Evaluation of Carotid Ultrasonography Screening Among Kidney Transplant Candidates: A Single-Center, Retrospective Study

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Background. Kidney transplant candidates undergo rigorous testing prior to clearance for transplantation. Because kidney transplant candidates may be at increased risk for carotid artery stenosis because of arteriosclerosis and atherosclerosis secondary to hypertension, vascular calcification, and diabetes, carotid ultrasound is often performed with the intent of preventing a cerebrovascular accident in the perioperative or posttransplant period. To our knowledge, there has not been a study investigating the utility of screening carotid ultrasonography in pretransplant candidates. The purpose of the present study was to investigate the yield of carotid ultrasonography in end-stage renal disease patients, at high risk for having clinically significant vascular disease evaluated at our center for kidney transplantation during the years 2009 to 2014. **Methods.** Data for carotid ultrasound findings and risk factors for carotid artery disease were extracted from the medical records. **Results.** A total of 882 patients were included in our study of which only 13 patients (1.47% of the cohort) had significant carotid artery stenosis (>70%) on ultrasound testing. Using multiple logistic regression on the outcome of carotid stenosis, congestive heart failure (adjusted odds ratio, 5.2), and peripheral vascular disease (adjusted odds ratio, 4.4) were positively associated with carotid stenosis. **Conclusions.** The prevalence of significant carotid artery stenosis was only 1.47% in our cohort of kidney transplant candidates, and the routine use of carotid ultrasound testing in this population may not be an efficient use of clinical resources. Use of risk factors, such as congestive heart failure or peripheral vascular disease, may identify patients who are more likely to benefit from carotid ultrasonography screening.

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Kidney transplant candidates undergo rigorous testing before clearance for listing on the United Network for Organ Sharing waiting list in the United States. Evaluation of renal transplant candidates is a complex, costly, and time-consuming process. A considerable amount of information

must be collected, reviewed, analyzed, and synthesized in a cost-effective manner. The pretransplant assessment is to ensure transplantation is technically possible, recipients' chances of survival are not compromised, and graft survival is not limited by premature disability or death caused by preexisting conditions. Furthermore, aggravating or exacerbating patients' underlying conditions, by the transplant or by immunosuppression, needs to be avoided whenever possible.

Patients being considered for kidney transplantation differ from the general population, and they often have systemic vascular calcification or atherosclerosis due to inflammation, oxidative stress, endothelial dysfunction, reduced nitric oxide bioavailability, and calcium-phosphate deposition.[1] Given the systemic nature of the vascular derangements encountered, carotid artery stenosis often results. Risk factors for carotid artery stenosis include advanced age, diabetes, coronary artery disease (CAD), hyperlipidemia, and current smoking.[2-4] The addition of these risk factors to the derangements found in end-stage renal disease (ESRD) further increase the risk of carotid artery stenosis.

At our institution, carotid ultrasound is among the many pretransplant screening tests. It is performed on candidates who had cardiovascular or cerebrovascular history or were over the age of 50 years with the expectation of preventing a cerebrovascular accident (CVA) in the perioperative or posttransplant period. However, there has not been a study investigating the utility of screening carotid ultrasonography

in pretransplant candidates that has come to our attention. The purpose of the present study was to investigate the yield of carotid ultrasonography in an ESRD population at high risk for having clinically significant vascular disease and to identify opportunities to improve efficiency by either eliminating routine screening or restricting screening to a subgroup of patients with specific risk factors.

MATERIALS AND METHODS

This observational, retrospective study assessed the prevalence of hemodynamically significant carotid artery stenosis in kidney transplant candidates who either had cardiovascular or cerebrovascular history or were over the age of 50 years. Data for carotid ultrasound findings, as well as for risk factors for carotid artery disease, were extracted from the medical records of consecutive patients evaluated at our center for kidney transplantation during the years 2009 to 2014. Risk factors evaluated included age, sex, race, body mass index (BMI), smoking history, family history of CVA or patient's medical history of hypertension, hyperlipidemia, diabetes mellitus, CVA, CAD, peripheral vascular disease (PVD), and congestive heart failure (CHF). We defined CAD, PVD, and CHF as the presence of these risk factors as established in the history, physical examination, stress testing, CT angiography, or echocardiogram.

Carotid ultrasound findings were classified as positive if greater than 70% or negative if less than 70% carotid artery stenosis was present based on the North American Symptomatic Carotid Endarterectomy Trial criteria. Ultrasound results revealing less than 70% stenosis were considered negative due to the fact that the clinical importance of asymptomatic carotid artery stenosis less than 70% remains unclear.[5] Carotid artery stenting, endarterectomy, or no treatment were offered as choices for patients with greater than 70% stenosis. Fisher exact test, odds ratios (OR), and a 95% confidence interval (CI) were used to analyze the data.

A multivariable logistic regression on the outcome of stenosis was developed to identify significant risk factors. Twelve candidate variables were selected based on clinical interest: age, sex, BMI, HTN, CAD, PVD, CHF, diabetes, transient ischemic attack (TIA)/CVA, HLD, family history of CVA, and smoking exposure. Five variables with sparse data were excluded, which was operationally defined as a cell count less than 3 on any cell of a contingency table between the variable of interest and stenosis. A multivariable logistic regression model containing the remaining 7 variables was built, and 4 variables with Wald test P greater than 0.2 were removed. Model fit and model performance of the final model containing 3 variables (CHF, PVD, and diabetes) were evaluated with Pearson χ^2 goodness of fit and area under the curve. Analyses were conducted using STATA version 13 (StataCorp LP, College Station, TX).

RESULTS

A total of 1382 transplant candidates were evaluated, of whom 500 were excluded due to incomplete workup, incomplete ultrasound reports, death, or chart being unattainable or illegible. A total of 882 patients were included in our study for which carotid ultrasound results and risk factors for vascular disease were available to be evaluated. The prevalence of significant carotid artery stenosis in this cohort was 1.47% (95% CI, 0.79-2.51%) for a total of 13 patients (10 men and 3 women).

Patient Demographics

There were a total of 882 patients, of whom 34% were white, 33% African American, 24% Hispanic, and 10% other races (Table 1). Men predominated, accounting for 63% of the cohort; 81% were over the age of 50 years and 45% were over the age of 60 years; and 80% of the cohort had a BMI greater than 25, of whom 43% had a BMI greater than 30.

Risk Factors

The prevalence of risk factors for vascular disease and carotid artery stenosis that were collected for this study is shown in Table 1. After systematic evaluation of 12 potential risk factors in this cohort, 3 variables were strongly correlated with carotid stenosis. Using multiple logistic regression

TABLE 1.

Patient demographics and previously identified risk factors for vascular disease and carotid artery stenosis

	Total patients (n = 882)		Prevalent stenosis, n		Logistic regression for stenosis[a]	
	n	%	n	%[b]	OR	95% CI
Race						
White	297	34%	5	2%	Reference	Reference
African American	287	33%	4	1%	0.8	0.2-3.1
Hispanic	213	24%	2	1%	0.6	0.1-2.9
Other	85	10%	2	2%	1.4	0.3-7.4
Sex						
Female	325	37%	3	1%	Reference	Reference
Male	557	63%	10	2%	2.0	0.5-7.2
Age, y						
≤40	22	3%	0	0%	N/A	N/A
41-49	147	17%	2	1%	Reference	Reference
50-59	315	36%	6	2%	1.4	0.3-7.1
>60	398	45%	5	1%	0.9	0.2-4.8
BMI						
≤18.5	12	1%	0	0%	N/A	N/A
18.6-24.9	169	19%	1	1%	Reference	Reference
25-29.9	324	37%	8	2%	4.3	0.5-34.3
≥30	377	43%	4	1%	1.8	0.2-16.2
Smoking status						
Nonsmoker	665	75%	7	1%	Reference	Reference
Past smoker	168	19%	6	4%	3.5	1.2-10.5
Active smoker	49	6%	0	0%	N/A	N/A
Medical history[c]						
Hypertension	814	92%	11	1%	0.5	0.1-2.1
Diabetes	493	56%	5	1%	0.5	0.2-1.5
Hyperlipidemia	316	36%			1.5	0.5-4.6
CAD	182	21%		2%	1.7	0.5-5.7
CHF	96	11%	5	5%	5.3	1.7-16.7
PVD	73	8%	3	4%	3.4	0.9-12.7
Prior TIA/CVA	83	9%	1	1%	0.8	0.1-6.2
Family history of CVA	45	5%	2	4%	3.5	0.8-16.3

[a] Odds ratios and confidence intervals were calculated using unadjusted logistic regression.

[b] Prevalence was calculated as the proportion of patients with stenosis in each row of the table.

[c] Present of comorbid conditions was not mutually exclusive. The reference category for each row is the absence of that comorbid condition, which is not shown.

N/A, not applicable.

on the outcome of carotid stenosis, CHF (adjusted OR, 5.2) and PVD (adjusted OR, 4.4) were positively associated with carotid stenosis; diabetes (adjusted OR, 0.4) was negatively associated with carotid stenosis (Table 2). The prevalence of significant carotid stenosis was 0.83% (6 of 722) among patients who were free from CHF and PVD, 3.97% (6 of 151) among patients with either CHF or PVD, and 11.1% (1 of 9) among patients with both CHF and PVD (Figure 1). Compared with 722 patients who were free from CHF and PVD, the odds for detecting significant carotid stenosis were increased for 160 patients with CHF or PVD (unadjusted OR, 5.5; 95% CI, 1.5-19.9; P = 0.004).

Screening Efficiency

Among all patients, 69 patients would have to be screened to identify 1 case of significant carotid stenosis. Among patients who were free from CHF and PVD, 121 patients would have to be screened to identify 1 case of significant carotid stenosis. Among patients with CHF or PVD, 23 patients would need to be screened to identify 1 case of significant carotid stenosis. Among ESRD patients in this study, the presence of CHF or PVD known before screening had 53.9% sensitivity, 82.4% specificity, 4.4% positive predictive value, and 99.2% negative predictive value for the outcome of significant carotid stenosis.
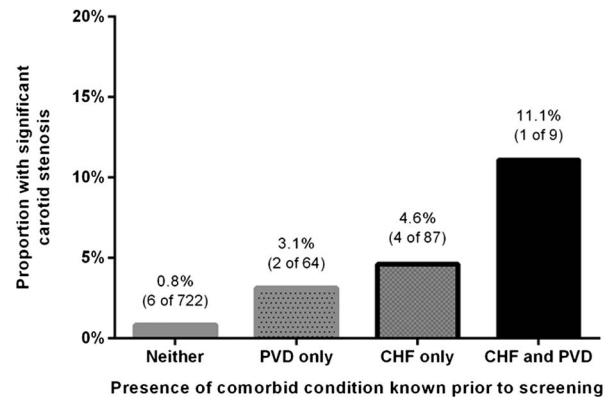
DISCUSSION

The prevalence of significant carotid stenosis detected during routine kidney transplant evaluation of 882 ESRD patients at our single center in Houston, Texas was 1.47%, which is within the estimated prevalence range of 0% to 3.1% for the general population.[6] Carotid artery stenosis causes up to 10% of all ischemic strokes, but the overall estimated prevalence of severe asymptomatic carotid artery stenosis varies from 0.5% to 1.6%.[6-9] Observational studies suggest the rate of stroke without an antecedent TIA ipsilateral to a hemodynamically significant extracranial carotid artery stenosis is about 1% to 2% annually.[10] The United States Preventive Services Task Force, as well as many other groups, recommend against screening for hemodynamically significant carotid artery stenosis in asymptomatic subjects in the general adult population. This is both because of the low yield and also because the risk of therapy may outweigh benefits of screening.[11-13] In the Carotid Revascularization Endarterectomy versus Stenting Trial, a randomized control trial in which 2502 participants were randomized to undergo carotid artery stenting vs. carotid endarterectomy, 7.2% of patients who underwent carotid artery stenting versus 6.8% of patients who had carotid endarterectomy met the primary endpoint of occurrence of any stroke, myocardial infarction,

CHF, congestive heart disease; PVD, peripheral vascular disease

Fisher's exact test, P=0.003.

FIGURE 1. Proportion of patients with significant carotid stenosis based on presence of comorbid conditions known prior to screening.

or death during the periprocedure period, or suffered ipsilateral stroke up to 4 years thereafter.[14] Postprocedure ipsilateral stroke over the 10-year follow-up occurred in 6.9% of the patients in the stenting group and in 5.6% of those in the endarterectomy group.[15]

Unlike the general population, however, patients with ESRD develop accelerated arteriosclerosis and vascular calcification.[1,16-20] It could not be certain, therefore, that the recommendations against screening of asymptomatic adults in the general population might be applicable to ESRD patients. Among ESRD patients listed for transplant, 1 case of significant carotid stenosis was identified for every 69 patients screened. However, if screening was restricted to patients with known CHF or PVD, only 23 patients would need to be screened to identify a new case of significant carotid stenosis. To improve the provision of healthcare resources for screening, our data support restriction of carotid ultrasonography screening to patients with CHF or PVD during routine evaluation for kidney transplant.

Patients with a history of CHF were five times more likely to have a positive ultrasound finding. We hypothesize that the link between these two conditions is likely the result of arterial stiffness known to occur in ESRD patients, and leads to left ventricular hypertrophy, diastolic dysfunction and CHF.[1,16-20] Further studies should consider evaluating pulse pressure as an indirect marker of arterial stiffness.[21,22]

Patients with a history of PVD were 4 times more likely to have a positive ultrasound finding. We hypothesize that this is possibly related to the fact that patients with arteriosclerosis and vascular calcification in 1 organ are likely to have involvement in multiple organs. Based on our findings, we recommend considering carotid ultrasound if kidney transplant candidates have multiple risk factors or history of CHF or PVD.

Limitations to our study include the fact that it is a retrospective chart review of secondary data extracted from medical charts. The presence or absence of underlying medical conditions may have been misclassified in the medical record. Our findings are important, however, to transplant programs as they could lead to the elimination of a potentially unnecessary routine screening test in pretransplant candidates. A larger study is needed to confirm our findings that the

TABLE 2.

Multiple logistic regression on the outcome of significant carotid stenosis

Predictor	Adjusted ORs	95% CI	P
CHF	5.2	1.7-16.5	0.005
PVD	4.4	1.1-17.6	0.037
Diabetes	0.4	0.1-1.3	0.125

Model fit was confirmed with Pearson χ^2 goodness of fit statistic of 5.40 and P = 0.249. The area under the receiver operating curve was 0.71.

efficiency of carotid ultrasonography screening among kidney transplant candidates would be improved if screening was restricted to patients with a medical history of CHF or PVD.

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