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Implantable cardioverter defibrillator use for primary prevention in ischaemic and non-ischaemic heart disease—indications in the post-DANISH trial era: results of the European Heart Rhythm Association survey

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Implantable cardioverter-defibrillator (ICD) is the standard of care for prevention of sudden cardiac death (SCD) in high-risk patients. For primary prevention of SCD, in patients with ischaemic heart disease, there is more robust data on the effect of ICD therapy compared with patients with non-ischaemic heart disease, but current real-life practice may differ substantially. The aim of this European Heart Rhythm Association survey was to evaluate the clinical practice regarding implantation of ICD for primary prevention among European countries in patients with non-ischaemic and ischaemic heart disease. Furthermore, we wanted to investigate the impact of the results of the recently published DANISH trial on clinical practice among European countries. In total, 48 centres from 17 different countries responded to the questionnaire. The majority did not implant ICD for primary prevention on a regular basis in patients with non-ischaemic heart disease despite current guidelines. Also, centres have changed their indications after the recent report on the efficacy of ICD in these patients. In patients with ischaemic heart disease, the guidelines for primary prevention ICD were followed on a regular basis, and no relevant change in indications were reported.

Keywords Implantable cardioverter-defibrillator • Cardiac resynchronization therapy • Pacing • Sudden cardiac death • Ventricular arrhythmias • Ischemic heart disease • Ischemic cardiomyopathy • Non-ischemic cardiomyopathy • Heart failure • Prevention • EHRA survey • EP wire

Introduction

Implantable cardioverter-defibrillator (ICD) is the standard of care for prevention of sudden cardiac death (SCD) in high-risk patients.[1,2] Indications for primary prevention ICD are stated in the current ESC guidelines; however, adherence to guidelines varies substantially among European countries. Current treatments of myocardial infarction (MI) and heart failure have improved substantially over the last decades, and thus, the patient population at risk of SCD may have been altered as well. Consequently, data on the high-risk patients after MI and with heart failure in the modern era are sparse and data from previous trials may no longer be applicable.

The aim of this European Heart Rhythm Association (EHRA) survey was to evaluate clinical practice regarding implantation of ICD for primary prevention among European countries. Furthermore, we wanted to investigate the impact of the results of the recently

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published DANISH (DANish randomized, controlled, multicentre study to assess the efficacy of Implantable cardioverter defibrillators in patients with non-ischaemic Systolic Heart failure on mortality) trial on the clinical practice among European countries.

Methods

A questionnaire was provided via the Internet to the participating centres of the EHRA electrophysiology (EP) research network, and responses were collected during January 2017. In this EP wire, we asked questions about policies and indications for ICD implantation for primary prevention of SCD in patients with non-ischaemic and ischaemic heart disease.

Patients with non-ischaemic disease fulfilling indications for primary prevention ICD according to current guidelines were defined as patients with non-ischaemic cardiomyopathy with ejection fraction (EF) ≤ 35% on optimal medical therapy and with >1 year life expectancy.[1] Patients with ischaemic disease fulfilling indications for primary prevention ICD were defined as patients >6 weeks after MI, with EF ≤35% on optimal medical therapy and with >1 year life expectancy.[1]

Results

Participating centres and proportions of primary prevention *implantable cardioverter-defibrillators*

In all, 48 centres from 17 different countries responded to the questionnaire. Of these, 80% were university hospitals, 12% were private hospitals, and 8% were non-university hospitals. The total number of implanted ICDs in the last 12 months were <50 in 4%, 50–99 in 33%, 100–199 in 39%, 200–300 in 14%, and >300 in 10% of the responding centres.

In most centres (63%), the proportion of primary prevention ICDs was 50–90% among all newly implanted ICDs, while the proportion was <50% in 35% of centres and >90% in 6% of centres. Decisions on ICD implantation for primary prevention were predominantly taken on an outpatient basis (63%) and more rarely on an inpatient basis (37%).

Patients with non-ischaemic cardiomyopathy

Only 40% of centres implanted patients with non-ischaemic cardiomyopathy fulfilling current indications for primary prevention on a regular basis (>75% of patients). About 30% of centres implanted ICD in these patients in 50–75% of cases and about 30% of centres implanted primary prevention ICD in these patients in <50% of cases. Notably, 4% of centres ($n = 2$) never implanted ICDs for primary prevention in these patients. Therefore, the majority of centres (60%) implanted ICD for primary prevention in <75% of patients fulfilling indications according to current guidelines.

The most common patient-related reasons for not implanting a primary prevention ICD in non-ischaemic patients fulfilling indications was advanced age (80%), followed by frailty (61%), co-morbidities, advanced heart failure, patient preferences, and renal replacement therapy. None of the centres reported gender or obesity to be a reason for not implanting, 6% reported disbelief in current guidelines, and 11% reported reimbursement issues as reasons for not implanting primary prevention ICD in patients fulfilling current indications. The timing for ICD implantation after the initial cardiomyopathy diagnosis was >90 days in 61% and <90 days in 34%.

Impact of the results from the DANISH study on current practice in patients with non-ischaemic cardiomyopathy

Most of the centres reported to have been influenced by the DANISH study regarding decisions on primary prevention ICD (*Figure 1*), with as much as 50% of centres reporting that they had either changed their practice or stopped implanting primary prevention ICDs in patients with non-ischaemic cardiomyopathy. One-third reported a need for further evidence, and 11% had not changed their practice.

Patients with ischaemic heart disease

Most centres (70%) implanted patients with ischaemic disease for primary prevention of ICD according to the current guidelines on a regular basis (>75% of patients). This was substantially higher rate compared with patients with non-ischaemic disease (40% of centres). Patient-related reasons for not implanting primary prevention ICDs were similar for those with non-ischaemic disease and included advanced age (76%), frailty (56%), patient preferences (53%), and advanced heart failure (51%). Timing for ICD implantation was shorter than for non-ischaemic cardiomyopathy: 40–90 days after MI in 60% of centres and >90 days in only 31% of centres.

Impact of the results from the DANISH study on current practice in patients with ischaemic heart disease

Only 7% of centres reported to have changed their practice regarding primary prevention indications in patients with ischaemic heart disease, while 93% had not changed their indications in this group (*Figure 2*).

Defibrillators in cardiac resynchronization therapy

Most centres regularly included defibrillation therapy when implanting cardiac resynchronization therapy (CRT) devices: 41% used CRT pacemaker (CRT-P)-only in only 0–10% of patients, and 50% of centres reported CRT-P-only in 10–50% of patients with CRT. Only 10% of centres reported CRT-P-only in >50% of CRT patients.

Patient-related reasons to favour CRT-P-only instead of CRT defibrillator (CRT-D) were most frequently advanced age (77%), frailty (55%) followed by patients preferences, advanced heart failure, renal replacement therapy and other comorbidities (all 34%). The diagnosis of non-ischemic cardiomyopathy favoured implanting CRT-P-only in 32% of centres.

Discussion

This survey showed that the majority of responding centres implanted ICDs for primary prevention in <75% of patients with non-ischaemic cardiomyopathy fulfilling indications according to current guidelines. The responding cardiologists reported to have been influenced by the recent DANISH study regarding the indications for primary prevention ICDs in these patients and admitted that the study had changed their clinical practice. In patients with ischaemic heart

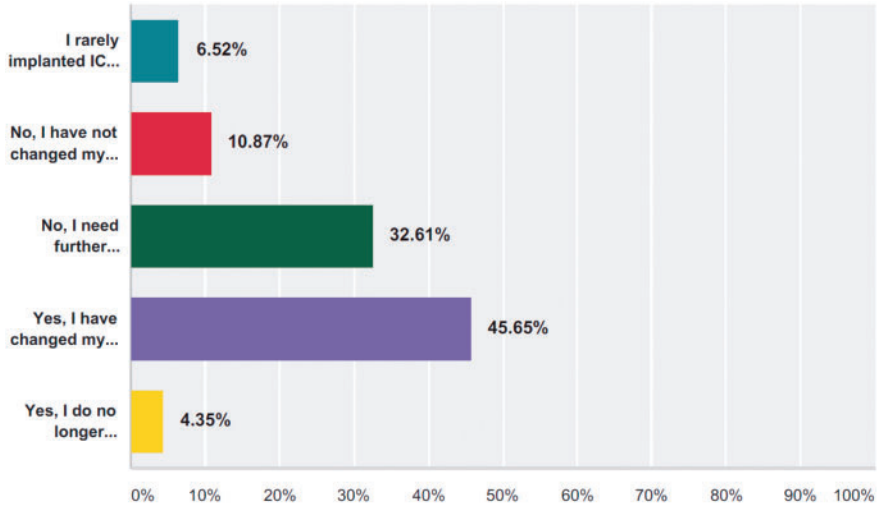

Figure 1 Results for non-ischaemic cardiomyopathy. Has the DANISH study changed your approach to ICD implantations for primary prevention in patients with non-ischaemic cardiomyopathy? (i) I rarely implanted ICD for primary prevention even before the DANISH trial. (ii) No, I have not changed my indications. (iii) No, I need further evidence and/or I will wait until the guidelines change before I modify my clinical practice. (iv) Yes, I have changed my practice. I am more selective and have implanted less ICDs on primary prevention for non-ischaemic cardiomyopathy after the study. (v) Yes, I do no longer systematically implant ICD for primary prevention in patients with non-ischemic cardiomyopathy.

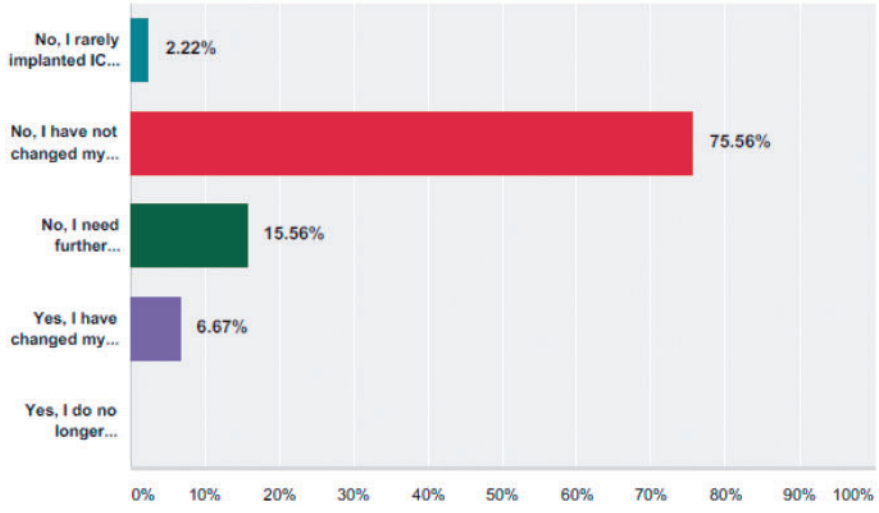

Figure 2 Results for ischaemic heart disease. Has the DANISH study changed your behaviour to implant ICD on primary prevention in patients with ischaemic heart disease? (i) No, I rarely implanted ICD for primary prevention even before the DANISH trial. (ii) No, I have not changed my indications. (iii) No, I need further evidence and/or I will wait until the guidelines change to modify my practice. (iv) Yes, I have changed my practice. I am more selective and have implanted less ICDs on primary prevention for ischemic heart disease after the study. (v) Yes, I do no longer systematically implant ICD for primary prevention in patients with ischaemic heart disease.

disease on the contrary, most centres reported to follow the current guidelines for primary prevention ICD and to have not been influenced by the DANISH study. These results indicate that high-impact studies can rapidly change clinical practice.[3]

Patients with non-ischaemic cardiomyopathy

Implantation of an ICD for primary prevention of SCD in patients with non-ischaemic cardiomyopathy and EF ≤35% has a Class I, level

of evidence B indication in the current guidelines.[1] In general, these guidelines have been less thoroughly applied by the medical community compared with the respective guidelines for patients with ischaemic heart disease, where ICD implantation for primary prevention of SCD has a Class I, level of evidence A indication. This survey showed that only 40% of reporting centres implanted ICD for primary prevention on a regular basis (>75% of patients) in patients with non-ischaemic heart disease. The lack of compliance with current guidelines may be explained by the results of previous studies, showing that primary prevention ICD in patients with non-ischaemic cardiomyopathy was less efficient for survival compared with patients with ischaemic heart disease.[4,5] A beneficial effect on all-cause mortality has only been shown in one randomized trial including patients with non-ischaemic heart disease [Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)], even if a predefined SCD-HeFT subgroup analysis demonstrated that the benefit was statistically significant only for the ischaemic subgroup.[6] However, medical treatment for heart failure has dramatically changed after the conduction of the landmark trials MADIT (Multicenter Automatic Defibrillator Implantation Trial) II[7] and SCD-HeFT that established primary prevention of SCD by ICD implantation. Thus, the effects might not be comparable anymore.

The DANISH study further showed the limited effect of primary prevention ICD on total mortality in these patients.[8] Interestingly, our EP wire survey data were collected only 4 months after the publication of the DANISH trial (on 27 August 27 2016). Nevertheless, more than half the cardiologists reported to have already changed their indication for primary prevention ICD in this patient group according to the results of the study. The DANISH study therefore seems to already have had a high impact on clinical decision making for primary prevention ICD in the medical community. Only 40% of centres reported to implant primary prevention ICD in >75% of all patients with non-ischaemic disease fulfilling current recommendations. Another 30% of centres implanted primary prevention ICDs in 50–75% of patients and the remaining 30% implanted in an even smaller proportion of patients. We do not know which centres were most influenced by the DANISH trial and if changes in indications were most predominant in those who already had a low proportion of implants or in centres with high proportion of implantations in non-ischaemic patients.

Patients with ischaemic heart disease

In patients with ischaemic heart disease, ICD for primary prevention has been shown to be associated with substantial reductions in the rate of sudden cardiac death in several trials.[7,9,10] This EP wire showed that the majority of centres followed the Class I, level of evidence A indications for primary prevention ICD on a regular basis.[1] The reasons for not implanting an ICD in rare cases were similar to those for patients with non-ischaemic disease, usually advanced age and frailty. This behaviour may originate from physicians' decisions reached on a case-by-case basis. The DANISH study had influenced indications for primary prevention in patients with ischaemic heart disease in only a small minority of cases, and therefore, we could not observe any interpolation of results from the DANISH study to patients with ischaemic heart disease. Nevertheless, a re-evaluation of the optimal strategies for prevention of SCD in the ischaemic population seems to be necessary.[11]

Defibrillators in cardiac resynchronization therapy

The majority of centres reported to implant CRT-D instead of CRT-P-only in accordance with the findings from patients with ischaemic heart disease. The diagnosis of non-ischaemic cardiomyopathy was an important factor favouring CRT-P-only rather than CRT-D and was reported in almost one-third of centres.[12]

Until now, no adequately powered study has provided evidence on the advantage of CRT-D vs. CRT-P, and a recent registry suggested similar outcome in CRT-D vs. CRT-P, with the preference for CRT-P-only similar to those described in this survey.[13]

Conclusions

Implantation of ICDs for primary prevention of SCD in patients with non-ischaemic cardiomyopathy fulfilling indications according to the current guidelines was not performed on a regular basis in the majority of centres. Also, the majority of centres reported to have changed their indications in these patients after the publication of the DANISH study. For patients with ischaemic heart disease, indications according to the current guidelines were followed by the majority and no changes in indications after the DANISH trial were reported. The DANISH study was able to rapidly change physicians' attitudes regarding ICD indications in the non-ischaemic patient population.

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