# Assessing Autonomic Nervous System Function by Pulse Rate Variability in Patients with Chronic Obstructive Pulmonary Disease

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## ABSTRACT

Heart rate variability (HRV) is measured to analyze autonomic nervous system function in humans, and pulse rate variability (PRV) assessed using the photoplethysmography method with a pulse oximeter has been proposed as a surrogate for HRV. To examine whether PRV is compatible with HRV in patients with chronic obstructive pulmonary disease (COPD), we simultaneously measured HRV with an electrocardiogram and PRV with a pulse oximeter in patients with COPD, and compared low-frequency and high-frequency components computed from HRV and PRV as indicators of autonomic nervous system function. In a Bland–Altman analysis, the low-frequency component computed from HRV exhibited good consistency with that computed from PRV. The high-frequency component showed a significant fixed error but relatively good consistency. Our results indicate that autonomic nervous system function may be estimated with the low-frequency component by measuring PRV with a pulse oximeter in patients with COPD.

**Key words**   autonomic nervous system; chronic obstructive pulmonary disease; heart rate variability; pulse oximetry; pulse rate variability

Sympathetic and parasympathetic nerves regulate heart rate, and heart rate variability (HRV) measured by an electrocardiogram (ECG) can be used to estimate autonomic nervous system function.[1, 2] The high-frequency (HF) component of the power spectrum calculated from HRV reflects cardiac vagal nerve activity, whereas the low-frequency (LF) component primarily reflects sympathetic nerve activity. The LF-to-HF ratio (LF/HF) has been used as an index of sympathetic nerve function and as an indicator of the balance between sympathetic and parasympathetic nerve functions.[1, 2]

Chronic obstructive pulmonary disease (COPD), which is the leading cause of chronic respiratory failure in Japan, is known to have negative effects on the autonomic nervous system.[3] The clinical condition of patients with COPD is monitored by assessing percutaneous arterial blood oxygen saturation ($SpO_2$) with a pulse oximeter,[4, 5] which can be used to also measure pulse rate variability (PRV) through the photoplethysmography method.[6] It has been reported that autonomic nervous system function can be analyzed by measuring PRV with a pulse oximeter instead of HRV, which appears satisfactory in healthy subjects at rest.[6] On the other hand, PRV has been reported to not be a surrogate for HRV in standing healthy subjects and in patients with low HRV.[7]

The aim of this study was to determine whether PRV is compatible with HRV in patients with COPD by analyzing and comparing HRV from an ECG and PRV from signals obtained at the fingers. To compare PRV and HRV in patients with COPD, we measured PRV using a pulse oximeter and HRV using an ECG, and compared the LF and HF components calculated from both as indicators of autonomic nervous system function.

## SUBJECTS AND METHODS

This study recruited patients with stable COPD. Patients with atrial fibrillation or premature ventricular contraction, and those taking autonomic nerve blockers were excluded. Written informed consent was obtained from all patients. The study was approved by the Ethical Review Board of the Faculty of Medicine, Tottori University (number: 18A008).

Measurements were taken with patients at rest in the supine position. A pulse oximeter (ATP-W03, Fukuda Denshi Co., Ltd., Tokyo, Japan) was attached to the index finger of the left hand, and the pulse wave was measured at a sampling rate of 200 Hz for 30 minutes using the photoplethysmography method. Furthermore, a Holter electrocardiography system (FM-980, Fukuda

Denshi Co., Ltd.) was attached to the chest, and the lead II ECG signal was simultaneously measured at a sampling rate of 125 Hz for 30 minutes. Thereafter, four sections of 128 seconds each without artifacts were selected from the measured records. The RR interval (RRI; i.e., the heart rate interval), which represents HRV, from the ECG and the pulse rate interval (PRI), which represents PRV, from the pulse oximeter were converted into time-series data for each 128-second section. We calculated the power spectrum from these time-series data using analysis software (SCM-850S, Fukuda Denshi Co., Ltd.) after resampling with 8 Hz of interpolated data, and used the power of the LF (0.031 Hz $\leq$ LF < 0.140 Hz) and HF (0.140 Hz $\leq$ HF < 0.390 Hz) components as indicators of autonomic nervous system function.

### Statistical analyses

The linear relationship between the RRI and PRI was analyzed in each patient. For comparing the LF and HF components and the LF/HF from HRV and PRV, we analyzed their linear relationships and performed a Bland–Altman analysis to calculate the fixed and proportional errors. Statistical analyses were performed using SPSS Statistics Version 27 (IBM Corp., Armonk, NY). A $P$ value <0.05 was considered to indicate statistical significance.

### RESULTS

A total of 10 male patients with stable COPD were included, and their mean age was 72.7 $\pm$ 6.1 years. A good significant correlation was found between the RRI and PRI in each patient (Appendix Figs. A1–A10). The linear relationship between the LF components calculated from HRV and PRV showed a gradient of 0.922 ($r$ = 0.874, $P$ < 0.0001, $n$ = 40), and the Bland–Altman analysis revealed no significant fixed or proportional error (Fig. 1). The linear relationship between the HF components calculated from HRV and PRV showed a gradient of 1.003 ($r$ = 0.845, $P$ < 0.0001, $n$ = 40), and the Bland–Altman analysis revealed a significant fixed error ($P$ < 0.01) but no proportional error (Fig. 1). The linear relationship of the LF/HF calculated from the HRV and PRV showed a gradient of 0.531 ($r$ = 0.915, $P$ < 0.0001, $n$ = 40), and the Bland–Altman analysis found both a significant fixed error ($P$ < 0.01) and a proportional error ($P$ < 0.01; Fig. 1).

### DISCUSSION

To evaluate the usefulness of PRV for assessing autonomic nervous system function in patients with COPD, we compared HRV measured using an ECG with PRV measured using a pulse oximeter. The LF component calculated from HRV exhibited good consistency with that calculated from PRV. Regarding the HF component, although a significant fixed error was observed in the Bland–Altman analysis, the HF component exhibited relatively good consistency. Consequently, the LF/HF calculated from the PRV was smaller than that calculated from the HRV, and thus, the results should be interpreted with caution. Our findings indicate that continuous measurement of PRV using the photoplethysmography method with a pulse oximeter has some validity for estimating autonomic nervous system function in patients with COPD at rest.

A review of studies found that PRV provides a sufficiently accurate estimate of HRV in healthy people at rest.[6] Moreover, another study found that the LF and HF components calculated from PRV measured using the photoplethysmography method and HRV measured using an ECG, were similar in healthy individuals at rest in the sitting position.[8] On the other hand, PRV was reportedly not a surrogate for HRV in standing healthy subjects and in patients with low HRV.[7]

In our study, besides measuring HRV using an ECG, we used the photoplethysmography method, a noninvasive method for continuously monitoring $SpO_2$, with a pulse oximeter to accurately measure the PRI and PRV. We found that the LF component calculated from PRV measured using a pulse oximeter was valid to a certain extent as an indicator of autonomic function. Thus, we suggest that autonomic nervous system function in patients with COPD at rest may be estimated by measuring PRV. Measuring the PRI and PRV simultaneously and evaluating the LF component to assess autonomic nervous system function in patients with COPD who frequently use a pulse oximeter may be clinically useful.

*The authors declare no conflict of interest.*
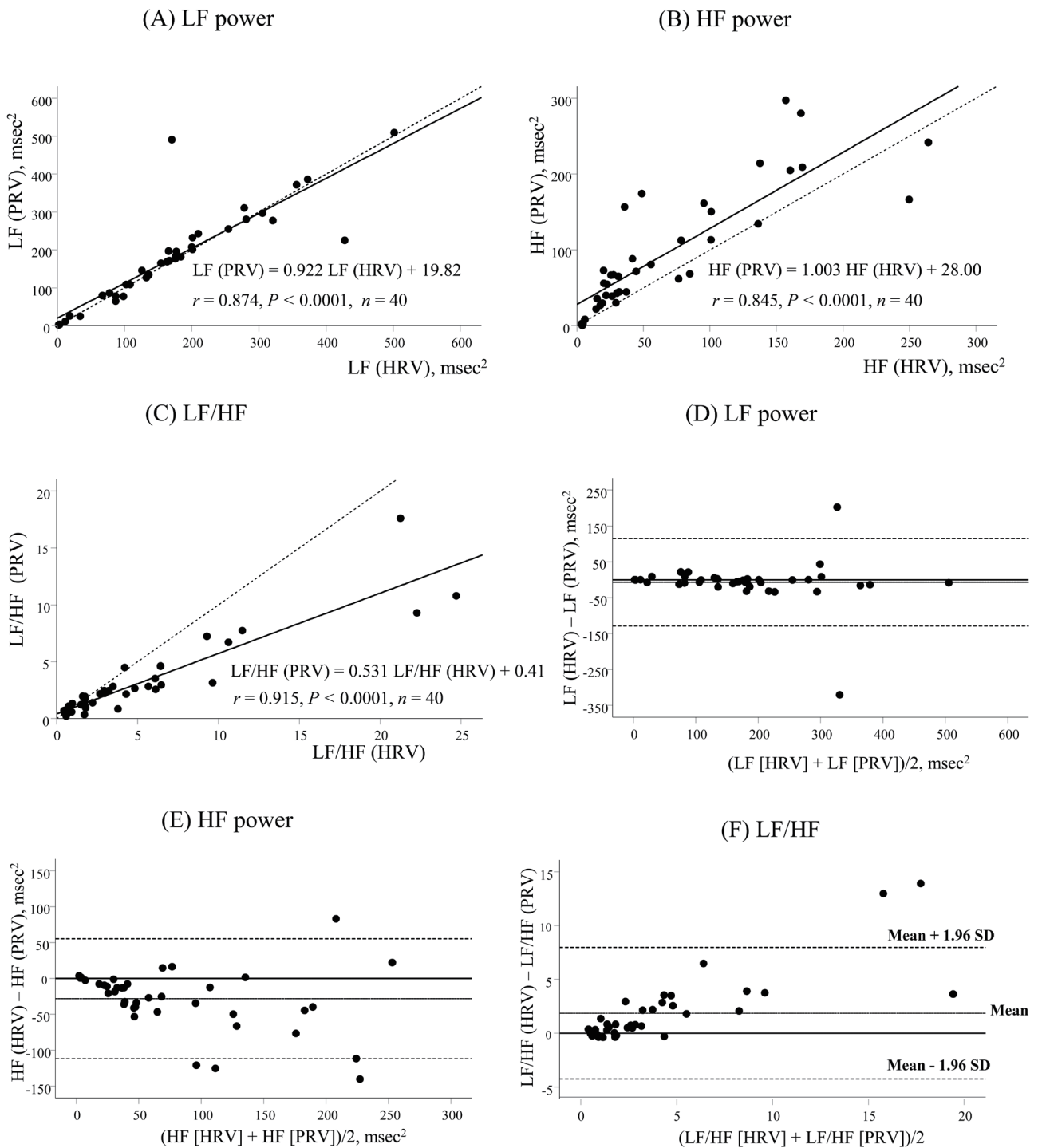
**Fig. 1.** The linear relationship between the low-frequency (LF) and high-frequency (HF) components of heart rate variability (HRV) and pulse rate variability (PRV), and Bland–Altman analysis of the LF and HF components and the LF-to-HF ratio (LF/HF). (**A**) The linear relationship of the LF components calculated from the HRV and PRV. (**B**) The linear relationship of the HF components calculated from the HRV and PRV. (**C**) The linear relationship of the LF/HF calculated from the HRV and PRV. (**D**) Bland–Altman analysis of the LF component. (**E**) Bland–Altman analysis of the HF component. (**F**) Bland–Altman analysis of the LF/HF. HF, high frequency; HRV, heart rate variability; LF, low frequency; LF/HF, LF-to-HF ratio; PRV, pulse rate variability.

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**APPENDIX**
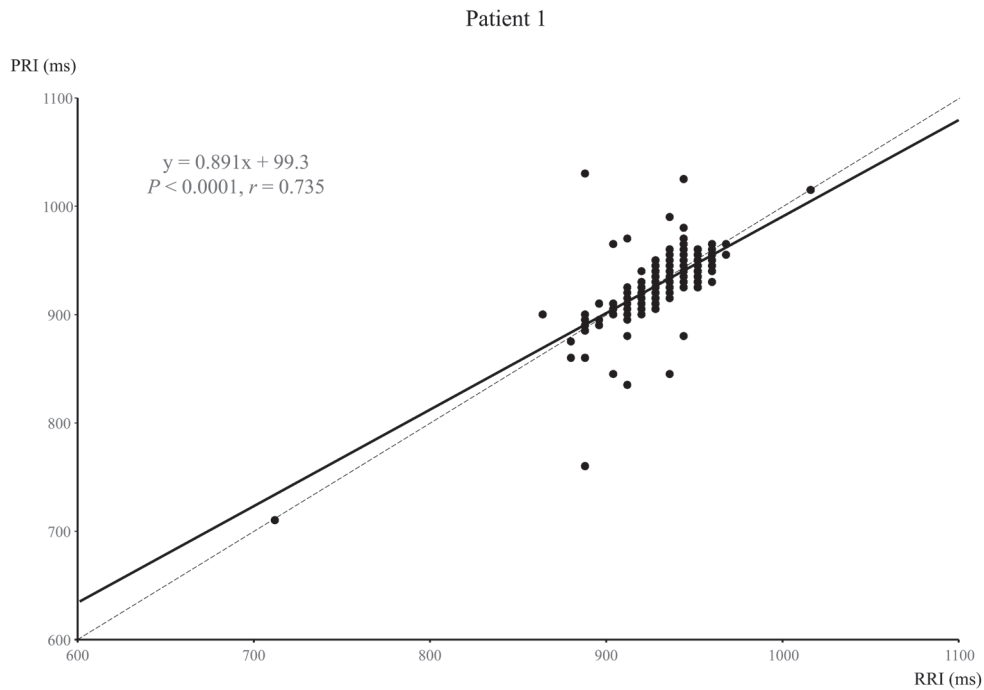
Patient 1
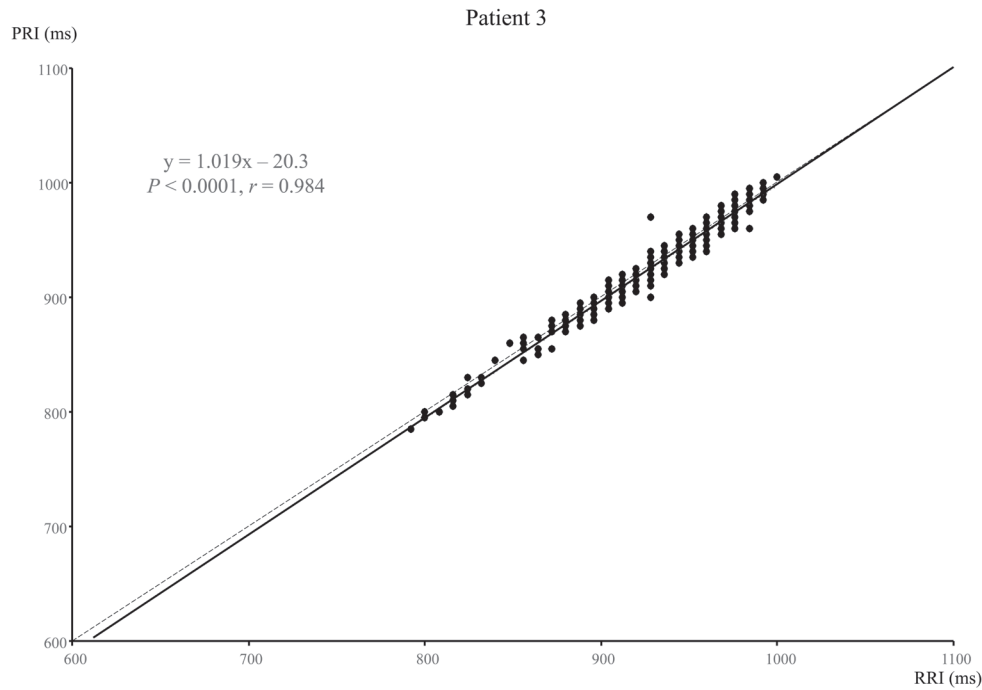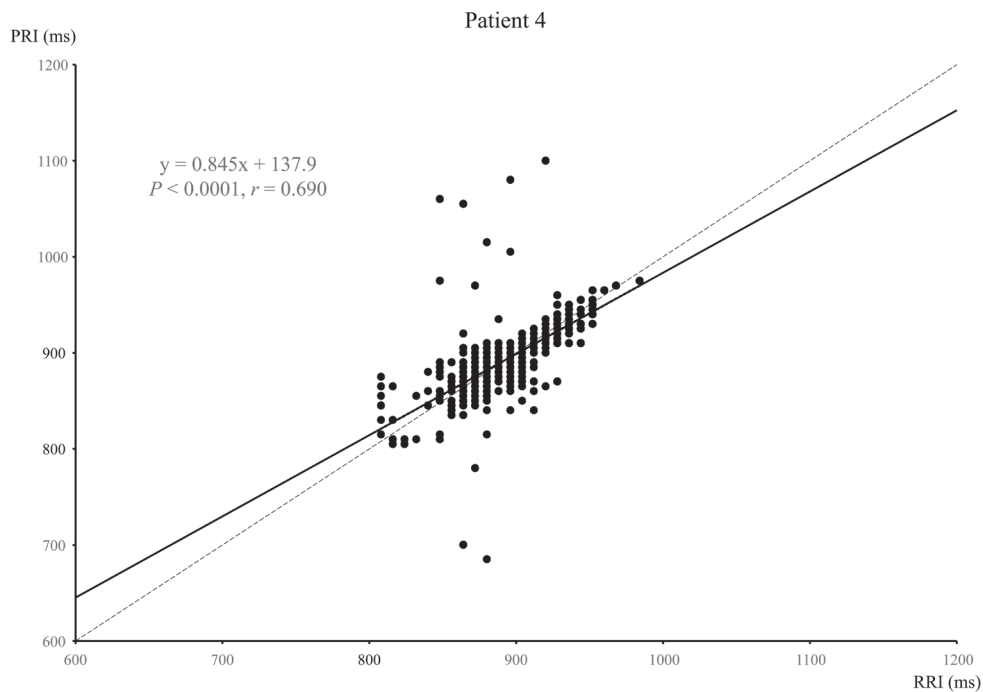


**Fig. A1.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in an 85-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found ($y = 0.891x + 99.3$, $P < 0.0001$, $r = 0.735$, $n = 546$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.
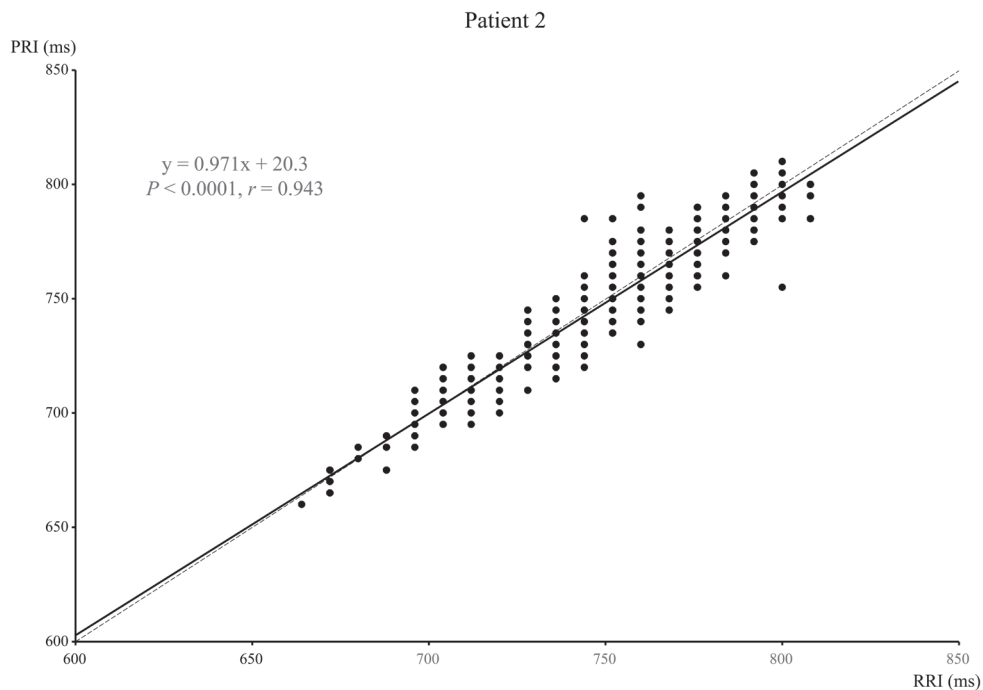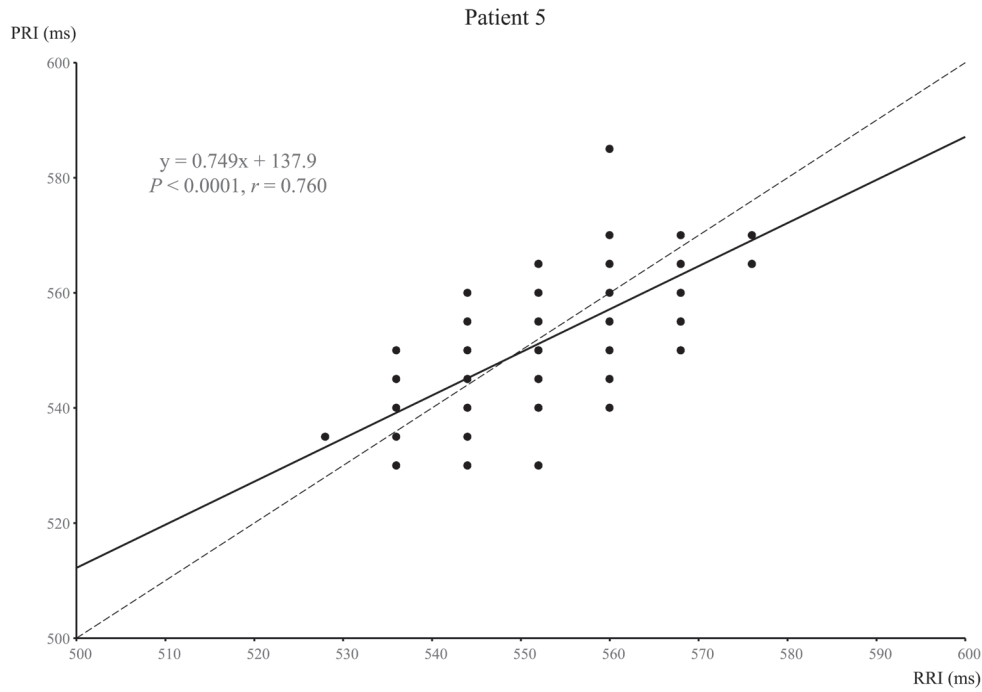
Patient 2



**Fig. A2.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 75-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found ($y = 0.971x + 20.3$, $P < 0.0001$, $r = 0.943$, $n = 682$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval

Patient 3

PRI (ms)

$y = 1.019x - 20.3$
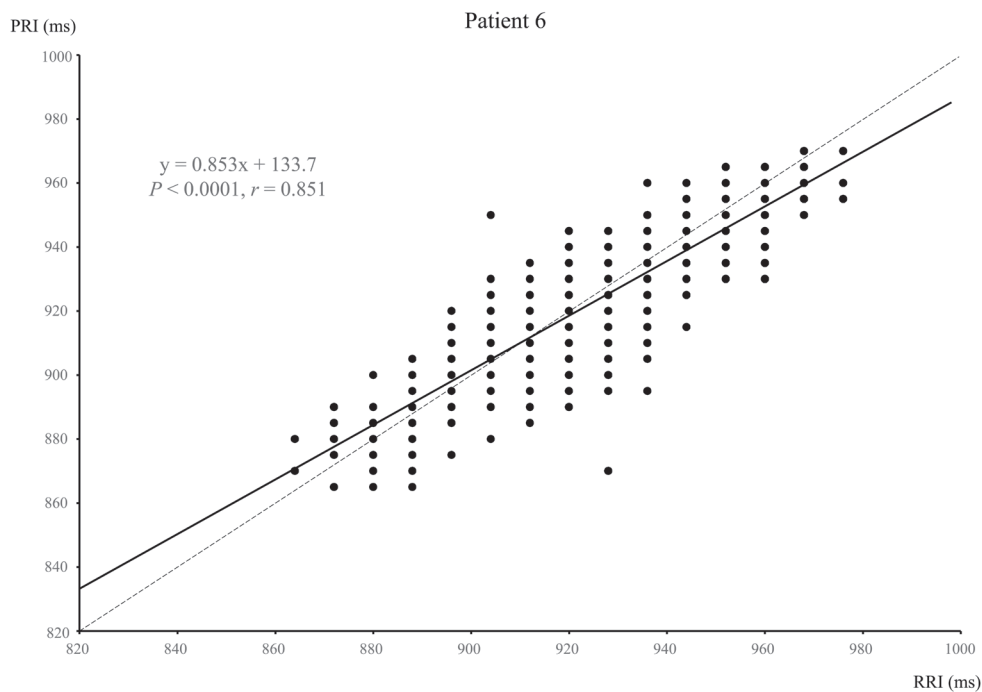$P < 0.0001, r = 0.984$

RRI (ms)

**Fig. A3.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 68-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 1.019x − 20.3, P < 0.0001, r = 0.984, n = 547). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval

Patient 4

PRI (ms)

$y = 0.845x + 137.9$
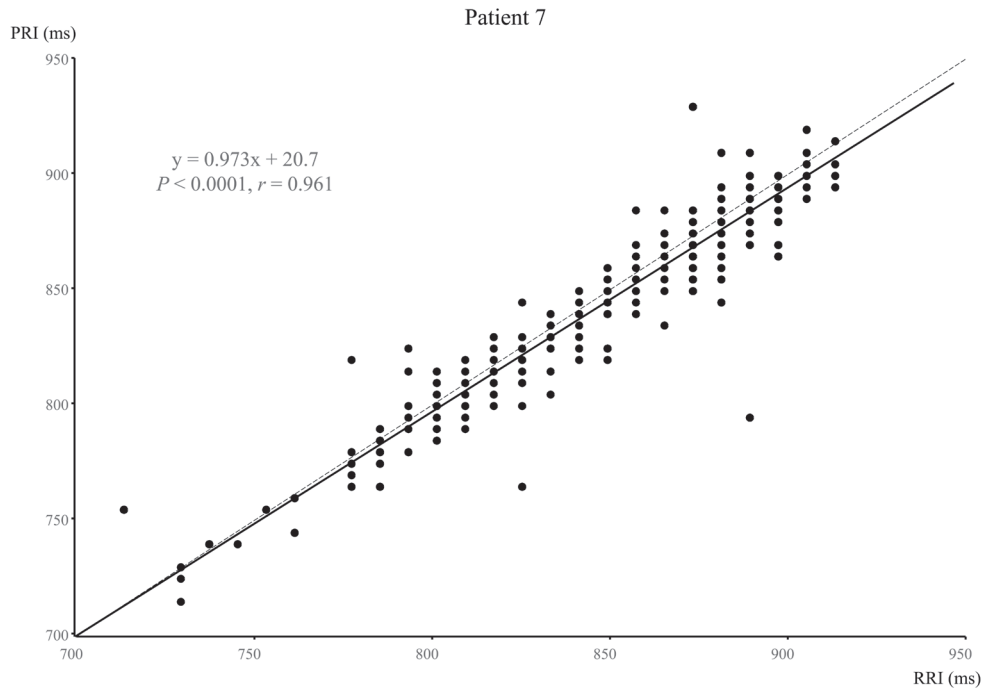$P < 0.0001, r = 0.690$

RRI (ms)

**Fig. A4.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 65-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 0.845x + 137.9, P < 0.0001, r = 0.690, n = 567). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.
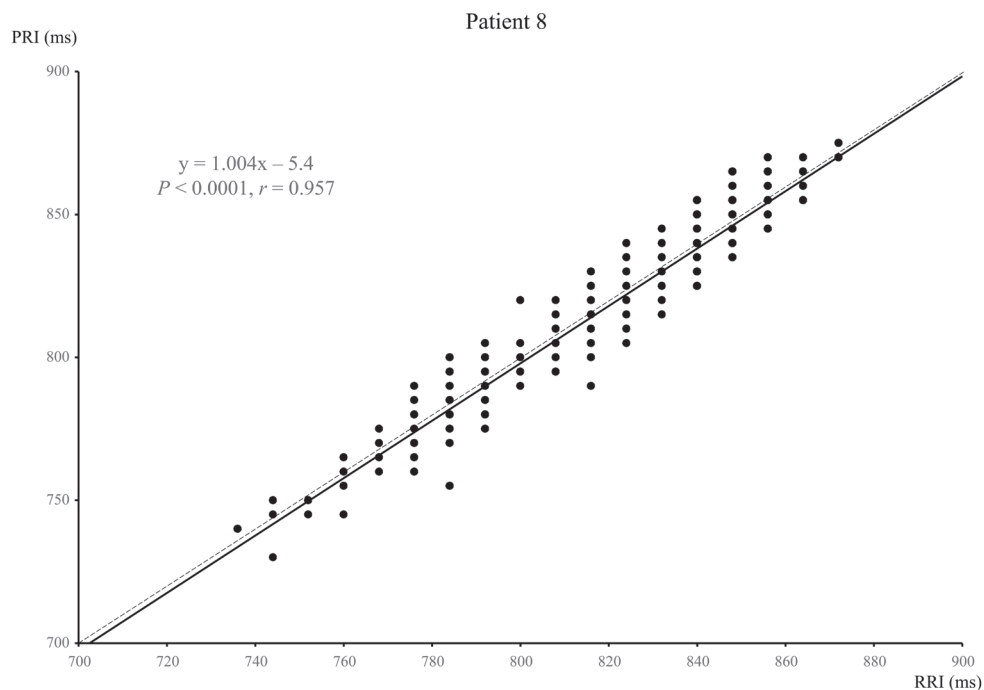
**Fig. A5.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 69-year-old male patient with chronic obstructive pulmonary disease and type 2 diabetes. A significant linear correlation was found (y = 0.749x + 137.9, $P < 0.0001$, $r = 0.760$, $n = 920$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.



**Fig. A6.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 70-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 0.853x + 133.7, $P < 0.0001$, $r = 0.851$, $n = 551$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.
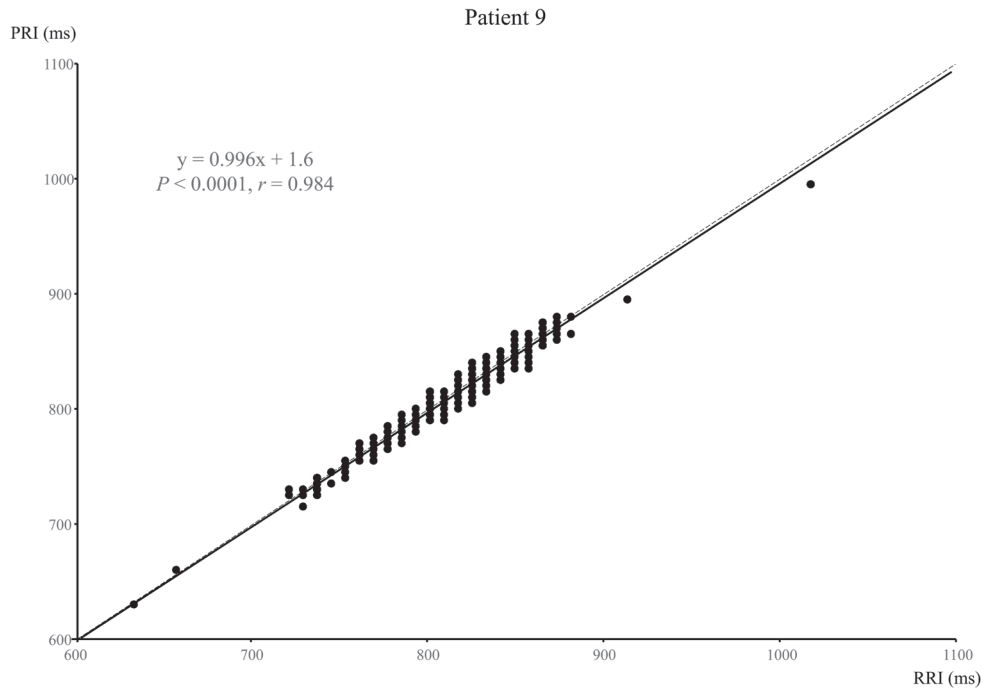
**Fig. A7.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 75-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 0.973x + 20.7, $P < 0.0001$, $r = 0.961$, $n = 700$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.
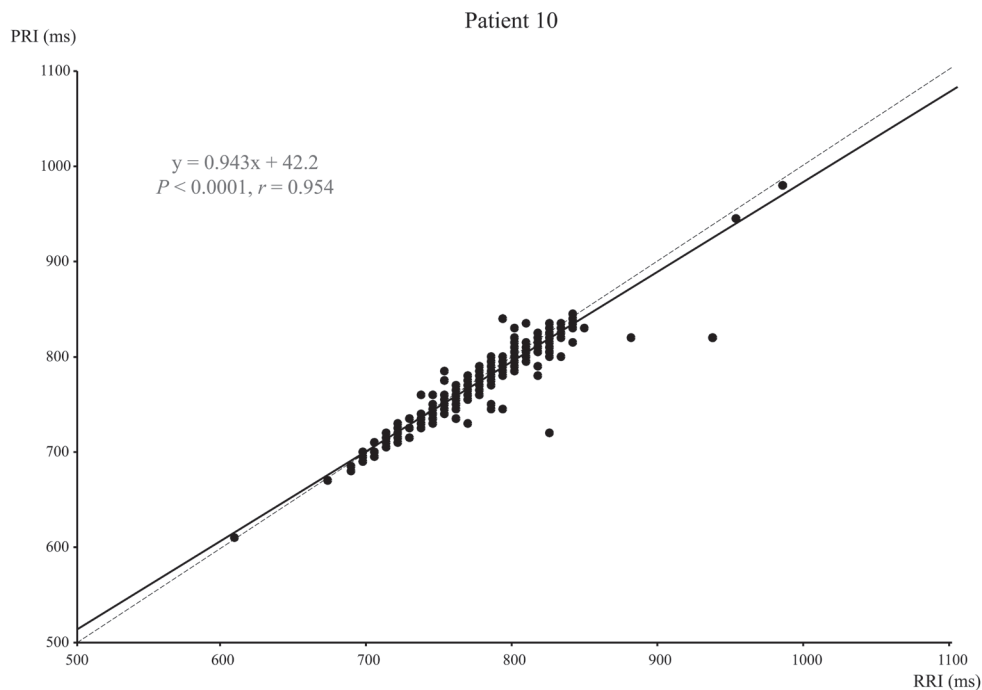


**Fig. A8.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 66-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 1.004x − 5.4, $P < 0.0001$, $r = 0.957$, $n = 620$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.

Patient 9



**Fig. A9.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in a 73-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 0.996x + 1.6, $P < 0.0001$, $r = 0.984$, $n = 624$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.

Patient 10



**Fig. A10.** The linear relationship between the RR interval (RRI) obtained using an electrocardiogram and the pulse rate interval (PRI) obtained using a pulse oximeter in an 81-year-old male patient with chronic obstructive pulmonary disease. A significant linear correlation was found (y = 0.943x + 42.2, $P < 0.0001$, $r = 0.954$, $n = 649$). The dotted line shows y = x. RRI, RR interval; PRI, pulse rate interval.