical practice [96]. This should promote the development of smaller devices meeting the clinical needs of paediatric patients.

### Elderly patients

Patient age is a crucial variable in the clinical course of HCM and a decisive factor for personalized management. In young adults and “midlife” HCM patients (i.e. 30-59 years of age), the most common age group in clinical practice, mortality is low (0.5% per year) and may be influenced importantly by the use of ICDs for primary prevention of SCD [97]. Conversely, HCM patients beyond midlife (i.e. ≥60 years of age) have low incidences of SCD or appropriate ICD interventions (0.2% per year), supporting the concept that, after the sixth decade of life, HCM has already declared its natural history with low arrhythmic propensity [12]. In this perspective, ICD implantation in patients >60 years of age should be evaluated on an individual basis, taking into account that non–arrhythmic events associated with HCM as well as acquired, age-related cardiovascular conditions and non-cardiac morbidity are most likely to impact outcome. Considering that ICD lead failure and infections are largely time-dependent, and that the rate of advanced AV block or slow AF increases markedly with age, use of non-transvenous technologies is less compelling in older patients, while traditional ICDs represent an affordable and appropriate option.

## CONCLUSIONS

Most HCM patients at risk for SCD are young and have low risk of dying for competing non-arrhythmic causes. The ICD exerts a major impact on the natural history of their disease and, therefore, device selection should be primarily tailored to preserve clinical benefit without introducing undesired morbidity (**Figure 4**). As a general rule, simpler ICD systems are associated with fewer long-term complications and should be preferred. Hence, single-chamber devices and the S-ICD are reasonable options for most HCM patients. When pacing is neither needed nor anticipated, the S-ICD could be implanted in view of the lower risk of lead-related complications and bloodstream dissemination of local infections. The use of dual-chamber ICDs should be limited to patients with symptomatic sinus node dysfunction or complete heart block when there is a need to preserve atrio-ventricular synchrony, mostly following septal reduction interventions in obstructive HCM patients. Current evidence does not support the use of dual-chamber ICDs as a strategy to reduce AF-related inappropriate shocks in HCM patients.

Many efforts are underway to enhance the long-term reliability of current devices and improve non-transvenous technologies with additional features that could address the clinical heterogeneity of HCM [89, 98]. We welcome forthcoming technology developments as long as they minimize long-term complications that erode the benefits of preventing SCD. *Primum, non nocere*.

## FIGURES

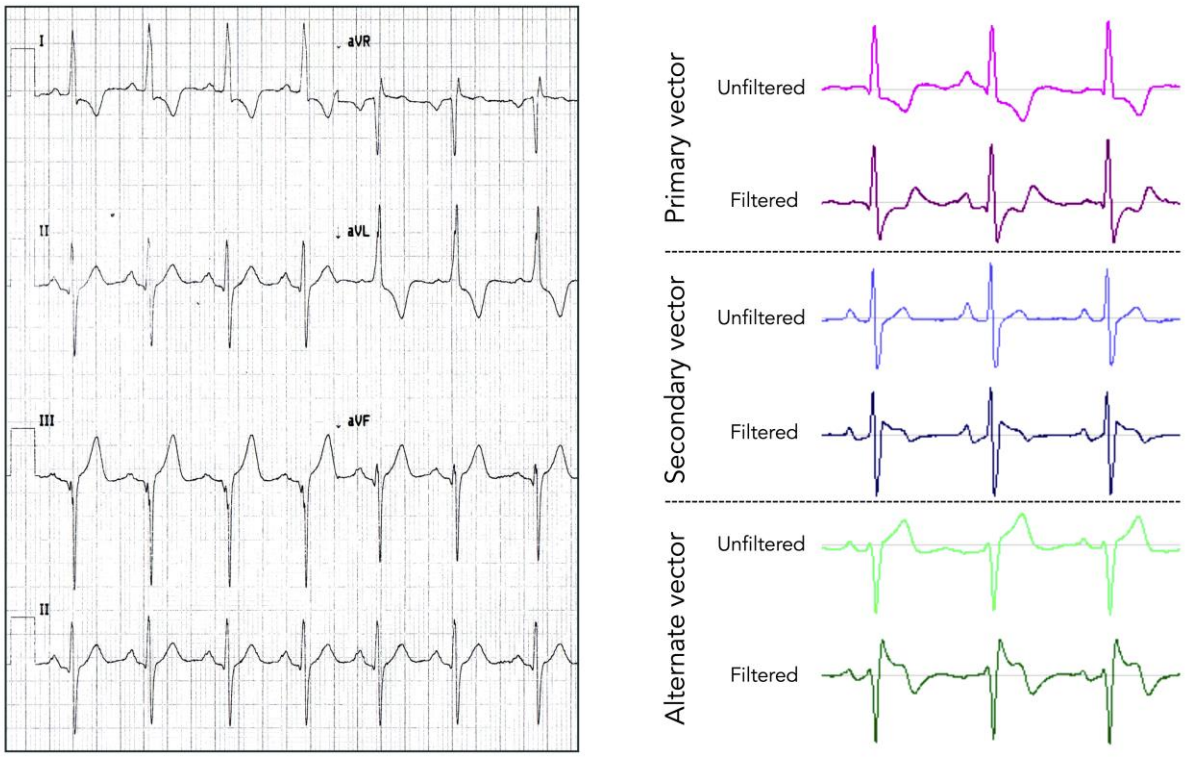


**Figure 1. Left.** Standard ECG from a 24 years-old patient with HCM and massive left ventricular hypertrophy. **Right.** Pre-implantation S-ICD screening with the automated screening tool in the same patient.

The R/T-wave ratio in leads I, II and aVF closely reflects eligibility according to the primary, secondary, and alternate S-ICD vectors. Automated screening tool approximates the implanted S-ICD sensing windows, as it processes the signals by applying a specific digital filter that is also embedded in the contemporary sensing algorithm of the S-ICD. As compared with unfiltered vectors, the T waves from digitally filtered signals are lower in amplitude and smoothed.

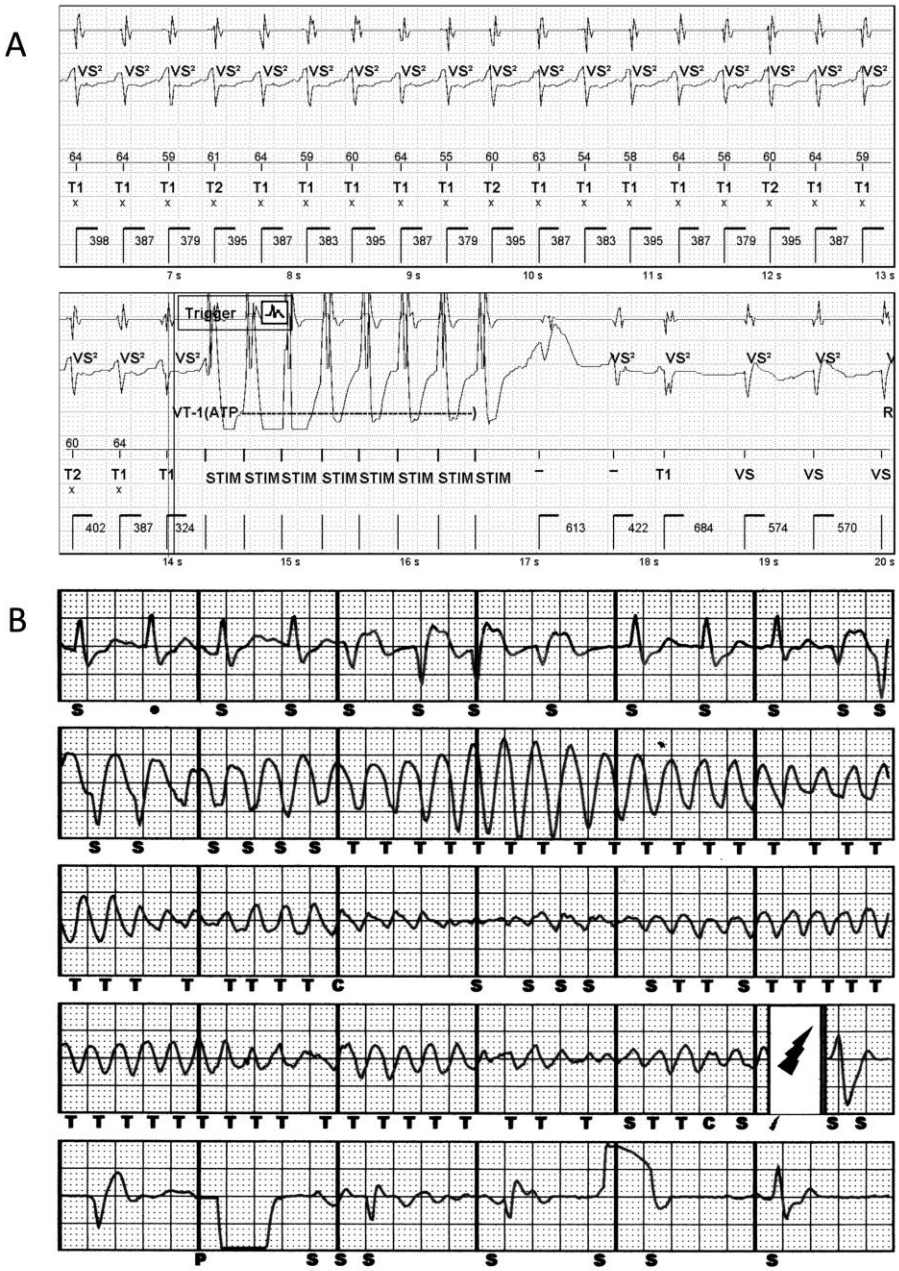


**Figure 2. (A)** Slow (156 bpm) monomorphic VT in a 75-years old patient with end-stage HCM implanted with a single-chamber ICD. The VT is appropriately recognized (T1 marker) and successfully treated with a single burst of anti-tachycardia pacing (STIM marker). **(B)** VF in a 36-years old HCM patient with massive LV hypertrophy

implanted with a subcutaneous ICD after resuscitated cardiac arrest. VF is promptly recognized (T marker) and treated with a 65J shock (lightening marker).

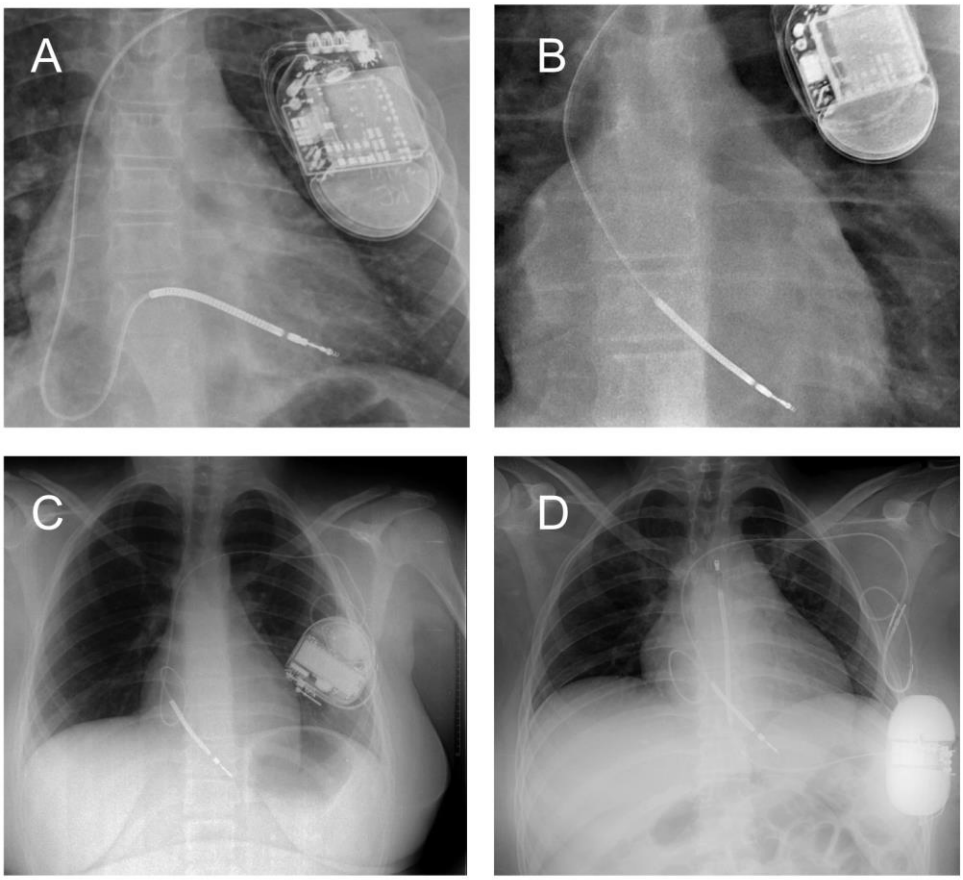


**Figure 3.** In young patients, lead displacement and fracture secondary to stretching during body growth is a concern with transvenous ICDs.

**Panels A and B**. A child with HCM and family history of end-stage disease and SCD was implanted at the age of 13 with a single-chamber ICD, leaving a portion of the lead prolapsing in the inferior vena cava (panel A). Nine years after implantation, the lead is markedly stretched although still properly functioning (panel B).

**Panels C and D**. A child with HCM and massive LV hypertrophy was implanted at the age of 14 with a single-chamber ICD. A large electrode loop was created within the atrium to allow for growth (panel C). Twelve years after implantation, lead fracture occurred causing multiple inappropriate shocks secondary to noise oversensing. As evident from chest radiograph,

lead fibrosis to the atrial wall precluded uncoiling with body growth (panel D). The patient underwent S-ICD implantation. The original electrode was provisionally abandoned, and the patient referred for extraction.

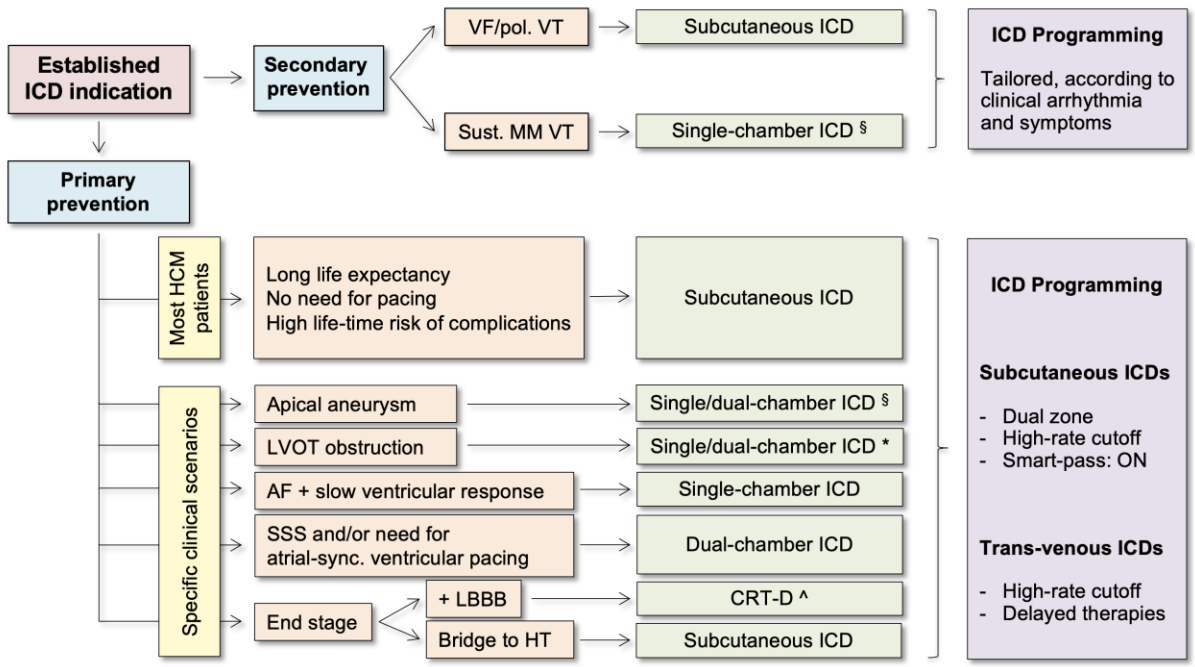


**Figure 4.** Suggested criteria for selecting the most appropriate ICD system and programming in HCM patients according to distinct clinical scenarios.

§ Consider also VT ablation or leadless ATP + subcutaneous ICD (*subject to approval*).

* Transvenous ICDs are preferred when there is no compelling indication to septal reduction, mostly in older patients. In case of AV block

following septal reduction, use of single/dual chamber ICDs becomes mandatory.

^ Specific indications for CRT are lacking in HCM patients and standard criteria for candidate selection are recommended [83].

VT, ventricular tachycardia; VF, ventricular fibrillation; pol, polymorphic; sust, sustained; MM, monomorphic HCM, hypertrophic cardiomyopathy; S-ICD, subcutaneous ICD; LVOT, left

ventricular outflow tract; AF, atrial fibrillation; SSS, sick sinus syndrome; CRT-D, cardiac resynchronization therapy ICD; SR, sinus rhythm; LBBB, left bundle branch block; HT, heart transplantation.

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