

## Research Article

# Predictors for Successful Outcome of Surgery Treatment in Carotid Stenosis with High Grade

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## Abstract

**Background and Purpose:** The safety of Surgery treatment for the patients was not clear. In order to determine predictors for successful surgery treatment in the patients of carotid severe stenosis.

**Methods:** 186 patients of carotid stenosis with high-grade undergoing Carotid Endarterectomy (CEA) or Carotid Artery Stenting (CAS) were enrolled in our study. The patients were divided into two groups according to the postprocedural complications (1year outcome of following-up) or nor. The univariate and multivariate logistic regression analysis were used to identify the risk factors including the grade of stenosis, age, Ischaemic Heart Disease (IHD), gender, stroke, associated with the postprocedural complications.

**Results:** The multivariate regression analysis of predictors to postprocedural complications shows that the grade stenosis of 90%-99% (OR: 4.85; 95% CI: 1.50-15.72), IHD (OR: 4.93; 95% CI: 1.66-14.58), Stroke (OR: 13.40; 95% CI: 4.46-12.28) were identified as indispensable positive predictor for the postprocedural complications in carotid stenosis. The c-index on the basis of area under the curve for the associations of risk factors predicting the postprocedural complications was 0.831 (95% CI: 0.759 to 0.903;  $p < 0.001$ ), with a sensitivity of 69.44% and a specificity of 84.00%.

**Conclusion:** The previous stroke, previous IHD, and the stenosis might be an adverse factor to the postoperative outcomes in the high-grade stenosis. The subgroup of 70%-79% stenosis without cardiovascular disease may be benefit for clinical treatment of carotid stenosis patients with the high grade.

**Keywords:** Carotid stenosis; Postoperative complications; Carotid artery stenting; Carotid Endarterectomy

## Introduction

Carotid stenosis is well known as one of the major cause of ischemic stroke, which can result in 10-15 percent of cerebral apoplexy [1]. The treatments of Carotid artery stenosis include Carotid Endarterectomy (CEA), Carotid Artery Stenting (CAS), and simple medication therapy. A series of clinical randomized trials confirmed CEA is the standard treatment for long-term of stroke prevention in carotid artery stenosis [2-4]. With technological advancements in endovascular therapy, CAS has emerged as a possible alternative treatment in carotid stenosis. The influential SAPHIRE trial demonstrated that CAS was found to be not inferior to CEA with regards to a composite endpoint of stroke, Myocardial Infarction (MI), and death, which is a major factor of CAS approved for high-risk patients with a symptomatic carotid artery stenosis (>70%) [5].

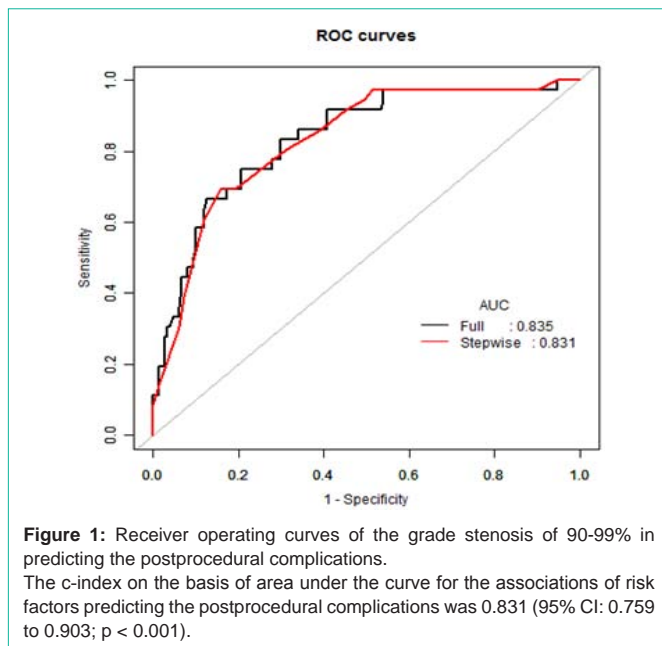
The above random trials fail to answer the question, CAS or CEA, which is the safe way protecting from adverse events. For the severe stenosis patients of symptomatic or asymptomatic, which kind of surgical option benefits more is a question, and the answers to this question are still not clear. Therefore, we present a retrospective analysis of the high-grade carotid stenosis (>70%) to identify predictors for the outcome of surgery treatment and to facilitate better case potation for beginning operators.

## Methods

### Patient

This study retrospectively reviewed patients who underwent carotid artery revascularization regardless of symptomatic or asymptomatic stenosis from 2010 January to 2014 December at the Vascular Department of Chang Hai Hospital affiliated to the second military medical university. The postoperative complications at 1 year with different surgical treatments for carotid stenosis patients were compared. The extracranial carotid artery stenosis was detected by duplex ultrasounds, computed tomography scanning, magnetic resonance imaging, or conventional angiography. According to criteria set by the American Heart Association [6], patients with a high-grade internal carotid artery stenosis of  $\geq 70\%$ , no matter symptomatic or asymptomatic, were included in this observational study.

All patients received the information about the advantages and disadvantages of CAS and CEA, involved the potential complications and risks, and signed the written consent. Patients who had unfavorable aortic arch anatomy, severe calcified carotid lesions, or extremely tortuous carotid anatomy, inadequate femoral arterial access for vascular disease were not applicable for CAS. High-neck carotid bifurcation, previous neck irradiation were contraindications



for CEA patients. A carotid stenosis treated with combined CEA and coronary artery bypass grafting and a patient who was carotid artery occlusion were excluded from the study. The clinical information and radiologic records of the patients who were in this retrospective study was approved by the local ethical committee.

### Design

The decisions which treatment intervened the carotid artery stenosis for each patient appropriately were made by the experienced surgical team comprising of vascular surgeons with proficient endovascular and operation skills. The patients who underwent CEA or CAS were performed by them. The patients were divided into two groups according to whether the occurrence of the postprocedural complications (1-year outcome of adverse event). The patients were broken up into three subgroups based on the degree of stenosis, which were stenosis of 70%-79%, 80%-89% and 90%-99%.

The following cardiovascular risk factors were date from medical history or direct measurements: hypertension (repeatedly measured blood pressure  $\geq 140/99$  mmHg or used antihypertensive drugs), hyperlipaemia (fasting serum cholesterol levels  $\geq 200$  mg/dl or presence of statin), diabetes mellitus (Fasting blood glucose  $\geq 120$  mg/dl or antidiabetic therapy), smoking (current or within the previous year), Ischaemic Heart Disease (IHD, history of angina, Myocardial Infraction (MI), percutaneous transluminal or surgery), and Chronic Obstructive Pulmonary Disease (COPD). The 1-year outcome of adverse events including myocardial infarction (MI), stroke and death, were compared between diverse operative methods.

### CAS procedural

All procedures were performed via the percutaneous femoral artery access under the local anesthesia. The interventions were carried out by experienced vascular surgeons. A distal cerebral protection device was used in all carotid stenting procedures. The type of the covered stent, cerebral protection device, and other interventional apparatus were selected by the operator according to various carotid lesion. All

stents were self-expanding. Pre-dilatation was done in most patients using 3 or 4mm balloons, after cerebral protection device released. Some stents were postdilated with a median size of 5mm balloon due to poor blood vessel filling. Before carotid-artery stenting, aspirin (100mg/day) was given at least 48 hours and clopidogrel (75mg/day) was given at least 3 days. After CAS, dual antiplatelet treatment was continued for a minimum of 4 weeks at least. Then, the Clopidogrel could be discontinued. Aspirin was administered continually for one year at least.

### CEA procedural

CEA was operated according to standard surgical techniques under general anesthesia with systemic heparin. Each member of our vascular surgical team had rich experience to perform CEA. No carotid shunt was used in the process of procedure. The ambulatory blood pressure monitoring was used during operation, and maintain the systolic pressure were not the higher than 120mmHg. Only one type of anti-platelet drug was given to all patients after surgical operation. Usually, the aspirin was preferred in our center and administered indefinitely.

### Follow-up

Most of patients had postoperative carotid duplex ultrasounds at 30 days, then reaped at 6 to 12 months using computed tomography angiography or magnetic resonance angiography. The complications of postprocedural period (1 year) were recorded and defined as the eventual endpoint of this study, including stroke, Myocardial Infarction (MI) and all-cause death. A stroke was referred to as any contralateral or ipsilateral neurologic deficit that was present for more than 24h. MI was defined as a new Q waves noted in two or more contiguous leads electrocardiograph or the level of Creatine Kinase (CK) was higher than the level of the upper limit of normal of Creatine Kinase-MB (CK-MB) three times at least without Q waves. Death referred to as death from any cause. The article carries on the analysis of the previous collected data of our center. These patients were not include in other research.

### Statistical analysis

All continuous variables with a normal distribution were expressed as mean  $\pm$  Standard Deviation (SD) and the categorical variables were expressed as count and percentages. The statistical comparison of continuous date was examined with Student's test. We used chi-square test or Fisher's exact test (if the group's number is 5 or less) to analyze the categorical variables. A 2-sides p value of 0.05 was set a statistically significant. All analyses were performed using Empower (R) ([www.empowerstats.com](http://www.empowerstats.com), X&Y solutions, inc, Boston, MA, USA) and R (<http://www.R-project.org>).

### Results

In total, 186 patients underwent CAS or CEA were enrolled in our study, whom 75(40.32%) underwent CAS and 111(59.68%) underwent CEA procedures. Most of patients were male (153(82.26%) vs 33(17.74%)). Among 186 carotid stenosis patients, 36 (19.35%) patients had postprocedural adverse events. The postprocedural adverse events included MI (n=9), stroke (n=22), death (n=5). As shown in Table 1, age distribution and other risk factors is presented according to the postprocedural complications or nor. Except for sex ( $p=0.033$ ), in hospital days ( $p=0.030$ ), ischaemic heart disease

**Table 1:** Characteristics of Study Participants Stratified by Postprocedural Complications.

Variable	Nor-PC,n=159	PC,n=36	P-value
Age, y	67.60 ± 8.37	70.42 ± 9.08	0.076
In the hospital days	9.11 ± 4.90	11.19 ± 5.99	0.030
Male, sex (%)	119 (79.30%)	34 (94.40%)	0.033
IHD,n(%)	31 (20.70%)	14 (38.90%)	0.022
Stroke	44 (29.30%)	27 (75.00%)	<0.001
Hyperlipemia	8 (5.30%)	3 (8.30%)	0.493
Hypertension	92 (61.30%)	26 (72.20%)	0.223
Diabetes mellitus	41 (27.30%)	12 (33.30%)	0.474
Amaurosis fugax	11 (7.30%)	1 (2.80%)	0.318
Smoking	37 (24.70%)	8 (22.20%)	0.758
Atrial fibrillation	4 (2.70%)	1 (2.80%)	0.970
TIA	42 (28.00%)	5 (13.90%)	0.080
COPD	3 (2.00%)	1 (2.80%)	0.773
Chronic renal insufficiency	2 (1.30%)	1 (2.80%)	0.537
Cancer	11 (7.30%)	1 (2.80%)	0.318
Aspirin	42 (28.00%)	13 (36.10%)	0.338
Antihypertensive	82 (54.70%)	22 (61.10%)	0.484
Clopidogrel	13 (8.70%)	2 (5.60%)	0.538
Statin	33 (22.00%)	8 (22.20%)	0.977
Operation			
CAS	60 (40.00%)	15 (41.70%)	0.855
CEA	90 (60.00%)	21 (58.30%)	0.855
Stenosis grade			
70-79%	65 (43.30%)	9 (25.00%)	0.048
80-89%	53 (35.30%)	13 (36.10%)	0.048
90-99%	32 (21.30%)	14 (38.90%)	0.048

Data are n (%) or mean (SD). Nor-PC indicates nor-postprocedural complications; PC: Postprocedural Complications; IHD: Indicates Ischemic Heart Disease; TIA: Transient Ischemic Attack; COPD: Chronic Obstructive Pulmonary Disease; CAS: Carotid Artery Stenosis; CEA: Carotid Endarterectomy; Y: Years.

( $P=0.022$ ), stroke ( $p<0.001$ ), degree of stenosis ( $P=0.048$ ), there were no statistical differences in the demographic and clinical data between the Postprocedural Complications (PC) group and the Nor-postprocedural Complications (Nor-PC) groups.

The stenosis grade was one of risk factors with statistical differences in our study. In 70%-79% stenosis grade, 9(25.00%) in PC group were compared to 65(43.30%) in nor-PC group. In 80%-89% stenosis grade, 13(36.10%) in PC group were compared to 53(35.30%) in Nor-PC group. In 90%-99% stenosis grade, 14(38.90%) in PC group were compared to 32(21.30%) in Nor-PC group.

To further analyze the relationship between the stenosis grade and the postprocedural adverse events, Univariate analysis was performed with logistic regression after adjusting gender, in hospital days, ischaemic heart disease, stroke (Table 2). The postprocedural complications were higher in the stenosis grade of 90%-99% (OR: 3.16; 95% CI: 1.24-8.08). After adjusting above factors, the stenosis grade of 90%-99% to predict the postprocedural complications became more

**Table 2:** The univariate analysis of the stenosis grade for Postprocedural Complications with adjusted.

Stenosis grade	N(%)	Non-adjusted			adjusted		
		OR	95% CI	P-value	OR	95% CI	P-value
70-79%	74 (39.8%)	1.0	-	-	1.0	-	-
80-89%	66 (35.5%)	1.77	0.70-4.46	0.2252	2.67	0.89-8.00	0.0793
90-99%	46 (24.7%)	3.16	1.24-8.08	0.0162	4.45	1.45-13.7	0.0092

Data are n (%); OR indicates Odds Ratio; CI indicates Confidence Interval.

**Table 3:** The multivariable regression analysis of predictors of postprocedural complications using stenosis grade with adjusted.

Predictor	Single			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
Stenosis grade						
70-79%	1.0	-	-	1.0	-	-
80-89%	2.55	0.87-7.45	0.0876	2.46	0.78-7.71	0.1229
90-99%	4.09	1.37-12.27	0.0118	4.85	1.50-15.72	0.0085
IHD	3.78	1.42-10.03	0.0076	4.93	1.66-14.58	0.0040
Age	1.03	0.98- 1.08	0.1851	1.04	1.66- 14.58	0.1898
Sex	0.33	0.07- 1.66	0.1795	0.31	0.06- 1.74	0.1838
Stroke	12.11	4.45- 32.96	<0.0001	13.40	4.46- 40.28	<0.0001

IHD indicates ischemic heart disease; OR indicates Odds Ratio; CI indicates Confidence Interval. Single means single factor analysis; Multivariable means multivariate analysis.

significant ((OR: 4.45; 95% CI: 1.45-13.66). Similarly, after adjusting the stenosis grade of 80%-89% as predictor for determining the postprocedural complications became stronger (from OR: 1.77; 95% CI: 0.70-4.46 to OR: 2.67; 95% CI: 0.89-8.00).

The multivariate regression analysis of predictors of postprocedural complications were shown in Table 3 when adjusted for in hospital days, smoking, TIA, COPD, DM, hyperlipemia, hypertension, surgical options. The grade stenosis of 90%-99% (OR: 4.85; 95% CI: 1.50-15.72), IHD (OR: 4.93; 95% CI: 1.66-14.58), Stroke (OR: 13.40; 95% CI: 4.46-12.28) were identified as indispensable positive predictor for the postprocedural complications in carotid stenosis.

As the Figure 1 shown, the c-index on the basis of area under the curve for the associations of risk factors predicting the postprocedural complications was 0.831 (95% CI: 0.759 to 0.903;  $p < 0.001$ ), with a sensitivity of 69.44% and a specificity of 84.00%.

## Discussion

In China, approximately 2 million residents experience an incidence stroke each year, of which 1.5 million patients succumb, while the majority of survivors (75%) become disabled. Carotid stenosis is one of the main risk factor for ischemic stroke and it contributes to >20% of incidence of ischemic stroke [7]. The extracranial carotid stenosis of the internal carotid is an important risk factors for ischaemic stroke, particularly in patients with recent ischaemic ocular symptoms, transient ischaemic attack, or stroke. The safety and effectiveness of CEA and CAS has been investigated many randomized or nonrandomized clinical trials, but these trials have failed to determine a clear answer for some limitations. Such as, a previous study evaluated the risk of perioperative stroke, MI, and

death associated with carotid stenosis and established a quantitative scoring system [8]. However, this study just paid attention to the assessment of high-risk patients with CAS and did not include these factors such as age, gender, history of IHD, and characteristics of lesions.

In our retrospective study, we analyzed the risk factors that are impact on the postprocedural complications of high-grade stenosis patients who underwent CAS or CEA. The risk factors include the grade stenosis, age, gender, IHD, in hospital days, smoking, TIA, previous stroke, COPD, DM, hyperlipemia hypertension, surgical options.

Previous stroke or TIA was recognized in the current analysis as an independent risk factor associated with a higher incidence of stroke, death, or their combination [9]. In our study, the rates of postprocedural complications with the previous stroke is higher than one without previous stroke, but the rates of postprocedural complications with or without TIA were no difference. One study found that risk of TIA with amaurosis fugax was higher than without [10]. Furthermore, IHD was as one independent risk factors associated with the postprocedural adverse events in some study [9]. In our study, the rates of IHD, as the same as stroke, was one risk factor can positively affect postprocedural complications.

Some study related to the treatment of carotid stenosis found that CAS used in patients at high Carotid endarterectomy risk due to co morbidities, vascular anatomy, or stenosis grade more than 70% [11,12]. This respective study found that the rates of postprocedural adverse events were not related with surgical operations. This founding may manifest that the CAS is not interior to the CEA during patients with stenosis grade more than 70%. Additionally, some research found that older age has been associated with an increased risk of adverse inpatient outcomes with CEA [13,14]. In the SAPHIRE worldwide study, age > 75 years was the most frequent high-risk surgical feature for CEA in these patients who underwent CAS [15]. However, the CREST trial manifested that age is also adverse impact on CAS and outcomes with CEA among patients of more than 70 years were better compare to CAS [16]. Our study no found the postprocedural complications was affected by age.

Some retrospective data have reported two-fold higher rates of CEA in men than women; especially in those with stenosis more than 70% to emergency for TIA were significantly less than the man [17-19]. In our study, the female with postprocedural complications was obviously less than the male, but the difference was absent when adjusting by in hospital days, smoking, TIA, COPD, DM, hyperlipemia, hypertension, surgical options.

As many study shown, the stenosis is the important risk factors associated with the postprocedural adverse events [2,17,20]. The patients of grade stenosis 70% was significantly impact on the postprocedural outcomes. But when grade stenosis more than 70% allocated into three subgroups, respectively as 70%-79%, 80%-89%, 90%-99%, the relationship between grade stenosis with the postprocedural complications were more obvious. The subgroup of 90%-99% stenosis grade as a predictor to determine the postprocedural adverse events is stronger than other subgroups. This may manifest that as the increasingly grade of stenosis, the impact on the rate of

postprocedural complications are more distinct. Meantime, we used the stenosis as a predictive tool to evaluate the postprocedural adverse events for individual carotid stenosis with more than 70%. It will be especially important and useful for beginner of the procedure, so that cases with the high rates of postprocedural complications may be avoided. In addition, it also provides a different approach in study of carotid stenosis.

## Limitations

The case number of the present study is relatively small, and this may obscure relevant factors and undermine the predictive power. More prospective patients are needed to validate current findings in the future. The present analysis only looked at factors associated with adverse events for a short time, without a long-term clinical outcome. Furthermore, we did not distinguish the patients with symptomatic or asymptomatic stenosis, avoiding the effect of them to the outcome.

## Conclusion

In summary, our data clearly demonstrate that the relationship between the risk factors and the postoperative complications. The previous stroke, previous IHD, and the stenosis might be an adverse factor to the postoperative outcomes in the high-grade stenosis. The subgroup of 70%-79% stenosis without cardiovascular disease may be benefit for clinical treatment of carotid stenosis patients with the high grade. Additionally, the previous stroke, previous IHD, and the degree of stenosis can be used to predict the risk of postoperative complications.

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