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Correlation of Intra-operative Duplex Findings During Carotid Endarterectomy with Neurological Events and Recurrent Stenosis at one Year*

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Objectives: *carotid endarterectomy has been used to treat both asymptomatic and symptomatic disease and this has meant that recurrent stenosis and its effect on late stroke risk have become increasingly important. In this study we compared anatomical defects and residual stenosis identified intra-operatively with recurrent stenosis and new symptoms developing in the first year after surgery.*
Design, Materials & Methods: *two hundred and forty-four consecutive patients undergoing carotid endarterectomy were studied prospectively. Residual anatomical defects were noted; residual stenosis was defined by intra-operative duplex ultrasound as >50%. New stenoses and clinical events during the one-year surveillance period were documented.*
Results: *there was an increased incidence of recurrent stenosis at one year in vessels with residual stenoses ($p < 0.001$) and in vessels containing a residual anatomical defect ($p = 0.037$). There was no significant difference in recurrent stenosis rate with respect to closure (primary or patch) or seniority of surgeon but recurrent stenosis was increased in females ($p = 0.026$). The majority (70%) of restenotic lesions were localised to the origin of the internal carotid artery. The late stroke rate was 0.9% and was not related to recurrent stenosis or symptoms.*
Conclusions: *residual stenosis and intra-luminal defects at completion increase the recurrent stenosis rate at one year. The aetiology of recurrent stenosis is multi-factorial and further studies are required to determine whether it is justified to modify the criteria for re-exploration with a view to reducing recurrent stenosis.*

Key Words: Carotid endarterectomy; Carotid artery stenosis; Duplex.

Introduction

It is generally accepted that carotid endarterectomy can be performed safely and with a low incidence of peri-operative stroke and death.[1,2] This has been achieved in part by the use of completion imaging techniques that ensure a technically precise repair and thus reduce the incidence of carotid thrombosis.[3–6] Carotid endarterectomy is becoming used more widely for treatment of both asymptomatic and symptomatic disease and this has meant that recurrent stenosis and its effect on late stroke risk have become increasingly important.[7] It has been suggested that residual intra-luminal defects, associated with flow abnormalities, have the potential to stimulate myointimal hyperplasia and to produce significant recurrent stenosis.[8,9] However, many of these residual lesions undergo regression and therefore the significance of residual defects and recurrent stenosis remains controversial.

The purpose of this study, which involved carotid surveillance with duplex, was to determine whether anatomical and/or haemodynamic factors identified at completion imaging were responsible for rapid recurrent stenosis and/or new symptoms developing in the first year after surgery.

Methods

Between June 1995 and May 2000, 244 consecutive patients (mean age 66 years; range 41–85; 157 male, 87 female) were entered prospectively into this study. There were 65 asymptomatic patients. Associated risk factors in the study group were cardiac (51), renal (10),

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hyperlipidaemia (117), diabetes (31), hypertension (161), gout (18) and smoking (201). Two hundred and twenty carotid endarterectomies were performed under general anaesthesia and the remaining 24 under local anaesthesia. An intra-luminal shunt was used selectively in 76 patients. The arteriotomy was closed primarily in 207 patients and with a synthetic patch in 37 cases. One hundred and forty-five procedures were performed by the consultant and the remaining 99 were performed by trainees under supervision.

Intra-operative duplex was carried out using a small footprint transducer (CL10-5 MHz, Philips, U.K.) placed in a sterile sheath containing acoustic gel and coupled directly to the vessel with the aid of saline. B-mode images and blood velocity spectra along the length of the endarterectomy were recorded to hard disc for subsequent analysis. The results of completion imaging were used to determine residual stenosis, which was defined as a $>50\%$ stenosis persisting immediately after carotid endarterectomy in the completion duplex scan. All duplex investigations were performed by the same operator using validated duplex criteria to grade carotid stenosis.[5] Any residual anatomical abnormalities left in the internal carotid artery (ICA) were classified as one of the following; an intimal shelf, intimal flap, a vessel kink, diffuse intimal irregularity or vasospasm.[6]

Duplex imaging was performed at 6 weeks, 6 months and 1 year post-operatively and the results were used to determine late recurrent stenosis occurring within the first year after surgery. The ultrasound operator was blinded to the intra-operative and previous duplex scans at successive duplex assessments. Changes from the completion findings were used to identify whether any lesions had undergone remodelling or were new stenoses. The location of the recurrent stenotic lesion in the internal carotid artery was also classified as proximal (at the origin of the internal carotid artery), entire (extending along the length of the endarterectomy) or at the distal extent of the endarterectomy.

New clinical events during this one-year surveillance period were documented, as were deaths and their causes. The relationship between arteriotomy closure (primary or patch), gender, grade of surgeon (consultant or trainee) and the incidence of recurrent stenosis were also investigated.

Statistical analysis was performed using Chi-squared analysis and Fisher's exact test to compare differences in disease progression between the patient groups with stenoses of less than and greater than 50% at one year. Multivariate analysis was performed to determine independent associations of factors with recurrent stenosis, controlling for potential predictors.

Results

Intra-operative (30 day) results

The incidence of neurological deficit occurring in the peri-operative period was 2%, comprising two strokes and three transient ischaemic attacks. There were three deaths, two were due to myocardial infarction and one of these was associated with a stroke. The third patient died 5 days post-operatively due to mesenteric ischaemia. The overall 30-day stroke rate was 0.8% and the 30-day stroke and death rate was 1.6%.

Intra-operatively 52 residual stenoses were identified. The criteria for immediate correction of residual lesions were a severe stenosis of $>70\%$ in the distal ICA associated with an intimal flap. There were nine such lesions that were re-explored, corrected and patched. There were nine further severe stenoses that were not associated with an intimal flap and were not corrected. There were no internal carotid thromboses. The final residual stenosis rate for all lesions was 17.6% (43/244) and the severe ($>70\%$) residual stenosis rate was 3.7% (9/244).

There were 16 stenoses in the distal CCA at the proximal endarterectomy site and all were due to a residual atheromatous shelf. One stenosis was severe ($>70\%$) but none of the lesions were corrected. The presence of an intra-operative defect was not significantly associated with either peri-operative stroke (chi squared $=0.43$, $p=0.51$) or peri-operative neurological events (chi squared $=0$, $p=1$).

One year results

During the follow-up period beyond 30 days, 16 patients died and 12 were lost to follow-up. The cause of death was ipsilateral stroke in two patients that occurred at 2 and 5 months respectively. One of these strokes had a residual 70% stenosis associated with a kink that was not corrected and there were no further follow-up scans. The second stroke had normal duplex scans at completion and at 6-week follow-up. In the remaining 14 patients death was due to; acute myocardial infarction (8), cancer (3), a ruptured aortic aneurysm in (1), hypoplastic anaemia and general debility (1) and sepsis secondary to pneumonia (1). There were no other neurological events in the one-year follow-up period.

The late stroke rate was 0.87% (2/229) and the late stroke and death rate was 7.0% (16/229). Duplex surveillance at one year was available in 213 patients as 19 had died and 12 were lost to follow-up.

Recurrent stenosis

The presence of a residual ICA stenosis at completion in the 213 patients was correlated with one-year duplex results. A residual stenosis was detected in 41 patients but persisted in only 21 (51%) of these, 20 lesions had reduced to less significant disease due to remodelling. Conversely in the 172 patients without residual stenosis at completion, 39 (23%) developed new recurrent stenoses. The difference in recurrent stenosis rate between these two groups was significant (51% vs 23%; $p < 0.0001$, Table 1; Fig. 1).

Table 1. Correlation between residual stenosis, anatomical defects and recurrent stenosis at one year.

Completion duplex	*n*	Recurrent stenosis		
		>50%	χ^2	*p*
Residual stenosis > 50%	41	21 (51%)	13.33	< 0.0001
Residual stenosis < 50%	172	39 (23%)		
No defect	106	23 (22%)	4.37	0.037
Intra-luminal defect	107	37 (35%)		

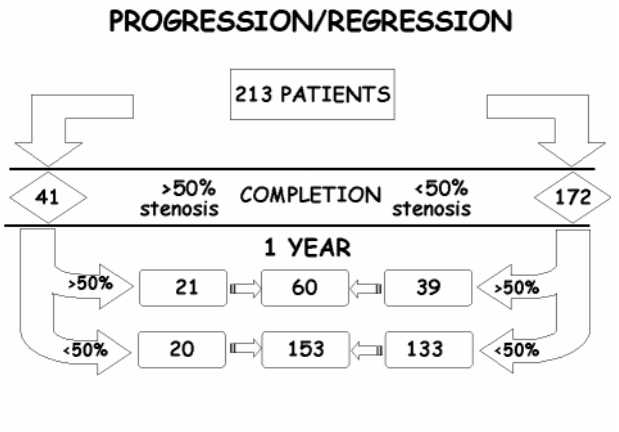

Fig. 1. Flow diagram illustrating progression and regression of carotid disease at one year.

There were nine residual severe ICA stenoses noted intra-operatively. All lesions showed some degree of regression. Two stenoses regressed to non-significant levels (<50%) and these were noted to have either vasospasm or a residual shelf on completion imaging. The remaining seven lesions regressed to moderate stenoses (50–65%). The anatomical defects noted at completion in these stenoses were; a kink in four cases, diffuse irregularity in two and vasospasm in one. None of the vessels scanned showed ICA thrombosis at one year.

At one year data were available on 15 of the 16 stenoses in the distal CCA (one patient had died). Stenoses persisted in only five vessels at one year but there were seven new CCA stenoses in vessels that had shown no stenosis intra-operatively. All stenoses were moderate (50–60%) and the one severe stenosis detected intra-operatively had resolved to non-significant levels (<50%).

Recurrent stenosis occurred in three distinct patterns in the 60 vessels. Forty-two (70%) lesions were localised to the origin of the internal carotid artery, five along the whole length of the endarterectomised segment and 13 were at the distal end of the endarterectomy (Fig. 2). Two of these 13 distal restenoses were

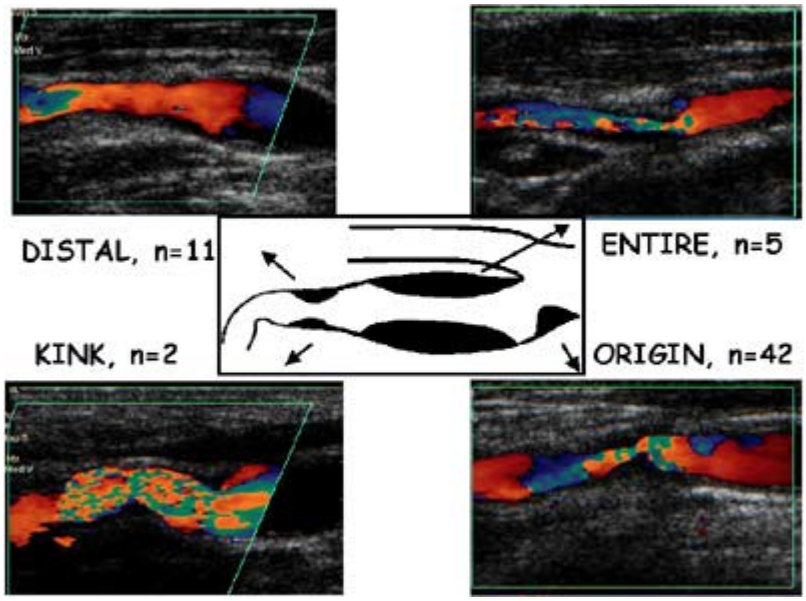

Fig. 2. The distribution of recurrent stenosis with respect to the carotid bifurcation.

associated with vessel kinking. The correlation between the type of intra-operative defect and location of recurrent stenosis is shown in Table 2. The numbers were insufficient for statistical analysis but did not indicate any relationship between the type of defect and the location of recurrent stenosis.

Anatomical defects

Half of the 213 vessels studied showed some defect at completion imaging. Correlation with one-year duplex findings showed that 35% of patients with intra-operative defects had recurrent stenosis compared to 21% of the vessels in vessels without defects. This difference was significant ($p = 0.037$, Table 1).

Table 3 summarises the individual defects and associated one-year stenosis. The results show that residual defects were not important in recurrent stenosis unless they were associated with a significant haemodynamic stenosis.

Table 2. Location of the 60 recurrent stenoses and their association with residual defects detected at completion imaging.

Completion finding	*n*	Site of stenosis			Recurrent stenosis at defect (%)
		Origin	Entire	Distal	
Normal	23	18	2	3	13
Shelf	3	1	0	2	67
Flap	7	5	2	0	0
Irregularity	13	9	1	3	23
Kink	13	8	0	5	38
Spasm	1	1	0	0	0

Table 3. Correlation between the 107 residual intra-luminal defects and recurrent stenosis at one-year.

Completion finding	*n*	Recurrent stenosis >50%	χ^2	*p*
Shelf	10	3 (30%)	0	1
Flap	21	7 (33%)	0.31	0.579
Irregularity	33	13 (39%)	2.43	0.119
Kink	40	13 (33%)	0.46	0.499
Spasm	3	1 (33%)	0	1

Table 4. Association between risk factors and recurrent stenosis at one-year.

Risk factor	Incidence of >50% recurrent stenosis	χ^2	*p*
Primary	29% (53/180)	0.93	0.334
Patch	21% (7/33)		
Male	23% (31/135)	4.94	0.026
Female	37% (29/78)		
Consultant	28% (35/125)	0	1
Trainee	32% (25/88)		

Other risk factors

Three other risk factors that have been implicated in recurrent stenosis were evaluated; the type of arteriotomy closure, gender and grade of surgeon. Univariate analysis demonstrated a significant increase in recurrent stenosis rate in females ($p = 0.026$; Table 4) but no significant difference in recurrent stenosis rate with respect to primary or patch closure or seniority of surgeon. Controlling for gender, did not reveal any significant associations between any of the other risk factors investigated and recurrent stenosis. Multivariate analysis did not demonstrate any independent associations between risk factors and recurrent stenosis at one year.

Discussion

The use of intra-operative duplex ultrasound to detect and correct residual, severe stenosis was associated with a low incidence of peri-operative stroke and no internal carotid thromboses from this series. During the one-year surveillance period, recurrent stenosis (defined as >50%) was comparatively high at over 20% but many studies define recurrent stenosis as >75% and the recurrent stenosis rate using this definition was 4.7% which was similar to that (1.4–8%) reported by other investigators.[10–12] In spite of an increased incidence of recurrent stenosis in patients with technically imperfect repairs, there was no increase in the incidence of late stroke or internal carotid thrombosis, suggesting that these lesions are relatively benign at early follow-up. Some residual stenoses had regressed to non-significant levels at one year. It is possible that some of this remodelling may be due to the variability in duplex estimates; because the accuracy of duplex estimation of stenosis has not been determined for duplex data obtained under general anaesthetic conditions.

Lesions that occur within one year after carotid endarterectomy are firm and homogeneous on gross pathological inspection and are related to intimal hyperplasia. However, lesions occurring more than two years post-operatively are generally due to atherogenesis although some report that true atherosclerosis may not occur until after 5 years.[13] Thus it has been suggested that surveillance is of questionable

value until after a period of at least two years following surgery.[14,15] Some reports however, suggest that severe (>75%) restenotic lesions are responsible for half of late ipsilateral strokes and so advocate prophylactic reintervention.[16–20]

The pattern of restenoses observed in this study suggests that residual technical defects are not always the focus for restenotic lesions. The majority of restenoses occurred in the proximal internal carotid artery and not at the distal extent of the endarterectomy where technical defects tended to be localised. It is recognised that the carotid bulb is a focus for disease because of its geometry coupled with pulsatile flow that produce boundary layer separation and low shear rates which in turn promote atherosclerosis in the sinus region opposite to the flow divider.[21] Hence the majority of these restenotic lesions were not linked to residual technical defect but may be linked to other risk factors. It has been suggested that patching reduces the significance of intimal hyperplasia because of the increase in vessel calibre and that female gender is associated with an increased rate of recurrent stenosis.[7,22,23] In this series we demonstrated an increase in recurrent stenosis in females but no significant decrease in vessels that were patched. The latter may be due to the small number of patients who were selectively patched in this series, providing insufficient numbers to reach statistical significance.

While the role of completion duplex in achieving a low peri-operative morbidity has been reported, criteria for re-intervention have not considered the association with recurrent stenosis. This study suggests that residual stenosis and intra-luminal defects at completion increase the recurrent stenosis rate at one-year, however, the aetiology of recurrent stenosis is multi-factorial. Further studies are required to determine whether it is justified to modify the criteria for immediate re-exploration with a view to reducing recurrent stenosis.

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