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Non-infected hemodialysis catheters are associated with increased inflammation compared to arteriovenous fistulas

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Although hemodialysis catheters predispose to infection which, in turn, causes inflammation, we studied whether they induce inflammation independent of infection. We compared the level of the inflammatory marker C-reactive protein (CRP) in maintenance hemodialysis patients, comparing those dialyzed using a non-infected catheter to those using arteriovenous fistulas. All incident patients had catheters and fistula placement at dialysis initiation. In 35 patients the fistulas matured, the catheters were removed and the patients were evaluated at 6 months (catheter–fistula). These results were compared to 15 patients in whom the fistula did not mature and catheter use persisted for 6 months (catheter–catheter). There was a significant 82% reduction in the CRP level in the catheter–fistula group but a 16% increase in the catheter–catheter group at 6 months. The changes in CRP did not differ by gender, diabetes status, or by race, and was not correlated with a change in phosphorus, age, or urea reduction ratio at 1 month following hemodialysis initiation. Decreased CRP was associated with increased hemoglobin and albumin. Patients with persistent fistula use from dialysis initiation through 6 months had consistently low CRP levels over that time period. Our study shows that catheters might contribute to increased inflammation independent of infection, and supports avoidance of catheters and a timely conversion to fistulas with catheter removal.

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The mortality rate for end-stage renal disease patients, especially for ones on maintenance hemodialysis (hemodialysis), is six times higher than in the general population.[1] Factors associated with poor clinical outcomes in hemodialysis patients include the presence of increased inflammation.[2] The increased levels of markers such as C-reactive protein (CRP) are associated with increased risk of premature death and hospitalization.[2–4] In addition, chronic inflammation is highly prevalent in patients receiving hemodialysis[5,6] and is linked to poor cardiovascular outcomes.[3]

Central venous catheters (catheters) are associated with infection and resultant higher CRP levels, suggesting that catheters may be an important determinant of the increased inflammatory response.[7–11] Catheter utilization in hemodialysis patients has increased by an alarming rate of 50% between 1998 and 2004, and data from the United States Renal Data System indicate that 81% of the patients initiate hemodialysis through a catheter.[1] Recent data show that changing from an arteriovenous access to catheters is associated with increased mortality in adult hemodialysis patients.[8] Therefore, avoidance or removal of catheters may represent an effective strategy to limit the inflammatory response in hemodialysis patients. In fact, a recent review suggested that 'nephrologists are ethically obligated to explain to patients the harms of tunneled catheters.'[7] Although catheters might predispose to infection and result in inflammation,[9] no data exist to assess catheter-induced inflammation independent of infection.

In this study, incident hemodialysis patients were evaluated to determine the influence of persistent use of a non-infected catheter versus use of a matured arteriovenous fistula (fistulas) on inflammation, using CRP as a marker. We hypothesized that the presence of persistent catheter use would be associated with higher CRP when compared with fistula use, and conversion to a fistula with catheter removal would lead to a decrease in CRP level. As dialysis vintage is associated with increased inflammation,[5,6,12] we examined another group of prevalent hemodialysis patients to evaluate if dialysis vintage could explain potential CRP differences between patients with a catheter versus a fistula.

RESULTS

The methodological description for each of the four study groups discussed below is depicted in Table 1. We observed no mortality during the 6-month study period in any of the three longitudinal groups. However, patients were not followed after the end of the 6-month study period, so long-term mortality data are not available.

Patients initiating hemodialysis through a catheter

A total of 35 incident patients (mean age 61.5 ± 7.8 years, 18 with diabetes, demographic characteristics shown in Table 2) initiated hemodialysis with a catheter but then had fistula maturation and were dialyzed with a fistula by 6 months after the catheter was removed (catheter–fistula group). Serum CRP decreased significantly at 6 months compared with the first month of hemodialysis (Figure 1), while serum albumin (Alb) and blood hemoglobin (Hb) increased and erythropoietin (EPO) doses decreased (all $P<0.0001$, Table 3). The erythropoesis resistance index (ERI) also decreased by 69%, but this was not statistically significant ($P=0.016$), given the increased stringency for significance we used to account for multiple univariate analyses ($P<0.01$, see Materials and Methods). Serum phosphorus (Phos) did not differ at initiation and 6 months. Blood Hb, serum Alb, and CRP concentrations did not differ between diabetic versus non-diabetic patients or by gender at either time point (not shown).

Fifteen incident patients (mean age 63.4 ± 4.6 years, nine with diabetes) did not have fistula maturation and were dialyzed with a catheter for the first 6 months of hemodialysis (catheter–catheter group). In contrast with the catheter–fistula group, CRP concentrations were no different at initiation and 6 months (Figure 1). Mean blood Hb levels increased insignificantly from initiation to 6 months (10.1 ± 0.5 versus 10.7 ± 0.5 g per 100ml). Furthermore, EPO dose and ERI did not change at 6 months (Table 3). Mean blood Hb, serum Alb, and median CRP concentrations did not differ between diabetic versus non-diabetic patients or by gender at either time point (not shown). In addition, no patient had evidence of fistula infection or thrombosis, which could conceivably lead to elevated CRP levels.

We compared change in CRP (Delta CRP = (6 month–1 month)/1 month × 100) between the catheter–fistula and catheter–catheter groups. Delta CRP was −82% (that is, an 82% mean reduction in CRP concentrations by 6 months) in the catheter–fistula group and + 16% in the catheter–catheter group ($P<0.001$). Delta CRP did not differ by gender (males: −50% versus females: −57%, $P=0.65$), diabetes status (no: −57% versus yes: −51%, $P=0.64$), or by race (Caucasian: −66% versus African-American: −53% versus Hispanic: −50%, $P=0.74$). Delta CRP was not correlated with Delta Phos ($r=-0.12$, $P=0.42$), age ($r=0.14$, $P=0.35$), or urea reduction ratio (URR) at 1 month of hemodialysis initiation ($r=0.01$, $P=0.92$). Decreasing CRP (a negative Delta CRP) was associated with increases in Hb (Delta Hb, $r=-0.48$, $P=0.004$) and Alb ($r=-0.67$, $P<0.001$).

When using partial correlation analysis (including Delta CRP, Delta Hb, Delta Alb, and Delta Phos) decreasing CRP was only significantly associated with increase in Hb (Delta Hb, partial $r=-0.57$, $P<0.001$), and not with Delta Alb

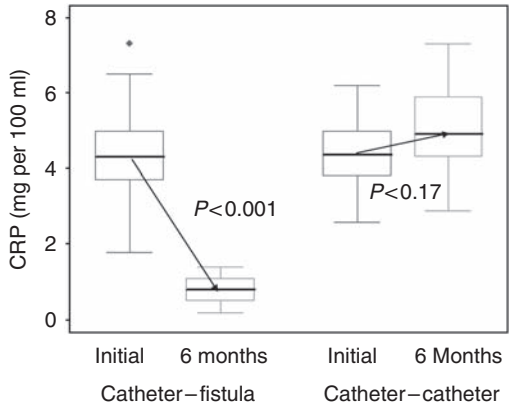

Figure 1 | C-reactive protein (CRP) levels (mg per 100 ml) decrease significantly in incident maintenance hemodialysis patients who initially dialyze with a non-infected catheter but with a fistula at 6 months ($P<0.0001$). By contrast, no change in CRP is observed in incident maintenance hemodialysis patients who initiated dialysis with a catheter and remained with a catheter at 6 months ($P=0.17$). CRP concentrations are shown as median (interquartile range) in the boxes.

Table 1 | Methodological description for each of the four study groups

Group (*n*)	Sample type	Access comparison
Catheter–fistula (35)	Incident	Catheters at initiation versus fistulas at 6 months
Catheter–catheter (15)	Incident	Catheters at initiation and at 6 months
Fistula-only (23)	Incident	Fistulas at initiation and 6 months
Prevalent maintenance hemodialysis (65)	Cross-sectional	Fistulas versus catheters

Table 2 | Demographic data for each of the four study groups

Group (*n*)	Age (years)	Vintage (years)	M/F	Race (*n*)	Diabetic
Catheter–fistula (35)	61.5 ± 7.8	NA	15:20	C(6), AA(17), H(12)	18/35
Catheter–catheter (15)	63.4 ± 4.6	NA	7:8	C(2), AA(8), H(5)	9/15
Fistula-only (23)	50.1 ± 17	NA	11:12	C(11), AA(10), H(2)	6/23
Prevalent (65)	52.6 ± 11.4	3.4 ± 2.2	38:27	C(13), AA(33), H(19)	29/65

AA, African-American; C, Caucasian; H, Hispanic; values mean ± s.d.

(partial $r=-0.23$, $P=0.12$) or Delta Phos (partial $r=-0.07$, $P=0.66$).

In a multiple linear regression analysis, being in the catheter–fistula group (fistula use by 6 months) was associated with a decrease in CRP (negative Delta CRP, $P<0.001$, model $R^2=0.88$, $P<0.001$) independent of age, gender, diabetes status, and race. We repeated this multiple linear regression analysis, replacing the race variables with Delta Hb and Delta Alb; being in the catheter–fistula group remained the only significant independent predictor of decreasing CRP ($P<0.001$). Of note, when only the presence of access change (catheter–fistula versus catheter–catheter) was included in the regression model, the model R^2 was 0.82 ($P<0.001$); addition of other variables in the model led to a minimal increase in the model R^2 (as high as 0.88), suggesting that access change at 6 months explained the majority of the variance in Delta CRP from dialysis initiation to 6 months.

Table 3 | Laboratory and CRP values for incident patients initiating maintenance hemodialysis with a catheter and fistula use at 6 months (catheter–fistula), persistent catheter use at 6 months (catheter–catheter) and fistula-only

	Initiation	6 months	*P*-value
Catheter–fistula			
Hb (g per 100 ml)	10.4 ± 0.5	12.5 ± 0.7	<0.0001
Alb (g per 100 ml)	3.4 ± 0.7	4.0 ± 0.2	<0.0001
CRP (mg per 100 ml)	4.3 (3.7, 5.0)	0.8 (8.6, 1.1)	<0.0001
EPO dose (U/week)	13,425 ± 225	5875 ± 175	<0.01
ERI (U/kg/(Hb))	537 ± 120	167 ± 75	<0.02
Phosphorus (mg per 100 ml)	5.1 ± 1.2	5.0 ± 0.8	0.42
Catheter–catheter			
Hb (g per 100 ml)	10.1 ± 0.5	10.7 ± 0.5	0.008
Alb (g per 100 ml)	3.2 ± 0.2	3.4 ± 0.9	0.47
CRP (mg per 100 ml)	4.4 (3.8, 5.0)	4.9 (4.3, 5.9)	0.17
EPO dose (U/week)	14,020 ± 330	15,250 ± 225	0.42
ERI (U/kg/(Hb))	624 ± 180	675 ± 210	0.38
Phosphorus (mg per 100 ml)	5.4 ± 1.0	5.0 ± 0.7	0.20
Fistula-only			
Hg (g per 100 ml)	10.5 ± 1.5	12.4 ± 1.8	0.0002
Alb (g per 100 ml)	3.8 ± 0.5	4.0 ± 0.4	0.18
CRP (mg per 100 ml)	0.5 (0.2, 1.0)	0.7 (0.3, 1.8)	0.24*

Alb, albumin; Ca, calcium; CRP, C-reactive protein; ERI, erythropoeisis resistance index; EPO, erythropoietin; Hb, hemoglobin; IQR, interquartile range; Phos, phosphorus; URR, urea reduction ratio.
All values mean ± s.d. except for CRP: median (IQR).
*P=0.88 for all 6-month CRP comparisons using Kruskal–Wallis test.

Out of the entire group, nine patients needed hospitalization. Seven of these patients were in the catheter–fistula group; two patients were in the catheter–catheter group. Six of the nine patients were female. Six of the nine were diabetics. Fluid overload was the most common cause of hospitalization (seven of the nine patients). No patient in either group was admitted with catheter-related sepsis.

Longitudinal assessment in patients who initiated hemodialysis with a fistula. Twenty-three incident patients (mean age 50.1 ± 17.0 years; six with diabetes, Table 2) were dialyzed with a fistula alone for the first 6 months. Mean serum Alb did not differ from initiation to 6 months (3.8 ± 0.5 versus 4.0 ± 0.4 mg per 100 ml, $P=0.18$), while blood Hb was significantly higher at 6 months (10.5 ± 1.5 versus 12.4 ± 1.8 g per 100 ml, $P<0.001$). EPO dose did not rise significantly during this period (data not shown). Median (interquartile range) serum CRP did not differ from dialysis initiation to 6 months (0.5 (0.2, 1.0) mg per 100 ml versus 0.7 (0.3, 1.8) mg per 100 ml, $P=0.24$) and was no different for patients with versus without diabetes or by gender (not shown). Sixteen patients had complete data on monthly CRP concentrations drawn during the first 6 months of dialysis; using repeated measures analysis of variance (and ln-transformed CRP levels), there was no significant change in CRP concentrations at any time point (Huyn-Feldt F-statistic = 1.69, $P=0.151$) across the 6 months of assessment (median CRP ranged from 0.5 to 0.8 mg per 100 ml).

We compared CRP concentrations in this group with CRP concentrations in the catheter–fistula and catheter–catheter groups at dialysis initiation and at 6 months. At dialysis initiation, median CRP levels were significantly lower in the fistula-only group compared with both the catheter–fistula and the catheter–catheter groups ($P<0.001$). At 6 months, median CRP concentrations for the fistula-only group were significantly lower than those in the catheter–catheter group ($P<0.01$), at which time the catheters was still in place, but no different compared with the catheter–fistula group ($P>0.05$), at which time the catheters had been removed.

Cross-sectional study of CRP concentrations and access type. Sixty-five prevalent hemodialysis patients (mean age 52.6 ± 11.4 years; 29 diabetic, shown in Table 4) had data available for cross-sectional analysis (44 fistulas, 21 catheters). Patients dialyzed with a fistula had significantly lower CRP concentrations than patients dialyzed with a catheter ($P<0.0001$, Figure 2), despite the fact that fistula patients had significantly longer dialysis vintage than catheter patients

Table 4 | Demographic, laboratory, and CRP values by access type in a prevalent group of maintenance hemodialysis patients

	Age (years)	Vintage (years)*	URR (%)	Alb (g per 100 ml)*	Hb (g per 100 ml)*	Ca (mg per 100 ml)	Phos (mg per 100 ml)	CRP (mg per 100 ml)*
Fistulas (44)	53.4 ± 11.9	4.6 ± 1.8	72.0 ± 3.3	4.0 ± 0.2	12.2 ± 0.4	8.9 ± 0.9	5.0 ± 0.6	0.4 (0.2,0.7)
Catheters (21)	51.0 ± 10.5	1.1 ± 0.8	73.0 ± 4.2	3.4 ± 0.3	10.2 ± 1.0	9.2 ± 0.6	5.2 ± 0.7	3.6 (1.8,6.5)

Alb, albumin; Ca, calcium; CRP, C-reactive protein; Hb, hemoglobin; Phos, phosphorus; URR, urea reduction ratio.
All values mean ± s.d. except for CRP: median (IQR).
*$P<0.001$ for catheters versus fistulas.

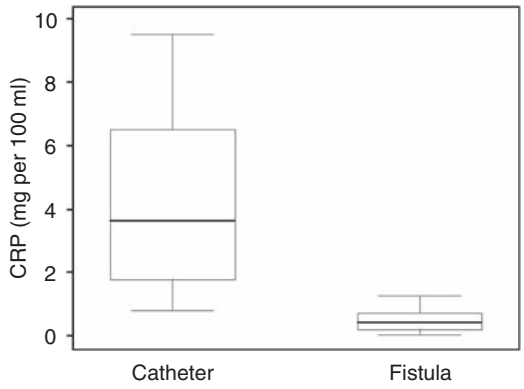

Figure 2 | C-reactive protein (CRP) levels (mg per 100 ml) are significantly lower for prevalent maintenance hemodialysis patients dialyzed with a fistula versus a non-infected catheter ($P < 0.001$). CRP concentrations are shown as median (interquartile range) in the boxes.

(Table 4). Mean URR did not differ between patients with either access, but serum Alb and Hb were significantly lower in catheter patients compared with fistula patients (Table 4). CRP did not differ by gender, diabetic status, race, or age (all $P > 0.05$, not shown).

In a multiple linear regression analysis, only access type (use of catheters) was significantly associated with higher CRP concentrations ($P < 0.001$), independent of age, gender, diabetes status, race, and dialysis vintage (model $R^2 = 0.61$, $P < 0.001$). When we replaced the race variables with URR and calcium–phosphate product, only access type (catheters use, $P < 0.001$) was significant in predicting higher CRP concentrations, independent of age, gender, dialysis vintage, URR, diabetes status, and calcium–phosphate product (model $R^2 = 0.63$, $P < 0.001$). When only access type was included in the regression model, the model R^2 value was still 0.57 ($P < 0.001$).

DISCUSSION

This study indicates that patients who receive dialysis through a non-infected catheter have an increased CRP when compared with patients who receive dialysis with a fistula. This finding was seen both in incident and prevalent patients and was independent of age, gender, diabetes status, and dialysis vintage (Tables 3 and 4).

A unique feature of our study was the ability to test our hypothesis in different groups of incident hemodialysis patients with varying access type to determine if changing access will improve markers of inflammation. In incident patients who initiated dialysis with a non-infected catheter and had elevated CRP levels, transition to a fistula at 6 months (catheter–fistula group) was probably accompanied by resolution of the inflammatory state as evidence by an 82% decrease in CRP, improvement of Alb and Hb, and decreased EPO dose and ERI (Figure 1, Table 3). By contrast, patients who initiated dialysis with a catheter (catheter–catheter group), which remained in place at 6 months follow-up, showed no change in these parameters (Figure 1, Table 3). Multivariate analysis of all incident patients dialyzed initially with a catheter (the catheter–fistula and catheter–catheter groups) provided sufficient sample size to reveal catheters to be associated with increased CRP independent of patient age, diabetes status, gender, ethnicity, serum Phos, or URR.

Moreover, incident patients who initiated dialysis with a fistula had significantly lower levels of CRP compared with incident patients who initiated dialysis with a non-infected catheter (Table 3). The lower level of CRP in incident patients with a fistula at initiation remained low for the following 6 months (Table 3).

Finally, a group of prevalent patients dialyzed with a fistula had significantly lower CRP, higher serum Alb, and higher Hb levels compared with patients with a catheter (Figure 2, Table 4). These findings were present despite the longer dialysis vintage of fistula patients. As patients with a positive surveillance bacterial culture or fever within 1 week before analysis were excluded from analysis of this cohort, infection *per se* had no impact on the difference in outcome in incident or prevalent patients using a catheter versus a fistula.

In the aggregate, these observations are consistent with our hypothesis that catheter use is associated with increased inflammatory response and its removal or avoidance could attenuate the background inflammation commonly observed in hemodialysis patients. To our knowledge, this is the first study to systematically show these associations and underscores the importance of avoiding catheter use even in the absence of active infection, and supports the current National Kidney Foundation-Kidney Disease Outcomes Quality Initiative recommendation of a fistula as the preferred vascular access type.[13]

Previous studies also show that catheters are associated with increased risk for all-cause mortality among incident and prevalent dialysis patients.[14–16] Interestingly, in these studies the increased mortality was seen after adjusting for infection, with cardiovascular mortality being the most common cause of death. This study might explain these findings, as the presence of a non-infected catheter induced a state of inflammation. Chronic inflammation in dialysis patients is linked to poor cardiovascular outcomes and is accompanied by malnutrition, decreased Alb, Hb, and urea clearance.[2,3,17]

Removal of infected clotted arteriovenous grafts,[18–20] removal of a failed kidney allograft,[21] and daily dialysis[22] are well-established measures that can ameliorate inflammation in selected patients. However, there are very few therapeutic options in the general dialysis population. This study offers a simple alternative, with a more general applicability to the dialysis population.

Why did we observe increased CRP in patients with catheters in the absence of clinical signs of infection? A prominent role for biofilm may have existed in some of our patients who remained asymptomatic and had negative surveillance catheter cultures.[23,24]

However, a more plausible explanation for the proinflammatory state observed in patients with catheters is an immunological reaction against the catheter material itself. A comparison of inflammation and infection rates in rabbits with indwelling catheters composed of silicone, polyurethane, polyvinylchloride, and Teflon, showed that silicone catheters induced the greatest inflammatory response, either in the presence or absence of infection.[25] In addition, infection rates were highest in silicone catheters. In a follow-up study, serum incubated in silicone catheters had significantly less opsonizing ability compared with sera incubated in polyurethane or polyvinylchloride catheters, suggesting that silicone may induce greater inflammation by excessive complement activation.[26]

Although it is important in this regard to recognize that the Tesio catheters (Medcomp, Harleysville, PA) that were used in this study are made of silicone, the presence of other catheter materials has also been associated with increased levels of CRP.[11] Furthermore, this study was not designed to study the effect of different kinds of catheters on CRP levels.

The strength of our study resides in the large cohort size without evidence of active infection. Furthermore, using incident patients with longitudinal follow-up allowed for patients to serve as their own control. This approach minimized the potential confounders of the study. Although this data does not prove causality, it offers the most supportive evidence at the present time for the role of non-infected catheters as a contributing factor of inflammation in dialysis patients.

However, there are also limitations with this study. The observational design, cross-sectional, or prospective, allows us only to evaluate associations and does not prove causality. In contrast, given the obvious ethical considerations, it is not possible to test these hypotheses through a randomized clinical trial. The concurrent comparative group allows us to obtain the most reliable evidence possible. Although we controlled for patient factors that may influence inflammation, there may be others unknown to us, which could have influenced our results. Although all patients were treated similarly, and we have attempted to avoid any bias in patient selection, the possibility remains that sicker, frailer, and, by inference, more inflamed patients are likely to have catheters and higher CRP levels.

In summary, patients who receive dialysis through a catheter show significant elevation CRP compared with patients dialyzed with a fistula. Moreover, inflammation is attenuated in incident and prevalent patients who change from a catheter to a fistula. Thus, our data support early and pre-emptive fistulas placement to avoid the use of catheters for hemodialysis.

MATERIALS AND METHODS

Study design and setting

This study represents a retrospective cohort analysis of 138 adult patients receiving maintenance hemodialysis (Table 1). No patient died during the study period. In addition, all patients in the groups studied longitudinally completed all 6 months follow-up. Seventy-three were incident and 65 were prevalent hemodialysis patients. Incident patients were followed prospectively with longitudinal analysis of laboratory values. The following were exclusion criteria: (1) a failed renal allograft in place, (2) a clotted, non-functional arteriovenous graft in place, (3) patients who were hospitalized for infection during the month of scheduled blood draw, and (4) patients with fever in the week before scheduled blood draw (fever defined as equal to or greater than 37.5°C). No patients in this study were excluded because of these exclusion criteria. Surveillance exit site cultures were drawn weekly in catheter patients. Exit site and blood cultures were drawn with CRP assessment. Patients with positive cultures were excluded from the study. As this was a retrospective cohort analysis, the study received expedited approval with a waiver for informed consent from the Baylor College of Medicine and Vanderbilt School of Medicine Institutional Review Boards.

Description of study groups

Catheter–fistula group. This group consists of 35 patients who initiated dialysis with a catheter with a fistula in place. These patients had fistula maturation with catheter removal and dialysis with a fistula alone by 6 months. CRP was measured in the first month of hemodialysis initiation and at 6 months.

Catheter–catheter group. This group consists of 15 patients initiating dialysis with a catheter with a fistula in place. They had fistula maturation failure with persistent catheter use by 6 months. Data from patients with fistula thrombosis were excluded. CRP was measured in the first month of hemodialysis initiation and at 6 months.

Fistula-only group. This group consists of 23 patients initiating hemodialysis with a fistula for 6 months. They never had a catheter in place. All patients had CRP measured in the first and sixth month of dialysis.

Prevalent maintenance hemodialysis patients

We studied a group of 65 prevalent patients receiving hemodialysis for at least 2 months.

Vascular access protocol

Fistulas were placed by one vascular surgeon in all incident patients after venous mapping of both arms to locate the best suitable vessels. In patients previously followed in the pre-dialysis clinic, fistula placement was carried out at least 3 months before dialysis initiation. In a subset of catheter–fistula and catheter–catheter patients without pre-dialysis care, dialysis was initiated with a catheter and fistula placement was carried out within 1 month of dialysis initiation. In catheter patients, all dressings were changed at each dialysis treatment to inspect for signs of exit site infection. All exit sites were cleaned with a standard Betadine solution after each treatment before re-dressing. All catheters had heparin instilled to prevent thrombosis between hemodialysis treatments; citrate or antibiotic locks were not used.

Dialysis prescription and patient care

Dialysis treatments used bicarbonate baths and polysulfone biocompatible membranes (Fresenius USA, Lexington, MA, USA) (blood flows were 400 ml/min and dialysis flows were 800 ml/min); dialysis times and frequency were 240 min per session, with a

frequency of three times per week. Dialysate was assessed monthly for bacteria and endotoxin levels and were below acceptable limits throughout the study (<50 CFU/ml and <0.99 EU/ml). All patients with catheters received dialysis with a Tesio catheter system.

Recombinant human erythropoetin and intravenous iron were prescribed to maintain Hb from 11 to 12 g per 100 ml, transferrin saturation $>20\%$ and serum ferritin >100 mg per 100 ml per established protocols. Phosphate binders were used to maintain pre-dialysis serum Phos below 5.5 mg per 100 ml, and serum calcium from 8.5 to 9.5 mg per 100 ml. Vitamin D was prescribed to maintain intact parathyroid hormone between 150 and 300 pg/ml. Aspirin (81 mg) was prescribed daily to all patients initiating dialysis with a catheter and fistulas together, and in 13% of patients who initiated dialysis with a fistula alone. All prevalent patients with a catheter or fistulas were prescribed daily aspirin (81 mg).

Data collection

The main outcome of the study was serum CRP concentration, measured in all four study groups immediately after the midweek hemodialysis session, as part of the standard monthly laboratory assessment. Serum CRP was measured using a nephelometry assay with an analytical sensitivity of 0.3 mg per 100 ml and an interassay variability of 5.9, 3.0, and 2.4% for low, medium, and highest values, and an intraassay variability of 1.3, 0.4, and 0.3% for low, medium, and highest values, respectively.

Erythropoietin resistance index, which is another putative inflammation marker in dialysis patients, was calculated as: weekly EPO dose (units)/post-dialysis weight (kg)/Hb concentration.[19] Other routine laboratory data were collected including URR, Hb, phosphate, calcium, calcium–phosphate product, and serum Alb (bromocresyl-green 'BCG' method). Demographic data and diabetes status were recorded.

Statistical analyses and analysis plan. Data were described using mean ± s.d. when the data were normally distributed or by median (lower, upper interquartile range) when the data were non-normally distributed. Univariate parametric tests were used (*t*-tests, one-way analysis of variance, Pearson's correlation) to evaluate normally distributed variable associations and non-parametric univariate tests (Mann–Whitney, Kruskall–Wallis, Spearman's correlation) were used to evaluate non-normally distributed variables. Categorical variables were compared using the χ^2-test. Variables following non-normal distributions were transformed to their natural logarithm for inclusion in regression analyses. Regression diagnostics were carried out to evaluate model assumptions. To account for the number of univariate tests carried out, we used $P<0.01$ for statistical significance to address the potential for a random chance of detecting significance with a standard P-value <0.05. Analysis was carried out using STATA 10 (College Station, TX, USA) and SPSS version 9 (Chicago, IL, USA).

Cross-sectional study of CRP concentrations and access type. Potential univariate associations between vascular access type (fistula versus catheter) and CRP, dialysis vintage, serum calcium and Phos, serum Hb, erythropoeitin doses, ERI, and serum Alb were evaluated. Potential univariate associations between CRP and patient age, dialysis vintage and URR were also evaluated. Multiple linear regression was used to evaluate for an independent association between access type and CRP concentrations (ln-transformed), controlling for potential confounding variables.

Comparison of CRP concentrations for catheter versus fistula use at 6 months

The catheter–fistula and catheter–catheter groups were included in these analyses. Change in CRP, serum calcium and Phos, blood Hb, EPO use and Alb at dialysis initiation to 6 months after dialysis initiation were assessed in both groups. To determine whether change in access type by 6 months predicted reduction in CRP concentrations by 6 months, we derived a CRP change score or Delta CRP: (6 month CRP−1 month CRP)/1 month CRP × 100. A negative Delta CRP thus represented a percent reduction in CRP from dialysis initiation to 6 months. This variable was used as the outcome in a multiple linear regression analysis, which included access type at 6 months, gender, age, diabetes status, and race as the main predictors. We also evaluated the potential effect of change in Hb and change in Alb on the association between access type and Delta CRP.

CRP evaluation in patients who initiated hemodialysis with a fistula. For patients in the fistula-only group, we compared dialysis initiation and 6-month CRP concentrations, Alb, Hb, and EPO dose, to evaluate for a significant change in CRP concentration over time when no catheters was ever used. For patients with complete data on monthly CRP for 6 months, we used repeated measures analysis of variance to determine if any change in CRP occurred over the 6-month study period.

DISCLOSURE

The authors declared no competing interests.

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