Clinical research

Does contralateral carotid artery occlusion affect the clinical and long-term outcomes of carotid artery stenting?

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Abstract

Introduction: Carotid artery stenting (CAS) has been used with increasing frequency in recent years as an alternative to surgery. Contralateral carotid occlusion (CCO) is present in approximately 2.3% to 25% of cases of re-vascularised carotid atherosclerotic stenosis. We aimed to compare the outcomes of 30-day, 6-month and 1-year stroke, transient ischaemic attack (TIA), death and myocardial infarction (MI) in patients with and without CCO who underwent CAS in our clinic.
Material and methods: The study was conducted with 288 consecutive patients who underwent CAS between September 2010 and June 2018. Patients with carotid stenting were divided into two groups: with (48 patients) and without CCO (240 patients).
Results: Total mortality (2.08% vs. 2.08% $p = 1$), stroke (2.08% vs. 0.83%, $p = 0.43$), TIA (0% vs. 0.83%, $p = 0.52$), MI (0% vs. 0%), and composite outcome (4.17% vs. 3.33%, $p = 0.77$) at 30 days were not significantly different between CCO and non-CCO groups. Also there was no statistically significant difference between the two groups in terms of the 6-month and 1-year outcomes ($p > 0.05$).
Conclusions: There was no difference between 30-day, 6-month and 1-year non-fatal MI, TIA, ischaemic stroke and mortality in the comparison of patients with and without CCO who underwent CAS. The outcomes were similar in terms of age and symptoms, and these data should be supported by prospective multicenter studies.

Key words: atherosclerosis, carotid artery stenting, contralateral carotid occlusion.

Introduction

Carotid artery (CA) diseases are frequently diagnosed due to the ongoing increase in average life expectancy and the widespread availability of imaging systems. Stroke is the most common cause of disability of CA diseases and ranks third in mortality [1]. About 15% to 20% of all strokes are caused by CA stenosis, and the most common location of stenosis is the margin of the proximal internal CA and common CA bifurcation [2, 3]. Although carotid artery endarterectomy (CEA) in conjunction with medical treatment is the gold standard therapy for CA stenosis, carotid artery stenting (CAS) has been used with increasing frequency in recent years as an alternative to surgery [4]. Contralateral carotid occlusion (CCO) is

present in approximately 2.3% to 25% of patients following revascularisation of the CA [5]. However, there is no consensus on a revascularisation strategy for CA stenosis in patients with CCO. Previous studies have shown that perioperative stroke and mortality are more common in patients with CCO following CEA [6, 7]. Although patients with CCO and CA stenosis scheduled for CEA are considered to be at high risk [8], the impact of carotid stenting is still less understood. The outcomes of patients with CCO following carotid stenting appear to be similar to those without CCO [9].

Thus, the aim of the present study was to compare the 30-day, 6-month and 1-year outcomes of stroke, transient ischaemic attack (TIA), death and myocardial infarction (MI) of patients with and without CCO who underwent CAS in our clinic.

Material and methods

The present study included 288 patients who underwent CAS between September 2010 and June 2018. Of these patients, 48 were diagnosed with CCO (16.6%). Patients who had an ischaemic stroke, TIA or amaurosis fugax over the last 6 months were considered symptomatic. Amaurosis fugax was defined as an isolated and transient loss of vision, TIA was defined as transient cerebral dysfunction of ischaemic origin, and stroke was defined as focal neurological deficits lasting more than 24 h. Each patient was evaluated by at least two interventional cardiologists, and those with symptomatic > 50% and asymptomatic > 70% common or internal CA stenosis, as determined angiographically by the North American Symptomatic Carotid Endarterectomy Trial method, were included in the study. A contralateral carotid occlusion was defined as 100% occlusion of the vessel opposite the artery undergoing carotid stenting. The exclusion criteria for the study were: acute stroke before CAS, spontaneous dissection, fibromuscular dysplasia and vasculitis. All patients were informed about the carotid stenting process and informed consent was obtained from all patients. The study was approved by the local ethics committee.

Clinical evaluation and medical treatment

All patients underwent complete pre- and post-CAS neurological examinations performed by an independent neurologist. To evaluate the pre-procedural anatomies of the CAs, intracranial arteries and aortic arch, each patient underwent one or more carotid Doppler ultrasonography, cranial computed tomography angiography or magnetic resonance angiography examinations. Upon discharge, all patients were prescribed at least 4 weeks of daily clopidogrel at 75 mg and lifetime acetylsalicylic acid at 100 mg after a 300-mg loading dose of clopidogrel.

Procedure

Cardiac activity, oxygen saturation and blood pressure were monitored during the procedure. Following local anaesthesia, an 8 Fr introducer sheath was placed in the main femoral artery and a 5 Fr Simmons type 2 catheter or 6 Fr Judkins R 4 diagnostic catheter over a 0.035-in hydrophilic wire was placed into the common CA to allow for selective imaging of each CA. The CAs and cranial vessels were evaluated on at least two images, including lateral and anterior views. A 0.035-in hydrophilic wire was guided towards the external CA. The diagnostic catheter over the hydrophilic wire was advanced towards the external CA and the hydrophilic wire was replaced with a stiff 0.035-in wire, which was left in the external CA, while the diagnostic catheter was removed. An 8 Fr Judkins R4 guiding catheter (Launcher, Medtronic, Inc., Minneapolis, MN, USA) was placed into the common CA and the stiff wire was removed. Intravenous heparin (5000–10,000 U) was administered, so that the average activated coagulation time would be approximately 250–300 s. Then, a distal embolic protection filter was placed in all patients (Emboshield NAV6; Abbott Laboratories, Santa Clara, CA, USA). Patients with stenosis of ≥ 90% or those with a lesion that did not allow passage for stenting underwent pre-dilatation with a 5.0 × 20-mm balloon (Viatrac 14 Plus; Guidant Corporation, Indianapolis, IN, USA). The procedure was performed with a self-expandable stent (XACT; Abbott Vascular, Galway, Ireland). Residual stenosis of 30% or less was accepted as the optimal range opening. Post-dilatation with 5 × 20-mm balloons (Viatrac 14 Plus; Guidant Corporation, Indianapolis, IN, USA) was performed if an optimal range opening could not be achieved. Prior to balloon and/or stent placement, 1 mg of atropine was intravenously administered to patients to avoid hypotension and bradycardia. At the end of the procedure, anterior-posterior and lateral cranial imaging was performed again and the procedure was terminated.

Statistical analysis

All statistical analyses were performed using SPSS Statistics for Windows, version 17.0. (SPSS Inc., Chicago, IL, USA). The normal distribution of variables was assessed using histograms and the Kolmogorov-Smirnov test. The number and percentile were used for descriptive analyses. Comparisons were made with 2 × 2 tables using Pearson's χ^2 and Fisher's exact tests. Cochran's Q test was used for comparisons of more than two

variables in dependent groups. Data are expressed as mean ± SD for parametric variables and median (minimum-maximum) for non-parametric variables. A p-value < 0.05 was accepted as being statistically significant.

Results

A total of 288 patients (range 51 to 93 years) who underwent carotid stenting were divided into two groups: those with (*n* = 48) and without CCO (*n* = 240). The demographic characteristics and risk factors of the patients are shown in Table I. Of the patients who underwent CAS, 39 (81.25%) with CCO and 195 (81.25%) without CCO were male. There was no statistically significant difference in the gender ratio between the two groups.

Before the procedure, 37 patients diagnosed with CCO and 193 without CCO were symptomatic. Although the baseline percentage of symptomatic patients was lower in those with CCO who underwent CAS, there was no statistically significant difference between the two groups. Of all 288 patients, 16 with CCO and 86 without CCO were aged ≥ 75 years, which was similar percentage-wise between the groups. As shown in Table II, there were no significant differences between the two groups in overall mortality (2.08% vs. 2.08%; *p* = 1.00), stroke (2.08% vs. 0.83%, *p* = 0.43), TIA (0% vs. 0.83%, *p* = 0.52), MI (0% vs. 0%), or composite outcome (4.17% vs. 3.33%, *p* = 0.77) at 30 days. Also there was no statistically significant difference between the two groups in terms of the 6-month and 1-year outcomes (*p* > 0.05). In patients aged < 75 years, the incidence of stroke at 30 days, 6 months and 1 year was higher in patients with CCO than those without CCO (*p* = 0.028), while in patients aged ≥ 75 years, the 1-year non-cardiac mortality rate was higher in patients with CCO than those without CCO (*p* = 0.020) (Table III). Also, there was no significant difference in the presence of CCO or complication rates between symptomatic and asymptomatic patients (Table IV).

Discussion

In this study, there was no difference in 30-day, 6-month or 1-year non-fatal MI, TIA, ischaemic stroke and mortality rates between patients with and without CCO who underwent CAS. In addition, there was no significant difference in composite outcomes between symptomatic and asymptomatic patients.

The prognosis of patients with CCO following medical treatment of CA stenosis is poor, and the risk of stroke within 2 years ranges from 40% to 70% [6, 10]. Therefore, in addition to medical treatment, the CA of patients with CCO must be revascularised, as the risk of stroke within 1 year is about 2% in our patients with CCO who underwent CAS.

The revascularisation strategy in patients with carotid stenosis and CCO remains controversial, as there have been no prospective studies comparing the benefits of surgery versus stent placement. Previous studies and meta-analyses have shown a greater perioperative risk in patients with CCO after CEA [11–13]. The advantages of CAS include a shorter ischaemia time, lack of shunt requirement and lack of sedation/general anaesthesia requirement during the procedure. Cerebral function may be reduced during CEA due to advanced atherosclerotic disease and lack of collateral circulation in these patients. In consideration of these findings, CAS may be a good option for patients with CCO.

Table I. Comparison of demographic characteristics between patients with CCO and without CCO

Parameter	With CCO	Without CCO	*P*-value
Age [years]	68.7 **±9.2**	71.0 **±8.6**	0.111
Age ≥ 75, *n* (%)	16 (33.3)	86 (35.8)	0.741
Male gender, *n* (%)	39 (81.2)	195 (81.2)	1.000
Hypertension, *n* (%)	42 (87.5)	183 (76.2)	0.085
Diabetes mellitus, *n* (%)	22 (45.8)	100 (41.7)	0.594
Hyperlipidemia, *n* (%)	12 (25.0)	60 (25.0)	1.000
Smoking, *n* (%)	14 (29.2)	42 (17.5)	0.062
Coronary artery disease, *n* (%)	18 (37.5)	64 (26.7)	0.129
Peripheral arterial disease, *n* (%)	6 (12.5)	25 (10.4)	0.671
Presence of symptom, *n* (%)	37 (77.1)	193 (80.4)	0.599

Continious variables are presented as mean±SD, whereas categorical variables are presented as frequency (percentage).

Table II. Comparison of complication rates between patients with CCO and without CCO

Variable	With CCO	Without CCO	P-value
30-day myocardial ınfarction, n (%)	0 (0.0)	0 (0.0)	***
6 months myocardial ınfarction, n (%)	0 (0.0)	1 (0.4)	0.654
1 year myocardial ınfarction, n (%)	1 (2.1)	1 (0.4)	0.204
Total death 30 days, n (%)	1 (2.1)	5 (2.1)	1.000
Total death 6 months, n (%)	1 (2.1)	7 (2.9)	0.748
Total death 1 year, n (%)	4 (8.3)	11 (4.6)	0.286
Cardiac death 30 days, n (%)	1 (2.1)	5 (2.1)	1.000
Cardiac death 6 months, n (%)	1 (2.1)	7 (2.9)	0.748
Cardiac death 1 year, n (%)	3 (6.2)	10 (4.2)	0.526
Non-cardiac death 30 days, n (%)	0 (0.0)	0 (0.0)	***
Non-cardiac death 6 months, n (%)	0 (0.0)	0 (0.0)	***
Non-cardiac death 1 year, n (%)	1 (2.1)	1 (0.4)	0.204
Stroke 30 days, n (%)	1 (2.1)	2 (0.8)	0.436
Stroke 6 months, n (%)	1 (2.1)	3 (1.2)	0.652
Stroke 1 year, n (%)	1 (2.1)	3 (1.2)	0.652
TIA 30 days, n (%)	0 (0.0)	2 (0.8)	0.526
TIA 6 months, n (%)	0 (0.0)	2 (0.8)	0.526
TIA 1 year, n (%)	0 (0.0)	3 (1.2)	0.436
Composite outcome 30 days, n (%)	2 (4.2)	8 (3.3)	0.773
Composite outcome 6 months, n (%)	2 (4.2)	13 (5.4)	0.722
Composite outcome 1 year, n (%)	6 (12.5)	18 (7.5)	0.253

*Categorical variables are presented as frequency (percentage). TIA – transient ischemic attack, ***not available.*

Nejim *et al.* found that the outcome of CAS was not superior to that of CEA in patients with asymptomatic CCO during the perioperative period, although the outcome of symptomatic patients was worse [14]. Ricotta *et al.* observed similar instances of major cardiac events, stroke, death and MI following surgery and stent placement in patients with CCO undergoing carotid revascularisation [15]. The outcomes of CAS vs. CEA were similar in regard to the absolute risk of periprocedural major adverse cardiovascular events (2.7% vs. 4.2%), mortality (1.1% vs. 0.7%), stroke (2.1% vs. 3.1%) and MI (0.3% vs. 0.6%). Texakalidis *et al.* found that risks of stroke, MI, and major cardiac events were similar for CAS and CEA during the revascularisation in patients with CCO. However, the 30-day periprocedural mortality rate was lower in the surgical branch [16].

Patients with CCO who underwent CAS may have a greater peri-procedural risk of chronic renal failure, heart failure and chronic obstructive pulmonary disease.

Mercado *et al.* found that the risks of in-hospital mortality, non-fatal MI and non-fatal ischaemic stroke were similar in patients with and without CCO after CAS, as there were no significant differences in composite outcomes (2.1% vs. 2.6%, *p* = 0.316). Likewise, the risks of mortality (0.8% vs. 0.4%, *p* = 0.08), non-fatal stroke (1.1% vs. 1.7% *p* = 0.103) and non-fatal MI (0.2% vs. 0.5%, *p* = 0.217) were similar between those with and without CCO [9]. In a study comparing patients with and without CCO who underwent carotid stenting, Keldahl *et al.* found no significant differences in 30-day mortality (0% vs. 0.5%, *p* = 0.99), stroke (2.6% vs. 1.9%, *p* = 0.55) and MI (0% vs. 0.5%, *p* = 0.8). Moreover, the long-term rates of mortality (25.6% vs. 22.2%, *p* = 0.63), stroke (5.3% vs. 3.4%, *p* = 0.64) and MI (15.4% vs. 14%, *p* = 0.81) were also similar [17]. In addition, Lago *et al.* reported similar 30-day and long-term complication rates between patients with and without CCO after CAS [18]. In the present study, the 30-day, 6-month and 1-year rates of mortality, stroke and

Table III. Comparison of complication rates in patients over and under 75 years of age

Variable	Age < 75 (*n* = 102)			Age ≥ 75 (*n* = 186)		
	With CCO (*n* = 16)	Without CCO (*n* = 86)	*P*-value	With CCO (*n* = 32)	Without CCO (*n* = 154)	*P*-value
30-day myocardial ınfarction, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
6 months myocardial ınfarction, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	1 (1.2)	0.665
1 year myocardial ınfarction, *n* (%)	0 (0.0)	0 (0.0)	***	1 (6,2)	1 (1.2)	0.178
Total death 30 days, *n* (%)	0 (0.0)	1 (0.6)	0.648	1 (6.2)	4 (4.6)	0.786
Total death 6 months, *n* (%)	1 (3.1)	3 (1.9)	0.676	0 (0.0)	4 (4.6)	0.379
Total death 1 year, *n* (%)	2 (6.2)	4 (2.6)	0.287	2 (12.5)	7 (8.1)	0.572
Cardiac death 30 days, *n* (%)	0 (0.0)	1 (0.6)	0.648	1 (6.2)	4 (4.6)	0.786
Cardiac death 6 months, *n* (%)	1 (3.1)	3 (1.9)	0.676	0 (0.0)	4 (4.6)	0.379
Cardiac death 1 year, *n* (%)	2 (6.2)	3 (1.9)	0.171	1 (6.2)	7 (8.1)	0.796
Non-cardiac death 30 days, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
Non-cardiac death 6 months, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
Non-cardiac death 1 year, *n* (%)	0 (0.0)	1 (0.6)	0.648	1 (6.2)	0 (0.0)	0.020
Stroke 30 days, *n* (%)	1 (3.1)	0 (0.0)	0.028	0 (0.0)	2 (2.3)	0.538
Stroke 6 months, *n* (%)	1 (3.1)	0 (0.0)	0.028	0 (0.0)	3 (3.5)	0.448
Stroke 1 year, *n* (%)	1 (3.1)	0 (0.0)	0.028	0 (0.0)	3 (3.5)	0.448
TIA 30 days, *n* (%)	0 (0.0)	2 (1.3)	0.517	0 (0.0)	0 (0.0)	***
TIA 6 months, *n* (%)	0 (0.0)	2 (1.3)	0.517	0 (0.0)	0 (0.0)	***
TIA 1 year, *n* (%)	0 (0.0)	3 (1.9)	0.426	0 (0.0)	0 (0.0)	***
Composite outcome 30 days, *n* (%)	1 (3.1)	3 (1.9)	0.676	1 (6.2)	5 (5.8)	0.946
Composite outcome 6 months, *n* (%)	2 (6.2)	5 (3.2)	0.417	0 (0.0)	8 (9.3)	0.204
Composite outcome 1 year, *n* (%)	3 (9.4)	7 (4.5)	0.270	3 (18.7)	11 (12.8)	0.525

*Categorical variables are presented as frequency (percentage). TIA – transient ischemic attack, ***not available.*

MI were similar between patients with and without CCO after CAS.

Previous studies comparing patients aged < 75 vs. ≥ 75 years who underwent CAS showed that the risks of procedural stroke and mortality were higher in older patients [19–21]. Guo *et al.* observed greater risks of stroke, MI, and mortality in patients aged > 75 vs. < 75 years with and without CCO after CAS [22]. In the present study, the risk of stroke was greater in those aged < 75 years, whereas the risk of non-cardiac mortality was greater in those aged > 75 years, while the 1-year composite outcome was similar between patients aged < 75 and ≥ 75 years.

Mercado *et al.* compared symptomatic and asymptomatic patients with and without CCO who underwent CCO. Mercado *et al.* found no difference in composite outcomes between symptomatic and asymptomatic patients with or without CCO (3.4% vs. 3.5%, respectively, *p* = 0.956) [9].

Similarly, in the present study, the clinical outcomes were similar between symptomatic and asymptomatic patients.

The most important restriction of our study was that it was a single-centred retrospective study. The other major restriction was that we were unable to compare patients who underwent CAS to those who underwent CEA.

In conclusion, no difference was found in terms of stroke, MI, or mortality between patients with and without CCO after CAS. We demonstrated that CAS is a safe and effective revascularisation strategy in patients with CCO. The outcomes were similar in terms of age and symptoms. However, these data should be verified in prospective multicentre studies.

Conflict of interest

The authors declare no conflict of interest.

Table IV. Comparison of complication rates of those with and without symptoms

Variable	Symptomatic (*n* = 230)			Asymptomatic (*n* = 58)		
	With CCO (*n* = 37)	Without CCO (*n* = 193)	*P*-value	With CCO (*n* = 11)	Without CCO (*n* = 47)	*P*-value
30-day myocardial ınfarction, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
6 months myocardial ınfarction, *n* (%)	0 (0.0)	1 (0.5)	0.661	0 (0.0)	0 (0.0)	***
1 year myocardial ınfarction, *n* (%)	1 (2.7)	1 (0.5)	0.090	0 (0.0)	0 (0.0)	***
Total death 30 days, *n* (%)	1 (2.7)	5 (2.6)	0.969	0 (0.0)	0 (0.0)	***
Total death 6 months, *n* (%)	1 (2.7)	6 (3.1)	0.895	0 (0.0)	1 (2.1)	0.626
Total death 1 year, *n* (%)	4 (10.8)	10 (5.2)	0.190	0 (0.0)	1 (2.1)	0.626
Cardiac death 30 days, *n* (%)	1 (2.7)	5 (2.6)	0.969	0 (0.0)	0 (0.0)	***
Cardiac death 6 months, *n* (%)	1 (2.7)	6 (3.1)	0.895	0 (0.0)	1 (2.1)	0.626
Cardiac death 1 year, *n* (%)	3 (8.1)	9 (4.7)	0.388	0 (0.0)	1 (2.1)	0.626
Non-cardiac death 30 days, *n* (%)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
Non-cardiac death 6 months (n, %)	0 (0.0)	0 (0.0)	***	0 (0.0)	0 (0.0)	***
Non-cardiac death 1 year, *n* (%)	1 (2.7)	1 (0.5)	0.190	0 (0.0)	0 (0.0)	***
Stroke 30 days, *n* (%)	1 (2.7)	2 (1.0)	0.413	0 (0.0)	0 (0.0)	***
Stroke 6 months, *n* (%)	1 (2.7)	3 (1.5)	0.625	0 (0.0)	0 (0.0)	***
Stroke 1 year, *n* (%)	1 (2.7)	3 (1.5)	0.625	0 (0.0)	0 (0.0)	***
TIA 30 days, *n* (%)	0 (0.0)	2 (1.0)	0.534	0 (0.0)	0 (0.0)	***
TIA 6 months, *n* (%)	0 (0.0)	2 (1.0)	0.534	0 (0.0)	0 (0.0)	***
TIA 1 year, *n* (%)	0 (0.0)	3 (1.5)	0.445	0 (0.0)	0 (0.0)	***
Composite outcome 30 days, *n* (%)	2 (5.4)	8 (4.1)	0.731	0 (0.0)	0 (0.0)	***
Composite outcome 6 months, *n* (%)	2 (5.4)	12 (6.2)	0.850	0 (0.0)	1 (2.1)	0.626
Composite outcome 1 year, *n* (%)	6 (16.2)	17 (8.8)	0.169	0 (0.0)	1 (2.1)	0.626

*Categorical variables are presented as frequency (percentage). TIA – transient ischemic attack, ***not available.*

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