Microvolt T-wave alternans profiles in patients with pulmonary arterial hypertension compared to patients with left ventricular systolic dysfunction and a group of healthy volunteers

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ABSTRACT

Objective: Microvolt T-wave alternans (MTWA) is a well-examined parameter for the risk stratification of sudden cardiac death (SCD) in patients with left ventricular dysfunction (LVD). However, the role of MTWA in pulmonary arterial hypertension (PAH) remains obscure. Consequently, the present study aimed to analyze the profile of MTWA among PAH patients in comparison with LVD patients and healthy volunteers.
Methods: The prospectively study included 22 patients with PAH (mean pulmonary artery pressure $\geq$ 25 mm Hg and pulmonary capillary wedge pressure $\leq$15 mm Hg during right heart catheterization; mean age, 40±17 years); 24 with LVD [left ventricular ejection fraction (LVEF) $\leq$35%; mean age, 40±11 years]; and 28 healthy volunteers (mean age, 41±8 years). Patients with persistent atrial arrhythmia were excluded. The MTWA (spectral method) categories were positive, negative, or indeterminate (MTWA_pos, MTWA_neg, or MTWA_ind, respectively). MTWA_pos and MTWA_ind were qualified as abnormal (MTWA_abn). Statistical analyses (Mann–Whitney U, chi-square with Yates's correction, Fisher's exact test) were performed.
Results: PAH patients had higher LVEF than LVD patients (61±7% vs. 27±7%; p<0.05). MTWA_abn was observed more frequently in the PAH and LVD groups than in the healthy volunteers. Patients with PAH were characterized by a considerable percentage of MTWA_pos and MTWA_abn (59% and 73%, respectively), but this did not differ from LVD patients.
Conclusion: Patients with PAH are characterized by a high rate of MTWA abnormalities similar to LVD patients, despite the relevant differences in LVEF. Further research is required to elucidate the clinical significance and prognostic value of this data, particularly in the context of SCD-underlying mechanisms in PAH patients. *(Anatol J Cardiol 2016; 16: 825-30)*
Keywords: pulmonary arterial hypertension, left ventricular systolic dysfunction, microvolt T-wave alternans

Introduction

Microvolt T-wave alternans (MTWA) is a well-known parameter helpful for the risk stratification of life-threatening ventricular arrhythmias and sudden cardiac death (SCD). This parameter has been well examined in patients with left ventricular systolic dysfunction (LVD) and left ventricular ejection fraction (LVEF) of <35% (1–7). In these patients, a potential source of life-threatening ventricular arrhythmias is located within the left ventricle, and MTWA testing can reveal the microvolt inhomogeneity of repolarization over these areas. An abnormal result of MTWA testing in LVD patients correlates with the incidence of spontaneous life-threatening ventricular arrhythmia, ventricular tachycardia induced on an electrophysiological study, and both arrhythmic and overall mortality.

Pulmonary arterial hypertension (PAH) is a progressive disorder with a complex pathology. It initially involves mostly small pulmonary arterioles, leading to morphological changes in the right ventricle, and eventually to its distension, dysfunction, and symptomatic insufficiency (8, 9). The treatment of PAH, previously mostly conservative, has been recently completed with new agents directly influencing the pathophysiology of the disease. However, despite such modern disease-specific therapy, patients with PAH are still characterized by a high overall mortality. Independent mortality risk factors include clinical characteristics (age, World Health Organization functional class, 6-min walk distance, etiology, family history), hemodynamic parameters (left atrial pressure, pulmonary pressure), echocardiography findings (pleural effusion), and laboratory tests (brain natriuretic peptide) (10, 11).

Although SCD is a complication for 30%–40% of PAH patients, this issue has not been studied extensively (1, 12), and neither the mechanisms underlying SCD in this group of patients nor the risk factors have been unequivocally defined. Data on MTWA testing that would enable detection of the substrates of ventricular arrhythmias have not been reported yet.

This study therefore aims to analyze the profile of MTWA testing among individuals with PAH in comparison to patients with LVD and a group of healthy volunteers.

Methods

This prospective study was performed within the framework of research on the risk stratification of life-threatening ventricular arrhythmias. The research protocol was approved by the Independent Bioethical Committee for Scientific Research of the Medical University of Gdansk. Written informed consent was obtained from all patients.

Study group

Among 28 patients with PAH who were consecutively admitted to the study, 22 patients were enrolled in the study (the remaining six patients were not enrolled due to permanent atrial fibrillation; the etiology of all these patients was congenital heart disease). PAH was diagnosed as a mean pulmonary artery pressure of ≥25 mm Hg at rest with a pulmonary capillary wedge pressure of ≤15 mm Hg during right heart catheterization) (13). All the PAH patients were treated in accordance with the program of the National Health Service. A firm diagnosis of PAH was established by echocardiography and right heart catheterization in these patients, after the exclusion of pulmonary, thromboembolic, and left heart disease (13, 14). Twenty-four LVD patients who were matched to the PAH patients with respect to age were also included. The diagnosis of LVD was made when LVEF was ≤35%. Additionally, a group of healthy volunteers was included in the further analysis. Patients were excluded from the study if they presented with functional class IV of the disease, a history or ECG-monitoring results of persistent spontaneous ventricular tachycardia and/or ventricular fibrillation or cardiac arrest, a persistent atrial fibrillation/flutter, a persistent grade II/III atrioventricular block, an implanted pacemaker, unstable angina pectoris, difficulties in walking on the treadmill, or a lack of consent for examination.

MTWA testing

MTWA testing was done in the morning hours during the treadmill exercise test. Patients did not withhold previously started pharmacotherapy, including beta-blockers. In order to minimize the artifact level, the patient's skin was cleansed with abrasive paper and the electrodes were placed in three orthogonal Frank leads: X, Y, and Z (High-Res high-resolution electrodes, Cambridge Heart, Spacelabs Healthcare, Snoqualmie, WA, USA) as well as in 12 standard leads. The exercise test was performed on a treadmill (Delmar Reynolds, Cambridge Heart, Spacelabs

Healthcare, Snoqualmie, WA, USA) following the protocol for MTWA testing, with a gradual increasing of the heart rate (HR) to 100–110 beats per min (bpm) and subsequently to 110–120 bpm (for at least 2 min). MTWA was analyzed using the spectral method (Cambridge Heart, Spacelabs Healthcare, Snoqualmie, WA, USA). The computer-guided analysis was completed with the evaluation by the physician performing the test. The result of the testing was classified as positive, negative, or indeterminate on the basis of literature-approved criteria (15, 16) as follows: positive MTWA (MTWA_pos): sustained alternans (lasting at least 1 min) with ≥1.9 µV amplitude, recorded at any orthogonal lead or in two consecutive precordial leads and an onset HR ≤110 bpm persisting with continued exercise and an increasing HR, or observed at rest; negative MTWA (MTWA_neg): does not meet the criteria of positive MTWA, and a maximum negative HR ≥105 bpm; indeterminate MTWA (MTWA_ind): the test cannot be definitely classified as either positive or negative. For MTWA_ind, the test was considered indeterminate mostly due to patient factors (inability to reach a target HR of 105–110 bpm, frequent ventricular premature beats exceeding 10% of the recording, and non-sustained alternans) or technical reasons (artifacts resulting from a high level of noise). The test was immediately repeated for the tests with indeterminate results caused by technical reasons (17). One patient was excluded from further analysis because the result of repeated testing was again indeterminate due to technical reasons. Both MTWA_pos and MTWA_ind results were qualified as abnormal MTWA (MTWA_abn) according to previous data (18).

Echocardiography (Vivid E9, GE Healthcare, Horten, Norway) was used to assess the left ventricular and right ventricular function. LVEF was calculated using the Simpson's biplane method. A cardiopulmonary exercise test was performed in all PAH patients using a cycloergometer (Lode Corival, Lode B. V. Netherlands) starting at 20 W with a constant (ramp) increment of 10 W/min. Oxygen uptake, carbon dioxide output, expiratory gas concentrations throughout the respiratory cycle, and minute ventilation were continuously measured on a breath-by-breath basis using Cortex equipment with Metasoft 3.9 software (Biophisik Gmbh, Germany). Additionally, in all patients, both electrocardiographic parameters (QRS width, a bundle-branch block—if present) and the existence of ventricular arrhythmias in 24-h ECG Holter monitoring (single ventricular extrasystoles, non-sustained ventricular tachycardias) were taken into account.

Statistical analysis

Collected data were analyzed by the STATISTICA 9.0 package (StatSoft, Tulsa OK, USA) on computerized media. Continuous variables were expressed as mean±standard deviation, and categorical variables were denoted as numbers and percentages. The quantitative variables were compared with the Mann–Whitney U test, whereas the qualitative variables were compared with the chi-square test with Yates's correction or Fisher's exact test, depending on the sample size. All the results were regarded as statistically significant if the p values were ≤0.05.

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Table 1. Clinical, demographic, and echocardiographic parameters of patients with pulmonary arterial hypertension (PAH), patients with left ventricular systolic dysfunction (LVD), and demographic characteristics of the group of healthy volunteers

	PAH group (n=22)	LVD group (n=24)	P*	Healthy volunteers (n=28)	P**	P***
Age, years	40±17	40±11	0.912	41±8	0.611	0.611
Males (n, %)	7 (32%)	16 (67%)	0.081	15 (54%)	0.114	0.275
NYHA/WHO class						
I (n, %)	0 (0%)	5 (21%)	<0.008	–	–	–
II (n, %)	7 (32%)	12(50%)		–	–	–
III (n, %)	15 (68%)	7 (29%)		–	–	–
ECG parameters						
QRS	101±13	122±28	<0.004	–	–	–
QRS ≥120 ms	1 (4.5%)	13 (59%)	<0.001	–	–	–
VPB	257±644	1786±4836	0.078	–	–	–
nsVT	2 (9%)	8 (36%)	0.072	–	–	–
ECHO parameters						
LVEF (%)	61±7	27±7	<0.005	–	–	–
RV, mm	35±12	28±5	<0.005	–	–	–
RVSP, mm Hg	80±26	31±12	<0.005	–	–	–
TAPSE, mm	17±3	22±3	<0.005	–	–	–
Comorbidities						
- CAD (n, %)	2 (9%)	12 (50%)	<0.010	–	–	–
- HA (n, %)	3 (14%)	8 (33%)	0.211	–	–	–
- DM	3 (14%)	2 (8%)	0.900	–	–	–
Pharmacotherapy						
B-blocker (n, %)	4 (18%)	24 (100%)	<0.005	–	–	–
ACEI/ARB (n, %)	3 (14%)	21 (95%)	<0.001	–	–	–
Digitalis (n, %)	3 (14%)	1 (4.5%)	0.600	–	–	–
Amiodarone (n, %)	0 (0%)	1 (4.5%)	1.000	–	–	–
Diuretic (n, %)	13 (59%)	12 (55%)	1.000	–	–	–
Calcium channel blocker (n, %)	2 (9%)	0 (0%)	0.469	–	–	–

Mann–Whitney U test (quantitative parameters), chi-square test with Yates's correction, and Fisher's exact test (qualitative variables), STATISTICA 9.0 (StatSoft, Tulsa OK, USA). Data are presented as the mean±standard deviation, or numbers and percentages. *P value between PAH and LVD groups. **P value between PAH group and healthy volunteers. ***P value between LVD group and healthy volunteers. ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; CAD - coronary artery disease; DM - diabetes mellitus; HA - arterial hypertension; LVEF - left ventricular ejection fraction; nsVT - non-sustained ventricular tachycardia; NYHA - New York Heart Association classification; TAPSE - tricuspid annular plane systolic excursion determined by M-mode technique; RV - transverse diameter of the right ventricle in the four-chamber apical view; RVSP - right ventricular systolic pressure (tricuspid insufficiency peak gradient+right atrial pressure); VPB - ventricular premature beats; WHO - World Health Organization classification

Results

The study involved a prospective review of 22 patients with PAH, 24 patients with LVD, and 28 healthy volunteers. All the groups were matched with respect to age. Fifteen patients with PAH had

Table 2. MTWA testing results in the group of patients with pulmonary hypertension (PAH) and patients with left ventricular systolic dysfunction (LVD)

	PAH (n=22)	LVD (n=24)	P
MTWA			0.648
MTWA_pos	13 (59.1%)	14 (58%)	
MTWA_neg	6 (27.3%)	7 (20%)	
MTWA_ind	3 (13.6%)	3 (13%)	
MTWA_abn	16 (73%)	17 (71%)	0.901
HR at rest, beats/min	84±15	91±10	<0.049
Max HR, beats/min	111±7	118±10	<0.012
Max neg HR, beats/min	105±8	109±5	<0.048
Onset HR, beats/min	102±7	105±3	0.06
Exercise duration (s)	399±179	493±228	0.070
Max amplitude, precordial leads, μV	8.2±2.3	9.1±2.6	0.190
Max amplitude, orthogonal leads, μV	4.7±1.9	5.0±3.4	0.420

Mann–Whitney U test (quantitative parameters), chi-square test with Yates's correction, and Fisher's exact test (qualitative variables), STATISTICA 9.0 (StatSoft, Tulsa OK, USA). Data are presented as the mean ± standard deviation, or numbers and percentages. HR - heart rate; MTWA_pos - positive result of MTWA; MTWA_neg - negative result of MTWA; MTWA_ind - indeterminate result of MTWA; MTWA_abn - abnormal results of MTWA (MTWA_pos + MTWA_ind)

an underlying congenital heart disease, while four patients were identified with idiopathic pulmonary hypertension, and three patients had PAH associated with connective tissue diseases. The treatment of all the patients was planned in accordance with the current recommendations, as shown in Table 1. All PAH patients enrolled in the study were on PAH-specific therapy, as well as symptomatic therapy: bosentan (n=11), sildenafil (n=6), diltiazem (n=2), sildenafil with bosentan (n=1), sildenafil with iloprost (n=1), and sildenafil with treprostinil (n=1). At the time of MTWA testing, all the PAH patients were in stable condition and on regular PAH-specific therapy; none of the patients was referred for the change of the therapy due to its ineffectiveness. Table 1 summarizes the demographic, clinical, and echocardiographic characteristics of the PAH and LVD patients and the demographic characteristics of the group of healthy volunteers. The functional class III disease was significantly more frequent among patients with PAH (p<0.008). When compared with the LVD patients, the patients with PAH had a significantly longer transverse diameter of the right ventricle, as well as a significantly higher LVEF and right ventricle systolic pressure (p<0.005 for all). However, tricuspid annular plane systolic excursion and QRS duration were significantly lower and the chronic administration of beta-blockers and angiotensin-converting enzyme inhibitors or angiotensin receptor blocker therapy was significantly less frequent in the PAH group (p<0.005 for both).

Regarding the MTWA results, there was only one healthy volunteer (3.6%) with abnormal MTWA (MTWA_pos). Both the LVD and PAH groups were statistically similar in respect of the MTWA results (Table 2). Abnormal MTWA results (MTWA_abn) were re-

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corded in over 70% of patients from both groups and the vast majority of those results (over 60%) were MTWA_pos. However, the LVD and PAH groups were significantly different in terms of resting and the maximum HR during MTWA testing, whereas HR was higher in patients from the LVD group. Table 3 presents the results of MTWA testing in PAH patients with regard to the etiology. Table 4 shows detailed clinical, electrocardiographic, and echocardiographic data in the PAH patients group with regard

Table 3. Results of MTWA testing in PAH patients according to the etiology

	All patients	MTWA_neg	MTWA_pos	MTWA_ind	MTWA_abn
Congenital heart disease	15	4	10	1	11
Connective tissue disease	3	–	1	2	3
Idiopathic	4	2	2	–	2
MTWA-pos - positive result of MTWA; MTWA_neg - negative result of MTWA; MTWA_ind - indeterminate result of MTWA; MTWA_abn - abnormal results of MTWA (MTWA_pos + MTWA_ind)					

Table 4. Clinical characteristics of PAH patients according to the MTWA result

	Overall (n=22)	MTWA_neg (n=6)	MTWA_pos (n=13)	MTWA_ind (n=3)	MTWA_abn (n=16)	P*	P**
Age, years	40±17	28±11	40±17	50±18	42±18	0.052	**<0.025**
Males (n, %)	7 (32%)	0 (0%)	5 (38%)	1 (33%)	6 (38%)	0.227	0.222
NYHA/WHO class							
I (n, %)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.767	0.544
II (n, %)	7 (32%)	3 (50%)	4 (31%)	0 (0%)	4 (25%)		
III (n, %)	15 (68%)	3 (50%)	9 (69%)	3 (100%)	12 (75%)		
ECG parameters							
QRS, ms	101±13	94±8	106±13	98±16	104±14	**<0.028**	**<0.039**
QRS ≥120 (n, %)	1 (4.5%)	0 (0%)	1 (8%)	0 (0%)	1 (6%)	1.000	1.000
RBBB	1 (4.5%)	0 (0%)	1 (8%)	0 (0%)	1 (6%)	1.000	1.000
RV hypertrophy	9 (41%)	3 (50%)	4 (31%)	2 (66%)	6 (32.5%)	0.767	0.965
VPB	257±644	5±6	413±822	85±148	351±740	**<0.047**	**<0.040**
nsVT (n, %)	2 (9%)	0 (100%)	2 (15%)	0 (0%)	2 (12.5%)	0.832	0.940
Syncope	5 (23%)	2 (33%)	3 (23%)	0 (0%)	3 (20%)	0.876	0.876
ECHO parameters							
LVEF (%)	61±7	67±2	56±8	59±7	56±8	**<0.001**	**<0.001**
RV, mm	35±12	37±3	40±8	53±2	42±9	0.120	**<0.039**
RV/LV	1.2±0.4	1.2±0.1	1.0±0.3	2.2±0.4	1.2±0.5	0.055	0.450
S' RV, cm/s	10.5±2.3	11.7±1.3	10.2±2.1	9.5±5.0	10.1±2.4	0.051	**<0.043**
RV FAC, %	36±9	39±8	36±9	26±15	35±10	0.272	0.165
RVSP, mm Hg	80±26	87±24	84±28	91±12	86±26	0.427	0.462
TAPSE, mm	17±3	17±2	18±4	17±7	17±5	0.464	0.491
Pericardial effusion	7 (3.2%)	2 (33%)	4 (31%)	1 (33%)	5 (31%)	1.000	1.000
Cardiopulmonary exercise test							
VO$_2$ peak (mL/kg/min)	10.8±2.2	12.2±2.9	10.3±1.8	10±1	10.2±1.7	0.107	0.104
VO$_2$ AT (mL/kg/min)	7.5±2.1	7.8±2.0	7.3±2.3	9±1	7.5±2.2	0.345	0.384
VE/VCO$_2$ slope	42.5±7.9	44.1±10.5	41.8±7.0	39±11	42±7.0	0.335	0.336
SBPmax, mm Hg	135±26	128±19	140±28	133±38	137±28	0.177	0.233
Other							
BNP, pg/mL	400±817	52±44	236±183	2250±1970	524±928	**<0.004**	**<0.004**
6-min walk test (m)	372±128	397±123	402±94	128±40	363±133	0.463	0.312

Mann–Whitney U test (quantitative parameters), chi-square test with Yates's correction, and Fisher's exact test (qualitative variables), STATISTICA 9.0 (StatSoft, Tulsa OK, USA). Data are presented as the mean±standard deviation, or numbers and percentages. *P value MTWA_neg and MTWA_pos groups. **P value between MTWA_neg and MTWA_abn groups. BNP - brain natriuretic peptide; LVEF - left ventricular ejection fraction; nsVT - non-sustained ventricular tachycardia; MTWA_pos - positive result of MTWA; MTWA_neg - negative result of MTWA; MTWA_ind - indeterminate result of MTWA; MTWA_abn - abnormal results of MTWA (MTWA_pos + MTWA_ind); NYHA - New York Heart Association classification; RV - transverse diameter of the right ventricle in the four-chamber apical view; RV/LV - the ratio of RV end-diastolic diameter to LV diastolic diameter (measured in the four-chamber apical view); RBBB - right bundle-branch block; RVSP - right ventricular systolic pressure (tricuspid insufficiency peak gradient+right atrial pressure); RVFAC - RV fractional area change; SBPmax - peak systolic arterial pressure; S'RV - tissue Doppler- derived tricuspid lateral annular systolic velocity; TAPSE - tricuspid annular plane systolic excursion determined by M-mode technique; VE/VCO$_2$ slope - ventilatory equivalent for VCO$_2$; VO$_2$ peak - peak O$_2$ uptake; VO$_2$AT - uptake measured at anaerobic threshold; VPB - ventricular premature beats; WHO - World Health Organization classification

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to their MTWA test results. Patients with a negative MTWA result were near 14 years younger, and were characterized by a 10 ms shorter QRS complex, more than 3000 fewer premature ventricular beats in 24-h ECG Holter monitoring, as well as better left (almost 10% LVEF) and right ventricular function parameters (5 mm less transverse diameter of RV in the four-chamber apical view and more than 1.5 cm/s tissue Doppler-derived tricuspid lateral annular systolic velocity). Also in patients with MTWA_neg, significantly lower levels of BNP were obtained during the study (near 500 pg/mL). However, in patients with an abnormal MTWA result, the functional WHO class III was identified more frequently, but the difference was not statistically significant.

The mean overall observation period was 24±8 months. During that time, two deaths were recorded in the LVD group (one of them was SCD and the second due to left ventricular heart failure exacerbation). In both cases, the MTWA results were positive. In the PAH group, four deaths were recorded: two SCDs (both of them with previous MTWA_pos result), one due to right ventricular heart failure exacerbation (in this patient, the MTWA result was indeterminate because the patient could not reach the required HR level), and one due to respiratory insufficiency in the course of pneumonia (this patient had an MTWA_pos result). However, on account of the small research group, we were unable to determine the prognostic value of MTWA testing in the PAH patients.

Discussion

In the present study, the most important finding was a high prevalence of abnormal results of MTWA testing among PAH patients. Although left ventricular systolic function in PAH patients is normal, this value was similar to the fraction of abnormal MTWA results observed in LVD patients. Data on MTWA testing in patients with PAH are scarce. Previous studies were mostly experimental (19, 20). For instance, Benoist et al. (19) analyzed the mechanisms underlying the development of ventricular arrhythmia in the rat model of right ventricular insufficiency associated with drug-induced pulmonary hypertension. In this particular study, the prevalence of right ventricular distension or hypertrophy was found to be related to MTWA abnormalities. The authors identified the electrical and structural heterogeneity of myocardium as a direct reason behind the alternans, along with an abnormal reuptake of calcium ions by the SERCA2 receptors of sarcoplasmic reticulum. Therefore, it would be reasonable to assume that similar pathophysiological mechanisms may exist in PAH patients.

Another interesting study was performed by Narayan et al. (20), who observed that acute overhydration in dogs caused a significant right ventricular overload, which resulted in significant alternans. However, it should be stressed that acute overhydration is not the same process as a chronic overload of the right ventricle in PAH patients. So far, a few publications based on clinical data, describing MTWA testing in patients with congenital heart diseases, have been published; however, only a small

portion of these analyses evaluated patients with PAH (21, 22). The first pilot clinical studies concerning MTWA assessment in PAH patients were published recently (23, 24). The first study established that abnormal MTWA results and positive test results are extremely frequent in patients with PAH, regardless of etiology (23). The second study revealed that positive MTWA could be attributed to the abnormal value of global longitudinal strain (assessed by 2D speckle-tracking echocardiography) and latent LVD, despite normal LVEF (24). The two above-mentioned publications focused only on patients with PAH, while the present study aimed to explore the profile of MTWA testing in PAH patients, with comparisons to that of LVD patients at high risk of sudden death. Since the value of MTWA in LVD patients is well documented and these patients raise highest clinical interest, they were considered as a reference group in this study (2–6). Aside from the differences regarding LVEF, these two groups differ significantly in terms of ischemic heart disease prevalence. Interestingly, despite a well preserved left ventricular systolic function, patients with PAH present functional class III disease more frequently. Such discrepancy may be attributed to the right ventricular dysfunction. Irrespective of these differences, patients with PAH and LVD were found to have a statistically similar frequency of MTWA abnormalities. Despite the preserved left ventricular systolic function in the PAH group as a whole, patients who had MTWA_pos and MTWA_abn presented significantly lower LVEF.

An abnormal MTWA result is related to spatial and temporal heterogeneity of the left ventricular myocardium during repolarization in LVD patients, where the right ventricular myocardial mass is small compared with the opposite ventricle, and contributes little to the formation of T-wave. As for PAH patients, both ventricles might be concerned with the T-wave form because of the right ventricle hypertrophy (signals originating from the left ventricle may be masked by those from the opposite ventricle), thus the reason for the MTWA phenomenon. In case of PAH, the right ventricle is under mechanical stress, which exposes the right ventricle to myocardial injury and, thus, arrhythmogenesis occurs. Even though the role of MTWA testing in estimating the risk of SCD in patients early after myocardial infarction is uncertain (25), it can raise interest as a tool in SCD risk estimation in patients with PAH.

Study limitations

The power of the present study is limited by the relatively small cohort size and the heterogeneity of the PAH patients with respect to the underlying etiology. Due to the small cohort size, we were unable to perform both the analysis of logistic regression of all parameters taken into account in the study and the assessment of the prognostic value of MTWA testing with respect to patients' mortality. Therefore, this study is a small-size pilot study and requires further research with follow-up analysis, as well as analysis of the relationships between MTWA abnormality, right ventricle function, and the WHO functional class.

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Conclusion

Patients with PAH are characterized by a high rate of MTWA abnormalities, mostly pertaining to positive results of the testing. The frequency of MTWA abnormality is similar to that observed in LVD patients. The prognostic value of MTWA abnormalities in PAH patients is still unclear, and it would be of importance to establish if MTWA testing in PAH patients is helpful in the identification of subjects with the highest risk of SCD. Large-scale, longitudinal studies are required to understand the significance of MTWA in prognostic evaluation and in the clinical follow up of PAH patients.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – L.D.S., E.L., G.R., A.D.K., A.N.M., K.R.; Design – L.D.S., E.L., A.D.K., A.N.M., Z.L.P; Supervision – J.K., G.R., E.S.; Fundings – L.D.S., E.L.; Materials – L.D.S., E.L., A.D.K., A.N.M., J.K., E.S.; Data collection &/or processing – L.D.S., E.L., A.D.K., A.N.M., J.K.; Analysis &/or interpretation – L.D.S., E.L., G.R., Z.L.P; Literature search – L.D.S., E.L., A.N.M., K.R.; Writing – L.D.S., G.R., E.L.; Critical review – G.R., A.N.M., Z.L.P, K.R., E.S.

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