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Original Article

The Correlation between Frailty and Recurrent Vascular Access Failure in the Elderly Maintenance Hemodialysis Patients

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SUMMARY

Background: Frailty is highly prevalent among the dialysis population and recent studies suggest that frailty affects dialysis outcomes such as vascular access failure (VAF). This study aimed to explore the correlation between frailty and one year recurrent VAF among the elderly.
Methods: A retrospective review enrolled the medical records for dialysis patients over 60 years of age who were first diagnosed with VAF and received angioplasty. Demographic data, arteriovenous fistula functions (vascular access blood flow) and dialysis efficiency calculated based on Kt/V calculator were analyzed. Frailty was assessed using the FRAIL scale which includes 5 components: fatigue, resistance, ambulation, illness, and weight-loss. Patients with FRAIL scale (3–5) were categorized into frail.
Results: A total of 73 records for elderly patients (mean age 68.8 ± 3.2 years; 56% male) were evaluated. The mean dialysis period for patients was 9.1 ± 7.3 years and 20 patients (27.4%) were previously diagnosed as frail in status. After one year of enrollment 25 (34.2%) patients experienced recurrent VAF required repeated percutaneous transluminal angioplasty or thrombectomy. Multivariate regression analysis indicated that age increased the risk of recurrent VAF during one year follow up (odd ratio [OR] 1.106, 95% confidence interval 1.029–1.190, p = 0.008), fatigue increased the risk of recurrent VAF (odd ratio [OR] 7.597, 95% confidence interval 1.411–40.833, p = 0.018) and loss of weight (odd ratio [OR] 4.803, 95% confidence interval 1.164–19.805, p = 0.030).
Conclusion: We assert that age, fatigue, and weight loss are useful prognostic indicators for the identification of recurrent VAF. Timely and regular assessment of frailty may allow for interventions that could mitigate potentially VAF.

1. Introduction

Arteriovenous fistula (AVF) is the preferred method of hemodialysis vascular access which is necessary prior to hemodialysis treatment. When an AVF is placed, an artery is anastomosed to a vein and over a period of 2–3 months the vein becomes arterialized. AVF provides the best access and fewest complications, however, a substantial number of these fistulas fail for unknown reasons. The pooled 12-month primary AVF patency rates were 53.6% (95% confidence interval [CI], 47.3–59.9).[1] Once venous stenosis occurs with clinical symptoms such as painful swelling of an extremity and subsequent poor function of the access point, treatment options include percutaneous transluminal angioplasty or surgical revision.[2]

Frailty, regardless of how it is assessed, remains highly associated with mortality in dialysis patients[3] and more recently frailty has been associated with negative outcomes such as falls, cognitive impairment, vascular access failure (VAF), and poor quality of life.[4] The prevalence of frailty is estimated to be between 7–16% among a non-institutionalized population and has been reported to be greater than 60% among dialysis-dependent chronic kidney disease patients.[5] Using Fried's widely accepted assessment of physical performance criteria, the frailty phenotype framework is a common geriatric syndrome.[6] Epidemiologic research has identified risk factors for frailty, including chronic diseases (such as cardiovascular disease, diabetes, chronic kidney disease, depression, and cognitive impairment physiologic impairments), inflammation,[7] anemia or coagulation systems,[8] and atherosclerosis.[9]

The Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommend autologous AVF as the primary vascular access in hemodialysis given its lower complication rates.[10] VAF may lead to negative clinical outcomes for patients who are exposed to inadequate dialysis performance and to infectious risks as a result of temporary placement of catheters. Vascular access-related morbidity accounts for 20% of all hospitalizations among hemodialysis patients, which leads to higher medical costs.[11] Previous research indicates that frailty is associated with an increased risk of VAF.[12] The goal of this study is to evaluate the factors, including frailty status and vascular access characteristics, demographic data, BMI, arteri-

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ovenous fistula functions, and biochemistry, that may be predictors for recurrent episodes among elderly dialysis patients who have experienced previous VAF.

2. Patients and methods

2.1. Methods

This retrospective study included 73 hemodialysis patients with previous episodes of VAF from a single medical center-based outpatient dialysis unit in Taipei between December 2016 and December 2018. Hemodialysis patients who were 60 years or older were recruited into this study once autologous AVF dysfunction was identified by the dialysis units. Only patients with AVF access issues due to stenosis were included and the stenosis of all AVF failure was confirmed by color Doppler ultrasonography.

Records of blood tests were obtained on the same day prior to angioplasty at the first occurrence of VAF for each patient. Demographic data (age, sex, body mass index (BMI) the status of frailty and hemodynamic measurement of VAF and dialysis efficiency calculator or Kt/V calculator, vascular access blood flow (VABF) were retrieved from the most recent regular medical record (less than one month). Following the detection of an issue in the color Doppler ultrasonography, all patients were further evaluated and received fistulography with angioplasty. If the thrill was easily identified with little pressure, a minimum of 4-h hemodialysis with > 300 mL/min was considered adequate.

The evaluation of recurrent AVF was conducted at the dialysis center 12 months after enrollment of each patient. Clinical patency was evaluated by nephrologists in the dialysis unit. Once a minimum of secondary venous stenosis occurred with clinical symptoms, such as painful swelling of an extremity and subsequent poor function of the access, evaluation and treatment option was performed according to standard protocols. The study program was approved by the Institutional Review Board of MacKay Memorial Hospital [18MMHIS171].

2.2. Definition of frailty

Frailty in our study was measured as a previously defined and validated phenotype which is based on 5 components among various ages and races.[13] The 5 components include fatigue (felt tired most of the time in past 4 weeks they scored 1 point); resistance (difficulty walking alone up 10 steps without resting = 1 point); ambulation (difficulty walking 300M alone = 1 point); and illness (presence of 5 or more illnesses out of list of 11 total = 1 point (these 11 illness included diabetes, hypertension, cancers, chronic heart failure, ischemic heart disease, acute myocardial infarction, peripheral arterial occlusive disease, hyperlipidemia, cerebral vascular accident, arthritis, and chronic obstructive pulmonary disease/asthma) and loss of weight (weight decline of more than 5% within past one year scored 1 point). A score of 1 was given to those with the presence of each measured component. The aggregate frailty score was calculated as the sum of the component scores (range 0–5) and categorized as robust (0), pre-frail (1–2), and frail (3–5).

2.3. Predictor variables

To determine which variables that we evaluated as components of frailty were associated with VAF, we identified a set of factors *a priori* that we suspected might be associated with frailty, including demographic factors such as age, sex, smoking history, body mass index, vascular access hemodynamic (Kt/V and VABF) and serum biochemistry (albumin Ca, P, cholesterol, triglyceride concentration). Recurrent VAF was defined as having received more than one percutaneous transluminal angioplasty within 12 months following study enrollment.

2.4. Statistical analyses

To evaluate the relative contributions of each of the components of the frailty phenotype and whether the components were independently associated with outcomes of recurrent of VAF, multivariable models were fit for the association with recurrent VAF between the individual components of frailty and other predictor variables. Student's t-test was used to compare the continuous variables, which were expressed as means ± standard deviations (SDs). Two-tailed $p < 0.05$ was considered statistically significant. The χ^2 test was used, as appropriate, for the comparison of the categorical data. All of the covariates were included in a logistic regression analysis, while a multivariate analysis was also conducted in order to evaluate the predictive factors. All analyses were completed using SAS 12 (SAS Institute, Cary, NC).

3. Results

3.1. Demography and clinical characteristics of patients

A total of 73 individuals over 60 years of age with a diagnosis of dialysis-dependent CKD who had experienced a first episode of VAF were incorporated into our analyses. Their mean age was 68.8 ± 3.2 years and 56% were male. They had a mean period of 9.1 ± 7.3 years of dialysis and according to the FRAIL scale, 20/73 = 27.4% were diagnosed as frail upon enrollment. The distribution of patient frequency for each level of the frail scale (0/1/2/3/4/5) was 2/18/14/11/3/0 respectively in the non- recurrent VAF group and 0/3/16/4/2/0 respectively in the recurrent VAF group. There was no significant difference between groups (Table 1).

Table 1
The demographics, biochemistries, arteriovenous fistula function and frailty status according to the grouping of recurrent vascular access failure.

	Non recurrent (n = 48)	Recurrent VAF (n = 25)	p-value
Age (mean ± SD)	64 ± 2.8	71.4 ± 3.4	0.002
Sex (M) (%)	24 (50%)	17 (68%)	0.141
Dialysis period (year)	9.4 ± 7.2	8.7 ± 7.6	0.709
Body mass index (%)	22.1 ± 3.2	22.5 ± 3.5	0.683
Smoking	10 (21.0%)	9 (36%)	0.161
Hb (g/dL)	10.4 ± 1.1	10.7 ± 1.0	0.276
Albumin (g/dL)	4.0 ± 0.3	4.1 ± 0.3	0.153
Cholesterol (mg/dL)	181.4 ± 55.5	182.6 ± 51.2	0.925
Triglyceride (mg/dL)	157.7 ± 122	152.3 ± 94.8	0.847
Calcium (mg/dL)	9.4 ± 0.7	8.9 ± 0.6	0.010
Potassium (mEq/L)	5.5 ± 1.7	5.8 ± 1.6	0.440
i-PTH (pg/mL)	516.9 ± 380.8	477.9 ± 444.8	0.696
Kt/V	1.55 ± 0.31	1.49 ± 0.24	0.364
VABF (mL/min)	718.5 ± 370.1	834.8 ± 452.3	0.255
Fatigue	26 (54%)	23 (92%)	0.001
Resistance	14 (50%)	3 (20%)	0.100
Ambulation	16 (33.3)	5 (20%)	0.232
Illness	8 (16.7%)	4 (16%)	0.942
Loss of weight	27 (56.2%)	20 (80%)	0.044
FRAIL SCALE (0/1/2/3/4/5)	2/18/14/11/3/0	0/3/16/4/2/0	0.150

i-PTH: intact parathyroid hormone; Kt/V: dialysis efficiency calculator; VABF: vascular access blood flow; VAF: vascular access failure.

3.2. The demographics, biochemistries, arteriovenous fistula function and frail status according to grouping of recurrent vascular access failure

One year after enrollment of each patient, 25 of 73 (34.2%) patients experienced recurrent VAF and required repeated percutaneous transluminal angioplasty or thrombectomy. The baseline mean age was higher for the recurrent VAF group than the group without VAF episodes (71.4 ± 3.4 vs. 64 ± 2.8 vs) (p = 0.002). Serum calcium levels were lower in the recurrent VAF group (8.9 ± 0.6 vs. 9.4 ± 0.7) (p = 0.010). The distribution of patients along the frail scale (0/1/2/3/4/5) was 2/18/14/11/3/0 in the non-recurrent VAF group and was 0/3/16/4/2/0, reactively in the recurrent VAF group and there was no significant between-group difference (p = 0.15). However, the percent of fatigue and loss of weight were found to be significantly higher in the recurrent AVF group 92% vs. 54% (p = 0.001) and 80.0% vs. 56.2% (p = 0.044) subsequently. No significant associations were observed between recurrent VAF and BMI, levels of phosphorus, cholesterol and the remaining variables. A comparison of laboratory parameters between the two groups is summarized in Table 1.

3.3. The predictors for recurrent vascular access failure in the dialysis baseline

Accounting for the demographics, biochemistries, arteriovenous fistula function and frailty status, multivariate regression analysis revealed that, during one year follow up, the following variables were associated with increased the risk of recurrent VAF: age (odd ratio [OR] 1.106, 95% confidence interval 1.029–1.190, p = 0.008), fatigue (odd ratio [OR] 7.597, 95% confidence interval 1.411–40.833, p = 0.018), and weight loss (odd ratio [OR] 4.803, 95% confidence interval 1.164–19.805, p = 0.030) (Table 2).

4. Discussion

The pathogenic mechanisms for VAF are not yet fully understood, but it is thought that thrombosis resulting in stenosis is due to neointimal hyperplasia. Turbulent flow, endothelial damage, cytokines or oxidative stress and possible genetic predisposition exacerbate vascular proliferation and smooth muscle injury may lead to neointimal hyperplasia.[14,15] Although frailty is associated with poor outcomes among the general elderly population, it is not yet common practice to assess frailty in dialysis patients, especially to aid in the prediction of recurrent VAF. Among dialysis patients with end-stage renal disease periodic vascular access surveillance to survey dialysis access outcomes indicated that after 15.7 months of follow-up, 37.3% participants developed VAF.[12] Here, one year after enrollment of each patients, 25 of 73 (34.2%) patients experienced recurrent VAF and required repeated percutaneous transluminal angioplasty or thrombectomy. To the best of our knowledge, this is the first study to evaluate the factors for predicting recurrent VAF among elderly dialysis patients.

An investigation of a potential link between a frailty construct and vascular access failure in a cohort of 51 prevalent dialysis patients in rural Taiwan revealed that frailty was associated with a higher risk of primary vascular access failure (hazard ratio: 2.63, 95% CI 1.03–6.71).[12] The simple FRAIL scale association aging process and nutrition status aims to screen for the presence of frailty, through 5 simple questions encompassing the entire spectrum of the frail phenotype (fatigue, resistance, ambulation, illness, and loss of weight).

In our study, the distribution of patients along the FRAIL scale (0/1/2/3/4/5) was 2/18/14/11/3/0 in the 48 non-recurrent VAF patients and was 0/3/16/4/2/0 in the 25 recurrent VAF patients and no between-group difference was observed (p = 0.15). Illness, one of the components of the frail scale, is relatively lower in our sample population from Taipei City. Only 16 % of patients in both groups had more than 5 of the 11 comorbidity illnesses. There are also potential differences between urban and rural regions. However, fatigue and weight loss ratio were significantly higher in the recurrent VAF group 92% vs. 54% (p = 0.001) and 80.0% vs. 56.2% (p = 0.044) respectively. Among dialysis patients, weight loss is associated with sarcopenia which in turn is accompanied by elevated oxidative stress and low-grade inflammation. In addition, fatigue and lethargy which potentially leads to delayed recognition of dialysis access dysfunction and causes irreversible VAF. The FRIAL scale is

Table 2
The predictors for recurrent vascular access failure among elderly maintenance hemodialysis patients.

	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.094	1.030–1.163	0.004	1.106	1.029–1.190	0.008
Gender (M)	0.470	0.170–1.295	0.145			
Dialysis period (year)	0.986	0.921–1.057	0.705			
Body mass index (%)	1.031	0.890–1.194	0.679			
Smoking	2.137	0.730–6.252	0.165			
Hb (g/dL)	1.291	0.816–2.043	0.274			
Albumin (g/dL)	3.048	0.655–14.181	0.155			
Cholesterol (mg/dL)	1.000	0.991–1.009	0.925			
Triglyceride (mg/dL)	0.999	0.995–1.003	0.845			
Calcium (mg/dL)	0.395	0.187–0.834	0.015	0.485	0.209–1.125	0.092
Potassium (mEq/L)	1.123	0.838–1.506	0.436			
i-PTH	0.999	0.998–1.000	0.692			
Kt/V	0.445	0.078–2.523	0.361			
VABF	1.000	0.999–1.001	0.254			
Fatigue	9.730	2.060–45.958	0.004	7.597	1.411–40.883	0.018
Resistance	0.331	0.085–1.286	0.111			
Ambulation	0.500	0.158–1.577	0.237			
Illness	0.952	0.256–3.534	0.942			
Loss of weight	3.111	1.001–9.667	0.050	4.803	1.164–19.805	0.030
Total score	1.291	0.816–2.043	0.274			

i-PTH: intact parathyroid hormone; Kt/V: dialysis efficiency calculator; VABF: vascular access blood flow; VAF: vascular access failure.

useful or validated in the uremia patients with initially VAF but only fatigue and weigh loss play a major role of the recurrent episodes in the elderly.

Serum calcium levels were lower in the recurrent VAF group (8.9 $\pm$ 0.6 vs. 9.4 $\pm$ 0.7) (p = 0.010). However, the multivariate regression analysis did not reveal the association. An increased calcium phosphate product level (Ca x P) but rather than serum calcium levels was noted decreased quality of fistula in patients with chronic renal failure.[16] We did not observe an association between recurrent VAF and BMI, phosphorus, and cholesterol which has been previously observed.[17,18]

Sex had no significant relationship with recurrent VAF in our study and the inconsistencies have been observed in previous studies on female sex as a risk factor for primary arteriovenous access dysfunction.[17] In our study, greater age was associated with an increased risk of recurrent VAF which is comparable with previous research on predictors for primary VAF study, i.e., the older the patient, the shorter the duration of vascular access.[18]

There are some limitations to this study. First, the study was conducted retrospectively. Second, the self-assessment of indicators for frailty may be influenced by misperceptions of subjective health, cognitive ability, and daily variations. More readily obtainable measurements in the dialysis unit have been suggested to include a measure of gait speed that can be instituted on dialysis rounds.[19] Lower case numbers and the presence of other unmeasured confounding factors (such as biomarkers of inflammatory) may limit the generalizability of our findings.

As more elderly patients begin dialysis, the assessment of frailty will become increasingly important. An assessment at dialysis initiation and 1–2 years after initiation can provide prognostic information that will inform dialysis practitioners and patients of potential risks of VAF on dialysis continuation. Early identification of frailty may also assist with improving overall outcomes and identification of frailty may be indicated at earlier stages of chronic kidney disease. Clinical trials have also suggested that exercise may improve physical functioning among dialysis patients.[20–22]

In conclusion, our results may aid in predicting recurrent VAF in hemodialysis patients who could be targeted for preventative interventions. Age, fatigue, and weight loss were identified as risk factors. However, further studies are required to assess whether exercise or increasing muscle mass may assist in decreasing the occurrence of VAF, especially among the elderly.

Conflicts of interest statement

I certify that all my affiliations with or financial involvement in, within the past 5 years and foreseeable future, any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, royalties). All authors have no financial interests related to the material in the manuscript.

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