

Combined Therapy with Peritoneal Dialysis and Hemodialysis in Japan: Current Status and Criteria for Initiation and Discontinuation

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Abstract

Background

Combined therapy with peritoneal dialysis (PD) and hemodialysis (HD) is widely used in Japan for patients with inadequate dialysis and/or who develop fluid overload during PD. However, current patterns of practice and criteria for initiating or discontinuing combined therapy remain inadequately defined. We investigated the contemporary status of combined therapy and the criteria used in clinical practice in Japan.

Methods

This study consisted of two parts. In Study 1, we analyzed data on patients receiving combined therapy extracted from the Japanese Society for Dialysis Therapy Renal Data Registry via the Web-based Analysis of Dialysis Data Archives system. In Study 2, we conducted a nationwide questionnaire survey of PD facilities registered with the Japanese Society for Peritoneal Dialysis to evaluate current practice patterns and physician criteria for transfer from PD to combined therapy and from combined therapy to HD alone.

Results

Study 1 identified 1,963 patients receiving combined therapy (age, 62 ± 12 years; 71.9% male). Approximately 90% were asymptomatic or had mildly symptomatic performance status. HD and hemodiafiltration (HDF) were used in 62.5% and 34.1% of patients, respectively, and 89.2% received HD/HDF once weekly. In Study 2, responses were obtained from 210 of 314 facilities (67%). Among the 616 patients included in the survey, 548 (89.0%) had transferred from PD to combined therapy and were included in subsequent analyses. The main reasons for transfer were fluid overload (43.6%), inadequate dialysis (26.7%), or both (23.9%). Frequently used indicators for treatment decisions include Kt/V, β 2-microglobulin, uremic symptoms, fluid overload-related symptoms, and natriuretic peptides. Common threshold values were a total weekly Kt/V of 1.7 and a β 2-microglobulin level of 30 mg/L. For discontinuation of combined therapy to prevent encapsulating peritoneal sclerosis (EPS), frequently used indicators included PD duration, PD-related peritonitis, and peritoneal deterioration, with frequently used thresholds of 10 years, three peritonitis episodes, and a high peritoneal equilibration test category.

Conclusions

In Japan, combined therapy is primarily introduced to manage inadequate dialysis and fluid overload while preserving PD, and objective measures such as Kt/V and β 2-microglobulin are widely used.

Evidence-based guidance for initiation and discontinuation, particularly criteria for preventing EPS, is needed.

INTRODUCTION

Peritoneal dialysis (PD) is recommended as a first-line kidney replacement therapy (KRT) for patients with end-stage kidney disease (ESKD). This is because of the similar or superior patient survival, particularly during the initial period after dialysis initiation, preserved residual kidney function (RKF), a flexible schedule, increased freedom from the patient's perspective, and lower cost [1]. However, declines in RKF and progressive deterioration of the peritoneal membrane can lead to inadequate dialysis and/or fluid overload, making long-term continuation difficult [2, 3]. International and Japanese guidelines state that both adequate solute and fluid removal are essential for the better management of PD, and transfer to another KRT should thus be considered when these can no longer be achieved [4–7].

In such situations, instead of direct transfer to conventional thrice-weekly hemodialysis (HD), combined therapy with PD and HD, generally in the form of 5–6 days of PD and 1–2 HD sessions per week, is widely used in Japan. Currently, approximately 10,000 patients are receiving PD in Japan, of whom about 20% are undergoing combined therapy [8]. The widespread use of combined therapy in Japan is largely attributable to two factors. The first is the over 14-year wait time for cadaveric kidney transplantation opportunities, resulting in prolonged dialysis dependence and leading many patients to remain on PD for extended periods. Second, under the universal health insurance system in Japan, dialysis-related medical expenses are largely covered by public funding regardless of dialysis modality. Although interventional studies are difficult to conduct, several observational studies have already reported that transfer from PD to combined therapy improves both inadequate dialysis and fluid overload [9–14]. In addition, several studies have suggested that combined therapy is associated with better quality of life [14, 15]. We conducted one retrospective and two prospective studies, and found that inadequate dialysis, fluid overload, function of the peritoneal membrane, and erythropoiesis-stimulating agent (ESA) responsiveness improved after transfer to combined therapy [16–18]. Regarding patient survival or hospitalization, as more important clinical outcomes, combined therapy has also been reported to be non-inferior to HD alone [18–23].

In clinical practice, lower Kt/V urea, higher levels of serum β_2 microglobulin, and uremic symptoms (including appetite loss, nausea or vomiting, malnutrition, ESA hyporesponsiveness, and restless leg syndrome) are used as indicators of inadequate dialysis, whereas hypertension, abnormal findings on chest radiography (including heart enlargement or pleural effusion), and clinical symptoms including edema or anasarca are used as indicators of fluid overload. The presence of these findings prompts consideration of transfer from PD to combined therapy, or from combined therapy to HD alone [24, 25]. In addition, longer duration of PD, frequent PD-related peritonitis, and peritoneal deterioration as represented by a higher dialysate-to-plasma ratio of creatinine (D/P Cr) obtained from a peritoneal equilibration test (PET) are generally used as criteria for PD discontinuation and transfer to HD alone, with the aim of preventing encapsulating peritoneal sclerosis (EPS) [24, 25]. However, the scientific

evidence in support of these criteria remains limited. Further, the actual implementation of combined therapy in clinical facilities across Japan is unclear.

The present study aimed to clarify how combined therapy is utilized in routine clinical practice in Japan and to elucidate the criteria used by Japanese physicians when considering transfer from PD to combined therapy or from combined therapy to HD alone. This study comprised two parts. In Study 1, we aimed to elucidate the recent epidemiology, including patient characteristics and prescriptions of combined therapy using a large-scale registry of Japanese dialysis patients. In Study 2, we aimed to elucidate the prescription practices of combined therapy and the criteria for transfer from PD alone to combined therapy or from combined therapy to HD alone, using data obtained from a nationwide questionnaire survey of institutions managing patients receiving PD.

MATERIALS AND METHODS

In Study 1, we used the Web-based Analysis of Dialysis Data Archives (WADDA) system. The Japanese Society for Dialysis Therapy (JSDT) has conducted annual surveys of dialysis facilities throughout Japan since 1968. The total number of patients receiving chronic dialysis therapy as of the end of 2022 was 347,474, and 2,138 patients received combined therapy with PD and HD [8]. The JSDT Renal Data Registry (JRDR) includes patient demographic data, laboratory findings, treatment conditions and outcomes. The WADDA system is an automated data-transfer platform in the JRDR, accessed through the JSDT website (<https://www.jsdt.or.jp/english/>). Since this system provides only anonymized and already aggregated data, we could only perform cross-sectional, descriptive epidemiological analyses without multivariable adjustment. Using this database, we collected data on patients receiving combined therapy as of the end of 2022, including demographic characteristics, medical condition, activity status, laboratory data and prescription, procedure and efficiency of dialysis.

In Study 2, a nationwide questionnaire survey was conducted among facilities managing patients receiving PD and registered with the Japanese Society of Peritoneal Dialysis (JSPD). This questionnaire survey consisted of the following three components (Additional file 1):

1. Conditions for the management of combined therapy in each facility.
2. Consciousness survey (opinions of dialysis physicians in each facility) for indication criteria of combined therapy, i.e., criteria for transfer from PD to combined therapy
3. Consciousness survey (opinions of dialysis physicians from each facility) regarding discontinuation criteria for combined therapy; i.e., criteria for transfer from combined therapy to HD alone

The questionnaire survey on conditions for combined therapy in each facility included the following items: PD prescription before the start of combined therapy; reasons for transfer to combined therapy; and dialysis prescription after transfer to combined therapy. On the other hand, the questionnaire survey on opinions regarding indications and discontinuation criteria for combined therapy included the following items: markers and threshold values for inadequate dialysis; fluid overload; clinical findings;

and other reasons. In addition, markers and threshold values for higher risk of EPS and transfer from combined therapy to HD alone were requested.

Categorical variables are presented as numbers and percentages, whereas continuous variables are presented as mean $\pm$ standard deviation or median and interquartile range, as appropriate.

RESULTS

Study 1

At the end of 2022, a total of 2,138 patients had received combined therapy with PD and HD. Among these, clinical data from 1,963 patients (males, $n = 1,411$ [71.9%]; mean age, 62 ± 12 years; median dialysis duration 4 years [3–7 years]) extracted from the WADDA system are presented in Table 1. The primary kidney disease was chronic glomerulonephritis in 626 (31.9%), diabetic kidney disease in 643 (32.8%) and nephrosclerosis in 258 (13.1%). The proportions of patients with a history of ischemic heart disease, cerebral hemorrhage, cerebral infarction or stroke, peripheral amputation, and EPS were 24.0%, 4.7%, 11.1%, 2.0%, and 0.6%, respectively. Regarding performance status, almost 90% were asymptomatic or only mildly symptomatic. Approximately 30% of patients had some form of regular exercise habit. Levels of blood urea nitrogen (BUN), creatinine (Cr), hemoglobin (Hb) and β_2 microglobulin were 57 ± 16 mg/dL, 12.1 ± 3.2 mg/dL, 11.3 ± 1.4 g/dL, and 33.0 mg/L (29.1–37.7 mg/L), respectively.

Clinical characteristics related to PD were as follows. The proportions of patients using icodextrin solution and automated peritoneal dialysis (APD) were 74.3% and 53.6%, respectively. The D/P Cr ratio obtained from PET was 0.65 ± 0.14 . Regarding PD exchange method, 75.2% of patients used device connection systems. Rates of PD-related peritonitis and exit-site infection were 0.15 ± 0.54 episodes/year and 0.40 ± 1.16 episodes/year, respectively.

Regarding clinical characteristics related to combined therapy, 62.5% of patients were receiving HD, whereas 34.1% were receiving hemodiafiltration (HDF) as combined therapy and 89.2% of patients were receiving combined HD/HDF once weekly. An arteriovenous fistula (AVF) was used for vascular access in 94.3% of patients.

Table 1. Current state of combined therapy with PD and HD in Japan (n = 1,963)			
Variable	Value	Variable	Value
Male [%]	1,411 (71.9%)	Laboratory data	
Age [years]	62 ± 12	BUN [mg/dL]	57 ± 16
Dialysis duration [years]	4 (3–7)	Cr [mg/dL]	12.1 ± 3.2
Primary kidney disease		Alb [g/dL]	3.2 ± 0.5
Chronic glomerulonephritis	626 (31.9%)	CRP [mg/dL]	0.17 (0.06–0.49)
Diabetic kidney disease	643 (32.8%)	Corrected calcium [mg/dL]	9.2 ± 0.8
Nephrosclerosis	258 (13.1%)	Phosphate [mg/dL]	5.5 ± 1.4
Polycystic kidney disease	56 (2.9%)	Hb [g/dL]	11.3 ± 1.4
Other/unknown	380 (19.4%)	β2 microglobulin [mg/L]	33.0 (29.1–37.7)
Medical history		PD-related characteristics	
Ischemic heart disease	360 (24.0%)	Icodextrin use	994 (74.3%)
Cerebral hemorrhage	68 (4.7%)	APD use	999 (53.6%)
Cerebral infarction or stroke	162 (11.1%)	PET performed	826 (63.8%)
Peripheral amputation	29 (2.0%)	D/P Cr ratio	0.65 ± 0.14
Hip fracture	28 (1.9%)	Dialysate volume [L/day]	7.5 (6.0–9.0)
EPS	9 (0.6%)	Urinary volume [mL/day]	20 (0–200)
Dementia	42 (3.3%)	UFR [mL/day]	1000 (600–1200)
Physical findings		PD exchange method	
Height [cm]	164 ± 9	Manual connection	326 (24.8%)
Body weight [kg]	65.8 ± 14.5	Device connection	989 (75.2%)
BMI [kg/m ²]	23.3 ± 3.8	Infection complication	
Blood pressure [mmHg]	150 ± 25 / 82 ± 14	PD-related peritonitis (in a year)	144 (10.6%)
Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; EPS, encapsulating peritoneal sclerosis; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; Alb, albumin; CRP, C-reactive protein; Hb, hemoglobin; APD, automated peritoneal dialysis; PET, peritoneal equilibration test; D/P Cr, dialysate-to-plasma ratio of creatinine; UFR, ultrafiltration rate; HDF, hemodiafiltration; AVF, arteriovenous fistula; AVG, arteriovenous graft.			

Table 1. Current state of combined therapy with PD and HD in Japan (n = 1,963)			
Performance status		Annual rate [episodes/year]	0.15 ± 0.54
Asymptomatic	724 (60.0%)	Exit-site infection (in a year)	269 (19.8%)
Mild symptoms	365 (30.2%)	Annual rate [episodes/year]	0.40 ± 1.16
Ambulatory > 50% of daytime	75 (6.2%)	Combined dialysis modality	
Bedridden > 50% of daytime	28 (2.3%)	Combined with HD	1,226 (62.5%)
Completely bedridden	15 (1.2%)	Combined with HDF	669 (34.1%)
Exercise habits		Other combinations	68 (3.5%)
None or almost none	545 (63.0%)	Frequency of combined HD/HDF	
Less than once per week	62 (7.2%)	Once per week	1,502 (89.2%)
About once per week	93 (10.8%)	Twice per week	118 (7.0%)
2–3 times per week	85 (9.8%)	Three times per week	37 (2.2%)
4–5 times per week	23 (2.7%)	Others	26 (1.5%)
Daily/almost daily	57 (6.6%)	Vascular access	
		AVF	1,153 (94.3%)
		AVG	35 (2.9%)
		Superficialized artery	26 (2.1%)
		Others (including catheter)	9 (0.7%)
Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; EPS, encapsulating peritoneal sclerosis; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; Alb, albumin; CRP, C-reactive protein; Hb, hemoglobin; APD, automated peritoneal dialysis; PET, peritoneal equilibration test; D/P Cr, dialysate-to-plasma ratio of creatinine; UFR, ultrafiltration rate; HDF, hemodiafiltration; AVF, arteriovenous fistula; AVG, arteriovenous graft.			

Study 2

A questionnaire survey was conducted at 314 facilities across Japan, of which 210 (67.0%) responded. The total number of patients who received combined therapy at a responding facility was 616. Among these, 548 (89.0%) were transferred from PD, 46 (7.5%) were transferred from HD, and 22 (3.6%) started

combined therapy at dialysis initiation. The following analyses were restricted to patients who transferred from PD to combined therapy.

Table 2 shows conditions for the management of combined therapy with PD and HD at these institutions. Before the start of combined therapy, PD was performed 7 days/week in 66.0% of patients and 6 days/week in 28.9%. Proportions of patients using icodextrin solution and APD were 82.6% and 55.5%, respectively. The main reasons for transfer to combined therapy were inadequate dialysis in 26.7%, fluid overload in 43.6%, both inadequate dialysis and fluid overload in 23.9%, and PD-related infection (including peritonitis and tunnel or exit-site infection) in 2.3%. Regarding the clinical characteristics related to combined therapy, 68.1% of patients received HD, whereas 28.9% received on-line HDF as combined therapy and 65.8% of patients received combined HD/HDF at the same PD management facility. Almost 30% of patients had at least one day each week when neither PD nor HD was performed, defined as a “PD holiday.”

Table 2
Conditions for management of combined therapy with PD and HD

Variable	Value
PD prescription just before the start of combined therapy	
Frequency of PD	
7 days/week	66.0%
6 days/week	28.9%
5 days/week	4.6%
4 days/week	0.5%
Icodextrin use	82.6%
APD use	55.5%
Main reasons for transfer to combined therapy	
Inadequate dialysis	26.7%
Fluid overload	43.6%
Both inadequate dialysis and fluid overload	23.9%
Decrease in abdominal capacity	0.2%
Pleuroperitoneal communication	0.4%
Difficulty of procedure	0.2%
PD-related peritonitis	1.6%
Tunnel or exit-site infection	0.7%
Other	2.8%
Dialysis prescription after transfer to combined therapy	
Combined dialysis modality	
Combined with HD	68.1%
Combined with online HDF	28.9%
Combined with I-HDF	2.9%
Dialysis session length	
< 3 h	0.3%
Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; APD, automated peritoneal dialysis; HDF, hemodiafiltration; I-HDF, intermittent infusion hemodiafiltration.	

Variable	Value
3–4 h	16.8%
≥4 h	82.6%
HD/HDF management facility	
Same as PD management facility	65.8%
Other than PD management facility	34.2%
PD holiday	31.2%
Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; APD, automated peritoneal dialysis; HDF, hemodiafiltration; I-HDF, intermittent infusion hemodiafiltration.	

Consciousness survey for indication criteria of combined therapy

From the survey, uremic symptoms leading to consideration of transfer from PD to combined therapy were appetite loss, nausea or vomiting (59.0%), ESA hyporesponsiveness (41.9%), malnutrition (35.7%), restless leg syndrome (27.1%), and others including skin rash, itchiness, cognitive disturbance, consciousness disturbance, fatigue, and peripheral neuropathy. Figure 1 shows survey responses regarding criteria for inadequate dialysis and the associated threshold values. Commonly used indicators were $\beta 2$ microglobulin (50.0%), total Kt/V urea (27.1%), BUN (15.7%), Cr (7.6%) and total weekly creatinine clearance (Ccr) (6.7%). Less frequent responses were phosphate, Hb, urinary volume, brain natriuretic peptide (BNP), pericardial effusion, and PET category. The most used threshold values for $\beta 2$ microglobulin and total Kt/V urea were 30 mg/L (60.0%) and 1.7 (65.8%), respectively. Figure 2 shows survey responses regarding criteria for fluid overload and threshold values. Commonly used indicators were clinical symptoms including edema, dyspnea, or orthopnea (84.8%), hypertension (36.2%), BNP (21.0%), human atrial natriuretic peptide (HANP) (10.5%), and N-terminal prohormone of brain natriuretic peptide (NTproBNP) (5.7%). The most used threshold values of BNP and HANP were 500 pg/mL (13.2%) and 100 or 200 pg/mL (22.2%), respectively. Some facilities reported that no clearly defined threshold values were in use, with decisions to initiate combined therapy instead based on individual patient circumstances, cardiac function, or a progressive increase in levels. Reasons for transfer from PD to combined therapy, other than inadequate dialysis and fluid overload, included difficulty performing PD (31.9%), PD-related peritonitis (30.0%), pleuroperitoneal communication (23.3%), tunnel or exit-site infection (19.5%), reduction in abdominal cavity capacity (14.8%), abdominal surgery (1.0%), and hernia (1.0%).

Consciousness survey regarding discontinuation criteria for combined therapy

Survey responses regarding uremic symptoms leading to consideration for transfer from combined therapy to HD alone were appetite loss, nausea or vomiting (55.7%), ESA hyporesponsiveness (41.4%), malnutrition (36.6%), restless leg syndrome (24.7%), and others including skin rash, itchiness, cognitive disturbance and consciousness disturbance. Figure 3 shows survey responses regarding criteria for inadequate dialysis and threshold values. Commonly used indicators were $\beta 2$ microglobulin (32.9%), total Kt/V urea (15.2%), BUN (14.3%), Cr (8.6%) and total weekly Ccr (3.3%). Other minority opinions were clear space, Hb, and PET category. The frequently used threshold values of $\beta 2$ microglobulin and total Kt/V urea were 30 mg/L (47.1%) or 35 mg/L (35.4%) and 1.7 (38.9%), respectively. Figure 4 shows survey responses regarding criteria for fluid overload and threshold values. Commonly used indicators were clinical symptoms including edema, dyspnea, or orthopnea (77.1%), hypertension (34.3%), BNP (21.0%), HANP (10.5%), NTproBNP (5.7%), and interdialytic weight gain (3.3%). The most used threshold values for BNP and HANP were 220 pg/mL (22.2%) and 100 pg/mL (42.9%), respectively. Some facilities reported that no clearly defined threshold values were in use, with the decision to discontinue combined therapy based instead on individual patient circumstances, cardiac function, or a progressive increase in levels. Reasons for transfer from combined therapy to HD alone, other than inadequate dialysis and fluid overload, included PD-related peritonitis (54.3%), difficulty performing PD (46.2%), tunnel or exit-site infection (34.3%), pleuroperitoneal communication (29.0%), reduction in abdominal cavity capacity (15.2%), hernia (1.0%), abdominal surgery (0.5%), and omental wrapping (0.5%).

Figure 5 shows survey responses regarding the criteria and threshold values used for discontinuing combined therapy, with the aim of preventing EPS. Commonly used indicators were PD duration (39.0%), PD-related peritonitis (34.8%), and peritoneal deterioration (28.1%). The most used threshold values for PD duration, number of episodes of PD-related peritonitis, and D/P Cr ratio were 10 years (48.6%), 3 times (69.6%), and 0.81 or “high” category (56.5%), respectively.

DISCUSSION

The present study clarified routine clinical practice for combined therapy and criteria for the initiation and discontinuation of combined therapy in Japan using a large-scale registry of Japanese dialysis patients and a nationwide questionnaire survey.

In Study 1, demographic data including sex, age, dialysis duration, primary kidney disease, medical history, performance status and exercise habits were similar to those of the patients on PD alone [8]. Interestingly, age was younger (62 ± 12 , 66 ± 15 , and 71 ± 11 for patients on combined therapy, PD alone, and HD/HDF, respectively) and performance status, defined as asymptomatic or mild symptoms, was better (90.2%, 82.9%, and 71.1% for patients on combined therapy, PD alone, and HD/HDF, respectively). These findings suggest that patients who are active and have a good performance status are more likely to undergo PD, especially combined therapy. Regarding PD-related characteristics, approximately three-fourths of patients used icodextrin solution and half of patients used APD systems. As expected, urinary volume was lower among patients on combined therapy than those on PD alone (20 (0-200) vs. 700 (300–1100)). Regarding the status of the management of combined therapy, approximately 60% of

patients underwent HD as a combined therapy and 90% of patients underwent HD/HDF once per week. Most patients used an AVF for vascular access. Of note, the incidence of PD-related peritonitis was 0.15 episodes/year, lower than the 0.20 episodes/year reported for the overall PD population [8].

In Study 2, we were able to elucidate how combined therapy is practiced in Japan by conducting a nationwide questionnaire survey. Most patients had been transferred from daily PD to combined therapy. Among them, 70% underwent HD and 30% underwent HDF, with each treatment session lasting at least 4 h. Regarding the main reasons for transfer to combined therapy, almost 95% of patients transferred to combined therapy due to inadequate dialysis and/or fluid overload. This proportion was similarly high to that reported in previous retrospective studies, suggesting that many patients on PD who experienced inadequate dialysis and/or fluid overload were able to continue PD, rather than discontinuing, thanks to the introduction of combined therapy [9, 10, 16].

Consciousness surveys revealed that Kt/V and β_2 microglobulin, in addition to uremic symptoms, are frequently used in the indication and discontinuation criteria for combined therapy among Japanese dialysis physicians. Frequently used threshold values are 1.7 for Kt/V and 30 or 35 mg/L for β_2 microglobulin. In previous guidelines, a total weekly Kt/V of 1.7 was recommended as the target for dialysis adequacy [4, 7]. Theoretically, Kt/V cannot be used for the assessment of dialysis efficacy among patients receiving combined therapy. However, indicators such as clear space [26], which have been reported as useful for evaluating dialysis efficacy in this patient population, have not yet been widely adopted in clinical practice in Japan. Meanwhile, β_2 microglobulin is well-known to predict mortality for patients on HD [27], and the Japanese guideline recommends maintaining predialysis β_2 microglobulin levels below 25 or 30 mg/L [28]. Among PD, we reported higher β_2 microglobulin levels as an independent risk factor for the development of EPS, and the optimal threshold was 37 mg/L [29]. Since then, higher β_2 microglobulin levels have been widely used as criteria for initiating and discontinuing combined therapy. However, a recent analysis using JRDR showed that higher β_2 microglobulin levels were not associated with patient survival among patients on PD, at least in univariate analyses [30]. Further discussion is thus warranted regarding the use of β_2 microglobulin as a marker for PD management. Regarding the indicators for fluid overload, physical findings including edema, dyspnea or orthopnea, hypertension and biomarkers including BNP, HANP or NTproBNP were frequently used. No solid threshold values were identified for these biomarkers.

Prevention of EPS, the most serious complication of PD, represents an important challenge for dialysis physicians. Prolonged PD duration, recurrent episodes of PD-related peritonitis, and peritoneal deterioration are well-known risk factors for EPS [7, 31]. Although unsupported by large-scale clinical studies, the present survey confirmed that a management strategy of discontinuing PD itself, taking into account the risk of EPS, has become widely accepted when patients have undergone PD for approximately 10 years, are classified to a high PET category, or have experienced three episodes of PD-related peritonitis. Notably, these indicators were derived from clinical experience during the era of acidic solutions, and the incidence of EPS has decreased in the era of biocompatible neutral solutions. Indeed,

whereas previous guidelines emphasized caution regarding long-term PD [32], this statement has been omitted from the most recent guidelines [7].

CONCLUSIONS

Using a nationwide dialysis registry and a nationwide questionnaire survey, we characterized contemporary clinical practice in combined therapy with PD and HD in Japan. Combined therapy was most commonly introduced in patients with inadequate dialysis and/or fluid overload and was typically performed as once-weekly HD or HDF in combination with ongoing PD. Japanese dialysis physicians frequently use Kt/V, β_2 microglobulin, uremic symptoms, and indicators of fluid overload when considering initiation or discontinuation of combined therapy. In addition, PD duration, PD-related peritonitis, and peritoneal deterioration are widely used as criteria for discontinuing PD to prevent EPS. However, many of these criteria are based on historical experience. Further studies are clearly needed to establish evidence-based indicators and threshold values for optimizing the initiation and discontinuation of combined therapy in patients receiving PD.

Abbreviations

PD	peritoneal dialysis
KRT	kidney replacement therapy
ESKD	end-stage kidney disease
RKF	residual kidney function
HD	hemodialysis
ESA	erythropoiesis-stimulating agent
D/P Cr	dialysate-to-plasma ratio of creatinine
PET	peritoneal equilibration test
EPS	encapsulating peritoneal sclerosis
WADDA	the Web-based Analysis of Dialysis Data Archives
JSDT	the Japanese Society for Dialysis Therapy
JRDR	

the Japanese Society for Dialysis Therapy Renal Data Registry

JSPD

the Japanese Society of Peritoneal Dialysis

BUN

blood urea nitrogen

Cr

creatinine

Hb

hemoglobin

APD

automated peritoneal dialysis

HDF

hemodiafiltration

AVF

arteriovenous fistula

Ccr

creatinine clearance

BNP

brain natriuretic peptide

HANP

human atrial natriuretic peptide

NTproBNP

N-terminal prohormone of brain natriuretic peptide

Declarations

Ethical approval and consent to participate

Regarding Study 1, the Medical Ethics Committee of the JSDT allows for approval from an ethics committee for each protocol to be waived, and all individual participants were provided the opportunity to opt out. Regarding Study 2, the Medical Ethics Committee of the JSPD approved the study (approval no. 2025-01), and the study was conducted in accordance with the Declaration of Helsinki. Since all data were fully anonymized, the need to obtain written informed consent from patients was waived by the ethics committee, and all individual participants were provided the opportunity to opt out.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the JSDT and the JSPD, but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. However, data are available from the authors upon reasonable request and with permission of the JSDT and JSPD.

Competing interests

YM received honoraria from Vantive International, Inc. and Terumo Corporation. KS received honoraria from Japan Medical Supply Corporation. No other authors have any conflicts of interest to declare.

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Authors' contributions

YM, KS, MI, HI, MB, MM, MT, TK, HY, and MN conceived and designed the study, developed the questionnaire, evaluated the survey results, and drafted the manuscript. YM analyzed the results and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures

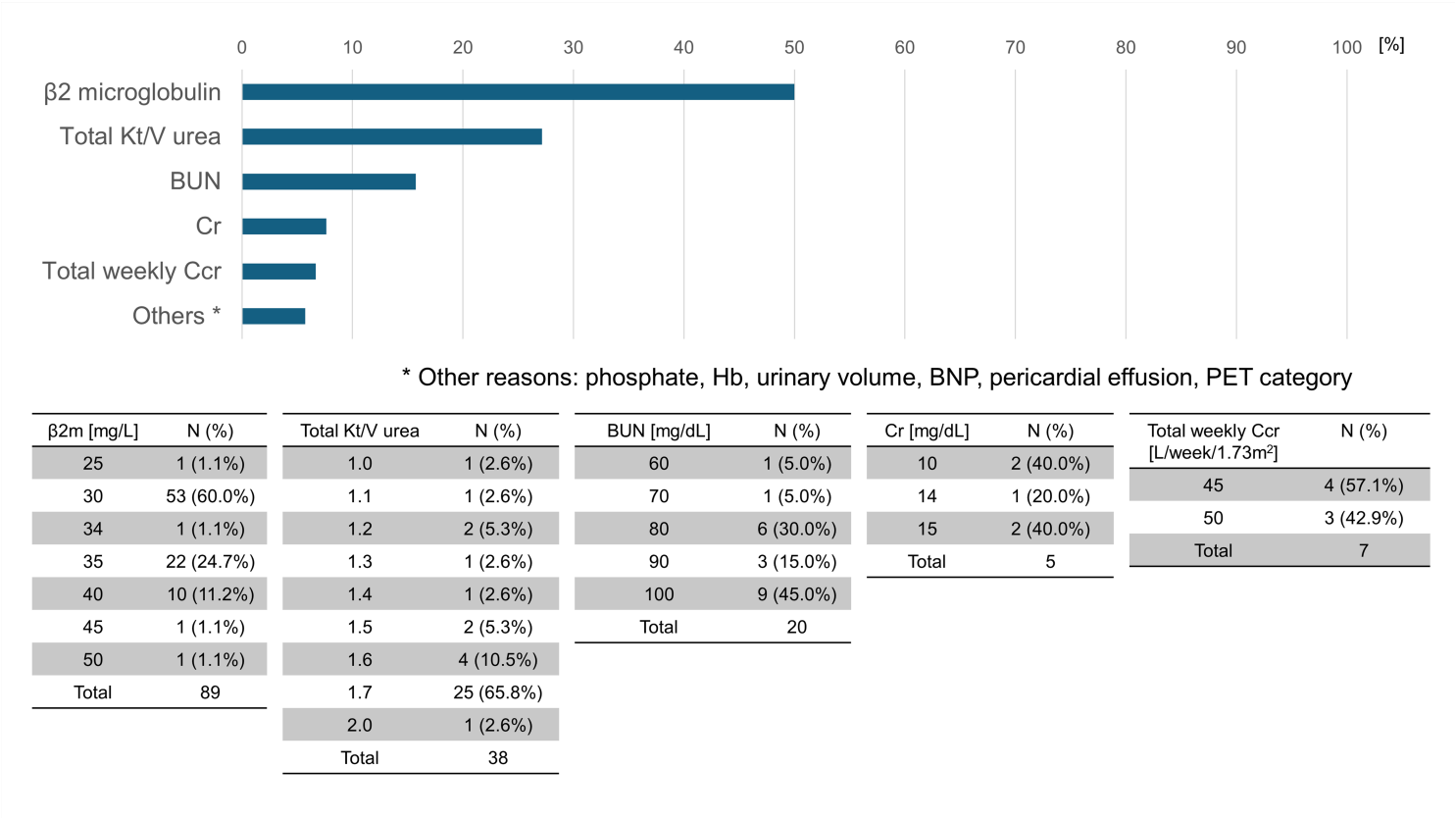


Figure 1

Indicators and threshold values for inadequate dialysis for transfer from PD to combined therapy with PD and HD

Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; BUN, blood urea nitrogen; Cr, creatinine; Ccr, creatinine clearance; Hb, hemoglobin; BNP, brain natriuretic peptide; PET, peritoneal equilibration test; β2M, β2 microglobulin.

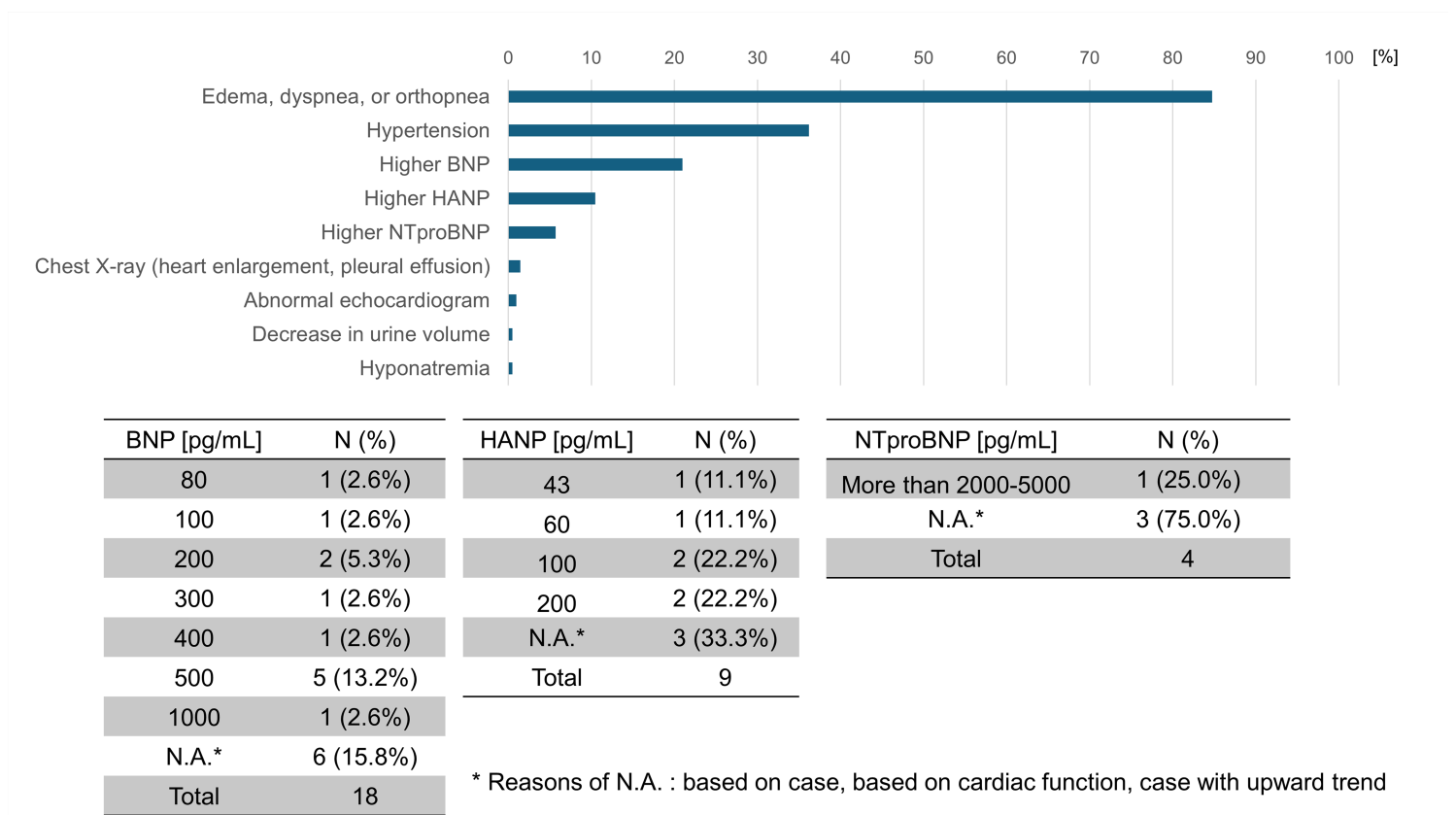


Figure 2

Indicators and threshold values for fluid overload for transfer from PD to combined therapy with PD and HD

Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; BNP, brain natriuretic peptide; HANP, human atrial natriuretic peptide; NTproBNP, N-terminal prohormone of brain natriuretic peptide; N.A., not applicable.

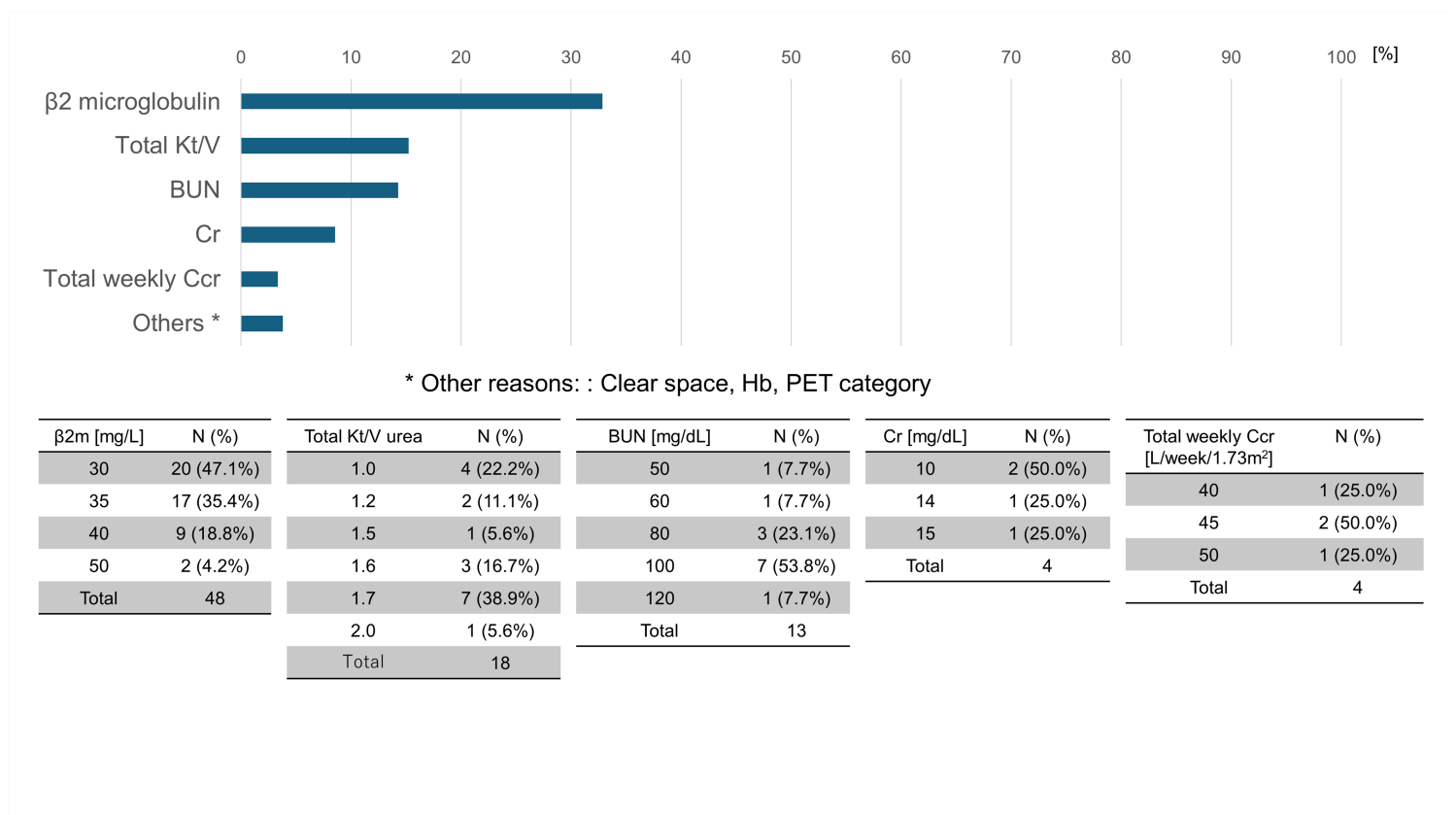


Figure 3

Indicators and threshold values for inadequate dialysis for transfer from combined therapy with PD and HD to HD alone

Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; BUN, blood urea nitrogen; Cr, creatinine; Ccr, creatinine clearance; Hb, hemoglobin; PET, peritoneal equilibration test; β2M, β2 microglobulin.

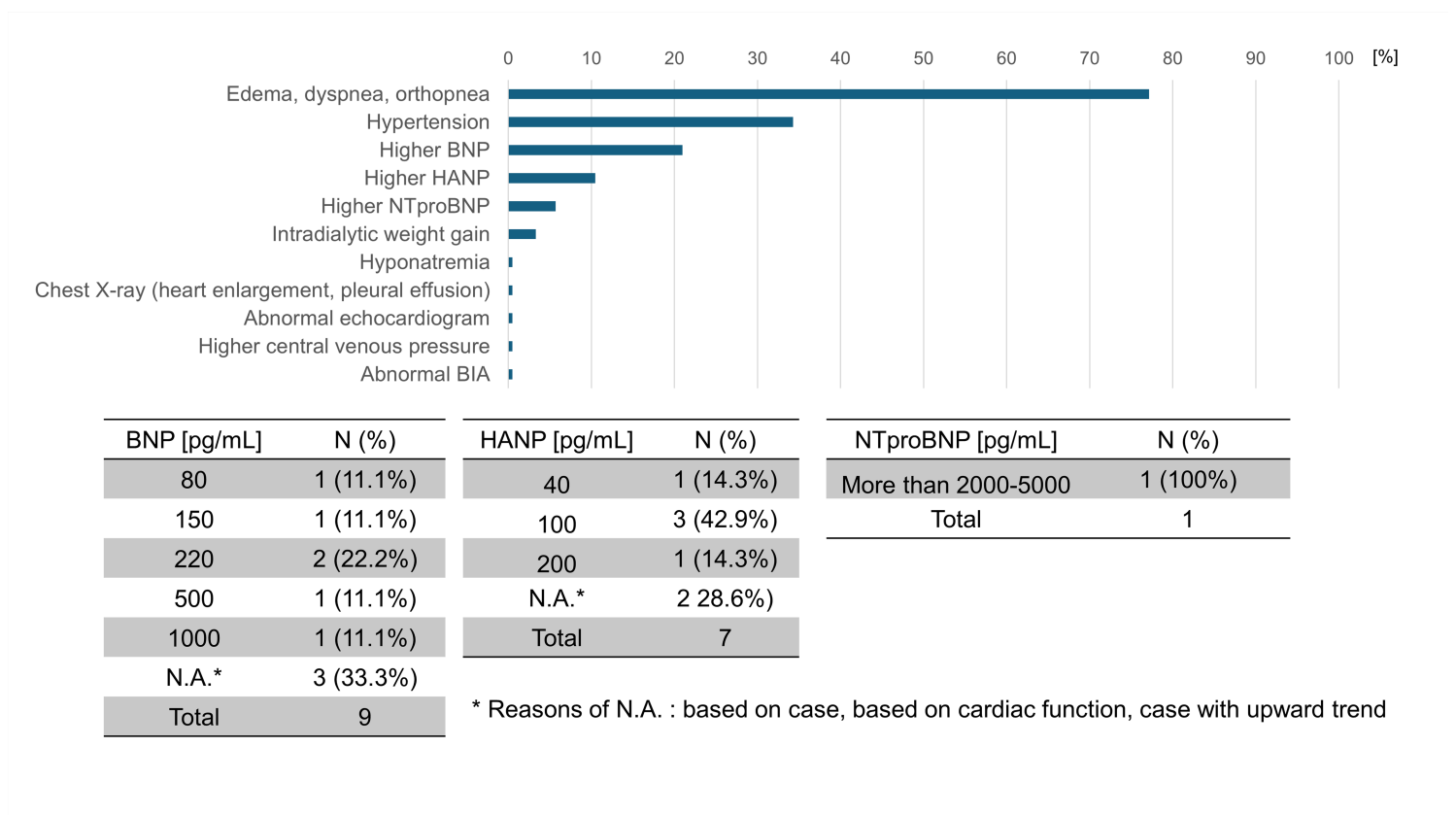


Figure 4

Indicators and threshold values for fluid overload for transfer from combined therapy with PD and HD to HD alone

Abbreviations: PD, peritoneal dialysis; HD, hemodialysis; BNP, brain natriuretic peptide; HANP, human atrial natriuretic peptide; NTproBNP, N-terminal prohormone of brain natriuretic peptide; BIA, bioelectric impedance analysis; N.A., not applicable.

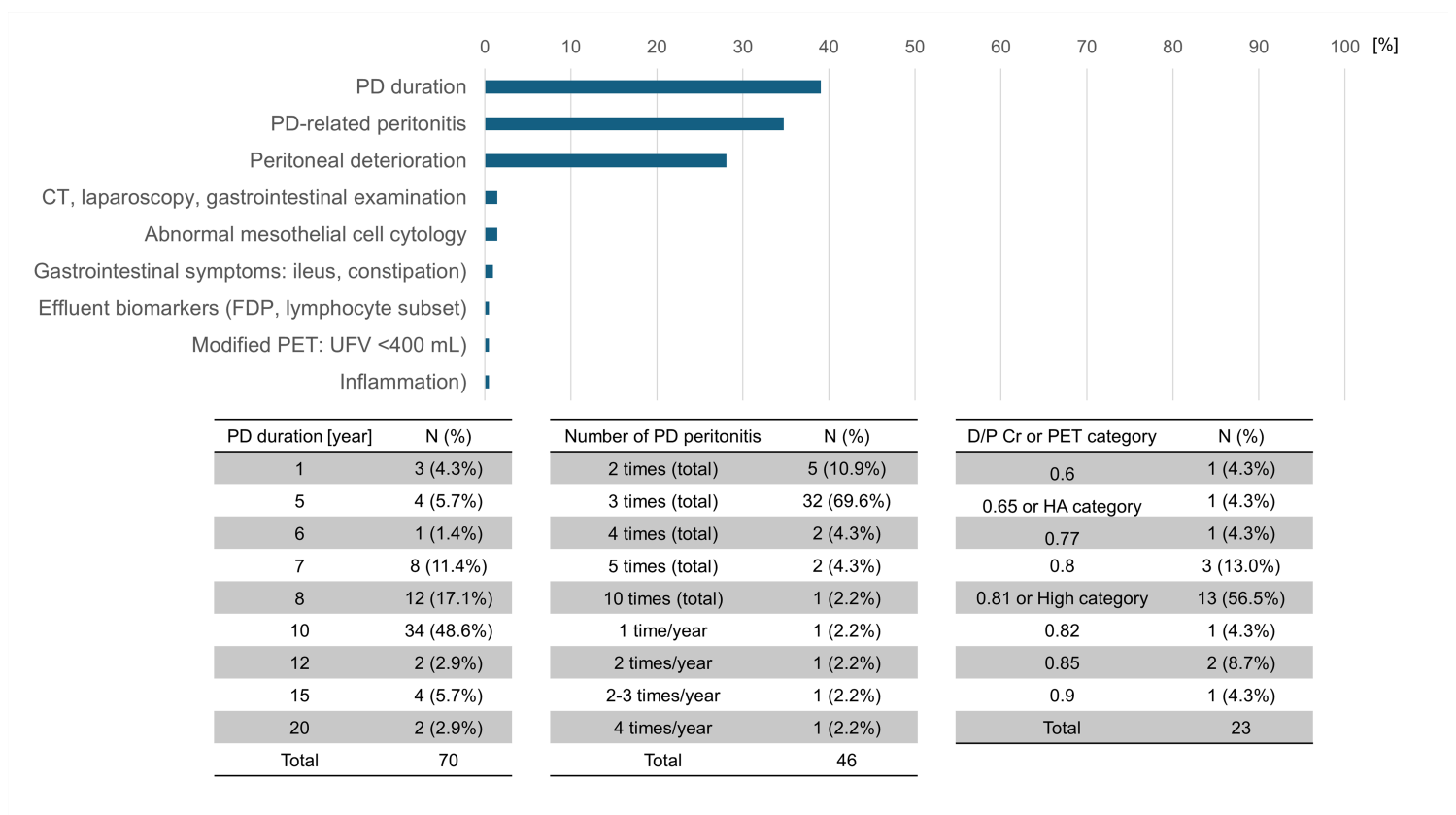


Figure 5

Indicators and threshold values for higher risk of EPS and transfer from combined therapy with PD and HD to HD alone

Abbreviations: EPS, encapsulating peritoneal sclerosis; PD, peritoneal dialysis; HD, hemodialysis; CT, computed tomography; FDP, fibrin degradation product; PET, peritoneal equilibration test; UFV, ultrafiltration volume; D/P Cr, dialysate-to-plasma ratio of creatinine.

Supplementary Files

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- [MaruyamaHybridQuestionnaireRRTSupplementarymaterial20260715.docx](#)