Electrocardiographic Predictors of Response to Vasoreactivity Testing in Patients with Pulmonary Arterial Hypertension

[1]E. Blinova, [1]T. Sakhnova, [1]O. Arkhipova, [1]N. Danilov, [1]T. Martynyuk,

[1]I. Chazova, [2]V. Trunov, [2]E. Aidu

[1]Cardiology Research Complex, Moscow, Russia,
[2]Institute for Information Transmission Problems RAS, Moscow, Russia
Email: blinova2009.73@gmail.com

Abstract. *The aim: to assess the possibilities of electrocardiography for prediction of response to vasoreactivity testing (VT) in patients with pulmonary arterial hypertension (PAH). 65 PAH patients who underwent right-heart catheterization and VT were evaluated. We analyzed P wave amplitude in lead II, QRS axis, QRS duration, R and S wave amplitudes in leads V1 and V5, spatial QRS-T angle, magnitude G and spatial components Gx, Gy, Gz of the "recovery acceleration" vector. 23 responders to VT had lower mean pulmonary artery pressure (46.6±11.0 mm Hg versus 61.3±19.0 mm Hg, p <0.01), PII (1.70±0.79 mm versus 2.34±0.97 mm, p <0.01), QRS-T angle (61.3±27.3 dgr versus 104.5±39.9 dgr, p <0.01), RV1+SV5 (8.98±5.04 mm versus 15.7±8.0 mm, p <0.01) and higher values of Gx (22.6±15.1 ms versus 5.3±17.9 ms, p <0.001) and Gy (22.6±11.2 ms versus 8.8±8.4 ms, p <0.001) as compared with non-responders. The most informative variables were Gx (the area under the ROC curve 0.77, SE 0.07), Gy (0.84±0.06) and QRS-T angle (0.81±0.05). On multivariate logistic regression analysis Gy emerged as an independent predictor of response (OR 1.17; 95% CI 1.06-1.30; p = 0.01). Decartographic parameters of repolarization may be helpful for predicting the results of VT in patients with PAH.*

Keywords: pulmonary arterial hypertension, electrocardiography, acute pulmonary vasodilator testing

1. Introduction

Vasoreactivity testing (VT) in patients with pulmonary arterial hypertension (PAH) is important for the optimization of the treatment and evaluation of prognosis [1], [2]. The commonly used test with inhaled nitric oxide (iNO) is well tolerated, has minimal side effects, but time-consuming and needs special equipment [3]. The use of simple noninvasive techniques for predicting the VT results may be of interest, but the available data about the predictors of response are small. The aim of the study was to assess the possibilities of electrocardiographic parameters for prediction of response to VT in patients with PAH.

2. Subject and Methods

Patients

65 patients (mean age 41.4±12.4 years; 81% women) with PAH who underwent right-heart catheterization and VT were evaluated. The diagnosis of PAH was made according to the current guidelines definition [4]. The presence of PAH was verified with clinical and instrumental methods. There were 10 patients with chronic thromboembolic disease, 4 patients with systemic sclerosis, 3 patients with septal defects, 2 patients with portal hypertension, in 46 patients after comprehensive clinical and instrumental examination PAH was considered to be idiopathic. All patients underwent echocardiographic examination using

a high-quality ultrasound machine (Vivid 7; GE, USA). The estimated systolic pulmonary artery pressure (SPAP) was defined as the right ventricular to right atrial pressure gradient added to the right atrial pressure. Right atrial pressure was estimated 5 to 15 mm Hg, according to the diameter and inspiratory collapse of the inferior caval vein.

Electrocardiography

Conventional 10-s digital electrocardiograms were recorded by certified ECG technicians using the standard 12-lead electrode configuration on commercially available digital electrocardiograph and averaged into 1 single beat. ECG parameters under investigation were: P wave amplitude in lead II (PII), QRS axis, QRS duration, R and S wave amplitudes in leads V1 and V5. The averaged beat was also converted into a derived orthogonal-lead beat and processed by means of software developed in Cardiology Research Complex and Institute for Information Transmission Problems. We studied spatial QRS-T angle and magnitude G (in ms) and spatial components Gx, Gy, Gz of the "recovery acceleration" vector (directed to the left, inferior, and anterior). Decartographic "recovery acceleration" map shows the distribution of the dipole component of the depolarized state duration over the heart surface, projected onto the image sphere which encloses the heart ventricles. The image sphere radius is taken equal to the maximum magnitude of the heart vector in the QRS period. The use of the maximal QRS vector as a scale helps to understand more clearly internal interrelationships between different parts of QRST complex. Concerning the electrophysiological meaning, "recovery acceleration" vector is close to the ventricular gradient vector.

Right Heart Catheterization with VT

All PAH patients underwent right heart catheterization, during which pulmonary artery pressure (PAP), right atrial and right ventricular pressure, pulmonary capillary wedge pressure were measured using Swan-Ganz catheter("Edwards", USA). Cardiac output was calculated using Fick's method. Pulmonary vascular resistance (PVR) was calculated by dividing the transpulmonary gradient (pressure difference between mean PAP and pulmonary capillary wedge pressure) by cardiac output. Following the measurement of baseline hemodynamic parameters, acute vasodilators (iNO or/and PGE1) were administered sequentially. iNO was administered via face mask at start concentration 10 ppm, with increase to 20 and 40 ppm every 5 minutes. After 15 minutes of administration hemodynamic parameters were measured. After 30 minutes of a washout phase PGE1 was administered intravenously at start dosage 0.4 mg/ml/kg which every 10 minutes was redoubled up to maximal dosage 1.6 mg/ml/kg. Responders were defined as patients who showed a decrease in mean pulmonary artery pressure of at least 10 mmHg to an absolute level below 40 mmHg with preserved or increased cardiac output at least with one vasodilator.

Statistical Analysis

Data were analyzed using MedCalc Statistical Software version 12.7.8 (MedCalc Software bvba, Ostend, Belgium). Results are presented as mean ± standard deviation. To evaluate the differences between two independent samples unpaired t-test was used. A value of $p<0.05$ was considered to be statistically significant.

3. Results

There were 23 (35%) responders to VT. Baseline clinical characteristics and hemodynamic findings in responders and non-responders are presented in Table 1. Statistically significant ($p<0.05$) differences are marked with *.

Table 1. Baseline clinical characteristics and hemodynamic findings in responders and non-responders to VT.

Parameter	Responders	Non-responders
Age, years	39.6±10.6	42.7±13.3
% females	96	74*
Functional class	2.13±0.55	2.67±0.68*
Heart rate, bpm	69.5±10.8	81.3±13.7*
SPAP, mm Hg	71,5±17.3	99.5±26.6*
Mean PAP, mm Hg	46.6±11.0	61.3±19.0*
PVR, dyn•s/cm5	837±447	1386±741

Baseline electrocardiographic characteristics in responders and non-responders are presented in Table 2. Statistically significant ($p<0.05$) differences are marked with *.

Table 2. Baseline electrocardiographic characteristics in responders and non-responders to VT.

Parameter	Responders	Non-responders
PII, mm	1.70±0.79	2.34±0.97*
QRS axis, degrees	89.7±42.2	105.6±51.8
QRS duration, ms	101.0±7.6	106.3±15.6
RV1+SV5, mm	8.97±5.04	15.72±8.01*
spatial QRS-T angle, degrees	61.3±27.3	104.4±39.9*
Gx, ms	22.56±15.08	5.31±17.87*
Gy, ms	22.57±11.24	8.76±8.43*
Gz, ms	6.87±19.64	4.55±18.43

At receiver operating characteristic curve analysis the most informative variables were Gx (the area under the ROC curve 0.77, SE 0.07), Gy (0.84±0.06), QRS-T angle (0.81±0.05) and RV1+SV5 (0.76±0.06). On multivariate logistic regression analysis after correction for age, sex, heart rate, WHO class, and echocardiographic systolic pulmonary artery pressure, Gy emerged as an independent predictor of response (odds ratio, 1.17; 95% confidence interval 1.06-1.30; $p = 0.01$).

4. Discussion

Predicting of the VT results in PAH patients by simple noninvasive techniques may be useful in clinical practice. Some attempts were made to do it by means of echocardiography [5]. Results of 6-minute walking test also may have predictive value. In our study non-responders as compared with responders were characterized with the more pronounced changes of electrocardiographic parameters, which corresponded to the more deteriorated hemodynamic state. It is interesting to note that parameters which describe cardiac repolarization in its relation to the preceding depolarization, namely spatial QRT-angle and components of the "recovery acceleration" vector were the most informative. Ventricular gradient, which is close to "recovery acceleration" vector, and especially spatial QRT-angle were shown to be important for mortality prediction in different clinical populations [6], [7], [8]. From theoretical point of view, these parameters may reflect the changes in myocardial electrophysiological properties, namely, the alteration in action potential duration heterogeneity in the ventricles. Further research of the mechanisms of ECG changes in right ventricular hypertrophy may contribute to the more accurate evaluation of the heart state in PAH patients.

5. Conclusions

The use of repolarization process mapping by DECARTO technique may be helpful for predicting the results of VT in patients with PAH.

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