Real-World Performance of High-Flux Dialyzers in Patients With Hypoalbuminemia

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There is little research on factors that influence the choice of dialyzer in patients undergoing hemodialysis. In patients at risk for poorer outcomes, including those with hypoalbuminemia, understanding how this choice impacts clinical parameters could inform patient management. The objective of this real-world analysis was to evaluate the use and performance of four single-use (*i.e.,* nonreuse [NR]), high-flux Optiflux dialyzers with varying surface areas (F160NR [1.5 m^2], F180NR [1.7 m^2], F200NR [1.9 m^2], and F250NR [2.5 m^2]) in patients (N = 271) with baseline hypoalbuminemia (≤3.5 g/dl) receiving hemodialysis at a medium-sized dialysis organization. Thrice weekly, in-center dialysis was delivered for 6 months without adjustments to the hemodialysis prescription. Larger dialyzers were more frequently used in men, patients with higher body mass indices, and those with diabetes. Increases in serum albumin from baseline (month 1) to month 6 ($p < 0.05$) were observed with all dialyzer sizes. A mean increase in hemoglobin of 0.31 g/dl was also observed ($p < 0.001$). Among patients exhibiting increased serum albumin levels (n = 177), reductions in the neutrophil-to-lymphocyte ratio, a marker of inflammation, were observed (mean: 0.90; $p < 0.001$). These results support the use of high-flux dialyzers in patients with hypoalbuminemia. *ASAIO Journal* 2022; 68;96–102

Key Words: hemodialysis, albumin, dialyzer, surface area, high flux

Approximately 470,000 patients with end-stage kidney disease (ESKD) receive hemodialysis (HD) in the United States.[1] Clinicians have a range of choices when selecting a dialyzer for patients receiving maintenance HD. Dialyzers differ in terms of how they are sterilized; the material, structure, and permeability of their membranes; and importantly, their membrane surface area.[2] Dialyzer selection and dialysis prescription aim to ensure dialysis adequacy, as assessed by Kt/V and the urea reduction ratio, while minimizing treatment time. Strategies to improve Kt/V include increasing dialyzer clearance by modifying the dialyzer size or increasing dialysis treatment time.[3]

The adequacy of dialysis delivered to a patient is governed by five variables: blood flow rate, dialysate flow rate, composition of dialysate fluid, duration of treatment, and dialyzer characteristics, including surface area of the membrane.[4] When other variables are held constant and flow rates are above thresholds for proper flow distribution, the delivered dose of dialysis can be increased by choosing a dialyzer with a greater surface area.[4] Dialyzers with higher surface areas also result in increased rates of small solute clearance and removal of β2-microglobulin.[5] Guidance on the selection of dialyzers by surface area and data on the real-world impact of membrane surface area on patient outcomes and clinical parameters, however, are limited.

Optiflux dialyzers (manufactured by Fresenius Medical Care North America, Waltham, MA) are single-use, electron-beam sterilized, biocompatible, high-flux dialyzers with polysulfone membranes designed to enhance small-molecule and middle-molecule clearance without albumin loss. They are available in four sizes, with four different membrane surface areas: 1.5 m^2 (F160NR), 1.7 m^2 (F180NR), 1.9 m^2 (F200NR), and 2.5 m^2 (F250NR). Key specifications of these dialyzers are summarized in **Table 1**.[6]

Patients with chronic kidney disease (CKD) have a markedly increased risk of hypoalbuminemia as a result of underlying metabolic derangements and nutritional alterations.[7] This risk is further increased in patients with ESKD receiving maintenance HD because of the potential for albumin loss during dialysis.[7–9] Inflammation, infection, and comorbid illnesses, all of which are common in HD populations, can also result in low levels of serum albumin. Hypoalbuminemia is well established as a key prognostic indicator of morbidity and mortality in this patient population, and even small reductions in serum albumin levels over time have been associated with significant increases in mortality.[10–13] As such, HD patients with baseline hypoalbuminemia represent a high-risk population for whom further reductions in serum albumin levels must be avoided. The objective of this analysis was to evaluate real-world performance of high-flux Optiflux dialyzers with varying surface areas in patients with hypoalbuminemia (serum albumin ≤3.5 g/dl) undergoing HD over a 6 month period.

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Table 1. Optiflux Dialyzer Specifications[6]

Parameters	F160NR	F180NR	F200NR	F250NR
Membrane surface area (m^2)	1.5	1.7	1.9	2.5
Ultrafiltration coefficient (ml/hr/mm Hg), Qb = 300 ml/min	61	76	74	111
Priming volume blood (ml)	87	102	113	142
KoA (ml/min), Qb = 300 ml/min, Qd = 500 ml/min	1,167	1,321	1,415	1,714
Flow resistance (mm Hg)				
Blood Qb = 300 ml/min	89	80	66	57
Dialysate Qd = 500 ml/min	17	15	15	19
Sieving coefficient for albumin, Qb = 300 ml/min, ultrafiltration rate = 29 ml/min	<0.01	<0.01	<0.01	<0.01

All dialyzers were manufactured by Fresenius Medical Care, Waltham, MA.
KoA, mass transfer area coefficient; Qb, blood flow rate; Qd, dialysate flow rate.

Materials and Methods

This retrospective cohort study utilized deidentified data extracted from the American Renal Associates (ARA) clinical data warehouse. As of June 2019, ARA operated 245 dialysis clinics and provided HD to more than 17,000 patients. Patients were adults (age ≥18 years) who received thrice weekly, in-center HD with an Optiflux dialyzer (F160NR, F180NR, F200NR, or F250NR) and acetate-acidified dialysate in 2019 and had at least 1 month (month 1; M1) of documented hypoalbuminemia (serum albumin ≤3.5 g/dl). Patients were required to have had no change in dialysis modality, vascular access type, or HD prescription over the course of the 6 month observation period. Patients with a current or history of liver disease, cancer, human immunodeficiency virus, or drug abuse were excluded from the study. Furthermore, the analysis cohort was limited to patients with at least five monthly (*i.e.*, months 2, 3, 4, 5, and 6 [M2, M3, M4, M5, and M6]) serum albumin assessments after M1 (baseline). The need for informed consent was waived by an independent institutional review board (Advarra, Inc., Columbia, MD) because of the anonymous and purely observational nature of the study.

Study Endpoints

Patient-level demographic characteristics (age, gender, race, ethnicity), body mass index (BMI), dialysis vintage, vascular access, and diabetes presence were evaluated at M1. Laboratory variables evaluated included pre-HD serum albumin levels, pre-HD hemoglobin concentrations, normalized protein catabolic rate (nPCR), single-pool Kt/V (spKt/V), and pre-HD neutrophil/lymphocyte ratio (NLR), a marker of inflammation. Laboratory tests were measured monthly except for hemoglobin, which was measured weekly per standard practice at ARA clinics. Albumin levels were assessed using an automated chemistry analyzer using bromocresol green (BCG) at a central laboratory. This colorimetric method measures albumin-BCG color complex. Dialysis treatment–related parameters included ultrafiltration volume (UFV; estimated using pre- and post-HD weights) and dialysis treatment time (actual and prescribed). Weight-related parameters (pre-HD weight, post-HD weight, and estimated dry weight [EDW]) and the use and quantity of nutritional supplements (liquid protein supplement and protein bar) were assessed at each dialysis session. For all parameters, repeated values within a month were averaged to account for short-term measurement variability.

Statistical Analysis

Demographic data are presented as mean ± standard deviation for continuous variables and the number and percentage of patients for categorical variables. Analyses were conducted to assess change from baseline to end of follow-up (M1 to M6) and change over all 6 months using longitudinal data analysis methods. Changes from M1 to M6 in clinical parameters were compared using paired *t* tests for continuous variables and McNemar tests for categorical variables. Changes over all months were summarized as least-squared means, with standard errors, and repeated-measures mixed-effects linear regression. Categorical clinical data were compared using the Cochran *Q* test and McNemar χ^2 test. Two-tailed *p* values <0.05 were considered statistically significant.

Analyses were performed for the overall cohort and by dialyzer subgroup. Because of the limited number of patients dialyzed with the F200NR and F250NR, data from these two subgroups were pooled for monthly analyses. To investigate the potential impact of dialysis vintage on dialyzer performance, a stratified analysis by dialysis duration (*i.e.*, <6 *vs.* ≥6 months) was carried out for variables of interest (serum albumin, NLR, spKt/V, and body weight). All analyses were conducted with SAS (version 9.4; SAS Institute Inc., Cary, NC).

Results

A total of 327 patients met baseline inclusion criteria, including the presence of hypoalbuminemia at M1. Follow-up serum albumin data were missing for 56 patients, leaving 271 patients in the final analysis cohort. Most patients received HD with either the F160NR or F180NR dialyzers (n = 128 and n = 112, respectively). Approximately 11% of the cohort received HD with an F200NR (n = 19) or F250NR (n = 12) dialyzer. Demographic and baseline characteristics of the dialyzer subgroups are shown in **Table 2**. Mean BMI and diabetes prevalence increased with dialyzer size. Increases in serum albumin level were observed in the overall cohort and in each dialyzer subgroup (**Table 3**; see Table S1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A676). Delivered and prescribed dialysis times remained unchanged from M1 to M6. Patients with shorter dialysis vintage (<6 months) exhibited greater increases in serum albumin (+0.32 *vs.* +0.17 g/dl; $p = 0.008$) and greater decreases in NLR (−1.13 *vs.* −0.19; $p = 0.10$), compared with patients receiving dialysis for at least 6 months (**Table 4**). Nearly all of the observed increases in serum albumin levels occurred between M1 and M2 and were

Table 2. Demographic and Baseline Characteristics of the Study Population

	All Patients (N = 271)	F160NR (N = 128)	F180NR (N = 112)	F200NR (N = 19)	F250NR (N = 12)
Age (yr), n (%)					
≤40	22 (8.1)	12 (9.4)	7 (6.3)	3 (15.8)	0
41–50	24 (8.9)	5 (3.9)	13 (11.6)	3 (15.8)	3 (25.0)
51–60	43 (15.9)	20 (15.6)	20 (17.9)	2 (10.5)	1 (8.3)
61–70	72 (26.6)	27 (21.1)	32 (28.6)	6 (31.6)	7 (58.3)
71–80	65 (24.0)	38 (29.7)	23 (20.5)	3 (15.8)	1 (8.3)
>80	45 (16.6)	26 (20.3)	17 (15.2)	2 (10.5)	0
Female, n (%)	144 (53.1)	79 (61.7)	54 (48.2)	7 (36.8)	4 (33.3)
Race, n (%)					
White	116 (42.8)	60 (46.9)	48 (42.9)	2 (10.5)	6 (50.0)
Black	101 (37.3)	42 (32.8)	48 (42.9)	9 (47.4)	2 (16.7)
Other	7 (2.6)	1 (0.8)	3 (2.7)	3 (15.8)	0
Unknown	47 (17.3)	25 (19.5)	13 (11.6)	5 (26.3)	4 (33.3)
Ethnicity, n (%)					
Hispanic or Latino	48 (17.7)	29 (22.7)	18 (16.1)	0	1 (8.3)
Not Hispanic or Latino	175 (64.6)	74 (57.8)	80 (71.4)	14 (73.7)	7 (58.3)
Unknown	48 (17.7)	25 (19.5)	14 (12.5)	5 (26.3)	4 (33.3)
BMI, kg/m^2, mean ± SD	29.6 ± 8.6	26.7 ± 7.0	30.5 ± 7.6	37.7 ± 9.4	38.7 ± 15.3
BMI classification, kg/m^2, n (%)					
<25	96 (35.4)	61 (47.7)	31 (27.7)	2 (10.5)	2 (16.7)
25–30	60 (22.1)	35 (27.3)	22 (19.6)	2 (10.5)	1 (8.3)
≥30	115 (42.4)	32 (25.0)	59 (52.7)	15 (79.0)	9 (75.0)
Dialysis vintage, n (%)					
<6 mo	51 (18.8)	26 (20.3)	22 (19.6)	1 (5.3)	2 (16.7)
6–12 mo	26 (9.6)	11 (8.6)	11 (9.8)	2 (10.5)	2 (16.7)
1–1.9 yr	37 (13.7)	17 (13.3)	13 (11.6)	6 (31.6)	1 (8.3)
2–3.9 yr	73 (26.9)	29 (22.7)	32 (28.6)	7 (36.8)	5 (41.7)
4–5.9 yr	42 (15.5)	22 (17.2)	18 (16.1)	2 (10.5)	0
≥6 yr	42 (15.5)	23 (18.0)	16 (14.3)	1 (5.3)	2 (16.7)
Diabetes, n (%)	140 (51.7)	63 (49.2)	57 (50.9)	10 (52.6)	10 (83.3)
Access, n (%)					
Fistula	159 (58.7)	75 (58.6)	63 (56.3)	11 (57.9)	10 (83.3)
Graft	58 (21.4)	25 (19.5)	28 (25.0)	5 (26.3)	0
Catheter	54 (19.9)	28 (21.9)	21 (18.8)	3 (15.8)	2 (16.7)

BMI, body mass index; NR, nonreuse; SD, standard deviation.

maintained over the follow-up period for the overall cohort (see Table S2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A676) and with each dialyzer (see Tables S3–S5, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A676). No significant changes in NLR, nPCR, spKt/V, UFV, or nutritional supplementation were observed in the overall cohort. Small reductions (≤1.1 kg; ≤1.2%) in pre-HD weight were observed in the overall cohort and within each dialyzer group. Nearly identical reductions were also observed for post-HD weights. In the overall cohort, hemoglobin concentrations increased by a mean of 0.31 g/dl from M1 to M6 ($p < 0.001$).

In the overall cohort, approximately two-thirds of patients (65%; 177/271) exhibited increases in serum albumin levels at M6 (**Figure 1**). The proportion of patients with observed increases was similar across the four dialyzer sizes. The proportion of patients with numeric decreases in serum albumin

Table 3. Mean Clinical Parameters at Month 1 and 6

	All Patients (N = 271)		F160NR (N = 128)		F180NR (N = 112)		F200NR (N = 19)		F250NR (N = 12)	
Parameter*	M1	M6–M1	M1	M6–M1	M1	M6–M1	M1	M6–M1	M1	M6–M1
sAlb (g/dl)	3.35	0.20†	3.36	0.17†	3.35	0.20†	3.33	0.22‡	3.25	0.33‡
Hgb (g/dl)	10.16	0.31†	10.13	0.36§	10.12	0.24	10.74	0.47	9.86	0.17
NLR	4.57	–0.33	4.58	–0.35	4.68	–0.37	3.50	0.67	4.99	–1.27‡
nPCR (g/kg/d)	0.97	–0.01	0.95	–0.02	0.98	0.01	1.00	–0.02	1.01	–0.12
spKt/V	1.58	–0.02	1.67	–0.05	1.52	–0.0003	1.43	0.04	1.39	–0.04
Pre-HD weight (kg)	85.2	–0.82†	72.5	–0.77‡	91.1	–1.1§	115.0	–0.33	118.4	0.05
Post-HD weight (kg)	83.1	–0.81†	70.7	–0.8‡	88.9	–1.0§	112.6	–0.29	115.4	0.02
UFV (L)	2.06	–0.01	1.8	–0.001	2.20	–0.03	2.43	–0.05	2.99	0.03
EDW (kg)	82.6	–0.75§	70.3	–0.8§	88.1	–0.8	112.0	–0.29	113.6	–0.48
Nutritional supplements (%)	64.9	–1.1	62.5	1.6	67.0	–2.7	73.7	–15.8	58.3	8.4

*Some parameters had missing values >10% and the sample sizes were: n = 203, n = 97, n = 83, n = 13, and n = 10 for NLR in all patients, F160NR, F180NR, F200NR, and F250NR, respectively; n = 112, n = 58, n = 42, n = 7, and n = 5 for nPCR in all patients, F160NR, F180NR, F200NR, and F250NR, respectively.

†$p < 0.001$; ‡$p < 0.05$; §$p < 0.01$.

EDW, estimated dry weight; HD, hemodialysis; Hgb, hemoglobin; M1, month 1; M6, month 6; NLR, neutrophil-to-lymphocyte ratio; nPCR, normalized protein catabolic rate; NR, nonreuse; sAlb, serum albumin; spKt/V, single-pool Kt/V; UFV, ultrafiltration volume.

Table 4. Mean Clinical Parameters at Month 1 and 6 by Dialysis Vintage Category (All Dialyzers)

Parameter*	<6 Month Vintage (n = 51)			≥6 Month Vintage (n = 220)			*p* Value (Change in <6 Month Subgroup *vs.* Change in ≥6 Month Subgroup)
	M1	M6	Diff	M1	M6	Diff	
sAlb (g/dl)	3.28	3.60	0.32†	3.36	3.53	0.17†	0.008
NLR	5.11	3.98	–1.13	4.47	4.28	–0.19	0.10
spKt/V	1.57	1.59	0.01	1.58	1.55	–0.03	0.24
Pre-HD weight (kg)	76.95	76.72	–0.24	87.11	86.14	–0.96†	0.23
Post-HD weight (kg)	75.20	74.68	–0.52	84.97	84.09	–0.88†	0.55

*Some parameters had missing values >10% and the sample sizes were: n = 32 and n = 171 for NLR in patients with <6 month vintage and patients with ≥6 month vintage, respectively.

†$p < 0.001$.

Diff, difference; HD, hemodialysis; M1, month 1; M6, month 6; NLR, neutrophil-to-lymphocyte ratio; sAlb, serum albumin; spKt/V, single-pool Kt/V.

varied from 8% (F250NR) to 32% (F200NR) with no clear relationship with dialyzer size. An analysis of albumin change categories (*i.e.*, increased, decreased, and unchanged) demonstrated consistent results across dialyzer groups ($p = 0.08$). At M6, 51% of patients had serum albumin levels greater than 3.5 g/dl (all ≤3.5 g/dl at M1). The percentages of patients in the individual dialyzer groups whose serum albumin levels rose to greater than 3.5 g/dl at M6 were 52%, 49%, 53%, and 50% among patients dialyzed with F160NR, F180NR, F200NR, and F250NR dialyzers, respectively.

Changes in clinical and laboratory parameters among those patients who experienced increases in serum albumin from M1 to M6 (n = 177) were further analyzed (**Tables 5**; see Table S6, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A676). Consistent with the results observed in the overall cohort, significant increases in hemoglobin concentrations (0.57 g/dl; $p < 0.0001$) and small reductions in pre-HD weight (–0.78 kg; $p = 0.01$) and post-HD weight (–0.75; $p = 0.01$) were observed. Although the reductions in NLR observed in the overall cohort (mean decrease: 0.33) did not reach statistical significance, the observed reductions were nearly twofold greater in the subgroup of patients that demonstrated increases in serum albumin levels at M6 (mean difference: 0.90; $p < 0.001$). Increases in serum albumin levels were not associated with increased use of nutritional supplements (65.5% at M1 *vs.* 62.7% at M6).

Discussion

The results of this analysis provide insights into the patterns of use of four sizes of high-flux dialyzers across a medium-sized dialysis organization. Dialyzers with increased surface area were generally used for patients with increased weight and BMI. Among those patients dialyzed with F200NR or F250NR, 77% had a BMI of at least 30 kg/m^2, 64% were male, and 81% were aged 70 years or younger. Dialysis treatment time and UFV increased with increasing dialyzer surface area. Our findings reinforce the concept that body weight and volume typically drive the choice of dialyzer size. Larger patients typically receive HD with larger dialyzers so as to enable them to receive "adequate" dialysis (as assessed by Kt/V) within a time range acceptable for the patient.[4,14] Using a larger dialyzer may avoid the necessity of undergoing additional or longer HD sessions to ensure adequate volume or solute removal.

The findings at the ARA centers regarding dialysis treatment time, dialysis adequacy, and vascular access are consistent

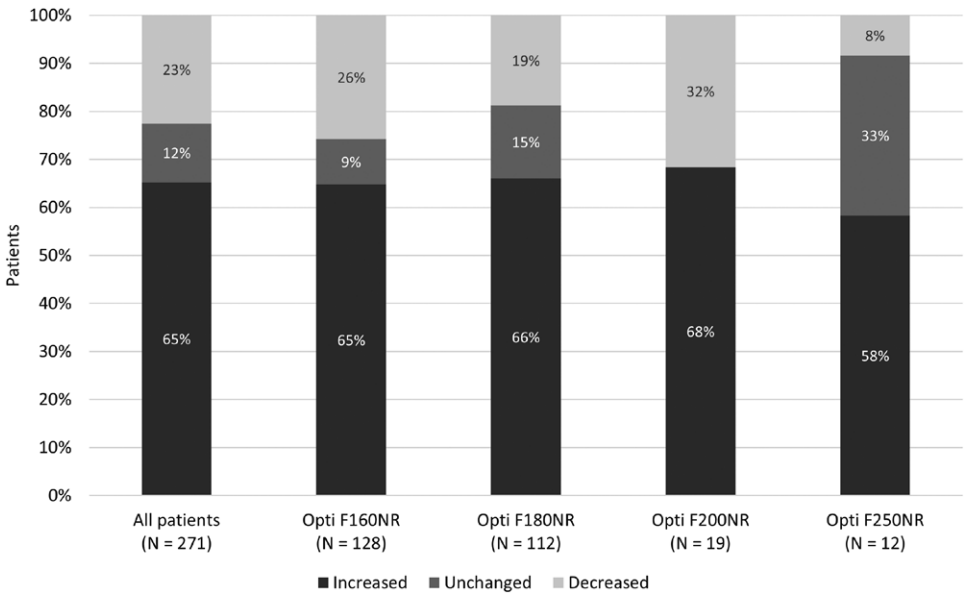

Figure 1. The percentage of patients with changes in albumin status from month 1 to 6. NR, nonreuse.

Table 5. Mean Clinical Parameters in Patients With Increased Serum Albumin Levels From Month 1 to 6

	All Patients (N = 177)		F160NR (N = 83)		F180NR (N = 74)	F200NR (N = 13)			F250NR (N = 7)	
Parameter*	M1	M6–M1	M1	M6–M1	M1	M6–M1	M1	M6–M1	M1	M6–M1
sAlb (g/dl)	3.32	0.40†	3.33	0.38†	3.32	0.39†	3.29	0.43†	3.17	0.57‡
Hgb (g/dl)	10.05	0.57†	9.95	0.62†	10.03	0.54†	10.85	0.72	10.01	0.02
NLR	4.66	−0.90†	4.46	−0.71‡	5.04	−1.20§	3.19	0.11	5.67	−1.81
nPCR (g/kg/d)	1.00	0.01	0.99	0.001	1.01	0.01	1.02	−0.001	0.90	0.13
spKt/V	1.58	−0.005	1.69	−0.03	1.51	0.03	1.39	0.02	1.36	−0.04
Pre-HD weight (kg)	84.6	−0.78‡	72.3	−0.84‡	90.3	−0.91	121.4	−0.18	103.5	−0.01
Post-HD weight (kg)	82.5	−0.75‡	70.4	−0.76‡	87.9	−0.90	118.8	−0.11	100.9	−0.17
UFV, L	2.16	−0.04	1.90	−0.08	2.32	−0.004	2.63	−0.07	2.56	0.17
Nutritional supplements										
LIQU/protein bar (%)	65.5	−2.8	60.2	0	68.9	−2.7	76.9	−23	71.4	0
LIQU use (%)	35.0	−2.8	39.8	−1.2	27.0	−2.7	46.2	−23.1	42.9	14.2
LIQU monthly dose (oz)	12.7	0.50	10.5	1.38‡	15.1	−1.1	21.0	1.0	13.0	−0.5
Protein bar use (%)	33.3	0.6	21.7	2.4	43.2	2.7	53.8	−15.3	28.6	−14.3
Protein bars monthly	10.7	1.15‡	10.7	1.35	10.9	0.90	9.2	2.40	13.0	−1.0¶

*Some parameters had missing values >10% and the sample sizes were: n = 127, n = 61, n = 51, n = 9, and n = 6 for NLR in patients overall, on F160NR, F180NR, F200NR, and F250NR, respectively; n = 72, n = 37, n = 26, n = 6, and n = 3 for nPCR in patients overall, on F160NR, F180NR, F200NR, and F250NR respectively.

†$p < 0.001$; ‡$p < 0.05$; §$p < 0.01$.

¶Significance statistics cannot be calculated, since n = 1.

HD, hemodialysis; Hgb, hemoglobin; LIQU, liquid protein supplement; M1, month 1; M6, month 6; NLR, neutrophil-to-lymphocyte ratio; nPCR, normalized protein catabolic rate; sAlb, serum albumin; spKt/V, single-pool Kt/v; UFV, ultrafiltration volume.

with national averages reported by the Dialysis Outcomes and Practice Patterns Study (DOPPS). In our study, mean prescribed dialysis time was 212 minutes (national average, ~220 minute).[15] Fistula access was present in 59% of our patients compared with 60% per DOPPS data.[16] Moreover, the mean spKt/V in our study (1.6) was consistent with national averages per DOPPS (~1.6) and in line with guidelines for HD adequacy issued by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI).[17,18] These guidelines recommend targeting an spKt/V of 1.4 per HD session for patients treated thrice weekly so as to ensure a minimum delivered spKt/V of 1.2.[18] Although there has been debate regarding whether Kt/V should be the primary measure of the adequacy of HD,[19] it continues to be emphasized in clinical guidelines and may influence reimbursement and payment decisions.[18,19]

Our observations regarding the impact of high-flux dialyzer use among hypoalbuminemic patients is consistent with data from other cohorts. In an analysis of 47 hypoalbuminemic patients managed in Fresenius Kidney Care facilities, 94% demonstrated increases in serum albumin levels after 6 months of dialysis with the F180NR dialyzer.[20] In another study of hypoalbuminemic patients receiving HD at Fresenius Kidney Care, 54% of patients achieved serum albumin levels greater than 3.5 g/dl at M6.[21] In the current study, 65% of patients had increased serum albumin levels at M6 and 51% achieved serum albumin levels greater than 3.5 g/dl at M6.

In patients undergoing HD, serum albumin concentrations can be influenced by inflammatory status, nutritional status, and albumin losses during dialysis. Data from DOPPS suggest that greater than 60% of HD patients have serum albumin levels less than 4.0 g/dl and ~13% have albumin levels less than 3.5 g/dl.[22] Although small, transient increases in serum albumin levels are often observed after the initiation of HD and steady reductions in serum albumin levels are frequently observed before death,[23–28] it is unlikely that our findings were influenced by either phenomenon or can be accounted for by the natural progression of illness. More than 80% of the population in the current study had been receiving dialysis for at least 6 months and, for most patients (77% of the overall cohort), serum albumin levels did not decrease beyond the level observed at M1. The absence of marked albumin losses with the four dialyzers studied is consistent with the sieving coefficient for albumin of less than 0.01. Because sieving coefficients are determined *via in vitro* testing however, they cannot be expected to dictate clinical performance which can be impacted multiple factors including blood flow rate, blood viscosity, and dialyzer design.[29]

The data in the current study do not allow determination of the cause of hypoalbuminemia recorded at baseline. Additionally, information on nutritional or pharmacologic (*e.g.*, anti-inflammatory) interventions that may have contributed to observed increases in serum albumin were not collected. However, given the absence of significant changes in nPCR during the study, it is unlikely that improvements in nutritional status accounted for the observed increases in serum albumin levels. Among patients whose serum albumin increased at M6, protein bar use increased by a mean of approximately one protein bar per month and liquid supplement use increased by a mean of 0.5 oz per month. The proportion of patients receiving any form of intradialytic oral nutritional supplements actually decreased by 2.8% among patients with serum albumin level increases. Changes between pre- and post-HD weights from M1 to M6 were similar, indicating that changes in fluid balance do not likely explain the improvement in albumin seen during the study.

Elevated NLRs have been associated with an increased risk of cardiovascular and all-cause mortality in ESKD[30,31] and are inversely correlated with serum albumin and hemoglobin levels.[30,32–34] The mean baseline NLR in the current study was 4.6, markedly higher than reference levels of 2–3 among patients on HD.[31] This finding suggests that increased inflammation may have been a contributing factor to the observed hypoalbuminemia. Numerical reductions in NLR (mean: 0.33) were observed in the overall cohort, with a mean decrease of

1.27 observed in patients dialyzed with the F250NR dialyzer ($p < 0.05$). Larger mean reductions in NLR were observed among those patients exhibiting increases in serum albumin levels, suggesting that reductions in systemic inflammation may have contributed to the observed increases in serum albumin levels. From M1 to M6, patients demonstrated mean hemoglobin increases of 0.31 g/dl; this inverse relationship between hemoglobin and NLR is consistent with prior research.[31]

Thus, it is plausible that the observed increases in serum albumin resulted from a reduction in systemic inflammation or a resolution of the numerous factors that can cause hypoalbuminemia in ESKD. The current study was not designed to identify factors that may have contributed to reduced inflammation, but potential explanations include resolution of infections or thrombotic events, improved management of comorbid conditions, changes in medication, dietary factors, and improved dialysate quality.[35] Such an explanation is consistent with the observed reductions in NLR. Reduced levels of inflammation could also explain observed increases in hemoglobin, a potential downstream consequence of improved erythropoiesis-stimulating agent (ESA) responsiveness or improved iron utilization.[36–38] In the current study, changes in iron use or ESA doses cannot be excluded as possible contributors to the observed hemoglobin increases.

Underlying differences in the inflammatory state of incident *versus*. prevalent dialysis populations may help explain the results across the dialysis vintage subgroups. Patients recently initiating dialysis had higher NLR and lower serum albumin levels at M1 than patients with a longer history of dialysis. These patients also demonstrated larger reductions in NLR and greater increases in serum albumin levels at M6. Such findings are aligned with the high rates of uremic symptoms (*e.g.,* fatigue, anorexia, pruritus, difficulty concentrating, and pain) and high levels of inflammatory markers observed in patients initiating dialysis.[39,40] Use of high-flux dialysis to clear uremic retention solutes associated with increased leukocyte activity and inflammation may contribute to reduced inflammation and the observed changes in laboratory parameters.[41–43] In prior studies, patients with the highest levels of inflammatory biomarkers on dialysis initiation exhibited sharp reductions in biomarker levels over the first year of dialysis.[40] Prior research also demonstrated increases in serum albumin over the first year of dialysis that inversely correlated with changes in markers of inflammation.[24] Such temporal changes have also been attributed to nutritional improvement or reduced proteinuria secondary to loss of residual renal function.

Limitations of the study included its retrospective, observational design and the lack of a comparator. Data on some parameters, including NLR and nPCR, were incomplete, with 25% of NLR data missing and 59% of nPCR data missing. By defining hypoalbuminemia at M1 on a single laboratory value, it is plausible that some patients with spurious laboratory results may have been included in the analysis. Additionally, the present analysis was not adjusted for potential seasonal variations in pre-HD albumin concentrations.[44,45] The absence of data on C-reactive protein, comorbidities, and potential factors leading to hypoalbuminemia or affecting the time course of the hypoalbuminemia also are important limitations of the study.

Conclusion

Dialyzers with larger membrane surface areas were generally reserved for patients with a larger BMI. All high-flux dialyzers studied, regardless of membrane surface area, were generally consistent in their clinical performance in this population of patients with hypoalbuminemia and increased markers of systemic inflammation. Significant improvements in serum albumin levels were observed within 1 month, and serum albumin increases were associated with reductions in systemic inflammation (as assessed by NLR). In summary, these results support the use of high-flux dialyzers in patients with hypoalbuminemia.

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