Original Article

Does Pulmonary Endarterectomy have Arrhythmia Prevention Effect?

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Abstract

Background: The aim of the present study was therefore to evaluate the evolution of electrocardiography (ECG) markers indicator of morbidity and mortality after pulmonary endarterectomy (PEA). It may be a good predictor of mortality and morbidity in chronic thromboembolic pulmonary hypertension (CTEPH) with patients who underwent PEA. PEA may be reduced risk of arrhythmia in patients with CTEPH. However, this claim must to be supported with long-term results. **Materials and Methods:** We collected demographic, ECG, and echocardiographic parameters data (baseline and after the operation) in patients undergoing PEA for CTEPH at our institution from 2009 to 2013.We assessed 62 CTEPH patients who underwent PEA. **Results:** P wave amplitude in DII, PR interval, *P* and QT dispersion changed significantly at 3 months after surgery. The P dispersion (17.66 ± 6.2, $P < 0.04$) and QT dispersion (23.75 ± 11.37, $P < 0.015$) were longer in before operation than in after operation. **Conclusions:** In our study, we found in ECG analyses of CTEPH with patients who are undergoing PEA that *P* dispersion, QT dispersion were changed when compared with before operation. For this reason, we think that PEA reduces the risk of atrial fibrillation and malignant arrhythmia.

Keywords: P wave dispersion, pulmonary endarterectomy, QT dispersion

Introduction

Several studies have evaluated the association between RV structure and ECG alterations in patients with either chronic thromboembolic pulmonary hypertension (CTEPH) or pulmonary arterial hypertension (PAH), which could be useful for diagnostic or prognostic purposes.[1-6] However, it is still unknown to what extent the different ECG criteria reflect the changes in mass and volume of the right ventricle, and they are related to the RV overload determined by the elevated pressures in the pulmonary circulation. Unlike other types of pulmonary hypertension, CTEPH can be successfully treated with surgery. It is well demonstrated that pulmonary endarterectomy (PEA) allows dramatic improvements in the right heart hemodynamic profile immediately after surgery.[7,8] On the contrary, regression of hypertrophy and restoration of regular RV systolic function requires more time and take place mainly during the first postoperative year.[9,10] The QT interval reflects electrocardiographic (ECG) parameter of the duration of ventricular repolarization. The QT dispersion is the interleaved variability of QT interval on ECG that reflects regional differences in myocardial repolarization. Enhanced the QT dispersion has been linked to the occurrence of malignant ventricular arrhythmias and sudden cardiac death.[11-13] P wave terminal force in lead V1 was found to be an independent predictor of stroke in a vital trial.[14] The aim of the present study was for this reason to evaluate the evolution of ECG parameters as potential predictors of future arrhythmias after PEA. However, this claim must to be supported with long-term results.

Materials and Methods

The present study is a retrospective evaluation of 62 CTEPH patients who underwent PEA between 2009 and 2013 in the Marmara University Hospital by thoracic surgery and were followed up for at 6 months after surgery. Thoracic surgeon evaluated patients. Patients with Stage 4 did not perform a surgical operation. Exclusion criteria were previous

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myocardial infarction, significant left valvular heart disease, congenital heart disease, the necessity of additional cardiac surgery, persistent atrial fibrillation/flutter (three patients), and significant chronic lung disease. All patients underwent echocardiographic examination and a 12-lead ECG recording before surgery, at 6 months after surgery as part of the routine PEA follow-up protocol at our center. Conventional 12-lead ECG was recorded with the patient in supine position with commercially available ECG at a paper speed of 25 mm/s, the sensitivity of 1 mV = 10 mm, a sampling frequency of 500 Hz. Every ECG recorded and analyzed was checked by two expert cardiologists and were used to assess intra- and interobserver variability. The ECG parameters were measured: Heart rate, PR interval, QRS width, P width, and P wave amplitude in DII, P wave amplitude in aVL, P wave amplitude in V5, QT duration in DII, QT duration in aVL, QT duration in V5, P dispersion, and QT dispersion. The P wave onset and end-points were considered as the intersection of the P wave by the isoelectric line and the junction of the end-point of the P wave with the isoelectric line, respectively. The maximum P wave duration was suggested as the most extended P wave and the longest atrial conduction time, and the variation between the longest and the shortest P waves were indicated as the P wave dispersion [Figure 1]. The interval between the points of the isoelectric TP segment intercepted by the onset of the QRS complex and the descending branch of the T wave was suggested as the QT interval and was respective calculated for each derivation. The QT dispersion was determined as the variation between the longest and shortest QT intervals in any origin in the standard 12-lead ECG [Figure 2].

Ultrasound examinations were performed using commercially available echocardiographic equipment (Vivid 7 System). The following parameters were measured to study the right and left ventricle: Left ventricle ejection fraction, right ventricle tissue Doppler value (S'), myocardial perfusion index, pulmonary systolic pressure, right atrium and ventricle diameters, tricuspid annular plane systolic excursion, and degree of tricuspid regurgitation. For statistical analysis, SPSS 16.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA). software was used. Categorical variables were defined as a percentage.

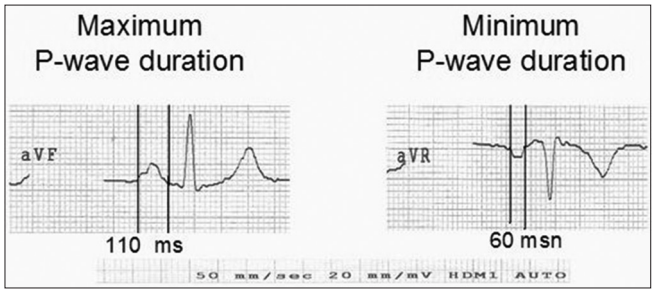

Figure 1: Two complexes extracted from 12-lead surface electrocardiography of a patient. In this case, maximum P-wave duration was observed from lead aVF and the minimum P-wave duration from lead automatic voltage regulator. Pine wilt disease was defined as the difference between the maximum and minimum P-wave durations

Quantitative variables were expressed as a mean ± standard deviation and for the comparison of variables between two paired groups "paired sample Student T" (parametric distributed parameters) and "Wilcoxon" (for the parameters showing the nonparametric distribution) tests were used. Correlation analyses were performed by Spearman correlation test. $P < 0.05$ was accepted statistically significant.

Results

The patient's clinical characteristic are shown in Table 1. A total of 39 of the patients were of the male gender; mean age was 57 years, the vast majority had severe symptoms, 45 of the patients had a history of deep vein thrombosis, few of them had associated diseases such as chronic obstructive pulmonary disease, diabetes mellitus, and systemic hypertension. Eighty-nine percent of patients had functional Class III-IV. Hemodynamic values are shown in Table 2: the mean pulmonary arterial pressure of patients was 48.7 ± 14.9.We assessed 62 CTEPH patients who underwent PEA. P wave amplitude (118.66 ± 2.77 vs. 109.16 ± 33.24. $P < 0.016$) India, PR interval (157.9 ± 31.51 vs. 139.35 ± 29.28, $P < 0.006$) P and QT dispersion changed significantly at 6 months after surgery. The P dispersion (27.93 ± 14.17 vs. 21.72 ± 11.04, $P < 0.04$) and QT dispersion (53.37 ± 313,76 vs. 42.00 ± 18.79, $P < 0.015$) were longer in before operation than in after operation [Table 3]. The patient's echocardiographic values are shown in Table 4. It showed a marked reduction in RA pressure after surgery. The correlation analyses were demonstrated that there was a positive correlation between RVS'2-MPI 2 (after PEA) and P dispersion wave 1 (before PEA) [Table 5]. We have no data with PR dispersion associated with postsurgical atrial fibrillation. Overall intra- and inter-observer variability rates were similar.

Discussion

The main result of the present study in patients with CTEPH is the differentiation, among the ECG markers of arrhythmia risk, of those more strictly related to the QT and P dispersion and those better reflecting the malign arrhythmia and atrial fibrillation. To the best of our knowledge, this is the first study to characterize the ECG changes in CTEPH patients

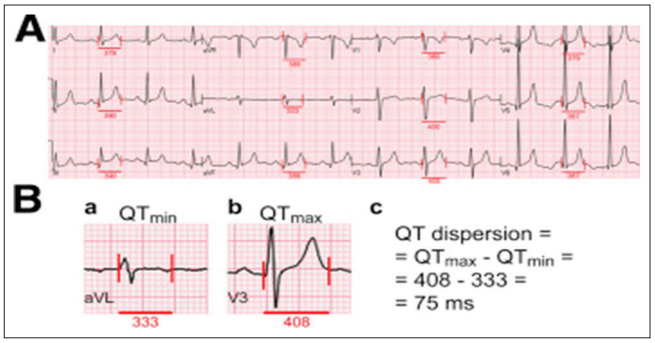

Figure 2: The QT dispersion is determined as the variation between the longest and shortest QT intervals in any origin in the standard 12-lead ECG

Table 1: Patients' clinical characteristics at baseline

	n (%)
Age	57±26
Male sex (*n*)	39 (62)
WHO class II/III/IV (%)	11/59/30
Previous deep venous thrombosis (*n*)	45 (72)
Systemic hypertension	18 (30)
Diabetes mellitus	4 (6)

WHO: World Health Organization

Table 2: Hemodynamic parameters of patients (before pulmonary endarterectomy)

Hemodynamic	values-average
mPAP (mmHg)	48.7±14.9
RAP (mmHg)	12.2±1.1
CO (l/min)	3.6±0.7
CI (l/min/m^2)	2.0±0.5
PVR (mmHg × min/l)	11.4±4.5
SVR (mmHg × min/l)	23.4±5.1
PVR/SVR	0.41±0.31

Data are presented as mean±SD. mPAP: Mean pulmonary artery pressure, RAP: Right atrial pressure, CO: Cardiac output, CI: Cardiac index, PVR: Pulmonary vascular resistance, SVR: Systemic vascular resistance, SD: Standard deviation

undergoing PEA, and arrhythmia-related morbidity and mortality are associated with reduced risk after surgery. Such patients are an excellent clinical model to study the effects of treatment of pulmonary hypertension on ECG markers of arrhythmia: first of all because the consequences of surgery on CTEPH patients by far exceed the impact of pharmacological therapy in other forms of pulmonary hypertension, with the only possible exception of the effects of calcium antagonists in patients with PAH responsive to vasodilators.[15] Second because in such patients there is apparent dissociation between the hemodynamic improvement, which is immediate after surgery, and the reverse remodeling of the right ventricle, which takes time, up to inadequate preservation of the right heart during the early postoperative period, with stunning being reversible over a few months, and tethering of the right ventricular wall due to adhesion between the heart and surrounding tissues.[15]Table 3 showed a marked reduction in RA pressure after surgery; this itself reduces the atrial stretching, which is surrogate for future remodeling and arrhythmia development.

We observed that PR interval in ECG, P wave amplitude in DII decreased significantly soon after the intervention at 6 months. Data in the literature in different forms of pulmonary hypertension indicate that a high P amplitude and a rightward-oriented QRS axis are linked to the presence of increased pulmonary pressures.[16-18] The magnitude of the P wave has also been previously reported to be of prognostic value in patients with PAH.[19] Finally, it has been suggested that an elevated P amplitude in lead DII, in association with changes in QRS and T wave axis, could be an important

Table 3: Patient's electrocardiography comparison between baseline (1) and 6 month (2)

	Mean±SD	SEM	95% CI of the difference	*P*
HR1 - HR2	17.61±−1.54	3,16	−8.01	0.628
PR1 - PR2	34.69±18.54	6.23	5.82	0.006
QRS1 - QRS2	19.89±5.96	3.57	−1.32	0.105
Pwidth1 - Pwidth2	0.72±0.01	0.13	−0.24	0.902
PD21 - PD22	27.07±12.93	5.02	2.63	0.016
PaVL1 - PaVL2	28.29±6.72	5.25	−4.03	0.211
PV51 - PV52	24.44±2.83	4.46	−6.29	0.531
QTD21 - QTD22	53.43±1.06	9.92	−19.25	0.915
QTaVL1 - QTaVL2	42.29±−4.55	7.85	−20.64	−0.579
QTV51 - QTV52	53.32±1.9	9.73	−18.01	0.847
Pdis1 - Pdis2	17.66±6.2	3.27	−0.51	0.04
QTdis1 - QTdis2	23.75±11.37	4.41	2.34	0.015

HR: Heart rate, PR: PR interval, QRS: QRS duration, PD2: P wave amplitüde in D2 derivation, PaVL: P wave amplitüde in aVL derivation, PV5: P wave amplitüde in V5 derivation, QTD2: QT duration in D2 derivation, QTaVL: QT duration in aVL derivation, QTV5: QT duration in V5 derivation, Pdis: P wave dispersion, QTdis: QT dispersion, SD: Standard deviation, SEM: Standard error of mean, CI: Confidence interval

Table 4: Patient's echocardiographic values at pulmonary endarterectomy before (1) and after (2)

	n	Minimum	Maximum	Mean±SD
EF1	62	50,00	80.00	64.73±7.06
EF2	62	50.00	80.00	64.50±6.94
TAPSE1	62	7.00	21.00	12.11±3.47
TAPSE2	62	7.00	27.00	14.30±3.96
RVS1	62	6.00	15.00	9.30±2.52
RVS2	62	7.00	13.00	10.24±1.94
MPI1	62	0.23	1.50	0.64±0.24
MPI2	62	0.24	0.85	0.49±0.16
TRGRA1	62	1.00	3.00	2±1
TRGRA2	62	0	2.00	1±1
SPAB1	62	32.00	127.00	83.07±27.50
SPAB2	62	15.00	67.00	32.34±13.39
RA1	62	10.00	41.00	25.42±8.68
RA2	62	11.00	33.00	17.72±5.50
RVED1	62	32.00	52.00	41.66±5.43
RVED2	62	28.00	41.00	34.92±3.98

SD: Standard deviation, EF: Ejection fraction, TAPSE: Tricuspit annular plane systolic excursion, RVS': Right ventricle systolic wave (cm/s), MPI: Myocardial Performance Index, TRGRA: Tricuspit regurgitation grade, sPAB: Systolic pulmonary artery pressure (mmHg), RA: Right atrium area (cm^2), RVED: Right ventricle end diastolic diameter (cm)

determinant of treatment response in PAH patients, implying that routine ECG evaluation could be a significant contribution to the assessment of therapy response in PAH patients.[20] The present study is in agreement with such previous findings, additionally, showing that the reduction in P wave amplitude in lead DII over the 3rd month.

The previous studies have shown that QT dispersion is an indicator for arrhythmia and CVD mortality[20]

Table 5: Correlation analyses between right heart function parameters and electrocardiographic parameters

	QTdis1	QTdis2	Pdis1	Pdis2
TAPSE1				
Correlation	−0.282	−0,286	−0.015	−0.165
P	0.172	0.165	0.942	0.430
n	62	62	62	62
TAPSE2				
Correlation	−0.028	−0.247	0.081	0.139
P	0.895	0.233	0.701	0.508
n	62	62	62	62
RVS1				
Correlation	−0.094	−0.052	−0.091	0.179
P	0.654	0.805	0.666	0.393
n	62	62	62	62
RVS2				
Correlation	0.159	−0.380	0.571	0.226
P	0.457	0.067	0.004	0.287
n	62	62	62	62
MPI1				
Correlation	−0.123	−0.097	0.027	−0.048
P	0.568	0.650	0.900	0.825
n	62	62	62	62
MPI2				
Correlation	−0.189	−0.322	0.003	−0.062
P	0.388	0.134	0.988	0.777
n	62	62	62	62
RA1				
Correlation	0.006	0.184	-0.178	0.280
P	0.977	0.379	0.394	0.175
n	62	62	62	62
RA2				
Correlation	−0.053	0.317	−0.068	0.047
P	0.806	0.131	0.751	0.828
n	62	62	62	62
RVED1				
Correlation	0.286	−0.231	−0.070	0.315
P	0.301	0.426	0.805	0.273
n	62	62	62	62
RVED2				
Correlation	0.120	0.125	0.081	0.332
P	0.697	0.670	0.791	0.246
n	62	62	62	62

TAPSE: Tricuspid annular plane systolic excursion, RV S': Right ventricle systolic wave (cm/s), MPI: Myocardial Perfusion Index, RA: Right atrium (cm^2), RVED: Right ventricle end-diastolic diameter (cm), Pdis: P wave dispersion, QTdis: QT dispersion (1: Before operation, 2: After operation)

Tuncer *et al*.[21] studied 25 patients with right ventricular hypertrophy without coexisting systemic hypertension, COPD, or PH who had emigrated from a high-altitude region to a low-altitude area 25 years previously and found that QT was significantly higher than in a healthy control group. Martin *et al*.[22] found that QT was prolonged (defined as ≥0.45 s) in two of 25 patients with right ventricular hypertrophy without other coexisting disorders but was not statistically significant in comparison with a healthy control group. Akgül *et al*.[23] found that among patients with sickle cell disease, those with PH had significantly higher mean QTd than patients without PH. We discovered that QT dispersion changed a great deal at 6 months after surgery. Thereby, we believe that PEA may be diminished the risk of malign arrhythmia. QTc dispersion was found to be higher in patients without PEA than in a patient with PEA, and increased QT dispersion was not correlated with echocardiographic parameters in our study. This might be originated from our trial population is small.

Prolonged P-wave duration and increased P-wave dispersion are reported to carry an increased risk for atrial flutter or fibrillation.[24] Many studies[25-27] have shown that many diseases, such as PAH, bronchial asthma, diabetes mellitus, and acute rheumatic fever, in which the heart may be affected, exhibit a significantly longer P-wave duration. Large prospective clinical trials have shown that chronic atrial dilatation is an important and independent risk factor for the development of atrial fibrillation.[28] In our study, there was a definite correlation between the MPI2-RVS2' (2: After PEA) and Pdis1 (1: Before PEA).The right ventricular systolic function may be increased as atrial stretch and preload decrease at the term of after operation.

We are aware that this study has some limitations. Foremost of these was a sample size smaller than that expected for a prospective cross-sectional study. The patients without PAH were determined by echocardiography alone, and right heart catheterization was not deemed to be ethical for these patients. This study should have an adequate number of patients in the mild, moderate, and severe groups to determine the correlation between the pulmonary artery pressure and dispersion durations.

Conclusions

Atrial and ventricular arrhythmia risks were found to be high in patients with PAH due to prolonged dispersion durations of P-wave, QT, and QTc. Further studies and multicentered studies are needed to enable an understanding of the underlying mechanisms and the diagnostic values of these electrophysiologic parameters. Physicians should pay close attention to possible atrial and ventricular arrhythmias during the clinical follow-up assessment and treatment of these patients.

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Conflicts of interest

There are no conflicts of interest.

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