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EHRA SURVEY

Contemporary clinical management of monomorphic idiopathic premature ventricular contractions: results of the European Heart Rhythm Association Survey

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Abstract

On behalf of the European Heart Rhythm Association, we designed a survey, whose aim was to understand the trend(s) in the clinical management of idiopathic monomorphic premature ventricular contractions (PVCs) among European cardiologists and cardiac electrophysiologists. A total of 202 participants in the survey answered 27 multiple-choice questions on the clinical presentation, diagnosis and treatment of idiopathic monomorphic PVCs. The most common symptom in patients with idiopathic monomorphic PVCs is palpitations, according to the majority of responders (87%), followed by fatigue (29%) and dizziness (18%). Complete blood cell count, renal function with electrolytes levels, and thyroid function are the blood tests requested by the majority of respondents (65%, 92%, and 93%, respectively). Coronary artery disease and structural heart disease needs to be ruled out, according to the vast majority of participants (99%). A 24-h Holter ECG is the preferred ECG modality to assess the burden of PVCs (86% of respondents). Among the different option treatments, beta-blockers and class I antiarrhythmic drugs are by far (81% of respondents) the preferred pharmacological option in comparison with calcium antagonists and class III antiarrhythmic drugs. Catheter ablation has also a good reputation: 99% of responders are keen to use it, especially in patients with high burden of PVCs and when signs of cardiomyopathy occur.

Keywords Premature ventricular contraction • Ventricular arrhythmias • Idiopathic • Cardiomyopathy • Antiarrhythmic drugs • Catheter ablation • EHRA survey

Introduction

Premature ventricular contractions (PVCs) are a frequent electrocardiographic finding in the cardiological clinical setting. The PVCs as single or repetitive phenomenon are sometimes associated with cardiomyopathies and structural heart disease, generally worsening their prognosis.[1] The PVCs may be a precursor of cardiac pathology and also accompany extra-cardiac pathologies such as uncontrolled hypertension,[2] thyroid dysfunction,[3] pulmonary disease,[4] and sleep apnoea syndrome.[5] In the absence of underlying cardiovascular pathology, ectopic ventricular beats are summarized under the term of idiopathic PVCs. The mechanisms for any given PVC may include

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triggered activity, automaticity, and re-entry, thus creating uncertainty and heterogeneity in treatment modalities. International guidelines are not providing univocal directions in their clinical management.[6,7] Therefore, the Scientific Initiatives Committee (SIC) of the European Heart Rhythm Association (EHRA) designed a survey to report the trend(s) in clinical diagnosis and management of idiopathic monomorphic PVCs among cardiologists and cardiac electrophysiologists.

Methods

This physician-based survey was promoted and disseminated by EHRA. An online questionnaire, consisting of 27 multiple-choice questions, was developed, amended and validated by SIC, and circulated to cardiologists and cardiac electrophysiologists via EHRA and selected national cardiac society mailing lists and via EHRA-related social media. The specific queries included in the questionnaire are shown in Supplementary material online.

Results were collected anonymously in compliance with the European General Data Protection Regulation (GDPR) 2016/679.

Survey results are expressed as categorical data (numbers and proportions).

Results

From 1 September to 30 September 30 2021, 202 respondents participated in the questionnaire. All of them were able to respond to most questions; therefore, the results of the survey were drafted from all their pooled answers.

The average age of the responders was 44 ± 10 years. The majority of responders was male (75%). European countries were the most represented in the survey, with France and Poland contributing half of the total responses (55%). Almost half the participants worked in university hospitals (49%), followed by private hospitals/clinics (19%), public hospitals (13%), and specialized public cardiology centres (9%). Only a minority worked in a private practice (7%). Most of the survey respondents were cardiac electrophysiologists (57%), followed by general cardiologists (28%), cardiac electrophysiology fellows (7%), and cardiac fellows (4%). Other healthcare professionals accounted for only 2% of the survey respondents.

Clinical presentation of idiopathic monomorphic premature ventricular contractions

The most common symptom in patients with idiopathic monomorphic PVCs was palpitations, according to the majority of responses (87%), followed by fatigue (29%) and dizziness (18%). Interestingly, 34% of the respondents reported that patients with PVCs remain asymptomatic (*Figure 1*).

Diagnostic investigations

Blood tests allow a non-invasive assessment of extracardiac and intra-cardiac causes possibly associated with PVCs. Of all the respondents, 75% agreed on the necessity of doing a blood test before diagnosis of idiopathic PVCs. Among various blood tests available, a high agreement on performing a complete blood cell count, thyroid function, and renal function tests in association with electrolyte levels (65%, 92%, and 93%, respectively) was reported (*Figure 2*). Of note, half of the respondents considered important checking the levels of NT-proBNP, whereas one-third are routinely testing C-reactive protein (CRP) to rule out active inflammation. Liver function tests, HbA1c, cholesterol, and troponine levels are routinely checked only by 25% of the physicians participating in the present survey.

Untreated hypertension may also promote PVCs[8] and aggravate any structural heart disease. Interestingly, of 74% of the respondents who believed in this possible association, 57% are basing their evaluation of blood pressure control on the office blood pressure measurements, while 17% usually employ ambulatory blood pressure monitoring with a cut-off of 135/85 mmHg to define uncontrolled blood pressure.

Sleep apnoea is another extracardiac disease, which is associated with high cardiovascular morbidity. Of all the respondents, 69% are routinely investigating if patients with monomorphic PVCs have also sleep apnoea.

Coronary artery disease (CAD) is a common intra-cardiac cause of PVCs. The respondents were almost all concordant (99%) on the necessity of ruling out CAD before making the diagnosis of idiopathic PVCs, with significant differences in the diagnostic modality and selection of patients. Indeed, only 25% considered useful to rule out CAD in all patients, regardless of their risk profile. On the contrary, 42% are usually excluding CAD only in those patients considered at risk according to the ESC guidelines. A minority of respondents reported testing for CAD only if PVCs are not originating from the outflow tracts or only if patients have repetitive phenomena, such non-sustained ventricular tachycardia (18% and 12%, respectively, *Figure 3*).

Among the non-invasive tests used routinely by respondents, a stress test is performed by 80% of them. A computed tomography (CT) coronary angiogram or an invasive coronary angiogram is always ordered by 12%, whereas the majority of respondents is ordering them only in particular cases: a positive stress test (52%), electrocardiographic documentation of non-sustained ventricular tachycardia (15%), or other reasons (12%). Only 8% are never performing a coronary artery imaging before the diagnosis of idiopathic monomorphic PVCs.

Cardiac magnetic resonance imaging (MRI) is a valuable diagnostic tool to rule out structural/non-ischaemic cardiac disease; 99% of respondents agreed with this statement, but only 32% of them are performing cardiac MRI in all patients with monomorphic idiopathic PVCs, 37% of them advise performing cardiac MRI only in the case of concomitant ECG or echocardiographic abnormalities, 11% in the case of PVC burden ≥ 15% during 24-h Holter monitoring, and 6% only PVC burden is ≥30% (*Figure 4*).

A 24-h or longer Holter ECG is the preferred diagnostic modality to measure the burden of idiopathic monomorphic PVCs (86% of the respondents), with 11% generally using a longer recording of 48 h, and only 1% using other monitoring modalities such as R test/remote cardiac telemetry or implantable loop recorders (*Figure 5*).

Treatment

Initiating a treatment was mainly driven by high burden of PVCs and the occurrence of PVCs-mediated cardiomyopathy. The burden cut-off chosen to start a treatment was heterogeneous (*Figure 6*), but the

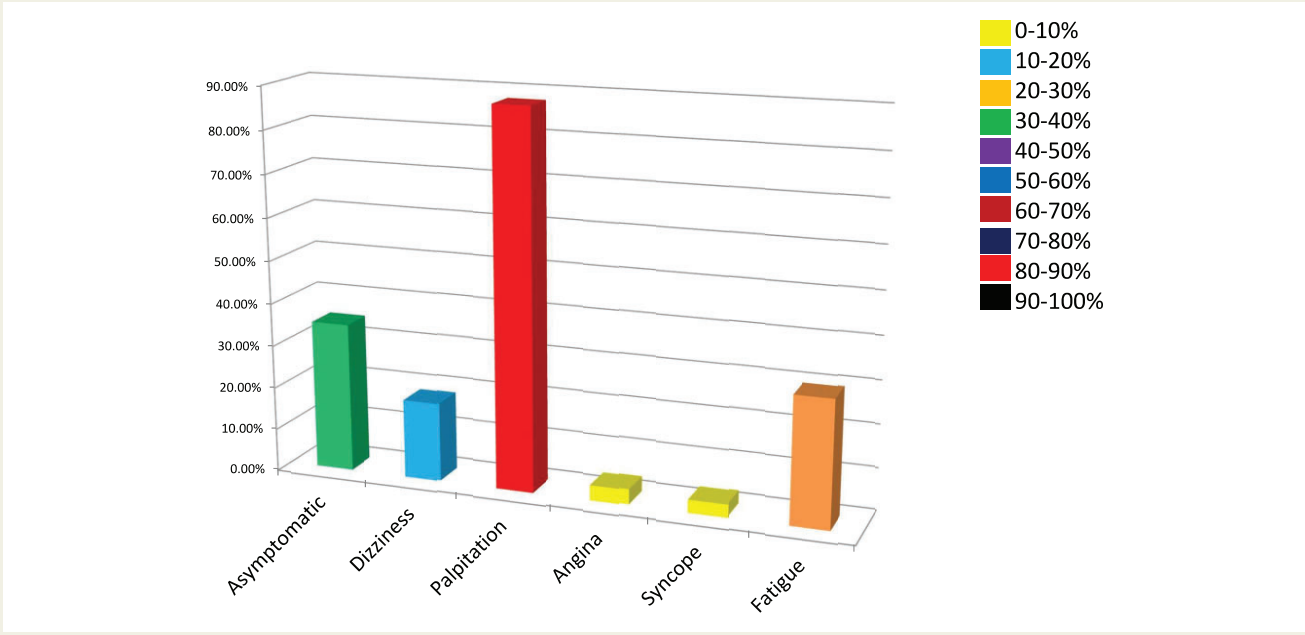

Figure 1 Type and frequency of symptoms associated with monomorphic idiopathic premature ventricular contractions.

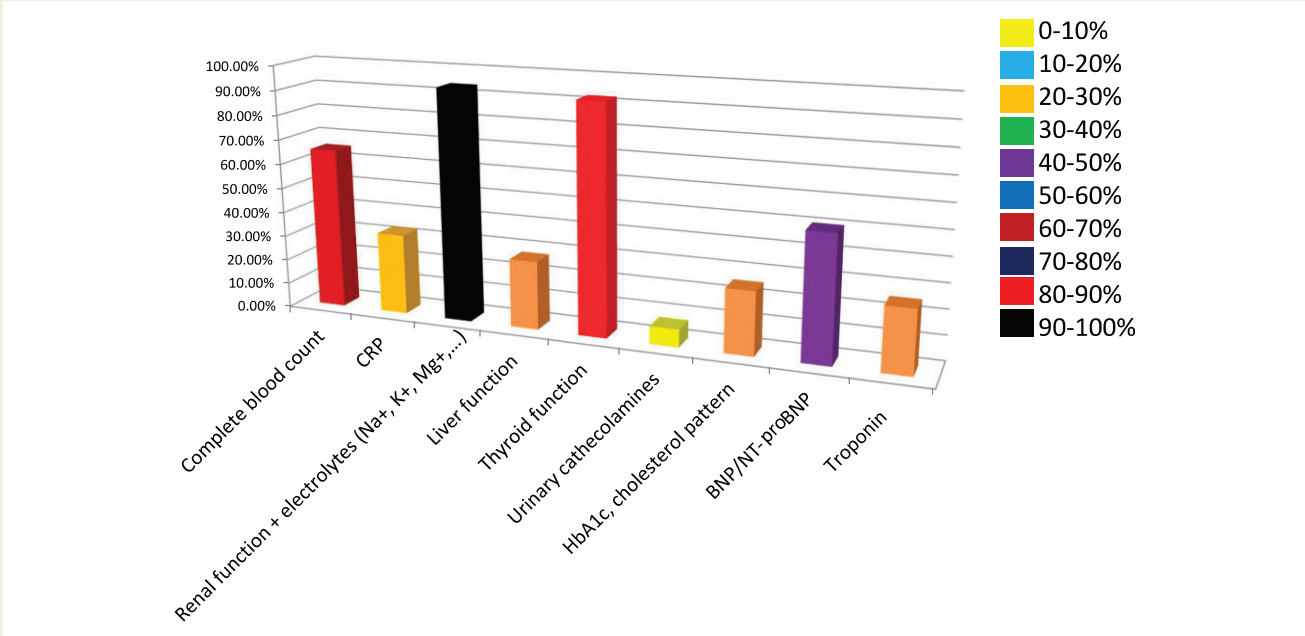

Figure 2 Type and frequency of blood tests ordered in patients with monomorphic idiopathic premature ventricular contractions. BNP, brain natriuretic peptide; CRP, C-reactive protein; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

majority of the respondents was in accordance with treatment initiation for PVC burden exceeding 10% of normal QRS complexes in a 24-h Holter ECG recording.

The survey reported a great diversity regarding the endpoint of an effective treatment for idiopathic PVCs: one-third of the respondents are not considering any specific cut-off for the reduction of PVC burden in a 24-h Holter ECG after treatment initiation and are reassessing the patient basing only on symptoms relief and on left ventricular function improvement. The other two-thirds are assessing treatment effectiveness according to the degree of PVC burden reduction prior to therapy initiation. Only 17% consider treatment successful in the case of complete absence of PVCs.

Beta-blockers are the preferred first choice treatment for 81% of the respondents, followed by class IC antiarrhythmic drugs (flecainide

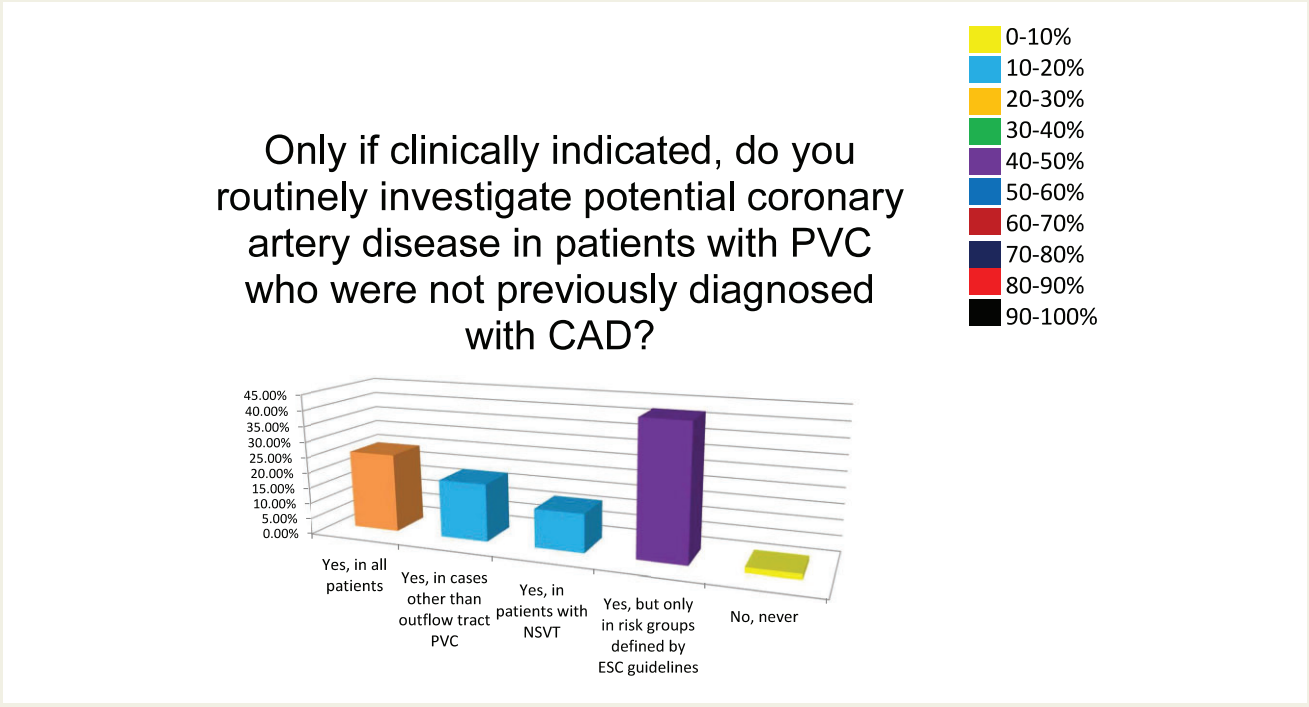

Figure 3 Coronary artery disease and monomorphic idiopathic premature ventricular contractions. CAD, coronary artery disease; ESC, European Society of Cardiology; NSVT, non-sustained ventricular tachycardia; PVCs, premature ventricular contractions.

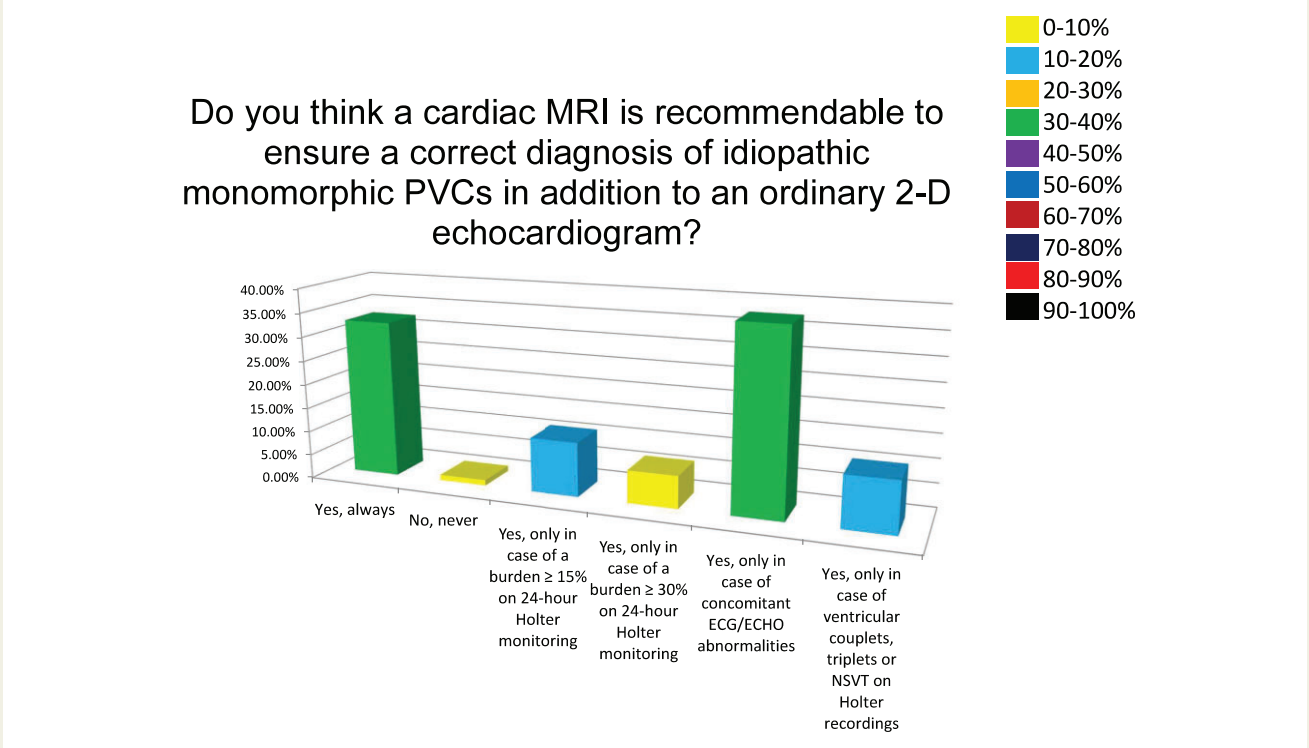

Figure 4 Cardiac magnetic resonance imaging and monomorphic idiopathic premature ventricular contractions. ECG, electrocardiogram; ECHO, echocardiogram; MRI, magnetic resonance imaging; NSVT, non-sustained ventricular tachycardia; PVCs, premature ventricular contractions.

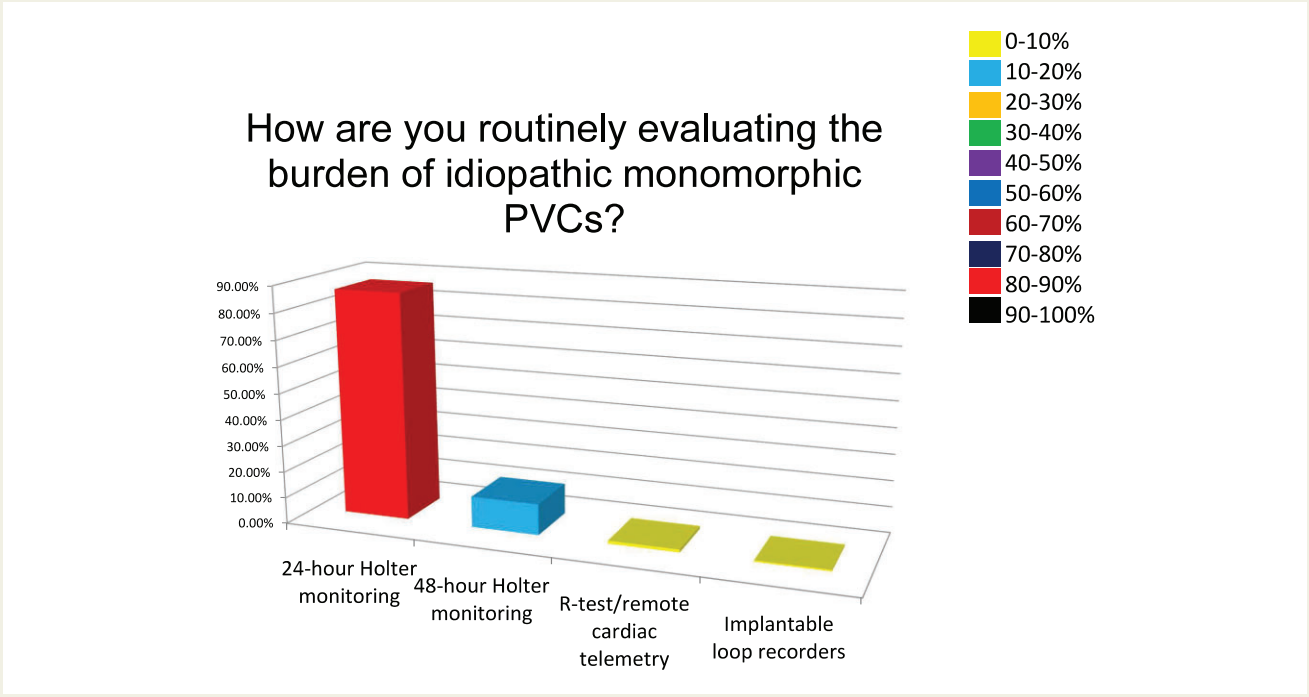

Figure 5 Type and frequency of the diagnostic tools used to evaluate the burden of monomorphic idiopathic premature ventricular contractions. PVCs, premature ventricular contractions.

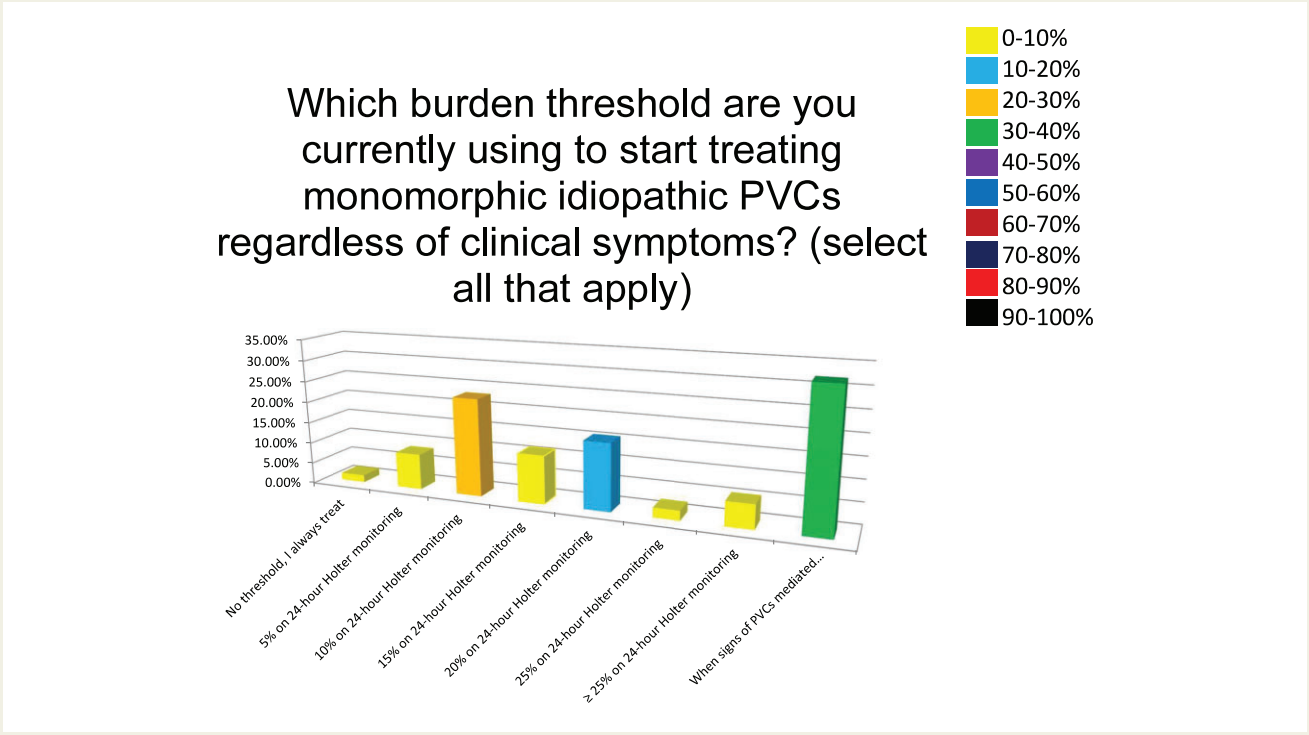

Figure 6 Burden threshold used to start any given treatment in patients with monomorphic idiopathic premature ventricular contractions. PVCs, premature ventricular contractions.

and propafenone) chosen by 11% of the respondents, and they are considered most effective (*Figure 7*). As expected, sotalol and amiodarone were never chosen as first choice treatment.

According to the vast majority of respondents, in their experience, PVC-mediated cardiomyopathy is developing rarely (maximum 10% of patients).

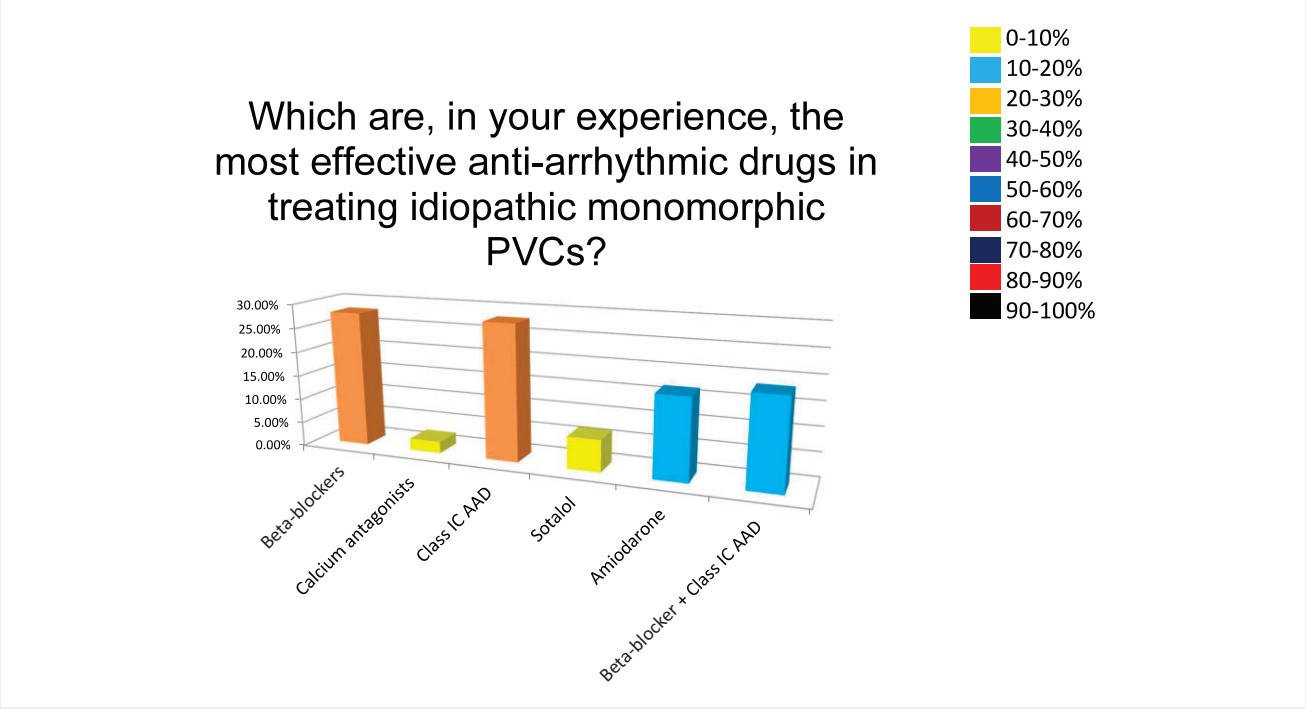

Figure 7 Antiarrhythmic treatments: perceived efficacy in patients with monomorphic idiopathic premature ventricular contractions. AAD, antiarrhythmic drugs; PVCs, premature ventricular contractions.

Involvement of cardiac electrophysiologists was deemed necessary mainly when signs of PVC- mediated cardiomyopathy are present, in the case of failure of antiarrhythmic medications, if PVC burden exceeds 15% of the normal QRS complexes during 24-h Holter monitoring, or if patients remained symptomatic.

Catheter ablation is considered an important treatment option by the majority of the respondents (99%, *Figure 8*). Patient consent to undergo an invasive treatment of idiopathic PVCs with radiofrequency catheter ablation was variable. According to 39% of the respondents, 62% of patients consider ablation as an option after failed pharmacological treatment, whereas 37% are opting for it as first line treatment.

The time intervals for scheduled clinical re-evaluations in patients with idiopathic monomorphic PVCs varied as well. Overall the tendency was to adapt it to each clinical case or to consider a time frame of 6–12 months.

Discussion

The main findings of our survey on the contemporary management of monomorphic idiopathic PVCs are the following:

- the most common symptoms associated with PVCs are palpitations, fatigue, and dizziness;
- blood cell count, renal function tests with electrolytes levels, and thyroid function tests are the most common laboratory items chosen by clinicians involved in the survey, but there was also some interest towards CRP and NT-proBNP;
- uncontrolled hypertension, sleep apnoea, and CAD need to be excluded in order to direct the diagnosis towards monomorphic idiopathic PVCs;
- cardiac MRI is one of the most preferred imaging modalities to rule out structural heart disease, but it should not be performed in all patients with idiopathic monomorphic PVCs;
- PVC burden and the presence of PVC-induced cardiomyopathy are the most important factors for treatment initiation; the most chosen burden cut-off was 10% calculated in a 24-h Holter ECG;
- treatment effectiveness is evaluated by the majority of participants re-assessing the burden of PVCs at follow-up, but there was absolutely no agreement on which burden threshold to use for this purpose;
- according to the participants of our survey, PVC-induced cardiomyopathy is perceived to occur rarely, in a range between 1% and 10% of the patients;
- there was good agreement among the participants of the survey on the fact that cardiac electrophysiologists should be involved in the treatment of idiopathic PVCs, especially in the presence of PVC-induced cardiomyopathy, antiarrhythmic drug failure, high burden of PVCs (≥15% on 24-h Holter monitoring) or, less commonly, intractable symptoms;
- catheter ablation is considered an important treatment option by the majority of respondents (99%), in selected cases as first-line option and more commonly as second-line options in the case of failure of one or more antiarrhythmic drugs.

Clinical presentation of idiopathic monomorphic PVCs is heterogeneous.[9] Our survey confirms this general impression and is in line with what has already been published in the literature.[10] Skipped heart beats and palpitations are the most common symptoms associated with PVCs. The reduced stroke volume associated with PVCs can explain symptoms such as fatigue and dizziness[11]: these symptoms are usually more frequent in patients with ventricular bigeny or trigeminy on the ECG and pulse deficit. However, PVCs may be completely asymptomatic, especially in patients with low arrhythmia burden.

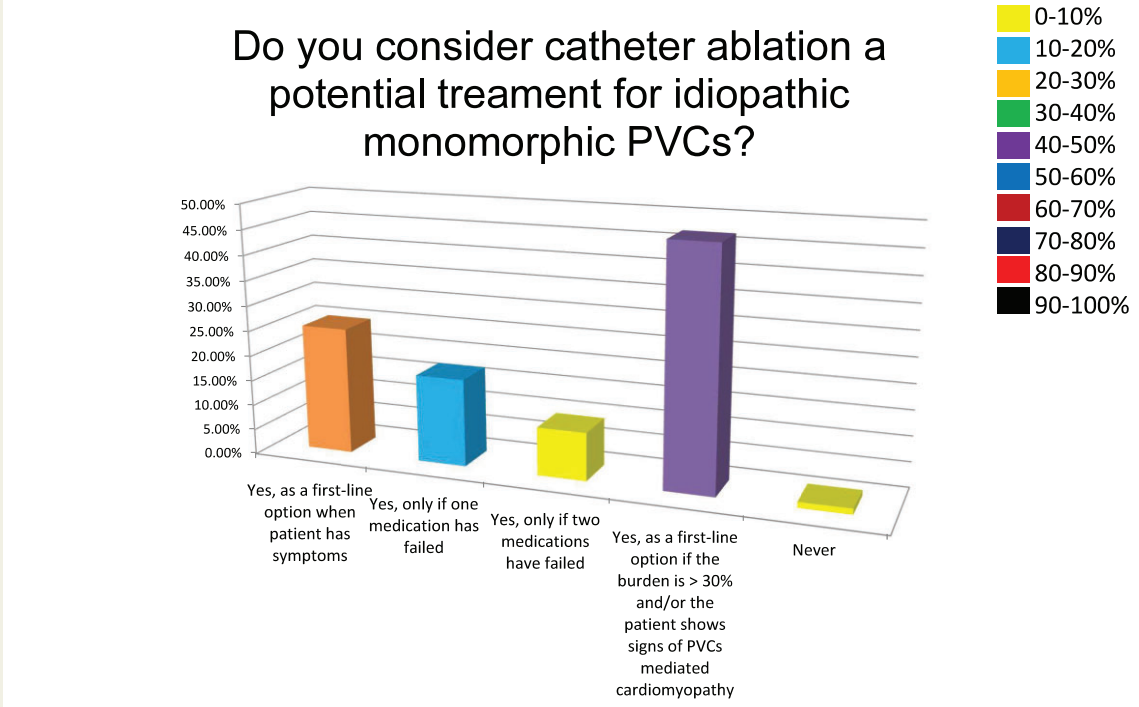

Figure 8 Candidates for catheter ablation of premature ventricular contractions. PVCs, premature ventricular contractions.

The diagnosis of monomorphic idiopathic PVCs is a diagnosis of exclusion. It is therefore plausible that the majority of participants in our survey stated that blood tests should be routinely used in this clinical scenario. Blood tests such as complete blood count, thyroid, and renal function tests were concordantly advised in order to exclude common extracardiac causes such as anaemia,[12] thyroid dysfunction,[13–15] or electrolyte imbalance,[16] which often trigger the occurrence of PVCs. The use of CRP[17] and NT-proBNP[18] was also seen favourably, given their strong association with inflammatory disease, infection, and heart failure.

Our respondents almost unanimously indicated that uncontrolled hypertension and sleep apnoea can contribute to the occurrence of PVCs. This finding is the natural consequence of the pathophysiologic link between sleep apnoea and hypertension.[19] Increased intra-thoracic pressure and intermittent hypoxia together with higher concentrations of angiotensin and catecholamines[20] can favour the development of left ventricular hypertrophy and an increase of the intracellular release of calcium, which may induce early or delayed afterdepolarizations with the consequent appearance of ectopic beats, both in the atria and in the ventricles.[21,22] Therefore, it is intuitive that detection and treatment of sleep apnoea and hypertension should be mandatory in patients with monomorphic idiopathic PVCs and should precede or accompany the arrhythmia-oriented treatment options.

The respondents to the survey were also concordant in advising to rule out CAD in patients with monomorphic idiopathic PVCs. If the role of ischaemia in the generation of PVCs was largely investigated in the past century[23,24]; the relationship with monomorphic idiopathic PVCs is vague at best. Our survey demonstrates also that it is important to exclude underlying CAD, especially in patients with cardiovascular risk factors, with non-outflow tract originating PVCs, prior to any pharmacologic or non-pharmacologic treatment for PVCs. The recommended modality of detection of cardiac ischaemia is all but univocal; stress test seems to be the most preferred option, whereas a CT coronary angiogram is rarely advised, probably due to the high rate of motion artefacts in concomitance with the occurrence of ectopics. Coronary angiography is the preferred option when there is documentation of ischaemia at the stress test or in case of non-sustained ventricular tachycardia.

The clinicians who participated in our survey indicated clearly the necessity to rule out myocarditis and/or structural heart disease by means of cardiac MRI. According to the ESC guidelines for the management of patients with ventricular arrhythmias and prevention of sudden cardiac death published in 2015,[1] cardiac MRI should be used when echocardiography does not provide the accurate assessment of cardiac function and/or evaluation of structural changes (class IIa indication). Cardiac MRI is the preferred imaging modality for myocardial tissue characterization and ruling out cardiomyopathies such as arrhythmogenic right ventricular dysplasia,[25] cardiac amyloidosis, and sarcoidosis.[26]

Our survey confirms a commonly used clinical practice: a 24-h Holter ECG is still the preferred electrocardiographic recording modality to quantify the burden of PVCs and to follow the clinical course of this group of patients, regardless of the type of selected treatment. Even if longer ECG recordings have been demonstrated to increase the accuracy of the detection of PVC burden in any given patient,[27] the easy availability of a 24-h ECG recording in comparison with other recording modalities can explain this finding. Furthermore, the vast majority of the literature on the topic has been produced using

24-h Holter ECGs: its use in the clinical practice can facilitate comparisons and allows to follow the evolution of a patient under a given treatment. It is important to underline though that this situation will probably fastly change in the incoming years, thanks to spreading of wearable ECG recording tools (patches, watches, etc.).[28] The main limitation of these new ECG recording modalities at present is that they are not providing reliable information on PVC number and burden.

Holter ECG seems central also in the evaluation of the effectiveness of treatment. No agreement was reported on the cut-off point to define a treatment successful. This is the consequence of a known extreme day-by-day variability of the frequency of PVCs. Indeed, Mullis *et al.*[29] have recently demonstrated that there is a significant variation in 24-h PVC burden when measured over a 14-day period in patients with PVC burden of >5%. They also speculated on the fact that this extreme variability can affect medical decisions (treatment vs. no treatment) and evaluation of treatment efficacy.

Beta-blockers (in particular bisoprolol and metoprolol) and, less commonly, class IC antiarrhythmic drugs (in particular flecainide and propafenone) are the preferred antiarrhythmic treatments. This finding is reassuring, as it is absolutely in line with the current ESC guidelines[1] and mirrors the general favourable profile of safety and efficacy of beta-blockers compared with class I antiarrhythmic drugs. Amiodarone and sotalol were never indicated as first choice treatment in our survey and their use as second choice is less and less frequent after the spread of catheter ablation.[30–32]

Our survey highlights the incremental involvement of the interventional cardiac electrophysiologists and the importance of invasive therapy with radiofrequency catheter ablation in the treatment of monomorphic idiopathic PVCs.[33] The general feeling coming out of the survey was that they should become first actors in the treatment when signs of PVC-induced cardiomyopathy are present, in the case of failure of anti-arrhythmic medications, and if there is burden of PVCs ≥ 15% during 24-h Holter monitoring. Along with this, catheter ablation is still considered more as rescue treatment when antiarrhythmic drugs fail, unless there is evidence of PVC-mediated cardiomyopathy.

The general impression emerging from the respondents to our survey is that the occurrence of PVC-mediated cardiomyopathy is somewhat rare. The majority of them has documented it in 1–10% of all patients with idiopathic monomorphic PVCs. The data on the epidemiology of monomorphic idiopathic PVCs are lacking. Even if there is evidence that the risk of developing left ventricular dysfunction and heart failure is proportional with the burden of PVCs[34] and that PVC-induced cardiomyopathy occur more often at burdens >10%,[35–37] there is still uncertainty regarding the individuals who are the most predisposed to have this unfavourable outcome.

Finally, our survey reflects the uncertainty of the recommendable frequency of follow-up visits for this category of patients: general consensus was that it should be adapted to each patient or be in the range of 6 months. Further research and guidelines are warranted on this particular matter.

Conclusions

Monomorphic idiopathic PVCs are a common clinical finding among cardiologists and cardiac electrophysiologists. Our survey denotes a correspondence with the published epidemiology and a substantial adherence of clinicians to the international recommendations.

Supplementary material

Supplementary material is available at *Europace* online.

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Conflict of interest: none declared.

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