Carotid endarterectomy in patients with significant renal dysfunction

W. Charles Sternbergh III, MD, C. Louis Garrard, MD, Mark D. Gonze, MD, Jeffrey D. Manord, MD, John C. Bowen, MD, and **Samuel R. Money, MD,** *New Orleans, La*

Purpose: **Recent reports suggest that carotid endarterectomy (CEA) should not be performed in patients with end-stage renal disease (ESRD) because of an unacceptable rate of perioperative stroke and other morbidity. Because these conclusions were based on a small number of patients, we reviewed the perioperative and long-term outcome of patients with ESRD and chronic renal insufficiency (CRI) who underwent CEA at our institution.**

Methods: **The 1081 patients who had a CEA between 1990 and 1997 were cross-referenced with those patients in whom renal insufficiency had been diagnosed. These charts were reviewed for patient demographics and perioperative and long-term outcome. Patients undergoing CEA during a 1-year period (1993) served as controls.**

Results: **Fifty-one CEAs were performed in 44 patients with CRI (32 in 27 patients) and ESRD (19 in 17 patients). In the CRI+ESRD group, 66.7% were symptomatic, and 70.7% of the control group were symptomatic. Six operations (11.8%) in the CRI+ESRD group were redo endarterectomies. There were no perioperative strokes in the CRI+ESRD group, but one patient died 29 days postoperatively because of a myocardial infarction, for a combined stroke-mortality rate of 2.0%. The control group had a 2.6% combined stroke-mortality rate. Long-term survival analysis revealed a 4-year survival rate of 12% for patients with ESRD and 54% for patients with CRI, compared with 72% for controls ($P < .05$).**

Conclusion: **CEA can be performed safely in patients with ESRD or CRI, with perioperative stroke and death rates equivalent to that of patients without renal dysfunction. However, the benefit of long-term stroke prevention in the asymptomatic patient with ESRD is in question because of the high 4-year mortality rate of this patient population. (J Vasc Surg 1999;29:672-7.)**

Each year, more patients survive chronic renal insufficiency (CRI) and start dialysis as end-stage renal disease (ESRD) patients. It is estimated that these numbers will increase significantly in the next century.[1] Because hypertension and diabetes mellitus are so prevalent in this population, these patients are at significant risk for having concurrent peripheral vascular disease.[2] As the number of these patients increases, more will come to vascular surgeons for evaluation of their vascular disease.

Patients with ESRD have been widely reported to have higher perioperative morbidity and mortality rates and worse long-term outcomes for both cardiac[3,4] and peripheral vascular[5,6] operations when compared with those patients without renal dysfunction. A recent report stated that carotid endarterectomy (CEA) in patients with ESRD had a prohibitive operative stroke and death rate, and it questioned the benefit of CEA in this patient population.[7] These conclusions, however, were based on an experience with few patients; larger series are needed to provide a clearer picture of the short- and long-term outcomes of patients with CRI and ESRD who undergo CEA. To better understand the perioperative and long-term outcomes of these patients, we performed a retrospective chart review of patients who had CRI or ESRD at the time of their endarterectomy.

From the Ochsner Clinic and Foundation.

Presented, in part, at the Twenty-second Annual Meeting of the Southern Association for Vascular Surgery, Rio Grande, Puerto Rico, Jan 21-24, 1998.

Reprint requests: W. Charles Sternbergh III, MD, Department of Surgery, Ochsner Clinic, 1514 Jefferson Hwy, New Orleans, LA 70121.

0741-5214/99/$8.00 + 0 **24/1/95750**

METHODS

All patients in whom CRI or ESRD had been diagnosed were cross-referenced with those who underwent a CEA at the Alton Ochsner Medical

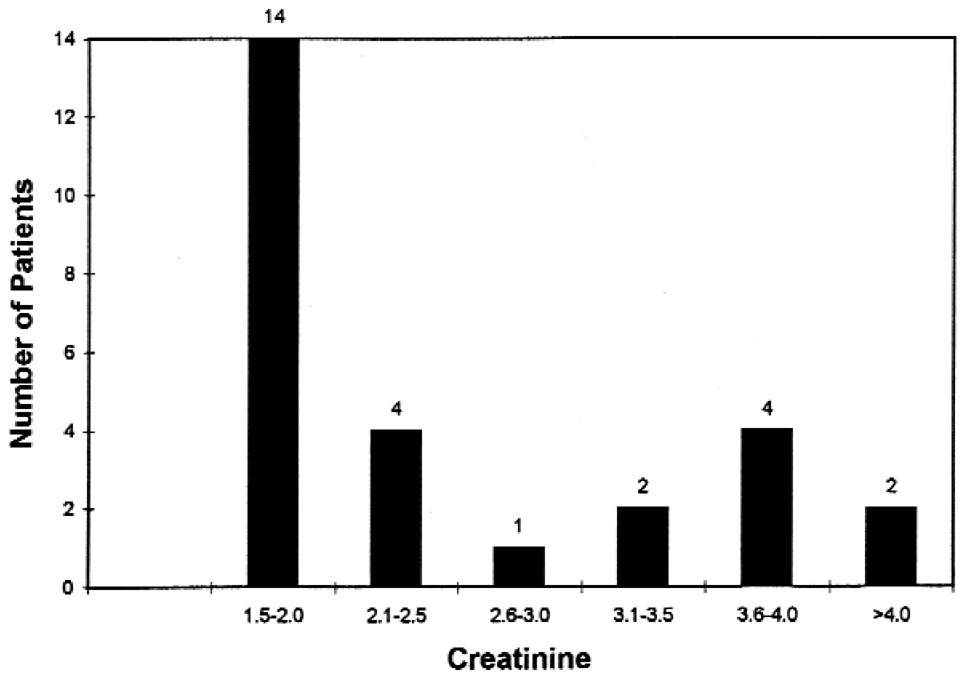

Fig 1. Creatinine levels of patients with chronic renal insufficiency at the time of carotid endarterectomy.

Table I. Baseline demographics

	CRI + ESRD (n = 44)	*Control (n = 105)*	*P*
Age	69.5 ± 1.4	68.3 ± 0.8	NS
Female	23 (52.7%)	35 (33.3%)	.054
Tobacco use	14 (31.8%)	69 (65.7%)	.0001
HTN	42 (95.5%)	70 (66.7%)	.0006
DM	18 (40.9%)	32 (30.8%)	NS
CAD	25 (56.8%)	61 (58.1%)	NS
PVD	26 (59.1%)	44 (41.9%)	NS

CRI, chronic renal insufficiency; *ESRD,* end-stage renal disease; *HTN,* hypertension; *CAD,* coronary artery disease; *PVD,* peripheral vascular disease.

Table II. Indications for carotid endarterectomy

	CRI + ESRD (n = 51)	*Control (n = 116)*	*P*
CVA	9 (17.6%)	27 (23.3%)	NS
TIA	15 (29.4%)	34 (29.3%)	NS
Amaurosis	9 (17.6%)	20 (17.2%)	NS
Global ischemia	1 (2.0%)	0 (0%)	NS
Asymptomatic	17 (33.3%)	34 (29.3%)	NS
Redo	6 (11.8%)	8 (6.9%)	NS

CRI, chronic renal insufficiency; *ESRD,* end-stage renal disease; *CVA,* cerebrovascular accident; *TIA,* transient ischemic attack.

Foundation between 1990 and 1997. Patients with a creatinine level of 1.5 mg/dL or higher at the time of their CEA were used in the evaluation. Those patients with acute renal failure were excluded. These charts were reviewed for patient demographics, renal function at the time of surgery, perioperative morbidity and mortality rates, and long-term follow-up. Follow-up data were based on routine postoperative clinic visits and hospital admissions when they occurred were supplemented with phone contact with patients whose long-term data were unavailable from the charts. For the purpose of survival analysis, the study patients were divided into two groups: those with CRI, defined as patients with a creatinine level of 1.5 mg/dL or higher; and those with ESRD, defined as patients on long-term hemodialysis or peritoneal dialysis. Excluding those with CRI or ESRD, all other patients who underwent CEA in 1993 (116 CEAs in 105 patients) were used as a control group. This group was chosen so that complete 4-year survival data would be available.

Survival data was analyzed by means of the Kaplan-Meier cumulative survival analysis, with statistical differences determined by means of the log-rank test. Baseline demographic data were compared with chi-square analysis, and perioperative stroke and death rates were analyzed with the Fisher exact

Table III. Late stroke

	ESRD + CRI	*Control*
Late stroke	2 (4.3%)	7 (6.0%)
Ipsilateral to CEA	1 (50%)	4 (57%)
Symptomatic at CEA	0 (0%)	6 (86%)

CRI, chronic renal insufficiency; *ESRD,* end-stage renal disease; *CEA,* carotid endarterectomy.

Table IV. Long-term survival rates (%)

Patient group	*1 yr*	*2 yr*	*3 yr*	*4 yr*
Control (n = 105)	94	92	85	72
CRI (n = 27)	88	70	65	54
ESRD (n = 17)	75	53	32	12

CRI, chronic renal insufficiency; *ESRD,* end-stage renal disease.

test. Significance was expressed as *P* being less than .05. Results were expressed as the mean ± standard error of the mean.

RESULTS

Demographics. Between 1990 and 1997, 1081 CEAs were performed at our institution, of which 51 were done in 44 patients with CRI or ESRD. Seventeen patients who had ESRD underwent 19 CEAs, and 27 patients who had CRI underwent 32 CEAs. The mean creatinine level of the patients with CRI was 2.4 ± 0.2 mg/dL; the creatinine levels of all patients with CRI are displayed in Fig 1. Table I lists the demographics of the study and control groups. In the CRI+ESRD group, there were significantly more women ($P = .054$) and a higher prevalence of hypertension ($P = .0006$), when compared with the control group. Smoking was more common in the control group (65.7% vs 31.8%; $P = .0001$). Age and incidence of coronary artery disease, peripheral vascular disease, and diabetes mellitus were similar between the two groups.

Indications for CEA were similar in the two groups (Table II). Two thirds of patients in both groups had ipsilateral focal symptoms. Redo endarterectomy comprised 11.8% (6 of 51) of patients in the CRI+ESRD group and 6.9% (8 of 116) in the control group.

Perioperative results. The combined 30-day perioperative stroke and death rate was 2.0% (0 strokes, 1 death) in the CRI+ESRD group and 2.6% (3 strokes with one leading to death) in the control group. In the CRI+ESRD group, the one perioperative death was from myocardial infarction, occurring on postoperative day 29; the patient had been discharged from the hospital 2 days after her CEA. In the control group, one death occurred in a patient with atrial fibrillation who sustained a massive left hemispheric cerebrovascular accident (CVA) 2 days after a redo right CEA. A second patient, also in chronic atrial fibrillation, was operated on urgently for free-floating thrombus at the carotid bifurcation after having an acute CVA; he had a worsening of his hemiparesis postoperatively. The third stroke in the control group occurred 10 hours after CEA in a patient who had sustained an ipsilateral CVA 6 weeks before operation.

Morbidity. In the CRI+ESRD group, perioperative morbidity included three transient cranial nerve injuries, three episodes of hypertension requiring prolonged hospitalization, one neck hematoma requiring evacuation, one clotted dialysis access, one episode of intraoperative cardiac arrest in a patient who was successfully resuscitated, and one case of worsening CRI progressing to ESRD. In the control group, there were two transient cranial nerve injuries, no neck hematomas requiring exploration, and one prolonged hospitalization for respiratory failure in a patient who had a thoracoabdominal aortic aneurysm repair 4 days after his CEA.

Late neurologic events. Table III contains information on late neurologic events. At a mean of 26 months, there were three (5.9%) transient ischemic attacks that had occurred in the CRI+ESRD group and six (5.2%) in the control group. Late strokes occurred in two (4.3%) patients in the CRI+ESRD group and seven (6.0%) patients in the control group. Strokes occurred on the ipsilateral side of previous CEA in 50% (1 of 2) of the CRI+ESRD group and 57% (4 of 7) of the control group. Most late strokes in the control group (86%) occurred in patients who were initially symptomatic at the time of CEA, whereas both late strokes in the CRI+ESRD group occurred in initially asymptomatic patients. The follow-up period was at least 1 year or the time of death in all patients.

Long-term mortality. The long-term mortality rate was significant (Table IV). The 4-year survival rate of those patients with ESRD and CRI was 12% and 54%, respectively, which was significantly less than the control group survival rate of 72% ($P = .04$ and $P < .0001$). In the CRI group, there were five deaths each in the subgroups, with creatinine levels ranging from 1.5 to 2.0 mg/dL (n = 14) and higher than 2.0 mg/dL (n = 13). Thus, in this small patient cohort, those with mild CRI had no better survival rates than those with more severe CRI. In

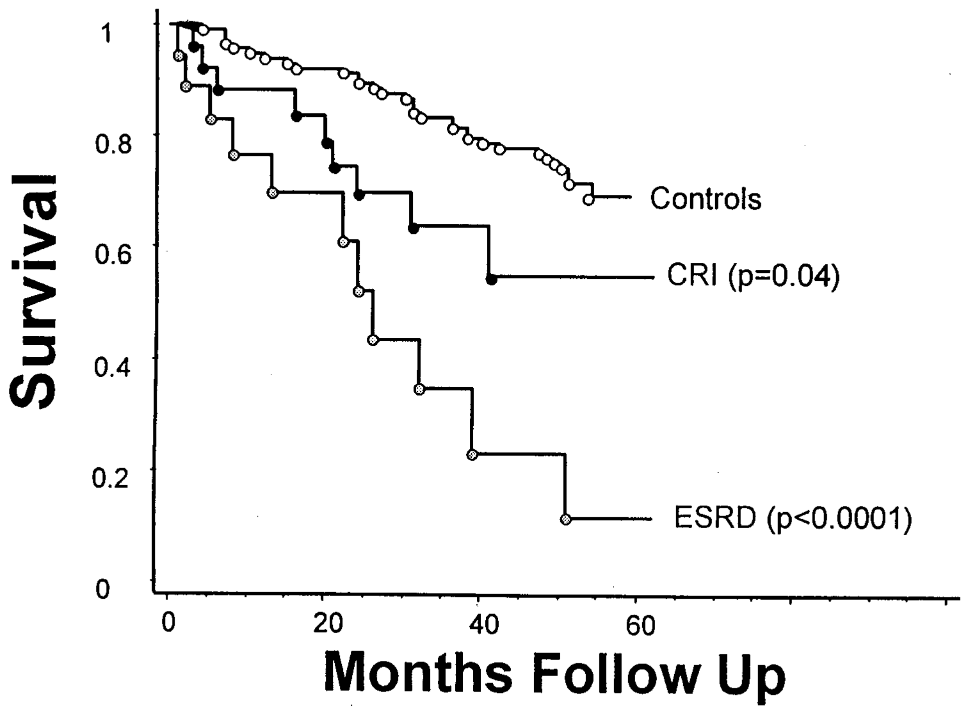

Fig 2. Kaplan-Meier survival curve of patients with chronic renal insufficiency (CRI), patients with end-stage renal disease (ESRD), and control patients. Survival is significantly worse in those patients with CRI and ESRD when compared with the control group, with $P = .04$ and $P < .0001$, respectively.

1997, the 1-year mortality rate for all ESRD patients, with an average age of 56 years, at Ochsner was 19%. The survival cures for all three groups are depicted in Fig 2.

There were 10 deaths each in the CRI and ESRD groups. Among the five patients in the CRI group with creatinine levels of 1.5 to 2.0 mg/dL, none died of renal failure, whereas two of the five patients with more severe CRI (creatinine levels higher than 2.0 mg/dL) died of complications of renal failure. The primary cause of death in the ESRD group was complications of renal failure (75%), which included withdrawal of dialysis, severe congestive heart failure with respiratory complications, and systemic infection. Cardiac disease (20%) was the second most common cause of death. None of the patients died of cerebral vascular disease.

DISCUSSION

There are few reports of CEA in patients with renal insufficiency in the literature. Rigdon et al[7] recently published a series of seven CEAs in six patients with creatinine levels higher than 2.9 mg/dL, two of whom were on dialysis. The perioperative stroke rate was 42% (3 of 7), with two additional strokes occurring at 3 and 4 months postoperatively. Long-term survival was not evaluated. In Plecha's review of 9795 CEAs, 216 (2.2%) patients had chronic renal failure. Both perioperative stroke and death were reported to be "significantly higher" in these patients than the 2.0% and 1.5%, respectively, in the entire patient cohort. Neither the magnitude of the increased perioperative morbidity/mortality nor long-term outcome were discussed.[8]

Our perioperative outcome was markedly different than these series, with a combined stroke/mortality rate of 2.0% in patients with CRI or ESRD. This event rate was not significantly different from the 2.6% stroke/death rate in the control group. Thus, the presence of significant renal disease did not appear to adversely affect early outcome. Incidence of late stroke in this patient group (4.3%) was not significantly different from our control group (6.0%). These data are in contrast to those of Rigdon et al, who noted a late stroke rate of 28.6% (2 of 7) in patients with CRI or ESRD. The morbidity was higher in our CRI+ESRD group when compared with the control group, but was not prohibitive.

The alarming finding in our study was the remarkably high long-term mortality rate of this patient cohort, especially those with ESRD. The 5-year survival rate for all ESRD patients is estimated at 40% for patients in the United States, a figure which drops to 15% in age-matched ESRD patients with diabetes mellitus.[9] This latter group is similar to our study group and, indeed, has a similar mortality rate. Our yearly mortality rate of 19% for all ESRD patients at our facility likely reflects the advanced age and significant comorbidities of this patient population.

In patients who do not have ESRD, the severity of CRI did not appear to correlate with death. Patients with mild CRI (creatinine levels of 1.5 to 2.0 mg/dL) had the same 4-year mortality rate as those with more severe CRI (creatinine levels higher than 2.0 mg/dL). Interestingly, none of the patients with mild CRI died of renal failure. Intuitively, one would expect that those with severe CRI would fare worse than those with mild CRI, but this hypothesis was not supported by the data. However, because of the small sample size of these subgroups, a type II error was certainly possible; no firm conclusions can be drawn.

Baseline demographics of the control group and the study group were fairly well matched. There were more women in the CRI+ESRD group, which would potentially bias the results against this group; women may have a higher perioperative stroke rate than men after CEA.[10,11] However, stroke rates were similar between the two groups. As expected, the nearly ubiquitous presence of hypertension in the CRI+ESRD group was higher than in the control group, but this variable has not been a predictor of perioperative outcome in CEA.[10] The control group (all patients undergoing CEA in 1993) was chosen so that complete survival data would be available, because this was a primary endpoint in this study. Indeed, the long-term survival rate in our control group was very similar to that reported in large randomized trials of carotid disease,[11,12] suggesting that it is indeed a representative control. Although the use of the entire cohort of CEA patients from 1990 to 1997, or a subgroup picked by a case control method, may have produced a more statistically "appropriate" control group, it is highly unlikely that the conclusions of this study would be altered with their use.

Does the high long-term mortality rate of these patients diminish or negate the effectiveness of CEA in preventing future stroke? In the North American Symptomatic Carotid Endarterectomy Trial (NASCET), the Kaplan-Meier curves for stroke diverged between the medically and surgically treated groups at approximately 3 months of follow-up, with clear benefit to the surgical group by 6 to 12 months.[12] At 2 years, the ipsilateral stroke rate was 26% in the medically treated patients and 9% in the surgically treated patients. In the Asymptomatic Carotid Artery Study (ACAS), a randomized trial of asymptomatic carotid disease, the Kaplan-Meier curves for stroke between surgically and medically treated groups did not begin to diverge until 18 to 24 months, and only at 5 years did the differences become statistically significant (5.1% vs 11% for surgery vs medical treatment, respectively).[11] Most patients with significant carotid disease and ESRD have died at 5 years of follow-up.[13]

Based on these data, it would appear that ESRD patients with symptomatic disease may still benefit from CEA, but those with asymptomatic disease may not live long enough to enjoy a significant reduction in stroke risk.

These speculations must be tempered, however, by the knowledge that the natural history of significant carotid disease in this patient cohort is largely unknown. These patients would not have been eligible for the NASCET and ACAS trials because of their renal disease. It may be possible that the risk of stroke in patients with ESRD is greater than that of the medically treated groups in these studies. Significant repetitive hypotension occurring during dialysis may predispose patients to hypoperfusion-induced stroke, for instance. However, most strokes caused by carotid bifurcation disease are embolic in nature and not hemodynamic.

The prevalence of ESRD is continuously increasing. In 1990, there were 180 cases of ESRD per 1,000,000 members of the US population, a rate which has increased by 7.5% each year. By the year 2001, there are expected to be 300,000 patients with ESRD, with 75,000 new patients in that year alone.[1] Patients with renal insufficiency have a greater propensity to develop carotid occlusive disease than age-matched controls.[13] Vascular surgeons can expect to see a larger number of patients with ESRD coming to them for evaluation of their carotid occlusive disease.

CONCLUSION

The high long-term mortality rate of the patients in our study suggests that the criteria for operative treatment that are applied to the routine patient population may not be applicable to those with CRI or ESRD. Although the operation can be performed safely in patients with CRI or ESRD, prophylactic CEA in the asymptomatic patient with renal dysfunction, especially one with ESRD, may have little effect in improving the long-term stroke-free survival of these patients. Although operative treatment decisions should be individualized to each patient, based on our data, we would not recommend CEA in asymptomatic patients with ESRD.

REFERENCES

1. Consensus Development Conference Panel. Morbidity and mortality of renal dialysis: NIH consensus conference statement. Ann Intern Med 1994;121:62-70.
2. Young EW. An improved understanding of the causes of end-stage renal disease. Semin Nephrol 1997;17;170-5.
3. Jahangiri M, Wright J, Edmondson S, Magee P. Coronary artery bypass surgery in dialysis patients. Heart 1997:78:343-5.
4. Christiansen S, Claus M, Philipp T, Reidemeister JC. Cardiac surgery in patients with end-stage renal failure. Clin Nephrol 1997;48:246-52.
5. Donayre CE. Results of revascularization for peripheral arterial insufficiency in chronic renal failure patients. Semin Vasc Surg 1996;9:253-61.
6. Johnson BL, Glickman MH, Bandyk DF, Esses GE. Failure of foot salvage in patients with end-stage renal disease after surgical revascularization. J Vasc Surg 1995;22:280-6.
7. Rigdon EE, Monaiem N, Rhodes RS. Is carotid endarterectomy justified in patients with severe chronic renal insufficiency? Ann Vas Surg 1997;11:115-9.
8. Plecha EJ, King TA, Pitluk HC, Rubin JR. Risk assessment in patients undergoing carotid endarterectomy. Cardiovasc Surg 1993;1:30-2.
9. Held PJ, Carroll CE, Liska DW, et al. Hemodialysis therapy in the United States: What is the dose and does it matter? Am J Kidney Dis 1994;24:974-80.
10. Hertzer NR, O'Hara PJ, Mascha EJ, Krajewski LP, Sullivan TM, Beven EG. Early outcome assessment for 2228 consecutive carotid endarterectomy procedures: The Cleveland Clinic experience from 1989 to 1995. J Vasc Surg 1997 26:1-10.
11. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-8.
12. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. N Engl J Med 1991;325:445-53.
13. Rossi A, Bonfante L, Giacomini A, et al. Carotid artery lesions in patients with nondiabetic chronic renal failure. Am J Kidney Dis 1996;27:58-66.

Submitted Sep 8, 1998; accepted Nov 11, 1998.