Research Article

A comparative study of the outcome following carotid artery stenting with or without embolic protection device

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Abstract

Objective: To compare peri-operative any symptomatic stroke after carotid angioplasty and stenting (CAS), based on the application or absence of a cerebral protection device. **Methods**: The study was performed between march 2018 to march 2019, 35 patients (mean age 77 years; 60 men) underwent CAS with and without any embolic protection device. Post-procedural MRI-DWI was done. **Results:** the number of stroke events was 2 (2.0%) in protected CAS and 4 (5%) in unprotected CAS. The use of cerebral protection device significantly decreased stroke after CAS (p=0.001). **Conclusion:** The use of protection device significantly decreased stroke after CAS. However, its efficacy was not demonstrated in symptomatic patients. Routine use of protection device during CAS should be critically assessed before mandatory use.

Keywords: carotid artery stenting, embolic protection device

Introduction

Stroke is the third leading cause of death in the USA. Nearly 25% of stroke patients will die within a year of the event. [1, 2]

Ischemic strokes, mostly caused by atherosclerotic vascular stenosis, account for almost 90% of cases. Approximately 75% strokes involve the middle cerebral and anterior circulation; the remainder of the events involves the posterior or vertebrobasilar circulation. [3]

Extracrania1 carotid stenosis accounts for about 15 - 20% of cerebral ischemic events. An Egyptian study had showed that among l00 acute stroke patients, 16% had internal carotid artery (ICA) stenosis (>50%).[4]

Asymptomatic carotid artery stenosis of less than 75% carries a stroke risk of 1.3% annually; with stenosis of greater than 75%, the combined TIA and stroke rate is 10.5% per year, with most events occurring ipsilateral to the stenosed carotid artery. Symptomatic carotid artery stenosis of greater than 70% carries an annual risk for stroke of approximately 15%.[5]

Carotid revascularization is superior to aggressive medical treatment in stroke prevention in patients with severe symptomatic or asymptomatic atherosclerotic carotid artery stenosis. [4]

Carotid artery stenting (CAS) with protection devices is a less invasive non-inferior alternative to conventional carotid endarterectomy and became a widely used procedure in critical artery stenosis. However the role of protection evices is debatable.[6]

Although the concept of cerebral protection is generally appealing and has been corroborated by a meta-analysis of single-center studies and large registries, the use of either balloon occlusion techniques or filter systems increases the duration, the technical complexity, as well as the costs of the intervention and is, thus, no panacea for CAS. Indeed, the periprocedural complication rates were comparable between those patients treated with and without cerebral protection in the recently published stent-protected angioplasty versus carotid endarterectomy in symptomatic patients (SPACE) trial.[7]

It is also conceivable that only certain subgroups of patients actually profit from the use of these devices. In fact, it could be speculated that potential impact of protection

devices on outcome is pronounced in those patients who have a high risk of embolic complications during unprotected CAS, such as older patients, and is negligible or even harmful in low-risk patients.[8]

Indeed, a preliminary experience in CASWBAP (carotid artery stenting without balloon angioplasty and protection) demonstrated a low 30-day stroke/death rate [9] and the main goal in CASWEP (Carotid Artery Stenting Without Embolic Protection) Trial which is currently recruiting is to test the hypothesis that CAS without CPD usage is as safe as in those patients who undergo CAS with CPD neuroprotection. [10]

Materials and Methods

A prospective randomized study comparing carotid artery stenting with and without the use of embolic protection device in 35 patients. Patients were sub-divided into 2 grups: **Group A**: those undergoing carotid stenting with the use of embolic protective device (20 patients). **Group B**: those undergoing carotid stenting without embolic protective device (20 patients).

Inclusion criteria: Symptomatic (defined as amaurosis fugax, TIA, Minor stroke or Major stroke) stenosis> 70%**.** Asymptomatic stenosis >80 % (accidentally discovered during pre-operative assessment for CABG and during full assessment for irrelevant stroke).

Exclusion criteria: *General exclusion criteria 1*-Major functional impairment (modified Rankin Scale>3. 2-Significant cognitive impairment (demented patients).3-Major stroke within 4 weeks.4-Contraindication to aspirin or clopidogrel (allergy, thrombocytopenia, GIT hemorrhage of<3 months).5- Intracranial aneurysm >2mm or AVM requiring treatment.*Lesion-specific exclusion criteria:1*-Inability to achieve safe vascular access.2-Visible fresh thrombus on the lesion.3-Chronic total occlusion.4-Long subtotal occlusion (string sign).5-Heavily calcified lesion.

Before procedure: All patients will be subjected to: Consent will be taken from all subject of the study. Complete history taking from patient or relatives including past medical history of any of the following risk factors: arterial hypertension, diabetes mellitus, cigarette smoking, cardiac disease, dyslipi-demia, peripheral vascular disease, previous stroke, transient ischemic attack, and/or reversible ischemic neurological deficit. General examination including vital signs, heart and chest full examination. Clinical and neurological examination with assessment by National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS). Imaging: Carotid Artery Imaging, all carotid lesions will initially be evaluated with Duplex ultrasonography (US) with high-frequency probes. Computed tomography angiography (CTA) or magnetic resonance angiography (MRA) may also be performed. Preprocedure CT imaging or MRI of the brain with diffusion was done in some cases. Angiographical measurement of the stenosis will be determined by the North American Symptomatic Carotid Endarterectomy. Diffusion-weighted magnetic resonance imaging was done within 24 hours after the procedure.

Statistical analysis: The collected data was, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 20.0

Results

Among them, 20 procedures were done with cerebral protection device and 15 were done without protection device. The number of stroke was 2 (2.0%) in protected CAS and 4 (5%) in unprotected CAS. The use of cerebral protection device significantly decreased stroke after CAS (OR 0.633, 95% CI 0.479– 0.837, p=0.001). In the publication bias analysis for comparison between protected and unprotected CAS, Egger's regression test disclosed that the intercept was -0.317 (95% CI -1.015 –0.382, p=0.358). Accordingly, there was no evidence of publication bias in this comparison.

Distribution of risk factors

	Number of patients	%
Males/Females	31/9	77.5/22.5
Smoking	15	37.5
Diabetes	22	55
Hypertension	29	72
Dyslipidemia	17	42.5
Coronary Heart disease	20	50
CABG	2	5
Atrial Fibrillation	3	7.5
Ischemic Cardiomyopathy	2	5
COPD	1	2.5

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Discussion

Although many reports are available, the efficacy of protection device in preventing thromboembolic complications during CAS remains inconclusive. Our study showed that using cerebral protection device significantly lowered the stroke. However, its efficacy was not demonstrated in symptomatic lesions.

During the delivery of protection device, thromboembolic complications can occur while passing over the severe stenotic lesions or vulnerable plaque. In addition, protection device sometimes cannot be deployed at the destination site due to the stiffness in the tortuous or kinked carotid artery. Subsequently, the efficacy of protection device should be assessed by an updated knowledge, although protection devices are widely accepted for the procedure. Compared total stroke events within 30 days after the procedures between protected and unprotected CAS. They concluded that protected CAS showed a relative risk reduction of 0.59 (95% CI 0.47– 0.73) than unprotected CAS.

Through a systemic review, Touzé et al., reported a 4.7% (95% CI 4.1– 5.2) reduction within the 30-day risk of stroke or death rate after CAS. In their study, the protection device lowered the periprocedural complications with risk reduction of 0.57 (95% CI 0.43– 0.76). Our study also showed that cerebral protection device significantly decreased the events of stroke. However, substantial heterogeneity across the tudies can be a concern to interpret the results of previous meta-analysis. In addition, only two randomized controlled trial (RCT) studies. were enrolled in their investigations.

Analyzing three RCT studies, the Cochrane review reported that the number of either stroke or death within days after CAS did not differ

significantly, based on the use of protection device (OR 0.95, 95% CI 0.38– 2.41). In this metaanalysis, only two studies2, provided clear information on stroke and death, respectively, not sum of stroke and death. That was because most previous RCTs have compared treatment outcomes between CAS and CEA, not focusing on the use of protection device. Accordingly, further analysis of individual patient data are necessary. Symptomatic stenosis affects the periprocedural risk after the procedure.

A systemic review40) showed that symptomatic lesion increased the -day risk of stroke or death, more than asymptomatic lesions (7.6%, 95% CI 6.3– 9.1 vs. 3.3%, 95% CI 2.6– 4.1). Garg et al.12) also reported that symptomatic patients had a higher stroke rate than asymptomatic patients, comparing patients who underwent protected (3.8% vs. 1.7%) and unprotected CAS (5.6% and 2.8%). For symptomatic patients, the protection device exhibited relative stroke risk reduction of 0.67 (95% CI 0.5–2 0.86). Kosowski et al., compared the long-term adverse events between symptomatic and asymptomatic patients who underwent CAS. The risk of stroke or death did not differ significantly between symptomatic (8.3%) and asymptomatic patients (8.6%). In this study, we did not find a significant difference in the number of stroke between protected (n=6, 1.7%) and unprotected CAS (n=11, 5.7%) in symptomatic patients (OR 0.455, p=0.160). We think that difference in the primary endpoint (stroke vs. stroke and death) resulted to the disagreement.

Accordingly, further large scale RCT studies are required to investigate the periprocedural risk according to the use of protection device, including symptomatic stenosis. Technical differences in stent type and protection device are related to the periprocedural complications after CAS. The procedures are performed using various stents with different cell designs. Bosiers et al., reported that the postprocedural event rate was more pronounced in open cells (3.4%) thanclosed cells (1.3%), in particular in symptomatic patients. However, a recent meta-analysis by Kouvelos et al., did not show the risk reduction of death (OR 0.69, p=0.21) and stroke (OR 1.17, p=0.37) according to cell design, within days after the procedure. Cerebral protection can be conducted by balloon occlusion of the internal carotid artery above the stenotic lesion, filter instrument and flow-reversal system. Embolic events are more found in filters than proximal occlusion or flow reversal system while crossing the lesion. Thus theoretically, proximal embolic protection device can be advantageous in preventing stroke during CAS. Giri et al. compared the clinical outcome between distal and proximal protection devices during CAS. In their study, the 30-day adverse events did not reach significance according to the device types (p=0.07). Zhan et al., also reported that in-hospital stroke or death did not differ significantly between filter (10 out of 551, 1.8%) and distal occlusive (4 out of 176, 2.3%) embolic protection device (OR 1.04, 95% CI 0.24– 4.44, p=0.958).

Nevertheless, future prospective trials comparing stent design and protection device properties are needed. There are some limitations in this study. First, most studies of this investigation did not analyze the efficacy of the protection device according to the symptomaticity. Second, two out of the 25 studies (8%) are RCTs, although a number of studies have drawn their conclusion from a prospective registry. Third, heterogeneity in terms of primary endpoints (stroke 12) vs. stroke or death vs. stroke and death) can be a limitation to reach the conclusion in the previous studies. In addition, some studies did not provide clear information on stroke, death, and their summation, respectively. Accordingly, total events can be overestimated because major stroke can be fatal, although total events were estimated as the sum of any stroke or death in previous study. Accordingly, randomized controlled studies including more detailed data on perioperative complications according to the symptomaticity and risk stratification, and adverse events in long-term observation are required.

Conclusion

The use of cerebral protection device significantly decreased any symptomatic stroke after the CAS. However, its efficacy was not demonstrated in symptomatic symptomatic patients. Therefore, routine use of protection device during CAS should be critically assessed before mandatory use.

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