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Carotid artery stenting: Rationale, technique, and current concepts

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ABSTRACT

Carotid stenosis is a major risk factor for stroke. With the aging of the general population and the availability of non-invasive vascular imaging studies, the diagnosis of a carotid plaque is commonly made in medical practice. Asymptomatic and symptomatic carotid stenoses need to be considered separately because their natural history is different. Two large randomized controlled trials (RCTs) showed the effectiveness of carotid endarterectomy (CEA) in preventing ipsilateral ischemic events in patients with symptomatic severe stenosis. The benefit of surgery is much less for moderate stenosis and harmful in patients with stenosis less than 50%. Surgery has a marginal benefit in patients with asymptomatic stenosis. Improvements in medical treatment must be taken into consideration when interpreting the results of these previous trials which compared surgery against medical treatment available at the time the trials were conducted. Carotid artery stenting (CAS) might avoid the risks associated with surgery, including cranial nerve palsy, myocardial infarction, or pulmonary embolism. Therefore and additionally to well-established indications of CAS, this endovascular approach might be a valid alternative particularly in patients at high surgical risk. However, trials of endovascular treatment of carotid stenosis have failed to provide enough evidence to justify routine CAS as an alternative to CEA in patients suitable for surgery. More data from ongoing randomized trials of CEA versus CAS will be soon available. These results will help determining the role of CAS in the management of patients with carotid artery stenosis.

1. Introduction

Carotid artery stenosis is a major risk factor for stroke and transient ischemic attack (TIA). Approximately 20% of strokes can be attributed to carotid artery occlusive disease [1]. Histological studies, showed the difference between symptomatic and asymptomatic carotid plaques [2], making the clear separation between symptomatic and asymptomatic patients with a carotid artery stenosis critical and necessary when considering an invasive treatment such as carotid endarterectomy (CEA) or carotid artery stenting (CAS). Therefore, when dealing with carotid artery occlusive disease, symptomatic and asymptomatic stenoses should be viewed as separate entities, because the risks and benefits of treatment are very different. The publication of the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial results established CEA as the treatment of choice for moderate and severe symptomatic carotid artery stenosis [3,4]. The Asymptomatic Carotid Surgery Trial showed a small benefit of early CEA in asymptomatic patients with stenosis greater than 60%, provided the periprocedural risk is lower than 3% [5].

However, these randomized controlled trials (RCTs), compared CEA to best medical treatment available at the time the studies were conducted. Since then, medical treatment has evolved, with newer antiplatelet agents, and the use of lipid-lowering medication, a more aggressive and effective management of risk factors associated with carotid artery stenosis is performed. Disadvantages of CEA include a neck incision with the risk of cranial nerve palsy and wound complications [6]. Medical risks associated with the procedure include myocardial infarction (MI) [7], and not all patients are suitable for surgery. During the past 2 decades, the rapid evolution of endovascular techniques that began with carotid artery angioplasty have evolved to stent-supported angioplasty and combined the use of different cerebral embolic protection devices. Carotid artery angioplasty and stenting have gained widespread acceptance after the publication of the first large series. This minimally invasive approach seemed interesting particularly in patients excluded from large RCTs which demonstrated the benefit of CEA over medical treatment in patients with carotid stenosis. Several randomized trials have then been undertaken to compare CAS and CEA, but have failed to demonstrate equivalence of the treatment modalities [8–10]. This article summarizes recent data on the management of carotid artery stenosis. Endovascular technique

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for carotid revascularization is described, indications, advantages, procedure-related limitations and complications are discussed. A review of recent randomized trials comparing CAS and CEA is presented.

2. Carotid artery revascularization strategies

2.1. Carotid endarterectomy

2.1.1. Symptomatic patients

In patients with symptomatic carotid artery disease, CEA is effective in preventing future ipsilateral ischemic events, provided that the perioperative combined risk of stroke and death is not higher than 6% [11].

Several randomized controlled trials demonstrated that carotid endarterectomy was more effective than medical therapy in patients with recently symptomatic carotid stenosis. The European Carotid Surgery Trial (ECST) [12] randomized patients with any degree of stenosis and compared patients treated by CEA with patients managed by best medical treatment alone. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) [4] had a similar design, but only recruited patients with more than 30% carotid stenosis. However, investigators have made different recommendations about the degree of stenosis above which surgery is effective. Different methods used to measure the carotid artery stenosis can explain this variability. Analysis of pooled data [13] from these two major randomized controlled trials including data from the Veteran Affairs Trial [14], allowed to accurately assess the overall effect of surgery by reanalysis of carotid angiograms. Data for 6092 patients, with 35,000 patient–years of follow-up, were pooled. The results showed that surgery was harmful in patients with less than 30% stenosis, had no effect in patients with 30–49% stenosis, was of marginal benefit in those with 50–69% stenosis. Surgery was highly beneficial in patients with 70% stenosis or greater, without near-occlusion (absolute risk reduction of 16% over 5 years). In patients with near-occlusion of the carotid artery (collapse of the internal carotid artery beyond the stenosis), no significant difference between CEA and medical treatment was found.

Pooled analysis of the RCTs suggested that the benefit from CEA was greatest if patients had the surgery within 2 weeks after the ischemic event. The benefit of surgery is reduced if patients with a previous TIA or non-disabling stroke are treated after 2 weeks from the symptoms onset. The risk of recurrent stroke with time while waiting for surgery is up to 40% when the treatment is delayed as long as 90 days after a qualifying event [15]. Recent guidelines for secondary stroke prevention recommend that CEA should be performed within 2 weeks for patients presenting with a TIA or minor stroke [11].

2.1.2. Asymptomatic patients

There have been two large randomized trials examining the benefits of CEA for asymptomatic stenosis [5,16]. These trials showed that CEA was more effective than medical treatment in preventing strokes in carefully selected patients who had severe carotid artery stenosis but no recent symptoms considered related to the carotid disease. In the analysis of these 2 trials and their conclusions, it is important to consider that the patients constituted a highly selected group which is not representative of the patients seen in clinical practice. These patients had no severe cardiac disease, or other serious comorbidities and were operated by selected surgeons who had low complication rates.

In these 2 trials, surgery provided a modest benefit in stroke prevention, reducing the risk of stroke from 2% per year to 1% per year. This benefit is only maintained when the perioperative risks of stroke and death are less than 3% [11,16]. Patients with a life expectancy of less than 5 years are unlikely to benefit from the modest risk reduction obtained by surgery [5]. In the Asymptomatic Carotid Surgery Trial, surgery did not benefit patients aged 75 years and above. A combined analysis of these 2 trials showed no apparent benefit during a mean follow-up of 2–3 years in women [17]. The results of these CEA trials need to be considered cautiously. In all the trials, surgery was compared with the medical treatment available at the time. The main difference today is the use of lipid-lowering medication. In the NASCET trial, the proportion of patients under lipid-lowering treatment varied from 16% at the beginning of the study, to 40% at the time the trial was completed [4]. Several trials have since found statins to lower the risk of recurrent stroke [18,19]. Identification of asymptomatic patients who are at increased risk of stroke would help clinicians in selecting the patients in whom an invasive treatment is indicated. Predictors of increased risk of ipsilateral ischemic events in asymptomatic patients with carotid stenosis are the following: a stenosis of increased severity, a progressive stenosis, a history of contralateral symptomatic carotid artery stenosis, and increased serum creatinine concentrations. [20] The place of CAS has to be determined in asymptomatic patients with severe carotid artery stenosis, particularly in patients aged 75 years or older in whom the Asymptomatic Carotid Surgery Trial [5], CEA did not show a clear benefit, but also in asymptomatic patients excluded from these trials because of severe comorbidities such as severe cardiac disease [3–5,12,16].

2.2. Carotid revascularization by angioplasty and stenting

2.2.1. Evolution and rationale

Since the 1980s, interventional neuroradiology techniques have become an important therapeutic alternative for many cerebrovascular diseases. Kerber et al. [21] published the first report of carotid artery balloon angioplasty in 1980.

A second small series was reported in 1983 [22] and in 1987, Theron et al. [23] published a larger series including 48 patients in whom technical success rate was 94% with a major stroke morbidity of 4.1%. By 1995, a review of worldwide experience among 523 patients claimed favorable results with 96.2% technical success, 2.1% morbidity, 6.3% transient minor complications, and no deaths [24]. Operator experience was important in determining the technical success and treatment outcomes: centers with limited experience (<50 cases) reported nearly twice the rate of complications (5.9% versus 2.6%) than those with more substantial experience [25,26].

The CAS procedure does not remove the source of intra-arterial emboli and carries the risk of plaque debris dislodgement during the passage of the stenosis and particularly during the postdilation of the stent. Therefore, it seemed necessary to develop a cerebral protection system during a CAS procedure. Theron was one of the pioneers who developed and used a temporary balloon occlusion device as a cerebral protection during angioplasty and stenting for carotid stenosis [27,28]. Three types of cerebral protection devices (CPDs) are nowadays available: distal filters and distal or proximal occlusion balloons, each has its advantages and disadvantages [29].

2.2.2. Patient selection and current indications of CAS

2.2.2.1. Patient selection and defining a "high surgical risk"?. Even though CEA became the standard method of treating carotid artery stenosis when the large randomized trials were published [3,4,12], these trials evaluating CEA have systematically excluded patients considered to be at "high risk for surgery"(Table 1). These important limitations were behind the rationale for developing CAS as a less-invasive endovascular approach to carotid revascularization. Endovascular treatment of carotid stenosis has been proposed as