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REVIEW

Current Device Therapies for Sudden Cardiac Death Prevention – the ICD, Subcutaneous ICD and Wearable ICD

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Defibrillator technology for sudden cardiac death (SCD) prevention now includes the transvenous implantable cardiac defibrillator (ICD), subcutaneous ICD (S-ICD) and wearable cardioverter defibrillator (WCD). ICD use improves survival in patients who survived previous sudden cardiac arrest (SCA) due to ventricular tachycardia (VT)/ventricular fibrillation (VF), as well as in patients who experienced haemodynamically significant VT. It is also currently indicated for primary prevention in ischaemic/non-ischaemic cardiomyopathies, certain congenital heart disease conditions and inherited channelopathies. In this review article, we hope to present an updated review on ICD use for SCD prevention, with a focus on contemporary issues affecting ICD selection. These include: the role of primary prevention ICD in patients with non-ischaemic cardiomyopathy (NICM) in light of the 2016 DANISH (Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality) trial; the role of defibrillator component (CRT-D) in patients receiving cardiac resynchronisation therapy (CRT-P); and the emerging role of cardiac magnetic resonance imaging (cMRI) in particular, the presence of late gadolinium enhancement (LGE), as an important SCD risk predictor. The current use of S-ICD and WCD, including clinical indications, evidence for efficacy and limitations, will also be discussed.

Keywords Sudden cardiac death • Implantable cardiac defibrillator • Subcutaneous-ICD • Wearable ICD • Cardiac Resynchronisation Therapy • Cardiac MRI

Introduction

Sudden cardiac death (SCD), which is the sudden and unexpected death within an hour of symptom onset, or death in patients within 24 hours of being asymptomatic, and likely due to cardiac arrhythmia, is the leading cause of cardiovascular mortality worldwide [1–3]. In Australia, it is estimated that 15,000 people die from SCD annually, accounting for 10% of all Australian deaths each year [4].

The implantable cardiac defibrillator (ICD) remains the most effective treatment for primary or secondary prevention of SCD [5]. However, ongoing challenges remain with the identification of individuals who are at risk of SCD and who might benefit from the prophylactic use of an ICD. About half of cardiac arrest cases in the general population occur in individuals without a known heart disease [2,6]. Additionally, there are age-related differences in the aetiology of cardiac diseases associated with SCD, with channelopathies and cardiomyopathies predominant in young people. The recent publication of the DANISH (Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality) trial has raised further questions about the utility of primary prevention ICD in patients with non-ischaemic cardiomyopathy (NICM) [7]. Patient selection aside, ICD technology has also undergone significant advancements to become sophisticated devices. Alternative approaches to

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defibrillation have now emerged to overcome limitations with transvenous ICDs, namely the subcutaneous ICD (S-ICD) and the wearable cardioverter defibrillator (WCD).

In this article, we aim to provide a brief review of current indications for ICD use in SCD prevention. We will also discuss issues affecting ICD selection, including the utility of a routine defibrillator component in patients receiving CRT devices, and the role of cardiac MRI in SCD risk prediction. The current indications, efficacy and safety data for newer defibrillator technologies, namely S-ICD and WCD, will also be discussed.

Current Indications for ICD Implantation

The current indications for the use of ICD for SCD prevention, based on the 2017 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) guidelines for management of patients with ventricular arrhythmias, and the 2015 European Society of Cardiology (ESC) guidelines for management of patients with ventricular arrhythmias, are summarised in Table 1 [2,6]. ICD implantation for secondary prevention in patients who survived sudden cardiac arrest (SCA) due to ventricular tachycardia/ventricular fibrillation (VT/VF); or in patients who experienced haemodynamically significant VT, has been accepted in recent years with class I indications in both major societal guidelines. This is based on earlier studies such as CIDS (Canadian Implantable Defibrillator Study), AVID (Antiarrhythmics Versus Implantable Defibrillators) and CASH (Cardiac Arrest Study Hamburg) [8–10]; with subsequent meta-analysis showing ICD use resulted in a 28% reduction in total mortality [11]. There are subgroups of patients who remain under-represented in ICD studies, including older patients (≥75 years of age), and patients with multiple medical co-morbidities. However, a recent systematic review suggested that even older patients with severe cardiomyopathy have a survival benefit from ICD. Additionally, patients with multiple medical co-morbidities and chronic kidney disease (CKD) may benefit from primary prevention ICD [12].

Primary Prevention in Ischaemic Cardiomyopathy

Current indications for primary prevention ICD in ischaemic cardiomyopathy have remain largely unchanged, having been shaped by the findings of earlier randomised controlled trials (RCT) namely MADIT (Multicenter Automatic Defibrillator Implantation Trial), MUSTT (Multicenter UnSustained Tachycardia Trial), MADIT–II, and SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) trials [13–16] (Table 2). These studies have focussed on left ventricular systolic function/ejection fraction (EF) and congestive cardiac failure CCF (CCF) symptoms (New York Heart Association (NYHA) classification) as the main risk stratification criteria. In addition, evaluation of patients for ICD implantation should be made at least 40 days after myocardial infarction (MI) as no survival benefit was demonstrated from early ICD use [17,18]. The use of an electrophysiological study to risk stratify patients, which carries a class I indication in the AHA/ACC/HRS guideline, was studied in the MUSTT trial, with higher overall mortality rates in patients with inducible VT as opposed to those without inducible VT [14]. This finding was further corroborated by an observational study where 22% of those who received an ICD for inducible VT had appropriate device therapy on follow-up, whereas none of the patients without inducible VT had arrhythmic events during follow-up [19].

Primary Prevention in Non-Ischaemic Cardiomyopathy (NICM)

Four earlier RCTs (CAT [CArdiomyopathy Trial], AMIOVIRT [Amiodarone Versus Implantable Cardioverter Defibrillator Trial], DEFINITE [Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation Trial], SCD-HeFT) studied outcomes of primary prevention ICD in NICM, with none of these studies showing significant survival benefit of an ICD (Table 3) [16,20–22]. However, a subsequent pooled analysis shows a significant 31% reduction in all-cause mortality for ICD relative to medical therapy [11]. Criticisms of earlier studies include low rates of anti-heart failure therapy such as angiotensin converting enzyme (ACE) −inhibitors, beta blockers, and mineralocorticoid antagonists; underpowered studies; and low overall event rates [2]. The most recent and largest study of NICM patients was the 2016 DANISH study (Table 3) [7], which randomised 1,116 NICM patients with LVEF <35% and NYHA class II–III (IV, if CRT planned) heart failure to receive an ICD or no ICD. The majority of patients were on optimal anti-heart failure therapy and CRT was used in 58% of the cohort. There was no significant difference in all-cause mortality, although ICD use did significantly reduce SCD rates from 8.4% to 4.3% [7]. Subsequent subgroup analyses showed a mortality benefit with ICD use in younger (<59 years old) patients and patients with lower NT pro–BNP levels [23]. This would suggest that the benefit of primary prevention ICD is likely to be greatest in patients with less severe symptoms of heart failure, younger age and fewer comorbidities.

Regardless, the findings of the DANISH study have resulted in significant controversy, and highlights the notion that SCD risk stratification in NICM is likely more complicated than the use of a single marker of left ventricular ejection fraction (LVEF) (and CCF symptoms) alone. Non-ischaemic CM encompasses a heterogeneous group of cardiac diseases with varying clinical progression, ranging from a stable myocardial substrate to progressive clinical progression/deterioration. NICM is also associated with an overall lower risk for ventricular arrhythmias than ICM, and these patients possibly have increased mortality associated with non-arrhythmic causes [24,25]. Thus, the benefit of having an

Table 1 Current indications for ICD implantation.

	2017 AHA/ACC/HRS	2015 ESC
Secondary Prevention		
SCA due to VT/VF or haemodynamically unstable VT not due to reversible causes or within 48 hours after MI who are on GDMT	Class I (level B)	Class I (level A)
Unexplained syncope with inducible sustained VT on EP study	Class I (level B)	–
Cardiomyopathy		
a) Ischaemic Cardiomyopathy		
LVEF ≤35% at least 40 days post MI and at least 90 days post revascularisation, with NYHA class II/III symptoms despite GDMT	Class I (level A)	Class I (level A)
LVEF ≤30% at least 40 days post MI and at least 90 days post revascularisation, with NYHA class I symptoms despite GDMT	Class I (level A)	–
LVEF ≤40%, NSVT, and inducible sustained VT/VF on EP study	Class I (level B)	–
b) Non-Ischaemic Cardiomyopathy (NICM)		
LVEF ≤35% with NYHA class II/III symptoms, despite GDMT	Class I (level A)	Class I (level B)
LVEF ≤35% with NYHA class I symptoms, despite GDMT	Class IIb (level B)	Class I (level B) (3 months of GDMT)
Patients who experience syncope due to presumed VT and who do not meet indication for a primary prevention ICD	Class IIa (level B)	–
NICM from Lamin A/C mutation who have 2 or more risk factors (NSVT, LVEF <45%, non-missense mutation, male sex)	Class IIa (level B)	–
c) Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)		
Patients with an additional marker of increased SCD risk (resuscitated SCA, poorly tolerated VT, significant ventricular dysfunction with RVEF or LVEF ≤35%)	Class I (level B)	Class I (level C)
Patients with one or more recognised risk factors for VT in adults with a life expectancy of >1 year (including syncope)	Class IIa (level B)	Class IIb (level C)
d) Hypertrophic Cardiomyopathy (HCM)		
Patients who have survived SCA due to VT/VF, or spontaneous sustained VT causing syncope/haemodynamic compromise	Class I (level B)	Class I (level B)
Patients with 1/> risk factors: Maximum LV wall thickness ≥3 cm SCD in 1/> first degree relatives presumed from HCM 1/> episodes of unexplained syncope within past 6 months	Class IIa (level B/C)	–(see below)
Patients with spontaneous NSVT or abnormal BP response to exercise, who also have SCD risk modifiers[γ] or high risk features[ς]	Class IIa (level B/C)	–(see below)
Risk stratification using HCM Risk-SCD calculator is recommended to estimate 5-year SCD risk in patients ≥16 years without history of resuscitated VT/VF or spontaneous sustained VT causing syncope or haemodynamic compromise	–	Class I (level B)
Patients with estimated 5-year risk of sudden death (based on HCM Risk-SCD calculator) of ≥6% and a life expectancy of ≥1 year	–	Class IIa (level B)
e) Cardiac Sarcoidosis		
Patients with sustained VT/survived SCA/LVEF of ≤35%	Class I (level B)	Class IIb (level C)
Patients with LVEF >35% who have syncope and/or evidence of myocardial scar by MRI/PET, and/or have an indication for permanent pacing	Class IIa (level B)	–
Patients with LVEF >35%, with inducible sustained VT on EP study	Class IIa (level C)	–
Patients with an indication for permanent pacing	Class IIa (level C)	–
f) Restrictive Cardiomyopathy		
Patients with sustained VA causing haemodynamic instability who are expected to survive >1 year with good functional status	–	Class I (level C)
Cardiac Channelopathies		
a) Congenital Long QT Syndrome		
High risk patients (including previous SCA/recurrent syncope) in whom beta blocker ineffective or poorly tolerated	Class I (level B)	Class I (level B)
Consider (with beta blocker therapy) in asymptomatic carriers of pathogenic mutation in KCNH2 or SCN5A when QTc >500 ms	–	Class IIb (level C)

Table 1. (continued).

	2017 AHA/ACC/HRS	2015 ESC
b) Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)		
Patients with previous cardiac arrest, recurrent syncope, or polymorphic/ bidirectional VT, whilst receiving beta blockade	Class I (level B)	Class I (level C)
c) Brugada Syndrome		
Patients who survived cardiac arrest, or experienced sustained VA	Class I (level B)	Class I (level C)
Patients with spontaneous type 1 Brugada ECG pattern and history of syncope	Class I (level B)	Class IIa (level C)
Patients with a diagnosis of Brugada syndrome who develop VF during PVS with 2/3 extrastimuli at two sites	–	Class IIb(level C)
d) Early Repolarisation "J wave" Syndrome		
Patients with cardiac arrest or sustained VA	Class I (level B)	–
e)Idiopathic Polymorphic VT/VF		
Patients resuscitated from cardiac arrest	Class I (level B)	–
Adult Congenital Heart Disease		
Patients with haemodynamcally unstable VT, after evaluation and treatment for residual lesion/ventricular dysfunction	Class I (level B)	Class I (level B)
Patients with SCA due to VT/VF in the absence of reversible cause	Class I (level B)	Class I (level B)
Patients with repaired TOF physiology, and inducible VT/VF or spontaneous sustained VT	Class IIa (level B)	–(see below)
Patients with repaired TOF and multiple risk factors for SCD (LV dysfunction, NSVT, QRS >180 ms, inducible sustained VT on PVS)	–	Class IIa (level B)
Patients with unexplained syncope and at least moderate ventricular dysfunction or marked hypertrophy	Class IIa (level B)	Class IIa (level B)
Patients with EF <35% and NYHA class II/III despite GDMT	Class IIb (level B)	Class I (level C)
Cardiac Transplantation		
NYHA class IV who are candidates for cardiac transplantation or LVAD, with expected meaningful survival of >1 year	Class IIa (level B)	Class IIa (level C)
Myocarditis		
Patients with giant cell myocarditis with SCA/haemodynamically unstable VT on GDMT	Class IIb (level C)	Class IIb (level C)

Abbreviations: SCA, sudden cardiac arrest; VT, ventricular tachycardia; VF, ventricular fibrillation; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; GDMT, guideline directed medical therapy; NSVT, non sustained ventricular tachycardia; PVS, programmed ventricular stimulation; EF, ejection fraction; SCD, sudden cardiac death; TOF, tetralogy of Fallot; MRI, magnetic resonance imaging; PET, positron emission tomography; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; EP, electrophysiological; VA, ventricular arrhythmia; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; BP, blood pressure; LVOT, left ventricular outflow tract.
[†]HCM risk modifier – age <30 years, delayed hyperenhancement on cardiac MRI, LVOT obstruction, syncope.
[‡]HCM high risk features – LV aneurysm, LVEF <50%.

ICD for SCD, as seen in ICM, may not be realised in these patients. Lastly, the possibility for a type II error in estimating the benefit of ICD in NICM could not be ignored, as lower-than-anticipated event rates attributable to improved medical therapy and CRT use could have led to under-powered primary prevention trials [26].

Various approaches have been studied to further refine risk prediction in NICM. Cardiac magnetic resonance imaging (cMRI), which is able to identify the presence of myocardial fibrosis through late gadolinium enhancement (LGE), is emerging as a powerful prognostic tool (this will be discussed further in the following section). Invasive electrophysiological (EP) study, with programmed ventricular stimulation (PVS), is able to detect circuits or foci which can potentially trigger ventricular arrhythmias. However, previous studies have provided conflicting findings on the usefulness of PVS in SCD risk stratification in NICM [27–29]. Additionally, there are limitations to this approach, including alterations in electrophysiological properties of cells from autonomic tone fluctuations, non-standardised methodology, and the invasive nature of performing a PVS. Underlying disease progression of NICM may also render PVS findings obsolete over time [30].

More recently, Dilaveris et al. have proposed a multi-tiered approach for risk stratification in NICM. This includes a clinical assessment of patients' expected survival from their underlying cardiomyopathy and co-morbidities; an assessment of non-invasive markers of electrical instability on ECG such as QRS fragmentation, late potentials, and complex ventricular ectopy; as well as the presence/absence of LGE

Table 2 Primary Prevention ICD Studies in Patients with Ischaemic Cardiomyopathy (ICM).

Clinical Trial Randomisation	Year Results	Patients	Sample	EF	NYHA
MADIT [15]	1996	Previous MI 196 NSVT Sustained VT on EPS	≤35%	I–III	ICD vs OMT	Significant reduction in mortality in ICD (HR 0.46; p = 0.009)
MUSTT [14]	1999	CAD 704 NSVT Sustained VT on EPS	≤40%	I–III	EPS guided therapy (ICD or AAD) vs no AAD	a) Significant reduction in cardiac arrest/ arrhythmic death in EPS guided therapy vs no AAD (RR 0.73; p = 0.04) b) No significant difference in overall mortality between EPS guided therapy vs no AAD (RR 0.8; p = 0.64) c) Significant reduction in cardiac arrest/ arrhythmic death in ICD group vs no ICD group (RR 0.24; p = < 0.001)
MADIT II [13]	2002	Previous MI (≥1 month) EPS not required	1232	≤30%	I–III	ICD vs OMT	Significant reduction in all cause mortality in ICD group (HR 0.69; p = 0.016)
DINAMIT [18]	2004	Previous MI (6–40 days) Abnormal HRV	676	≤35%	I–III	ICD vs OMT	a) No significant difference in mortality (HR 1.08; p = 0.06) b) Significant reduction in arrhythmic death in ICD group (HR 0.42; p = 0.009) c) Significant increase in non arrhythmic death in ICD group (HR 1.75; p = 0.02)
SCD-HEFT [16]	2005	52% – IHD	2521	≤35%	II–III	ICD vs amio vs placebo	Significant reduction in mortality in ICD group cf placebo (HR 0.79; p = 0.05) No benefit for Amio vs placebo
IRIS [17]	2009	Previous MI (5–31 days) NSVT/HR >90 bpm	898	≤40%	N/A	ICD vs OMT	a) No significant difference in mortality (HR 1.04; p = 0.78) b) Significant reduction in arrhythmic death in ICD group (HR 0.55; p = 0.049) c) Significant increase in non arrhythmic death in ICD group (HR 1.92; p = 0.001)

Abbreviations: MI, myocardial infarction; EF, ejection fraction; NYHA, New York Heart Association; NSVT, non sustained ventricular tachycardia; EPS, electrophysiologic study ; ICD, implantable cardiac defibrillator; OMT, optimal medical therapy; AAD, anti-arrhythmic drugs; IHD, ischaemic heart disease; HRV, heart rate variability; Amio, amiodarone; MADIT, Multicenter Automatic Defibrillator Implantation Trial; MUSTT, Multicenter UnSustained Tachycardia Trial; MADIT II, Multicenter Automatic Defibrillator Impltantation Trial II; DINAMIT, Defibrillator in Acute Myocardial Infarction Trial; SCD-HeFT, Sudden Cardiac Death in Heart Failure Trial; IRIS, Immediate Risk Stratification Improves Survival Trial.

on cardiac MRI. The authors propose the use of invasive PVS to provide the ultimate adjudication in LGE positive cases and/or in cases with one or more ECG risk factors [30]. Further studies are needed to validate this approach.

CRT–Pacing (CRT-P)Versus CRT–Defibrillator (CRT-D)

Cardiac resynchronisation therapy (CRT) has been shown to decrease morbidity and mortality in selected patients with severe left ventricular (LV) systolic dysfunction, NYHA class II–IV (ambulatory) symptoms, with ECG evidence of left bundle branch block (LBBB) and wide QRS complex of >150 ms [31,32]. An important consideration at the time of implantation is whether to add a defibrillator component, with higher associated cost, to CRT pacing. Studies thus far have not provided clear evidence on the incremental survival advantage of CRT-D to CRT-P, even within the specific subgroups of ICM/NICM [33]. In the landmark COMPANION (Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure) trial, comparison between CRT-D versus CRT-P arms showed a non-significant 14% reduction in all-cause mortality in the CRT-D arm. Patients with NICM had greater survival benefit with CRT-D over CRT-P, but this was not observed in patients with ICM [31]. Subsequently, in a

Table 3 Primary Prevention ICD Studies in Patients with Non-Ischaemic Cardiomyopathy (NICM).

Clinical Trial Randomisation	Year Results	Patients		Sample	EF	NYHA
CAT [20]	2002	NICM (≤9 months onset)	104	≤30%	II–III	ICD vs OMT	No significant difference in mortality (73% vs 58%; p = 0.554)
AMIOVIRT [21]	2003	NICM NSVT	103	≤35%	I–III	ICD vs amio	No significant difference in mortality (96% vs 88%; p = 0.08)
DEFINITE [22]	2004	NICM NSVT or PVC ≥10/hour	458	≤35%	I–III	ICD vs OMT	a) No significant difference in mortality (HR0.65; p = 0.08) b) Significant reduction in arrhythmic death in ICD group (HR 0.2; p = 0.006) c) Significant reduction in mortality in males/ NYHA class III with ICD
SCD-HEFT [16]	2005	47% – NICM	2521	≤35%	II–III	ICD vs amio vs OMT	No significant difference in mortality (HR 0.73; p = 0.06)
DANISH [7]	2016	NICM 58% had CRT	1166	≤35%	II–IV(if CRT)	ICD vs OMT	a) No significant difference in mortality (HR 0.87; p = 0.28) b) Significant reduction in SCD in ICD group (HR 0.5; p = 0.005)

Abbreviations: NICM, non ischaemic cardiomyopathy; EF, ejection fraction; NYHA, New York Heart Association; ICD, implantable cardiac defibrillator; OMT, optimal medical therapy; NSVT, non sustained ventricular tachycardia; PVC, premature ventricular complex; CRT, cardiac resynchronisation therapy; SCD, sudden cardiac death; amio, amiodarone; CAT, Cardiomyopathy Trial; AMIOVIRT, Amiodarone Versus Implantable Cardioverter Defibrillator Trial; DEFINITE, Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation Trial; SCD-HeFT, Sudden Cardiac Death in Heart Failure Trial; DANISH, Danish Study to Assess the Efficacy of ICDs in Patients with Non-Ischemic Systolic Heart Failure on Mortality.

2015 meta-analysis by Barra et al. comparing CRT-D with CRT-P, CRT-D patients had significantly lower mortality rates compared with CRT-P patients. However, there were baseline differences in the patient cohorts, with CRT- D recipients being younger, and consisting of more males; as well as having lower NYHA class, lower atrial fibrillation rates, and higher prevalence of ischaemic heart disease. In comparison, CRT-P recipients were older, and had more advanced heart failure and medical comorbidities [33]. An implantable cardiac defibrillator was found to benefit patients with ICM more than patients with NICM, in contrast to the findings from COMPANION [33]. More recently, CRT-D was compared with CRT-P (through propensity matching) in a registry of 5,307 patients in Europe, and it showed no survival benefit with the addition of ICD in NICM patients, whereas ICM patients did benefit [24].

It has been suggested that the proportional risk of SCD primarily determines the benefit of ICD over CRT-P. An implantable cardiac defibrillator has a greater benefit when the proportion of SCD is high, whereas CRT-P has greater benefit when the proportion of SCD is low [34]. Improvements in LVEF seen in CRT responders is itself associated with reduced ventricular arrhythmia and SCD [35]. In the DANISH trial (where 58% of the cohort received CRT), SCD constituted 35% of all deaths [7], and it is plausible that this lower proportion of SCD attenuates the ICD benefit. Additionally, the difference in outcomes between ICM and NICM patients could be partly attributable to the fact that NICM patients respond better to CRT with greater left ventricular reverse remodelling [36]; whereas, sudden death risk is more closely related to markers of ischaemic heart disease [24].

Thus, ICDs have been proposed to provide the greatest benefit in CRT patients with the following: high proportion of sudden death (>35%), sudden death rate ≥1.2% per year, and annual mortality rate of ≤25% (mean survival of 3 years) [34]. This would imply that an ICD would likely be inappropriate in those with ambulatory NYHA class IV symptoms, elderly patients, and those with extensive medical co-morbidities, where the risk of non-SCD related deaths are high [33]. The Seattle Proportional Risk Model, which incorporates various clinical, biochemical and demographic variables, was published as a predictive tool for sudden death and non-sudden death in patients with cardiomyopathy [37]. However, more evidence is needed to confirm the validity of this approach. In all situations, however, discussions with patient and families on the choice of CRT-D or CRT-P, including goals of care, are important to decide on the most appropriate device therapy.

The Emerging Role of Cardiac MRI (cMRI) as a Risk Stratification Tool

There has been an increasing number of studies in recent years demonstrating the prognostic value of the presence of late gadolinium enhancement (LGE) in SCD risk prediction,

both in patients with ICM and NICM [38,39]. In a meta-analysis on NICM patients, LGE was significantly associated with increased SCD or aborted-SCD risk [40]. Recently, Leyva et al. also showed that cMRI could be used as a risk stratifier to determine which CRT patients would benefit from the addition of ICD (ie CRT-D). Patients with left ventricular mid-wall LGE on cMRI had significantly lower mortality and heart failure hospitalisations with CRT-D than with CRT-P [36]. Even in patients with milder CCF (LVEF >35%), who would not have met the criteria for primary prevention ICD implantation, the presence of LGE significantly correlated with life-threatening arrhythmias and SCD [26]. This was further corroborated in a recent meta-analysis on NICM by Marco et al., where the association between LGE and an arrhythmic endpoint remained significant among studies with mean LVEF >35%. Importantly, the study showed that the prognostic value of LGE was superior and independent from LVEF [41]. This could potentially lead to a paradigm shift in prophylactic ICD implantation, given that the majority of SCD burden lies in patients with less severe degrees of cardiomyopathy with lower risk of non-sudden death, and who, therefore, stand to benefit the most from SCD prevention with an ICD [39,41]. An Australia-led RCT (CMR-Guide) is currently ongoing which seeks to further evaluate the benefit of ICD implantation in patients with LVEF 36-50% and LGE on cMRI [42].

There are still important unanswered clinical questions regarding the use of LGE as a risk stratifier, such as whether patients with LGE would benefit from primary prevention ICDs irrespective of their LVEF, and conversely whether patients without LGE can avoid having a preventive ICD despite underlying severe cardiomyopathy [41]. In addition, it remains unclear whether the location and extent of LGE matter in terms of arrhythmic risk prediction as studies thus far have shown conflicting findings [30,39,43]. Even patients without LGE on cMRI can still experience arrhythmic events, and in patients with NICM, this could possibly be due to the presence of diffuse fibrosis. Diffuse fibrosis would not be readily detected through gadolinium contrast, but could be detected with T1 mapping [44,45].

It is also worth noting that, in certain cardiac conditions, namely hypertrophic cardiomyopathy (HCM) and cardiac sarcoidosis, the detection of LGE on cMRI has now been accepted as a part of the diagnostic/risk stratification process for ICD. In patients with HCM, LGE is recognised as a risk modifier in the 2017 AHA/ACC/HRS guidelines and carries a class IIb recommendation [46]. Additionally, larger amounts of LGE have been shown to confer higher SCD risk. With regards to cardiac sarcoidosis, LGE was added to the 2014 HRS guidelines as a diagnostic criterion for a probable clinical diagnosis of cardiac sarcoidosis [47]. Patients with LGE had higher risk of all-cause mortality, ventricular arrhythmia, and SCD; even among those with LVEF >50% [48]. The burden of LGE has also been shown to correlate with the risk of malignant VT/SCD [49].

Subcutaneous ICD (S-ICD)

The S-ICD was developed to overcome limitations of the transvenous ICD, in particular lead-related issues which can occur in up to 20% of patients. The device consists of a pulse generator and single electrode (Figure 1). The electrode has an 8 cm shock coil at the distal end, flanked by two sensing poles. Under general anaesthesia, the pulse generator is inserted into a subcutaneous pocket at the left midaxillary line, at the fifth/sixth intercostal space. The electrode is tunnelled subcutaneously from the pocket medially towards the xyphoid incision and then cranially along the left side of the sternum using either a two or three incision technique. There are three sensing vectors: primary (proximal sensing pole to generator), secondary (distal sensing pole to generator) or alternative (distal to proximal sensing poles). If a ventricular arrhythmia is detected, an 80J shock is then delivered. Post-shock bradycardia pacing at 50 bpm can be delivered for up to 30 seconds [3].

Patients are screened for suitability prior to device implantation, as up to 16% of patients are found to be unsuitable due to inadequate sensing. This process involves collecting a modified ECG tracing taken in both the supine and standing positions to evaluate for adequate R- to T-wave ratios. At least one (preferably two) of the three sensing vectors should be acceptable in both positions for an implant to proceed. To further reduce the rates of inappropriate shocks, which are predominantly from T-wave oversensing, all devices should be programmed with a conditional zone (range of 170–240 bpm) and shock zone (200–250 bpm) [3,50].

Indications for S-ICD

Initial experience with S-ICD has been in younger patients who face a potential lifetime of device therapy, patients with

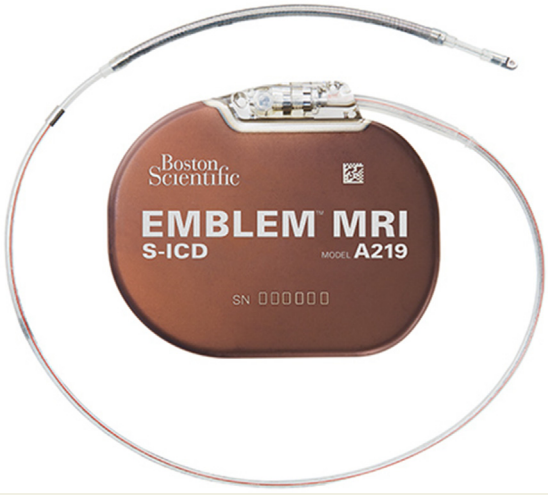

Figure 1 Subcutaneous implantable cardiac defibrillator (ICD) with pulse generator and electrode.
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limited vascular access, patients with higher risk of infection (including patients with previous transvenous ICD infection/diabetes mellitus/immunosuppression and renal failure), patients with channelopathies, and patients with congenital heart diseases (where anatomical complexity may result in difficulty with transvenous lead placement) [3,5,51]. As experience has been gained over the last few years, most primary prevention ICD candidates are now considered suitable to receive a S-ICD. However, in patients who require pacing, CRT or anti-tachycardia pacing for ventricular tachycardia, S-ICDs remain contra-indicated.

Efficacy

Subcutaneous ICDs have been shown in observational studies to be efficacious in termination of VT/VF in various patient populations including ICM, NICM and genetic cardiac disorders [3,5,50]. At present, the largest data on S-ICD efficacy is derived from the 2-year pooled analysis of the investigational device exemption trials (IDE) and the Boston Scientific Post Market S-ICD Registry (EFFORTLESS) registry [52], which included 882 patients. One hundred and eleven (111) spontaneous VT/VF events were treated, with 90.1% terminated with one shock and 98.2% terminated within five available shocks. This is similar to the reported shock efficacy reported in transvenous ICD of between 97.3 and 99.6% [53]. At present, no data from RCTs exist which compares S-ICDs with transvenous ICDs, although the PRAETORIAN (Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter-defibrillator therapy) trial is currently underway with the primary study endpoints of device shock efficacy, complications, and overall mortality rates [54].

Safety and Complications

The main advantage of the S-ICD is the avoidance of procedural complications associated with transvenous leads, including pneumothorax, haemothorax, cardiac tamponade, lead dislodgement and endocarditis [55,56]. The risk of infection with an S-ICD is generally thought to be lower than with a transvenous ICD [50], and it is certainly easier to manage as complex extraction procedures are not required. A recent systematic review showed that pocket infection affected 2.7% of patients [57]. In the IDE study/EFFORTLESS registry analysis, infection rates were even lower with 0.3% of patients having superficial infection treated conservatively, whereas 1.7% of patients had infection requiring device removal [3].

Inappropriate device shocks from S-ICDs are mainly from cardiac oversensing (predominately T-wave), supraventricular tachyarrhythmias (SVT), and sensing of non-cardiac events (eg myopotentials) [3]. Other risk factors include patients with hypertrophic cardiomyopathy (HCM) (from T-wave oversensing), patients with atrial fibrillation, and the use of secondary or alternative sensing vectors (as opposed to a primary vector). Whilst early experience with S-ICD suggested high rates of inappropriate shocks, these have declined significantly with pre-implantation patient screening, as well as refinements in device programming. In particular, dual zone programming with a conditional zone (range of 170–240 bpm) and shock zones (200–250 bpm) have resulted in a 70% reduction in inappropriate shocks [58]. In the conditional zone, discrimination algorithms including beat-to-beat morphology changes, and morphology comparison to stored sinus rhythm template, have been shown to result in 98% specificity for appropriately withholding therapy for SVT, whilst maintaining 100% sensitivity for detection of VT/VF [59]. Pre-implantation exercise testing has also been suggested for patients with HCM to reduce rates of inappropriate shocks from T-wave oversensing [53]. Recent evidence has demonstrated overall rates of inappropriate shocks from S-ICD to be between 4–16%, which is comparable to transvenous ICD [56,60,61].

Limitations

Subcutaneous ICDs lack the capacity for bradycardia pacing except for a brief 30 seconds post defibrillation shock and are, therefore, unsuitable for patients who require pacing support/CRT [53]. They are not able to deliver anti-tachycardia pacing to terminate tachyarrhythmias which may limit their use in some secondary prevention patients who present with ventricular tachycardia. Current S-ICD models have a significantly shorter battery life than conventional transvenous ICD, with median time to replacement of around 7 years. This affects the cost effectiveness of the device, although next generation S-ICDs are likely to have battery longevity comparable to current transvenous devices [3].

Wearable Cardioverter Defibrillator (WCD)

The only commercially available wearable cardioverter defibrillator, the LifeVest WCD (ZOLL, Pittsburgh, PA, USA), was approved in 2001 and consists of an elastic chest garment which holds the defibrillation electrodes, as well as four monitoring electrodes. The defibrillation electrodes contain a vibration plate and gel capsules. Upon detection of a shockable rhythm, the vibration plate provides a tactile warning (in addition to an audible alert) of an impending shock, and the device wearer can self-abort the shock by pushing two buttons simultaneously [54]. If no attempt to abort is made, then shock therapy is delivered with gel released from the capsules concurrently.

Indications for WCD

The use of WCDs currently has a class II indication in the AHA/ACC/HRS guidelines in several clinical situations, with the common denominator being patients who are at high risk of SCD for a limited period–until either definitive therapy is provided, or the SCD risk resolves over time [62]. This includes patients with ischaemic heart disease and severe LV dysfunction who have been recently

revascularised, patients with newly diagnosed severe cardiomyopathy with recent commencement of guideline-directed medical therapy, patients with myocarditis (who are expected to make a full recovery), and patients with a clear indication for an ICD who require device removal (usually for infection). In these situations the WCD provides a bridging therapy until expected patient recovery, device re-implantation or cardiac transplantation [2,6,63].

Efficacy

As with S-ICD, there is no RCT comparing the use of WCDs with transvenous ICDs [63]. Early data on WCD efficacy is derived from the WEAR-IT (Wearable Cardioverter Defibrillator Investigational Trial), which enrolled patients with NYHA class III or IV (ambulatory) CCF and an LVEF <30%; and the BIROAD (Bridge to ICD in Patients at Risk of Arrhythmic Death) trial, which included patients post myocardial infarction or coronary artery bypass surgery who were at high risk for SCD due to ventricular arrhythmia, syncope or low LVEF <30% [64].

Seventy-five per cent (75%) of defibrillation attempts (six of eight) were successful. There were six sudden deaths, five of which occurred whilst patients were not wearing the WCD; whereas one patient had the device on incorrectly at the time of cardiac event. Subsequently, the WEARIT-II (Prospective Registry of Patients Using the Wearable Defibrillator) data was published which included patients with ICM, NICM, and congenital heart disease. There were 120 sustained VT/VF events in 41 patients, of whom 54% received an appropriate shock. The study concluded that a WCD can adequately protect patients during high-risk periods until primary prevention ICD is implanted [65]. Furthermore, an observational US study found that first shock success was 99% for all VT/VF events, with survival post VT/VF of 89.5% [66]. More recently, the VEST (Vest Prevention of Early Sudden Death Trial) trial (ACC 2018) randomised 2302 patients post MI with moderate–severe LV impairment (EF < 35%) to WCD and optimal medical therapy versus optimal medical therapy alone. Using intention to treat analysis, the use of WCDs resulted in a reduction in the primary endpoint of SCDs at 90 days, although this did not reach statistical significance (1.6% vs 2.4% p = 0.18). Interestingly, all cause mortality was significantly reduced with WCD (p = 0.04). Twenty (20) patients in the control group crossed over to receive the WCD, whereas 19% in the WCD arm did not wear the vest and compliance decreased with time. These were likely to have influenced the non-significant SCD reduction [67].

Safety, Complications and Limitations

In order for a WCD to be effective, it needs to be worn for a prolonged period of time. Unfortunately in the WEARIT/BIROAD studies up to 22.5% of patients discontinued use due to discomfort, skin irritation or lifestyle interference [64]. Similar discontinuation rates were also seen in the VEST trial. Wearable cardiac defibrillators do appear to be associated with a low risk of inappropriate shocks, which is related to noise artefacts or T-wave oversensing [68]. In the WEARIT–II study 10 patients (out of 2,000 enrolled) received inappropriate shocks [65]. As with S-ICDs, a WCD is not able to provide anti-bradycardic nor anti-tachycardic pacing.

The Future in Device Therapy

Gaps in current knowledge still exist on the appropriate selection of devices for SCD prevention. These include patients with NICM, adult congenital heart disease, and inherited cardiomyopathies/channelopathies, where further refinement in risk stratification is required [2]. Particularly in NICM patients, the current notion of NICM as a single clinical entity with sufficient risk prediction based on EF alone is flawed and inadequate. It is likely that the risk of SCD varies significantly depending on the exact underlying aetiology, although more data is needed on aetiology-based specific risks and how to combine that information with other patient variables to determine the need for ICD implantation. Additionally, the role of cMRI variables in particular LGE and newer T1 mapping sequences in risk prediction/prognostication requires further study. The role of novel biomarkers (eg. brain natriuretic peptide [BNP]), genetic information and other imaging markers, also remain to be determined.

The S-ICD is continuously evolving and it is likely within a couple of years S-ICD will be able to be paired with a leadless pacemaker, for example the Micra Transcatheter Pacing System (TPS) (Medtronic Inc., Dublin, Ireland), which will overcome limitations associated with the current device. Whilst the randomised PRAETORIAN study will provide further objective data on the comparative efficacy of S-ICD with transvenous ICD, long-term data is still needed on S-ICDs including lead performance and inappropriate shock rates.

The role of the WCD in SCD prevention, particularly the specific patient subgroups most likely to derive benefit from it, still requires further research. Whilst the recent negative overall finding of the VEST trial was disappointing, the fact that a reduction in SCD was seen would still suggest a benefit in the high risk subgroup of post myocardial infarction patients. What is clear, however, is that the current version is associated with high rates of discontinuation, and therefore efforts to improve the tolerability and compliance of the WCD have to be made.

Conclusions

Defibrillator technology has advanced significantly over the past few decades with current availability of the transvenous ICD (with or without CRT), S-ICD and WCD. Selecting the appropriate device for patients should take into account patients' clinical characteristics and the advantages/disadvantages of each device. More work still needs to be done to refine our risk stratification of patients at high risk of SCD to ensure appropriate primary prevention use of devices. Furthermore, randomised, long-term data on S-ICDs and WCDs

is needed to establish their efficacy in comparison with the established standard of transvenous ICDs.

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