Outcome of Carotid Artery Stenting in Asymptomatic and Asymptomatic Carotid Artery Stenosis Patients in Siriraj Hospital

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Background: *Carotid artery stenosis represents one of the most common etiologies of stroke. One of current treatment modalities available for the treatment of carotid artery stenosis is carotid artery stenting (CAS). CAS is a less invasive revascularization strategy than carotid endarterectomy (CEA) in carotid artery stenosis.*
Objective: *To determine outcome of CAS in symptomatic and asymptomatic carotid artery stenosis patients in Siriraj Hospital.*
Material and Method: *The authors enrolled 82 patients with carotid artery stenosis that underwent carotid artery stenting between January 2006 and January 2010. Baseline characteristics were collected. Comorbid medical conditions (age ≥ 80 years, congestive heart failure class III/IV, angina pectoris class III/IV, left main or ≥ 2 vessels coronary artery disease, urgent heart surgery < 30 days, left ventricular ejection fraction < 30%, recent myocardial infarction < 30 days, severe chronic lung disease, severe renal disease) and anatomic features (lesion at second cervicle or higher, lesion below clavicle, prior radical neck surgery or radiation, prior ipsilateral CEA, contralateral laryngeal nerve palsy, tracheostomy) that are associated with increased complications after CEA were analyzed. Primary end point of the present study was the cumulative incidence of a major adverse cardiovascular event (MACE) at 30 days (a composite of death, stroke or myocardial infarction within 30 days after the intervention).*
Results: *There were 60 male (73.2%). Majority of age group (60-79 years) was 64 patients (78.0%). Symptomatic patients accounted for 69.5%. Eight patients (9.7%) developed a major cardiovascular event which was observed at 30 days. No correlation existed between either comorbid medical conditions or anatomic features to major cardiovascular event. Univariate and multivariate analysis showed that age ≥ 80 years (p = 0.04) and history of transient ischemic attack (TIA) (p = 0.03) increased unfavorable outcomes.*
Conclusion: *CAS is the alternative treatment to CEA for carotid artery stenosis. Risk factor for unfavorable outcomes at 30 days were age ≥ 80 years and history of TIA.*

Keywords: *Outcome, Carotid artery stenting, Carotid artery stenosis*

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Carotid artery stenosis is responsible for 20-30% of ischemic stroke[1]. The natural history of the disease is directly related to the severity of the lesion[2]. There is a direct relationship between the degree of carotid artery stenosis and the risk of ipsilateral stroke. Asymptomatic patients have a much lower annual stroke rate than symptomatic patients. In general annual stroke risk is less than 1.0% in patients with carotid stenosis less than 60% and 1-2.4% for those with carotid stenosis greater than 60%[3]. Carotid revascularization by means of carotid endarterectomy has proved highly successful in reducing the incidence of stroke among patients with moderate to severe symptomatic carotid artery stenosis as well as among those with severe asymptomatic carotid stenosis[4]. The efficacy of carotid endarterectomy (CEA) to prevent stroke in patients with carotid stenosis is well established, particularly in those who have symptomatic stenosis.

Percutaneous transluminal angioplasty (PTA)

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of carotid stenosis was first performed by Kerber's group in 1980 and rapidly developed during the subsequent 2 decades[5]. Carotid artery stenting (CAS) a potential alternative treatment to CEA, has been evaluated in a few randomized trials and many nonrandomized studies and involving many specialists, including neurologists, radiologists, cardiologists, vascular surgeons and neurosurgeons, most of whom have already implemented the technique in their clinical practice[6]. CAS has been increasingly performed in patients considered high risk for CEA since its introduction in the mid-1990s[7-9]. Less commonly, CAS is indicated in anatomically high-risk patients who have a history of neck irradiation or surgery (radical neck dissection or CEA) or some other anatomic reason, such as tracheostomy, that would make CEA particularly hazardous.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial investigators demonstrated that CAS could be performed with emboli-protection device with similar rates of complications as CEA in patients considered high risk for surgery[10]. Criteria for high risk for CEA were included medical conditions such as comorbid medical conditions (age $\geq$ 80 years, congestive heart failure class III/IV, angina pectoris class III/IV, left main or $\geq$ 2 vessels coronary artery disease, urgent heart surgery < 30 days, left ventricular ejection fraction < 30%, recent myocardial infarction < 30 days, severe chronic lung disease and severe renal disease) and anatomic features (lesion at second cervicle or higher, lesion below clavicle, prior radical neck surgery or radiation, prior ipsilateral CEA, contralateral laryngeal nerve palsy and tracheostomy).

Previous randomized trials demonstrate that revascularization with CEA reduces stroke risk in both symptomatic and asymptomatic patients. Stenting has been shown to be noninferior compared with CEA in high surgical risk patients[10], with clinical equipoise maintained at 3 years[11].

Some studies have shown that the risk of complications after CAS is likely to be related to some particular patient characteristics and technical aspects. However, the number of complications observed in individual studies was usually small, precluding any reliable conclusion. Moreover, many studies have focused on patients with a perceived high surgical risk, with the hypothesis that those patients should be good candidates for CAS. However, it is possible that comorbidities associated with a greater perioperative risk with CEA may also increase the periprocedural risk with CAS.

There is no previous data on result of CAS in Thailand. Therefore the authors conducted this retrospective research to determine whether the short term outcome of CAS and factors that can influence the major adverse cardiovascular event (MACE), a composite of death, stroke or myocardial infarction within 30 days after the intervention, and these were recorded after intervention at 72 hours and in 30 days

Material and Method

Study protocol

The present study included all consecutive patients, both symptomatic and asymptomatic undergoing CAS in the region of the carotid bifurcation at the Division of Cardiology, Department of Medicine, Siriraj Hospital, between January 2006 and January 2010. Symptomatic patients were defined as those with a stroke or TIA. The patients were treated by angioplasty with stenting, arterial route and the use of cerebral protection. The number of events (stroke, MI, or death) were extracted. Eighty-two patients were retrospectively reviewed. Data retrieval and handling were done via case record form. The present study was approved by the Ethics Committee for Human Rights Research. Postoperative major adverse cardiovascular event (MACE), a composite of death, stroke or myocardial infarction within 30 days after the intervention, was recorded after intervention at 72 hours and 30 days.

Statistical analysis

Baseline characteristic and Categorical data were described as count and percentages compare between patient with and without MACE. The statistical package used was SPSS version 13. The authors compared risk factors, symptom of the patients, investigations, medical comorbidities, anatomical factors and angiographic findings to MACE by Chi-square tests and Fisher's exact test. A p-value < 0.05 was considered to be statistically significant. Forward Stepwise logistic regression analysis was used to estimate odds ratio (OR) and 95% confidence intervals (95% CI), was designed for each variable with a significant p-value.

Results

Eighty-two patients were enrolled. The majority of patients were male (73.2%). The majority of ages was in range of 60-79 years (78.0%). The main underlying diseases more than 90%, were hypertension

(96.3%) and dyslipidemia (92.7%). Fifty-seven patients had symptomatic carotid artery stenosis which include TIA 15 (18.3%) and stroke 42 (51.2%). The intervention was performed at common carotid artery in 6 patients. Eight patients had bilateral severe carotid stenosis and 2 of them had both sides done CAS at the same occasion. One patient had only Percutaneous transluminal angioplasty (PTA) with balloon due to unsuccessful deployment of stent. Nine patients did not use an emboli-protection device due to failure to advance the devices (p-value = 0.21). Table 1 showed comparison of baseline characteristic between patients with and without MACE. The patients with history of TIA developed MACE more often than those without history of TIA (p-value = 0.03). Total MACE was occurred in 8 patients (9.7%).

MACE in 72 hours and 30 days are described in Table 2. Table 3 showed the association of anatomical factor and comorbidities factor with MACE. Age > 80 years is the only factor that associated with MACE, p-value = 0.04.

The present study had no significant

Table 2. Description of MACE after carotid artery stenting in 72 hours and 30 days

	MACE in 72 hours (n = 8)	MACE in 30 days (n = 8)
TIA	3	3
Stroke	4	4
Intracerebral hemorrhage and death	1	1

Table 1. Comparison of baseline characteristic and MACE

	Total (n = 82)	No MACE (n = 74)	MACE (n = 8)	p-value
Age				
< 6o	11 (13.4%)	8 (10.8%)	3 (37.5%)	0.75
60-79	64 (78.0%)	62 (83.8%)	2 (25%)	
≥ 80	7 (8.6%)	4 (5.4%)	3 (37.5%)	
Sex				
Male	60 (73.2%)	53 (71.6%)	7 (87.5%)	0.68
Female	22 (26.8%)	21 (28.4%)	1 (12.5%)	
Underlying disease				
Diabetic mellitus	39 (47.6%)	35 (47.3%)	4 (50%)	1.0
Hypertension	79 (96.3%)	71 (95.9%)	8 (100.0%)	1.0
Dyslipidemia	76 (92.7%)	68(91.9%)	8 (100.0%)	1.0
CKD or ESRD	28 (34.1%)	23 (31.1%)	5 (62.5%)	0.12
Current smoker	12 (14.6%)	10 (13.5%)	2 (25.0%)	0.33
Atrial fibrillation	4 (4.9%)	4 (5.4%)	0 (0%)	1.0
CHF	5 (6.1%)	3 (4.1%)	2 (25%)	0.07
PAD	15 (18.3%)	15 (20.3%)	0 (0%)	0.34
Prior MI	18 (22.0%)	15 (20.3%)	3 (37.5%)	0.36
Prior PCI or CABG	23 (28.0%)	22 (29.7%)	1 (12.5%)	0.43
Symptom				
TIA	15 (18.3%)	11 (14.9%)	4 (50.0%)	0.03
Stroke	42 (51.2%)	40 (54.1%)	2 (25.0%)	0.15
Investigation				
Duplex ultrasound	44 (53.7%)	37 (50.0%)	7 (87.5%)	0.06
CTA	21 (25.6%)	18 (24.3%)	3 (37.5%)	0.42
MRA	29 (35.4%)	27 (36.5%)	2 (25.0%)	0.71
Instrumental used				
Emboli-protection device	73 (89.0%)	67 (90.5%)	6 (75.0%)	0.21

CKD indicates chronic kidney disease; ESRD, end stage renal disease; CHF, congestive heart failure; PAD, peripheral arterial disease; MI, myocardial infarction; PCI percutaneous coronary intervention; CABG; coronary artery bypass graft surgery; TIA, transient ischemic attack; CTA, computed tomography angiography; MRA, Magnetic Resonance Angiography

correlation between angiographic finding and MACE (Table 4). From multivariate analysis, age > 80 years and history of TIA before intervention remained significant predictors for MACE (Table 5).

Using SAPPHIRE trial's primary endpoint (Death, MI and stroke without TIA at 30 days), MACE in our study was 6.1% (5 from 82 patients). There was 7.0% (4 from 57 patients) in symptomatic group and 4.0% (1 from 25 patients) in asymptomatic group.

Discussion

In general, the indications for carotid revascularization relating to symptomatic status and lesion severity are similar for the endovascular and surgical strategies. The North American Symptomatic Carotid Endarterectomy Trial[12] and Asymptomatic

Table 3. Comparison between anatomical factor and medical comorbidities with MACE

	Total (n = 82)	No MACE (n = 74)	MACE (n = 8)	p-value
Anatomical factor				
High lesion or low lesion	13 (15.9%)	11 (14.9%)	2 (25.0%)	0.61
Contralateral carotid occlusion	5 (6.1%)	5 (6.8%)	0 (0%)	1.0
Prior radical neck surgery or radiation	2 (2.4%)	1 (1.4%)	1 (12.5%)	0.19
Total anatomical factor	19 (23.2%)	16 (21.6%)	3 (37.5%)	0.38
Medical Comorbiditiesfactor				
Age ≥ 80 yrs	9 (11.0%)	6 (8.1%)	3 (37.5%)	0.04
Congestive heart failure class III/IV	4 (4.9%)	3 (4.1%)	1 (12.5%)	0.34
Angina pectoris class III/IV	5 (6.1%)	5 (6.8%)	0 (0%)	1.0
Left main/≥ 2 vessels coronary artery disease	45 (54.9%)	39 (52.7%)	6 (75.0%)	0.28
Urgent heart surgery < 30 days	13 (15.9%)	10 (13.5%)	3 (37.5%)	0.11
LVEF < 30%,	7 (8.5%)	6 (8.1%)	1 (12.5%)	0.53
Recent myocardial infarction < 30 days	4 (4.9%)	3 (4.1%)	1 (12.5%)	0.34
Severe chronic lung disease	2 (2.4%)	1 (1.4%)	1 (12.5%)	0.19
severe renal disease	1 (1.2%)	1 (1.4%)	0 (0%)	1.0
Total medical comorbidities factor	47 (57.3%)	41 (55.4%)	6 (75.0%)	0.46

Table 4. Correlation between angiographic findings and MACE

	Total (n = 82)	No MACE (n = 74)	MACE (n = 8)	p-value
Excessive tortuosity	12 (14.6%)	10 (13.5%)	2 (25.0%)	0.33
Heavy calcification	39 (47.6%)	36 (48.6%)	3 (37.5%)	0.72
≥ 2 90° bends within 5 cm of the lesion	7 (8.5%)	5 (6.8%)	2 (25.0%)	0.14
Concentric circumferential calcified. Width ≥ 3 mm	64 (78.0%)	58 (78.4%)	6 (75.0%)	1.0
Total angiographic findings	73 (89.0%)	66 (89.2%)	7 (87.5%)	1.0

Table 5. Crude odds ratio and Adjusted odds ratio by Logistic Regression analysis

	Univariate analysis		Multivariate analysis	
	Crude odds ratio	p-value	Adjusted odds ratio	p-value
Hx of TIA	5.7 (1.2-26.4)	0.034	20.7 (2.1-204)	0.009
Age ≥ 80	6.8 (1.3-35.7)	0.039	28.5 (2.6-319)	0.007

Carotid Atherosclerosis Study, or ACAS[13], set the bar for acceptable periprocedural complication rates for carotid endarterectomy. ACAS identified a limited benefit relative to periprocedural risk of CEA in asymptomatic patients, discouraging revascularization unless the risk is below 3%. The American Heart Association guidelines for CEA reflect these studies and recommend an upper limit of perioperative risk of 6% for symptomatic patients and of 3% for asymptomatic patients. The goal of CAS is to passivate the lesion and decrease the risk of stroke with an acceptable moderate residual stenosis of 30-40%. Results from our study showed that MACE occurred in 9.7% (8 from 82 patients) at 30 days. The incidence of 30 day stroke in the symptomatic patients was 10.53% (6 from 57 patients) and in the asymptomatic patients 8% (2 from 25). From SAPPHIRE trial, study in high-risk patients, The 30-day incidence of MI, stroke, or death was 4.8% after CAS and 9.8% after CEA. From our study, MACE (not include TIA) was 6.1% that was more than CAS but less than CEA in SAPPHIRE trial. The reason for a higher rate of MACE compare to previous studies may be due to the incomplete use of a cerebral protective device especially at the beginning of the study. There may also be significant heterogeneity among baseline characteristics of the included patients, with varying degrees of baseline stenosis and time since symptom onset since being considered for treatment. History of TIA and age > 80 years are the independent predictors of MACE.

CAS may be considered a revascularization option in most elderly patients. Better patients selection may help to reduce unwarranted procedures and to optimize the likelihood of survival[14].

Although CAS is an acceptable option in selected patients, much remains to be explored to identify those patients who will derive greater benefit from CAS than from CEA and to identify the factors related to patient characteristics, arterial anatomy, operator experience and the procedure itself that are associated with increased risk of unfavorable outcome after CAS.

Limitation

The present study shows lack of association between anatomical or medical comorbidities factor and MACE which is probably due to relatively small sample size and the variety of techniques used.

Conclusion

CAS is the alternative treatment to CEA for carotid artery stenosis. Risk factor for unfavorable outcomes at 30 days were age ≥ 80 years and history of TIA.

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Potential conflicts of interest

None.

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ผลลัพธ์ของการใส่ขดลวดคาโรติดในผู้ป่วยหลอดเลือดแดงคาโรติดตีบที่มีอาการและไม่มีอาการในโรงพยาบาลศิริราช

อิศรา สันตอรรณพ, สุวัจชัย พรรัตนรังสี

***ภูมิหลัง**: ภาวะหลอดเลือดแคโรติดตีบนั้นเป็นสาเหตุหนึ่งของโรคสมองขาดเลือด การรักษาด้วยการใส่ขดลวดคาโรติดเป็นหนึ่งในการรักษาหลอดเลือดแดงคาโรติดตีบ โดยที่รุกรานน้อยกว่าการผ่าตัดเปิดหลอดเลือดแดงใหญ่ในผู้ป่วยหลอดเลือดแดงคาโรติดตีบ*

***วัตถุประสงค์**: ประเมินผลลัพธ์ของการใส่ขดลวดคาโรติดในผู้ป่วยหลอดเลือดแดงคาโรติดตีบที่มีอาการ และไม่มีอาการในโรงพยาบาลศิริราช*

***วัสดุและวิธีการ**: รวบรวมผู้ป่วยหลอดเลือดแดงคาโรติดทุกรายที่ได้รับการใส่ขดลวดที่หลอดเลือดคาโรติดที่โรงพยาบาลศิริราช ตั้งแต่เดือนมกราคม พ.ศ. 2549 ถึง เดือนมกราคม พ.ศ. 2553 โดยมีผู้ป่วย 82 คน ข้อมูลของผู้ป่วยได้รับการรวบรวมและวิเคราะห์ใน 2 หัวข้อหลักคือ ภาวะร่วม และลักษณะทางกายวิภาคของหลอดเลือด โดยภาวะร่วม ประกอบไปด้วยภาวะ อายุมากกว่าหรือเท่ากับ 80 ปี, มีภาวะหัวใจล้มเหลวระดับ 3-4, มีอาการเจ็บหน้าอกระดับ 3-4, มีการตีบของหลอดเลือดโคโรนารีมากกว่าหรือเท่ากับ 2 เส้น หรือพบการตีบที่เส้นซ้ายหลัก, ต้องผ่าตัดหัวใจในช่วง 30 วัน, การบีบตัวของหัวใจน้อยกว่า 30 เปอร์เซ็นต์, มีภาวะหัวใจขาดเลือดในช่วง 30 วัน, โรคปอดเรื้อรังที่รุนแรงและไตวายรุนแรง ส่วนลักษณะทางกายวิภาคของหลอดเลือดประกอบไปด้วยรอยโรคอยู่สูงกว่าหรือเท่ากับระดับของกระดูกต้นคอชิ้นที่ 2, ระดับต่ำกว่ากระดูกไหปลาร้า, เคยได้รับการการผ่าตัดหรือฉายรังสีบริเวณคอมาก่อน, เคยได้รับการผ่าตัดเปิดหลอดเลือดแดงใหญ่ข้างนั้นมาก่อน, เส้นเสียงแหบข้างตรงกันข้าม และได้รับการเจาะคอมาแล้ว ซึ่งปัจจัยต่างๆ เหล่านี้สัมพันธ์กับภาวะแทรกซ้อนหลังการผ่าตัดเปิดหลอดเลือดแดงใหญ่ เป้าหมายหลักเพื่อศึกษาจุดจบอย่างรุนแรงของการเกิดการเสียชีวิต, โรคหลอดเลือดสมอง และกล้ามเนื้อหัวใจขาดเลือดภายใน 30 วัน หลังการขยาย*

***ผลการศึกษา**: ผู้ป่วยชาย 60 คน คิดเป็น 73.2 เปอร์เซ็นต์ ส่วนใหญ่อายุอยู่ระหว่าง 60-79 ปี 64 คน คิดเป็น 78 เปอร์เซ็นต์ พบผู้ป่วยที่มีอาการ 69.5 เปอร์เซ็นต์ พบจุดจบอย่างรุนแรง 8 คน คิดเป็น 9.7 เปอร์เซ็นต์ ภายใน 30 วัน ไม่พบมีความสัมพันธ์ระหว่างจุดจบอย่างแรงกับภาวะร่วม และลักษณะทางกายวิภาคของหลอดเลือดจากการวิเคราะห์ทั้งหนึ่งและหลายตัวพบว่า ทั้งอายุมากกว่าหรือเท่ากับ 80 ปี และมีประวัติของภาวะสมองขาดเลือดชั่วคราว มีผลต่อผลที่ไม่น่าพึงพอใจ*

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