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Association of frequent premature ventricular complex >10% and stroke-like symptoms without a prior diagnosis of stroke or transient ischemic attack

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ABSTRACT

Introduction: Premature ventricular complex (PVCs) detected from long-term ECG recordings have been associated with an increased risk of ischemic stroke. However, there was limited data about the association between high PVCs burdens (>10%) and stroke-like symptoms without a prior diagnosis of stroke or transient ischemic attack in the long-term follow up.

Methods: The Kosin University 24-hours holter monitoring, echocardiography, electrocardiogram (ECG) database were reviewed from 2013 to 2015 to identify patients with frequent PVCs (>10%). We compared the long-term clinical outcomes between the patients with frequent PVCs (>10%) and control group without PVC.

Results: Among 572 patients who underwent 24-hours holter monitoring, finally, 373 consecutive patients (mean age; 59.5 ± 15.8 years, 45.2% male) were enrolled. Among them, 203(54.4%) patients had high PVCs burdens (>10%). There was no difference of the baseline characteristics. In the long term follow-up, PVCs burden was not associated with PVCs -related symptoms ($P = 0.210$). In univariate analysis, female, non-sustained ventricular tachycardia (VT), sinus QRS duration, PVC coupling interval (CI), post- PVC CI, and late precordial R-wave transition of PVCs were associated with PVCs-related symptoms. In multivariate analysis, non-sustained VT ($P = 0.022$) and late precordial R-wave transition of PVCs ($P = 0.044$) were independent risk factors for PVCs-related stroke-like symptoms with frequent idiopathic PVCs > 10%.

Conclusion: High PVCs burdens (>10%) were associated with and stroke-like symptoms without a prior diagnosis of stroke or transient ischemic attack in the long-term follow up, suggesting more intensive medical therapy with close clinical follow-up will be required.

1. Introduction

Stroke is the leading cause of disability and the third leading cause of death in the World. Etiologies of ischemic stroke are well-documented but remain undetermined in 15% to 40% of patients. Numerous risk factors have been identified as targets of preventive strategies [1,2].

Premature ventricular complex (PVCs) are mostly asymptomatic irregular heart rhythms commonly seen on electrocardiograms (ECGs) of the middle-aged and elderly [3,4].

PVCs have been examined as predictors of cardiovascular morbidity and mortality, especially with pre-existing heart disease. The presence of PVCs was associated with a 2-fold increase in the rate of fatal coronary heart disease [5]. Frequent PVCs are associated with impaired ventricular relaxation and have the potential to remodel the heart. In addition to their additive arrhythmogenic potential, such adverse remodeling may increase the risk of atrial fibrillation (AF), potentially increasing the risk of clot formation and embolization. In contrast to the established association of AF with incident stroke, the relationship of ventricular rhythm abnormalities with stroke has not been much study [6,7]. In a recent report from the Atherosclerosis Risk in Communities (ARIC) study, the presence of PVCs on 2-minute ECG rhythm strips was associated with a higher risk of ischemic stroke, suggesting that incidentally detected PVCs, typically dismissed as benign findings, may be a risk marker for future stroke [8].

However, there was limited data about the association between high PVCs burdens (>10%) and stroke-like symptoms without a prior diagnosis of stroke or transient ischemic attack (TIA) in the long-term follow up. The aim of this study was to evaluate the association of frequent PVCs > 10% and stroke-like symptoms without a prior diagnosis of stroke or TIA.

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2. Methods

2.1. Study populations

We retrospectively reviewed the medical records of 572 patients who underwent 24 h holter monitoring at Kosin university gospel hospital from January 2013 to November 2015.

Inclusion criteria included patients with/without PVCs. Patients with a history of PVC documented by a standard electrocardiogram (ECG) or Holter-ECG were enrolled.

Exclusion criteria included a history of cardiomyopathy, or valvular or congenital heart disease; hepatic or renal disease (known chronic liver disease or aspartate aminotransferase [AST] >3 times than normal range, more advanced CKD or stage 3); an acute cardiovascular or cerebrovascular event within the preceding 3 months [Brain magnetic resonance imaging were done in all patients and all patients were consulted with neurologist for selection of the patients with stroke-like symptoms]; any major trauma or surgery within the preceding 3 months; hyperthyroidism; uncontrolled hypertension; malignancy; connective tissue disease; or any acute or chronic inflammatory disease; ischemic heart disease.

Finally, 373 consecutive patients (mean age; 59.5 ± 15.8 years, 45.2% male) at Kosin university gospel hospital from January 2013 to November 2015 were enrolled. And all patients were monitored to evaluate stroke-like symptoms, thromboembolic events, arrhythmic events, re-hospitalization and death during follow-up according to the frequent PVCs > 10%. Symptom evaluation was determined by reviewing the cardiology records, created by cardiologist. If the patient felt painless weakness, sudden numbness or a dead feeling on one side of the body, sudden painless loss of vision, and sudden loss of ability to understand what people were saying related PVCs observed on an ECG, this was defined as stroke-like symptoms [9,10]. The baseline characteristics of the patients are presented in Table 1.

Table 1
Baseline demographics, medications, ECG and echocardiographic findings according to frequent idiopathic premature ventricular complex >10%.

Variables	Control group ($n = 170$)	PVC > 10% group ($n = 203$)	*P*-value
Age (years)	57.6 ± 16.4	61.0 ± 15.2	0.042
Gender (Male, %)	80 (47.3)	88 (43.3)	0.465
DM (%)	34 (20.0)	34 (17.5)	0.591
HTN (%)	52 (30.6)	55 (28.4)	0.647
CAD (%)	21 (12.4)	22 (11.3)	0.871
PCI (%)	8 (4.7)	16 (8.2)	0.207
CABG (%)	1 (0.6)	0 (0)	0.467
Medication			
Anti-arrhythmics (%)			
Amiodarone (%)	0 (0)	15 (7.7)	<0.001
Propafenone (%)	0 (0)	2 (1.0)	0.501
Digoxin (%)	8 (4.8)	10 (5.2)	0.484
Beta-blocker (%)	14 (8.2)	104 (53.6)	<0.001
CCB (%)	34 (20)	42 (21.6)	0.989
ARB & ACEi (%)	28 (16.4)	33 (17.0)	0.896
Statins (%)	64 (37.6)	80 (39.4)	0.464
Aspirin (%)	43 (25.3)	50 (24.6)	0.268
Clopidogrel	20 (12.0)	26 (13.4)	0.118
VKA	19 (11.2)	19 (9.8)	0.732
Laboratory findings			
WBC (10^3/uL)	7.8 ± 3.0	7.4 ± 2.7	0.598
Creatinine (mg/dL)	1.3 ± 0.9	1.2 ± 0.6	0.436
TSH (mg/dL)	2.8 ± 1.7	2.7 ± 1.6	0.898
fT4	1.2 ± 0.5	1.2 ± 0.4	0.683
Pro-BNP	1281.1 ± 231.5	1469.5 ± 876.4	0.700
Echo parameters			
LVEF (%)	59.1 ± 11.9	62.9 ± 13.5	0.006
LVIDs (mm)	31.2 ± 9.4	34.5 ± 7.9	0.001
LVIDd (mm)	46.8 ± 8.0	50.6 ± 6.6	<0.001
IVSD (mm)	12.1 ± 3.7	10.8 ± 2.7	<0.001
LVPWD (mm)	10.4 ± 2.2	9.9 ± 2.2	0.030
LAVi (mL/m^2)	22.1 ± 17.9	24.8 ± 12.1	0.193
E velocity (cm/s)	0.7 ± 0.2	0.8 ± 0.3	0.266
A velocity (cm/s)	0.7 ± 0.2	0.7 ± 0.2	0.111
E′	0.1 ± 0.03	0.1 ± 0.04	0.427
E/E′	11.4 ± 6.6	11.9 ± 7.0	0.511

Values are mean ± SD (range). PVC indicates premature ventricular complex; DM, diabetes mellitus; HTN, hypertension; CAD, coronary artery disease; PCI, percutaneous coronary intervention, CABG, coronary artery bypass graft surgery; CCB, calcium channel blocker; ARB, angiotensin II receptor blocker; ACEi, angiotensin converting enzyme inhibitor; VKA, vitamin K antagonist; WBC indicates white blood cell count; fT4, free thyroxine 4; proBNP, pro-B type N-terminal peptide; LVEF, left ventricular ejection fraction; LVIDs, left ventricular systolic diameter; LVIDd, left ventricular diastolic diameter; IVSd, interventricular septal diameter; LAVi, left atrial volume index; E, the peak mitral flow velocity of the early rapid filling wave; A, peak velocity of the late filling wave due to atrial contraction; E′, early diastolic mitral annulus velocity; A′, late diastolic mitral annulus velocity.

2.2. Data collection

After ECG and chest X-ray, cardiovascular status was evaluated for each patient using echocardiography, an exercise test, 24-h Holter recordings, and blood laboratory data from the initial visit, as determined by the attending physicians. From the database, the following information was collected: (1) patient data, including sex, age, height, and weight; (2) cardiovascular risk factors, including hypertension (use of antihypertensive agents, systolic blood pressure ≥ 140 mm Hg, or diastolic blood pressure 90 mm Hg on admission) and diabetes mellitus (use of oral hypoglycemic agents or insulin, or glycosylated hemoglobin ≥6.5%); (3) cardiovascular disease status, including structural heart disease, congestive heart failure, or a history of a disabling cerebral infarction or TIA; and (4) use of medication. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

2.3. Definitions of premature ventricular complex, arrhythmia and electrocardiographic measurement

Participants were requested to fast and to refrain from smoking and consuming caffeinated beverages before the examination. Electrocardiographic data processing, monitoring, and quality control have been described elsewhere. Rhythm strips were classified 3 times by independent trained coders for total supraventricular, ventricular complexes, and ventricular runs, bigeminy, trigeminy, and multiform complexes. Coding for PVCs was done before this study's hypothesis was formulated and before stroke-like symptomatic outcomes were ascertained. Adjudication of disagreements was performed by the ECG center principal investigator or coding supervisor. PVCs and heart rate were determined from the rhythm strip.

The presence of any PVCs was classified by the frequency of their occurrence on 24 hours Holter monitoring. Mean 2.8 times/person of 24 hours Holter monitoring were done during the follow-up.

Several other ECG parameters were measured including 1) Baseline sinus cycle length (ms), from the R peak of one sinus beat to the R peak of the next sinus beat; 2) PVC QRS width (ms), from the onset of the PVC to the terminal S wave; 3) PVC coupling interval (CI, ms), from the onset of the R wave of the previous sinus beat to the onset of the PVC; 4) PVC CI ratio (%), PVC CI/sinus cycle length × 100%; 5) Post- PVC CI, from the onset of the PVC to initiation of the next sinus beat; 6) Post-PVC CI ratio (%), post- PVC CI/sinus cycle length×100%; 7) PVC amplitude (mV), highest amplitude of the PVC in the precordial leads [11]. The Muse® Cardiology Information System (GE Healthcare, Piscataway, NJ, USA) was used to measure the width and amplitude of the PVCs, as well as CI and cycle length of both the PVCs and sinus beats. To assess intra-observer variation, parameters were measured for five consecutive normal sinus rhythms and PVC beats.

In our study, paroxysmal AF was defined as sinus rhythm on ECG and previous diagnosis of paroxysmal AF by referring physicians. Patients whose AF was estimated to continue for ≥7 days after the initial visit were considered to have persistent AF originally. Asymptomatic AF