Renal Replacement Therapy

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Clinical advantages of a newly launched anti-thrombotic PMMA membrane for the nutritional status and dialysis-related symptoms in older chronic dialysis patients: a multicenter pilot study

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Abstract

Background: Malnutrition that is associated with inflammation is a key factor of poor outcome in chronic hemodialysis patients, especially in older dialysis patients. Polymethyl methacrylate (PMMA) membrane has been reported to improve the inflammatory status by removing pro-inflammatory cytokines via adsorption. However, older dialysis patients occasionally have multiple uncomfortable dialysis-related symptoms, which decrease their quality of life and survival rate. We investigated whether a new PMMA membrane, Filtryzer NF, can improve malnutrition and dialysis-related symptoms in older hemodialysis patients.

Methods: Patients over 70 years of age who were dialyzed using a polysulfone (PS) membrane were enrolled and randomly allocated into one of two groups: control or NF. In the NF group, the PS dialyzers were changed to NF, whereas in the control group, the PS membrane was continuously used. The primary outcome was the malnutrition–inflammation score (MIS). Secondary outcomes were C-reactive protein, normalized protein catabolism rate, percent of creatinine generation rate, arm circumference, and eight dialysis-related symptoms. The primary and secondary outcomes were measured every 3 months for 1 year.

Results: Fifty-four hemodialysis patients were randomly assigned to the NF group (n = 28) or the control group (n = 26). During the 12-month study period, 11 and 10 patients were withdrawn from the NF and control groups, respectively. There was no significant difference in the MIS between the groups during the study or between the beginning and the end of the study within each group. For the secondary outcomes, there was a significant reduction in the total score of dialysis-related symptoms in the NF group but not in the control group. During the study period, the total dialysis-related symptoms score in the NF group was significantly decreased from 6 (range, 1–16) to 3 (range, 0–11) (median [minimum–maximum], $p < 0.05$). Other secondary outcomes were not different between the groups or between the beginning and the end of the study.

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Conclusions: This study showed no advantage for the nutritional status in older hemodialysis patients using NF compared with PS. However, our results indicated that NF may improve several dialysis-related symptoms. To clarify this clinical finding, large-scale prospective randomized clinical trials are required.

Trial registration: This study was registered with the Clinical Trials Registry of the University Hospital Medical Information Network (registration ID, UMIN000032990).

Keywords: Dialysis, PMMA membrane, Protein adsorption, Filtryzer NF, Nutrition, Dialysis-related symptoms

Background

The polymethyl methacrylate (PMMA) membrane consists of two types of polymers, isotactic and syndiotactic PMMA polymers, which have different structures. This membrane has several features including good hemocompatibility, protein adsorption properties, and a uniform structure with homogenized pores [1, 2]. Filtryzer is a hollow-fiber hemodialyzer that is made with a PMMA membrane, and it was reported to show a variety of advantages including an anti-inflammatory effect [3, 4] and improvement of anemia [5, 6], itchiness [7, 8], nutrition status [9], and immune response [10, 11] in dialysis patients. Recently, Abe et al. reported that 1- and 2-year mortality rates in dialysis patients who were dialyzed using a PMMA membrane were significantly lower compared with polysulfone (PS) membrane dialyzers [12, 13]. For the new PMMA membrane Filtryzer NF (NF), we reported that platelet activation and the reduction of peripheral blood circulation during dialysis were lower, and it improved dialysis-related symptoms compared with the previous type of PMMA membrane [14]. Additionally, NF was reported to potentially maintain the patient's nutritional status compared with PS dialyzers in a pilot multicenter randomized controlled study, although there was no significant difference between them [15].

The age of the dialysis population has been increasing worldwide, and aging is a risk for malnutrition, which affects the prognosis of dialysis patients. However, older dialysis patients occasionally have multiple dialysis-related symptoms, so it is important to avoid malnutrition and these symptoms for better survival and a better quality of life in older dialysis patients. In this study, we evaluated the usefulness of the new NF membrane on the nutritional status and dialysis-related symptoms in older dialysis patients compared with the PS membrane.

Methods

Patient recruitment

Chronic maintenance hemodialysis patients from 11 facilities were recruited into the study groups for randomization. The inclusion criteria were as follows: patients over 70 years of age who were dialyzed three times per week; patients treated using a PS membrane-type dialyzer (PS dialyzers) excluding the vitamin E-coated PS membrane and the novel hydrophobic polymer-coated PS membrane (NV) [16]; and patients without residual urine volume (> 100 mL). The exclusion criteria were as follows: patients whose serum albumin concentrations were less than 3.0 g/dL; patients who had a cerebral or cardiovascular event within past 3 months; patients who had obvious inflammatory disorders; patients who had evidence of an active infectious disease; or patients who were over 90 years old or could not walk independently.

Study protocol

The flow diagram of this study is shown in Fig. 1. Enrolled patients who met the eligibility requirements were randomly allocated into the NF group or the control group (PS dialyzer). To reduce the bias due to differences in dialysis methods among participating dialysis centers, when multiple patients were registered from one dialysis center, the same number of patients were randomly allocated to the NF group and control group (see Appendix 1 and Appendix 2). Then, in patients who were allocated to the NF group, previous PS dialyzers were switched to the Filtryzer NF (TORAY Inc., Japan, Tokyo). The primary outcome was the total malnutrition–inflammation score (MIS). Secondary outcomes were dry weight (DW) which means body weight after dialysis, normalized protein catabolism rate (nPCR), percent of creatinine generation rate (%CGR), arm circumference (AC), C-reactive protein (CRP), and dialysis-related symptoms. The primary outcome and secondary outcomes were assessed every 3 months. Evaluation of the MIS was conducted on the basis of a previous report [17]. We also evaluated eight patient-reported dialysis-related symptoms which are frequently observed in the clinical practice, as follows: joint pain, itchiness, irritation, fatigue, headache, intradialytic hypotension, leg cramp, and leaving bed after dialysis. These eight symptoms were evaluated using five-point scales, as shown in a previous report [18]. The total score of these dialysis-related symptoms was calculated as the sum of these eight items.

Patients were excluded from the study protocol when the following occurred: an adverse event that was suspected to be related to hemodialyzers such as allergic reactions, sudden drop in blood pressure just after the start of dialysis, or abnormal clinical test result; when a patient chose to withdraw from the study; or when a doctor considered that the patient should be withdrawn from the study.

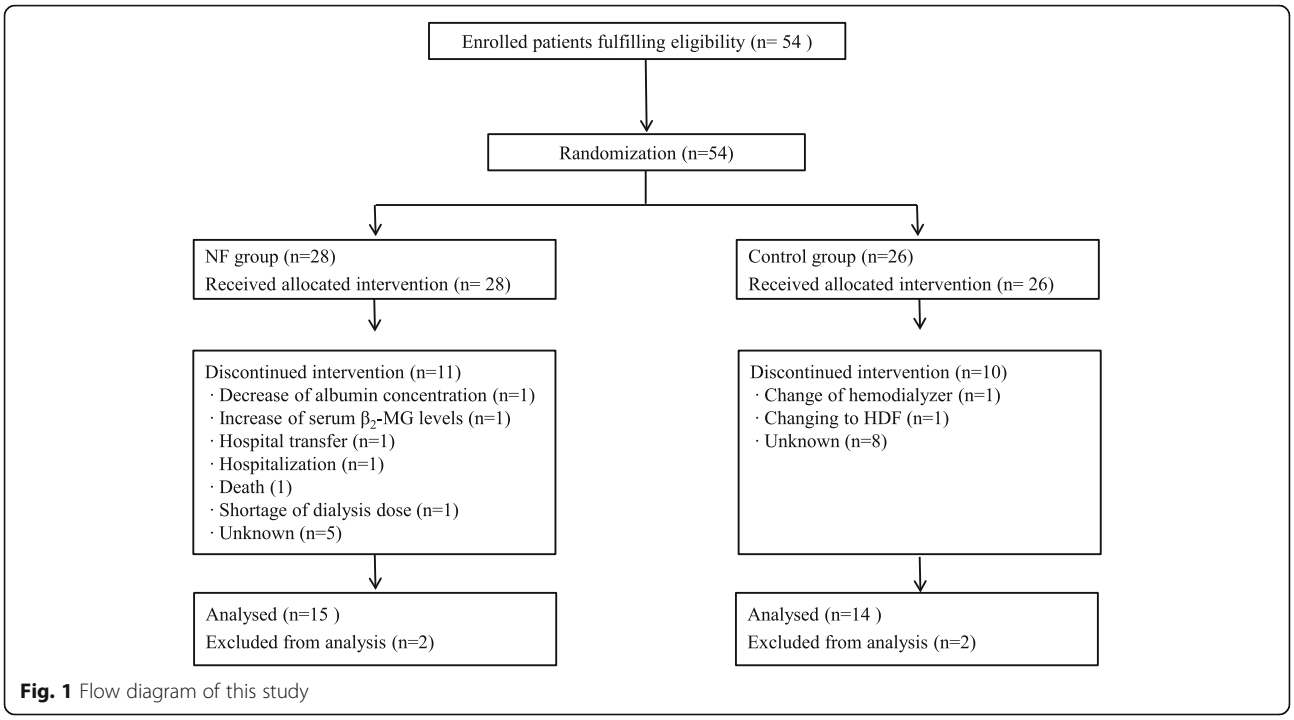

Fig. 1 Flow diagram of this study

All of participating dialysis centers used ultrapure dialysis fluid during the study period in accordance with the "Standard on Microbiological Management of Fluids for Hemodialysis and Related Therapies by the Japanese Society for Dialysis Therapy 2008" [19]. Endotoxin or microorganisms were not detected in the dialysates at any time point during the study period.

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Yabuki hospital (the approval number: 66). Written informed consent was obtained from all the patients before they were enrolled into this study.

Clinical trials registry

This study was registered in the Clinical Trial Registry of the University Hospital Medical Information Network (UMIN-CTR) (Registry ID: UMIN000032990).

Data and statistical analysis

Data analysis was conducted excluding patients who were withdrawn from this study and/or who had incomplete clinical data. The scores that were obtained from the MIS and dialysis-related symptoms between the NF and Control groups were compared using the Mann–Whitney *U* test. DW, CRP, nPCR, %CGR, and AC were compared between the groups, and an unpaired Student's *t* test or Welch's *t* test was used, as appropriate. A Friedman test was used to compare the MIS and dialysis-related symptoms within each group. Categorical variables were tested using the chi-square test. $P < 0.05$ was considered to be significant. Statistical analysis was performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

Results

Study outline

Fifty-four patients who met the study entry criteria were randomly allocated into the NF group (28 patients) or the control group (26 patients). The patients' demographic data are summarized in Table 1. The number of patients who were treated using acetate-free dialysis fluid was significantly greater in the NF group than the control group, but there was no significant difference between other items between the groups. During the 12-month study period, 11 patients in the NF group and 10 patients in the Control group were withdrawn from the study for several reasons, as shown in Fig. 1. Seventeen patients in the NF group and 16 patients in the control group completed the study. Two patients in each group were excluded because of missing data related to the primary endpoint, and the final data analysis was conducted with 15 patients in the NF group and 14 patients in the control group. There was no significant difference in the background data between the two groups except for the ratio of the patients who were treated using acetate-free dialysis fluid (Table 2).

Primary outcome

There were no significant differences in the MIS between the NF and Control groups throughout the study period

Table 1 Patient demographic data

Items	All	NF group	n	Control group	n	p
Number of patient	54	28	28	26	26	
Sex (male/female)	36/18	17/11	28	19/7	26	*n.s.*[a]
Age (years)	76.4 ± 5.0 (70.0–87.0)	77.1 ± 4.8 (70.0–87.0)	28	75.6 ± 5.0 (70.0–87.0)	26	*n.s.*[b]
Dialysis vintage (years)	8.3 ± 6.2 (0.5–30.0)	9.8 ± 7.4 (0.5–30.0)	28	6.8 ± 4.2 (1.0–15.0)	26	*n.s.*[c]
Dry weight (kg)	52.5 ± 9.8 (33.8–90.0)	50.8 ± 8.8 (33.8–67.8)	28	54.3 ± 10.6 (34.5–90.0)	26	*n.s.* [b]
Albumin concentration before dialysis (g/dL)	3.6 ± 0.3 (3.0–4.4)	3.6 ± 0.3 (3.1–4.0)	27	3.6 ± 0.3 (3.0–4.4)	25	*n.s.* [b]
Dialysis condition						
Blood flow rate (mL/min)	219.3 ± 30.3 (150–300)	218.9 ± 32.7 (150–300)	28	219.6 ± 28.2 (150–250)	26	*n.s.* [b]
Dialysis time (h)	4.0 ± 0.4 (3.0–5.0)	4.0 ± 0.4 (3.0–5.0)	28	4.0 ± 0.3 (3.0–5.0)	26	*n.s.* [b]
Effective surface area (m^2)	1.7 ± 0.3 (1.3–2.1)	1.7 ± 0.3 (1.3–2.1)	28	1.7 ± 0.3 (1.4–2.1)	26	*n.s.* [b]
Dialysis membrane (PS/PES/PEPA)	(32/12/10)	(13/8/7)	28	(19/4/3)	26	*n.s.* [a]
Classification of dialyzer[#] (I·II/III/IV/V)	(0/6/26/22)	(0/1/16/11)	28	(0/5/10/11)	26	*n.s.* [a]
Dialysate (with acetate/without acetate)	(44/10)	(20/8)	28	(24/2)	26	$p < 0.05$ [a]
Medical history						
Diabetes mellitus (Y/N)	(18/36)	(9/19)	28	(9/17)	26	*n.s.* [a]
Cerebrocardiovascular event (Y/N)	(12/42)	(7/21)	28	(5/21)	26	*n.s.* [a]

Results are presented as the mean ± standard deviation, and the values in parentheses represent the minimum and maximum values
[#]Classification of dialyzers in the Japanese reimbursement system
[a]Chi-square test
[b]Unpaired *t* test
[c]Welch's test

(Table 3). In the NF group, MIS became significantly worse at 6 and 9 months compared with the baseline, and it recovered at 12 months (Fig. 2A). In the control group, MIS at 9 months was significantly higher compared with the baseline and 3 months, but it was significantly improved at 12 months (Fig. 2B).

Secondary outcomes

There were no significant differences in DW between the groups throughout the study period. Additionally, no significant time-dependent changes were observed in each group (Table 4).

There was no significant difference in nPCR between the groups during the study period. nPCR in the control group did not change during the study period, but that in the NF group tended to decrease and was significantly lower at 9 and 12 months compared with the baseline (Table 4).

The average %CGR at the baseline, 6 months, and 9 months was significantly higher in the NF group than in the control group. In both groups, %CGRs at 12 months were significantly lower compared with that at 3 months (Table 4). There was no significant difference in AC between the groups. In the control group, AC at 12 months was significantly higher than that at 9 months (Table 4). There were also no differences in CRP between the groups, and this result did not change during the study period in each group.

The total scores of the dialysis-related symptoms were not different between the groups at each point during the entire study period (Table 4). However, the average of the total score for symptoms significantly improved in the NF group between baseline and 12 months, whereas it did not change in the control group (Fig. 3A, B). We evaluated the score-distributions of symptoms in both groups (Fig. 4). The number of patients with a high score (i.e., greater than 3) decreased in the NF group compared with the control group, but there were no symptoms that were specifically improved by the NF membrane (Fig. 4).

After switching to NF, we did not observe adverse events such as elevated blood pressure and changes in anti-coagulant doses.

Discussion

Malnutrition in chronic kidney disease is more prevalent and qualitatively differentiated from malnutrition in the general population in relation to inflammation and accelerating atherosclerosis (MIA syndrome) [20]. Therefore, we expected that the PMMA membrane would improve the nutritional status because it has been reported to have anti-inflammatory effects [3, 4]. The PS membrane has been the most widely used dialysis membrane material throughout the world, but several adverse effects that were associated with the PS membrane were reported, and these adverse effects seemed to be derived from its bio-incompatibility. It is a unique insight of the current study to improve the nutritional status by providing a biocompatible anti-inflammatory dialysis modality.

Previously, we showed that body weight increased when switching from a PS dialyzer to a conventional type of PMMA dialyzer in older hemodialysis patients [9]. In the current randomized controlled study, to clarify the

Table 2 Demographic data for patients included in the analysis

Items	NFgroup	n	Control group	n	p
Number of patient	15		14		
Sex (male/female)	9/6	15	11/3	14	*n.s.*[a]
Age (year)	76.1 ± 5.0 (70.0–87.0)	15	74.7 ± 4.2 (70.0–87.0)	14	*n.s.*[b]
Dialysis vintage (year)	9.8 ± 9.1 (0.5–30.0)	15	6.5 ± 4.2 (1.0–13.0)	14	*n.s.*[c]
Dry weight (kg)	52.0 ± 9.1 (33.8–63.5)	15	57.8 ± 11.4 (43.2–90.0)	14	*n.s.* [b]
Albumin concentration before dialysis (g/dL)	3.7 ± 0.3 (3.1–4.0)	15	3.6 ± 0.2 (3.3–4.1)	13	*n.s.* [b]
Dialysis condition					
Blood flow rate (mL/min)	217.3 ± 28.4 (200–300)	15	220.0 ± 22.2 (200–250)	14	*n.s.* [b]
Dialysis time (h)	4.1 ± 0.3 (4.0–5.0)	15	4.1 ± 0.3 (4.0–5.0)	14	*n.s.* [b]
Effective surface area (m^2)	1.7 ± 0.3 (1.3–2.1)	15	1.8 ± 0.3 (1.5–2.1)	14	*n.s.* [b]
Dialysis membrane (PS/PES/PEPA)	(8/5/2)	15	(12/1/1)	14	*n.s.* [a]
Classification of dialyzer[#] (I·II/III/IV/V)	(0/0/8/7)	15	(0/4/5/5)	14	*n.s.* [a]
Dialysate (with acetate/without acetate)	(9/6)	15	(13/1)	14	$p < 0.05$ [a]
Medical history					
Diabetes mellitus (Y/N)	(6/9)	15	(3/11)	14	*n.s.* [a]
Cerebrocardiovascular event (Y/N)	(3/12)	15	(4/10)	14	*n.s.* [a]

Results are presented as the mean ± standard deviation, and the values in parentheses represent the minimum and maximum values
[#]Classification of dialyzers in the Japanese reimbursement system
[a]Chi-square test
[b]Unpaired *t* test
cWelch's test

advantages of the biocompatible modality, we used the newly developed PMMA membrane, which has improved antithrombogenicity compared with the conventional membrane [14]. However, we did not observe significant advantages of the NF membrane for the primary outcome compared with the control group with PS dialyzer. We hypothesized that the different results in the current study compared with the previous studies might be caused by refinements of the PS membrane and the difference of the dialysate that was used in the studies. After reports that suggested that there were bio-incompatible aspects of PS membrane, the biocompatibility of dialyzers that were composed of PS were improved by modifying its membrane surface and/or chemical characteristics, and this improved their clinical usefulness [21–23]. Thus, the advantages of PMMA compared with the PS membrane might have decreased compared with the previous studies.

In this study, acetate-free bicarbonate dialysate was used more often in the NF group compared with the control group. Kuragano et al. [24] reported that acetate-free bicarbonate dialysate has a nutritional advantage because it increases the serum albumin concentration compared with the conventional acetate-containing dialysate in dialysis patients with low albuminemia. Acetate-free bicarbonate dialysate was also reported to reduce the inflammatory response in dialysis patients [25]. On the basis of these suggestive studies, the nutritional situation before the current study might have been better in the NF group compared with the control group, although significant differences were not detected at the start of the study. The advantages of acetate-free dialysate might have made the nutritional advantage of the NF membrane unclear.

We chose an open-label design for the clinical design in this trial with an evaluation period of 1 year. We chose this design because we were concerned about the influence of the evaluation period for the results in a crossover trial, although the differences in the results might show differences in the degree and susceptibility to symptoms among the patients.

In the current study, we observed a significant improvement in the total score for dialysis-related symptoms in each measurement month that was compared with the baseline results within each group, and a significant improvement was found in the NF group but not in the control group, as we previously reported [14]. When the change in the number of patients is investigated on the basis of the score for each

Table 3 Primary outcome

	n	0	3	6	9	12
NF group	15	5 (2–10)	6 (2–10)	7[#] (2–9)	7[#] (4–10)	6 (3–12)
Control group	14	5 (3–8)	5 (2–7)	5.5 (3–8)	6.5[#,$] (2–10)	5.5[&] (2–9)

Friedman test: #, $p < 0.05$ vs. baseline; $, $p < 0.05$ vs. 3 months; &, $p < 0.05$ vs. 9 months
Results are presented as the median (minimum–maximum values)

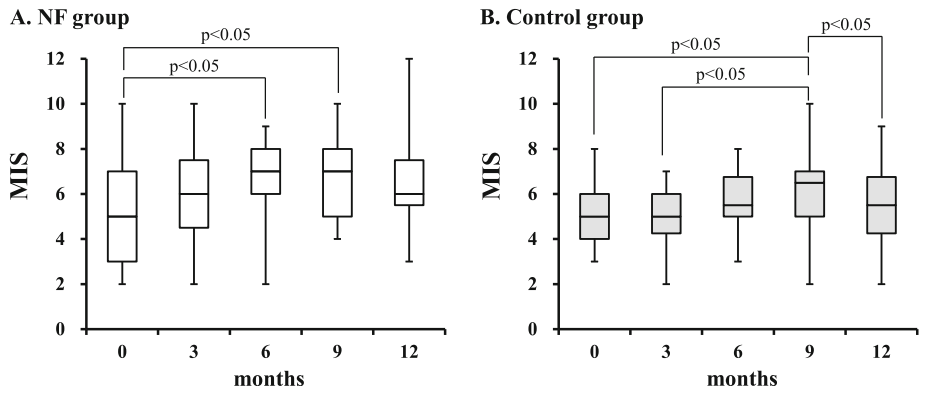

Fig. 2 Primary endpoint results for the MIS evaluation. **A** Results from the NF group (n = 15). **B** Results from the control group (n = 14). Results are presented as the interquartile range

symptom, the number of patients with fewer symptoms in the NF group tended to increase for all of the symptoms. However, there were no specific symptoms that were dramatically improved by the NF membrane. We speculated that the bio-compatibility and protein adsorptive properties of NF membrane had an important role to ameliorate the total score of dialysis-related symptoms, and we can consider this an improvement in the quality of life for the patients. This is a very important result for patients because we believe that quality of life is the most important outcome in the management of older dialysis patients, and we must pay attention to it.

In a previous study, we reported that the NF membrane improved the peripheral circulation and preserved the blood pressure stability during the dialysis session, which suggests good hemocompatibility of the NF membrane [14]. There have been few studies that have addressed the usefulness of intense removal of low molecular-weight proteins on the quality of life in chronic dialysis patients. Sakurai et al. [26] reported that an alpha-1 microglobulin removal rate of over 35% was effective to ameliorate severe restless leg syndrome. The protein adsorption capacity of the NF membrane was remarkably improved compared with the conventional PMMA, so it might have had some favorable effects on the improvement of multiple dialysis-related symptoms in the patients.

To objectively evaluate each patient's condition, it is important to consider the changes in the blood test results data and the removal of solutes including protein. However, because this study was conducted as pilot study, blood test result data and the removal of solutes were not evaluated in the study plan. We will add these evaluation items to a future clinical study that will enroll more patients.

Table 4 Secondary outcomes

Items		n	0	3	6	9	12
DW (kg)	NF	15	52.1 ± 9.2	52.5 ± 8.9	52.5 ± 8.8	52.0 ± 8.8	52.0 ± 9.0
	Cont	14	56.2 ± 11.0	56.4 ± 10.9	56.6 ± 10.9	56.5 ± 11.0	56.4 ± 11.1
nPCR (g/kg/day)	NF	15	0.95 ± 0.15	0.87 ± 0.15	0.86 ± 0.20	0.75 ± 0.15$^{***, \&\&, \dagger\dagger}$	0.83 ± 0.16$^{***, \ddagger}$
	Cont	13	0.86 ± 0.20	0.89 ± 0.22	0.86 ± 0.20	0.83 ± 0.22	0.87 ± 0.24
%CGR (%)	NF	15	124.4 ± 17.3	126.4 ± 13.2	124.3 ± 15.7$^{\#}$	124.6 ± 19.2$^{\#}$	117.7 ± 20.7$^{\&}$
	Cont	13	107.4 ± 26.9	109.4 ± 28.5	106.5 ± 25.3	106.3 ± 25.5	98.2 ± 30.8$^{\&}$
Arm circumference (cm)	NF	15	25.0 ± 3.1	24.8 ± 3.1	24.2 ± 3.0	24.9 ± 3.0	25.6 ± 3.0
	Cont	13	25.0 ± 3.2	24.9 ± 3.0	25.4 ± 3.4	24.9 ± 2.1	25.1 ± 3.1‡
CRP (mg/dL)	NF	15	0.14 ± 0.11	0.26 ± 0.26	0.30 ± 0.48	0.11 ± 0.08$^{\&}$	0.23 ± 0.16‡‡
	Cont	13	0.24 ± 0.31	0.18 ± 0.23	0.16 ± 0.22	0.24 ± 0.34	0.34 ± 0.62
dialysis-related symptoms	NF	15	6 (1–16)	4 (1–16)	5 (0–12)	4 (0–11)	3$^{\$}$ (0–11)
	Cont	14	5 (0–13)	4 (0–13)	4.5 (0–17)	4.5 (0–15)	4.5 (0–13)

DW, nPCR, %CGR, arm circumference, and CRP are presented as the mean ± standard deviation. Dialysis-related symptoms are presented as the median (minimum–maximum values)
Unpaired *t* test: #, $p < 0.05$; NF group vs. Cont group
Paired *t* test: ***, $p < 0.001$ vs. 0 months; &, $p < 0.05$ vs. 3 months; &&, $p < 0.01$ vs. 3 months; ††, $p < 0.01$ vs. 6 months; ‡, $p < 0.05$ vs. 9 months; ‡‡, $p < 0.01$ vs. 9 months
Friedman test: $, $p < 0.05$ vs. 0 months
NF NF group, *Cont* control group, DW dry weight, *nPCR* normalized protein catabolism rate, *CGR* creatinine generation rate, *CRP* C-reactive protein

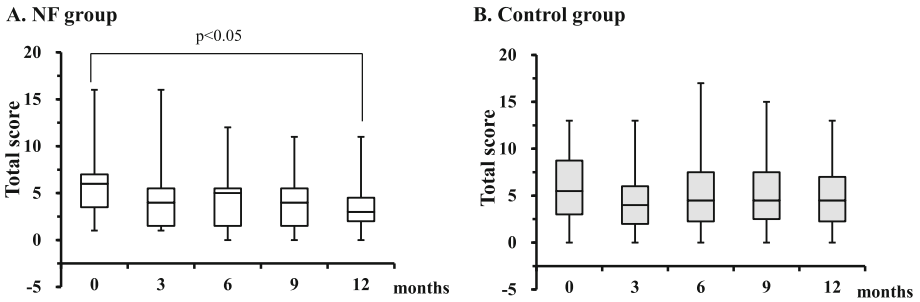

Fig. 3 Indefinite complaint results. **A** NF group (n = 15) results. **B** Control group (n = 14). Results are presented as the interquartile range

Our study has some limitations. First, the number of patients was too small to evaluate clinical differences between the membranes. Second, one-third of the allocated patients dropped out of the study. Third, despite random allocation of the patients, there was a bias in the dialysate that was used in the treatment. These issues might affect the results of our study. An investigation excluding these factors and enrolling a larger number of patients should be planned and conducted in the future to verify the results of this study.

Conclusions

In the current study, we did not observe a nutritional advantage for the NF membrane compared with the PS membrane, which has been previously reported, in older dialysis patients. However, we confirmed a significant improvement in the total score of dialysis-related symptoms only in the NF group. This finding indicates that the NF membrane could improve older hemodialysis patients' quality of life.

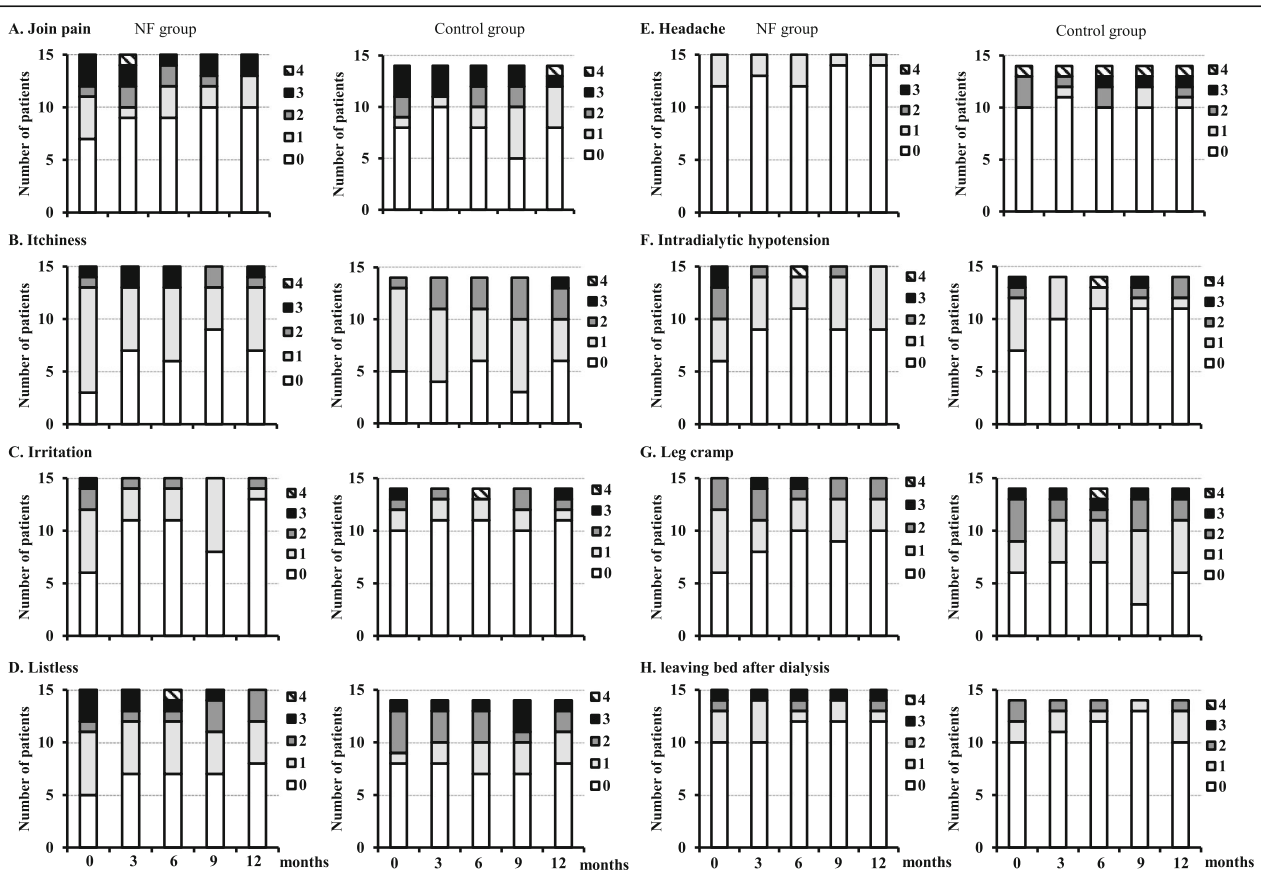

Fig. 4 Results of each score for patients with each dialysis-related symptom. Each score is presented as follows: 0, none; 1, mild; 2, moderate; 3, moderately severe; 4, severe. NF group, n = 15, control group, n = 14

Appendix 1

Table 5 Information related to dialysis therapy for each patient (control group)

Pt, no.	Dialysis membrane (PS/PES/PEPA)	Surface area (m^2)	Classification of dialyzer[a] (I·II/III/IV/V)	Blood flow rate (mL/min)	Dialysate flow rate (mL/min)	Dialysate (Acetate:+/−)	Dialysis time (h)
1	PS	2.1	Type V	230	500	+	4.0
2	PS	2.1	Type V	230	500	+	4.0
3	PS	2.1	Type V	200	500	+	4.0
4	PS	2.1	Type V	240	500	+	4.0
5	PS	2.1	Type V	250	500	+	4.0
6	PS	1.4	Type IV	150	500	+	3.0
7	PS	1.4	Type IV	150	500	+	4.0
8	PES	1.5	Type V	230	500	+	4.0
9	PS	1.8	Type V	230	500	+	4.0
10	PES	1.5	Type V	230	500	+	4.0
11	PEPA	1.8	Type V	250	500	+	4.0
12	PES	2.1	Type IV	250	500	+	4.0
13	PEPA	1.5	Type IV	250	500	+	4.5
14	PEPA	1.5	Type IV	230	500	+	4.0
15	PS	1.8	Type IV	250	500	+	4.0
16	PS	2.1	Type V	200	500	+	5.0
17	PES	1.8	Type IV	230	500	+	3.5
18	PS	1.5	Type V	250	500	+	3.5
19	PS	1.5	Type IV	240	500	+	4.0
20	PS	1.8	Type IV	200	500	+	4.5
21	PS	1.5	Type IV	220	500	+	4.0
22	PS	1.5	Type III	200	500	−	4
23	PS	1.5	Type III	200	500	+	4
24	PS	1.5	Type III	200	500	−	4
25	PS	1.5	Type III	200	500	+	4
26	PS	2.1	Type III	200	500	+	4

[a]Classification of dialyzers in the Japanese reimbursement system

Appendix 2

Table 6 Information related to dialysis therapy for each patient (NF group)

Pt, no.	Dialysis membrane (PS/PES/PEPA)	Surface area (m^2)	Classification of dialyzer[a] (I·II/III/IV/V)	Blood flow rate (mL/min)	Dialysate flow rate (mL/min)	Dialysate (Acetate:+/−)	Dialysis time (h)
1	PEPA	1.5	Type IV	300	500	−	4
2	PEPA	1.5	Type V	300	500	−	4
3	PS	2.1	Type V	250	500	+	4
4	PEPA	1.5	Type IV	230	500	+	4
5	PEPA	2.1	Type IV	200	500	+	4
6	PS	2.1	Type V	200	500	+	4
7	PS	1.4	Type IV	150	500	+	3
8	PS	1.4	Type IV	200	500	+	3.5
9	PES	1.3	Type V	230	500	+	4
10	PES	1.5	Type V	200	500	+	4
11	PES	1.5	Type V	220	500	+	4
12	PES	1.5	Type V	250	500	+	4
13	PES	1.5	Type V	200	500	+	4
14	PEPA	1.5	Type IV	250	500	+	4
15	PES	2.1	Type V	180	500	+	4
16	PEPA	1.5	Type IV	200	500	+	4
17	PEPA	1.8	Type IV	230	500	+	4
18	PS	2.1	Type V	250	500	+	5
19	PS	1.6	Type IV	230	500	+	3.5
20	PS	2.1	Type IV	240	500	+	4.5
21	PES	1.5	Type IV	200	500	+	4
22	PES	2.1	Type IV	220	500	+	5
23	PS	1.5	Type III	200	500	−	4
24	PS	1.8	Type IV	200	500	−	4
25	PS	1.3	Type IV	200	500	−	4
26	PS	1.8	Type V	200	500	−	4
27	PS	1.3	Type IV	200	500	−	4
28	PS	1.8	Type IV	200	500	−	4

[a]Classification of dialyzers in the Japanese reimbursement system

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Authors' contributions
IM planned the study, analyzed the data, and drafted the manuscript. IY, YM, KA, YK, MN, YM, TT, KS, HA, and AK recruited patients and collected data. All authors read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this article.

Declarations

Ethics approval and consent to participate
This clinical study was approved by the Institutional Review Board at the Yabuki Hospital, and written informed consent was obtained from each study participant.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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