Exploration and treatment of carotid stenoses in 1996

Guy Leseche and Joy Zoghbi

Department of Vascular and Thoracic Surgery, Beaujon Hospital, Clichy, France

Introduction

Every year in France, ~12000 cerebrovascular accidents (CVA) can be blamed on atherosclerotic stenosis of the extracranial carotid artery, which represents 10–15% of all first-occurrence CVA recorded. The human and socio-economic consequences of these strokes can be qualified as tragic because, 6 months after the CVA, roughly one-third of patients have died and another third retain sequelae, half of which are invaliding. In addition to the localized risk of ipsilateral stroke, carotid stenoses, either symptomatic or asymptomatic, carry a general risk of myocardial infarction and vascular death of 4 and 6% per annum, respectively [1–3]. This dual local and general risk of carotid stenoses raises the issue of estimating the cost-effectiveness ratio of systematic screening of the general population. This issue is all the more relevant as carotid stenoses are easy to detect in a non-invasive manner by Doppler ultrasonography and are accessible to treatment (medical in all cases, surgical in some) capable of reducing the incidence of brain infarctions and cardiovascular events in the population studied. Systematic auscultation of the cervical area at all clinical examinations is a crucial part of screening. However, the non-specificity of cervical bruit justifies the preference given to Doppler ultrasonography for carotid stenosis screening. A cost study of systematic screening of carotid stenosis by ultrasonography in the general population does not justify such a position [4]. On the other hand, screening is justified in a selected population at high risk of high-grade stenosis, hence of stroke. Such a population can be defined as possessing at least two of the following factors: presence of cervical bruit, presence of vascular risk factors or presence of one (or several) atherosclerotic complications.

In the ACAS (Asymptomatic Carotid Atherosclerosis Study), 75% of stenoses with a grade ≥60% were accompanied by cervical bruit detectable at auscultation [5]. The prevalence, grade and progressiveness of asymptomatic carotid stenoses are correlated with vascular risk factors in the following decreasing order of importance: age, male gender, smoking habit, hypertension and diabetes melitus [2,6–8]. After age 65, the prevalence of carotid stenoses with a grade significantly higher than 50% is of the order of 5–10%. This steadily increases with age, and most high-grade stenoses ≥80% are found in elderly subjects above age 75 [6,7]. Smoking is a predominant factor; the relative stenotic risk increases with age and duration of smoking, from 1.36 in a 40-year-old subject who smoked for 10 years, to 3.7 in a 70-year-old subject who smoked for 50 years [8]. A number of studies have revealed an increased incidence of carotid stenosis in patients who presented with atherosclerotic disease complications. Thus, the prevalence of high-grade stenoses or carotid occlusions is 8% in patients with coronary arterial disease and 39% in subjects with lower limb arteriopathy [2]. The NASCET study (North American Symptomatic Carotid Endarterectomy Trial) showed that subjects with contralateral carotid occlusion run a very high risk (56% at 2 years) of stroke and death [9]. Whether stenosis is detected at screening or after ischaemic stroke, practitioners must reach a decision for or against surgery. Thanks to the European ECST (European Carotid Surgery Trial) and American NASCET and VASC#309 randomized studies, the situation is now more clear regarding symptomatic carotid stenoses [10–12]. (i) Carotid endarterectomy ensures quick and lasting improvement in patients with symptomatic stenoses of grade ≥70%, regardless of the severity of their atherosclerosis. (ii) Carotid endarterectomy is of no benefit to patients with symptomatic stenoses <30%. (iii) The best strategy has not been established for patients seen more than 6 months after the stroke and with stenoses between 30 and 70%.

The situation of asymptomatic stenoses was expected to become more clear (and quieter) after the publication of the ACAS study [5]. In that study, 1659 patients presenting with asymptomatic stenoses ≥60% and aged between 40 and 79 were followed up for 2.7 years on average, with 4657 patient-years of observation. The aggregate risk of ipsilateral stroke and any peri-operative stroke or death at 5 years was estimated as 5.1% for surgical patients and 11.0% for patients treated medically (aggregate risk reduction of 53%
[95% confidence interval, 22–72%]. This difference was statistically significant in men but not in women. Despite the ACAS results, controversy continues [13], and will continue as long as a simplistic blanket answer to the issue of carotid surgery is sought. As recently reiterated by Bousser [14], good clinical practice requires individual assessment of the risks of spontaneous or recurrent infarction ipsilateral to stenosis and those linked to surgery, in order to obtain a case-by-case estimate of the cost–benefit ratio of surgery and to decide accordingly, taking into consideration the wishes expressed by properly informed patients.

The risk of stenotic ipsilateral stroke

Cohort studies and, more recently, prospective, randomized multicentre trials have clearly identified and singled-out certain risk markers of carotid stenosis.

Symptoms

The risk of stroke is multiplied by two or three in symptomatic stenoses by comparison with those which are asymptomatic. In the year following transient ischaemic attack (TIA), the risk of brain infarction varies from 6.6 [3] to 11.6% [15], whereas in asymptomatic stenoses the risk is 3–4% [1,2]. This greater risk of brain infarction in relation to the symptomatic character of stenosis has been confirmed by major controlled trials. High-grade symptomatic stenoses (≥70%) carry a risk of ipsilateral stroke of 10% per year on average [10,11] vs 2.3% in asymptomatic stenoses [5,16]. Among symptomatic stenoses, prognosis differs according to the type of symptoms. Thus the risk of ipsilateral stroke is increased in cases of repeated TIA, crescendo TIA and prolonged (>1 h) TIA, and also in cases of embolic occlusion of the retinal artery and stroke. Conversely, transient monocular blindness (TMBl) carries a risk of ipsilateral stroke three times less than hemispheral TIA [9]. This relative innocuity of TMB, however, should be weighed against the increased risk of permanent monocular blindness (personal experience). A computerized tomography (CT) scan visualization of a ‘silent’ infarction in the ipsilateral carotid territory is another risk factor. In the NASCET, the risk of infarction on the same side as stenosis was 6 and 11% per year in the absence or presence of such silent infarctions, respectively. It is too early to determine whether Doppler detection of high-intensity transient signals (HITS) in the median cerebral artery is a risk marker of clinical event occurrence [17]. Micro-emboli have been shown to be much more frequent in symptomatic than asymptomatic stenoses, and more frequent in the latter than in controls. There is also a correlation between the frequency of these signals and plaque characteristics. In practice, transcranial ‘Holter’ could prove useful for the detection of highly emboligenic ulcerated stenoses [18].

Characteristics of stenosis

In cohort studies and in most but not all controlled trials, the risk of ipsilateral brain infarction increases with the grade of stenosis.

In cohorts of asymptomatic stenoses, the risk of stroke is multiplied by 3 if stenosis is narrow, from 2% per annum for stenoses less than 75%, to 6% if greater [1,2]. Contralateral carotid analysis in 2295 patients included in the ESCT revealed a 5.7% risk of brain infarction on the side of asymptomatic stenosis after 3 years for stenoses between 70 and 79%, a 9.8% risk for stenoses between 80 and 89%, and a 14% risk beyond those grades [19]. One of the ‘curiosities’ of the ACAS study was that no correlation was found between the risk of brain infarction and the grade of stenosis. In symptomatic stenosis, that correlation is very clear. If the risk of ipsilateral infarction is almost nil when stenosis is below 30%, it increases sharply with high-grade stenosis of ≥70%. In the NASCET, the ipsilateral infarction risk varied from 10%/year in the 70–79% stenosis range to 14% in the 80–89% range, and 17% beyond that range. It thus appears that the narrower the stenosis, the greater the risk of ipsilateral brain infarction. This appears to be especially true when stenosis is poorly compensated for, for instance because of the existence of an occlusion of a communicating artery or significant contralateral internal carotid artery stenosis.

The progressiveness of asymptomatic stenosis is another well known risk factor, and there is strong evidence that the same applies to symptomatic stenosis. The risk of ipsilateral infarction is tripled when stenosis progresses to ≥70% [1,2]. The occurrence of haemodynamic changes in the sylvian artery seen by transcranial Doppler and the reduced or reverse flow of the ophthalmic artery are excellent markers of the progressiveness of stenosis. The presence of ulceration constitutes a recognized risk factor of high-grade symptomatic stenosis and, more questionably, of asymptomatic stenosis, but with a greater risk with large ulcerations [2]. In that respect, the potential use of transcranial Doppler in this pathological situation deserves to be reiterated [18].

Among all the characteristics of stenosis, its grade appears to be correlated best with the risk of ipsilateral infarction. Rather than a watershed figure of 60 or 80%, it is the notion of haemodynamically significant high-grade stenosis that should be noted. Indeed, the uncertainties inherent in angiographic and velocimetric measurements of the grade of stenosis are similar, and the excellent concordance of both techniques was ascertained for the measurement of high-grade stenosis [20].

Vascular risk factors and complications of atherosclerosis

The risk of ipsilateral brain infarction upstream of symptomatic or asymptomatic stenosis increases in parallel with vascular risk factors and complications of atherosclerosis. The risk of infarction and death is four times greater in the presence of contralateral
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Carotid occlusion, up to 56%/2 years [9,11]. The influence of vascular risk factors and complications of atherosclerosis on the progression of symptomatic stenosis was studied prospectively in NASCET [11]. In medically treated patients with stenosis ≥70%, the risk of ipsilateral infarction at 2 years was 17% when fewer than five risk factors were present, 25% when six were present, and 39% with more than seven risk factors. In contrast, in surgical patients, the weight of risk factors did not significantly alter the incidence of ipsilateral brain infarction of 9%/2 years in all three groups. Therefore, the patients who had the largest number of atherosclerosis severity markers and who ran the highest surgical risk were those who benefited most from surgery.

The surgical risk

The second fact to consider in the choice of treatment is the surgical risk. It is worth remembering that in all controlled trials (requiring pre-operative angiography), the surgical risk was determined from the cumulative risk of the operation proper and of pre-operative angiography. In the NASCET, angiography-related morbidity-mortality was 0.7% and that of surgery was 2%. In ACAS, the angiography-related morbidity-mortality was 1.2%, equal to the surgical risk. Systematic pre-operative angiography, justified by the lack of validation of non-invasive exploration methods at the time of those studies, is now unnecessary in 80% of cases [21], thus proportionally reducing the current risks linked to carotid endarterectomy. The relevancy of surgical risk assessment in the choice of treatment becomes essential when stenosis is asymptomatic, because then the risk of stroke is low (2%/year on average). The factors which modify the surgical risk have not been evaluated prospectively in large-scale controlled trials but were subjected to sub-group retrospective analysis [10,22]. Among these factors, some relate to the surgeons and their techniques, and others are related to the patients themselves. Too short or too long an operation, a temporary shunt, non-use of anticoagulants and peri-operative blood pressure variability emerged as pejorative prognostic factors in the ESCT. In this respect, it is worth highlighting the very significant impact, in our opinion, of local or regional anaesthesia. Relative to general anaesthesia, local or regional anaesthesia permits optimization of the endarterectomy technique without any time constraint imposed by clamping-related risks, avoiding unnecessary shunting and better peri-operative haemodynamic stability [23–25]. With regard to the patient, a number of factors have been incriminated, such as age, female gender, severity of vascular risk factors and presence of atherosclerotic complications, although scientific evidence has not been shown for any of these factors. In all published series on carotid surgery, the main cause of death was myocardial infarction. Despite the poor scientific value of this statement, it does, however, seem worth underlining that in three recent French series totalling nearly 2000 patients operated on under local or regional anaesthesia, no death from myocardial infarction was noted [32,26,27]. To some authors, the ‘assumed’ life expectancy of patients is an important criterion of therapeutic choice. In the NASCET, individuals over 79 were excluded; the benefits of surgery were apparent after only 3 months and persisted for at least 30 months. In the ACAS, individuals over 80 were excluded; the beneficial effects of surgery occurred in the tenth month and became significant after 3 years. In the ESCT, there was no age limit and that factor did not emerge as a significant prognostic variable of the surgical risk. The mean life expectancy of subjects between 80 and 85 is 6.7 years [28]. There is, therefore, no case, in our view, for refusing surgery to patients on the grounds that their life expectancy would preclude them from benefiting from it, except in special cases and provided the surgical risk is less than that of stroke. Because the final decision is the patients’, they must be accurately and objectively informed of the spontaneous risk of brain infarction and of the surgical risk. If vascular surgeons have to accept that the spontaneous risk of stroke is low in asymptomatic stenosis, neurologists have to be aware that carotid surgery is increasingly applicable to out-patient surgery, whose morbidity-mortality is <1% in specialized centres [23,26,27]. Nevertheless, the implementation in France of an independent system to evaluate ambulatory surgery practice is highly recommended, to be assigned to the surgical teams with the lowest morbidity-mortality rates.

Angiography, justifiably considered for a long time as the mandatory preoperative examination which was the only procedure to explore cervical arteries as well as proximal supra-aortic trunks and brain arteries, has gradually lost its importance, in favour of non-invasive exploration methods. It was readily accepted that angiography was unnecessary to diagnose the very rarely significant lesions of proximal supra-aortic trunks and that moderate lesions at that level did not change the indication or results of carotid endarterectomy [29]. Later, velocimetric criteria of high-grade stenoses (≥60%) were clearly established by Moneta et al. [20] with a positive predictive value of 95% in relation to the ‘gold standard’ of angiography. More recently, Patel et al. [21] definitively validated Doppler ultrasonography by comparison with angiography and compared these results with those of three-dimensional magnetic resonance imaging (3D MRI) angiography. Doppler ultrasonography has 94% sensitivity, 83% specificity and 86% accuracy. Identical values were obtained with 3D MRI (94, 85 and 88%). Results were even better when both examinations were concordant (80% of cases): 100% sensitivity, 91% specificity and 94% accuracy. Some authors still maintain that detection of severe ipsilateral saphenous stenosis associated with carotid bifurcation stenosis (tandem stenosis) justifies systematic preoperative arteriography. In large-scale controlled trials on carotid surgery, detection of ipsilateral saphenous stenosis exceeding proximal stenosis was an exclusion criterion. This indication limitation, whose corollary is the systematic perform-
ance of preoperative angiography, no longer appears to be justified for at least three reasons. First, published data do not permit the conclusion that the existence of ipsilateral siphon stenosis associated with carotid bifurcation stenosis would significantly modify results and subsequently the indications for carotid endarterectomy [2,30–32]. Secondly, risk-free 3D MRI arteriography perfectly displays intracranial (and extracranial) arteries, including the circle of Willis. Lastly, as intracerebral artery angioplasty is now a feasible reality [33], it is logical, rather than advocating surgical abstinence, to first treat the carotid stenosis, so as to permit later and less risky angioplasty of ipsilateral siphon stenosis. Angiography has also lost its relevance to the detection of other intracranial pathological lesions such as tumours, arterio-venous malformations and aneurysms, which can be detected by CT scan or MRI. These methods have the added advantage of detecting possible silent infarctions, whose prognostic value need not be reminded.

Conclusion

Ultrasoundographic screening for carotid stenosis is justified in a selected population at high risk of high-grade stenosis and hence of stroke. Thanks to cohort studies and controlled trials, the risk markers of stenosis ipsilateral infarction are now known. Carotid stenosis carries a dual risk, both local and general, which in all cases justifies medical management, combining global management of atherosclerosis and its risk factors together with antiplatelet therapy (aspirin or ticlopidine). Large-scale controlled trials have established that surgery was beneficial in haemodynamically significant high-grade stenosis despite 5.8–7.5% morbidity–mortality rates (including that of angiography) for symptomatic and 2.3% for asymptomatic stenosis. There is no longer any justification for imposing the risk and inconvenience of pre-operative angiography or general anaesthesia on patients. Optimized management in a specialized centre reduces surgical risks to <2%, leading surgeons to be able to consider extending surgical prerogatives to the treatment of intermediate-grade symptomatic stenosis with a free mind.

References