Comparative Effectiveness of Dialyzers: A Longitudinal, Propensity Score-Matched Study of Incident Hemodialysis Patients

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Differences in dialyzer design may have consequences for patient outcomes. We evaluated the comparative effectiveness of commonly used dialyzers with respect to measures of dialysis treatment, anemia management, inflammation, and dialyzer clotting. Patients receiving hemodialysis between January 1, 2009, and December 31, 2013, and using polyarylethersulfone–polyvinylpyrrolidone (PAS-PVP; Polyflux Revaclear) or polysulfone (PS; Optiflux 160 or Optiflux 180) dialyzers were followed for 1 year or until end of study or censoring for dialyzer switch, modality change, or loss to follow-up. For each comparison, eligible patients were propensity score-matched 1:1 on a range of baseline characteristics. Outcomes were assessed using generalized linear mixed models. Dialysis adequacy was similar in both dialyzer groups. Erythropoiesis-stimulating agent (ESA) doses were lower for patients using PAS-PVP *versus* patients using PS-160 (difference range: 75–589 units/treatment; statistically significant in months 1–5 and 7) and for patients using PAS-PVP *versus* patients using PS-180 (difference range: 27–591 unit/treatment; statistically significant in months 1–9). Intravenous iron doses trended lower for patients using PAS-PVP *versus* patients using PS, but hemoglobin concentrations were equivalent. In conclusion, use of PAS-PVP *versus* PS dialyzers was associated with equivalent dialysis adequacy, lower ESA doses, modestly lower Intravenous iron doses, and equivalent hemoglobin concentrations. *ASAIO Journal* 2016; 62:613–622.

Key Words: dialysis, dialyzer composition, outcomes

Dialyzer composition and architecture have biological and clinical implications. Classical examples of this include the effect of surface area of the dialyzer on efficiency, the effect of dialyzer pore size on flux and middle molecule clearance, and the effect of membrane biocompatibility on inflammatory responses.[1,2] In the contemporary era, dialyzers are highly efficient, high-flux, and highly biocompatible by historical standards.[3–7] This has led to an inherent complacency, whereby the effects of subtle but real differences among modern dialyzers that impact outcomes may not be considered.

Differences among modern dialyzers include fiber number, configuration and diameter, length, pore size, and membrane polymer.[8] These differences may influence blood flow dynamics, cytokine expression, and thrombogenicity and, thereby, affect urea clearance, time requirements for dialysis, sequestration of blood in the dialyzer, hemoglobin concentration and other iron storage measures, and utilization of medications to treat anemia.[9–12] There is the potential, therefore, for dialyzer selection to affect patient outcomes and, by extension, health care expenditures.

Dialyzer comparison studies performed to date have generally assessed small numbers of patients over relatively short time periods and may, therefore, not be large enough to demonstrate potential differences in clinical outcomes. In this comparative effectiveness analysis, we have examined outcomes in a large cohort of incident in-center hemodialysis (HD) patients over the course of 1 year following initiation of dialysis with either a polyarylethersulfone–polyvinylpyrrolidone (PAS-PVP) membrane (Polyflux Revaclear) or a polysulfone (PS) membrane (Optiflux); both are single-use dialyzers with similar mass transfer coefficients and are used extensively in the United States.[13–16]

Methods

Study Design

The study was a retrospective, observational analysis of preexisting, deidentified data from a large dialysis organization (LDO) in the United States. Thus, according to 45 CFR Part 46 from the United States Department of Health and Human Services, this study was exempt from institutional review board or ethics committee approval. We adhered to the Declaration of Helsinki; informed consent was not required.

Study Patients and Exposure

Patients eligible for inclusion in the analysis were those who began in-center HD at LDO facilities at least 3 times per week during the period January 1, 2009, to December 31, 2013, using a study dialyzer (Polyflux Revaclear, Optiflux F160NR, or Optiflux F180NR). Patients were excluded from the analysis if they were less than 18 years of age, were Veterans

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Administration beneficiaries, or were on a dialysis modality other than in-center HD.

Polyflux Revaclear dialyzers (Baxter International Inc., Deerfield, IL) have a PAS-PVP membrane with a surface area of 1.4 m^2, membrane wall thickness of 35 μm, fiber inner diameter of 190 μm, and are steam sterilized. Optiflux dialyzers (Fresenius Medical Care North America, Waltham, MA) have a PS membrane and are available in varying sizes, including Optiflux F160NR (here represented as PS-160), with a surface area of 1.5 m^2, and Optiflux F180NR (here represented as PS-180), with a surface area of 1.8 m^2. Both of these PS membrane dialyzers have a membrane wall thickness of 40 μm, fiber inner diameter of 200 μm, and are sterilized by electron beam. For the primary analysis, outcomes among patients using PAS-PVP or PS-160 dialyzers were compared. In the secondary analysis, outcomes among patients using PAS-PVP dialyzers or the larger surface area PS-180 dialyzers were compared.

Study Time Period

Patient time began on the first day of the first calendar month after patients started dialysis using a study dialyzer. Patients were followed forward in time for 1 year or until end of study (31 December 2013) or censoring (upon dialyzer change, modality change, transplant, transfer of care away from LDO, withdrawal from dialysis, renal recovery, or death).

Propensity Score Matching

Propensity score matching was used to construct comparable populations of PAS-PVP and PS membrane dialyzer users from among all eligible users such that differences that are obvious sources of potential bias were minimized. Separate but analogous propensity score-matched comparisons were performed for PAS-PVP *versus* PS-160 and PAS-PVP *versus* PS-180 analyses. Propensity scores were estimated using logistic regression models that considered age, sex, race, body weight, dialysis access type, diabetes, peripheral vascular disease, congestive heart failure, coronary artery disease, cerebrovascular disease, gastrointestinal bleed, Charlson comorbidity index score, baseline serum albumin, normalized protein catabolic rate, and serum phosphate. For each comparison, PAS-PVP and PS dialyzer patients were matched 1:1 without replacement.

Outcomes

Outcomes were assessed longitudinally for each comparison as follows:

Dialysis treatment parameters. Kt/V was considered as the mean monthly value for each patient. Dialysis treatment time was considered as the mean treatment duration in minutes for each patient in each month.

Anemia management-related parameters. Utilization of erythropoiesis-stimulating agent (ESA; which was empirically observed to be epoetin alfa for all patients in this study, consistent with treatment patterns at the LDO) was considered as the mean dose delivered per dialysis treatment attended during each month for each patient. Intravenous (IV) iron utilization was considered as the cumulative dose per month for each treated patient. Hemoglobin concentration (measured twice monthly per clinical protocol) was considered as the mean monthly value for each patient.

Inflammation markers. Transferrin saturation (TSAT), serum ferritin concentration, and serum albumin concentration (each typically measured once monthly per clinical protocol) were considered as the mean (where more than one measurement was recorded) monthly value for each patient.

Dialyzer clotting-related parameters. Heparin utilization was considered as the monthly mean dose per dialysis treatment for each patient, including all attended treatments whether heparin was administered or not. As a surrogate of fiber clotting (which is not measured directly), we considered the rise in venous pressure during the course of dialysis. To account for ramp up of blood flow at the start of dialysis treatments (which is common in clinical practice), venous pressure change was considered only for the period where blood flow had been maximized for the treatment: venous pressure change was defined as the difference between the highest and the first venous pressure during this interval. Data were considered as the mean monthly value for each patient. Platelet count was considered as the mean monthly value (if more than one value was available per month) for each patient.

Hospitalizations were determined from LDO electronic health records and considered as number of admissions per patient-year.

Statistical Analysis

Baseline patient characteristics of the propensity score-matched cohorts were summarized as means, standard deviations, medians, interquartile ranges, counts, and proportions and were formally compared using standardized differences (differences of magnitude >10% were considered indicative of imbalances that are likely to confound).

Outcomes in the matched groups were assessed using generalized linear mixed models, with random effects intercepts for individual patients and fixed-effects terms for dialyzer, time, and the two-way cross-product of dialyzer group-by-time. Robust variance estimators were used to account for the matched design in treatment groups. For models of hospitalization rates, group-by-time interactions were not statistically significant for either comparison (indicating that between-group differences were constant over time), and reduced models were fit containing fixed-effect terms for dialyzer group and time only; the resultant single time-invariant effect estimate is presented. Results from significance testing for fixed effects in all models are provided in Supplementary Data Tables S1 and S2 (see Tables, Supplemental Digital Content, http://links.lww.com/ASAIO/A104).

Empiric transformations were applied as needed to meet distributional assumptions. Where transformations were applied, model output was back-transformed, and results are presented on the native scale. Models for continuous response parameters were specified using natural links and Gaussian distributions where possible. Models for hospitalization rates were specified using log links and Poisson distributions.

All analyses were performed using SAS 9.3.

Results

Primary Comparisons: PAS-PVP Versus PS-160

Comparisons of baseline characteristics of matched incident patients beginning dialysis using PAS-PVP and PS-160

dialyzers during the period January 1, 2009, to December 31, 2013, are presented in **Table 1**. Dialyzer groups were well matched across all variables considered (magnitude of standardized differences was <10% for all characteristics). It should be noted that serum ferritin and TSAT measurements were not included in the propensity score match; baseline values were 404 ng/mL (PAS-PVP) *vs*. 442 ng/mL(PS-160) for ferritin and 21.0% (PAS-PVP) *vs*. 21.9% (PS-160)

Table 1. Baseline Characteristics of Matched PAS-PVP *vs.* PS-160 Dialyzer Patients

	PAS-PVP (N = 9,396)	PS-160 (N = 9,396)	Standardized Difference	*P* Value*
Age (years)				
Mean ± SD	63.8 ± 15.3	64.1 ± 15.5	+1.9%	0.07
Median [p25, p75]	65 [54, 75]	66 [55, 76]		
Gender, n (%)				
Male	5,116 (54.5)	5,072 (54.0)	–0.9%	0.52
Female	4,280 (45.6)	4,324 (46.0)	+0.9%	
Race, n (%)				
White	4,701 (50.0)	4,788 (51.0)	+1.9%	0.66
Black	2,479 (26.4)	2,445 (26.0)	–0.8%	
Hispanic	1,438 (15.3)	1,400 (14.9)	–1.1%	
Asian	394 (4.2)	370 (3.9)	–1.3%	
Other/unknown	384 (4.1)	393 (4.2)	+0.5%	
Vascular access, n (%)				
Arteriovenous fistula	1,503 (16.0)	1,468 (15.6)	–1.0%	0.88
Arteriovenous graft	282 (3.0)	287 (3.1)	+0.3%	
Central venous catheter	7,608 (81.0)	7,637 (81.3)	+0.8%	
Unknown	3 (0.03)	4 (0.04)	+0.5%	
Dialysis vintage (months)				
Mean ± SD	0.1 ± 0.0	0.1 ± 0.0	0%	0.36
Median [p25, p75]	0 [0, 0]	0 [0, 0]		
Etiology of ESRD, n (%)				
Diabetes	3,992 (42.5)	3,892 (41.4)	–2.2%	0.34
Hypertension	2,812 (29.9)	2,862 (30.5)	+1.2%	
Other	2,592 (27.6)	2,642 (28.1)	+1.2%	
Census region, n (%)				
Midwest	2,069 (22.0)	2,189 (23.3)	+3.1%	
Northeast	1,011 (10.8)	1,013 (10.8)	+0.1%	
South	1,274 (13.6)	1,154 (12.3)	–3.8%	0.05
South Atlantic	3,258 (34.7)	3,231 (34.4)	–0.6%	
West	1,784 (19.0)	1,809 (19.3)	+0.7%	
CCI score				
Mean ± SD	5.6 ± 2.0	5.6 ± 2.0	0%	0.96
Median [p25, p75]	6 [4, 7]	6 [4, 7]		
Body weight (kg)				
Mean ± SD	79.9 ± 22.2	79.4 ± 22.4	–2.2%	0.06
Median [p25, p75]	76.7 [64.0, 92.1]	75.9 [63.8, 91.4]		
Diabetes, n (%)	5,921 (63.0)	5,824 (62.0)	–2.1%	0.14
Congestive heart failure, n (%)	1,107 (11.8)	1,101 (11.7)	–0.2%	0.89
Coronary artery disease, n (%)	203 (2.2)	213 (2.3)	+0.7%	0.62
Cerebrovascular disease, n (%)	57 (0.6)	61 (0.7)	+0.5%	0.71
Peripheral vascular disease, n (%)	363 (3.9)	360 (3.8)	–0.2%	0.91
GI bleed, n (%)	31 (0.3)	31 (0.3)	0%	>0.99
nPCR (g/kg/day)				
Mean ± SD	0.42 ± 0.15	0.42 ± 0.14	0%	0.99
Median [p25, p75]	0.39 [0.33, 0.46]	0.39 [0.33, 0.46]		
Serum albumin (g/dL)				
Mean ± SD	3.41 ± 0.54	3.41 ± 0.55	0%	0.54
Median [p25, p75]	3.4 [3.1, 3.8]	3.4 [3.1, 3.8]		
Serum phosphate (mg/dL)				
Mean ± SD	4.62 ± 1.52	4.58 ± 1.51	–2.6%	0.07
Median [p25, p75]	4.4 [3.6, 5.4]	4.4 [3.5, 5.4]		
Serum ferritin† (ng/mL)				
Mean ± SD	403.9 ± 424.8	441.9 ± 430.9	+8.9%	0.09
Median [p25, p75]	289 [142, 552]	308 [150, 600]		
Transferrin saturation† (%)				
Mean ± SD	21.0 ± 10.1	21.9 ± 11.5	+8.3%	0.29
Median [p25, p75]	19 [15, 25]	20 [15, 26]		
Transplant, n (%)	0 (0)	0 (0)	0.0%	NA

**P* values are provided but standard differences were used to evaluate the propensity score match.

†Variable not included in propensity score match.

CCI, Charlson comorbidity index; ESRD, end-stage renal disease; GI, gastrointestinal; nPCR, normalized protein catabolic rate; p25, 25th percentile; p75, 75th percentile; PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone; SD, standard deviation.

for TSAT (standardized differences were 8.9% and 8.3%, respectively).

Kt/V and dialysis treatment times were comparable for the PAS-PVP and PS-160 groups over the study period (**Figure 1**, left panels). For both groups, Kt/V increased over months 1 through 5 and remained constant thereafter. Also for both groups, dialysis treatment time increased from month 1 to month 2 and subsequently declined gradually. Treatment times were shorter for patients using PAS-PVP in months 1–7, but differences were small, ranging from 1.2 to 1.7 minutes/treatment. Comparisons of measures of anemia management between PAS-PVP and PS-160 users are presented in the left panels of **Figure 2**. For both dialyzer groups, ESA utilization increased from month 1 to month 2 and subsequently declined over the remainder of study follow-up. Erythropoiesis-stimulating agent use was significantly lower for patients using PAS-PVP in months 1–5 and month 7 and numerically lower in all other months. The magnitude of difference ranged from 75 to 589 units/HD treatment month-over-month throughout the follow-up period. Cumulative monthly IV iron utilization was modestly lower among PAS-PVP users than PS-160 users, except in month 2; although statistically significant, the magnitude of difference is unlikely to be clinically relevant (2–5 mg/month). Over the course of follow-up, IV iron use fell in parallel for both groups. Hemoglobin concentrations increased in both groups over the first 4 months of study follow-up, declining gradually thereafter. Hemoglobin concentrations were essentially comparable for both groups at all time points. Statistically significant differences were observed in months 2 and 3 (with hemoglobin higher among patients using PAS-PVP *versus* patients using PS-160), but the magnitude of difference was modest and unlikely to be of clinical significance (0.01–0.08 g/dL).

Comparisons of markers of inflammation among PAS-PVP and PS-160 users are presented in the left panels of **Figure 3**. Transferrin saturation increased over time in both groups and was significantly higher for patients using PAS-PVP than for patients using PS-160 in months 3, 4, and 9; the magnitude of the between-group difference in TSAT during these months was approximately 1%. Serum ferritin values increased over time in both groups but were lower for patients using PAS-PVP, except in month 3. The between-group difference was statistically significant only in month 1, and it should be considered that a difference of similar magnitude was observed at baseline for patients with available data. Serum albumin concentrations increased over time and were lower for patients using PAS-PVP from month 2; although differences were statistically significant in several months, the magnitude of the difference was small (<0.04 g/dL).

Comparisons of potential dialyzer clotting indicators are presented in the left panels of **Figure 4**. Heparin doses declined over follow-up in both groups: doses were higher for PAS-PVP users than PS-160 users in month 1 (difference: 121 unit/HD treatment) but comparable between groups thereafter. Venous pressure change during dialysis treatment was of a lesser magnitude for patients using PAS-PVP than

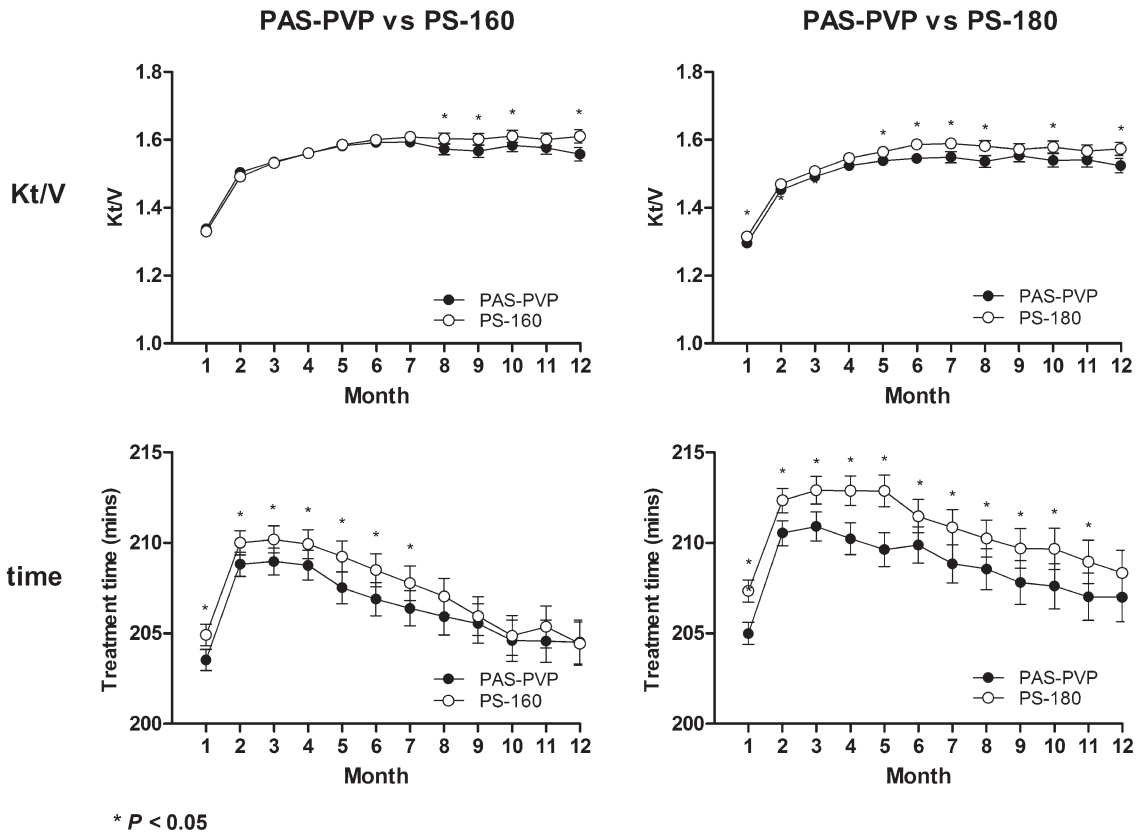

Figure 1. Dialysis parameters (Kt/V, top panels; treatment time, bottom panels) over the course of the study are presented. The left panels show comparison of PAS-PVP *vs.* PS-160, and the right panels show PAS-PVP *vs.* PS-180. PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone.

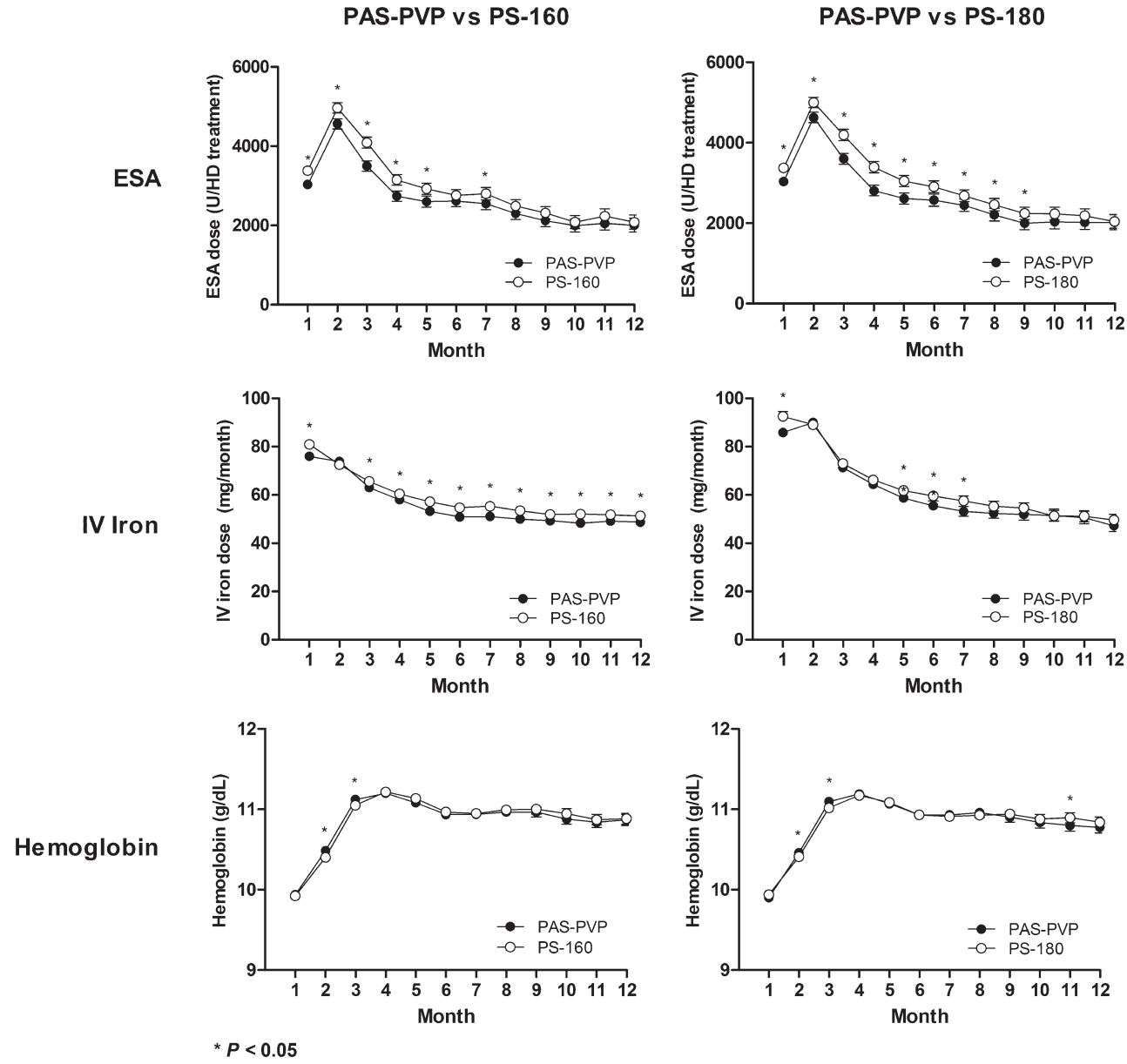

Figure 2. Measures of anemia management (erythropoiesis-stimulating agent [ESA], top panels; intravenous [IV] iron, middle panels; hemoglobin, bottom panels) over the course of the study are presented. The left panels show comparison of PAS-PVP *vs.* PS-160, and the right panels show PAS-PVP *vs.* PS-180. PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone.

for patients using PS-160 from month 2 onwards, with statistically significant differences in months 5, 6, 9, 10, and 12; between-group differences generally increased over the study, reaching a maximum difference of 2.4 mm Hg in month 9. Platelet counts declined over time in both groups; platelet counts were greater for patients using PAS-PVP than for those using PS-160 at all time points. Differences ranged from 5.0×10^9/L to 11.2×10^9/L and were statistically significant in all except month 11.

Hospitalization rates (**Table 3**) were slightly lower for PAS-PVP users than for PS-160 users, with overall estimates of 2.42 and 2.55 admissions/patient-year, respectively, corresponding to an incidence rate ratio (IRR) for PAS-PVP of 0.95 (95% confidence interval [CI]: 0.90, 1.00; $P = 0.05$) referent to PS-160.

Secondary Comparisons: PAS-PVP Versus PS-180

Secondary comparisons were made between PAS-PVP and PS-180 users. Baseline characteristics of the matched PAS-PVP and PS-180 groups are shown in **Table 2**. The two groups were well matched across all variables. Again, serum ferritin and TSAT were not included in the propensity score match algorithm; TSAT was comparable between groups, but serum ferritin concentrations were lower for patients using PAS-PVP than for patients using PS-180 (388 *vs.* 430 ng/mL; standardized difference = 9.9%). As expected, the observed body weights of 86.1 and 86.3 kg for PAS-PVP and PS-180 users, respectively, were greater than those observed for the matched PAS-PVP/PS-160 patient groups (at 79.9 and 79.4 kg, respectively).

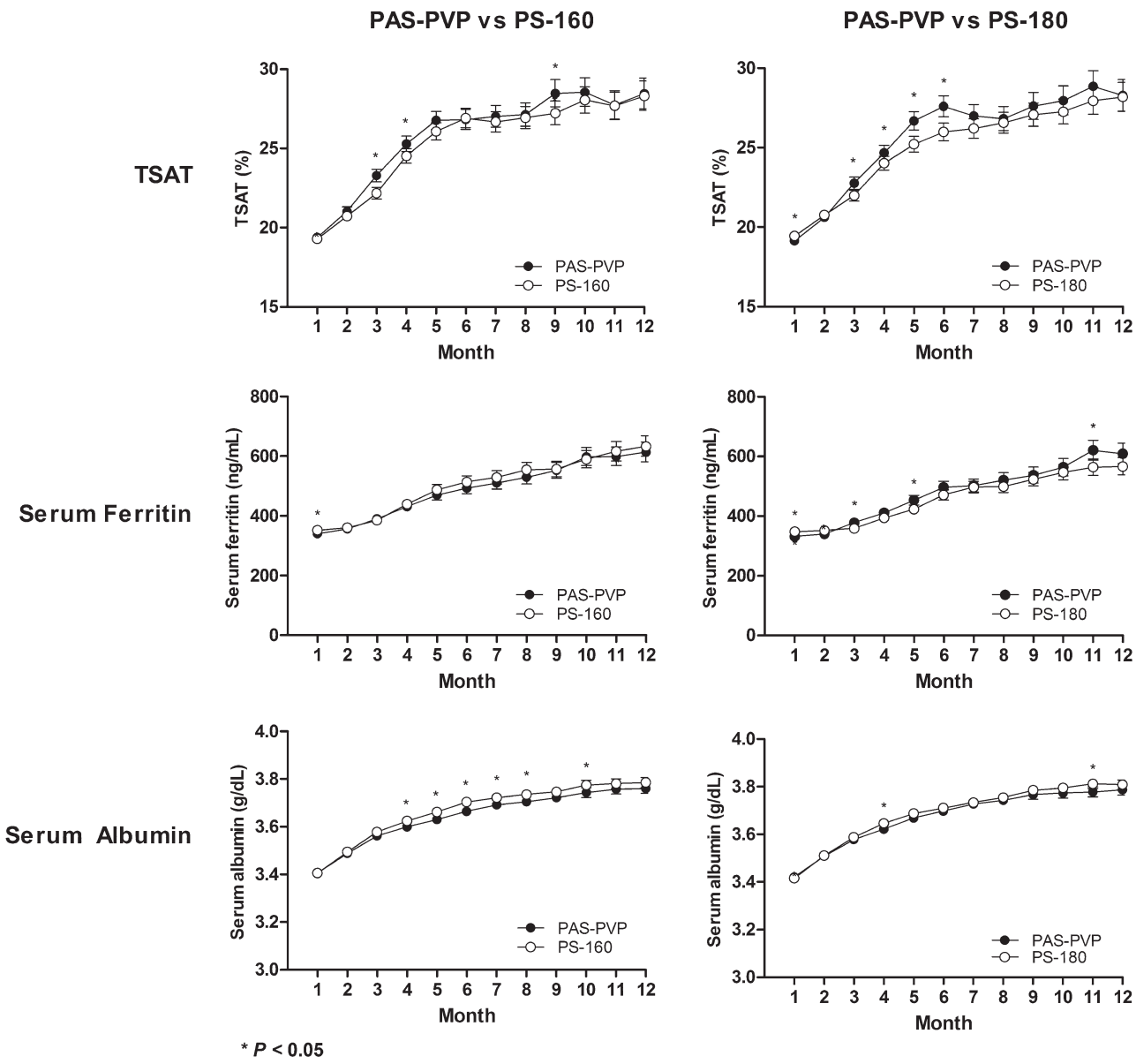

Figure 3. Markers of inflammation (transferrin saturation [TSAT], top panels; serum ferritin, middle panels; serum albumin, bottom panels) over the course of the study are presented. The left panels show comparison of PAS-PVP *vs.* PS-160, and the right panels show PAS-PVP *vs.* PS-180. PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone.

In general, both temporal patterns and between-group differences for outcomes mirrored findings from the PAS-PVP/PS-160 comparison. No substantive differences in monthly mean Kt/V were observed between PAS-PVP and PS-180 users. Although differences were statistically significant at several time points, the magnitude of differences was not clinically meaningful (0.02–0.05). Mean dialysis treatment time was lower among PAS-PVP users than among PS-180 users in all months; differences ranged from 1.4 to 3.2 mins/treatment (**Figure 1**, right panels).

Erythropoiesis-stimulating agent utilization was lower among PAS-PVP users in all months, with differences ranging from 27 to 591 unit/HD treatment and achieving statistical significance in months 1–9. Cumulative monthly IV iron utilization was lower among PAS-PVP users than among PS-180 users in all except months 2 and 10, although between-group differences were very small (0–6.7 mg/month). Hemoglobin concentrations were comparable for both groups at all time points.

Transferrin saturation increased over time in both groups: values were lower among PAS-PVP users than among PS-180 users in months 1 and 2 and were higher for PAS-PVP users than for PS-180 users thereafter, with differences in values of 0.3–1.6%. Serum ferritin values increased over the study for both groups. Values were lower for patients using PAS-PVP than for patients using PS-180 in months 1 and 2 and greater for patients using PAS-PVP than for patients using PS-180 thereafter; differences were significant in months 1, 3, 5, and 11. Serum albumin levels were lower among PAS-PVP users than among PS-180 users in all but month 1, but the magnitude of difference was small (<0.03 g/dL; **Figure 3**, right panels).

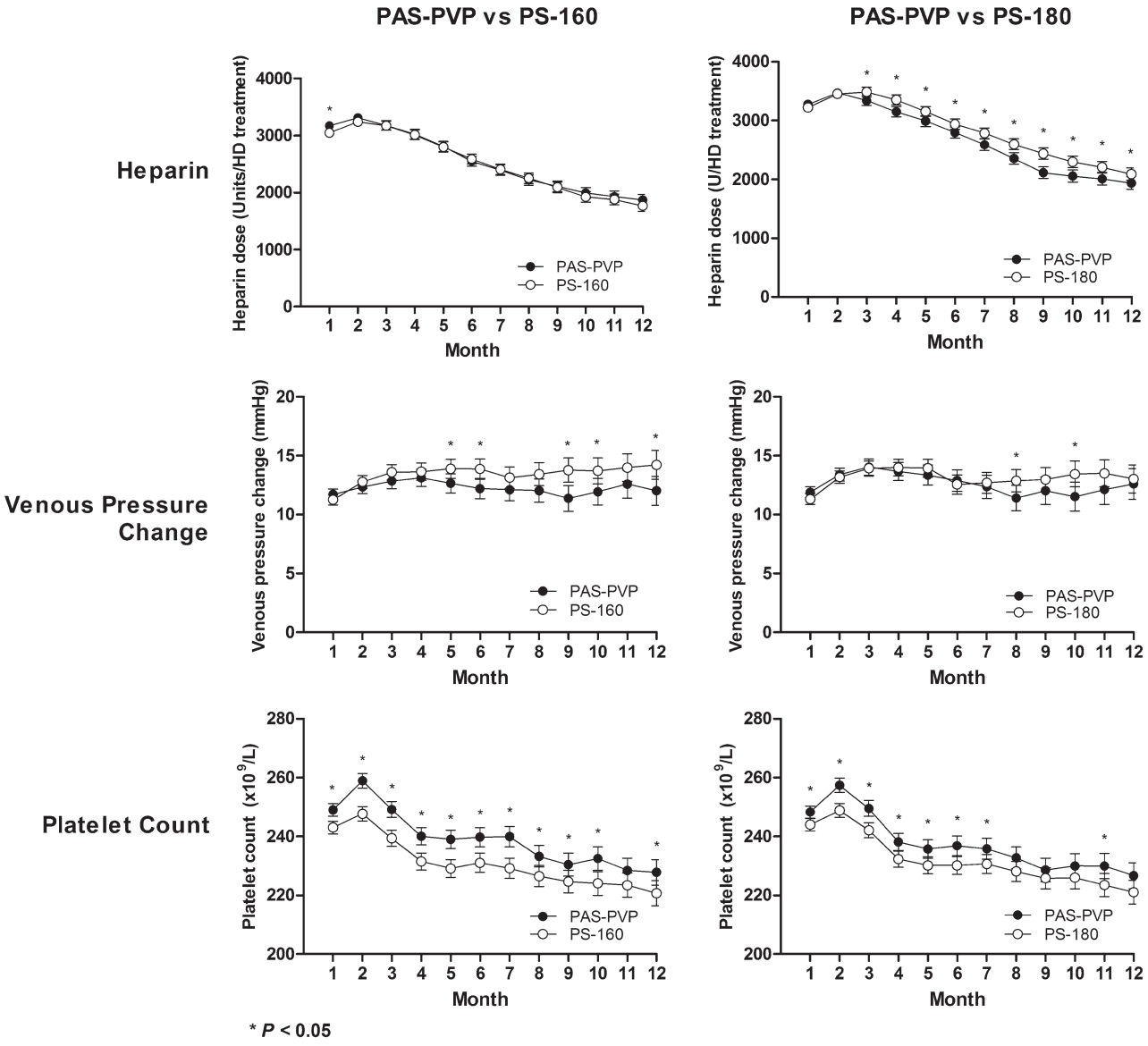

Figure 4. Dialyzer clotting indicators (heparin, top panels; venous pressure change, middle panels; platelet count, bottom panels) over the course of the study are presented. The left panels show comparison of PAS-PVP *vs.* PS-160, and the right panels show PAS-PVP *vs.* PS-180. PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone.

Heparin utilization declined over the study follow-up period for both groups but was lower in PAS-PVP users than in PS-180 users from month 3 onward. Differences ranged from 142 to 324 unit/HD treatment during these months. Venous pressure change was greater for PAS-PVP users than for PS-180 users in months 1–3 and month 6, but greater for PS-180 users than for PAS-PVP users in all other months; between-group differences were statistically significant in months 8 and 10. Platelet counts were greater for PAS-PVP users than for PS-180 users at all time points; differences ranged in magnitude from 2.8×10^9/L to 8.6×10^9/L and were statistically significant in months 1–7 and month 11 (**Figure 4**, right panels).

Hospitalization rates were comparable for PAS-PVP and PS-180 cohorts (**Table 3**), with overall estimates of 2.55 and 2.58 admissions/patient-year, respectively, corresponding to an IRR for PAS-PVP of 0.99 (95% CI: 0.94, 1.04; $P = 0.62$) referent to PS-180.

Discussion

In this retrospective, propensity score-matched analysis, we assessed differences between commonly used dialyzers with respect to measures of dialysis treatment, anemia management, inflammation, and potential dialyzer clotting over the course of 1 year among patients initiating in-center HD.

Results from our study did not clearly favor one dialyzer type over another with respect to dialysis adequacy: Kt/V values were lower for PAS-PVP users compared with matched PS-160 and PS-180 users at later time points, although differences were small in magnitude and unlikely to be of clinical significance. It should also be noted that although Kt/V is commonly used as a marker of dialysis adequacy, it is calculated based on urea clearance[17] and, thus, does not allow comparison of the effectiveness of the dialyzers at removing other higher molecular weight toxins. Treatment times were slightly shorter for patients

Table 2. Baseline Characteristics of Matched PAS-PVP *vs.* PS-180 Dialyzer Patients

	PAS-PVP (N = 9,636)	PS-180 (N = 9,636)	Standardized Difference	*P* Value*
Age (years)				
Mean ± SD	62.1 ± 15.4	62.0 15.2	–0.7%	0.56
Median [p25, p75]	63 [52, 74]	63 [52, 73]		
Gender, n (%)				
Male	5,661 (58.7)	5,688 (59.0)	+0.6%	0.69
Female	3,975 (41.3)	3,948 (41.0)	–0.6%	
Race, n (%)				
White	4,468 (46.4)	4,488 (46.6)	+0.4%	0.96
Black	3,243 (33.7)	3,212 (33.3)	–0.7%	
Hispanic	1,284 (13.3)	1,277 (13.3)	–0.2%	
Asian	253 (2.6)	252 (2.6)	–0.1%	
Other/unknown	388 (4.0)	407 (4.2)	+1.0%	
Vascular access, n (%)				
Arteriovenous fistula	1,282 (13.3)	1,286 (13.4)	+0.1%	0.66
Arteriovenous graft	309 (3.2)	282 (2.9)	–1.6%	
Central venous catheter	8,044 (83.5)	8,066 (83.7)	+0.6%	
Unknown	1 (0.01)	2 (0.02)	+0.8%	
Dialysis vintage (months)				
Mean ± SD	0.1 ± 0.3	0.1 ± 0.3	0%	0.41
Median [p25, p75]	0 [0, 0]	0 [0, 0]		
Etiology of ESRD, n (%)				
Diabetes	4,167 (43.2)	4,138 (42.9)	–0.6%	0.79
Hypertension	2,839 (29.5)	2,826 (29.3)	–0.3%	
Other	2,630 (27.3)	2,672 (27.7)	+1.0%	
Census region, n (%)				
Midwest	2,092 (21.7)	2,242 (23.3)	+3.7%	
Northeast	912 (9.5)	938 (9.7)	+0.9%	
South	1,061 (11.0)	983 (10.2)	–2.6%	
South Atlantic	3,156 (32.8)	2,990 (31.0)	–3.7%	
West	2,415 (25.1)	2,483 (25.8)	+1.6%	0.007
CCI score				
Mean ± SD	5.5 ± 2.0	5.5 ± 2.0	0%	0.51
Median [p25, p75]	5 [4, 7]	5 [4, 7]		
Body weight (kg)				
Mean ± SD	86.1 ± 25.5	86.3 ± 24.7	+0.8%	0.11
Median [p25, p75]	81.7 [68.3, 99.6]	82.8 [69.0, 99.3]		
Diabetes, n (%)	6,210 (64.5)	6,189 (64.2)	–0.5%	0.75
Congestive heart failure, n (%)	1,246 (12.9)	1,264 (13.1)	+0.6%	0.70
Coronary artery disease, n (%)	275 (2.9)	270 (2.8)	–0.3%	0.83
Cerebrovascular disease, n (%)	62 (0.6)	67 (0.7)	+0.7%	0.66
Peripheral vascular disease, n (%)	347 (3.6)	334 (3.5)	–0.7%	0.61
GI bleed, n (%)	19 (0.2)	18 (0.2)	–0.2%	0.87
nPCR (g/kg/day)				
Mean ± SD	0.42 ± 0.16	0.42 ± 0.16	0%	0.72
Median [p25, p75]	0.39 [0.33, 0.47]	0.39 [0.33, 0.47]		
Serum albumin (g/dL)				
Mean ± SD	3.42 ± 0.55	3.41 ± 0.56	–1.8%	0.59
Median [p25, p75]	3.5 [3.1, 3.8]	3.5 [3.1, 3.8]		
Serum phosphate (mg/dL)				
Mean ± SD	4.66 ± 1.53	4.63 ± 1.50	–2.0%	0.57
Median [p25, p75]	4.5 [3.6, 5.4]	4.5 [3.6, 5.4]		
Serum ferritin† (ng/mL)				
Mean ± SD	388.4 ± 389.3	429.8 ± 445.1	+9.9%	0.35
Median [p25, p75]	290 [148, 497]	294 [144, 549]		
Transferrin saturation† (%)				
Mean ± SD	21.4 ± 11.5	21.6 ± 11.7	+1.7%	0.81
Median [p25, p75]	19 [14, 25]	19 [15, 25}		
Transplant, n (%)	0 (0)	0 (0)	0.0%	NA

**P* values are provided but standard differences were used to evaluate the propensity score match.

†Variable not included in propensity score match.

CCI, Charlson comorbidity index; ESRD, end-stage renal disease; GI, gastrointestinal; nPCR, normalized protein catabolic rate; p25, 25th percentile; p75, 75th percentile; PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone; SD, standard deviation.

using PAS-PVP compared with patients using PS-160 (≈1 minute/treatment) and PS-180 (≈2 minutes/treatment) and might offer an explanation for the minor differences between groups in Kt/V. Hospitalization rates were slightly lower for PAS-PVP users than for PS-160 users (IRR, 0.95), but were essentially identical for the matched PAS-PVP and PS-180 groups. Taken together, these findings suggest no substantive effect of dialyzer choice on longer-term patient outcomes.

Table 3. Comparison of Hospitalization Rates Between Matched PAS-PVP *vs.* PS-160 and Matched PAS-PVP *vs.* PS-180 Dialyzer Patients

	Group 1		Group 2	
	PAS-PVP	PS-160	PAS-PVP	PS-180
Hospitalization rate (95% CI) admissions/patient-year	2.42 (2.31, 2.53)	2.55 (2.44, 2.66)	2.55 (2.43, 2.66)	2.58 (2.47, 2.69)
Incidence rate ratio (95% CI)	0.95 (0.90, 1.00); $P = 0.05$	1 (ref)	0.99 (0.94, 1.04); $P = 0.62$	1 (ref)

CI, confidence interval; ref, referent; PAS-PVP, polyarylethersulfone–polyvinylpyrrolidone; PS, polysulfone.

The most striking finding among the outcomes assessed was that ESA utilization was lower for PAS-PVP dialyzer users than for PS dialyzer users (for both the PS-160 and PS-180 comparisons). Differences of ≈100–600 unit/treatment were observed; differences were evident throughout follow-up, although they decreased in magnitude slightly in later months. The lower ESA utilization among PAS-PVP dialyzer users cannot be explained by greater utilization of IV iron: iron use was found to be equivalent-to-lower among PAS-PVP users. Similarly, lower ESA utilization among patients using PAS-PVP cannot be explained by a more permissive attitude toward anemia control as hemoglobin was found to be equivalent among PAS-PVP patients.

One plausible explanation for the increased ESA requirement among PS dialyzer users might be that inflammation is inhibiting iron transport and storage pathways.[18–21] However, analysis of markers of iron storage and inflammation (TSAT, serum ferritin, and albumin) yielded little consistent supportive evidence for this hypothesis: TSAT levels were generally higher in PAS-PVP *versus* PS users, as might be consistent with an inflammation-mediated effect; however, serum ferritin levels were equivalent. Serum albumin was also not significantly different between groups, and trends were toward lower concentrations among patients using PAS-PVP, a finding that is inconsistent with an inflammation-mediated effect. Thus, it is not possible to draw any definitive conclusions on the role of inflammation in mediating observed differences in ESA utilization, but the lack of consistent effect across the 3 markers assessed here would seem to argue against this being the primary mechanism.

An alternative hypothesis is that patients using PAS-PVP may have experienced less sequestration of blood in the extracorporeal circuit. There are two means by which this can happen: frank episodes of circuit clotting and subclinical microfiber clotting. We were unable to compare the former because of limitations in the source data, while the latter could not be measured directly but was assessed indirectly in terms of venous pressure changes during dialysis and platelet counts. Venous pressure tended to rise less during dialysis for PAS-PVP *versus* PS users; this finding is consistent with, but not proof of, less fiber clotting among PAS-PVP dialyzer users. Moreover, platelet counts fell less over time among PAS-PVP *versus* PS users, which is again consistent with a microfiber clotting mechanism. Importantly, if microfiber clotting is the operative mechanism, this cannot be explained by differential use of heparin, which was equivalent in PAS-PVP and PS-160 users and was lower in PAS-PVP users than in PS-180 users. However, we cannot exclude the possibility that differences in platelet levels were mediated through pathways other than microfiber clotting.

The current study had several limitations. As a retrospective study, all data assessed were those collected as part of routine care. Measures of inflammation are limited in the data set: C-reactive protein, a commonly used marker of inflammation, is not measured routinely and would only be ordered by a physician if there was a specific indication (*e.g.*, to monitor for resolution of osteomyelitis); therefore, the sparse existing data would not be representative of the entire patient population. In addition, no direct measure of dialyzer clotting is captured in the database. Propensity score matching was used to identify comparable patient groups to allow comparison of outcomes, and dialyzer-type groups were well-matched at baseline, but TSAT and ferritin levels were not included in the propensity matching. However, as with all retrospective studies, the possibility of residual confounding cannot be excluded. Because of the large sample sizes, statistically significant differences that were very small in absolute magnitude and not clinically meaningful were observed in a number of instances. Data interpretation should, therefore, be guided by both statistical significance and clinical relevance.

In summary, we show that use of PAS-PVP *versus* PS membrane dialyzers was associated with lower ESA utilization and modestly lower IV iron doses at equivalent hemoglobin concentrations over the first year of dialysis. The mechanism(s) leading to differing ESA requirements among PAS-PVP *versus* PS dialyzer users cannot be definitively determined in retrospective studies and would require dedicated and carefully conducted prospective study. However, this does not negate the empiric observation that ESA requirements were lower for PAS-PVP dialyzer users. Under current reimbursement, injectable medications are covered by Medicare bundled payments for dialysis,[22] and the vast majority of end-stage renal disease patients receiving dialysis are Medicare beneficiaries. Differences in ESA utilization may be economically significant to dialysis providers at the population level; further studies considering ESA costs, as well as other relevant costs (including dialyzer acquisition costs), will be required to quantify the health economic impact.

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