Clinical Application of the Spatial QRS-T Angle for the Prediction of Pulmonary Arterial Hypertension in Patients with Acute Pulmonary Embolism

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Research

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Abstract

Background: The objective of our study was to assess the clinical application of the spatial QRS-T angle for the prediction of pulmonary arterial hypertension (PAH) in patients with acute pulmonary embolism.

Methods: The study group of 162 patients with acute pulmonary embolism was stratified on the basis of color doppler echocardiographic findings into two subgroups: non-PAH group (n = 92) and PAH group (n = 70). Then PAH group patients were stratified into mild, moderate, and severe PAH group. Independent t-test was used to compare the indexes of non-PAH group and PAH group. One-way ANOVA was used to compare the indexes of mild, moderate, and severe PAH group. Pearson correlation analysis was used to evaluate the significance of the correlation between acute pulmonary arterial systolic pressure (PASP) and spatial QRS-T angle.

Results: The spatial QRS-T angle was larger in patients with PAH than those with non-PAH (109.010±30.970° VS 68.098±18.010°, $P < 0.05$). Significant differences of spatial QRS-T angle values were found between patients with mild, moderate and severe PAH (73.714±15.716°, 104.790±20.675°, 139.57±23.196°, respectively, $P < 0.05$). There was a positively linear correlation between the spatial QRS-T angle and PASP in patients with PAH.

Conclusions: Spatial QRS-T angle are potentially useful for differentiation between acute pulmonary embolism patients with PAH from those without PAH, and possibly also for predicting PASP in acute pulmonary embolism patients.

Background

Acute pulmonary embolism is a frequent cause of cardiovascular morbidity and mortality [1]. Pulmonary arterial hypertension (PAH) is a progressive and debilitating condition associated with a sustained increase in pulmonary artery pressure that results from excessive vasoconstriction and remodeling of the pulmonary arteries [2]. Residual PAH persists in acute pulmonary embolism [3]. People who has PAH is easy to develop right heart failure and lead to death [4]. Its diagnosis is often delayed, with more than 20% of patients with PAH being symptomatic for more than 2 years before PAH is diagnosed [5]. Right heart catheterization is the gold standard to confirm a diagnosis of PAH. However, its wide application is limited by its invasive feature. Therefore, clinically, most PAH evaluations are based on tricuspid regurgitation velocity by echocardiography. However, this assessment may be affected by cardiac cycle, breathing and operators' manipulation. Electrocardiogram (ECG) is one of the first tests to be performed in the emergency department when a patient presents with cardiac or respiratory symptoms. It is a rapidly interpretable, noninvasive test with minimal associated risk or cost, and it is available in remote areas where modern technology may not be. It can reflect the changes of cardiac structure and hemodynamics caused by PAH in patients with pulmonary embolism from the perspective of cardiac electrical activity, and has important electrophysiological significance. By vectorcardiography, one can measure a spatial angle between depolarization and repolarization, specifically a spatial angle between the spatial QRS

vector and spatial T vector, namely spatial QRS-T angle [6]. The spatial QRS-T angle has been shown to be associated with sudden cardiac death, ventricular arrhythmia and heart failure. Furthermore, the spatial QRS-T angle has been shown to be increased in patients with various cardiac risk factors, including smoking, diabetes and hypertension [7]. Henkens et al. reported that in Wistar rats with experimentally induced-PAH can be detected with increased spatial QRS-T angle [8]. The aim of the study was to assess the clinical application of the spatial QRS-T angle for the prediction of PAH in patients with acute pulmonary embolism.

Methods

Study population

We studied patients with acute pulmonary embolism according to 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism [9] in our hospital between June 2017 and June 2019. The exclusion criteria encompassed intraventricular conduction disturbances (the right or left bundle branch block, non-specific intraventricular conduction block), atrial fibrillation or flutter during ECG recordings, other types of arrhythmia (e.g. numerous ventricular and supraventricular extra beats) disturbing the analysis of ECG recordings, heart stimulation, old myocardial infarction, chronic heart failure, chronic obstructive pulmonary disease, chronic respiratory failure, chronic kidney diseases (stages 3–5), liver failure, acute infectious diseases. All of the subjects gave their informed consent, and the study was approved by the Local Ethics Committee.

162 consecutive patients collected were evaluated with a color Doppler echocardiography, and defined as non-PAH group (92 patients), PAH group (70 patients). The averaged anthropometric and physiological parameters of the participants were given in Table 1. The PAH group comprised of 14 patients with mild PAH, 35 patients with moderate PAH and 21 patients with severe PAH.

Table 1
Baseline characteristics of acute pulmonary arterial hypertension (PAH) group and non-PAH group subjects

Variable	PAH group	non-PAH group	P
N	70	92	
Male/female	33/37	52/40	
Age, years	65.957 ± 9.227	67.652 ± 11.932	0.326
Height, cm	163.390 ± 8.196	164.570 ± 7.231	0.333
Weight, kg	56.614 ± 10.660	57.957 ± 14.475	0.515
Resting HR, beats/minute	100.240 ± 17.423	97.478 ± 18.498	0.335
Resting SBP, mmHg	129.940 ± 22.153	125.050 ± 18.489	0.128
Resting DBP, mmHg	87.214 ± 8.915	85.174 ± 8.054	0.129
Blood glucose, mmol/L	5.260 ± 0.298	5.203 ± 0.244	0.182
Total cholesterol, mmol/L	4.313 ± 0.691	4.199 ± 0.556	0.247
LDL cholesterol, mmol/L	2.721 ± 0.653	2.646 ± 0.556	0.428
HDL cholesterol, mmol/L	1.170 ± 0.356	1.086 ± 0.246	0.078
Triglycerides, mmol/L	1.613 ± 0.652	1.450 ± 0.671	0.125
Creatinine, umol/L	68.709 ± 11.940	69.710 ± 9.485	0.553

Note: The results were given as means ± SD. SD indicates standard deviation. HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

Experimental protocol

The assessment of pulmonary artery systolic pressure (PASP) using transthoracic color doppler echocardiography

Echocardiograms were performed by one technician using a Philips Sonos 5500 with a 3.2 MHz transducer (Philips Medical Systems, Andover, MA, USA). PASP was obtained from the formula: PASP = RAP + 4V2, RAP was right atrial pressure and the V refers to velocity of tricuspid regurgitation. RAP was estimated by evaluating the inferior vena cava (IVC) size and change with respiration. Briefly, RAP was estimated to be 5 mmHg when the IVC diameter was less than 20 mm and the collapsibility greater than 50%; 10 mmHg when IVC diameter was less than 20 mm and collapsibility less than 50%; 15 mmHg when IVC diameter was greater than 20 mm and collapsibility greater than 50%; and 20 mmHg when IVC diameter was greater than 20 mm and collapsibility less than 50%. PAH was defined as PASP beyond 37 mmHg. Patients were stratified according to the classification of PAH into those with normal

pulmonary arterial systolic pressure (< 37 mm Hg), and mild (37–40 mm Hg), moderate (41–70 mm Hg), and severe (> 70 mm Hg) PAH [3, 10, 11].

Three-dimensional Vectorcardigram Analysis

SCA-II type three-dimensional vectorcardiogram (VCG) (Beijing Cadiz Medical Technology Co., Ltd, Beijing, China) was applied. A baseline 12-lead ECG and VCG were recorded (paper speed 25 mm/s, gain 10 mm/mV). The ECG and VCG were recorded on a Wilson system and Frank orthogonal lead system, respectively. In order to exclude the effect of respiration on QRS complex, the ECG and VCG were recorded when the patient was breath holding (three complexes were recorded). The measured data were mean value calculated from three QRS complexes. The data from each patient were acquired digitally and analyzed by two independent cardiologists who were also blinded to the transthoracic echocardiography results and patients' symptoms and signs.

Observed index

Maximum QRS and T vectors were computed for each patient from their averaged QRS-T complexes. The spatial QRS-T angle is an angular difference between the maximum QRS vector and maximum T vector. Usually, the degree from QRS maximum vector clockwise to T maximum vector is positive, and vice versa.

Statistical analysis

The results were given as mean ± standard deviation. Independent t-test was used to compare the indexes of non-PAH group and PAH group. One-way ANOVA was used to compare the indexes of mild, moderate, and severe PAH group. When the ANOVA was significant, the differences between mild, moderate, and severe PAH group were tested by the SNK comparisons test. The correlation between the spatial QRS-T angle and PAH was analyzed by using pearson correlation analysis. Correlation coefficient (r) ≥ 0.7 can be considered highly correlated; $0.4 \leq r < 0.7$ can be considered moderately correlated. $0.2 \leq r < 0.4$ can be considered low correlated. All statistical analysis were performed using SPSS 16.0. A P-value < 0.05 was considered significant.

Results

Study population

The averaged anthropometric and physiological parameters of the participants were given in Table 1. There were no statistically significant differences between the two groups.

Comparison of spatial QRS-T angle in study subgroups

The spatial QRS-T angle was larger in patients with PAH than those with non-PAH (109.010 ± 30.970° VS 68.098 ± 18.010°, $P < 0.05$), see Fig. 1. There were 84 patients with PAH, including 14 patients with mild,

48 with moderate, and 22 with severe PAH. Significant differences of spatial QRS-T angle values were found between patients with mild, moderate and severe PAH (73.714 ± 15.716°, 104.790 ± 20.675°, 139.57 ± 23.196°, respectively, $P < 0.05$), see Fig. 2.

The correlation between the spatial QRS-T angle and PAH

There was a positively linear correlation between the spatial QRS-T angle and PASP in patients with PAH ($r = 0.676$, $P < 0.05$), see Fig. 3. The PASP increase was moderately associated with a increase in QRS-T angle.

Discussion

Acute pulmonaryembolism is one of the most frequent cardiovascular causes of death [1]. Thromboembolic PAH causes high morbidity worldwide, and its diagnosis and treatment remain challenging. Residual PAH persists in both acute and chronic embolism [3, 12]. Approximately 80% of patients with acute pulmonary embolism suffer from PAH [3]. Acute pulmonary embolism-induced PAH results from the interaction of at least three main factors: the mechanical obstruction of pulmonary vessels, general pulmonary arteriolar constriction attributable to a neurogenic reflex, and the release of vasoconstrictors by activated platelets, leukocytes, and endothelial and lung cells [13]. The most common cause of death in acute pulmonary embolism is right heart failure [14]. After acute pulmonary embolism, pulmonary circulation resistance increased in a short time, right ventricular afterload increased sharply, and cardiac structural changes mainly occurred with right ventricular enlargement; persistent hypoxia further aggravated pulmonary artery pressure, hemodynamic deterioration, and then aggravated right ventricular load and dysfunction gradually appeared.

VCG has reemerged with the advent of digital electrocardiography. VCG visualizes movement of the heart vector through cardiac cycle as loops. The QRS loop reflects depolarization, whereas the T loop reflects repolarization. By VCG, one can measure a spatial angle between depolarization and repolarization, specifically a spatial angle between the spatial QRS vector and spatial T vector, namely spatial QRS-T angle [6, 15]. While normal ranges for spatial QRS-T angle vary by method and by study, most studies have suggested that normal values lie below 100°-110° for men and below 90° for women. Of note, an increased spatial QRS-T has been reported as an independent predictor of cardiac arrhythmias and sudden cardiac death [16]. Several pathologies increase spatial QRS-T angle. In the Rotterdam Study, spatial QRS-T angle 105° was noted in 20% of diabetic patients [17]. In patients with chronic kidney diseases, both disease duration and poor outcome of dialysis is associated with increased spatial QRS-T angle [18]. Severe coronary atherosclerosis is also an independent predictor of increased QRS-T both in patients with chronic kidney diseases and in patients with isolated coronary artery disease [18, 19]. Additionally, some anaesthetics and sedatives can affect VCG and increase risk of sudden cardiac death. Interestingly, rapidly induced intraabdominal hypertension to 15 mmHg also acutely increases spatial QRS-T angle to above 100° in some healthy young women undergoing elective gynaecological laparoscopy [20]. In this present study, it showed spatial QRS-T angle values are significantly higher in

patients with PAH than in non-PAH. The moderately positive correlation between PASP and QRS-T angle was significant ($r = 0.676$, $P < 0.05$). Henkens et al. carried out experimental study on Wistar PAH rats which also showed increased spatial QRS-T angle can help the recognition of PAH [8]. Therefore, the angle of QRS-T is helpful to objectively evaluate the changes of the disease, and take effective treatment measures as soon as possible to improve the prognosis of patients.

The mechanisms of QRS-T angle change in PAH are as follows: (1) The effect of PAH on ventricular depolarization: QRS maximum vector is the maximum instantaneous integrated ECG vector generated during ventricular depolarization, which usually occurs at 0.04 s in normal conditions and is produced by left ventricular lateral wall and right ventricular basal depolarization. In the early stage of acute pulmonary embolism, pulmonary trunk and cone of pulmonary artery and supraventricular ridge (the last depolarization part of right ventricle) were dilated, which made the maximum vector of QRS shift backward [21, 22]. With the increase of pulmonary artery pressure, the right ventricular afterload gradually increased, and the maximum vector of QRS gradually shifted backward to the right. When the right ventricle expands and hypertrophy causes the right power to exceed the left power, the QRS maximum vector moves to the right rear. (2) The effect of PAH on repolarization: PAH can significantly slow down the repolarization velocity of the endocardial surface at the site (right ventricular basement) where the systolic pressure of the right ventricle is significantly increased, resulting in repolarization vectors deviating from the endocardial surface [23, 24]. The direction of change of T vectors caused by the repolarization vectors tends to change with the influence of the above analysis on QRS vectors (codirectional change). Therefore, the change of QRS-T angle is helpful for the analysis of PAH in patients with acute pulmonary embolism.

Study Limitations

This study is only a single-center study with small sample size. A multicenter prospective study with large sample is necessary to demonstrate that the diagnostic value of QRS-T angle in patients with acute pulmonary embolism before and after treatment.

Conclusions

Our results suggest that spatial QRS-T angle may be useful for identifying PAH from those without RVH and predicting PASP in patients with acute pulmonary embolism, .

Declarations

Abbreviations

PAH, Pulmonary arterial hypertension; PASP, pulmonary arterial systolic pressure; ECG, electrocardiogram; IVC, inferior vena cava; VCG, vectorcardiogram

Declarations

Authors' contributions

All authors fulfill the criteria for authorship. QHC and WSC conceived and designed the research. QHC, CJL, WSC, HYF, CCZ acquired the data. QHC, CJL, WSC, HYF, CCZ performed statistical analysis. QHC, CJL, WSC, HYF, CCZ drafted the manuscript and made critical revision of the manuscript for key intellectual content. All authors read and approved the final version of the manuscript. All authors have agreed to authorship and order of authorship for this manuscript.

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Availability of data and materials

All relevant data supporting the conclusions of this article is included within the article.

Ethics approval and consent to participate

All of the subjects gave their informed consent, and the study was approved by the Local Ethics Committee of the First Affiliated Hospital of Liaoning Medical University.

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None.

Competing interests

None declared.

Consent for publication

Not applicable.

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Figures

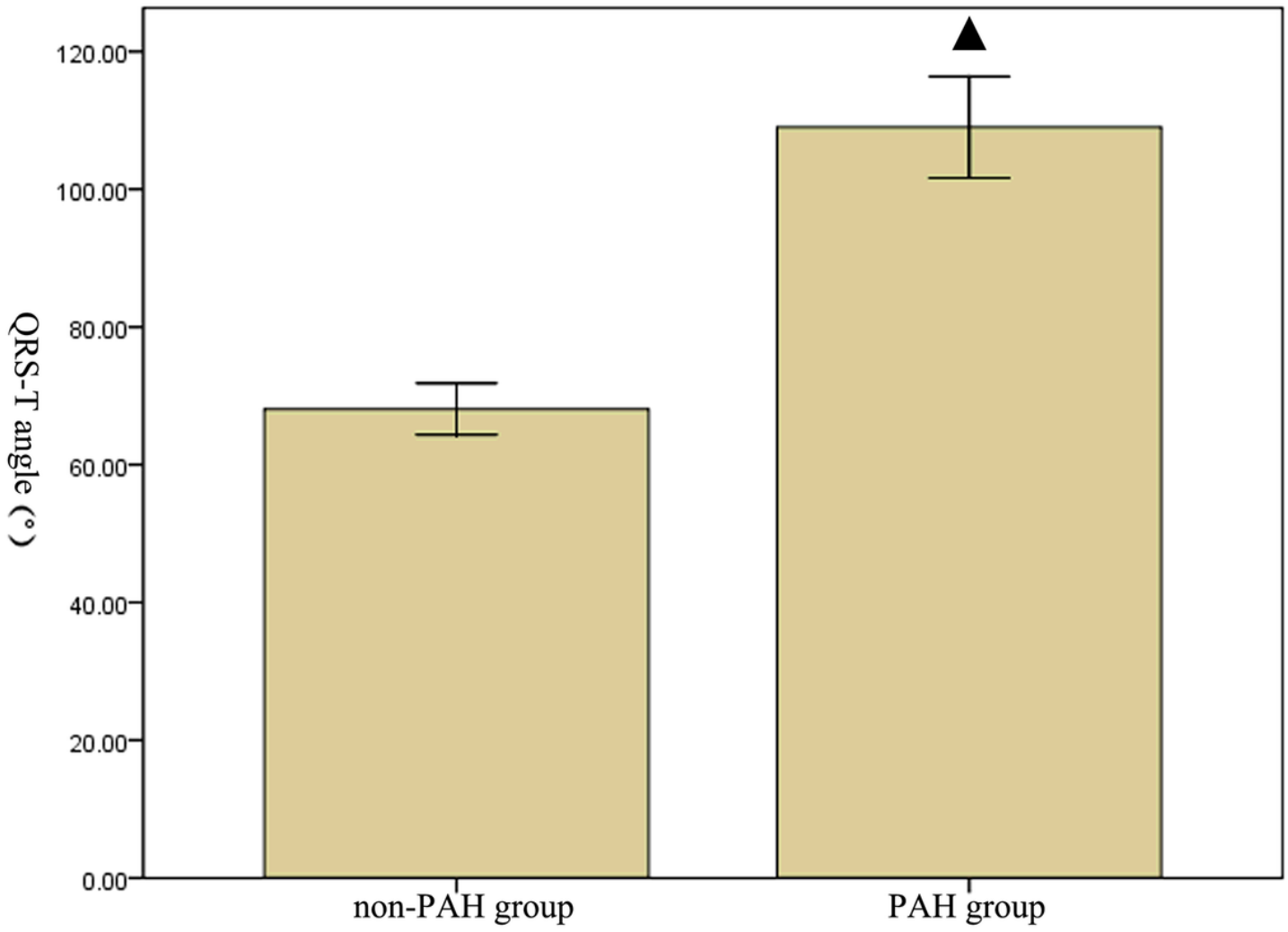

Figure 1

Comparative study of spatial QRS-T angle in pulmonary arterial hypertension (PAH) group and non-PAH group. Compared with non-PAH group, ▲ indicates $P < 0.05$.

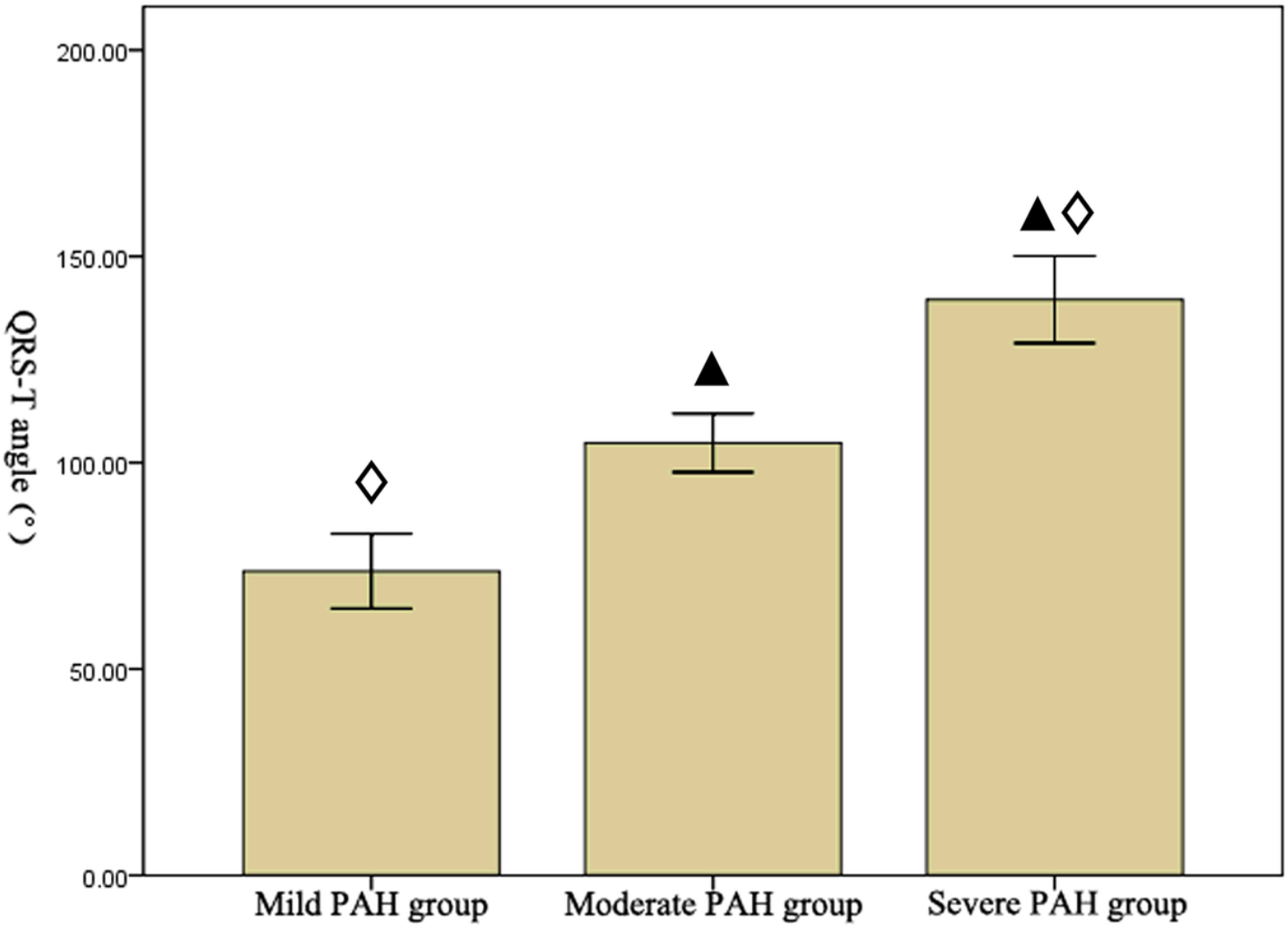

Figure 2

Comparative study of spatial QRS-T angle in mild, moderate, and severe pulmonary arterial hypertension (PAH). Compared with mild PAH group, ▲ indicates $P < 0.05$. Compared with moderate PAH group, ◊ indicates $P < 0.05$.

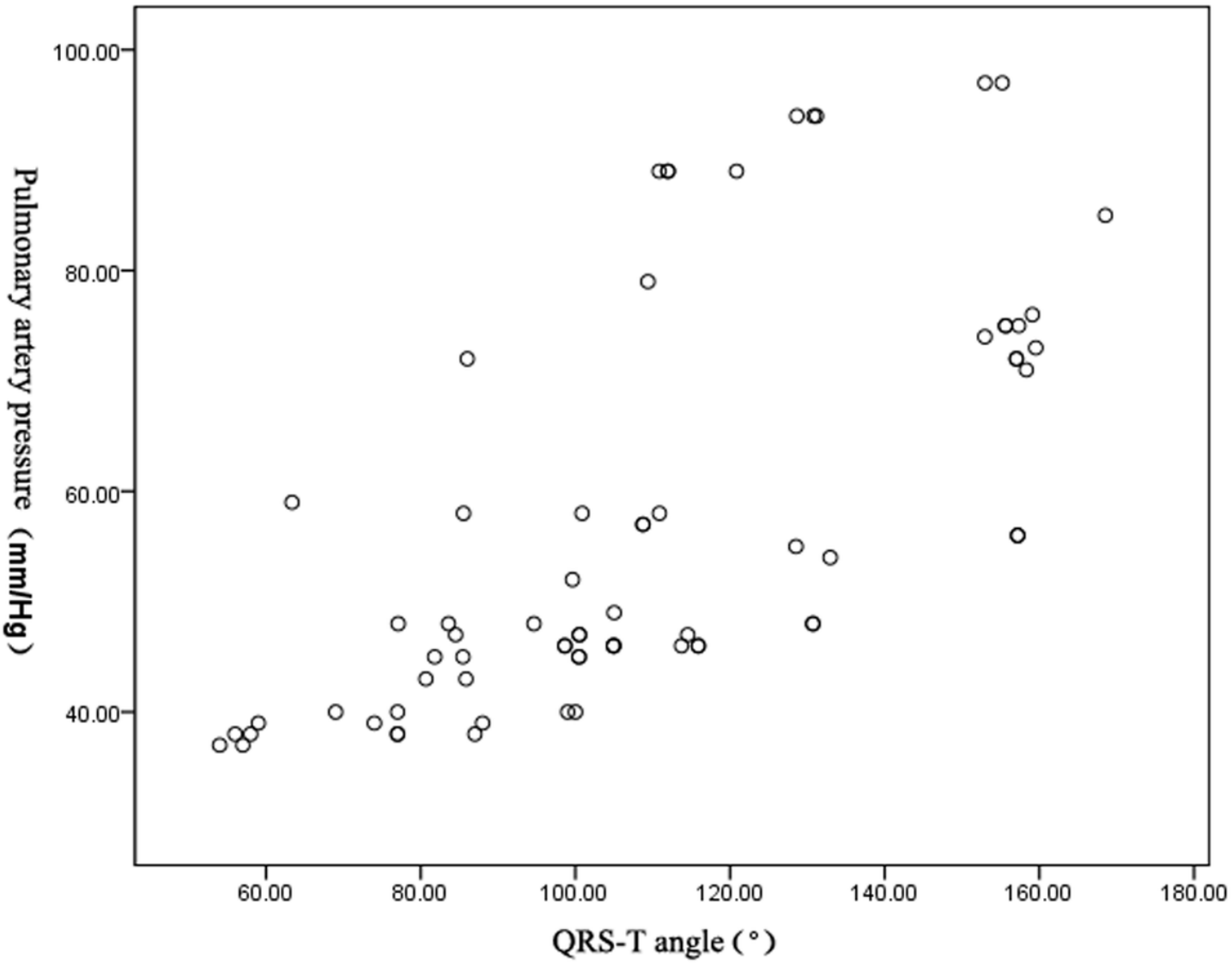

Figure 3

Pearson correlation analysis between the spatial QRS-T angle and pulmonary artery systolic pressure (PASP) in patients with PAH. PASP was significantly positively associated with QRS-T angle ($r = 0.676$, $P < 0.05$).