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# Distribution characteristics and prognostic value of 12-lead ECG PR interval in hospitalized patients with heart failure

X.-X. ZHANG, L. WANG

Department of Cardiology, Jincheng People's Hospital, Jincheng, China

**Abstract. – OBJECTIVE: The aim of this study was to explore the distribution characteristics and prognostic value of the distance from the start of the P wave to the start of the QRS wave (PR interval) in 12-lead electrocardiogram (ECG) of hospitalized patients with heart failure.**

**PATIENTS AND METHODS: A total of 354 heart failure patients treated in our hospital from June 2018 to April 2020 were retrospectively selected as the study subjects. Among them, 86 cases were classified as the 101 ms-156 ms group, 92 cases as the 157 ms-169 ms group, 94 cases as the 170 ms-191 ms group, and 82 cases as the 192 ms-321 ms group based on the PR interval quartile. The clinical data of the subjects were collected and the changes in clinical data at different PR intervals were analyzed. The patients were followed up for 48 months and were further divided into 92 cases in the death group and 262 cases in the survival group. The changes in the levels of 12-lead ECG indexes in patients with different prognoses were analyzed. The receiver operating characteristic (ROC) curve was established to analyze the predictive value of 12-lead ECG on the prognosis of heart failure patients. The Kaplan-Meier survival curve was adopted to analyze the relationship between 12-lead ECG and survival time of heart failure patients.**

**RESULTS: There were significant differences in age, body mass index (BMI), cardiac function classification, left ventricular ejection fraction (LVEF) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) among patients with different PR intervals ($p<0.05$). P-wave, PR interval, and QRS complex levels increased with increasing PR staging fraction ($p<0.05$). Compared with the survival group, the proportion of P wave, PR interval 192 ms-321 ms, and the level of QRS complex in the death group were much higher ($p<0.05$). ROC curve analysis showed that the P wave, PR interval, and QRS complex were all factors influencing the poor prognosis of patients with heart failure ($p<0.05$, Table IV). QRS complexes were all predictive of prognosis in heart failure patients ($p<0.05$). The median survival time (MST) of patients with P wave ≥113 ms was 35 months, which was sharply shorter than the patients in P wave <113 ms group (46 months, $p<0.05$). The MST of patients with PR interval of 101 ms-156 ms was 45.5 months, 42 months in the 157 ms-169 ms group, 39 months in the 170 ms-191 ms group, and 35 months in the 192 ms-321 ms group, exhibiting significant differences among the groups ($p<0.05$). The MST of patients with QRS complex ≥121.44 ms was 38 months, which was memorably shorter than 44.5 months of the patients with QRS complex <121.44 ms ($p<0.05$).**

**CONCLUSIONS: The 12-lead ECG of hospitalized patients with heart failure is significantly abnormal, and the PR interval, P wave width, and QRS complex are significantly prolonged. The P wave, PR intervals, and QRS complex had a certain correlation with the prognosis of heart failure patients.**

*Key Words:*
Twelve-lead electrocardiogram, PR interval, Heart failure, Distribution characteristics, Prognosis, Predictive value.

## Introduction

Heart failure refers to the symptoms and signs induced by the heart's inability to pump enough blood to meet the body's needs. Heart failure is the main cause of death from various cardiovascular diseases such as hypertension and coronary heart disease, and it is more common in the elderly. With the improvement in life expectancy and population aging, the incidence rate of heart failure is also rising[1]. Cardiac output, cardiac contractility, filling pressure, ventricular wall pressure, and heart rate during systolic and diastolic function are the pathophysiological basis of heart failure[2]. Hemodynamic disturbances, neurohormonal activation, excessive tubular sodium reabsorption, inflammation, oxidative stress, and nephrotoxic drugs are important drivers of cardiac and renal dysfunction



*Corresponding Author:* Li Wang, BM; e-mail: wanglilyeah@21cn.com

in patients with heart failure[3]. With the continuous progress of clinical medicine, the mortality rate of patients has gradually decreased, but cardiovascular disease is still one of the most important causes of death worldwide.

12-lead electrocardiogram (ECG) is a routine examination in cardiology, which is often used to detect and record abnormal electrical activity in patients. It is reported[4] that 12-lead ECG is an initial mapping tool for predicting the most likely origin site, which has important guiding significance for selecting an appropriate treatment plan in clinical practice. The distance from the onset of the P wave to the onset of the QRS wave (PR interval) was defined as the time required for an electrical pulse to travel from the sinoatrial node through the atrioventricular node to the Purkinje fibers. Some studies[5] have shown that PR interval plays an important role in the occurrence of atrial fibrillation and the potential process of atrial remodeling. However, the effect of PR interval on the prognosis of patients with heart failure remains unclear.

Patients with heart failure treated in our hospital from June 2018 to April 2020 were retrospectively selected as the research subjects, in order to explore the distribution, distribution characteristics and prognostic value of PR interval of 12-lead electrocardiogram in hospitalized patients with heart failure, so as to provide a relevant reference for the prognosis evaluation of these patients.

## Patients and Methods

### General Materials

A total of 354 heart failure patients treated in our hospital from June 2018 to April 2020 were retrospectively selected as the study subjects. Among them, 86 cases were classified as the 101 ms-156 ms group, 92 cases as the 157 ms-169 ms group, 94 cases as the 170 ms-191 ms group, and 82 cases as the 192 ms-321 ms group based on the PR interval quartile. There were 263 males and 91 females, with an average age of 54.79±12.85 years old. Inclusion criteria: (1) all subjects met the guidelines for the diagnosis and treatment of heart failure[6] and were detected by ECG. (2) Informed consent of patients and their families were signed. (3) The clinical and pathological data were complete, and the mental symptoms were good. Exclusion criteria: (1) patients with clearly abnormal liver and kidney function. (2) Patients accompanied with infectious diseases such as acquired immune deficiency syndrome (AIDS) and hepatitis B. (3) Patients with infectious diseases. This study was approved by the hospital Ethics Committee and conformed to the relevant principles of Medical Ethics (JCPH.NO 20230210001). The experimental process is shown in Figure 1.

### 12-Lead ECG Detection[7]

12-lead ECG (Nippon Kohden, Japan, Model number: ECG-2250) was performed on all subjects in a quiet environment in a supine position. V 1 and V 2 were placed in the fourth intercostal space, V 3 to V 6 were placed in the fifth intercostal space, where V 4 was located in the middle line of the left clavicle, V 6 was located in the middle line of the left armpit, and the limb wires (left and right, upper and lower limbs) were connected according to the standard configuration. The parameters of P wave, PR interval, QRS complex, and QT interval in patients' ECG were obtained by using 12-lead ECG (Nippon Kohden, Japan, Model number: ECG-2250) at a paper speed of 25 mm/s and a low-frequency limit of 0.05 Hz. All these results were obtained under the supervision of an experienced cardiologist.

### Clinical Data Collection

The clinical data of the patients were collected. Gender (male, female), age, body mass index (BMI), blood pressure (systolic blood pressure, diastolic blood pressure), disease history (smoking history, hypertension history, diabetes history, stroke history), cardiac function classification (grade I, II, III, IV), left ventricular ejection fraction (LVEF), N-terminal pro-B-type natriuretic peptide (NT-proBNP) and white blood cell count (WBC) were collected.

### Outcome Measures

The basic data of patients with different PR intervals and the changes in 12-lead ECG indexes were analyzed. Patients were followed-up by telephone, wechat or outpatient examination, and the follow-up time was 48 months, with death as the endpoint. The patients were divided into the death group (92 cases) and the survival group (262 cases). The changes in 12-lead electrocardiogram parameters in patients with different prognoses were analyzed.

### Statistical Analysis

In this study, the enumeration data such as gender, disease history, and cardiac function grading were expressed in [cases (%)] and compared

using $\chi^2$ test. Age, BMI, blood pressure, LVEF, NT-proBNP, WBC, 12-lead ECG indicators, and other measurement data were all in accordance with normal distribution through the normal distribution test and were all expressed in the form of ($x\pm s$). Independent sample $t$-test was used to compare the measurement data between two groups, and an analysis of variance was used to compare the measurement data between multiple groups. The receiver operating characteristic (ROC) curve was used to analyze the predictive value of intervention factors for the prognosis of patients with heart failure. The Kaplan-Meier survival curve was used to analyze the relationship between 12-lead ECG and the survival time of patients with heart failure. In this study, SPSS 23.0 (IBM Corp., Armonk, NY, USA) software was used for statistical data analysis, and $p<0.05$ was regarded as the difference with statistical significance.

## Results

### *Comparison of Basic Data of Patients with Different PR Intervals*

No significant difference was detected in gender, blood pressure, disease history, angiotensin-converting enzyme inhibitors (ACEI), diuretics, and WBC between patients with different PR intervals ($p>0.05$). The differences in age, BMI, cardiac function class, LVEF, and NT-proBNP were statistically significant in patients with different PR intervals ($p<0.05$, Table I).

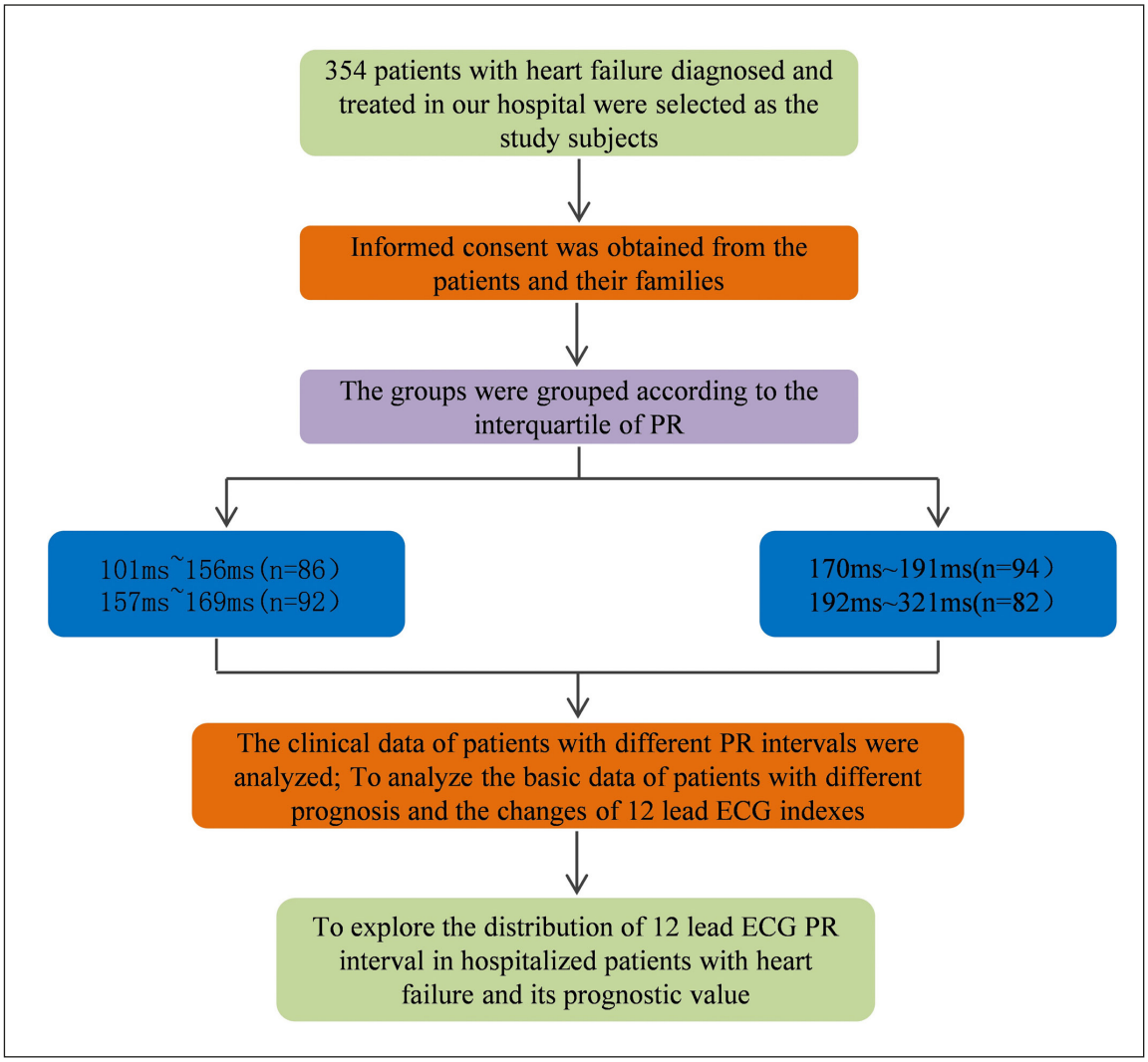


**Figure 1.** The experimental process.

**Table I.** Comparison of basic data of patients with different PR intervals [cases (%), ($\bar{x}$±s)].

| Groups | 101 ms-156 ms group (n=86) | 157 ms-169 ms group (n=92) | 170 ms-191 ms group (n=94) | 192 ms-321 ms Group (n=82) | $\chi^2$/F | p |
|---|---|---|---|---|---|---|
| Gender (%) | | | | | 7.433 | 0.059 |
| Female | 30 (34.88) | 26 (28.26) | 20 (21.28) | 15 (18.29) | | |
| Male | 56 (65.12) | 66 (71.74) | 74 (78.72) | 67 (81.71) | | |
| Age (year) | 52.85±10.72 | 53.14±11.18 | 55.27±10.24 | 58.62±13.74 | 4.53 | 0.004 |
| BMI (kg/m$^2$) | 24.46±3.25 | 25.47±3.52 | 25.75±3.88 | 26.15±2.53 | 3.93 | 0.009 |
| Blood pressure (mmHg) | | | | | | |
| DBP | 72.52±12.41 | 74.28±11.66 | 73.68±13.26 | 72.08±12.41 | 0.58 | 0.626 |
| SBP | 121.85±19.85 | 122.15±20.41 | 123.47±18.87 | 120.68±21.19 | 0.29 | 0.834 |
| Disease history (%) | | | | | | |
| History of smoking | 37 (43.02) | 41 (44.57) | 39 (41.49) | 44 (53.66) | 3.056 | 0.383 |
| History of hypertension | 46 (53.49) | 52 (56.52) | 45 (47.87) | 44 (53.66) | 1.468 | 0.690 |
| History of diabetes | 21 (24.42) | 31 (33.70) | 29 (30.85) | 29 (35.37) | 2.781 | 0.427 |
| History of stroke | 6 (6.98) | 4 (4.35) | 7 (7.45) | 5 (6.10) | 0.883 | 0.830 |
| Cardiac function grading (%) | | | | | 18.651 | 0.028 |
| Grade I | 10 (11.63) | 4 (4.35) | 3 (3.19) | 23 (28.05) | | |
| Grade II | 27 (31.40) | 24 (26.09) | 18 (19.15) | 14 (17.07) | | |
| Grade III | 38 (44.19) | 49 (53.26) | 55 (58.51) | 46 (56.10) | | |
| Grade IV | 11 (12.79) | 15 (16.30) | 18 (19.15) | 20 (24.39) | | |
| LVEF (%) | 40.35±7.26 | 37.27±8.52 | 33.25±6.21 | 30.58±4.15 | 34.62 | <0.001 |
| NT-proBNP (pg/mL) | 1,254.63±346.58 | 1,758.15±663.27 | 2,017.58±679.64 | 2,862.46±716.54 | 98.35 | <0.001 |
| WBC (×10$^9$/L) | 7.63±1.64 | 7.53±2.35 | 7.46±2.38 | 7.60±2.36 | 0.11 | 0.957 |

SD: standard deviation, n: number, AFC: antral follicle count; AMH: anti-Müllerian hormone, FSH: follicle-stimulating hormone, ns: not statically significative.

### Comparison of 12-Lead ECG Indexes in Patients with Different PR Intervals

No notable difference was observed in heart rate (HR) and QT intervals between patients with different PR intervals ($p$>0.05). P wave, PR interval and QRS complex levels increased with increasing PR staging fraction ($p$<0.05, Table II and Figure 2).

### Comparison of 12-Lead ECG Indexes in Patients with Different Prognosis

No remarkable difference was detected in QT interval between the death group and the survival group ($p$>0.05). Compared with the survival group, the proportion of P wave, PR interval 192 ms-321 ms and the level of QRS complex were much higher. The HR level was much lower in the death group ($p$<0.05, Table II).

### Prognostic Value of 12-lead ECG in Patients with Heart Failure

ROC curve analysis was established, and the analysis showed that the P wave, PR interval, and QRS complex were all factors influencing the poor prognosis of patients with heart failure ($p$<0.05, Table IV).

### Kaplan-Meier Survival Curve Analysis of the Relationship Between 12-lead ECG and Survival Time in Patients with Heart Failure

These 354 patients were followed-up for 48 months, and the survival rate was 74.01% (262/354). Kaplan-Meier survival curve analysis showed that the median survival time (MST) of patients with P wave ≥113 ms was 35 months, which was sharply shorter than the patients in P wave <113 ms group (46 months, $p$<0.05). The MST of patients with PR interval of 101 ms-156 ms was 45.5 months, 42 months in the 157 ms-169 ms group, 39 months in the 170 ms-191 ms group, and 35 months in the 192 ms-321 ms group. The difference between the groups was statistically significant ($p$<0.05). The MST of patients with QRS complex ≥121.44 ms was 38 months, which was shorter than 44.5 months of the patients with QRS complex <121.44 ms ($p$<0.05, Figure 3).

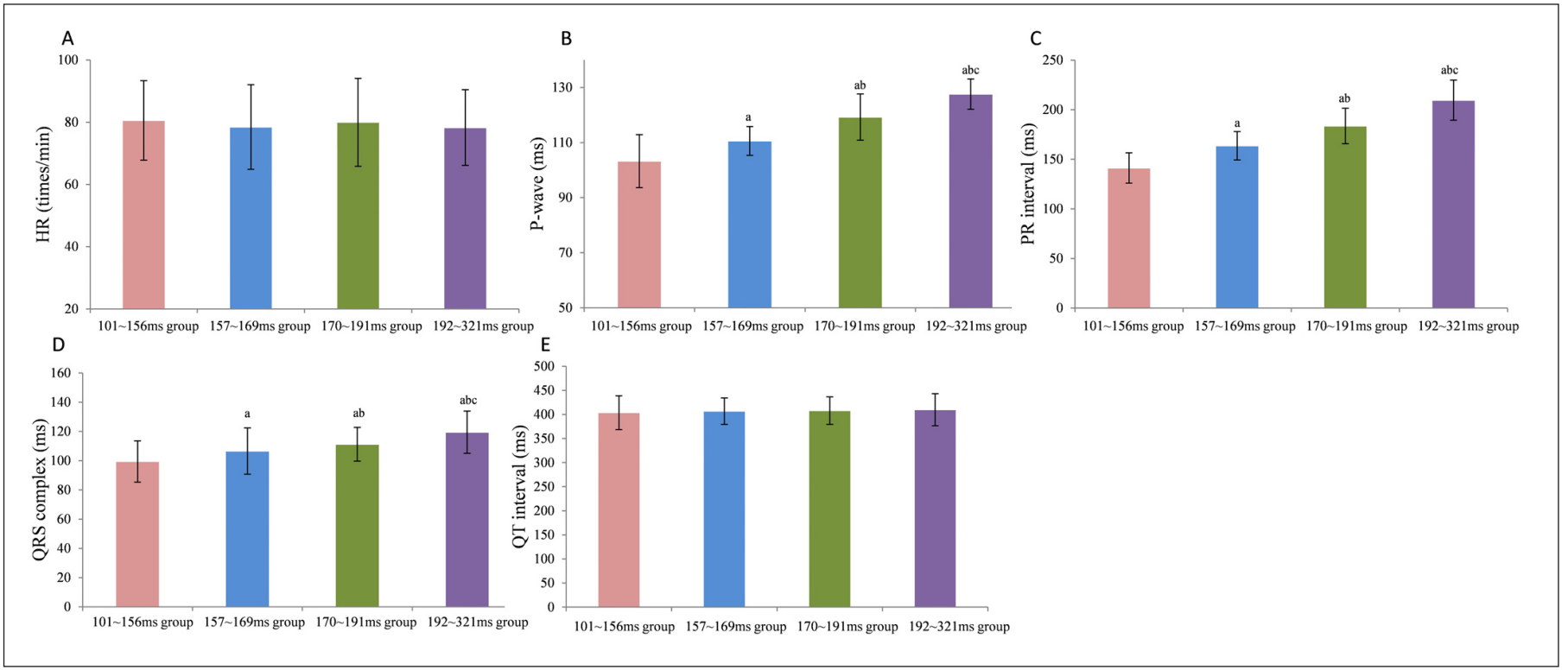


**Figure 2.** Comparison of 12-lead ECG indexes in patients with different PR intervals. **A**, Comparison of HR in patients with different PR intervals; (**B**) comparison of P wave in patients with different PR intervals; (**C**) comparison of PR intervals in patients with different PR intervals; (**D**) comparison of QRS complex in patients with different PR intervals; (**E**) comparison of QT intervals in patients with different PR intervals. [a]$p<0.05$ compared with 101 ms-156 ms group, [b]$p<0.05$ compared with 157 ms-169 ms group, [c]$p<0.05$ compared with 170 ms-191 ms group.

**Table II.** Comparison of 12-lead ECG indexes in patients with different PR intervals ($\bar{x} \pm s$).

| Groups | 101 ms-156 ms group (n=86) | 157 ms-169 ms group (n=92) | 170 ms-191 ms group (n=94) | 192 ms-321 ms | F | p |
|---|---|---|---|---|---|---|
| HR (times/min) | 80.57±12.80 | 78.46±13.57 | 79.96±14.13 | 78.28±12.17 | 0.63 | 0.598 |
| P wave (ms) | 103.26±9.58 | 110.57±5.24[a] | 119.23±8.41[ab] | 127.56±5.53[abc] | 170.45 | **<0.001** |
| PR interval (ms) | 141.25±15.33 | 163.58±14.37[a] | 183.58±17.94[ab] | 209.55±20.26[abc] | 245.45 | **<0.001** |
| QRS complex (ms) | 99.47±14.14 | 106.59±15.86[a] | 111.28±11.52[ab] | 119.53±14.41[abc] | 30.28 | **<0.001** |
| QT intervals (ms) | 403.63±35.16 | 406.70±27.46 | 407.85±28.76 | 409.86±33.29 | 0.55 | 0.621 |

[a]$p<0.05$ compared with 101 ms-156 ms group. [b]$p<0.05$ compared with 157 ms-169 ms group. [c]$p<0.05$ compared with 170 ms-191 ms group.

**Table III.** IComparison of 12-lead ECG indexes in patients with different prognoses [cases (%), ($\bar{x} \pm s$)].

| Groups | The death group (n=92) | The survival group (n=262) | $\chi^2$/t | p |
|---|---|---|---|---|
| HR (TIMES/MIN) | 73.25±13.78 | 82.46±14.79 | 5.228 | **<0.001** |
| P WAVE (MS) | 117.05±10.23 | 109.25±12.41 | 5.416 | **<0.001** |
| PR INTERVAL(MS) | | | 21.555 | **<0.001** |
| 101MS~156MS GROUP | 9 (9.78) | 77 (29.39) | | |
| 157MS~169MS GROUP | 22 (23.91) | 65 (26.39) | | |
| 170MS~191MS GROUP | 27 (29.35) | 52 (25.57) | | |
| 192MS~321MS GROUP | 34 (36.96) | 68 (18.32) | | |
| QRS COMPLEX (MS) | 128.46±46.57 | 114.02±52.18 | 2.346 | **0.020** |
| QT INTERVAL (MS) | 406.02±57.80 | 388.18±95.52 | 1.685 | 0.093 |

**Table IV.** Prognostic value of 12-lead ECG in patients with heart failure.

| Indicators | AUC | Specificity (%) | Sensitivity (%) | Yoden index | p-value | 95% CI |
|---|---|---|---|---|---|---|
| HR | 0.712 | 50.36 | 57.33 | 0.077 | 0.742 | 0.634-0.789 |
| P WAVE | 0.668 | 76.24 | 70.36 | 0.466 | **0.001** | 0.597-0.739 |
| PR INTERVAL | 0.840 | 84.63 | 87.28 | 0.719 | **<0.001** | 0.742-0.937 |
| QRS COMPLEX | 0.568 | 70.32 | 72.28 | 0.426 | **0.021** | 0.504-0.632 |
| QT INTERVAL | 0.519 | 67.82 | 68.07 | 0.359 | 0.174 | 0.504-0.619 |

## Discussion

Heart failure is caused by structural and functional changes in the myocardium caused by cardiomyopathy, myocardial infarction, hemodynamic overload, and inflammation. Ultimately, ventricular pumping or filling hypoperfusion may occur. Heart failure is also one of the leading causes of death from cardiovascular disease[8]. Early diagnosis and active intervention are of great significance in improving the prognosis of patients. With the progress of clinical diagnosis technology and the continuous development of instruments, ECG detection has become an important auxiliary means for the diagnosis of various heart diseases[9]. PR interval of ECG is the time required for electrical pulse transmission from the sinus node to the Purkinje fiber through the atrioventricular node. It is reported[10] that any part of the conduction delay or extension of the conduction path from the sinus node to the Purkinje fiber path through the atrioventricular node may cause the prolongation of the PR interval. It may be related to the structural remodeling of the atrial myocardium caused by fibrosis.

In this study, the PR interval of 12-lead ECG was used to evaluate the changes in PR interval-related indicators in patients. The results showed that there were differences in age, BMI, cardiac function classification, LVEF, NT-proBNP, P wave, PR interval and QRS complex in patients with different PR intervals, and PR interval had a certain correlation with the above indicators. The electrical activity of the heart can be manifested in different waveform forms on electrocardiogram (ECG), including P wave, PR in-

terval, QRS complex, etc. However, the incidence of heart failure increased significantly with age and BMI. In patients with heart failure, the accumulation of collagen between myocardial cells or the impairment of sodium ion transmission leads to abnormal cardiac electrical activity[11]. Some studies[12] found a significant correlation between the patients' BMI and the cardio-atrial conduction tissue, namely, the P wave width and PR interval. Therefore, it is important to evaluate the PR interval of patients through the above indicators to judge the condition of patients.

This study found that P wave, PR interval, and QRS complex had certain predictive value for the prognosis of patients with heart failure. Compared with the survival group, the P wave and QRS complex in the death group were significantly prolonged, and the ratio of PR interval 192 ms-321 ms was significantly increased. It suggested that P wave, PR interval, and QRS complexes could be used as effective indicators of cardiac function deterioration. Some scholars[13] found in the study of myocardial infarction that lower calcium values and older age during hospitalization were related to the prolongation of male PR interval. During a median follow-up of 31 months, 64 patients died. After adjusting for confounding covariates by Cox regression analysis, prolonged PR interval was independently associated with poor prognosis. Previous studies[14] found that a long PR interval is closely related to heart failure, sudden death, tachycardia, and other heart diseases. These results suggest that PR interval can be used as an independent predictor of long-term poor prognosis in patients with myocardial infarction during hospitalization. It is reported[15] that the left atrial cavity of patients

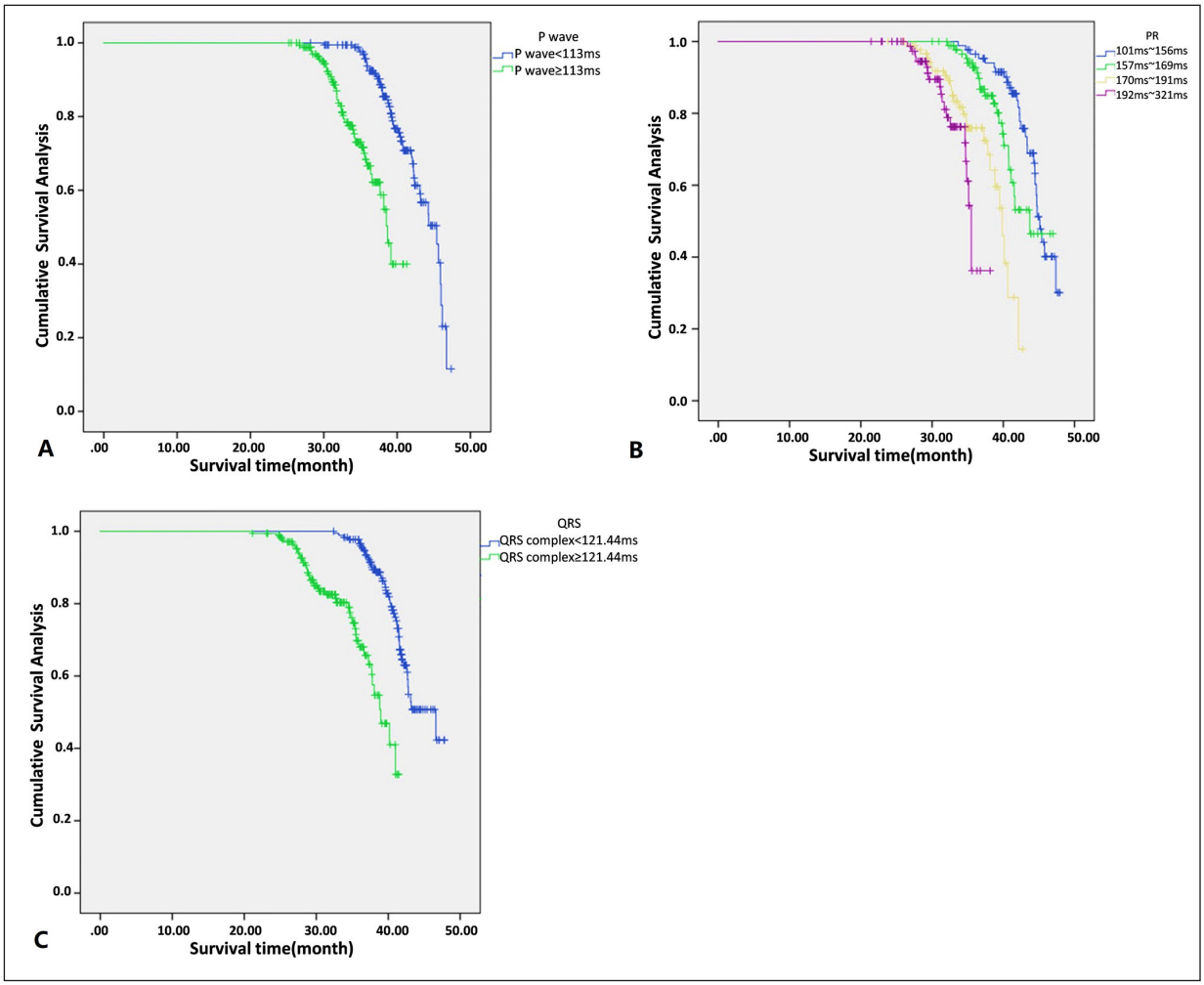


**Figure 3.** Kaplan-Meier survival curve analysis of the relationship between 12-lead ECG and survival time in patients with heart failure. **A**, Survival curve of patients with different P waves; (**B**) survival curves of patients with different PR intervals; (**C**) survival curve of patients with different QRS waves.

with atrial fibrillation is clearly enlarged. P-wave axis abnormality and left atrial size can be used as important factors to evaluate the prognosis of patients. In addition, some studies[16-18] have confirmed that the small increase in the duration of the QRS complex is related to the decrease of left ventricular ejection fraction, the increase of cardiac cavity size, and the risk of heart failure. Therefore, understanding the factors affecting the prognosis of patients with heart failure and timely intervention and treatment are expected to improve the prognosis and survival rate of patients.

## Conclusions

There are obvious abnormalities in 12-lead ECG of hospitalized patients with heart failure, mainly manifested as prolonged PR interval, P wave width, and QRS complex. P wave, PR interval, and QRS complex have a certain correlation with the prognosis of patients with heart failure. However, due to the limited sample size and the retrospective study, the experimental results may have some bias. Further multicenter prospective studies with larger sample sizes are needed to confirm the present results and conclusions. In addition, the follow-up period in this study was relatively short at 4 years. Therefore, the correlation between PR interval of 12-lead ECG and long-term prognosis of patients is worthy of further exploration in the future.

### Conflict of Interest
The Authors declare that they have no conflict of interests.

### Informed Consent
Patients and their families signed informed consent forms.

### Ethics Approval
This study was approved by the hospital Ethics Committee and conformed to the relevant principles of Medical Ethics (JCPH. NO 20230210001).

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### ORCID ID
Xiaoxia Zhang: 0009-0004-3903-7465.
Li Wang: 0009-0000-3914-7913.

### Data Availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Funding
None.

### Authors' Contributions
XX Z, and L W: guarantor of integrity of the entire study, study concepts and study design, definition of intellectual content, literature research, clinical studies, experimental studies, data acquisition and analysis, and statistical analysis. All authors have prepared, read, and approved the manuscript.

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