

Ventricular arrhythmias and sudden cardiac death

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Summary

The 2015 European Society of Cardiology guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death (SCD) is a European update of the joint guidelines with American College of Cardiology / American Heart Association published in 2006. The new SCD guideline is an extensive document that was subject to a thorough and extensive evaluation by 74 peer reviewers.

Preventive measures against the burden of coronary artery disease and heart failure have, in the past 20 years, resulted in reduced cardiovascular mortality in high-income countries. Cardiovascular diseases still account for a significant 17 million deaths every year worldwide, of which approximately 25% are SCD. In the aging population, coronary artery disease and heart failure dominate whereas in the young rarer disorders such as channelopathies, cardiomyopathies and myocarditis are the commoner cardiac causes of SCD. The new SCD guidelines give a detailed description of how to conduct an adequate autopsy in order to not overlook genetic disorders, a policy that will have important implications for screening of relatives. Other updated and new recommendations for the prevention of sudden death relate to the use of implantable cardiac defibrillators, cardiac resynchronisation therapy and catheter ablation in different patient populations. In this review, the most important updated and new recommendations are summarised, compared with previous guidelines and related to their support in the literature.

Key words: ventricular tachycardia; ventricular fibrillation; defibrillator; sudden cardiac death; guidelines; heart failure

Background

The 2015 European Society of Cardiology (ESC) guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death (SCD) [1] is a European update of the joint guidelines published in 2006 by the American College of Cardiology / American Heart Association and the ESC on this topic. The new SCD guideline is an extensive document that has been subject to thorough and extensive evaluation by 74 peer reviewers.

Risk evaluation

Preventive measures against the burden of coronary artery disease and heart failure have in the past 20 years resulted in reduced cardiovascular mortality in high-income countries [2]. Cardiovascular diseases, however, still account for approximately 17 million deaths every year in the world, of which approximately 25% are SCD. The risk of SCD increases with age related to the increasing coronary artery disease with age. The SCD rates are approximately 1.40 per 100 000 person-years in women, 6.68 per 100 000 person-years in men [3] and 0.46–3.7 events per 100 000 person-years in younger individuals [4]. In the aging population, coronary artery disease, valvular heart diseases and heart failure are the most common causes of SCD, whereas in the young rarer disorders, including channelopathies, cardiomyopathies, myocarditis and substance abuse, dominate. The majority of SCD victims suffer from previously undetected ischaemic heart disease. None of the many risk markers of SCD that have been proposed for patients with coronary artery disease have so far proved to influence outcome. Left ventricular ejection fraction (LVEF) is the only and best risk marker that has shown an association with increased risk of SCD in the setting of myocardial infarction, and is still used to identify patients for implantation of a cardioverter-defibrillator as primary prevention of SCD [6, 7]. The only broad screening programme for SCD is the existing recommendation for preparticipation screening in athletes, including clinical evaluation, personal or family history and a baseline 12-lead ECG. There are no other clear data supporting broad screening programmes for identifying high-risk patients in the general population.

Conditions such as inherited channelopathies or drug-induced arrhythmias are not unmasked even at autopsy as both are devoid of structural abnormalities, which makes expert post-mortem examination a reasonable approach to improve the detection of heritable diseases. Such an autopsy should be able to clarify whether the death was related to a cardiovascular disease and if so which type, if the death was arrhythmic

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and if the disease is inheritable. The new guidelines give a detailed description of how to conduct an adequate autopsy in order not to miss genetic disorders, a policy that will have important implications for screening of relatives (table 1). The pathologist should take samples of tissues, and blood and other fluids for toxicology and molecular pathology before fixing the heart in formalin, and should secure further biological samples for DNA extraction to allow a “molecular” autopsy [5]. Such procedures will make it possible to extend the genetic screening to family members of SCD victim.

The diagnosis of an arrhythmogenic disorder that is inheritable (long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, subtle forms of hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy or familial hypercholesterolaemia) is made in only approximately half of the families of a SCD victim. It is therefore important that when an autopsy is not available or reveals normal findings, the first-degree rela-

tives of the victim should be informed about the potential risk of being affected themselves by similar events and should be offered cardiac evaluation, as well as a complete three-generation pedigree evaluation of all SCDs and cardiac diseases. If tissue or blood samples from the victim are missing and an inheritable disease in family members is suspected, targeted molecular screening in first-degree relatives may be considered.

A detailed screening programme with noninvasive and invasive evaluation of patients with suspected or known ventricular arrhythmias is presented in the new guideline, emphasising the importance of a resting 12-lead ECG, ECG monitoring systems, signal averaged ECG, exercise stress testing and echocardiography for adequate evaluation and diagnosis for the patient at risk.

Electrophysiological studies are a class I recommendation for evaluation of symptoms, such as palpitations, presyncope and syncope, that are potentially ventricular tachyarrhythmias in postmyocardial infarction patients.

Table 1: Indications for autopsy and molecular autopsy in sudden death victims.

Recommendations	Class and level of evidence
An autopsy is recommended to investigate the causes of sudden death and to define whether a SCD is secondary to arrhythmic or nonarrhythmic mechanisms (e.g. rupture of an aortic aneurysm).	I C
Whenever an autopsy is performed, a standard histological examination of the heart is recommended and it should include mapped labelled blocks of myocardium from representative transverse slices of both ventricles.	I C
NEW: The analysis of blood and other adequately collected body fluids for toxicology and molecular pathology is recommended in all victims of unexplained sudden death.	I C
NEW: Targeted post-mortem genetic analysis of potentially disease-causing genes should be considered in all sudden death victims in whom a specific inheritable channelopathy or cardiomyopathy is suspected.	Ila C

SCD = sudden cardiac death.

Table 2: Secondary prevention of sudden cardiac death and ventricular tachycardia.

Recommendations	Class and level of evidence
ICD implantation is recommended in patients with documented VF or haemodynamically not tolerated VT in the absence of reversible causes or within 48 hours post-myocardial infarction, who are receiving chronic optimal medical therapy and have reasonable expectation of survival with a good functional status for more than 1 year.	I A
ICD implantation should be considered for patients with recurrent sustained VT (not within 48 hours after myocardial infarction), who are receiving chronic optimal medical therapy, have a <i>normal</i> LVEF, and reasonable expectation of survival with a good functional status for more than 1 year.	Ila C This panel of experts

ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; VF = ventricular fibrillation; VT = ventricular tachycardia

Treatment

Available antiarrhythmic drugs, except for beta-blocking agents, have not consistently been shown to be effective in randomised clinical trials (RCTs) for primary prevention of life-threatening ventricular arrhythmias or SCD.

Implantable cardioverter defibrillator (ICD) therapy prevents sudden death and prolongs life in patients at high risk of sudden arrhythmic death, provided that the patient does not suffer from other conditions that limit life expectancy to <1–2 years. Long-term studies have demonstrated the efficacy of ICDs and cardiac resynchronisation therapy-defibrillators (CRT-Ds) over a mean follow-up of 8 and 7 years, respectively (table 2). Implantation of an ICD for secondary prevention of SCD and ventricular tachycardia is the same class I recommendation as in the previous guidelines. The three trials supporting this recommendation [8–10] compared ICD with antiarrhythmic drug therapy, predominantly amiodarone, and included patients suffering cardiac arrest or haemodynamically unstable ventricular arrhythmia or tachycardia with syncope. The meta-analysis of the three trials demonstrated that ICD therapy was associated with a 28% (95% confidence interval [CI] 0.60–0.87, $p = 0.006$) reduction in total mortality (table 3) [11].

An important new recommendation is the use of a subcutaneous defibrillator as an alternative to a transvenous defibrillator for the prevention of sudden

Table 3: Meta-analysis of ICD secondary prevention trials.

Trial	N	Total mortality		
		Events	Hazard ratio	95% CI
AVID [8]	1016	80	0.62	0.47–0.81
CIDS [9]	659	83	0.82	0.61–1.10
CASH [10]	191	37	0.83	0.52–1.33
Cumulative	1866	200	0.72	0.60–0.87

AVID = Antiarrhythmic drugs Versus Implantable Defibrillator; CIDS = Canadian Implantable Defibrillator Study; CASH = Cardiac Arrest Study Hamburg; ICD = implantable cardioverter defibrillator. P-value for heterogeneity = 0.306.

death. Data on long-term tolerability and safety are lacking, but a more recent meta-analysis including 852 patients showed no electrode failures, the need for right ventricle pacing in only 3 patients, and the frequency of inappropriate shocks was <5% in the latest quartile of enrolment, which is lower than the reported frequencies in earlier studies [12]. The subcutaneous device is not suitable for patients who require bradycardia pacing or who need cardiac resynchronisation therapy (CRT), nor for patients who need anti-

tachycardia pacing, but it should be considered as an alternative to transvenous defibrillators in all other patients with an indication for an ICD (table 4). It may be useful in young patients who expect a lifelong device therapy, if venous access is difficult, and in patients at increased risk of infection. Battery longevity needs to be improved and large-scale late follow-up information about lead performance of subcutaneous ICDs is lacking. Ongoing prospective randomised trials comparing the efficacy and complications of the subcutaneous ICD with those of the conventional ICD will give better guidance for usage in the future.

An external defibrillator wearable as a vest has been shown in many case series and registries to successfully identify and terminate ventricular tachycardia and fibrillation in vulnerable patients [13], but there are no prospective RCTs evaluating its efficacy. The wearable cardioverter defibrillator (WCD) may be used in patients with transiently impaired LVEF until left ventricular function has recovered sufficiently (table 4), including patients with myocardial infarction, postpartum cardiomyopathy or myocarditis, or after interventions such as revascularisation associated with transient left ventricular dysfunction, or in patients with life-threatening ventricular arrhythmias who are scheduled for cardiac transplantation.

With the advent of electroanatomical mapping systems and contact force catheters, catheter ablation has evolved into an important treatment option for patients with scar-related ventricular tachycardia or fibrillation (table 5). Randomised multicentre trials reported that catheter ablation for ventricular tachycardia decreases the rate of subsequent ICD shocks and prevents ventricular tachycardia recurrences in patients with ischaemic heart disease [14]. Several studies have confirmed that ICD shocks are associated with higher mortality and impaired quality of life. Scar-related ventricular tachycardia is typically monomorphic, and since multiple ventricular tachycardia morphologies may be induced in the same patient, a 12-lead surface ECG recording of the clinical ventricular tachycardia can aid in the mapping and ablation procedure. That catheter ablation should already be considered after a first episode of sustained ventricular tachycardia in patients with ischaemic heart disease and an ICD is new in the 2016 recommendations. Catheter ablation has also proven to control incessant ventricular tachycardia or electrical storms [14]. Polymorphic ventricular tachycardia, defined as a continually changing QRS morphology, is often associated with acute myocardial ischaemia and in patients refractory to drug treatment, Purkinje-fibre triggered polymorphic ventricular tachycardia may be amenable to catheter ablation.

Table 4: Alternative implantable or wearable cardioverter defibrillators.

NEW: Recommendations for a subcutaneous implantable cardioverter defibrillator (ICD)	Class and level of evidence
Subcutaneous ICD should be considered as an alternative to transvenous ICD in patients with an ICD indication, when pacing therapy for bradycardia support, cardiac resynchronisation, or antitachycardia pacing is not needed.	Ila C
The subcutaneous ICD may be considered as a useful alternative to a transvenous ICD system when venous access is difficult, after the removal of a transvenous ICD for infection, or in young patients with a long-term need for ICD therapy.	Ilb C
NEW: Recommendation for wearable cardioverter defibrillator (WCD)	
The WCD may be considered for adult patients with poor left ventricular systolic function who are at risk of sudden arrhythmic death for a limited period, but are not candidates for an implantable defibrillator (e.g. bridge to transplant, bridge to transvenous implant, peripartum cardiomyopathy, active myocarditis and arrhythmias in the early post-myocardial infarction phase).	Ilb C

Table 5: Catheter ablation for the treatment of sustained monomorphic ventricular tachycardia.

Recommendations	Class and level of evidence
UPGRADE: Urgent catheter ablation is recommended in patients with scar-related heart disease presenting with incessant ventricular tachycardia or electrical storm.	I B
Catheter ablation is recommended in patients with ischaemic heart disease and recurrent ICD shocks due to sustained ventricular tachycardia.	I B
NEW: Catheter ablation should be considered after a first episode of sustained ventricular tachycardia in patients with ischaemic heart disease and an ICD.	Ila B

Therapies for patients after myocardial infarction

The timing of ICD placement after myocardial infarction and assessment of left ventricular dysfunction before and after discharge has gained more attention in the present guidelines (table 6). The recommendation to re-assess LVEF 6–12 weeks after a myocardial infarction to identify the need for a primary preventive ICD is new and was not emphasised in a table of recommendation in the previous guidelines, which may explain why primary preventive ICD use has not gained full acceptance in many European countries. The evaluation should be structured and offered to all patients. Specific disease states such as preexisting LVEF dysfunction, incomplete revascularisation, and ventricular arrhythmia occurring >48 hours after the onset of acute coronary syndrome may urge the need for an early (<40 days) ICD implantation or a temporary (<40 days) use of a WCD.

Therapies for patients with left ventricular dysfunction, with or without heart failure

Treatment with angiotensin converting-enzyme inhibitors or, if intolerant, angiotensin II receptor blockers, beta-blockers or mineralocorticoid receptor antagonist is recommended in patients with heart failure with systolic dysfunction (LVEF ≤35–40%) as a class I

recommendation for primary prevention of total mortality and SCD.

ICD use for primary prevention of SCD in patients with heart failure and reduced LVEF has in the new guidelines the same class I recommendation as in the previous guideline (table 7). There are two large trials supporting this recommendation: the SCD-HeFT study¹⁵ (inclusion criteria New York Heart Association [NYHA] class II–III, LVEF <0.35), in which absolute mortality decreased by 7% with ICD after 5 years; and the MADIT II study¹⁶ (inclusion criteria postmyocardial infarction, LVEF <0.30), in which the absolute mortality decreased by 6%. Nonischaemic aetiology also received a class I recommendation based on a meta-analysis of five primary prevention trials including 1854 patients with nonischaemic heart failure, in which the use of an ICD was associated with a significant 31% reduction in total mortality (hazard ratio 0.69, 95% CI 0.55–0.87, $p = 0.002$) [17].

The recommendation that ICD implantation should be considered for primary and secondary prevention of SCD in patients who are listed for heart transplant is based on studies including ambulatory class IV patients listed for heart transplantation, which suggested survival benefit with ICD (table 7) [18].

After consideration of the trials and meta-analyses published on CRT and the importance of a left bundle-branch block, a certain QRS duration and NYHA functional class, separate recommendations for various group settings were given (table 8). The new recommendations are different from the previous ESC heart failure guidelines from 2012, which only referred to patients with QRS duration >150 ms (IIa A recommendation) and gave no recommendation for patients with a QRS of 120–150 ms. They are also different from the recently published ESC heart failure guidelines [19], which introduced a CRT contraindication for patients with QRS duration <130 ms. It is beyond the scope of this summary to discuss how these divergent recommendations came about, although the issue of QRS duration cut-off deserves a more thorough analysis with respect to gender, because of the higher CRT response rates in women which may have important implications for the chosen cut-off for the QRS duration.

Two large RCTs in patients with moderate to severe (class III–IV) heart failure and in sinus rhythm have shown that CRT reduces mortality in this population: the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart failure (COMPANION) Trial [20] and the Cardiac Resynchronization – Heart Failure (CARE-HF) Trial [21].

The COMPANION and CARE-HF studies both provided strong evidence favouring the use of a CRT-pacemaker

Table 6: Timing of ICD placement after myocardial infarction and assessment of left ventricular dysfunction before and after discharge.

Recommendations	Class and level of evidence
Early (before discharge) assessment of LVEF is recommended in all patients with acute myocardial infarction.	I C
NEW: Re-evaluation of LVEF 6–12 weeks after myocardial infarction is recommended to assess the potential need for primary prevention ICD implantation.	I C

Table 7: ICD recommendations.

ICD in patients with left ventricular dysfunction	Class and level of evidence
ICD therapy is recommended to reduce SCD in patients with symptomatic heart failure (NYHA class II–III) and LVEF ≤35%, after ≥3 months of optimal medical therapy, who are expected to survive for at least 1 year with good functional status:	
Ischaemic aetiology, and at least 6 weeks after myocardial infarction.	I A
Nonischaemic aetiology.	I B
ICD in patients with NYHA IV listed for heart transplantation	
UPDATE: ICD implantation should be considered for primary and secondary prevention of SCD in patients who are listed for heart transplant.	IIa C

NYHA = New York Heart Association class.

Table 8: Cardiac resynchronisation therapy in the primary prevention of sudden cardiac death.

Recommendations for in-patients in sinus rhythm and NYHA functional class III – ambulatory class IV	Class and level of evidence
CRT is recommended in patients with an LVEF $\leq 35\%$ and <i>LBBB</i> , despite at least 3 months of optimal pharmacological therapy, who are expected to survive at least 1 year with good functional status, to reduce all-cause mortality:	
– With a QRS duration of >150 ms	I A
– With a QRS duration of 120–150 ms	I B
CRT should or may be considered in patients with an LVEF $\leq 35\%$, <i>without LBBB</i> , despite at least 3 months of optimal pharmacological therapy, who are expected to survive at least 1 year with good functional status, to reduce all-cause mortality:	
– With a QRS duration of >150 ms	IIa B
– With a QRS duration of 120–150 ms	IIb B
Recommendations for CRT-D in patients in sinus rhythm with mild (NYHA class II) heart failure	
CRT-D is recommended in patients with QRS duration of ≥ 130 ms, with an LVEF $\leq 30\%$, and with a <i>LBBB</i> , despite at least 3 months of optimal pharmacological therapy, who are expected to survive at least 1 year with good functional status, to reduce all-cause mortality.	I A
CRT-D may be considered in patients with QRS duration of ≥ 150 ms, irrespective of QRS morphology, and an LVEF $\leq 35\%$, despite at least 3 months of optimal pharmacological therapy, who are expected to survive at least 1 year with good functional status, to prevent hospitalisation for heart failure.	IIb A
CRT = cardiac resynchronization therapy; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; ms = milliseconds.	

(CRT-P) or CRT-D in heart failure patients with moderate to severe symptoms, who have a prolonged QRS duration, especially in those with left bundle-branch block morphology. A QRS duration ≥ 120 ms was required and additional criteria for dyssynchrony had to be met in patients with a QRS interval of 120–149 ms in the CARE-HF trial. The majority of studies and meta-analysis have favoured the view that QRS morphology with left bundle-branch block identifies a subgroup of patients with increased benefit, including the REVERSE study [22], MADIT-CRT [23], RAFT study [24] and two meta-analyses [25, 26]. None of these studies could demonstrate benefit in patients without left bundle-branch block QRS morphology. CRT is not recommended in heart failure patients with QRS duration <120 ms. CRT is a class I recommendation in patients with an LVEF $\leq 35\%$ and left bundle-branch block, and a QRS duration of at least 120 ms (table 8). It should /may be considered in patients without left bundle-branch block, but wide QRS without left bundle-branch block morphology still remains an area of uncertainty for CRT.

The MADIT-CRT study [23] enrolled mildly symptomatic patients in NYHA class I or II with LVEF $\leq 30\%$, and a QRS duration ≥ 130 ms. It showed a 34% reduction

in the composite primary endpoint of all-cause death or heart failure events (25.3% vs 17.2% for ICD vs CRT-D; hazard ratio [HR] 0.66, 95% CI 0.52–0.84, $p = 0.001$). In long-term follow-up, CRT-D significantly reduced mortality compared with ICD only, which was confined to patients with left bundle-branch block at baseline. The RAFT trial [24], which enrolled patients with NYHA class II or III, LVEF $\leq 30\%$, and a QRS duration ≥ 120 ms, showed a 25% relative risk reduction in all-cause mortality in the CRT-D group (HR 0.75, 95% CI 0.62–0.91, $p = 0.003$) compared with ICD only patients. CRT-D use is therefore a class I indication in patients with mild heart failure (NYHA class II), LVEF <0.3 , left bundle-branch block and QRS duration >130 ms (table 8).

In patients with atrial fibrillation, CRT should be considered for those with markedly reduced LVEF, although it has not been shown to reduce mortality or sudden death in these patients (class IIa). The outcome of CRT in patients with atrial fibrillation depends on the degree of biventricular pacing, which can be achieved only by means of atrioventricular junction ablation in many patients. CRT should be considered in patients with NYHA functional class III / ambulatory class IV heart failure, permanent atrial fibrillation, QRS ≥ 120 ms and LVEF $\leq 35\%$ if: (i) ventricular pacing is required or the patient otherwise meets CRT criteria; and (ii) near 100% ventricular pacing is achieved by CRT with atrioventricular junction ablation or pharmacological rate control (table 8).

Prospective studies evaluating the role of catheter ablation for treatment of sustained ventricular tachycardia have in the majority of cases shown freedom from ventricular tachycardia over 6–8 months of follow-up, and, if using a substrate-directed approach, a significant reduction in the incidence of ventricular tachycardia episodes during follow-up. Several prospective studies have evaluated the role of catheter ablation for sustained ventricular tachycardia [27, 28] and for eliminating all inducible ventricular tachycardia [27, 28], by use of electroanatomical mapping systems [29] and targeting of the substrate scar during sinus rhythm [30]. In the study using a substrate-guided approach and targeting abnormal ventricular potentials during sinus rhythm there was a significant reduction in the incidence of ventricular tachycardia episodes, from 33% in the control group to 12% in the ablation arm. Another study showed that the rate of survival free from recurrent ventricular tachycardia over 24 months was higher in the ablation group compared with the control arm (47% vs 29%, HR 0.61, $p = 0.045$) [31]. However, catheter ablation did not affect mortality.

Because of the improved results in various studies, ventricular tachycardia ablation has a broader indica-

Table 9: Prevention of ventricular tachycardia recurrence in patients with left ventricular dysfunction and sustained ventricular tachycardia.

Recommendations	Class and Level of Evidence
UPGRADE: Urgent catheter ablation in a specialised or experienced centre is recommended for patients presenting with incessant ventricular tachycardia or electrical storm resulting in ICD shocks.	I B
Amiodarone or catheter ablation is recommended in patients with recurrent ICD shocks due to sustained ventricular tachycardia.	I B
ICD implantation is recommended in patients undergoing catheter ablation whenever they satisfy eligibility criteria for ICD.	I C
NEW: Amiodarone or catheter ablation should be considered <i>after a first episode</i> of sustained ventricular tachycardia in patients with an ICD.	IIa B

tion in the new as compared with the previous guidelines (table 9). In view of the lack of data and the rather high risk for recurrence of sustained ventricular tachycardia following catheter ablation, ICD implantation should be considered in all patients with left ventricular dysfunction (EF <45%) and sustained ventricular tachycardia. Patients with ventricular tachycardia related to a post-myocardial infarction scar tend to have a better outcome after catheter ablation than patients with ventricular tachycardia due to nonischaemic cardiomyopathy.

The recently published DANISH trial, a randomised, controlled, multicentre study designed to assess the effect of ICD use on mortality in patients with nonischaemic systolic heart failure, deserves some comment in this context. Patients with clinical heart failure, LVEF ≤35%, nonischaemic aetiology and levels of the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) above 200 pg/ml were randomised to ICD (560 patients) or standard therapy for heart failure (560 patients). Fifty-eight percent of both groups received CRT. The primary outcome was death from any cause and the secondary was sudden death.

In patients with symptomatic nonischaemic systolic heart failure, the death rate from any cause was not significantly lower in the primary preventive ICD group (21.6%) than in the control group (23.4%) after a median follow-up of 67.6 months (HR 0.87, 95% CI 0.68–1.12; $p = 0.28$). SCD occurred less frequently in the ICD group (4.3%) than in the control group (8.2%) (HR 0.50, 95% CI 0.31–0.82; $p = 0.005$).

The findings are, however, not surprising for several reasons. There is no reason to expect ICD therapy to reduce total mortality unless in the population under study, the proportion of SCDs (amenable to ICD therapy) is significantly higher than deaths related to cardiovascular/heart failure plus other deaths. Indeed, 31% of deaths were attributed to noncardiovascular causes, not unexpected in this elderly population, which underlines the importance of careful patient selection for ICD implantation. Moreover, more modern guideline-directed heart failure therapy that results in a lowering of heart failure-related event rates is more likely to benefit younger patients with less advanced heart failure and less comorbidity, making them more responsive to ICD. This is supported by the fact that there was an important interaction with age, suggesting that younger patients (<59 years) had a total survival benefit in association with ICD implantation, an effect that was independent of CRT status. Further long-term studies are, however, needed to more carefully guide us in the selection of the patients most suitable for ICD therapy.

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References

The full list of references is included in the online article at www.cardiovascmed.ch

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