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EHRA SURVEY

Management of patients with ventricular arrhythmias and prevention of sudden cardiac death—translating guidelines into practice: results of the European Heart Rhythm Association survey

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Prevention of sudden cardiac death (SCD) remains a partly unsolved task in cardiology. The European Society of Cardiology (ESC) guidelines on management of patients with ventricular arrhythmias and prevention of SCD published in 2015 considered the new insights of the natural history of diseases predisposing to SCD. The guidelines improved strategies for management of patients at risk of SCD and included both drug and device therapies. The intention of this survey was to evaluate the extent of the disparities between daily clinical practice and the 2015 SCD ESC guidelines among electrophysiology centres in Europe. The results suggest that the adherence to guidelines is reasonably high and strategies for the management of ischaemic disease are well-established. Implantable cardioverter-defibrillator indications for primary prevention are a difficult topic, particularly in non-ischaemic dilated cardiomyopathy. Disparities in the use of genetic testing are probably due to differences in local availability.

Keywords Sudden cardiac death • Ventricular arrhythmias • Prevention • European Society of Cardiology guidelines • European Heart Rhythm Association • Survey

Introduction

Prevention of sudden cardiac death (SCD) remains a partly unsolved task in cardiology. The European Society of Cardiology (ESC) guidelines on management of ventricular arrhythmias and prevention on SCD published in 2015 considered the new insights of the natural history of diseases predisposing to SCD.[1] The guidelines improved strategies for management of patients at risk of SCD and included both drug and device therapies. Furthermore, they included risk stratification for genetic cardiac diseases with risk of SCD.

Current European clinical practice at the patient level may differ from the ESC guideline recommendations. The intention of this survey was to evaluate the extent of the disparities between daily clinical practice and the 2015 SCD ESC guidelines among electrophysiology centres in Europe.

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Methods and results

Participating centres

An on-line questionnaire prepared by members of the Scientific Initiatives Committee of the European Heart Rhythm Association (EHRA) was sent to members of the EHRA Electrophysiology Research Network including 17 countries. In all, 40 centres (26% response rate) from 17 different countries responded to the questionnaire. Of these centres, 91% were University hospitals, 7% were private centres, and the rest were non-University hospitals.

Screening of sudden cardiac death victims and family members

In a victim of unexplained SCD <35 years of age with no findings at autopsy, 53% of respondents would perform genetic testing of the victim and subsequent screening of the family if a positive result was found in the victim. Of those not performing genetic screening of the victim, half would perform clinical family screening including electrocardiogram (ECG) and echocardiography and the other half also included exercise test and Holter monitoring in the family screening (23%).

Coronary artery disease and non-ischaemic dilated cardiomyopathy

In patients with acute coronary syndrome and recurrent sustained ventricular tachycardia (VT), 95% of respondents would include urgent coronary angiography in first-line management, with most also including beta-blockers (88%) and amiodarone (60%) as first-line treatment.

To reduce SCD risk after myocardial infarction almost all respondents would include beta-blockers, dual antiplatelet therapy, statins, and optimize heart failure treatment as needed, while 21% would consider the wearable cardioverter-defibrillator in patients with left ventricular ejection fraction (LVEF) <35% as a bridging therapy.

Patients with preserved LVEF and stable coronary artery disease after myocardial infarction with unexplained syncope were considered for programmed ventricular stimulation (PVS) by 59% of respondents; however, 36% of respondents would not use PVS for risk assessment.

The management strategy for patients with non-ischaemic dilated cardiomyopathy (DCM) with LVEF 45% and asymptomatic non-sustained VT (NSVT) on optimal medical therapy differed between respondents (*Figure 1*). The majority (85%) of respondents chose conservative heart failure therapy with regular clinical follow-up.

All respondents considered implantable cardioverter-defibrillator (ICD) implantation in cardiac arrest survivors, and 90% in patients with documented VT or haemodynamically non-tolerated VT in the absence of reversible causes and in patients >40 days after myocardial infarction with LVEF <35%. Only 70% considered ICD implantation in patients with non-ischaemic DCM and LVEF <35%. One-fifth considered ICD implantation in patients with non-ischaemic DCM and LVEF <35% only if the patient was relatively young (<68 years of age).

The respondents were also asked if they discussed with the patient what to do with the ICD in the case of the patient's end-of-life situation, in patients with severe left ventricular dysfunction fulfilling ICD criteria for primary prevention. Almost one quarter (24%) always discussed this issue, 32% if they considered that the patient psychologically suitable, 37% in special cases, 5% never discussed this topic, and 3% did not disable ICD therapies in end-of-life situations.

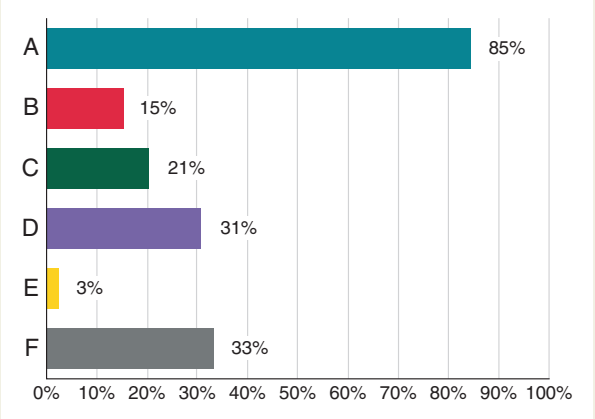

Figure 1 Which is your strategy in a patient with non-ischaemic dilated cardiomyopathy, ejection fraction 45%, and asymptomatic non-sustained ventricular tachycradia (non-bundle branch re-entry, non-outflow tract morphology) on optimal medical therapy? (multiple answers): (*A*) Conservative heart failure therapy with regular clinical follow-up. (*B*) Electrophysiological study for risk stratification. (*C*) Catheter ablation. (*D*) Amiodarone. (*E*) ICD implantation. (*F*) Perform genetic analysis for *LMNA* mutation and/or family history of sudden death and accordingly decide for ICD implantation. ICD, implantable cardioverter-defibrillator.

Hypertrophic cardiomyopathy

Almost all respondents included maximum wall thickness (97%), family history of SCD (97%), unexplained syncope (95%), and NSVT (82%) in the risk stratification for SCD in a patient with hypertrophic cardiomyopathy (HCM). Furthermore, 66% included left ventricular outflow tract gradient, 52% the left atrial diameter, and 50% included results from cardiac magnetic resonance imaging (MRI) for risk stratification. Less commonly included in the risk stratification were exercise stress test (42%), genotyping (39%), and PVS (13%). Approximately one-fifth (21%) of respondents reported that they used their clinical experience in risk stratification. Most of the respondents always used the ESC risk calculator and none used this calculator in children or after septal reducing therapy.

Most (82%) recommended avoidance of competitive sports in HCM patients, with 5% recommending avoidance of all sports. Almost half (47%) discussed sports participation with the patient and decided on this on an individual basis, with 42% imposing no restrictions to family members with maximum wall thickness <12 mm.

Arrhythmogenic cardiomyopathy

Most (79%) respondents recommended avoidance of competitive sports in patients with definite arrhythmogenic cardiomyopathy (AC) and 27% recommended avoidance of all sports. No respondent let the patients exercise *ad libitum*. Another 38% discussed with the patients and decided on sports participation on an individual basis.

A total of 35% also recommended mutation positive family members to avoid competitive sports.

The majority of respondents (76%) treated AC patients with a definite AC diagnosis with beta-blockers and 54% added amiodarone in patients with frequent premature ventricular complexes or NSVT intolerant for or with contraindications to beta-blockers.

All respondents considered ICD implantation in patients with definite AC with a history of aborted SCD and haemodynamically poorly tolerated VT. Around half (51%) considered ICD in patients with one or more risk factors for SCD; 35% considered primary prevention ICD on a case-by-case basis.

Inherited primary arrhythmia syndromes

Long QT syndrome

The majority of respondents (84%) considered long QT syndrome (LQTS) diagnosis in patients with unexplained syncope and QTc >460 ms in repeated a 12-lead ECGs. This diagnosis was also considered in presence of a confirmed pathogenic LQTS mutation irrespective of QT duration (73%). As many as 60% considered a LQTS diagnosis in patients with QTc >480 ms and in male patients with QTc >450 ms and women with QTc >460 ms (59%). Most (84%) recommended beta-blockers to all LQTS patients and 35% interestingly recommended beta-blockers in LQTS mutation positive patients with normal QTc. Only 41% considered primary prevention ICD in patients with LQT2 and LQT3 and QTc >500 ms, whereas 43% of respondents considered only secondary prevention ICD in LQTS patients.

Brugada syndrome

All respondents considered ICD implantation in SCD survivors with a Brugada type ECG. The majority (76%) considered ICD in patients with syncope and type 1 Brugada ECG, whereas 24% considered ICD in the same patients only after a positive PVS (*Figure 2*).

In a 30-year-old patient with spontaneous type 1 Brugada ECG with no additional risk factors for SCD and a history of a suspected reflex syncope, the majority (71%) performed only regular follow-up. Half of respondents considered further investigations with tilt test to explore the suspected reflex syncope and half of respondents considered implantation of a loop recorder. Around half (46%) suggested PVS, and 25% suggested ICD implantation (11% single chamber ICD and 14% subcutaneous ICD). The LifeVest wearable defibrillator was not suggested by any of the respondents in this setting.

Discussion

This EHRA survey provides a snap-shot overview of cardiologists' adherence to the European SCD guidelines.[1] Despite the relative low response rate, this survey is able to demonstrate relatively clear adherence to the ESC 2015 management of ventricular arrhythmias and SCD prevention guidelines, but with some important exceptions. The main topics interrogated were (i) screening of SCD victims and family members (ii) strategies in patients with coronary artery disease and non-ischaemic cardiomyopathy, (iii) risk stratification and management of patients with cardiomyopathies, and (iv) risk stratification and management of patients with ion channel disease.

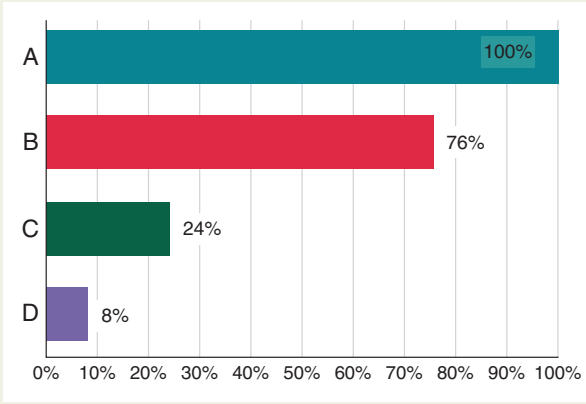

Figure 2 In patients with Brugada syndrome, I consider ICD implantation under the following scenario (multiple answers): (*A*) In an SCD survivor with a Brugada type ECG. (*B*) In a patient with syncope and a spontaneous type 1 Brugada ECG. (*C*) In patients with syncope and a spontaneous type 1 Brugada ECG, only after positive electrophysiological study. (*D*) In first-degree relatives of a Brugada patient with (aborted) SCD. ECG, electrocardiogram; ICD, implantable cardioverter-defibrillator; SCD, sudden cardiac death.

Screening of sudden cardiac death victims and family members

The survey showed that only half of respondents performed genetic screening of SCD victims <35 years of age with no findings in standard autopsy, despite genetic screening in this setting having a Class IA recommendation. The remaining centres performed clinical screening of the family members. The relatively low frequency of genetic screening may indicate that this test is not available in all centres. Molecular autopsy allows for the identification of ion channelopathies and explains 15-25% of SCD when standard autopsy is normal. Furthermore, if a genetic test identifies the cause of death in a victim, family screening can be performed efficiently focusing clinical resources on family members at risk and can reassure the non-carriers.

Strategies in patients with coronary artery disease and non-ischaemic dilated cardiomyopathy

First-line treatment for patients with coronary syndrome and recurrent sustained VT were in accordance to the SCD guidelines, including high frequency of beta-blocker and amiodarone medication and urgent coronary angiography. There was also high concordance of medication after myocardial infarction with use of beta-blocker therapy, dual antiplatelets, statins and optimization of heart failure therapy, reflecting agreement in this common and well-established patient group. Interestingly, one-fifth considered a wearable cardioverter-defibrillator in patients with LVEF <35% during the first 40 days after myocardial infarction, (Class IIB), showing rapid implementation of this relatively novel strategy.[2,3] Future studies will shed light on the usefulness of a wearable cardioverter-defibrillator.

The use of PVS for risk stratification of SCD risk has been debated, but is recommended (Class I) in patients after myocardial infarction with symptoms suggestive of VT.[1,4] In this survey, 60% of the

respondents considered using this method in such patients. However, as many as 36% reported that they would not use PVS for risk stratification reflecting the limited consensus on this topic.

The strategies in non-ischaemic patients with asymptomatic NSVT on optimal medical treatment and LVEF <45% were more diverse. The majority have chosen a conservative strategy with regular follow-up, which is in accordance with the guidelines. Only 15% considered PVS (Class IIB indication) and may reflect that the majority of centres do not perform PVS for risk stratification in non-ischaemic DCM patients. Interestingly, one-third of respondents added amiodarone although this is not recommended in the guidelines (Class III) in asymptomatic patients. Knowledge of increased risk among patients with *LMNA* mutations was evident as one-third of respondents considered genetic testing for further risk stratification. The guidelines and current literature support that patients with *LMNA* mutations have a more severe outcome and are frequently in need of an ICD before left ventricular function is severely reduced (LVEF < 35%).[5,6]

Implantable cardioverter-defibrillators

The chosen strategies for ICD implantation in patients with coronary artery disease were strictly adherent to guidelines. The obvious IA indication for ICD for secondary prevention was acknowledged by almost all respondents, and strategies for ICD for primary prevention were also in accordance with guidelines in ischaemic patients. Guidelines for ischaemic patients therefore seem to be well-established and supported by the EP community. In contrast, as reported in a previous EHRA wire,[7] the strategies differed in patients with non-ischaemic DCM. Only 70% considered ICD in patients with non-ischaemic DCM fulfilling current IB recommendations, with 20% considering ICD only in younger individuals (<67 years). These results are similar to the previously reported disparities[7,8] and may have even been augmented by the publication of the DANISH study.[9] The primary prevention ICD indications for non-ischaemic cardiomyopathy therefore remain challenging.

The question of management of the ICD device in an end-of-life situation has been discussed previously in an EHRA patients' survey.[10] The results from this survey, from the physicians' point of view, have confirmed the results of the patients' survey that this difficult discussion is often not performed. Only one in four respondents discussed this topic on a regular basis, and one in three took into consideration the patient's psychological status before they eventually addressed this topic.

Hypertrophic cardiomyopathy

Risk stratification of patients with HCM was adherent to guidelines and also included the guidelines for HCM incorporating the calculation of 5 years risk of SCD.[11] Almost all respondents used the risk markers included in the HCM risk calculation, however, with less attention given to atrial diameter (only 50% of respondents). A recent echocardiogram reporting atrial diameter may not always be available in the patient follow-up setting, and this may be one of many reasons explaining the less frequent use. In addition, half of respondents also included results from cardiac MRI studies for risk stratification, although this is only recommended in cases with intermediate risk.[11] The ESC HCM calculator was a commonly used tool by the respondents of this study and has been evaluated in recent studies.[12] Furthermore, all respondents were aware of its limitations in children, after septal reducing therapy and in other entities such as Anderson-Fabry disease.

The majority of respondents recommended avoidance of competitive sports in patients with HCM, which is in agreement with the guidelines (Class I). Half of respondents discussed participation in sports with the patient and made the decision on an individual basis. Only 40% gave no restrictions to asymptomatic family members with normal wall thickness. This answer could indicate the lack of specific indication in guidelines for these individuals. Recent reports indicate the participation in sports is not harmful in these individuals.[13] Future guidelines should clearly address this topic to avoid unnecessary restrictions to health beneficial physical activity in HCM mutation positive family members.

Arrhythmogenic cardiomyopathy

The awareness of the harmful effects of sports participation in AC disease was high and all respondents recommended avoidance of sports in patients with AC according to the guidelines. Only 35% recommended mutation positive family members to avoid competitive sports. Again this important question is not addressed in the current SCD guidelines and should clearly be included in future versions as reports indicate vigorous exercise may accelerate and aggravate AC disease also in family members.[14,15]

Medical therapy in AC patients was consistent with the guidelines with the majority of respondents giving beta blockers (Class I) to definite AC patients, with the addition or replacement by amiodarone in some cases. ICD recommendations were followed by all respondents for secondary prevention ICD. The difficulty in selection of patients for primary prevention ICD were obvious with more than one third reporting that this was performed on a case-by-case basis in their centre. Risk stratification for ventricular arrhythmias in the growing cohort of AC mutation positive family members is still very difficult and tools for selection of these patients are limited.[16,17]

Inherited primary arrhythmia syndromes

The strategies for diagnosing LQTS among the respondents were consistent with the guidelines, although only 70% considered an LQTS diagnosis in individuals with confirmed pathogenic mutations (Class I). The genetic diagnosis seems to be lingering behind, which may be explained by the fact that this diagnostic test is not yet available throughout Europe. In accordance to the guidelines, the respondents treated the majority of LQTS patients with beta blockers, but only 35% considered beta-blocker medication in genotype positive patients with a normal QTc. The latter is a Class IIA recommendation and other factors including personal experience may play a role in the management strategy in these individuals.

Implantable cardioverter-defibrillator for secondary prevention was acknowledged by all respondents and 40% stated that they considered only secondary prevention ICD in LQTS. The answers may be biased by the different number of LQTS patients in different centres and many centres may not have large cohorts of LQTS patients. Referral to experienced centres in these cases may be the preferred approach.

Implantable cardioverter-defibrillator implantation in patients with Brugada syndrome was clear for secondary prevention and also in patients with type 1 Brugada ECG and syncope, with the majority of

respondents advocating an ICD (Class IIA). However, one in four preferred a positive PVS study (Class IIB) before the decision of an ICD in the latter group of patients. The prognostic value of PVS has been debated and most clinical studies have not confirmed either a positive or a negative predictive value of PVS for arrhythmic events.[4]

Conclusion

This survey suggests that electrophysiologists' adherence to the ESC guidelines is reasonably high and strategies for ischaemic heart disease are well established. Implantable cardioverter-defibrillator indications for primary prevention are difficult topics and in particular for non-ischaemic DCM. There seems to be disparities in the use of genetic testing, probably due to differences in local availability. Future guidelines should address strategies for the growing population of mutation positive family members.

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References

1. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J *et al.* 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Europace* 2015;**17**:1601–87.
2. Reek S, Burri H, Roberts PR, Perings C, Epstein AE, Klein HU *et al.* The wearable cardioverter-defibrillator: current technology and evolving indications. *Europace* 2017;**19**:335–45.
3. Lenarczyk R, Potpara TS, Haugaa KH, Hernandez-Madrid A, Sciaraffia E, Dagres N. The use of wearable cardioverter-defibrillators in Europe: results of the European Heart Rhythm Association survey. *Europace* 2016;**18**:146–50.
4. Brembilla-Perrot B, Suty SC, Houriez P, Claudon O, Beurrier D, de la Chaise AT. Value of non-invasive and invasive studies in patients with bundle branch block, syncope and history of myocardial infarction. *Europace* 2001;**3**:187–94.
5. Hasselberg NE, Edvardsen T, Petri H, Berge KE, Leren TP, Bundgaard H *et al.* Risk prediction of ventricular arrhythmias and myocardial function in Lamin A/C mutation positive subjects. *Europace* 2014;**16**:563–71.
6. Hasselberg NE, Haland TF, Saberniak J, Brekke PH, Berge KE, Leren TP *et al.* Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation. *Eur Heart J* 2018;**39**:853–60.
7. Haugaa KH, Tilz R, Boveda S, Dobreanu D, Sciaraffia E, Mansourati J *et al.* 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. *Europace* 2017;**19**:660–4.
8. Tilz RR, Lenarczyk R, Scherr D, Haugaa KH, Iliodromitis K, Purerfellner H *et al.* Management of ventricular tachycardia in the ablation era: results of the European Heart Rhythm Association Survey. *Europace* 2018;**20**:209–13.
9. Køber L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E *et al.* Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med* 2016;**375**:1221–30.
10. Haugaa KH, Potpara TS, Boveda S, Deharo JC, Chen J, Dobreanu D *et al.* Patients' knowledge and attitudes regarding living with implantable electronic devices: results of a multicentre, multinational patient survey conducted by the European Heart Rhythm Association. *Europace* 2018;**20**:386–91.
11. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P *et al.* 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J* 2014;**35**:2733–79.
12. Ruiz-Salas A, Garcia-Pinilla JM, Cabrera-Bueno F, Fernandez-Pastor J, Pena-Hernandez J, Medina-Palomo C *et al.* Comparison of the new risk prediction model (HCM risk-SCD) and classic risk factors for sudden death in patients with hypertrophic cardiomyopathy and defibrillator. *Europace* 2016;**18**:773–7.
13. Dejgaard LA, Haland TF, Lie OH, Ribe M, Bjune T, Leren IS *et al.* Vigorous exercise in patients with hypertrophic cardiomyopathy. *Int J Cardiol* 2018;**250**:157–63.
14. Saberniak J, Hasselberg NE, Borgquist R, Platonov PG, Sarvari SI, Smith HJ *et al.* Vigorous physical activity impairs myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy and in mutation positive family members. *Eur J Heart Fail* 2014;**16**:1337–44.
15. Haugaa KH, Haland TF, Leren IS, Saberniak J, Edvardsen T. Arrhythmogenic right ventricular cardiomyopathy, clinical manifestations, and diagnosis. *Europace* 2016;**18**:965–72.
16. Leren IS, Saberniak J, Haland TF, Edvardsen T, Haugaa KH. Combination of ECG and echocardiography for identification of arrhythmic events in early ARVC. *JACC Cardiovasc Imaging* 2017;**10**:503–13.
17. Corrado D, Wichter T, Link MS, Hauer R, Marchlinski F, Anastasakis A *et al.* Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. *Eur Heart J* 2015;**36**:3227–37.