European Journal of Therapeutics

DOI: 10.5152/eurjther.2020.20058

Original Research

Subclinical Coronary Atherosclerosis in Patients Undergoing Catheter Ablation for Idiopathic Premature Ventricular Complexes

Ahmet Hakan Ateş[1], Hikmet Yorgun[1], Uğur Canpolat[1], Muhammet Dural[2], Yusuf Ziya Şener[1], Metin Oksul[1], Sevilay Karahan[3], Kudret Aytemir[1]

[1]Department of Cardiology, Hacettepe University School of Medicine, Ankara, Turkey

[2]Department of Cardiology, Eskisehir Osmangazi University School of Medicine, Eskisehir, Turkey

[3]Department of Biostatistics, Hacettepe University School of Medicine, Ankara, Turkey

ABSTRACT

Objective: Idiopathic premature ventricular complexes (PVC) occur in the absence of clinically apparent structural heart disease (SHD) and are treated effectively with catheter ablation. We aimed to evaluate the association of PVC characteristics with subclinical coronary artery disease (CAD) during catheter ablation.

Methods: A total of 116 patients (age: median 55 years; sex: 58.6% men), without SHD, in whom PVC ablation and coronary angiography had been performed simultaneously were enrolled. PVC localizations were categorized into 4 groups as; right ventricular outflow tract (RVOT), left ventricular outflow tract (LVOT), left ventricle (LV)-body, and right ventricle (RV)-body. PVC frequency was also classified as moderate (5,000–10,000 PVCs/day) and frequent (≥10,000 PVCs/day). Coronary artery stenoses were categorized as normal, non-critical (<50%), and critical (≥50%).

Results: Co-incidental CAD was more frequent among patients with LV-body originated PVCs (non-critical, 51.6 % and critical, 22.6 %); while most of the patients with LVOT, RVOT, and RV-body originated PVCs had normal coronary arteries (58.8%, 56%, and 55.6%, respectively; p=0.019). There was no significant association between PVC frequency and coronary artery lesion severity (p=0.080) or between PVC recurrence and PVC frequency (p=0.748), PVC localization (p=0.188), coronary artery lesion severity (p=0.080), number of involved coronary artery segments (p=0.566), and number of involved coronary artery vessels (p=0.729).

Conclusion: Subclinical CAD was more frequent among patients with LV-body originated idiopathic PVCs. Thus, its routine pre-procedural assessment may be considered for LV-body originated PVCs.

Keywords: Coronary artery disease, premature ventricular complex, radiofrequency ablation

INTRODUCTION

Premature ventricular complexes (PVCs) develop due to automaticity, micro-re-entry, or triggered activity with a prevalence of 1%–4% on 12-lead electrocardiography (ECG) and 40%–75% on Holter monitorization (1-3). Although, PVCs generally have a benign course, they can be associated with more serious conditions, such as ventricular tachycardia and ventricular fibrillation, causing sudden cardiac death, particularly in patients with SHD or ionic channel disorders. PVC-induced cardiomyopathy is another manifestation that responds well to either antiarrhythmic medications or catheter ablation (4). Among several landmark studies that evaluated the association between PVC and survival after acute coronary syndrome, the GISSI trial (5) demonstrated that more than 10 PVCs per hour, detected by Holter monitorization, were associated with an increased mortality risk after a myocardial infarction. It has also been reported that implantable cardioverter-defibrillator prolongs survival in patients with coronary heart disease and asymptomatic non-sustained ventricular tachycardia (VT) (6). However, data regarding the relationship between subclinical coronary atherosclerosis and PVC characteristics in patients without structural heart disease (SHD) who underwent catheter ablation is limited.

Catheter ablation offers safe and effective treatment for AAD resistant symptomatic PVCs in patients with and without SHD (7, 8). We aimed to evaluate the association between PVC characteristics and coincidentally detected coronary atherosclerosis, and predictors of PVC recurrence, in patients without known SHD.

How to cite: Ateş AH, Yorgun H, Canpolat U, Dural M, Şener YZ, Oksul M, et al. Subclinical Coronary Atherosclerosis in Patients Undergoing Catheter Ablation for Idiopathic Premature Ventricular Complexes. Eur J Ther 2020; 26(3): 245–50.

ORCID iDs of the authors: A.H.A. 0000–0001–5414–7268; H.Y. 0000–0001–7673–229X; U.C. 0000–0002–4250–1706; M.D. 0000–0001–7227–8114; Y.Z.Ş. 0000–0001–5151–5133; M.O. 0000–0002–4759–4868; S.K. 0000–0002–8692–7266; K.A. 0000–0001–9279–8424.

Corresponding Author: Yusuf Ziya Şener **E–mail:** yzsener@yahoo.com.tr

Received: 20.06.2020 • **Accepted:** 28.07.2020

METHODS

Study Population

Patients who underwent catheter ablation due to frequent and symptomatic PVCs between May 2015 and June 2019 were screened. Those who concurrently underwent diagnostic coronary angiography (CAG) were included in the study. Coronary angiography indications during catheter ablation were as follows: presence of any risk factor for ischemic heart disease, moderate-to-severe mitral regurgitation, reduced left ventricular ejection fraction (HFrEF), and previous history of coronary artery disease (CAD). Patient data including demographic, clinical, laboratory, procedural, and follow-up parameters were obtained from the electronic database of our university hospital. Exclusion criterias were: age <40 years, lack of CAG assessment, history of myocardial infarction, presence of polymorphic PVCs, ischemic signs and/or symptoms, and previous diagnosis of cardiomyopathy; including, arrhythmogenic right ventricle cardiomyopathy, non-compaction cardiomyopathy, hypertrophic or dilated cardiomyopathy, etc. Patients with systolic blood pressure of ≥140 mmHg and/or diastolic BP (DBP) of ≥90 mmHg, or those receiving antihypertensive medications were considered as hypertensive (9). Diabetes mellitus was defined by the presence of one of the following conditions: HbA1c levels≥6.5%, fasting plasma glucose levels≥126 mg/dL, random plasma glucose levels≥200 mg/dL, plasma glucose levels 2 hours after oral glucose loading≥200 mg/dL, or administration of antidiabetic medications (10). Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR)<60 mL/min/1.73 m^2 in at least two measurements at three months interval. PVCs were categorized into 4 groups according to the anatomic localization: 1) PVCs originating from the right ventricular outflow tract (RVOT), 2) PVCs originating from the left ventricular outflow tract (LVOT) including outflow tract and aortic cusps, 3) LV-body originating PVCs including papillary muscle, aortico-mitral continuity region, and LV summit, and 4) RV-body originating PVCs including free wall, moderator band, and papillary muscle. PVC frequency was classified as moderate (5,000-10,000 PVCs/day) and frequent (≥10,000 PVCs/day). Ethical approval was received from the Local Ethical Committee of Hacettepe University, School of Medicine. All patients were hospitalized and signed a hospitalization form that included the permission to use their clinical data for future clinical studies. Due to the retrospective design of the study no additional informed consent was obtained from the patients.

Mapping and Ablation Procedure

Antiarrhythmic drugs were stopped for a duration of five half-lives of the drugs before the intervention. Anticoagulant and antiplatelet drugs (P2Y12 receptor antogonists), except aspirin, were discontinued before the procedure for the recommended time interval.

Main Points:

- There is not any relationship between the frequency of PVC and coronary artery lesion severity.
- LV-body originated PVCs are associated with the presence and severity of CAD in patients with a structurally normal heart
- PVC frequency and localization is not a predictor of recurrence after cathether ablation.

Since PVC suppression may occur under general anesthesia, electrophysiological studies and catheter ablation were performed under conscious sedation using intravenous midazolam. Clinical PVC templates were recorded at the beginning of the procedure. If spontaneous PVCs were not seen, isoproterenol infusion was administered to induce them. After femoral access, a thorough electrophysiological study was performed in all patients using coronary sinus, RV, and His catheters. In all patients, three-dimensional electroanatomical mapping system was used (Ensite Precision, Abbott or CARTO, Biosense Webster). If PVCs were of RV origin on the surface ECG, activation mapping of RV and RVOT was performed initially; while, for those of LV origin and/or without any early site at the RV, activation mapping of the LV including aortic cusps was performed. LV mapping was performed via the retrograde transaortic approach. Heparin was administered to maintain an activated clotting time between 300 and 350 seconds in patients who underwent LV mapping. Intravenous heparin (50 IU/kg) was also administered to all patients if only right-sided mapping and ablation were performed. Additionally, pace-mapping was also used to localize the PVC exit site and a pace-map score ≥90% was applied for an appropriate ablation site. Radiofrequency (RF) current ablation using irrigated tip catheters (maximum energy: 30–40 W; duration: 60–120 s) was performed at the site of earliest local bipolar activation (≥30 ms from the onset of the QRS) and with the presence of a QS pattern in the unipolar signal. After ablation at the appropriate site, procedural success was defined as the complete elimination of the PVCs after a 30 minute waiting period, including isoproterenol infusion, and the absence of clinical PVCs in the 24-hour post-ablation period.

Coronary Angiography

Coronary angiography was performed using the Judkins technique via the femoral approach. Coronary arteries were visualized by injecting contrast medium in the right and left oblique positions at the cranial and caudal angles. Patients were grouped into three groups according to the coronary lesion presence and severity. These included normal coronary arteries (no visible atherosclerotic plaque), non-critical stenotic lesions (atherosclerotic plaque with <50% stenosis), and critical stenosis (atherosclerotic plaque with ≥50% stenosis).

Follow-up

Patients with normal coronary arteries were discharged and prescribed aspirin for a month. Patients with non-critical lesions were discharged with aspirin and statin therapy if their LDL-cholesterol levels were above recommended values. Patients with critical coronary artery stenosis were referred to the interventional cardiology team for optimal medical therapy, percutaneous coronary intervention, or coronary artery by-pass grafting. Patients were scheduled for outpatient clinic visits at 1, 3, and 6 months and yearly visits thereafter; wherein; resting 12-lead ECG, transthoracic echocardiography, and 24-hr Holter monitorization were performed. The PVC recurrence was defined as the detection of ≥5000 PVCs/day on 24-hr Holter monitorization on follow-up that had the same morphology as the previously ablated PVCs.

Statistical Analysis

Continuous variables were expressed as a mean with standard deviation or median with interquartile range (IQR). Categorical

Table 1. Baseline characteristics of the study population

Male gender	68 (58.6%)
Age, years	55 (14)
Comorbidities	
– Coronary artery disease	17 (14.6%)
– Diabetes mellitus	17 (14.7%)
– Hypertension	45 (38.8%)
– HFrEF	17 (14.6%)
– Chronic kidney disease	7 (6.0%)
Smoking	34 (29.3%)
Medications	
ACE inhibitor	20 (17.2%)
Anigotensin receptor blocker	28 (24.1%)
Beta–blocker	71 (61.2%)
Calcium channel blocker	6 (5.2%)
Statin	20 (17.2%)
Duration between symptom onset and ablation, months	6 (3–19.5)
Duration of follow–up, months	16.23 (8.75–26.00)
Recurrence during follow–up	11 (9.5%)
Re–do catheter ablation	9 (7.7%)
Recurrence free survival, months	15.43 (7.86–25.31)
LV end–diastolic diameter, mm	51.49 ± 7.14
LVEF, %	60 (50–62)
Mitral regurgitation	
–Mild	70 (60.3%)
–Moderate	37 (31.9%)
–Severe	4 (3.4%)
BNP, pg/mL	83.20 (28–176.75)
TSH, mIU / L	1.4 (0.8–2.4)
Hb, gr/dL	13.92 ± 1.45
Serum creatinine, mg/dL	0.8 (0.6–0.9)
Localization of VPBs	
– RVOT	25 (21.6%)
– LVOT	51 (44.0%)
– LV body	31 (26.7%)
– RV body	9 (7.8%)
PVCs frequency	
Moderate (5000–10 000 per day)	78 (67.2%)
Frequent (≥10 000 per day)	38 (32.8%)
Coronary artery stenosis severity	
– Normal	57 (49.1%)
– Non–critical	40 (34.5%)
– Critical	19 (16.4%)
Involved coronary segments	1 (4)
Coronary artery with severe stenosis	
– LAD	8 (6.8%)
– Cx	6 (5.1%)
– RCA	6 (5.1%)
Number of coronary artery with any plaque	
– One vessel	5 (4.3%)
– Two vessels	11 (9.4%)
– Three vessels	43 (37.0%)

ACE: Angiotensin converting enzyme; BNP: brain natriuretic peptide; Cx: circumflex artery; Hb: hemoglobin; HFrEF: heart failure with reduced ejection fraction; LAD: left anterior descending artery; LV: left ventricle; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract; PVC: premature ventricular complex; RCA: right coronary artery; RV: right ventricle; RVOT: right ventricular outflow tract; TSH: thyroid stimulating hormone

variables were expressed as a number (percentage). Independent groups were compared with chi-square, independent samples t-test, or one-way ANOVA as appropriate. The Cox proportional hazards model was performed to identify predictive factors for PVC recurrence. Predictors of PVC recurrence with $p<0.2$ in univariate analyses were further included as covariates in the multivariate model. Recurrence-free survival was performed using Kaplan-Meier curves and log-rank tests. Statistical analyses were performed using the SPSS statistical software (version 20; IBM SPSS Corp.; Armonk, NY, USA). All tests of significance were two-sided and $p<0.05$ was considered as statistically significant.

RESULTS

A total of 116 patients (median age, 55; sex, 58.6% men) were included in the final analysis. Hypertension was present in 45 (38.8%), diabetes in 17 (14.7%), and CKD in 7 (6.0%) patients. The median duration between the onset of PVC-related symptoms and catheter ablation was 6 (3–19.5) months and the median follow-up after catheter ablation was 16.23 (8.75–26.00) months. Baseline characteristics including demographic, comorbidities, medications, echocardiographic, and laboratory parameters are represented in Table 1. Most of the PVCs originated from LVOT (44.0%); while, other sites had a lower frequency in this

Table 2. PVC localization and coronary artery disease

	LVOT	LV body	RVOT	RV body	p
Coronary artery stenosis severity					
–Normal	30 (58.8%)	8 (25.8%)	14 (56%)	5 (55.6%)	0.019*
–Non–critical	11 (21.6%)	16 (51.6%)	10(40%)	3 (33.3%)	
–Critical	10 (19.6%)	7 (22.6%)	1 (4%)	1 (11.1%)	
Number of involved segments	0 (0–7)	4 (0–8)	0 (0–6)	0 (0–5)	0.027*
Number of involved vessel	0 (0–3)	3 (0–3)	0 (0–3)	0 (0–3)	0.062

PVC: premature ventricular complex

Table 3. PVC frequency and coronary artery disease

	Moderate–frequent	Very frequent	p
Lesion severity;			
–Normal coronary arteries	44 (56.4%)	13 (34.2%)	0.080
–Non–critical stenosis	23 (29.5%)	17 (44.7%)	
–Critical stenosis		11 (14.1%)	8 (21.1%)
Number of involved segments	0 (0–8)	3 (0–7)	0.049*
Number of involved vessel	0 (0–3)	2 (0–3)	0.041*

PVC: premature ventricular complex

study group (LV-body, 26.7%; RVOT, 21.6%; and RV-body, 7.8%). Thirty-eight (32.8%) patients had frequent PVCs, while others showed moderate PVCs.

Severe coronary artery stenosis was detected in 19 (16.4%) patients. Distribution of the severe coronary artery stenotic lesions was as follows: eight (6.8%) lesions were located in LAD, six (5.1%) in the circumflex artery, and six (5.1%) in the right coronary artery. The median number of coronary artery segments with atherosclerotic plaques was 1 (0–4). Atherosclerosis severity, localization, and burden are also shown in Table 1.

The presence and severity of coronary artery lesions were also assessed with respect to PVC localization, and are represented in Table 2. Most of the patients with LV-body originated PVCs had coronary artery stenosis (non-critical, 51.6% and critical, 22.6%), while most of the patients with LVOT, RVOT, and RV-body related PVCs had normal coronary arteries (58.8%, 56%, and 55.6%, respectively, p=0.019). Number of involved coronary artery segments was significantly higher in patients with LV-body originated PVCs (median, 4; range, 0–8) than in patients with PVCs originating from LVOT (median, 0; range, 0–7), RVOT (median, 0; range, 0–6), and RV-body (median, 0; range, 0–5) (p=0.027). Number of involved coronary vessels was higher in patients with LV-body originated PVCs (median, 3; range, 0–3) than in patients with PVCs originating from LVOT (median, 0; range, 0–3), RVOT (median, 0; range, 0–3), and RV-body (median, 0; range, 0–3); however, the difference was not statistically significant (p=0.062) (Table 2). Critical coronary artery stenosis was seen in 11 (14.1%) and 8 (21.1%) patients with moderate and frequent PVCs, respectively. PVC frequency and coronary artery lesion severity were not significantly associated (p=0.080). The number of the involved coronary artery segments and coronary artery vessels were significantly higher in patients with frequent PVCs than in patients with moderate PVCs (median 3 vs. 0; range 0–7 vs. 0–8; p=0.049 and median 2 vs. 0; range 0–3 vs. 0–3; p=0.041, respectively) (Table 3).

PVC recurrence occurred in 11 (9.5%) patients and nine of them underwent repeat catheter ablation. Median recurrence-free survival was 15.43 (7.86–25.31) months. No significant association was found between PVC recurrence and PVC frequency (p=0.748), PVC localization (p=0.188), coronary artery lesion severity (p=0.080), number of involved coronary artery segments (p=0.566), and number of involved coronary artery vessels (p=0.729).

DISCUSSION

In this study, the relationship between PVC characteristics and coronary atherosclerosis was evaluated in patients without SHD. LVOT was the most common site of PVC origin. PVCs originating from LV-body had higher coronary artery stenosis than in patients with other PVC localization. However, we did not find a significant relationship between coronary artery lesion severity and PVC frequency. Conversely, the burden of coronary atherosclerosis was higher in the frequent PVC group than in the moderate

PVC group. There was no association of PVC recurrence with PVC frequency, localization, and coronary arteriosclerotic lesion characteristics.

PVCs can be seen in 40%–75% of healthy individuals on 24–48 hr Holter recordings (1). The association of PVCs with long-term prognosis in patients without identifiable heart disease has been variably reported. While, some studies have shown that long-term risk is similar to that of healthy individuals (11, 12), according to another study PVCs and short-term NSVTs may increase the risk in individuals older than 30 years (13). In many studies, the frequency of PVCs was associated with LV dysfunction and dilatation (14, 15). In patients with outflow tract PVCs, catheter ablation is recommended in symptomatic patients and/or in patients with a failure of antiarrhythmic drug therapy (7). The ablation success rate is high in these patients and this rate reached up to 95% in RVOT-originated PVCs (16, 17). The recurrence rate of 9.5% and median recurrence-free survival of 15.43 (7.86–25.31) months in our study was in accordance with that in the literature. No association has been reported between the PVC frequency and the success of the ablation procedure (18). The same was observed in our study by the absence of a relationship between PVC recurrence and its frequency. Further, there was no significant association between PVC recurrence and coronary atherosclerotic lesion severity and extent. This showed that CAD and its characteristics in patients with a structurally normal heart did not affect the long-term success of ablation.

Ventricular outflow tracts are the most common origin of idiopathic PVCs (19, 20). Furthermore, 70% of them are reported to be of RVOT origin (21). In our study, most of the PVCs originated from LVOT. This may be attributed to several factors, including the inclusion of patients who underwent simultaneous coronary angiography and the enrollment of patients older than 40 years. Moreover, because of the proximity of the coronary artery ostium to the ablation areas in LVOT-originated PVCs, coronary imaging was almost always required to prevent possible injury to the coronary arteries during ablation.

One of the main objectives of our study was to investigate the relationship between PVC characteristics and CAD. Although, the association between PVCs and CAD has always been a subject of concern, data regarding the appropriate selection of patients who may benefit from coronary angiography is limited. In a previous study involving 343 patients with an intermediate-to-high probability of CAD who underwent single-photon emission computed tomography and a stress test, it was found that patients with stress-induced PVCs of right bundle-branch block morphology had higher rates of known CAD, ischemia, scar, and ST-segment changes (22). It was shown that exercise-induced PVCs were associated with a higher risk of cardiovascular mortality and all-cause mortality over long-term follow-up (23). In patients without SHD, PVC ablation is mostly performed in symptomatic patients refractory to medical therapy, or in those with systolic left ventricular dysfunction. The relationship between PVC characteristics and CAD in patients undergoing PVC ablation without SHD has not been assessed previously. CAD characteristics were associated with PVC localization in our study. CAD was significantly more frequent in patients with LV-body originated PVCs than in patients with LVOT, RVOT, and RV-body originated PVCs. Further, the extent of atherosclerosis was higher in patients with LV-body originated PVCs than at other sites. Consequently, those with LV-body originated PVCs may require assessment for CAD during the ablation procedure. Conversely, there was no relationship between PVC frequency and coronary artery stenosis severity in our study. Furthermore, the number of involved coronary segments and coronary artery vessels were significantly higher in patients with frequent PVCs than in patients with moderate PVCs. Thus, our findings have important implications regarding the relationship between PVC subtypes and CAD characteristics in patients with a structurally normal heart.

There were some limitations in our study. Firstly, the study was of a retrospective design with a small sample size. Secondly, it was conducted in patients in whom PVC ablation was primarily targeted. If ischemic symptoms were predominant, these patients may not have been enrolled in the study, despite the presence of PVCs. Thus, our findings cannot be generalized to the whole population with PVCs. Large scale long-term prospective studies are needed to clarify the relationship between CAD and PVC characteristics in such patient populations.

CONCLUSION

Our study showed that LV-body originated PVCs were associated with the presence and severity of CAD in patients with a structurally normal heart. There was no significant relationship between the frequency of PVC and coronary artery lesion severity. Furthermore, it was shown that PVC frequency and localization, and CAD characteristics were not predictors of PVC recurrence after catheter ablation. In patients with LV-body originated PVCs, a more detailed assessment of CAD during the ablation procedure may be required.

Ethics Committee Approval: Ethics committee approval was received for this study from the Local Ethics Committee of Hacettepe University, School of Medicine (09.07.2019-Decision No: 2019/18-04).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.Y. ; Design - A.H.A.; Supervision - K.A.; Resources - M.O.; Data collection and processing - Y.Z.Ş., M.O; Analysis and/or interpretation - S.K., Y.Z.Ş.; Literature research - A.H.A., U.C.; Writing - M.D., A.H.A.; Critical review - U.C.

Conflict of Interest: KA & HY: Proctoring for Abbott and Medtronic. All other authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Ng GA. Treating patients with ventricular ectopic beats. Heart 2006; 92: 1707-12. [Crossref]

2. Enriquez A, Frankel DS, Baranchuk A. Pathophysiology of ventricular tachyarrhythmias : From automaticity to reentry. Herzschrittmacherther Elektrophysiol 2017; 28: 149-56. [Crossref]
3. Lerman BB. Ventricular tachycardia: mechanistic insights derived from adenosine. Circ Arrhythm Electrophysiol 2015; 8: 483-91. [Crossref]
4. Ahn MS. Current Concepts of Premature Ventricular Contractions. J Lifestyle Med 2013; 3: 26-33.
5. Maggioni AP, Zuanetti G, Franzosi MG, Rovelli F, Santoro E, Staszewsky L, et al. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. GISSI-2 results. Circulation 1993; 87: 312-22. [Crossref]
6. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996; 335: 1933-40. [Crossref]
7. Priori SG, Blomstrom-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: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015; 36: 2793-867. [Crossref]
8. Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, et al. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. J Arrhythm 2019; 35: 323-484. [Crossref]
9. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018; 39: 3021-104. [Crossref]
10. American Diabetes A. Diagnosis and classification of diabetes mellitus. Diabetes care 2011; 34: S62-9. [Crossref]
11. Engstrom G, Hedblad B, Janzon L, Juul-Moller S. Ventricular arrhythmias during 24-h ambulatory ECG recording: incidence, risk factors and prognosis in men with and without a history of cardiovascular disease. J Intern Med 1999; 246: 363-72. [Crossref]
12. Kennedy HL, Whitlock JA, Sprague MK, Kennedy LJ, Buckingham TA, Goldberg RJ. Long-term follow-up of asymptomatic healthy subjects with frequent and complex ventricular ectopy. N Engl J Med 1985; 312: 193-7. [Crossref]
13. Chiang BN, Perlman LV, Ostrander Jr LD, Epstein FH. Relationship of premature systoles to coronary heart disease and sudden death in the Tecumseh epidemiologic study. Ann Intern Med 1969; 70: 1159-66. [Crossref]
14. Niwano S, Wakisaka Y, Niwano H, Fukaya H, Kurokawa S, Kiryu M, et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart 2009; 95: 1230-7. [Crossref]
15. Kanei Y, Friedman M, Ogawa N, Hanon S, Lam P, Schweitzer P. Frequent premature ventricular complexes originating from the right ventricular outflow tract are associated with left ventricular dysfunction. Ann Noninvasive Electrocardiol 2008; 13: 81-5. [Crossref]
16. Ling Z, Liu Z, Su L, Zipunnikov V, Wu J, Du H, 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; 7: 237-43. [Crossref]
17. Yamada T, Murakami Y, Yoshida N, Okada T, Toyama J, Yoshida Y, et al. Efficacy of electroanatomic mapping in the catheter ablation of premature ventricular contractions originating from the right ventricular outflow tract. J Interv Card Electrophysiol 2007; 19: 187-94. [Crossref]
18. Latchamsetty R, Yokokawa M, Morady F, Kim HM, Mathew S, Tilz R, et al. Multicenter Outcomes for Catheter Ablation of Idiopathic Premature Ventricular Complexes. JACC Clin Electrophysiol 2015; 1: 116-23. [Crossref]
19. Morady F, Kadish AH, DiCarlo L, Kou WH, Winston S, deBuitlier M, et al. Long-term results of catheter ablation of idiopathic right ventricular tachycardia. Circulation 1990; 82: 2093-9. [Crossref]
20. Tada H, Hiratsuji T, Naito S, Kurosaki K, Ueda M, Ito S, et al. Prevalence and characteristics of idiopathic outflow tract tachycardia with QRS alteration following catheter ablation requiring additional radiofrequency ablation at a different point in the outflow tract. Pacing Clin Electrophysiol 2004; 27: 1240-9. [Crossref]
21. Yamada T, McElderry HT, Doppalapudi H, Murakami Y, Yoshida Y, Yoshida N, et al. Idiopathic ventricular arrhythmias originating from the aortic root prevalence, electrocardiographic and electrophysiologic characteristics, and results of radiofrequency catheter ablation. J Am Coll Cardiol 2008; 52: 139-47. [Crossref]
22. Biere L, Mezdad TH, Dupuis JM, Vervueren L, Rakotonirina H, Prunier F, et al. Long-term prognostic significance of right bundle-branch morphology ventricular ectopy induced during stress test in patients with intermediate to high probability of coronary artery disease. Europace 2018; 20: 528-34. [Crossref]
23. Lee V, Perera D, Lambiase P. Prognostic significance of exercise-induced premature ventricular complexes: a systematic review and meta-analysis of observational studies. Heart Asia 2017; 9: 14-24. [Crossref]