



Premature ventricular complexes. Systematic review, evaluation and management

Vanesa Alonso-Ventura, Javier Jimeno Sánchez, Elena Gambó Ruberte, David de las Cuevas León, Belén Peiró Aventín, Gabriel Hurtado Rodríguez, Teresa Simón Paracuellos, Pablo M. Corredoira, Carlos Ruben Lopez Perales, Rodrigo Gallardo

Department of Cardiology, University Hospital Miguel Servet, Zaragoza (Spain)

Corresponding author:

Rodrigo Gallardo, University Hospital Miguel Servet – Paseo Isabel la Católica, 1-3 – 50007 Zaragoza (Spain)

E-mail: rgallardol@salud.aragon.es

Premature ventricular complexes (PVCs) are a common finding in general population and can be even considered physiologic in most cases. Nevertheless, very frequent isolated PVCs may lead to the development of a usually reversible left ventricular dysfunction or be a manifestation of an underlying cardiac condition that could be associated with more severe ventricular arrhythmias, heart failure or cardiac death.

Three causative mechanisms of the PVCs have been proposed: abnormal automaticity, triggered activity and reentry supposing different diagnostic and therapeutic implications.

Although many patients with PVCs remain completely asymptomatic, others may suffer from a wide range of symptoms like palpitations, fatigue, dyspnoea or dizziness of a variable degree.

Proper characterisation of the PVCs, their burden and features, as well as the identification of their sites of origin and mechanisms should be pursued to establish the convenience of a conservative or therapeutic approach.

Specific treatment with medical therapy or catheter ablation must be contemplated in symptomatic patients or in those who develop related systolic dysfunction or other kind of complications.

Keywords: premature ventricular complexes, cardiac arrhythmia, pvc-induced cardiomyopathy

Premature ventricular complexes (PVCs), also known as premature ventricular contractions, ventricular premature beats or ventricular extrasystoles, can be defined as any cardiac single depolarization originated below the atrioventricular node, either in His-Purkinje tissue or in ventricular myocytes. They represent the most common ventricular arrhythmia and are frequently observed even in healthy individuals. Global prevalence varies between 1% to 4% on simple ECG and 40% to 75% on a 24 or 48-hour Holter monitoring.

Some risk factors for the appearance of PVCs are male gender, African-American ethnicity, hypertension and advanced age, showing an exponential increase in prevalence after the third or fourth decade of life (1–3).

Aetiology

Most frequently, PVCs have an idiopathic origin, not associated with any underlying cardiac disease, and arise mainly from some specific ventricular areas, being particularly common in the right ventricular outflow tract (RVOT) remaining unclear the reason for this preferential location. Other prevalent foci are the left ventricular outflow tract (LVOT), the aortic sinus of Valsalva, the atrioventricular valve annulus, the Purkinje fibres or the papillary muscles. Idiopathic PVCs can appear spontaneously or favoured by increased sympathetic tone in situations such as anxiety, sleep deprivation, physical exercise, electrolyte disturban-

ces and intake of drugs like cocaine, caffeine, alcohol or tobacco (4).

In some occasions PVCs may be related to an underlying cardiac condition, either affecting the electrical properties of the heart such as Brugada or long QT syndromes or being linked to structural heart disease (SHD) like hypertrophic or dilated cardiomyopathy, ischaemic heart disease, mitral valve prolapse... implying a poorer prognosis (5, 6).

Mechanisms

The pathophysiology of this phenomenon remains not totally clarified. Three possible mechanisms have been proposed (6, 7).

Abnormal automaticity

It consists in the spontaneous progressive depolarisation of the resting membrane potential (phase 4 of the action potential) until it finally reaches the electrical threshold and initiates a new action potential.

It is mainly observed in cells of the specialised conduction system but also occasionally in normal myocytes from certain regions like the outflow tract and it may be enhanced by several factors like increased sympathetic tone, use of inotropic agents, electrolyte imbalances or ischaemic states (6).

One phenomenon explained by this mechanism is parasystole in which a group of cells turns into an independent focus firing at a rate that is typically unaffected by the electrical activity of the rest of the myocardium, linked to a functional unidirectional block that protects the parasystolic focus (8, 9).

Triggered activity

Here, impulse formation results as a consequence of oscillations in the membrane potential related to the previous action potential (afterdepolarisations) which, if they are of sufficient amplitude, can trigger a new action potential.

Based on their temporal relationship, afterdepolarisations are classified as early (if they happen in phase 2 or 3 of the action potential) or delayed (phase 4) (6, 7).

- Early afterdepolarisations occurring during phase 2 are related to persistent inward calcium currents through $ICa-L$ channels (10) and those in phase 3 are mainly associated with IK_1 channels (11). In both cases, action potential prolongation is the main predisposing condition that is manifested on surface ECG with a prolonged QT interval. Resulting PVCs may induce polymorphic ventricular tachycardia (VT) or torsades de pointes particularly in patients affected with long QT syndromes (12).
- Delayed afterdepolarisations occur in phase 4 as a result of an intracellular calcium overload initially from extracellular source and then from additional

calcium release from sarcoplasmic reticulum via ryanodine receptors. The increased intracellular concentration of calcium activates the Na-Ca exchanger that can finally trigger a new action potential (13).

This mechanism is favoured by increased sympathetic tone and also by some drugs like digitalis (first drug in which this effect was observed) (14) or catecholamines. It is considered the most common mechanism of PVCs in patients with no SHD, associated generally with a benign course but also involved in possible malignant arrhythmias like in patients with catecholaminergic polymorphic ventricular tachycardia syndrome (6).

Reentry

In this mechanism the electrical impulse propagates around a circuit enclosed by functional or physical barriers (usually scars) of unexcitable tissue. Due to the different electrophysiological properties of the fibres along the circuit, we can simplify it as formed by two distinct pathways with different conduction velocities and refractoriness. In normal conditions, the electrical impulse enters the circuit through both pathways leading to a final collision of wavefronts and no arrhythmia is originated. Under certain circumstances, and mainly because of the difference in refractoriness, unidirectional block may happen in one of the pathways so that the wavefront transmitted along the other pathway can cross the usual region of collision of wavefronts, advance retrogradely through the first pathway and close the circuit if the area of block has recovered the excitability. Reentry is the main mechanism for ventricular arrhythmias in patients with SHD, most typically involved in sustained VT but also possible for single PVCs (6, 7, 15, 16).

Clinical Presentation

There can be a wide variety of symptoms related to the presence of PVCs ranging from patients completely asymptomatic to others with more severe or even disabling symptoms.

The most common clinical presentation consists in palpitations attributed to the abnormal heart contraction produced by the PVC itself, the compensatory pause and the consecutive hypercontractile beat or a combination of these. Frequently, the patients describe these palpitations either as irregular heart rhythm with the sensation of the heart skipping a beat or as pulsations in the neck in relation to cannon atrial waves that can be noticed also in the physical examination.

Some patients may experience light-headedness or presyncope in relation to ventricular bigeminy especially if the PVC shows a short coupling interval with the preceding beat resulting in insufficient ventricular filling and consequently ineffective contraction of the PVC leading to a functional relative bradycardia (6).

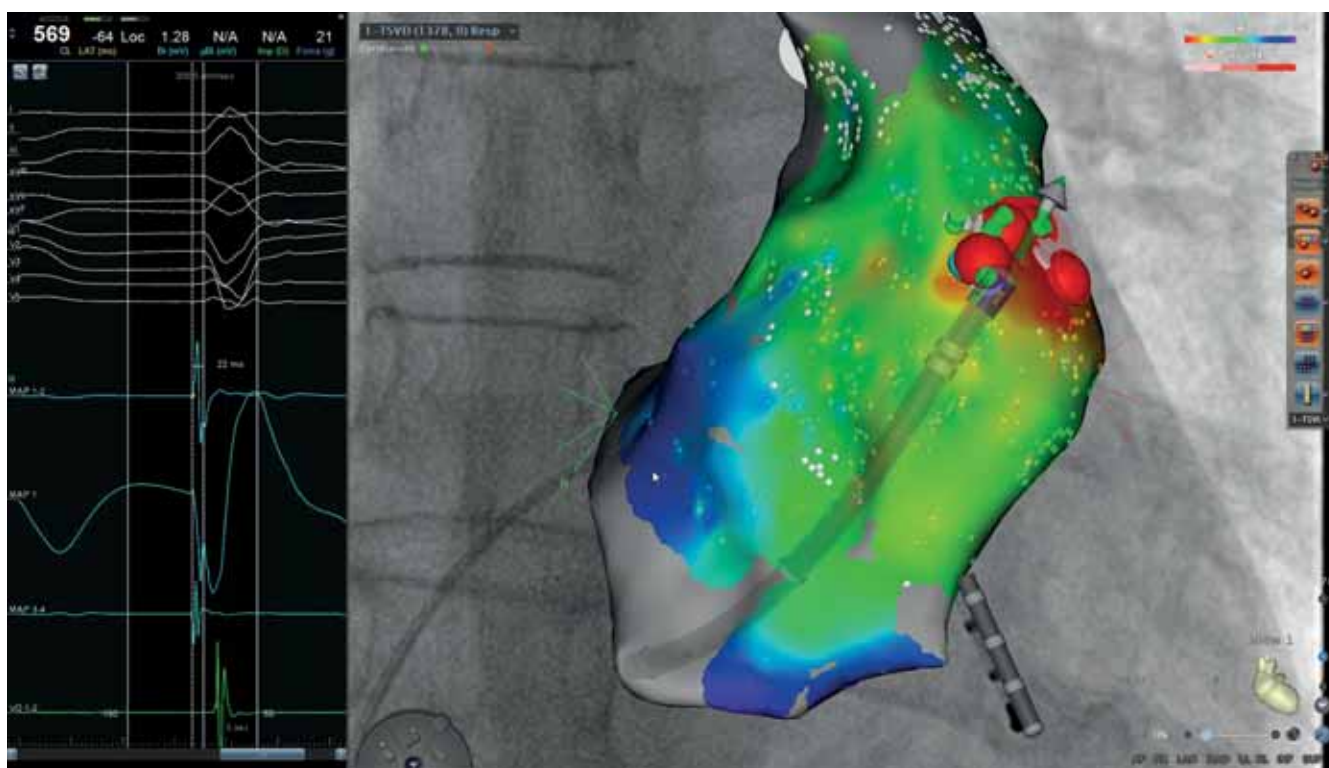


FIGURE 1. PVC with origin in RVOT. **LEFT PANEL:** Typical ECG pattern with tall R waves in the inferior leads and LBBB morphology with late precordial transition. Below the ECG, mapping catheter electrograms showing early activity and QS pattern in the unipolar configuration. These signals are compatible with the catheter being located on the site of origin of the PVC. **RIGHT PANEL:** 3D electroanatomic map confirming earliest activation area on the anterior wall of the RVOT

Other possible symptoms could be chest discomfort, dyspnoea, exertional limitation or even overt heart failure particularly in those patients with very frequent PVCs who can develop ventricular systolic dysfunction. This condition called PVC induced cardiomyopathy (PIC) is generally reversible following the reduction of the PVC burden after adequate treatment (17).

If the PVCs are associated with another heart condition there can be specific symptoms related to the latter, for instance chest pain in patients with ischaemic heart disease.

Malignant arrhythmias or sudden cardiac death (SCD) have also been reported even in the absence of any other apparent heart disease (although exceptional in these cases), happening mainly when PVCs present with short coupling intervals (18).

Evaluation

ECG

Initial diagnostic evaluation usually starts with a resting 12-lead ECG showing one or more PVCs, sometimes as an incidental finding in a routine physical examination. On other occasions PVCs are discovered on a Holter monitoring during the investigation of the symptoms of the patient.

In any case, following the anamnesis about the clinical

and family history of the patient, the first step should be a thorough analysis of the resting ECG looking for clues of a possible underlying substrate.

Then, if the PVC is visible on the ECG, we must try to identify its site of origin as this could have diagnostic, therapeutic and prognostic implications. Many different algorithms have been proposed for this matter.

In general terms, when the PVC presents with a right bundle branch block (RBBB) pattern in lead V1 the site of origin is very likely to be in the left ventricle whereas a left bundle branch block (LBBB) morphology in V1 suggests an origin in the right ventricle or interventricular septum.

Secondly, the inferior or superior direction of the PVC axis would point to an origin in the superior or inferior aspect of the ventricle respectively.

Thirdly, a QS pattern in lead V6 suggests a PVC origin near the apex as this lead is anatomically positioned close to this region. Conversely, positive wave in V6 would suggest the base as the origin of the PVC and intermediate patterns would reflect base-to-apex intermediate locations.

Another key aspect is the total QRS duration. Relatively narrow QRS generally indicates septal origin or early entry to the preferential conduction fibres of the His-Purkinje system.

Finally, signs of initial slow depolarisation would sug-

gest an epicardial origin instead of the most common endocardial origin of the PVC (19).

Globally, the most frequent location of PVCs is the RVOT, generally not related to any underlying cardiac disease. Analysis of the morphology of these PVCs deserves special attention. The typical pattern consists of tall R waves in the inferior leads with an LBBB pattern in V_1 with precordial transition happening after V_3 (Figure 1). If precordial transition occurs before V_3 , the origin is more likely to be in the LVOT or within the aortic root on the right or left coronary cusps. When precordial transition occurs at V_3 , the site of origin is more unpredictable and may be either right or left sided.

ECG monitoring

During assessment of patients with PVCs, it is of paramount importance to determine the PVC burden, defined as the number of PVCs per day or as the percentage in relation to the total number of heart beats, which is ultimately related to the risk of developing PIC. Other important factors to analyse are the number of different PVC morphologies, if one or more morphologies are predominant, if there are only isolated PVCs or they group in couplets or even VT and if there is clinical correlation between the presence of PVCs and the symptoms of the patient.

For these purposes, an ECG monitoring for a minimum of 24-hours would be advisable for all patients under investigation for PVCs.

Taking into account that PVC burden may be variable one day from another, mobile telemetry for a period of 7 days may reflect the overall PVC burden more accurately. Further than that, monitoring for 2 weeks or longer would provide little additional information (20).

Imaging tests

Although most of the times PVCs have an idiopathic origin, they may sometimes be associated with underlying SHD, with a poorer prognosis and would warrant a specific treatment. Consequently, investigation with cardiac imaging techniques is usually required.

These imaging tests however might be unnecessary if there is no evidence of high PVC burden, patient is otherwise healthy and physically active, no history of syncope or symptoms compatible with VT, no family history of early or sudden death or cardiomyopathy, and neither the resting ECG nor physical examination suggest the presence of other abnormalities (6).

Transthoracic echocardiography (TTE) is the preferable initial imaging modality for both screening for SHD and evaluation of possible PIC in patients with high PVC burden (6). When conventional TTE is non-diagnostic but suspicion of possible SHD remains, additional techniques like myocardial strain, transoesophageal echocardiography and particularly cardiac magnetic resonance imaging (MRI) may be necessary.

Thanks to its high resolution and sensitivity for iden-

tification of early stages of SHD and the possibility of scar analysis, cardiac MRI plays a key role in uncovering undiagnosed cardiac structural abnormalities even in those patients with previously presumed idiopathic PVCs. Several studies have indeed demonstrated that routine diagnostic tests could be suboptimal, enhancing the role of cardiac MRI. Specific findings that suggest arrhythmogenic substrates are: late gadolinium enhancement, myocardial oedema, fatty infiltration or altered T1 mapping and increased extracellular volume (21, 22).

Cardiac MRI should therefore be considered in situations that have proven a positive connection with underlying SHD like the presence of multifocal PVCs, induction of PVCs or more complex ventricular arrhythmias during exercise, PVCs with a non-LBBB inferior axis morphology or clinical factors like male gender, advanced age or family history of SCD or cardiomyopathy (22).

Exercise testing

Exercise testing should be taken into consideration in those patients with PVCs which occur or worsen during exertion. It can also be used as a tool to add diagnostic and prognostic values. The appearance of PVCs or even VT during exercise is more frequent in individuals with SHD, fact that implies a worse prognosis and a need for deeper evaluation.

In a study with otherwise apparently healthy athletes, those with repetitive PVCs during exercise were found to represent a high-risk subgroup and the presence of exercise-induced non-sustained polymorphic VT was associated with a probability of an underlying LV scar of 67% (22, 23). Anyway, patients with idiopathic PVCs who develop monomorphic VT during exercise testing are still considered to have good prognosis, but a thorough investigation is necessary to ensure its benign nature (24).

Electrophysiology study (EPS)

It may serve to determine the mechanism and origin of the PVCs which can later be used to plan proper treatment, sometimes even catheter ablation during the same procedure.

In terms of the mechanisms, PVCs mediated by reentry are generally easily inducible by programmed stimulation. Conversely, induction of PVCs mediated by triggered activity or abnormal automaticity is more unpredictable, responding to the use of sympathomimetic drugs or to atrial or ventricular burst pacing with variable success rates (25).

During the EPS, the site of origin of the PVCs can be identified as the area with the earliest activation time or alternatively through pace mapping manoeuvres in cases of non-inducibility (26).

The creation of voltage maps depicting areas of scar tissue can also be useful since these zones are usually linked to sites of origin of ventricular arrhythmias in patients with SHD.

Management

Specific treatment to reduce PVC burden will be necessary in symptomatic patients or in those who develop PIC as this condition is generally reversible after adequate control of PVCs. In addition, some patients diagnosed of idiopathic dilated cardiomyopathy with impaired systolic function and a high PVC burden may have a certain component of PIC. It has been reported that some of these patients experience a significant improvement in ventricular contraction and volumes after successful reduction of their PVC burden, particularly in the ones with a ventricular dysfunction that is out of proportion in relation to the degree of myocardial fibrosis detected in cardiac MRI (17).

Another situation in which treatment of PVCs should be pursued is in cases where PVCs are followed by initiation of malignant ventricular arrhythmias. Successful ablation of these PVCs can lead to a decrease of the risk of ICD shocks (1).

Lifestyle changes

Abuse of caffeine, theine, alcohol, tobacco or illicit drugs as well as high levels of stress and anxiety have been related to a higher risk of PVCs. Nevertheless, a randomized trial evaluating PVC burden after total abstinence of caffeine, smoking and reduced alcohol intake in healthy individuals failed to demonstrate a reduction of total PVCs (27). Since SHD patients were not investigated, further studies are needed to evaluate the potential benefit of lifestyle modifications in this population.

Electrolyte correction

Low blood levels of potassium and magnesium can favour the development of PVCs or other types of atrial and ventricular arrhythmias. A blood test for determining electrolyte levels is mandatory in these patients and prompt correction of hypokalaemia or hypomagnesemia as well as their possible causes would be necessary.

Medical Therapy

Beta-blockers and non-dihydropyridine calcium channel blockers remain first-line pharmacological therapy for patients with frequent and symptomatic PVCs. A favourable safety profile and the added benefit of beta-blockers in patients with ischaemic heart disease or with heart failure with reduced ejection fraction make them the best initial medical therapy. Nevertheless, several studies have showed only a slight reduction (between 12 and 24%) of PVC burden in patients with symptomatic outflow tract PVCs treated with these agents (6).

If these drugs were ineffective or poorly tolerated, catheter ablation should be the next therapeutical option. Anyway, other antiarrhythmic drugs could be regarded in those with a failed ablation or preference for medical treatment. Some of these antiarrhythmic drugs could be amiodarone (70% efficacy rate, although concerns

about side effects in long-term treatment may limit its use) or sotalol (particularly in ischaemic heart disease patients). Flecainide and propafenone are other possible options provided that SHD has been ruled out as they were associated with a higher mortality rate in this patient population (6, 28).

Catheter Ablation

Catheter ablation is the preferable treatment if medical therapy is not tolerated, not effective or rejected by the patient. It has indeed a higher success rate (up to 80-95%) and low incidence of complications (0-5%), mostly related to vascular access. Success rate diminishes in cases of non-inducibility during the procedure, presence of polymorphic PVCs or if the sites of origin of the PVCs are of difficult access like epicardial foci or located in areas where catheter contact is more unstable or close to important anatomical structures (17, 29). In these latter circumstances use of imaging techniques such as intracardiac echocardiography, computed tomography, MRI or angiography may facilitate the ablation procedure (Figure 2).

Follow up

Although, as previously mentioned, isolated PVCs are often thought to have minimal clinical significance in patients without SHD, persistence of high PVC burden may conduct to development of PIC in the long term, even if this condition is not present at the time of the initial evaluation. In spite that no clear cut-off value has been established, several studies have shown increa-



FIGURE 2. Image integration of 3D electroanatomic map and aortic angiography during catheter ablation of PVC arising from the aortic root. The visualisation of the origin of the coronary arteries provides safer guidance during the ablation procedure

sing risk of development of PIC in accordance with the degree of PVC burden, being this risk of up to 40% in patients with a PVC burden greater than 10% and exceptional if PVC burden is below 6% (17). Therefore, annual echocardiogram is recommended in patients with high PVC burden and medical or ablative therapy should be reconsidered in case of progression to systolic dysfunction.

In addition to the degree of PVC burden, other factors that have been proposed as risk predictors of systolic dysfunction are long QRS duration (> 150 ms) and short coupling interval of the PVCs (30). In the presence of these features a closer follow up could be convenient.

Declaration of interest

The authors below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

- Luebbert J, Auberson D, Marchlinski F. Premature Ventricular Complexes in Apparently Normal Hearts. *Card Electrophysiol Clin* 2016 Sep; 8(3): 503–14. <https://doi.org/10.1016/j.ccep.2016.04.001>.
- Frigy A, Csiki E, Caraşca C, et al. Autonomic influences related to frequent ventricular premature beats in patients without structural heart disease. *Medicine (Baltimore)* 2018 Jul; 97(28): e11489. <https://doi.org/10.1097/MD.00000000000011489>
- Hiss RG, Lamb LE. Electrocardiographic findings in 122,043 individuals. *Circulation* 1962 Jun; 25: 947–61. <https://doi.org/10.1161/01.cir.25.6.947>
- Ahn M-S. Current Concepts of Premature Ventricular Contractions. *J Lifestyle Med* 2013 Mar; 3(1): 26–33.
- Maggioni AP, Zuanetti G, Franzosi MG, et al. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. GISSI-2 results. *Circulation* 1993 Feb; 87(2): 312–22. <https://doi.org/10.1161/01.cir.87.2.312>.
- Marcus GM. Evaluation and Management of Premature Ventricular Complexes. *Circulation* 2020 Apr 28; 141(17): 1404–18. <https://doi.org/10.1161/CIRCULATIONAHA.119.042434>
- Hoogendijk MG, Géczy T, Yap S-C, et al. Pathophysiological Mechanisms of Premature Ventricular Complexes. *Front Physiol* 2020; 11: 406. <https://doi.org/10.3389/fphys.2020.00406>
- Keating MT, Sanguinetti MC. Molecular and cellular mechanisms of cardiac arrhythmias. *Cell* 2001 Feb 23; 104(4): 569–80. [https://doi.org/10.1016/s0092-8674\(01\)00243-4](https://doi.org/10.1016/s0092-8674(01)00243-4)
- Hoffman BF, Rosen MR. Cellular mechanisms for cardiac arrhythmias. *Circ Res* 1981 Jul; 49(1): 1–15. <https://doi.org/10.1161/01.res.49.1.1>
- Yamada M, Ohta K, Niwa A, et al. Contribution of L-type Ca²⁺ channels to early afterdepolarizations induced by I Kr and I Ks channel suppression in guinea pig ventricular myocytes. *J Membr Biol* 2008 Apr; 222(3): 151–66. <https://doi.org/10.1007/s00232-008-9113-9>
- Maruyama M, Lin S-F, Xie Y, et al. Genesis of phase 3 early afterdepolarizations and triggered activity in acquired long-QT syndrome. *Circ Arrhythm Electrophysiol* 2011 Feb; 4(1): 103–11. <https://doi.org/10.1161/CIRCEP.110.959064>
- Morita H, Wu J, Zipes DP. The QT syndromes: long and short. *Lancet Lond Engl* 2008 Aug 30; 372(9640): 750–63. [https://doi.org/10.1016/S0140-6736\(08\)61307-0](https://doi.org/10.1016/S0140-6736(08)61307-0)
- Clusin WT. Calcium and cardiac arrhythmias: DADs, EADs, and alternans. *Crit Rev Clin Lab Sci* 2003 Jun; 40(3): 337–75. <https://doi.org/10.1080/713609356>
- Rosen MR, Gelband H, Merker C, et al. Mechanisms of digitalis toxicity. Effects of ouabain on phase four of canine Purkinje fiber transmembrane potentials. *Circulation* 1973 Apr; 47(4): 681–9. <https://doi.org/10.1161/01.cir.47.4.681>
- Zipes DP. Mechanisms of clinical arrhythmias. *J Cardiovasc Electrophysiol*. 2003 Aug; 14(8): 902–12. <https://doi.org/10.1046/j.1540-8167.2003.03228>
- Gaztañaga L, Marchlinski FE, Betensky BP. Mechanisms of cardiac arrhythmias. *Rev Espanola Cardiol Engl Ed* 2012 Feb; 65(2): 174–85. <https://doi.org/10.1016/j.recesp.2011.09.018>
- Latchamsetty R, Bogun F. Premature Ventricular Complex-Induced Cardiomyopathy. *JACC Clin Electrophysiol* 2019 May; 5(5): 537–50. <https://doi.org/10.1016/j.jacep.2019.03.013>
- Ip JE, Lerman BB. Idiopathic malignant premature ventricular contractions. *Trends Cardiovasc Med* 2018 May; 28(4): 295–302. <https://doi.org/10.1016/j.tcm.2017.11.004>
- Yamada T. Twelve-lead electrocardiographic localization of idiopathic premature ventricular contraction origins. *J Cardiovasc Electrophysiol* 2019 Nov; 30(11): 2603–17. <https://doi.org/10.1111/jce.14152>
- Hsia BC, Greige N, Patel SK, et al. Determining the optimal duration for premature ventricular contraction monitoring. *Heart Rhythm* 2020 Dec; 17(12): 2119–25. <https://doi.org/10.1016/j.hrthm.2020.07.013>
- Muser D, Santangeli P, Selvanayagam JB, et al. Role of Cardiac Magnetic Resonance Imaging in Patients with Idiopathic Ventricular Arrhythmias. *Curr Cardiol Rev* 2019; 15(1): 12–23. <https://doi.org/10.2174/1573403X14666180925095923>
- Muser D, Santangeli P, Castro SA, et al. Risk Stratification of Patients With Apparently Idiopathic Premature Ventricular Contractions: A Multicenter International CMR Registry. *JACC Clin Electrophysiol* 2020 Jun; 6(6): 722–35. <https://doi.org/10.1016/j.jacep.2019.10.015>
- Crescenzi C, Zorzi A, Vessella T, et al. Predictors of Left Ventricular Scar Using Cardiac Magnetic Resonance in Athletes With Apparently Idiopathic Ventricular Arrhythmias. *J Am Heart Assoc* 2021 Jan 5; 10(1): e018206. <https://doi.org/10.1161/JAHA.120.018206>
- Michowitz Y, Viskin S, Rosso R. Exercise-induced Ventricular Tachycardia/Ventricular Fibrillation in the Normal Heart: Risk Stratification and Management. *Card Electrophysiol Clin* 2016 Sep; 8(3): 593–600. <https://doi.org/10.1016/j.ccep.2016.04.008>
- Gorenk B, Fisher JD, Kudaiberdieva G, et al. Premature ventricular complexes: diagnostic and therapeutic considerations in clinical practice : A state-of-the-art review by the American College of Cardiology Electrophysiology Council. *J Interv Card Electrophysiol Int J Arrhythm Pacing* 2020 Jan; 57(1): 5–26. <https://doi.org/10.1007/s10840-019-00655-3>
- Shirai Y, Liang JJ, Santangeli P, et al. Catheter ablation of premature ventricular complexes with low intraprocedural burden guided exclusively by pace-mapping. *J Cardiovasc Electrophysiol* 2019 Nov; 30(11): 2326–33. <https://doi.org/10.1111/jce.14127>
- DeBacker G, Jacobs D, Prineas R, et al. Ventricular premature contractions: a randomized non-drug intervention trial in normal men. *Circulation* 1979 Apr; 59(4): 762–9. <https://doi.org/10.1161/01.cir.59.4.762>
- Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991 Mar 21; 324(12): 781–8. <https://doi.org/10.1056/NEJM199103213241201>
- Ling Z, Liu Z, Su L, et al. Radiofrequency ablation versus antiarrhythmic medication for treatment of ventricular premature beats from the right ventricular outflow tract: prospective randomized study. *Circ Arrhythm Electrophysiol* 2014 Apr; 7(2): 237–43. <https://doi.org/10.1161/CIRCEP.113.000805>
- Yokokawa M, Kim HM, Good E, et al. Impact of QRS duration of frequent premature ventricular complexes on the development of cardiomyopathy. *Heart Rhythm* 2012 Sep; 9(9): 1460–4. <https://doi.org/10.1016/j.hrthm.2012.04.036>