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Accessory papillary muscles and papillary muscle hypertrophy are associated with sudden cardiac arrest of unknown cause☆

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ABSTRACT

Background: The present study was performed for elucidating the associations between the morphology of the papillary muscles (PMs) and sudden cardiac arrest (SCA).
Methods: We retrospectively reviewed history, laboratory data, electrocardiography, echocardiography, coronary angiography, and cardiac CT/MRI for 190 patients with SCA. The prevalence of accessory PMs and PM hypertrophy in patients with SCA of unknown cause was compared with that in patients with SCA of known causes and 98 age- and sex-matched patients without SCA. An accessory PM was defined as a PM with origins separated from the anterolateral and posteromedial PMs, or a PM that branched into two or three bellies at the base of the anterolateral or posteromedial PM. PM hypertrophy was defined as at least one of the two PMs having a diameter of ≥1.1 cm.
Results: In 49 patients (age 49.9 ± 15.9 years; 38 men) the cause of SCA was unknown, whereas 141 (age 54.2 ± 16.6 years; 121 men) had a known cause. The prevalence of accessory PMs was significantly higher in the unknown-cause group than in the known-cause group (24.5% and 7.8%, respectively; $p = 0.002$) or the no-SCA group (7.1%, $p = 0.003$). The same was true for PM hypertrophy (unknown-cause 12.2%, known-cause 2.1%, $p = 0.010$; no SCA group 1.0%, $p = 0.006$). By logistic regression, accessory PM and PM hypertrophy were independently associated with sudden cardiac arrest of unknown cause.
Conclusions: An accessory PM and PM hypertrophy are associated with SCA of unknown cause.

1. Introduction

The major known causes of sudden cardiac arrest (SCA) are coronary artery disease, cardiomyopathies, and channelopathies [1]. During the last five decades, researchers have identified some causes of SCA that had been considered idiopathic SCA or idiopathic ventricular fibrillation. These include long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome, short QT syndrome, and early repolarization syndrome [2–7]. However, the causes of SCA remain unknown in a considerable number of patients. Some forensic pathologists have reported autopsy cases of patients with sudden cardiac death who had accessory or anomalous papillary muscles (PMs) [8,9]. Although the PMs are known to be an arrhythmogenic structure [10], it is not known whether they have any association with SCA. The present study was performed to elucidate the association between the morphology of the PMs of the left ventricle (LV) and SCA.

2. Methods

2.1. Study population and patient workup

The study design was approved by the institutional review board and was conducted in compliance with the Declaration of Helsinki. Informed consent and a critical event committee were exempted by the board because this was a retrospective study. We retrospectively evaluated 213 patients who were hospitalized because of out-of-hospital SCA in a single university hospital between January 2012 and October 2013. Among 213 patients, we included 190 patients who had undergone electrocardiography (ECG) and at least one of cardiac imaging studies. Personal medical and family histories were taken in detail. A twelve-lead ECG was performed at the first visit and at least once a day during hospitalization in all patients. Transthoracic echocardiography was performed as soon as spontaneous circulation recovered. Coronary angiography was performed whenever patients' medical condition was

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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permitted and whenever patients' family members agreed. A coronary vasospasm provocation test with ergonovine was performed in the patients whose coronary angiography showed no significant coronary artery disease. Positive criteria of the coronary vasospasm provocation test included a transient total or subtotal occlusion in at least one major coronary artery with ECG changes and/or typical chest pain [11,12]. If coronary vasospasm provocation test was positive, we considered coronary vasospasm as a possible cause of sudden cardiac arrest. Cardiac computed tomography (CT) or magnetic resonance imaging (MRI) was performed when the cause of SCA was not revealed by ECG, echocardiography, and coronary angiography, or when cardiomyopathy was suspected on the basis of the echocardiography findings. An exercise stress test was performed when exercise-induced arrhythmia was suspected. Drug provocation tests (including flecainide, epinephrine, and isoproterenol challenges) were performed when Brugada syndrome, long QT syndrome, or ventricular tachyarrhythmias was suspected. A signal-averaged ECG was recorded in the limited patients whose 12-lead ECG showed suspicious late potentials in the terminal portion of the QRS complex. Analysis filter of signal-averaged ECG was 40–250 Hz. For an additional comparison with the patients with SCA of unknown cause, we retrospectively and randomly included age- and sex-matched patients without SCA who have undergone ECG and transthoracic echocardiography in the same period (between January 2012 and October 2013) by R Package, version 2.0 (R Foundation for Statistical computing, Vienna, Austria).

2.2. Study design and review of the imaging studies

The patient's medical history, family history, laboratory data, ECG, echocardiography, coronary angiography with/without vasospasm provocation test, cardiac CT, cardiac MRI, exercise stress test, and drug provocation test findings were meticulously reviewed and analyzed to elucidate the cause of SCA. Two independent cardiologists reviewed the echocardiography findings and a radiologist reviewed the cardiac CT and MRI findings for evaluation of the morphology of the LV PMs, false tendon, and trabeculation pattern in a blind fashion. The cardiologists and a radiologist had no patients' clinical information when they reviewed the imaging studies. We classified the patients into two groups: patients with SCA of unknown cause (n = 49) and patients with SCA of known cause (n = 141). SCA of unknown cause included idiopathic ventricular fibrillation. Known causes were classified into coronary artery disease, cardiomyopathies, channelopathies, myocarditis, congenital heart disease, and other. Coronary artery disease included acute myocardial infarction, coronary vasospasm, and ischemic cardiomyopathy. Cardiomyopathies included hypertrophic, dilated, restrictive, and arrhythmogenic right ventricular cardiomyopathies. Channelopathies included Brugada syndrome, early repolarization syndrome, long QT syndrome, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia. We compared the prevalence of accessory PMs, PM hypertrophy, false tendon, and hypertrabeculation in the LV between the unknown-cause group and the known-cause group. In an additional exploratory study to validate the associations between the PM morphology and SCA, we made similar comparisons between the patients with SCA of unknown cause and age- and sex-matched patients without SCA (n = 98, i.e., twice the number). In addition, we analyzed the risk for SCA of unknown cause in relation to the presence of an accessory PM or PM hypertrophy in the patients with SCA. An accessory PM was defined as a third or fourth PM with an origin separate from the anterolateral and posteromedial PMs, or a PM that branched into two or three bellies at the base of the anterolateral or posteromedial PM. PM hypertrophy was considered to be present when at least one of the two PMs had a diameter of ≥1.1 cm in the end-diastolic phase [13]. False tendons were defined as chord-like structures attached to the septum and free wall of the LV [14]. LV hypertrabeculation was defined as more than 3 prominent trabeculous formations along the LV endocardial border at end-systole [15].

2.3. ECG and hemodynamic changes according to PM morphology

In addition to the associations between PM morphology and SCA, we also analyzed the associations between accessory PM or PM hypertrophy and the ECG and hemodynamic changes. ECG findings analyzed included a notched QRS complex, LV hypertrophy by voltage, J wave, T wave inversion, and U wave. Echocardiographic findings analyzed

Table 1
Baseline characteristics and prevalence of accessory papillary muscles, papillary muscle hypertrophy, left ventricular hypertrabeculation and false tendon in the unknown-cause, known-cause, and no-SCA groups.

	Unknown-cause (n = 49)	Known-cause (n = 141)	No-SCA (n = 98)	p-Value[a]	p-Value[b]
Age (years)	49.9 ± 15.9	54.2 ± 16.6	49.9 ± 15.9	0.117	
Male sex, n (%)	38 (77.6)	121 (85.8)	76 (77.6)	0.177	
Hypertension, n (%)	14 (28.6)	66 (46.8)	14 (14.3)	0.026	0.038
Diabetes, n (%)	10 (20.4)	32 (22.7)	5 (5.1)	0.740	0.004
History of CAD, n (%)	6 (12.2)	52 (36.9)	17 (17.3)	0.001	0.422
EF (%)	54.4 ± 14.8	48.7 ± 16.7	63.2 ± 9.8	0.038	<0.001
Rhythm on the first ECG					
VF, n (%)	34 (69.4)	82 (58.2)		0.178	
VT, n (%)	3 (6.1)	18 (12.8)		0.291	
TdP, n (%)	0 (0.0)	2 (1.4)		–	
Asystole, n (%)	6 (12.2)	16 (11.3)		0.802	
PEA, n (%)	3 (6.1)	10 (7.1)		>0.999	
Unknown, n (%)	3 (6.1)	13 (9.2)		0.766	
ICD, n (%)	22 (44.9)	41 (29.1)		0.053	
Survival at discharge, n (%)	44 (89.8)	124 (87.9)		0.716	
Accessory PM, n (%)	12 (24.5)	11 (7.8)	7 (7.1)	0.002	0.003
Third or fourth PM, n (%)	5 (10.2)	6 (4.3)	4 (4.1)	0.155	0.160
Branched PM, n (%)	4 (8.2)	3 (2.1)	2 (2.0)	0.074	0.096
Uncertain[c], n (%)	3 (6.1)	2 (1.4)	1 (1.0)	0.109	0.108
PM hypertrophy, n (%)	6 (12.2)	3 (2.1)	1 (1.0)	0.010	0.006
PM diameter (mm)	9.3 ± 1.4	9.1 ± 1.0	8.6 ± 1.0	0.529	0.058
LV hypertrabeculation, n (%)	1 (2.0)	5 (3.5)	3 (3.1)	>0.999	>0.999
False tendon, n (%)	10 (20.4)	31 (22.0)	23 (23.5)	0.817	0.675

Abbreviations: CAD, coronary artery disease; EF, ejection fraction; ICD, implantable cardioverter-defibrillator; LV, left ventricle; PEA, pulseless electric activity; PM, papillary muscle; SCA, sudden cardiac arrest; TdP, torsades de pointes; VF, ventricular fibrillation; and VT, ventricular tachycardia.

[a] Comparison between unknown-cause group and known-cause group.

[b] Comparison between unknown-cause group and no-SCA group.

[c] Accessory PM that is uncertain whether it is third or fourth PM or branched PM.