Complications of cerebral angiography in patients with symptomatic carotid territory ischaemia screened by carotid ultrasound

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Abstract

After nearly 40 years, carotid endarterectomy has been shown to be of benefit to patients with symptomatic carotid territory ischaemia and greater than 70% stenosis of the relevant internal carotid artery. Cerebral angiography is performed before surgery and is not without risk. These risks must be added to those of surgery before recommending the procedure to patients. The study evaluated the local, systemic and neurological complications following digital subtraction angiography with selective catheterisation of the carotid arteries in 200 patients presenting to a cerebrovascular clinic for assessment of cerebral ischaemia. All patients had carotid ultrasound screening before angiography to screen out those with normal arteries or mild disease (less than 30% stenosis of symptomatic internal carotid artery). Complications occurred in 28 patients. There were six (3%) local, two (1%) systemic and 20 (10%) neurological complications. Seventeen neurological complications occurred within 24 hours and there were three late complications (24-72 hours). Neurological complications occurred more frequently when angiography was performed by a trainee rather than a consultant neuroradiologist ($p < 0.01$). The neurological complications were transient (resolved within 24 hours) in 10/200 (5%), reversible (resolved within seven days) in two (1%) and permanent in 8/200 (4%). Two patients died after a stroke and two other patients suffered a disabling stroke. At 24 hours post angiography the permanent (persisting beyond seven days) neurological complication rate was 2.5%. The incidence of total neurological complications and post angiographic strokes was higher in patients with greater than 90% stenosis of the symptomatic internal carotid artery ($p < 0.001$). The increased use of non-invasive Doppler duplex screening will reduce the absolute number of patients put at risk of angiography, yet the rate of post angiographic complications is likely to increase as patients with severe stenosis of the symptomatic internal carotid artery are probably most at risk of complications and have most to gain from carotid endarterectomy.

Although carotid endarterectomy has been performed since 1954¹ its value in the prevention of stroke has been unproven. Recently two large studies, the North American Symptomatic Carotid Endarterectomy Trial (NASCET)² and the European Carotid Surgery Trial (ECST)³ have been published which show the benefit of surgery in patients with symptomatic carotid territory ischaemia and greater than 70% stenosis of the relevant internal carotid artery (ICA). In both studies carotid endarterectomy reduced the risk of major or fatal ipsilateral stroke by 80% over the following two to three years. The perioperative risk of severe stroke or death was 3.7% (3) and 2.1% (2). Conversely, the European trial³ reported that in patients with mild (0-29%) stenosis of ICA the perioperative stroke and death rate outweighed the benefit of surgery.

In most centres cerebral angiography is performed before carotid endarterectomy to delineate the extent of the disease, but this is not without hazard.⁴ There is a large variation in the published morbidity rates following cerebral angiography ranging from 0-28% due to differences in study design, patient population and definition of complications.⁵⁻⁸ Hankey *et al*⁹ published an overview of twenty one cerebral angiography studies performed in patients with ischaemic cerebrovascular disease. The overall risk of a neurological complication was about 4% (stroke or TIA), the risk of a permanent neurological deficit about 1% and mortality was low at less than 0.1%. Neither the NASCET nor the ECST studies could take account of the risks of cerebral angiography before surgery.^{2,3} To reduce the potential risks of cerebral angiography patients must be appropriately selected, have had a recent carotid territory ischaemic event and be willing to consider carotid endarterectomy. It is important that angiography is not performed unnecessarily in patients with normal or mild (0-29%) stenosis of the ICAs.

Ultrasound examination of the extracranial vessels, using B mode imaging and Doppler flow studies is non invasive, safe and the most cost effective way of screening patients before angiography.¹⁰ B mode imaging is most sensitive in detecting mild to moderate disease,¹¹⁻¹³ while Doppler studies are more reliable in detecting stenoses greater than 50%.¹²⁻¹⁴ The combination of continuous wave Doppler and B mode ultrasound imaging improves the detection of significant stenosis (>50%) with a sensitivity of 90% and specificity of

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93%,¹²⁻¹⁵ although it is unreliable in the diagnosis of occlusion.¹²⁻¹³ It is therefore recommended that all patients with features of occlusion should have angiography, as their management will be radically altered by the finding of a tight stenosis.¹⁶

The aim of this study was to delineate prospectively the post-angiographic complication rate in patients with recent non-disabling carotid territory ischaemic events and greater than 30% stenosis of the symptomatic ICA who will now be considered for endarterectomy. This is the first study to examine the complication rate of cerebral angiography in patients with symptomatic carotid territory ischaemia in which ultrasound has been used to exclude patients with normal ICAs or mild atheroma. With the increased use of ultrasound screening and endarterectomy for carotid disease, clinicians will need to know the angiographic complication rate in this group of patients to enable the doctor and patient to decide if they wish to proceed with angiography and endarterectomy.

Methods

All patients had Doppler duplex scanning (Kranzbuhler Doppler 761, 4 MHz and 8 MHz transducers, Diasonics CV 400, 10 MHz transducer) of both carotid arteries before cerebral angiography. Angiography was performed to assess a potentially resectable vascular lesion within the extra cranial vessels. Patients only proceeded to angiography if they were considered fit for carotid artery surgery. All patients were screened for possible vascular risk factors; smoking, hypertension, ischaemic heart disease and hypercholesterolaemia. All patients had a full neurological assessment before angiography, some of the patient information was collected retrospectively in 18 patients. All other data were collected prospectively.

Angiography was performed by a consultant neuroradiologist or senior registrar with consultant supervision. Digital subtraction angiography was performed by selective catheterisation, usually of both carotid arteries (using Mani and pigtail catheters), via a femoral puncture except in one patient where a brachial approach was used. All angiography was performed under local anaesthesia, with Niopam 300 or Ultravist 300 non-ionic contrast. The volume of contrast used varied between 40 and 75 mls. The extent of disease demonstrated on angiography was classified as mild (<30% stenosis), moderate (30-69% stenosis), severe (70-99% stenosis) or complete occlusion of the vessel. Each patient was classified according to the lesion in the symptomatic vessel whether there was disease present in the contralateral vessel or not. The patients were observed during and immediately after angiography by the radiologist. A neurologist completed a neurological assessment on return to the ward and before discharge.

Local, systemic, neurological complica-

tions and deaths were recorded. A neurological complication was defined as any neurological symptom or sign occurring during the procedure or in the subsequent 72 hours, whether it was considered to be a manifestation of the primary disease or not. All neurological complications of angiography were recorded and classified according to their duration as transient, reversible and permanent.

The number of patients undergoing angiography, rather than the number of vessels imaged was used as the denominator for expressing the frequency of complications.

DEFINITIONS

Transient ischaemic attack (TIA)—an acute loss of focal cerebral or ocular function with symptoms lasting less than 24 hours which after adequate investigation is presumed to be caused by embolic or thrombotic vascular disease.¹⁷

Stroke—rapidly developing signs of local (or global) disturbance of cerebral function with symptoms lasting 24 hours or longer, or leading to death, with no other apparent cause than vascular origin.¹⁸

Retinal infarct—an acute painless and persistent for more than 24 hours monocular loss of visual acuity or visual field with ophthalmoscopic findings of pallor of all or a section of the posterior pole of the retina.

Hypertension—Diastolic blood pressure (phase V) >100 mmHg and/or known treated hypertension.

Ischaemic heart disease (IHD)—ischaemic changes on ECG, documented previous myocardial infarction, positive stress (exercise) test or previous coronary artery bypass surgery.

Hypercholesterolaemia—fasting plasma cholesterol >5.8 mmol/l and/or known treated hypercholesterolaemia.

PATIENTS

A total of 205 consecutive patients with symptomatic carotid territory ischaemia admitted for cerebral angiography following Doppler duplex scanning were studied between August 1989 and February 1992. One patient sustained a myocardial infarct before angiography and four angiograms failed for technical reasons and had to be abandoned. These five patients are excluded from the analysis.

The presenting diagnoses were TIA of the brain 62 (31%), amaurosis fugax 57 (29%), retinal infarction 11 (5%), non disabling stroke 56 (28%), and non disabling stroke preceded by TIA of the brain or eye 11 (5%). Three patients (2%) were assessed for pulsatile tinnitus or possible vertebro-basilar TIAs associated with subclavian steal syndrome. Up to January 1991 all patients were randomised for surgery on the basis of angiography as part of the ECST study.

Statistical analysis on categorical data was performed using Chi square or Fisher's Exact tests as appropriate. A confidence interval of 95% was chosen.

Table Post angiographic neurological complication rate (0–72 hours)

Diagnosis	Pts	Transient number (%)	Reversible number (%)	Permanent <24 hours (%)	24–72 hours (%)
TIA (brain and eye)	119	9 (8)	2 (2)	4 (3)	0
Stroke	67	1 (1)	0	1 (1)	3 (4)
Total	186	10 (5)	2 (1)	5 (3)	3 (2)

TIA—Transient ischaemic attack

Results

Cerebral angiograms were performed in 200 patients, imaging 379 vessels. Twenty one patients had the single symptomatic vessel imaged. Angiography was performed by a consultant radiologist in 85%. The median age of the patients was 61 (range 25–79) years with a male predominance (64%). Risk factors for vascular disease were present: smoking 121 (61%), hypertension 77 (39%), IHD 62 (31%) and hypercholesterolaemia 112 (56%).

Thirty one (16%) patients had complete occlusion of the ICA and one patient occlusion of the common carotid artery. Severe stenosis (70–99%) was present in 90 (45%), moderate (30–69%) stenosis in 50 (25%) and mild (<30%) stenosis in 22 (11%). Dissection of the ICA was demonstrated in four (2%) patients, one had carotid syphon disease, and one angiogram proved to be normal.

Carotid endarterectomy was subsequently carried out in 95 patients. Seventy of 90 patients (78%) with severe stenosis and 23 of 50 (46%) with moderate stenosis had surgery. At the beginning of the study patients were randomised to surgery as part of the ECST, therefore 20 patients with severe stenosis had medical treatment only and one patient with mild stenosis had a carotid endarterectomy. One patient with an occlusion of the left ICA and subclavian steal was referred for surgery.

Complications occurred in 28 patients. There were six local complications, two systemic and 20 (10%) neurological. Local complications occurred in six patients; five sustained large haematomas in the groin and thigh sufficient to delay hospital discharge, one patient developed pain and “heaviness” of the leg but without neurological signs. General complications occurred in two patients; one developed persistent vomiting for eight hours following the angiogram, the other developed a severe frontal headache and vomiting for 24 hours. Neither patient had neurological symptoms or signs.

Neurological complications occurred in twenty (10%, 95% confidence interval (CI) 6–14.0) patients. Seventeen patients (table) developed complications within 24 hours of the procedure. Three patients developed complications after 24 hours but within 72 hours (table). The neurological complication was a TIA in ten patients, seven occurring within 24 hours. All TIAs occurred within six hours of angiography. In six of the 10 patients the TIA was compatible with the lesion detected at angiography (was in the territory

of the affected vessel) and in seven there was severe stenosis of the symptomatic ICA. Seven patients sustained an early (<24 hours) post-angiographic stroke of which one died, in two the neurological deficit resolved in two and five days respectively, two others suffered disabling strokes, the remaining two patients recovered fully. Three patients with late onset strokes had permanent neurological deficits, one of these died, the other two had non-disabling strokes. The time of onset of the stroke varied between during the angiogram and up to 60 hours after. Nine of the ten patients had severe stenosis of the ICA. The patients who sustained a neurological complication were similar to the group as a whole, with a median age of 60 years and a male predominance (70%). The prevalence of vascular risk factors was not significantly different from the remainder of the group.

The rate of post angiographic stroke was not significantly different between those presenting with TIA of the brain or eye and stroke (table). Neurological complications occurred in 7/20 (35%) patients whose angiogram was performed by a senior registrar, compared with 13/116 (11%) performed by a consultant neuroradiologist (Fisher's exact; $p < 0.01$, odds ratio (OR) = 4.25, 95% CI of OR: 1.3–14.3). Three of the twenty patients sustaining a neurological complication had persistent neurological deficits following the presenting episode at the time of angiography. None of the remaining 180, who did not sustain a neurological complication had persistent deficits (Chi square (Yates corrected) = 18.2, OR = 72, 95% CI of OR = 4.2–317, $p < 0.001$).

The degree of vessel stenosis influenced the development of neurological complications. These occurred in two patients with mild (<30%) stenosis (both transient), two patients with moderate (60–70%) stenosis (one transient, one permanent) and 16 with severe (70–99%) stenosis (seven transient, two reversible and seven permanent). In particular in patients with greater than 90% stenosis the incidence of post angiographic complications was significantly higher. Twelve of the twenty patients (60%) suffering a post angiographic neurological complication had stenosis greater than 90% compared with 18 of the 180 patients (10%) who did not (Chi square (Yates correction) = 31.5, OR = 12.9, 95% CI of OR = 4.4–42.4, $p < 0.001$). When only strokes (not TIAs) are included in the analysis, eight of ten patients had greater than 90% stenosis of the symptomatic carotid artery compared to 22/190 (11.6%) who did not (Chi square (Yates correction) = 29.7, OR = 25.4, 95% CI of OR = 5.4–224, ($p < 0.001$)).

One patient with total occlusion of the ICA developed a stroke 60 hours after the procedure. No other patient with complete occlusion developed a neurological complication.

Discussion

The total neurological complication rate up to 72 hours in our study following cerebral

angiography in 200 patients under consideration of carotid endarterectomy, was 10% (95% CI = 5.8–14). The neurological complications were transient in 5% (95% CI = 2–9), reversible in 1% and permanent in 4% (95% CI = 1.7–7.7). Seventeen of twenty (85%) complications occurred within 24 hours of angiography and there were three late (24–72 hours) complications, all strokes. Two patients suffered disabling strokes. There were two deaths, a mortality rate of 1% (95% CI = 0.1–3), both following dense strokes, although the onset of the stroke was 40 hours after the angiogram in one patient.

It is usual to assume any event occurring after angiography has been caused by it but it may be a manifestation of the primary disease and part of the natural history. In this study 65% of the complications occurred in the territory of the symptomatic vessel. Events occurring between 24 and 72 hours after angiography may be more likely to be a part of the disease but it remains difficult to differentiate them from complications. Seventy two hours is an arbitrary cut off time for monitoring complications but has been used by other authors.^{19,20} If we had taken 24 hours post angiography as the cut off point the permanent neurological complication rate would be 2.5% (95% CI = 0.8–5.7). This demonstrates the importance of defining the time period over which the complications are registered.

Accurate comparison of this study with others is difficult owing to differences in study design, patient selection, sampling errors, angiographic technique and definition of complications. Hankey *et al.*⁹ reviewed seven retrospective studies, the overall combined total neurological complication and mortality rate was 1.9% (95% CI = 1.6–2.2), the permanent complication rate 0.6% (95% CI = 0.4–0.8) and mortality rate 0.6% (95% CI = 0.4–0.8). The comparative figures for eight prospective studies show higher complication rates, the total neurological complication and mortality rate 4.1% (95% CI = 3.3–5.0), the permanent complication rate (all strokes) 1.0% (95% CI = <1–1.5) and mortality rate 0.06%. The confidence intervals of our permanent neurological complication rate of 2.5% (95% CI = <1–5.7) at 24 hours and 4% (95% CI 1.7–7.7) at 72 hours overlap those given in the overview.⁹

Hankey *et al.*⁹ in the most recent prospective study, looked at 382 patients undergoing cerebral angiography for symptomatic carotid ischaemia and reported 10 (2.6%, 95% CI = 1.0–4.2) neurological complications occurring up to 72 hours after the procedure. The complications were transient in two, reversible in three and permanent in five (1.3%, 95% CI = 0.2–2.4) patients. The patients in this study were not screened by Doppler duplex scanning, and only 127/382 (33%) had greater than 50% stenosis of the symptomatic ICA. The degree of atheroma in our patients is more severe than in other studies but is likely to represent the current

situation if non invasive ultrasound is used as a screening test before angiography.

Several risk factors for the development of post angiographic neurological complications have been suggested: older age,²⁰ poor general health and presence of systemic disease,²¹ hypertension and diabetes,^{22,23} cerebrovascular disease rather than other conditions such as cerebral aneurysm or tumour as the indication for angiography,²⁰ frequent cerebral events or recent stroke,^{22,23} severity of symptomatic ICA stenosis,^{22,24,25} performance of angiogram by a trainee rather than a consultant neuroradiologist²⁵ and raised serum creatinine.²³

The patients who had a neurological complication in this study were not significantly older than the patients who did not (61 versus 60 years). They were all medically fit, biochemically normal and there was no significant difference in the frequency of vascular risk factors in the group developing complications. The only three patients with persistent neurological deficits from previous cerebral events developed complications, two developed strokes and one of these patients subsequently died. Faught *et al.*²² found no excess of complications in patients with previous neurological deficit while Patterson *et al.*²⁶ showed a trend of increased risk with more severe deficits.

The major complication of post angiographic stroke (10 patients) occurred with equal frequency in patients being investigated for TIA (5.2%, 95% CI = 1.8–10.6) as for stroke (6%, 95% CI = 1.6–14.4). Although most studies have not categorised the indication for cerebral angiography Hankey *et al.*¹⁹ found post angiographic stroke to be more common in patients investigated for stroke (6.2%) compared with TIA (0.8%) while McIvor *et al.*²⁵ reported no significant difference.

In the present study the radiological technique was consistent throughout the study. The complication rate was higher in patients whose angiogram was performed by a senior registrar in training compared with a consultant. McIvor *et al.*²⁵ also reported a significantly higher neurological complication rate when the angiogram was performed by a trainee. It is commonly assumed that the degree of ICA stenosis present predicts the complication rate of cerebral angiography. Internal carotid artery stenosis of greater than 90% was present in 60% of the patients sustaining a neurological complication compared with 10% who did not (OR = 12.9, 95% CI = 4.4–42.4). The confidence interval of the odds ratio is wide because of the small number of complications, but when looking at the stroke group alone the presence of greater than 90% stenosis remains significant (OR = 25.4, 95% CI or OR = 5.4–224). Transient complications also occurred in two patients with mild stenosis and one with 40% stenosis of the symptomatic ICA. Only two other prospective studies have looked at the correlation between ICA stenosis and the

complication rate but with differing conclusions.^{19,25} Hankey *et al*¹⁹ found that seven of 127 (5.5%) patients with greater than 50% stenosis of the symptomatic ICA sustained a post angiographic stroke and three of these seven had greater than 95% stenosis of the symptomatic ICA. McIvor *et al*²⁵ did not find a statistically significant correlation between the degree of ICA stenosis and the total neurological complication rate. No firm conclusions can be drawn from the retrospective studies.^{22,24,27}

The findings of this study suggest that the risk of neurological complications following cerebral angiography is increased by the presence of severe ICA stenosis. Yet it is these patients who are probably at greatest risk of stroke as part of their disease and are the patients who are now known to benefit most from carotid endarterectomy.^{2,3} The risk of neurological complications in the presence of ICA occlusion remains uncertain, one of 31 patients with ICA occlusion in this study developed a stroke 60 hours after the angiogram. McIvor *et al*²⁵ reported complications in two patients with ICA occlusion.

In the light of the recent studies^{2,3} showing the benefit of carotid endarterectomy in patients with symptomatic cerebral ischaemia and ICA stenosis of 70% or more and our findings of a permanent neurological complication rate of 4%, it is imperative that patients not suitable for carotid endarterectomy are screened out and not put at risk from cerebral angiography. Doppler duplex scanning is non-invasive and although operator dependent it is accurate in experienced hands. When used with clinical assessment it can reliably select patients for angiography.

The complication rate reported here cannot be applied to other medical centres because of differences in patient selection, availability of Doppler duplex scanning and radiological expertise. In this centre over the same time period angiography was performed in 110 patients (age range 14–52) under consideration of surgery for focal epilepsy. Three patients (2.7%) sustained hemispheric TIAs following the procedure (D Smith, personal communication). This suggests it is the disease and not the procedure which puts patients at risk. Patients with severe ICA stenosis on Doppler duplex screening should have angiography performed by experienced neuroradiologists. The higher complication rate is likely to reflect the selection of high risk patients who all have definite carotid ultrasound evidence of ICA stenosis. Centres performing cerebral angiography need to monitor their complication rate by prospective audit.

It is not yet known whether patients with moderate (30–69%) stenosis of the symptomatic ICA will benefit from carotid endarterectomy. If no benefit is shown it will be increasingly important to offer accurate screening of patients before angiography.

With Doppler duplex screening the absolute number of patients undergoing

angiography will be substantially reduced. The rate of post angiographic complications is likely to rise as patients with severe stenosis appear to be at greatest risk of developing complications and have most to gain from carotid endarterectomy. Most centres continue to require angiography before surgery. It is important that patients with symptomatic carotid ischaemia have the risks of both cerebral angiography and surgery explained to them before they accept the recommendation to undergo carotid endarterectomy. In this unit we now tell patients there is a 2% risk of serious complications with angiography.

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