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Association between prognostic nutritional index and peritoneal dialysis discontinuation: a retrospective cohort study

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Abstract

Background Malnutrition is associated with discontinuing peritoneal dialysis (PD). The prognostic nutritional index (PNI), composed of serum albumin level and total lymphocyte count, has been suggested as a prognostic marker for mortality in patients undergoing PD. However, the relationship between PNI and PD discontinuation has not yet been well addressed. We evaluated the relationship between PNI and PD discontinuation in patients with end-stage kidney disease who initiated PD treatment.

Methods This retrospective cohort study included patients who underwent PD at a single academic hospital between 2007 and 2022. We examined the association between PNI (< 40 vs. ≥ 40) and PD discontinuation using Cox proportional hazards regression models. We used restricted cubic spline analysis to examine the continuous associations between the PNI and outcomes.

Results The mean age (and standard deviation) of the 91 patients was 57.1 ± 13.4 years; 72 (79.1%) discontinued PD during the median follow-up period of 25.0 months. Lower PNI was associated with an increased risk of PD discontinuation. The hazard ratios (95% confidence intervals) with three levels of adjustments were 1.74 (1.08, 2.79), 2.21 (1.32, 3.66), and 1.81 (1.01, 3.24) (reference: PNI ≥ 40). Restricted cubic spline analysis showed that a PNI < 40 was continuously associated with a higher risk of PD discontinuation.

Conclusion A lower PNI (< 40) was associated with a higher risk of PD discontinuation. Our findings suggest that evaluating the PNI may help identify patients at high risk of PD discontinuation and lead to appropriate nutritional management for dialysis maintenance.

Keywords Peritoneal dialysis, Prognostic nutritional index, Malnutrition, Albumin, Lymphocyte

Background

Peritoneal dialysis (PD) accounts for approximately 11% of the treatment modalities for end-stage kidney disease (ESKD) worldwide [1]. PD has several advantages over hemodialysis (HD), such as cost-effectiveness, fewer harmful hemodynamic effects, and preservation of residual kidney function [2, 3]. However, patients are often unwilling to discontinue PD and are forced to transition to HD after a shorter-than-expected period

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of PD treatment. Therefore, detecting patients at high risk of PD discontinuation is important for both dialysis modality selection and maintenance of PD treatment [2].

Malnutrition is an important factor in PD discontinuation and can be a modifiable factor [4]. Objective screening tools comprising laboratory markers and anthropometric parameters have been used to assess nutritional status [5]. The prognostic nutritional index (PNI) is a simple and useful nutritional marker calculated from the serum albumin level and total lymphocyte count. It has been widely used in the risk assessment of surgical intervention in patients with cancer [6]. In patients with ESKD, some studies have investigated the association between PNI and mortality, showing that a lower PNI is associated with higher mortality in both HD and PD patients [7–10]. However, there have been few reports on the relationship between PNI and PD discontinuation, and only one retrospective study has assessed the predictive values of nutritional indices for PD discontinuation [4].

In clinical settings, biomarkers and indices are often divided into categories based on optimal cutoff values. These objective criteria can help clinicians interpret data and select the optimal treatment [11]. To our knowledge, the association between well-recognized PNI cutoff values and PD discontinuation has not yet been examined. It may be important to investigate the association between the PNI and PD discontinuation using a well-recognized and reasonable cutoff value for the practical use of the PNI in clinical settings.

Consequently, this study aimed to examine the relationship between PNI and PD discontinuation in patients with ESKD who initiated PD treatment at an academic hospital by determining a certain cutoff value for PNI.

Methods

Study population and data source

This retrospective cohort study was conducted at a single academic hospital. The study cohort included patients who initiated PD treatment between April 1, 2007, and March 31, 2022. Patients aged < 20 years at baseline, those who did not receive PD treatment for at least a month, or those who switched from maintenance HD to PD were excluded from the study. All data were obtained from the electronic records of the Kumamoto University Hospital. Due to the anonymity of the patients included and the nonintrusive nature of the research, the requirement for written consent was waived. This study was approved by the Institutional Review Committee of the Kumamoto University Hospital (No. 2529).

Demographic, clinical, and laboratory measures

We obtained data on age, sex, height, weight, blood pressure, urine volume, information on the primary disease of ESKD, comorbidities, cardiovascular disease (CVD) events, CVD history or death, PD prescription, PD treatment period and peritonitis, HD treatment period, the use of renin–angiotensin–aldosterone system inhibitors, statins, diuretics, phosphate binders, vitamin D, and erythropoiesis-stimulating agents, and laboratory results from electronic medical records. Weight and height were used to calculate the body mass index (BMI).

Most laboratory parameters measured were obtained from the nearest day of PD initiation, which was within a week before or after initiation, including the levels of hemogram, albumin, urea nitrogen, creatinine, and electrolytes. Serum levels of ferritin, iron, total iron binding capacity, lipids, plasma brain natriuretic peptide (BNP), and intact parathyroid hormone (PTH) were measured within a month before or after PD initiation. Hemoglobin (Hb) A1c levels were measured within 3 months. The PNI was calculated using the following formula: (10 × serum albumin [g/dL]) + (0.005 × total lymphocyte count [/mm^3)] [6].

Outcome ascertainment

The outcome of interest was the discontinuation of PD. Based on previous reports, the discontinuation of PD was defined as a switch to HD or hybrid therapy with HD, kidney transplantation, or death [12, 13]. Censoring was performed at another dialysis clinic or at the end of the study.

Statistical analysis

Data are described as proportion, mean (± standard deviation, SD), or median (interquartile range, IQR), as appropriate. We divided the PNI levels into two categories (< 40 and ≥ 40) according to previous reports [6, 8]. We used the t-test, Mann–Whitney U test, chi-square test, or Fisher's exact test to assess patients' characteristics between PNI categories. We conducted a Kaplan–Meier analysis to estimate the survival rates between the PNI groups, and the survival estimates were compared using the log-rank test. To assess the relationship between PNI and PD discontinuation, we used Cox proportional hazards regression models using PNI ≥ 40 as a reference. Plots of log [− log (survival rate)] against log (survival time) were generated to test the proportionality of this assumption.

In Cox proportional hazards regression models, three models were examined based on the level of multivariate adjustment: (a) model 1: a minimally adjusted model that included PNI (< 40 and ≥ 40), (b) model 2: PNI, age, and

Table 1. Demographic and clinical characteristics of 91 PD patients, including patients in 2 groups of PNI

		Overall	PNI		*P* value
			<40	≥ 40	
		(n = 91)	(n = 42)	(n = 49)	
Age (years)	Mean (SD)	57.1 (13.4)	59.6 (12.9)	55.1 (13.7)	0.104
Sex (men)	n (%)	56 (61.5)	27 (64.2)	29 (59.2)	0.777
Diabetes mellitus	n (%)	40 (44.0)	25 (59.5)	15 (30.6)	0.011
Cause of end stage kidney disease					0.013
Diabetes nephropathy	n (%)	30 (33.0)	20 (47.6)	10 (20.4)	
Glomerulonephritis	n (%)	34 (37.4)	10 (23.8)	24 (49.0)	
Nephrosclerosis	n (%)	14 (15.4)	6 (14.2)	8 (16.3)	
Others	n (%)	10 (11.0)	6 (14.2)	4 (8.1)	
Unknown	n (%)	3 (3.2)	0	3 (6.1)	
CVD history	n (%)	22 (24.2)	14 (33.3)	8 (16.3)	0.100
Height (cm)	Median (IQR)	160.4 (152.3,169.8)	157.9 (149.7,169.3)	162.4 (154.1,170.0)	0.232
Weight (kg)	Median (IQR)	60.4 (51.5,69.3)	59.4 (51.5,70.0)	60.8 (52.0,69.1)	0.846
BMI (kg/m^2)	Median (IQR)	23.0 (21.0,26.3)	24.4 (20.9,27.0)	22.5 (21.0,25.0)	0.210
Systolic blood pressure (mmHg)	Mean (SD)	136.0 (19.4)	140.3 (21.8)	132.3 (16.3)	0.048
Diastolic blood pressure (mmHg)	Mean (SD)	78.0 (12.2)	78.3 (14.2)	77.7 (10.2)	0.797
Urine volume (ml)	Median (IQR)	1263.5 (1005.5,1652.2)	1168.5 (1000.0,1560.0)	1367.5 (1125.8,1897.0)	0.025
RAAS inhibitor	n (%)	69 (76.7)	34 (81.0)	35 (72.9)	0.516
Statin	n (%)	39 (43.3)	15 (35.7)	24 (50.0)	0.250
Diuresis	n (%)	52 (57.8)	29 (69.1)	23 (47.9)	0.070
Icodextrin	n (%)	36 (40.0)	24 (57.1)	12 (25.0)	0.004
CAPD	n (%)	50 (55.0)	24 (57.1)	26 (53.0)	0.858
Laboratory variables					
WBC(10^3/μl)	Median (IQR)	6.1 (4.8,7.1)	6.0 (4.9,7.1)	6.2 (4.5,7.1)	0.918
Lymphocyte (%)	Mean (SD)	22.1 (8.1)	19.0 (6.8)	24.8 (8.1)	<0.001
Hb (g/dL)	Median (IQR)	9.5 (8.5,10.2)	8.9 (8.2,9.8)	9.9 (9.2,10.4)	0.002
Alb (g/dl)	Mean (SD)	3.3 (0.5)	2.9 (0.4)	3.7 (0.4)	<0.001
Cr (mg/dL)	Mean (SD)	9.0 (2.6)	8.2 (2.8)	9.6 (2.2)	0.010
$eGFR_{cr}$ (mL/min/1.73m^2)	Median (IQR)	5.0 (4.0,6.0)	6.0 (5.0,7.0)	5.0 (4.0,5.0)	0.007
CRP (mg/dl)	Median (IQR)	0.2 (0.05,0.6)	0.4 (0.1,1.3)	0.07 (0.05,0.3)	<0.001
Ca (mg/dl)	Median (IQR)	8.3 (8.0,8.8)	8.1 (7.8,8.4)	8.6 (8.3,8.9)	<0.001
P (mg/dl)	Median (IQR)	5.8 (5.0,6.6)	5.3 (4.2,6.4)	6.0 (5.3,6.8)	0.021
intPTH (pg/ml)	Median (IQR)	251.0 (170.0,355.2)	212.0 (129.0,278.0)	294.0 (210.0,383.0)	0.001
PNI	Mean (SD)	40.0 (6.1)	34.6 (3.5)	44.6 (3.7)	<0.001

Categorical variables are presented as percentage; continuous variables are presented as mean±SD or median (IQR)

PNI prognostic nutritional index, *PD* peritoneal dialysis, *IQR* interquartile range, *SD* standard deviation, *CVD* Cardiovascular disease, *BMI* body mass index, *RAAS* renin angiotensin aldosterone system, *CAPD* continuous ambulatory peritoneal dialysis, *WBC* white blood cell, *Hb* hemoglobin, *Alb* albumin, *Cr* creatinine, *eGFR* estimated glomerular filtration rate, *CRP* C reactive protein, *intPTH* intact parathyroid hormone

sex, (c) model 3: PNI, age, sex, presence of diabetes mellitus, CVD history, Hb, and urine volume. The selected variables were based on previous studies [14–18]. Associations between continuous PNI and PD discontinuation across the three adjustment levels were also modeled using restricted cubic splines with knots at 10, 50, and 90 percentiles of the PNI.

Most analyses were performed using JMP version 12 (SAS Institute Inc., Cary, NC, USA). Kaplan–Meier and spline analyses were performed using Stata version 17.1 (Stata Corporation, College Station, TX, USA). Statistical significance was set at $P < 0.05$.

Results

In total, 119 patients had initiated PD in Kumamoto University Hospital during the study period. After excluding patients who switched from HD, discontinued PD within a month, or had missing data in the main analysis, the

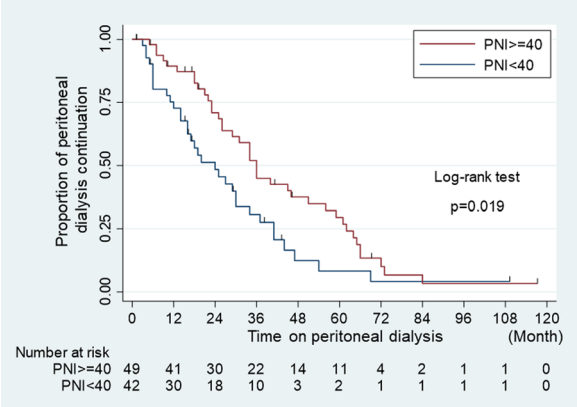

Fig. 1 Kaplan–Meier survival plots between two categories of PNI for PD discontinuation. The differences in survival were compared using the log-rank test for the entire cohort of 91 patients who underwent PD. The number at risk in each group divided by PNI < 40 and ≥ 40 is shown below the plots

final study population consisted of 91 patients (Additional file 1: Figure S1). The mean age of patients was 57.1 ± 13.4 years; 61.5% were males, and 44.0% had diabetes. Table 1 shows the baseline demographic, clinical, and laboratory characteristics of all patients and those in each PNI subset (< 40, and ≥ 40). Patients with PNI < 40 had a significantly higher prevalence of diabetes and exhibited significantly lower urine volume and Hb level than those with PNI ≥ 40 (Table 1).

The duration of PD therapy averaged 25.0 months (median) in the total cohort (Additional file 2: Table S1): 17.5 months in patients with PNI < 40 and 34.0 months in patients with PNI ≥ 40 ($P < 0.05$). A total of 72 patients (79.1%) discontinued PD therapy during the study period; 33 (78.6%) had PNI < 40, and 39 (79.6%) had PNI ≥ 40 (Additional file 3: Table S2). The incidences of peritonitis, CVD events, and death until PD discontinuation or censor were not significantly different between the two PNI categories (Additional file 2: Table S1). The causes of PD discontinuation are shown in Additional file 4: Figure S2 and Additional file 5: Table S3. When we compared the PNI < 40 group with the PNI ≥ 40 group, there was a significant difference in survival estimates by the log-rank test ($P = 0.019$) (Fig. 1).

In the Cox proportional hazards regression models before and after adjustment for age, sex, diabetes, CVD history, Hb level, and urine volume, a lower PNI was significantly associated with a higher risk of PD discontinuation (Table 2). When comparing the PNI < 40 group with the PNI ≥ 40 group, the hazard ratios (HRs) (95% confidence interval) of PD discontinuation in each model were 1,74 (1.08, 2.79), 2.21 (1.32, 3.66), and 1.81 (1.01, 3.24), respectively (Table 2). Additional file 6: Table S4 shows the HRs of the other adjusted variables in Models 2 and 3. Restricted cubic spline analysis showed that a lower PNI was continuously associated with a higher risk of PD discontinuation when the reference was set at PNI = 40 (Fig. 2). However, a higher PNI level showed no significant difference in the HR for PD discontinuation (Fig. 2).

Discussion

In this retrospective cohort study, we examined the association between PNI and PD discontinuation using the clinical data of PD patients in an academic hospital. A lower PNI level (< 40) was associated with a higher HR for PD discontinuation, and this association was consistent when we examined continuous associations between PNI and outcome with a reference level of PNI (PNI = 40).

The PNI consists of blood albumin level and lymphocyte count, and this index represents nutritional status [6]. PNI could be useful as a prognostic marker, including mortality, in patients with ESKD [7–10]. As malnutrition has been reported to be an important factor in PD discontinuation [18], the PNI may also serve as a useful marker for PD discontinuation. One observational study examined the association between several nutritional indices and PD discontinuation. The authors found that the PNI was a better prognostic marker than the geriatric nutritional risk index (GNRI) and controlling nutritional status (CONUT) scores, both of which are well-known prognostic markers for nutritional status

Table 2. Association of PNI with PD discontinuation using Cox proportional hazards models in 91 PD patients

Variables	Univariate analysis Model 1 HR (95% CI)	*P* value	Multivariate analysis Model 2 HR (95% CI)	*P* value	Multivariate analysis Model 3 HR (95% CI)	*P* value
PNI (≧40)	Ref		Ref		Ref	
PNI (＜40)	1.74 (1.08, 2.79)	0.022	2.21 (1.32, 3.66)	0.002	1.81 (1.01, 3.24)	0.046

Model 1: unadjusted

Model 2: adjusted age, sex

Model 3: adjusted age, sex, diabetes, CVD history, Hb, urine volume

PNI prognostic nutritional index, *PD* peritoneal dialysis, *HR* hazard ratio, *CI* confidence intervals, *CVD* Cardiovascular disease, *Hb* hemoglobin

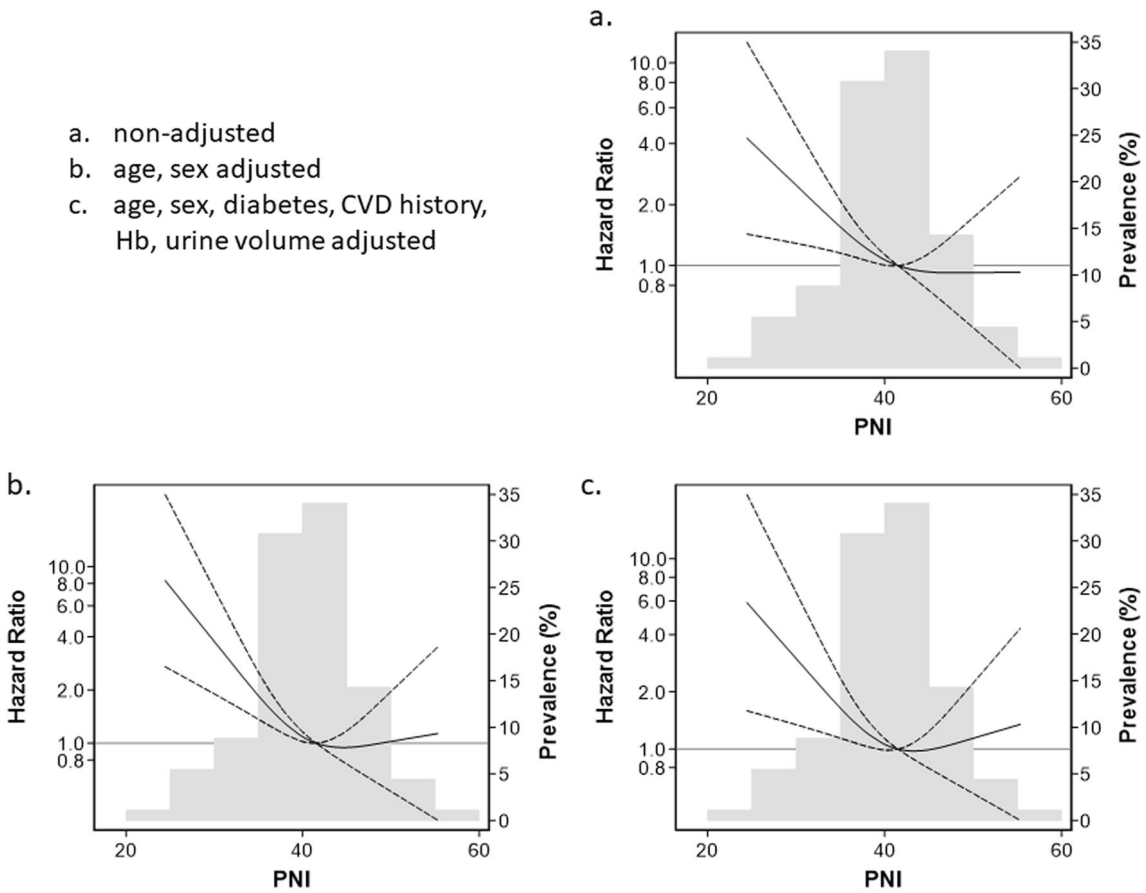

Fig. 2 Hazard ratios of PD discontinuation according to PNI by cubic splines of Cox regression analyses. Cubic spline models of Cox proportional regression analyses reflecting hazard ratios for PD discontinuation according to the PNI in a cohort of 91 patients who underwent PD are shown (**A**: model 1; **B**: model 2; **C**: model 3). Histograms show the frequencies of the participants. Solid and dotted lines represent hazard ratios and 95% confidence intervals, respectively. The reference value was set at PNI = 40

[4]. Additionally, they set the PNI cutoff value from the receiver operating characteristic (ROC) curve. They also discussed the need for further studies to determine and validate the optimal PNI cutoff value. In the present study, we used a PNI value of 40, a well-used cutoff value in the risk assessment of several diseases [6, 8, 19–23]. We found that a PNI < 40 can be a useful cutoff level for identifying the risk of PD discontinuation.

This study found an association between the PNI during the initiation period of dialysis and withdrawal from PD. Notably, up to 75% of patients are reported to be malnourished at PD initiation [24]. Malnutrition in PD patients has been reported to be associated with increased mortality and infections such as peritonitis, which may be reflected in the high mortality and infection rates as causes of PD discontinuation in the low PNI group in this study (Additional file 5: Table S3) [8–10, 25]. In addition, patients undergoing PD tend to lose protein more easily via the PD fluid [26]. Therefore, nutritional management and adequate dialysis prescriptions based on the assessment of nutritional status at PD initiation are extremely important for maintaining PD. Nutritional management is one of the most important topics in patients with kidney disease from the non-dialysis-dependent phase to the dialysis-dependent phase [27]. Based on our findings that nutritional status during PD initiation was associated with the risk of PD discontinuation, it is also important to ensure adequate nutritional status during the initiation period of dialysis through preemptive nutritional management. As the current study highlighted the PNI upon PD initiation, further studies are needed to clarify whether continuous nutritional intervention with adequate assessment, including PNI over time, can influence prognosis, including PD discontinuation.

Although the proportion of inadequate dialysis, including ultrafiltration failure and insufficient dialysis, among the causes of PD discontinuation was similar to that in a previous report [12], ultrafiltration failure was the

leading cause of PD discontinuation in the present study (Additional file 4: Figure S2). In previous studies, fluid overload was associated with PD technical failure, and hypoalbuminemia was associated with overhydration [28, 29]. From these points, it could be argued that an abnormal PNI may indicate fluid overload during the induction phase of dialysis because albumin is the main component of PNI. In this regard, Kang et al. showed an independent association between PNI and mortality by adjusting for fluid status in PD patients [8]. Therefore, in this study, we adjusted for residual urine volume, a predictor of overhydration, as a confounding factor and showed an association between PNI and PD discontinuation [30]. This association remained consistent when we adjusted for BNP levels instead of urine volume (Additional file 7: Table S5). These findings suggest that PNI is not only an indicator of fluid overload but may also be used as a marker of malnutrition and that PD patients with a low PNI level will require measures to improve nutritional status and fluid control.

This study had several limitations. First, because of the nature of the observational study, we could not clarify the causal relationship between PNI and PD discontinuation. Second, we could not exclude the possibility of residual confounding due to unmeasured confounders and the limitation of adjusting for variables due to the relatively small sample size. Third, because the participants' data were from a single academic hospital, generalizability should be considered when adapting the evidence of our findings.

Conclusions

We showed that a lower PNI was associated with a higher risk of PD discontinuation in a single academic hospital cohort. We propose that upon initiation of dialysis treatment, patients must be evaluated for their nutritional status and potential risks of PD treatment. To this end, our findings suggest that evaluating the PNI may help identify patients at high risk of PD discontinuation and lead to appropriate nutritional management for dialysis maintenance.

Abbreviations

PD	Peritoneal dialysis
ESKD	End-stage kidney disease
HD	Hemodialysis
PNI	Prognostic nutritional index
CVD	Cardiovascular disease
BMI	Body mass index
BNP	Brain natriuretic peptide
PTH	Parathyroid hormone
SD	Standard deviation
IQR	Interquartile range
Hb	Hemoglobin
HR	Hazard ratio
GNRI	Geriatric nutritional risk index
CONUT	Controlling nutritional status
ROC	Receiver operating characteristic

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41100-023-00511-1.

Additional file 1: Figure S1. Flowchart of patient selection in the study cohort.

Additional file 2: Table S1. Time on peritoneal dialysis therapy and incidence of peritonitis, cardiovascular event, and death until peritoneal dialysis discontinuation or censor in 91 PD patients and patients in 2 groups of PNI.

Additional file 3: Table S2. Case numbers of each outcome in all 72 cases and cases in 2 groups of PNI.

Additional file 4: Figure S2. The causes of PD discontinuation.

Additional file 5: Table S3. The causes of PD discontinuation in all 72 cases and cases in 2 groups of PNI.

Additional file 6: Table S4. The hazard ratios of other adjusted variables for PD discontinuation using Cox proportional hazards models in 91 PD patients.

Additional file 7: Table S5. Association of PNI with PD discontinuation in Cox proportional hazards models adjusting BNP.

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Author contributions

YM, JM, and MM designed the study. YM collected the data. YM and JM analyzed the data. YM and MM drafted the manuscript. HI, YN, MA, YI, YK, TM, TN, DF, AO, and TK supervised the study. All authors contributed substantially to the conception and interpretation of the work and critically revised the manuscript. The final manuscript was approved by all listed authors.

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Availability of data and materials

As the participants in this study did not agree that their data would be shared publicly, supporting data were not available.

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. It was approved by the Institutional Review Committee of Kumamoto University Hospital (No. 2529). Because of the anonymity of the patients studied and the nonintrusive nature of the research, the requirement for written consent was waived via the opt-out method on the hospital's information website.

Consent to publication

Because of the anonymity of the patients studied and the nonintrusive nature of the research, the requirement for written consent was waived via the opt-out method on the hospital's information website.

Competing interests

The authors declare no competing interests relevant to the contents of this article.

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