Recurrent Stenosis at Site of Carotid Endarterectomy

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SUMMARY

Five patients studied by the authors and 28 mentioned in the literature indicate that recurrent stenosis occurs in no less than 0.6% of patients after carotid endarterectomy. The pathology of the recurrent stenosis was stated in only 10 cases indicating atheromatous dissection as the primary mechanism. The other patients. Seventeen symptomatic patients had surgical correction of the re-stenosis (endarterectomy 9, vein patch 6, arterial homograft 1, not detailed 1). The incidence of recurrent stenosis after carotid endarterectomy is low and usually the operation provides a patent artery for life.

Methods

Two patients with asymptomatic recurrent stenosis died 5 years and 11 years after operation. Two patients with symptomatic recurrent stenoses 16 months and 11 years after first endarterectomy died 51 days and 32 days respectively after repeat endarterectomy. The carotid arteries were removed at postmortem examination, fixed in formalin, decalcified if necessary, and the endarterectomy site sectioned transversely at several levels or serially. Tissue sections were stained for light microscopy with hematoxylin and eosin, Gomori connective tissue stain and Weigert's or Verhoeff's elastic tissue stains.

One patient with a symptomatic recurrent stenosis 6 years after first operation had it removed uneventfully by repeat endarterectomy.

Surgical specimens from all patients were examined to determine plaque morphology and thickness of intima and media which had been removed.
Case Histories and Pathological Findings

Case 1: A 44-year-old man had numerous 1 minute episodes of flashing lights in the right eye one month prior to the sudden onset of weakness and numbness of his left arm. The deficit progressed over a few hours to include weakness of his left face, tongue, arm, and leg and a left homonymous hemianopia. Bruits were absent but the right carotid pulsation felt diminished. Emergency right retrograde brachial arteriogram showed complete occlusion of the right internal carotid artery at its origin. Nine hours after onset of neurologic deficit a right carotid endarterectomy removed an atherosclerotic plaque causing a nearly complete stenosis and fresh occluding thrombus extending several centimeters distally. The neurologic deficit improved immediately postoperatively leaving only a mild left hemiparesis at discharge. No postoperative anticoagulation was given.

Elective postoperative arteriography 5 months later showed a patent internal carotid artery with a diverticulum directed anteriorly at the arteriotomy site. Bruits were absent and only a mild left facial weakness and left hyperreflexia remained from the previous episode of cerebral ischemia. A second arteriogram 11 months postoperatively showed no change in the diverticulum. During the remaining 5 years of his life the patient remained neurologically well until death from myocardial infarction.

Postmortem examination showed a completely patent right carotid artery with a smooth, thick, covering of neointima. The neointima lining the diverticulum contained scant extracellular lipid indicative of early atheroma. There was no luminal encroachment or discontinuity of the overlying endothelium.

Comment: This patient had normal blood pressure, blood sugar, serum cholesterol, and electrocardiograms during the 5 years prior to death. Despite the lack of significant risk factors for atherosclerosis he developed a high grade atherosclerotic stenosis and subsequent thrombotic occlusion of the right internal carotid artery at the age of 44 years, and 5 years after endarterectomy early atheroma had re-formed in the thick neointima lining a diverticulum.

Case 2: A 37-year-old man had three brief episodes of right frontal headache and numbness of the left hand 5 months prior to the onset of weakness of the left face and arm, cortical sensory loss in the left hand, and left hemianopia. Bruits were absent but the right carotid pulsation felt diminished. A carotid arteriogram showed an irregular plaque 1.5 centimeters long at the origin of the right internal carotid artery. During 3 weeks on oral anticoagulation the sensation in the patient's left hand returned to normal and hand power improved to Grade 2 out of 5. Following this improvement a carotid endarterectomy under hypothermia via a transverse arteriotomy at the right internal carotid artery origin was performed. Oral anticoagulation was continued 12 months postoperatively.

Elective postoperative arteriography at 4 months showed a normal right carotid bifurcation.

Eleven years after surgery, at age 48 years, he suddenly developed a weak and numb right arm. Arteriography showed an ulcer at the left internal carotid artery origin and poor filling of the left anterior and middle cerebral arteries. There was a smooth 50% stenosis at the origin of the previously operated right internal carotid artery (fig. 20 in reference 2). His deficit progressed to a right hemiplegia and coma within a few hours after arteriography and he died 2 days later.

Postmortem examination showed that recent thrombosis of the left internal carotid artery had caused massive left cerebral infarction and secondary brain stem hemorrhages. The right internal carotid artery origin was stenosed by encroachment of typical chronic atheromatous material in the posterior wall at the site of the previous endarterectomy (fig. 1).

Comment: On repeated examination this patient had normal blood sugar, cholesterol, and electrocardiograms during the 11 years prior to his death. He had only mild diastolic hypertension yet he developed a symptomatic right internal carotid atheromatous plaque at the age of 37 years. As well, asymptomatic recurrent atheroma formed at the site of the previous endarterectomy in the 11 years after operation and a fatal atherothrombotic occlusion occurred in the unoperated left internal carotid artery.

Case 3: A 56-year-old woman noted brief episodes of a "film" descending over her right eye for 1 month followed by an episode of numbness and weakness of her left arm that cleared incompletely. One week later the deficit suddenly progressed to a mild weakness of her left face and arm. A right carotid bruit was present. A right retrograde brachial arteriogram demonstrated a severe stenosis of the right internal carotid artery origin (fig. 2). A right carotid endarterectomy removed an atherosclerotic lesion and a postoperative arteriogram at 17 days showed a patent right
carotid bifurcation (fig. 3). Oral anticoagulation was continued 6 months postoperatively.

She remained well until 16 months later when she again developed a mild paraplegia of the left arm. A new, harsh bruit was heard over the right carotid bifurcation. A right retrograde brachial arteriogram revealed a severe recurrent stenosis of the right internal carotid origin (fig. 4). Repeat right carotid endarterectomy removed "a collagenous looking ridge" and the lumen was enlarged with a vein patch. Microscopy showed intimal atheroma with a ragged, partly ulcerated luminal surface with adherent organized thrombus. Postoperative anticoagulation was again given but 51 days after operation the patient died from a massive intracerebral hemorrhage.

Postmortem examination revealed a completely patent right internal carotid artery with thick neointima overlying the vein patch and the surgically thinned media of the right internal carotid artery (fig. 6 in reference 1).

*Comment:* This patient had an abnormal glucose tolerance test at age 44 years but her diabetes did not require treatment until age 56 years when an 1800 calorie diabetic diet was prescribed. Serum cholesterol was mildly elevated on occasion but serum triglycerides and lipoprotein electrophoresis were normal. Mild systolic hypertension had been recorded. Myocardial infarctions occurred at 51 and 57 years of age, the latter episode occurring between the two endarterectomies. Asymptomatic peripheral vascular disease was suggested by a left femoral artery bruit and bilaterally absent posterior tibial pulses.

This woman had several risk factors associated with an increased chance of atherosclerotic disease and developed both symptomatic coronary artery disease and carotid occlusive disease. Recurrent symptomatic atherosclerotic occlusive disease developed at the first endarterectomy site 16 months after the first operation.

**Case 4:** A 51-year-old man noted transient episodes of slurred speech as well as numbness and weakness of his right arm for 3 months until persistent weakness of his right face and hand and a mild expressive dysphasia developed. A left supraclavicular and carotid bruit were present. A left carotid arteriogram demonstrated a severe stenosis of the left internal carotid artery origin. A left carotid endarterectomy removed an atherosclerotic plaque. Oral anticoagulation was given for 6 months postoperatively. No postoperative angiography was performed.

He remained neurologically well during the next 4 years but required a total of 7 operations on his aortoiliac and femoral arterial systems to maintain adequate circulation to his lower limbs. Four of the operations were necessitated by occlusion of various limbs of the arterial prostheses. One of the responsible limbs of a Dacron prosthesis had an area of atherosclerosis in the neointima lining the graft.

Six years after the left carotid endarterectomy 3 episodes of transient numbness of his right face and arm occurred.
Sulfinpyrazone* was given and he had no further sensory symptoms but episodic left amaurosis fugax developed while he was taking the antiplatelet medication. A left carotid arteriogram showed a marked stenosis in the origin of the left internal carotid artery (fig. 5). A repeat left carotid endarterectomy removed a friable mass of tissue without difficulty (fig. 6) from the left internal carotid artery origin clearly within the boundaries of the neointima formed after the first endarterectomy. Microscopy showed organizing thrombus containing cholesterol clefts in the neointima and more recent thrombus on the surface of the lesion. The patient was neurologically well postoperatively and oral anticoagulation was given for 6 months.

Comment: During 6 years of active carotid and aortoiliac-femoral occlusive disease this patient's blood sugar, serum cholesterol and triglycerides, blood pressure and electrocardiograms had been normal. Thus a man with none of the usual risk factors for atherosclerotic disease developed symptomatic recurrent stenosis of the left internal carotid artery origin 6 years after first endarterectomy, as well as severe occlusive disease of his aortoiliac and femoral arterial systems. The occurrence of atheroma in a Dacron arterial prosthesis attests to the activity of the atherosclerotic process.

Case 5: A 50-year-old man noted transient episodes of numbness of his left face and arm and clumsiness of his left hand. Bruits were absent. A right carotid arteriogram was normal. He remained well for 9 months until similar transient symptoms for three weeks preceded the onset of progressive weakness of his left face and arm and a cortical sensory loss of his left hand. Bruits were again absent. A right carotid arteriogram showed a complete occlusion of his right internal carotid artery at its origin. A right carotid endarterectomy performed with hypothermia restored good flow after removal of an atherosclerotic plaque with superimposed occlusive thrombus. A Teflon patch enlarged the origin of the internal carotid artery. There was good neurological recovery and oral anticoagulants were continued 6 months postoperatively.

Six years later he suffered the onset of right hemianopia and numbness and weakness of his right arm. A right carotid bruit was present. A left carotid arteriogram was normal. A

*Anturan, Geigy
right carotid arteriogram to evaluate his previous endarterectomy site showed slight irregularity at the origin of the internal carotid artery but no stenosis (WP in fig. 11 and fig. 22 in reference 2). Oral anticoagulation had to be stopped after 6 weeks therapy due to hematuria.

Nine years after the onset of cerebral ischemia an aortoiliac endarterectomy relieved claudication in the right leg.

Eleven years after right carotid endarterectomy brief episodes of numbness of his left face and arm and weakness of his left hand recurred for 1 month before the sudden onset of left hemianopia, left face and arm paresis, and severe cortical sensory loss in his left hand. The right carotid bruit had disappeared. A right carotid arteriogram revealed occlusion of the internal carotid artery 1 centimeter above the origin. Emergency endarterectomy was performed by opening the artery along one edge of the Teflon patch and removing a recurrent atherosclerotic plaque from the patch and vessel wall as well as recent and organized mural thrombus. A postoperative arteriogram 24 days later showed a widely patent right internal carotid artery. Thirty-two days after operation the patient died of a myocardial infarction.

Postmortem examination showed a patent right carotid artery with thick neointima overlying the surgically thinned media (fig. 5 in ref. 1). Marked atherosclerosis of the aorta was noted and severe coronary atherosclerosis with occlusion of the left circumflex artery found.

Comment: During 11 years with evidence of active atherosclerotic disease of the carotid and aortoiliac systems, this patient’s cholesterol, blood sugar, and electrocardiograms were normal on repeated measurements. Moderate hypertension was recorded 5 years prior to death but was not treated. Although hypertension was this patient’s only known risk factor he suffered recurrent atherosclerotic occlusive disease of the right internal carotid artery 11 years after endarterectomy and Teflon patch graft. He also had symptomatic peripheral atherosclerotic occlusive disease.

Discussion

The recurrence of occlusive disease is well documented after vascular operations throughout the human arterial system except for the carotid artery after endarterectomy. Mundth and Austen6 reviewed the literature concerning progressive fibrous intimal hyperplasia in venous aorto-coronary bypass grafts as a cause of late graft failure. Lixfeld et al.4 reported typical atheromatous deposits in the hyperplastic intima of a human aortocoronary vein bypass graft 4 years after insertion. Szilagyi et al.5 listed recurrence of atheroma in endarterectomized segments of aorta, iliac, and femoral arteries as one cause of late failure in reconstructive arterial surgery. Beebe et al.6 is only one of several authors to report typical atheromatous deposits developing in the hyperplastic intima of a femoropopliteal autogenous vein bypass graft 6 years after insertion in a patient with hypercholesterolemia. DeBlakey et al.7 noted an atherosclerotic plaque in the neointima lining an abdominal aortic Dacron prosthesis 5 years after insertion.

Several animal models develop typical atheroma or lesions believed to be a precursor of atheroma. Hypercholesterolemic dogs develop atheroma within the hyperplastic intima of autogenous vein grafts inserted into the aorta or iliofemoral arterial systems and to a lesser degree in the neointima of the Dacron prostheses.8 Atheroma develops at an accelerated rate at the site of aortic endarterectomy in hyperlipemic dogs9 and rabbits10 and at the site of balloon-induced arterial endothelial injury in hypercholesterolemic swine.11 There are normolipemic animal models12,13 which develop possible precursor lesions for the “complicated lesion”13 of typical atheroma (hemorrhage, calcification, cell necrosis, mural thrombus). Prathap12 produced “hard plaques” in the femoral arteries of normocholesterolemic monkeys by transfixing the artery with a catgut suture to produce platelet rich non-occlusive thrombi. Nam et al.14 found that balloon-induced arterial endothelial injury in normocholesterolemic swine produced lesions similar to the “fibromusculoelastic lesion of the intima.”15

Despite this rich background of human and animal evidence for development of occlusive disease in vein grafts, arterial prostheses, and endarterectomized arterial segments there is relatively little on the extracranial carotid artery after endarterectomy. In fact, the English language literature mentions 31 cases of recurrent disease at the site of previous carotid endarterectomy1.16-29 and this report adds 2 additional cases for a total of 33. Thirty-one patients had recurrent disease sufficient to cause re-stenosis of the arterial lumen and 20 of these cases were symptomatic. Two patients had asymptomatic non-stenotic recurrences in the neointimal layer discovered at postmortem examination.

FIGURE 6. (Case 4). Specimen removed at second endarterectomy. The white tissue (black arrow) is the plane of cleavage in the neointima and the open arrow indicates the thrombus adherent to the recurrent neointimal atheroma.
TABLE 1  Recurrent Disease at Site of Carotid Endarterectomy

<table>
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<tr>
<th>Case</th>
<th>5 BP</th>
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<th>PVD (Antemortem)</th>
<th>Postoperative anticoagulation</th>
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ASHD = arteriosclerotic heart disease; PVD = peripheral vascular disease.

Site of Recurrent Disease

A new intimal layer completely covers the endarterectomy site within 30 days after operation with further thickening and maturation as time passes.\textsuperscript{1} A truly recurrent lesion must develop within this neointimal layer in the distal common and proximal internal carotid artery. Thirteen patients had truly recurrent stenosis suggested by serial arteriography in 4 patients (Case 3),\textsuperscript{1,14,18} postmortem examination in 3 (Case 2),\textsuperscript{1,16} or stated to be at the origin in 6 (Case 4).\textsuperscript{20,21,27,28} Technical factors contributed to recurrent stenosis in 8 patients suggested by the location of the stenosis at the distal extent of the endarterectomy in 5,\textsuperscript{14,17,19} the proximal extent of the endarterectomy in 2,\textsuperscript{16} and at the site of a carotid clamp in 1.\textsuperscript{26}

In 12 patients the site of re-stenosis was not indicated by the author.\textsuperscript{14,18,20-25}

Pathology of Recurrent Disease

In only 14 of the 33 patients reported have there been comments upon the pathology of the recurrent lesion. Seven patients had atherosclerotic disease varying from early to chronic determined by pathological examination of the surgical specimen in 4 patients (Case 4),\textsuperscript{1,17} or at postmortem examination in 3 patients (Case 1, Case 2).\textsuperscript{1,14} Edwards et al.\textsuperscript{16} found 3 patients with symptomatic recurrent stenoses to have "a tough, thick, fibrous lining." A vein patch was placed to enlarge the lumen since this tissue was without a cleavage plane and difficult to remove in 2 patients and was not removed in a third. A picture of the microscopic specimen appears to be a thick layer of neointima without evidence of atheromatous change. The arteriograms in 2 of these patients showed the re-stenosis at the common carotid-internal carotid bifurcation, presumably at the lower end of the endarterectomy site. Four patients were stated to have atheroma\textsuperscript{16,19} or a plaque\textsuperscript{29,29} but no pathological details were provided. Twenty patients had no pathological diagnosis related by the authors.

Experimental animal models show a correlation between the pathology of the lesion after intimal or endothelial damage and the level of the serum lipids. Hyperlipemic dogs,\textsuperscript{6-8} rabbits,\textsuperscript{19} or swine,\textsuperscript{11} form typical atheroma in various stages of development. However, the normolipemic monkey\textsuperscript{22} and swine\textsuperscript{11} models develop hard plaques containing little or no lipid. This correlation certainly does not fit the human situation as shown in table 1. All 5 patients had atheroma in various stages of development and yet only one patient (Case 3) had a mildly elevated serum cholesterol as well as hypertension and diabetes. Patients 2, 4 and 5 had chronic atheroma and normal lipid levels. In particular, patient 4 had recurrent atheroma at the carotid endarterec-

![Figure 7](http://stroke.ahajournals.org/)

A left carotid arteriogram shows irregularity of the internal carotid artery origin presumed to be the source of cerebral emboli.
be controlled but our patients suggest that control of risk factors is not the entire answer in the prevention of recurrent carotid occlusive disease.

There is experimental evidence that heparin and dextran can retard the development of atheroma in hypercholesterolemic dogs after aortic endarterectomy by means of a combination of altered coagulation and a mild decrease in serum cholesterol. Four of our 5 patients had oral anticoagulation at the time of surgery continued for up to 6 months postoperatively (table 1) but they still developed recurrent atheroma. Two other patients cited in the literature received prophylactic oral anticoagulation postoperatively and later had evidence of recurrent atheroma.

Schutz et al. demonstrated that irregularities seen on early postoperative arteriograms tended to disappear as time passed indicating a progressive restructuring of the neointimal layer. The general belief that a patent endarterectomy segment is permanent is supported by the few reports of recurrent stenosis. However, the true incidence of the phenomenon is difficult to determine as only symptoms or routine postoperative angiography will detect a re-stenosis. Sixteen instances of recurrent stenosis (12 symptomatic, 3 asymptomatic, 1 not stated) have been reported by authors performing a total of at least 2,827 endarterectomies in 2,417 patients for an incidence of 0.6%. This
figure probably would be increased if there were detailed long-term follow-up of operated patients and exclusion of patients with early postoperative thrombosis.

Twenty symptomatic patients have been mentioned in the literature and the time from first operation to recurrent symptoms is given for 18 (table 2). The shortest respite from symptoms is our third patient (figs. 2, 3, 4) who developed recurrent stenosis 16 months after surgery and the longest to date is our fifth patient who developed occlusive thrombus superimposed upon recurrent chronic atheroma 11 years after surgery. Table 2 indicates that recurrent symptoms developed in 44% by 3 years, 67% by 5 years, and 83% by 7 years. Those patients believed to have technical factors contributing to re-stenosis did not develop recurrent symptoms earlier than other patients but spanned 2, 3, 4, 4½, 5, and 6 years.

Seventeen of the 20 symptomatic patients had operation to correct the recurrent stenosis. Nine patients had repeat endarterectomy (Case 4), 1, 3, 10, 14, 21, 6 had a vein patch to enlarge the lumen, 1, 4, 15 had an arterial homograft (subsequently demonstrated to have thrombosed) and 1 was not described. Six of the operated patients were reported to be well but 2 patients in our series died postoperatively.

Technical Factors Contributing to Re-stenosis

The neointima incorporates irregularities of the endarterectomy site and, with time, the neointima thickens as shown on pathological examination and as suggested by serial arteriography. Therefore, any stenosis of the lumen produced at the time of surgery by vascular clamps, by intimal or medial tags, by suturing faults which stenose the upper (figs. 7, 8) or lower end of the arteriotomy or by failure to remove the distal tongue of plaque (fig. 9) may predispose to progressive stenosis. The neointima gradually thickens over any excrescence of the wall and factors of turbulent flow, etc., may produce a greater response-to-injury on the part of the neointima and encourage further hyperplasia and stenosis. Javid et al. and Julian et al. recognized the necessity of complete removal of the distal extent of the plaque and attribute their 3 instances of distal re-stenosis to incomplete removal.

Technical errors in endarterectomy may be more common than generally believed as suggested by Blaisdell et al. who found 25% of 100 carotid endarterectomies in need of immediate revision at the time of intraoperative arteriography. The recently described technique of carotid artery endoscopy may be applicable to the intraoperative assessment of the arterial lumen prior to complete closure of the arteriotomy.

Two recent patients illustrate the two problems of the distal end of the endarterectomy site. One demonstrates a iatrogenic stenosis at the distal extent of the arteriotomy likely due to suture technique (figs. 7, 8). The other shows residual plaque at the distal end (fig. 9). If these patients had repeat arteriography years later, these early surgical errors plus neointimal thickening could falsely present a picture of "distal recurrent occlusive disease."

Conclusion

The endarterectomy site is not a static segment in a "reamed-out pipe." It is a dynamic area of regenerating tissue fully capable of re-forming the disease just eradicated. The patient's risk factors for the development of atherosclerotic disease should be controlled but such treatment will not totally solve the problem of recurrent stenosis. Prophylactic anticoagulation has not prevented recurrent atheroma in the few patients reported. Careful surgical technique is necessary to remove the distal tongue of plaque and to close the arteriotomy. The incidence of re-stenosis can be estimated at 0.6% from the existing literature, but this figure is unrealistically low. The fact that 33% of the reported symptomatic re-stenoses occurred later than 5 years after operation indicates that prolonged follow up by the operating surgeon will be necessary to detect many cases. Asymptomatic re-stenosis and occlusions will rarely be detected clinically unless postoperative arteriography or noninvasive techniques to assess patency and flow are routinely performed.

![Figure 9. Carotid endarterectomy specimen obtained 1 hour after operation and death from myocardial infarction. At the distal end of the arteriotomy (black arrow) in the internal carotid artery is a thick residual fibromuscular plaque (open arrow). Gomori stain, X 17.](image-url)
Recurrent occlusive disease at the site of carotid endarterectomy does occur but the incidence as judged from the existing literature appears to be acceptably low. In the vast majority of patients, carotid endarterectomy should provide a satisfactorily patent artery for the remainder of that individual's life.

References

Recurrent stenosis at site of carotid endarterectomy.
B N French and N B Rewcastle

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