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Review

Carotid stenting and endarterectomy

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ABSTRACT

Stroke, either ischemic or hemorrhagic, remains the second commonest cause of death worldwide in the last decade. Etiologies for ischemic stroke (IS) vary widely. Atherothrombotic occlusion is an essential cause to which carotid artery stenosis (CAS) is a major contributor. Administration of anti-platelet agent to patients with CAS has been shown to reduce incidence of long-term IS. In additional, in patients with symptomatic CAS, clinical trials have demonstrated that carotid endarterectomy (CEA) is superior to medical therapy for prevention of future CAS-related IS. However, CEA is not suitable for CAS post-radiotherapy or those located at higher level of the internal carotid artery; and major complications of this procedure including cranial nerve injuries have stimulated the interest of using percutaneous transfemoral carotid stenting as an alternative approach. Although transfemoral arterial approach of carotid stenting is not inferior to CEA in improving clinical outcomes, it has been reported to be associated with vascular complication and has its limitations in patients with atheroocclusive disease of abdominal aorta or bilateral iliac arteries, level II or III aortic arch, or bovine type carotid arterial anatomy. Therefore, transradial/transbrachial arterial approach has emerged as a novel method for carotid stenting. This article provides a critical review on interventional approaches for the treatment of CAS.

Stroke shatters a lot of patients' hopes and takes more than ten million of lives every year worldwide [1–5]. Despite state-of-the-art therapy which includes thrombolytic therapy by tissue plasminogen activator [6–8], more aggressive treatment with endovascular therapy [9–11] for acute ischemic stroke (IS), surgical intervention for acute hemorrhagic stroke [12–14] as well as regular update of guidelines [15,16], stroke is still the second commonest cause of death and the third commonest cause of disability-adjusted life-years worldwide [3] in the last decade [5,17,18].

There are two main types of stroke, namely IS due to lack of intracerebral blood flow and hemorrhagic stroke due to intracranial bleeding [18]. The etiologies of IS vary widely [9–12] which include atherothrombotic stroke, embolic stroke, cerebral hypoperfusion and venous thrombosis. However, atherothrombotic occlusion is the principal cause of IS [19–21] and carotid artery stenosis (CAS) is a major contributor to atherothrombotic IS or transient ischemic attack (TIA) [22–24].

Clinical studies have shown previously that anti-platelet therapy [6,25–27] has effectively reduced the incidence of CAS-induced IS. On the other hand, further investigations have demonstrated that surgical carotid endarterectomy (CEA) is more effective than anti-platelet therapy in reducing the incidence of IS or death in patients with symptomatic (defined as IS, TIA or retinal TIA) severe (defined as ≥70% to 99% of stenosis) CAS [28–31]. Accordingly, CEA is the first established gold standard treatment of symptomatic CAS [28–34]. However, CEA is not without limitations. Firstly, it is not suitable for patients who had received radiotherapy which usually causes fibrosis and deformity over the skin and muscle layers of the neck area. Secondly, patients with the CAS located at higher level of internal carotid artery are not amenable to CEA due to limited surgical field accessibility. Thirdly, the result of CEA is much less favorable in the high-risk subset with severe coronary artery disease, pulmonary disease or renal dysfunction [35]. Fourthly, CEA may cause cranial nerve injuries and associated with the risk of ipsilateral ischemic events following the procedure [36–40]. These limitations of CEA raise the need of an alternative option for the treatment of CAS. Growing data have shown that carotid stenting (CS) by transfemoral arterial approach is not inferior to CEA for improving the

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short- and long-term prognosis in patients with symptomatic CAS [41–43]. Accordingly, CS is currently being adopted as a complementary treatment to CEA for patients with CAS [41–45]. However, CS by transfemoral arterial approach is associated with vascular puncture site complications and is not feasible for patients with atherosclerotic occlusion of abdominal aorta or bilateral iliac arteries, level II–III aortic arch and carotid arterial anatomy of bovine arch [46–48]. Therefore, transradial/transbrachial arterial approach has emerged as a novel method for CS [49–51]. This review will describe, and compare the clinical values between CEA and CS of different vascular approaches for patients with CAS.

1. Carotid endarterectomy—a milestone for the treatment of CAS

Previously clinical observational studies have clearly shown that the annual incidence of major IS was up to 5–6% in patients with symptomatic CAS [52–55]. Further analysis has shown that the 2-year cumulative neurologic event rate was estimated to be up to 20% in this group of patients [52]. The results of these clinical observational studies illustrated the need for aggressive and strategic management for symptomatic CAS by CEA [28–34].

As a matter of fact, the CEA was initially introduced in the 1950s as a therapeutic modality for treatment of sporadic patients with recurrent IS [56,57]. Later, with the improvement and refinement of surgical technique and accumulating clinical experience [58–62], the number of the patients with symptomatic CAS who underwent CEA treatment in the United States raised rapidly from 15,000 cases in 1970 to 107,000 cases in 1985 [63,64]. However, in the mid- and late-1980s, the use of CEA as prophylactic treatment against stroke declined dramatically [64] due to a number of reasons [28,64–69]. These included inappropriate categorization of CAS, inappropriate criteria and indication for CEA, uncertainties of whether the pre-operative risk is high enough to justify medical treatment alone, high rates of complications, and continuous uncertainty about marked geographic variation of the efficacy of CEA. On the other hand, with the improvement of risk factor modifications, recognition and education for preventing stroke, and the prompt utilization of antiplatelet agents in preventing the CAS-related stroke [70–74] had reduced the need of CEA in CAS. Furthermore, despite CEA has been accepted widely as an important stroke-prevention strategy since 1950s, up to the mid 1980s, there has not been any strong evidence of its efficacy based on randomized, controlled clinical trials in symptomatic patients. Subsequently, two randomized clinical trials showed negative results of CEA [75,76], and the indication and benefits of CEA in symptomatic patients were being questioned [66,69,77,78]. These raised the opportunity to re-evaluate the efficacy and safety of CEA in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (phase I) [28]. The results from this study demonstrated that CEA is highly beneficial to patients with symptomatic and ipsilateral high-grade stenosis (70 to 99%) of the internal carotid artery [28]. Three further randomized trial in the 1990s [28,30,31] have also showed that as compared with medical treatment, the CEA can effectively reduce the risk of subsequent death or cerebral IS with sustained benefit at long-term follow-up (Table 1). Taking together the results of these large randomized clinical trials [28,30,31] and the NASCET (phase II) trial [29], the following clinical questions were being addressed: Whether CEA offers real benefit for those asymptomatic CAS patients? How large is the benefit of CEA when compared to medical treatment alone? What kind of patients should receive CEA? What is the acceptable complication rate of CEA? How sustainable are the benefits of CEA?

In NASCET (phase II) trial [29], the investigators focused on the examination of the benefit of CEA in patients with asymptomatic moderate stenosis (defined as <70%). They found that among patients with CAS of 50% to 69%, the five-year rate of any ipsilateral stroke (i.e., defined as failure rate) was 15.7% among patients treated surgically and 22.2% among those of patients treated medically (P = 0.045) [29]. Moreover, they further identified that patients with CAS of <50% did benefit from CEA [29]. The results have provided important information to guide the currently practice in the treatment of CAS patients.

Clinical evidence to support the use of CEA in asymptomatic patients with severe CAS (i.e., >70%, <99%) is also compelling [79–82]. All except one randomized trial [79] have clearly demonstrated that CEA reduced the incidence of long-term stroke or death when compared with patients who received medical therapy alone [80–82]. Based on the results of the randomized clinical trials, CEA became the gold standard therapy for patients with severe CAS, irrespective of whether they are symptomatic [28,30,31] or asymptomatic [79–82] (Table 1).

2. Complications and contraindications of CEA

While the benefit of CEA on improving the clinical outcome of patients with severe CAS has been well-established, the complications of the procedure reported by randomized clinical trials and observational studies should not be undermined [28–31,64–69,77,78,80–82]. Cranial nerve injury has been reported to be one of the commonest complications with an estimated incidence from 4.0% to 16.0% [40,83–85]. In another large study that enrolled 3061 patients received CEA over a 10-year period, the prevalence of the composite end point (i.e., stroke, myocardial infarction or death) has been reported to be up to 7.4% in the high-risk subgroup (defined as patients who had severe coronary artery disease or renal insufficiency) [35]. In addition, another randomized trial observed that the frequency of a major stroke or death at 3-year follow-up is up to 14.9% [31]. Of these complications, the high-risk patient group has been identified as the major contributors. Therefore, initial clinical evaluation for the suitability of CEA should be carefully undertaken in such high-risk population (Table 2).

The CEA procedure also has major contraindications. Accumulated experiences have identified that the following patient groups are not suitable for the procedure. These include post-radiotherapy for head and neck cancers, obstructions at higher level of internal carotid artery or lower level of common carotid artery (i.e., below the clavicle level),

Table 1
Benefit of Carotid Endarterectomy (CEA) versus Medical Treatment in improving future clinical outcome in patients with symptomatic and asymptomatic severe carotid artery stenosis based on randomized clinical trials.

Name of clinical trials	CEA	Medical treatment	Follow-up duration	Absolute RR (%)	p-Value
Symptomatic CAS					
NASCET [28] trial: end point (major or fatal ipsilateral stroke)	2.5%	13.1%	2 years	10.6%	<0.001
VA [30] trial: end point (stroke or TIA)	7.7%	19.7%	1 year	11.7%	0.011
ECST [31] trial: end point (major stroke or death)	14.9%	26.5%	3 years	11.6%	<0.001
Asymptomatic CAS					
ACAS [80] trial: accumulative end point (5-years for ipsilateral stroke & any perioperative stroke or death)	5.1%	11.0%	5 years	53.0%	<0.001
VA [81] trial: end point (combined incidence of ipsilateral neurologic events)	8.0%	20.6%	4 years	38.0%	<0.001
ACST [82] trial (stroke)	4.1%	10.0%	5 years	59.0%	<0.001

RR = relative risk; TIA = transient ischemic stroke; NASCET = North American Symptomatic Carotid Endarterectomy Trial; VA = Veterans Affairs; ECST = European Carotid Surgery Trial; ACAS = Asymptomatic Carotid Atherosclerosis Study; ACST = Asymptomatic Carotid Surgery Trial.