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Cartoid Near Occlusion: Time to Re-think Endarectomy?

ABSTRACT

Objectives: Carotid near occlusion (CNO) treatment is still controversial. In the discussion of surgical revascularization of these patients, periprocedural complications and technical failure should be considered in addition to the long-term results. We examined the efficacy and safety of surgical treatment in CNO and non-CNO patients undergoing carotid endarterectomy (CEA).

Methods: Data from 152 patients (118 male and 34 female) who underwent isolated CEA between January 2018 and June 2020 without critical contralateral lesions were retrospectively analyzed. Patients were divided into 2 groups: CNO (n=52) and non-CNO (n=100). The groups were compared regarding postoperative transient ischemic attack (TIA), ipsilateral ischemic stroke, and mortality.

Results: The success rate of the procedure was 100% in the CNO group and 99% in the Non-CNO group. In the Non-CNO group, 1 patient had ipsilateral ischemic stroke on postoperative day 0, and this patient was treated with carotid artery stenting. While the number of patients who died in the non-CNO group was 3 (3%) overall, the exitus rate was 1 (1.9%) in the CNO group ($P > .05$). In the CNO group, retinal TIA was observed in 1 patient (1.9%), ischemic stroke in 2 patients (3.8%), and TIA in 1 patient (1.9%). In the non-CNO group; Retinal TIA was observed in 1 patient (1.0%), ischemic stroke in 2 patients (2.0%), and TIA in 2 patients (2.0%). There was no statistically significant difference between the groups in terms of postoperative neurologic complications and primary endpoints at 12-month follow-up ($P > .05$).

Conclusions: Carotid endarterectomy is a safe, feasible, and advantageous procedure in selected CNO patients, as in non-CNO carotid artery patients. Therefore, we recommend a surgical approach to prevent neurological events in CNO patients.

Keywords: Carotid artery disease, carotid near occlusion, endarterectomy

ORIGINAL INVESTIGATION

INTRODUCTION

Carotid artery near occlusion (CNO) indicates a decrease in the diameter of the distal internal carotid artery (ICA) lumen as well as severe carotid artery stenosis.[1] Carotid artery near-occulsion treatment is still controversial. It can be misdiagnosed and can be mistaken for total occlusion.

In the literature, patients with CNO account for almost 20% of all patients with severe (>70-94%) carotid artery stenosis.[2] However, while thousands of patients are included in randomized controlled studies, near-occlusion patients were excluded.[3] This raises the suspicion that near-occlusion patients are underrepresented in the literature. Thus, it prompted a comparison in carotid endarterectomy (CEA) patients, including isolated near-occlusion patients.

Furthermore, as is known, according to the 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS), CEA and carotid artery stenting (CAS) were not recommended for patients with CNO.[4] Because an individual meta-analysis of 5-year stroke risk (including perioperative risk) from pooled data from ESCT, NASCET, and SVACS studies was performed, 262 patients with CNO were divided into 2 groups: those with CEA + best medical therapy (BMT) and those who followed up with BMT alone. There was no statistically significant difference between groups in terms of "relative risk of stroke reduction"

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and "number of treatments needed in 5 years for stroke prevention." Therefore, no clear benefit of applying CEA to CNO patients has been established.[4] However, in the ESVS 2023 Clinical Practice Guidelines for the Management of Atherosclerotic Carotid and Vertebral Artery Disease, it was reported that 33/114 (29%) CNO patients randomized to BMT subsequently underwent CEA but were analyzed as the BMT group. This has led to the notion that this may confuse meaningful data interpretation and potentially underestimate the benefit conferred by CEA on these patients. Nevertheless, BMT was offered to asymptomatic CNO patients with distal collapse in line with previous guidelines. On the other hand, it was suggested that revascularization could be considered in symptomatic CNO patients with distal collapse only after a multidisciplinary team review.[5]

In addition to the guideline recommendations, other studies have also reported that surgical treatment in CNO is a high-risk procedure. In a recent multicenter registry study on this topic, Garcia-Pastor et al[6] reported that revascularization is associated with high technical failure and periprocedural complications in patients with CNO.[6] Based on these data, CEA is typically not performed in patients with CNO in current practice.

Apart from this generalization, high success rates in the treatment of CNO with CEA or CAS are reported in some studies.[7,8] Recently reported studies have shown high stroke rates in CNO patients followed up with BMT alone, reinforcing that revascularization is appropriate and safe for this group of patients.[9]

These studies, which do not overlap with guideline information, have also raised a debate: What if CNO patients are treated surgically? Would CEA surgery performed on CNO patients be harmful to the patient?

In this study, we attempted to interpret surgical treatment in terms of efficacy and safety in these 2 patient groups by comparing CNO patients treated surgically in our clinic with those without CNO but with severe carotid artery stenosis in terms of postoperative symptoms and re-intervention.

HIGHLIGHTS

- We need an answer in the treatment of carotid near occlusion (CNO) patients: Is the carotid endarterectomy (CEA) procedure harmful for the patients with CNO?
- Looking at our results, there was no statistically significant difference between the groups in terms of postoperative neurologic complications ($P > .05$) and primary endpoints (postoperative transient ischemic attack, ipsilateral ischemic stroke, and mortality) at 12-month follow-up ($P > .05$).
- Our experience has shown that in selected CNO patients, CEA is a safe, feasible, and advantageous procedure instead of follow-up with best medical therapy, as in the non-CNO group.

METHODS

Study Population

A total of 152 patients, 118 male and 34 female, who underwent an isolated carotid artery endarterectomy without a contralateral critical lesion between January 1, 2018 and June 1, 2020, were included in the study. The Local Ethics Committee approved the study. Patient demographics, treatment details, and outcome data were collected and analyzed retrospectively. All patients signed written informed consent.

Inclusion and Exclusion Criteria

Patients were divided into 2 groups: non-CNO and CNO patients, by visual assessment of angiographic images according to carotid artery lesions with surgical operation indication (n = 100, n = 52, respectively). In the angiographic evaluation, patients who met the diagnostic criteria previously defined in the literature were included in the CNO group. Patients with at least 2 of the following 4 criteria were evaluated as CNOs:[2]

1. Delayed contrast filling of the ipsilateral ICA compared to the external carotid artery (ECA)
2. Evidence that filling of ipsilateral intracranial vessels with angiographic contrast material by collaterals
3. Decrease in the diameter of the ipsilateral distal cervical ICA compared to the contralateral ICA
4. Decrease in the ipsilateral distal diameter of the ICA compared to the diameter of the ECA beyond the origin of the facial and occipital arteries

Symptomatic or asymptomatic, all CNO patients without distal collapse are included in the study.

Exclusion criteria were determined based on surgical risk and severe comorbidity. Contralateral carotid stenosis >50%, history of longitudinal radiotherapy, history of neck dissection, anatomical difficulties (high bifurcation), cardiac insufficiency (such as recent MI), severe cognitive decline, etc. secondary protective revascularization of the patient. A history of CEA or CAS and non-atherosclerotic lesions were also excluded.

Endpoints and Follow-Up

Postoperative transient ischemic attack (TIA), ipsilateral ischemic stroke, and mortality were the primary endpoints. Other postoperative symptoms of tinnitus and dizziness were also recorded.

Preoperative symptoms (clinical presentation) consisted of TIA and an ipsilateral ischemic attack.

Postoperative symptoms include dizziness, tinnitus, retinal TIA, TIA and ipsilateral ischemic stroke.

Reoperations: redo CEA, including CAS. Post-operatively, symptomatic patients who were ineligible for surgery and CAS were followed up with the BMT.

The preoperative evaluations of the patients included in the study were routinely performed by the joint council of neurology, cardiology, anesthesia, and cardiovascular surgery, and the intervention decision was taken with this council.

All the patients were operated on by the same surgical and anesthesia team. All patients were monitored by cerebral oximetry from the beginning to the end of the procedure. At the end of each procedure, a complete neurological examination was performed. The patients were observed 24 hours a day with hourly neurological tests along with continuous cardiac monitoring. All patients were followed up with postoperative aspirin and clopidogrel. All patients were followed up by the same team for 1 year, as mentioned before.

Preoperative, operative, and postoperative early period data, all in-hospital data, were obtained by retrospectively scanning their files.

The preoperative variables of the patients were recorded. In this context, age, gender, diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HLP), chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD), smoking, peripheral arterial disease (PAD), preoperative neurological sequelae, and clinical presentation were obtained retrospectively from the file data. The intraoperative data, lesion side, surgical technique, and anesthesia procedure were discussed.

Surgical and Perioperative Management

All patients received aspirin, clopidogrel, and statins. Aspirin and clopidogrel were discontinued 5 days before surgery and replaced with low-molecular-weight heparin. The conventional CEA or eversion method was performed under general anesthesia, cervical block, and local anesthesia.

Electrocardiograms, blood pressure, and oxygen saturation were monitored for 24-48 hours after surgery in all patients. Systolic blood pressure was tightly controlled at ≤140 mmHg. Aspirin (100 mg/day) was started 1 day after the operation and was recommended to be continued for life. Clopidogrel (75 mg/day) was started 1 day postoperatively and continued for 1 year.

Statistical Analysis

Descriptive statistics were calculated for the baseline characteristics of patients. The Kolmogorov–Smirnov test and the Shapiro–Wilk test were employed to test the normality of data. Continuous variables were described as mean (standard deviation), and categorical variables were presented as counts (percentages). We tested factors in univariate analyses (*t* test and chi-square test). A *P*-value < .05 was considered statistically significant. All analyses were performed using Statistical Package for Social Sciences Statistics software for Windows, version 22.0 (Chicago, Ill, USA).

RESULTS

Demographics and Clinical Features:

A total of 152 patients were included in the study, including 100 non-CNOs and 52 CNOs. There were 77 males and 23 females in the non-CNO group, and the mean age was 67.0 ± 7.2 years. There were 41 men and 11 women in the CNO group, and the mean age was 65.3 ± 7.3 years.

No significant differences were found between the patient groups in terms of age, gender, DM, HLP, smoking, COPD, PAD, and CRF (*P* > .05). In group 2, HT and coronary heart disease (CAD) were found to be significantly higher than in group 1 (Table 1). When patient groups were evaluated on preoperative clinical variables, no statistically significant differences were found between groups in terms of clinical presentation and permanent preoperative neurological sequelae (*P* > .05) (Table 2).

Table 1. Patient's Demographics and Clinical Features

	Group 1 Non-CNO (n = 100)	Group 2 CNO (n = 52)	*P*
Age (years), Mean (SD)	67.0 (7.2)	65.3 (7.3)	.180
Gender, n (%)			.796
Female	23 (23.0)	11 (21.2)	
Male	77 (77.0)	41 (78.8)	
Hypertension, n (%)	51 (51.0)	36 (69.2)	**.031**
Diabetes, n (%)	37 (37.0)	21 (40.4)	.684
Hyperlipidemia, n (%)	26 (26.0)	16 (30.8)	.533
COPD, n (%)	14 (14.0)	6 (11.5)	.670
PAD, n (%)	20 (20.0)	8 (15.4)	.486
CAD, n (%)	43 (43.0)	39 (75.0)	**<.001**
Chronic renal failure, n (%)	14 (14.0)	3 (5.8)	.127
Smoking, n (%)	49 (49.0)	17 (32.7)	.054

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CNO, cartoid near occlusion; PAD, peripheral arterial disease; SD, standard deviation; *P* < .05, statistically significant.

Perioperative Variables

The success rate of the procedure was 100% for CNO patients. In the non-CNO group, 1 patient had an ipsilateral

Table 2. Patient's Clinical and Surgery Features

	Non-CNO (n = 100)	CNO (n = 52)	*P*
Side of the lesion operated, n (%)			.504
Left	48 (48.0)	22 (42.3)	
Right	52 (52.0)	30 (57.7)	
Preoperative neurological sequelae, n (%)	21 (21.0)	9 (17.3)	.587
Clinical presentation, n (%)			.155
Asymptomatic	38 (38.0)	26 (50.0)	
Symptomatic	62 (62.0)	26 (50.0)	
Anesthesia procedure, n (%)			.636
General	51 (51.0)	30 (57.7)	
Cervical block	45 (45.0)	21 (40.4)	
Local	4 (4.0)	1 (1.9)	
Surgical procedure, n (%)			**<.001**
Classic/Conventional	78 (78.0)	28 (53.8)	
Eversion	21 (21.0)	14 (26.9)	
Patchplasty	0	9 (17.3)	
Graft Interposition	1 (1.0)	1 (1.9)	
Postoperative symptoms, n (%)	11 (11.0)	9 (17.3)	.275
Secondary intervention, n (%)	11 (11.0)	9 (17.3)	.275
Mortality, n (%)	8 (8.0)	4 (7.7)	1.000

CNO, cartoid near occlusion, *P* < .05, statistically significant.

ischemic stroke on postoperative day 0, and this patient was treated with CAS. The success rate of the procedure was 99% in the non-CNO group. There was no statistically significant difference between the groups.

When the patient groups were evaluated according to the operative variables, no statistically significant differences were found between the groups in terms of the side of the lesion operated on and the type of anesthesia procedure (Table 2).

Primary Endpoints and Follow-Up

One patient in the non-CNO group died due to an ipsilateral stroke. While the total number of patients who died in the non-CNO group was 3, this number was 1 in the CNO group. It was determined that 1 patient in the non-CNO group and 1 patient in the CNO group died of an acute myocardial infarction. There was no statistically significant difference between groups regarding exit rate ($P > .05$).

In the CNO group, retinal TIA was observed in 1 patient, ischemic stroke in 2 patients, and TIA in 1 patient. All of these patients underwent emergency carotid computed tomography angiography imaging. One patient with an ischemic stroke underwent reoperation in the ninth follow-up month. The second patient with an ischemic stroke was in his 11th month of follow-up. It was diagnosed that the lession was intracranial and not suitable for CAS. Both patients with TIA in this group were in the fifth month after surgery. They continued to recieve the best medical treatment after the TIA attack.

In the non-CNO group, retinal TIA was observed in 1 patient, ischemic stroke in 2 patients, and TIA in 2 patients. All these patients underwent emergency carotid CTA imaging too. One patient underwent CAS due to ipsilateral paralysis on postoperative day 0. After emergency carotid digital subtraction angiography, it was seen that the lesion was intracranial. Therefore, thrombus aspiration and CAS were preferred. And this patient died due to a stroke. Also, in the same group, CAS was performed on 1 patient during the 7th month of follow-up for restenosis.

Accordingly, there was no statistically significant difference between groups (7.0% and 7.69%, respectively) when rates of ipsilateral TIA, cerebrovascular event, and exitus were examined during the 12-month follow-up period ($P > .05$) (Table 3).

Table 3. Patient's 12 Month Primary Endpoints

	Non-CNO (n = 100)	CNO (n = 52)	*P*
Ischemic stroke, n (%)	2 (2.0)	2 (3.8)	.607
TIA, n (%)	2 (2.0)	1 (1.9)	1.000
Retinal TIA, n (%)	1 (1.0)	1 (1.9)	1.000
Other symptoms (tinnitus, vertigo), n (%)	3 (3.0)	3 (5.7)	.412
Exitus, n (%)	3 (3.0)	1 (1.9)	1.000
Re-intervention, n (%)	2 (2.0)	1 (1.9)	1.000
Primary endpoints, n (%)	7 (7.0)	4 (7.7)	1.000

CNO, cartoid near occlusion; TIA, transient ischemic attack.

DISCUSSION

The treatment strategy for CNO is still controversial.[1] Randomized controlled trials and current guidelines indicated that there was no statistically significant difference between groups in stroke risk reduction between those who underwent CEA + BMT in CNO patients and those who were followed up with BMT alone. Therefore, it was reported that these patients would not sufficiently benefit from CEA.[10]

In the recent guideline (ESVS 2023), BMT is recommended to asymptomatic CNO patients with distal collapse in line with the previous guideline recommendations. It has been reported that revascularization may be considered in symptomatic CNO patients with distal collapse only after a multidisciplinary team review.[5]

Although BMT has been recommended in these patient groups, studies have reported that nearly 40% of CNO patients can become total occlusion patients within the first year.[11] This means that the patient completely loses the opportunity to undergo surgery. Of course, the difficulty of performing endarterectomy for CNO lesions cannot be ignored due to the anatomical difficulties. In fact, high rates of technical failure and periprocedural complications in the revascularization of CNO patients are reported in the literature.[6]

Guideline recommendations and the expectation of high perioperative and postoperative complications in CNO lesions have naturally led to the avoidance of CEA or CAS in CNO patients. However, since 2018, we have been surgically treating patients with CNO. The main reason for this is stenosis or occlusions that may develop in the future, especially in patients without lesions on the contralateral side. Because in patients with CNO, the collateral circulation developed on the opposite side provides the ipsilateral circulation. Of course, logically, the supply of this collateral network is the counterlateral system that is currently intact. Indeed, we sought to revascularize the side with CNO to provide a safety valve for ischemic events caused by lesions that may develop on the contralateral side in the future. Encouraged by the good results of the CEA in CNO patients in the current literature, we operated on these patients. Naturally, we wondered about the process security.

In this context, we designed this study based on the hypothesis that CNO patients can be operated on safely like other non-CNO patients with severe carotid arteries and may benefit from surgical revascularization. And in our study, we compared consecutive CNO patients who underwent CEA operation with non-CNO severe carotid artery stenosis patients in terms of postoperative symptoms and re-interventions.

In the literature, among the risk factors for ipsilateral stroke in patients with symptomatic extracranial carotid atherosclerosis, factors such as age, gender, degree of stenosis, patient's clinical presentation, and plaque morphology are the main ones.[12] Therefore, we compared the preoperative demographics and clinical presentations of patients. There was no

statistically significant difference between groups regarding major risk predictors such as age, gender, and clinical presentation. The HT and CAD were statistically significantly higher in the CNO group than the in non-CNO group. We have seen that our patients in the CNO group are at higher risk in terms of these preoperative parameters that may affect the postoperative results. We think we should consider this when considering our study's postoperative results.

Although the surgical treatment of CNO patients is still controversial, it is undeniable that surgery is advantageous in the medium and long term for these patients, as well as the risk of perioperative complications and the difficulty of the surgical technique. In light of the different results reported in the literature, the main question to be asked in this group of patients is: will CEA surgery performed on CNO patients harm the patient?

In their current study, which included 141 CNO patients, Garcia-Pastor et al[6] reported that they performed CEA on 23 patients. And they reported the CEA procedure success rate at 83.6% and also reported the rate of periprocedural ischemic stroke or death at 13%. Consistent with these findings, they reported that revascularization is associated with high technical failure and perioperative complications in patients with CNO.[6] On the contrary, in their meta-analysis, Meershoek et al[13] evaluated 17 CNO patients undergoing CEA, and the 30-day stroke or death rate was reported to be 1.8% in these patients. When the results were compared with the results of non-CNO patients[14] undergoing CEA in the literature, it was reported that the CNO patients were not at high risk for surgery.[13] In another recent study of 122 CNO patients, the success rate of the procedure was reported to be 100%, and the perioperative surgical risk in CNO patients was similar to that of non-CNO patients.[15]

Our study aimed to investigate the safety of surgery for CNO patients. Therefore, we tested the procedure's safety by comparing CNO patients with non-CNO patients. There was no statistically significant difference between groups regarding periprocedural complications and procedural success. From this point of view, according to the results of our study, CNO patients can be operated on as safely as non-CNO patients.

Although the primary objective of this study is not to assert that CEA is superior to BMT in patients with CNO, we wanted to evaluate our study data in terms of the utility of the CEA procedure in addition to the safety of the CEA procedure. As is known, the most important indicators of the procedure's efficacy, which is the main objective of the CEA, are ipsilateral postoperative symptoms and reoperations.

In Antonopoulos et al's[9] study, the combined stroke rate in CNO patients was reported to be 1.52% after CEA, and 8.39% in patients followed up with BMT. Furthermore, it was reported that BMT alone is not better than CEA or CAS in terms of 30-day or 1-year stroke prevention or death prevention. It has been reported that they concluded that BMT is not superior to CEA or CAS. Another meta-analysis involving CNO patients showed lower stroke rates after CEA and CAS than after medical treatment.[16] Zhang et al[15] evaluated CNO patients (n=54, CNO with total collapse vs. n=68, CNO without total collapse) in whom they performed CEA and reported restenosis at 8 months postoperatively in 1 patient in the entire non-collapsed group. The same study concluded that CEA outcomes for CNO patients with recurrent symptoms were not worse than those described in historical control groups.[15] In our study, postoperative TIA, ipsilateral ischemic stroke, and mortality rates, which were the study's primary endpoints, were similar among our patient groups. We have no data on CNO patients, followed by BMT. However, our results showed that CEA can achieve acceptable results in these patients when our CNO group, which we operated on, and CNO patients followed with BMT alone in the literature were compared in terms of ipsilateral stroke rate.[9]

Study Limitations

There may be several limitations to this study. First, data were collected and analyzed retrospectively. Secondly, the follow-up time is relatively short. We have no long-term results. However, the purpose of the study is to investigate the safety of the surgery, considering the procedural risk and technical difficulties. Therefore, the lack of long-term results does not limit our study. The sample size is relatively small. However, using predefined diagnostic criteria for the CNO group strengthened our study.

CONCLUSION

In conclusion, our experience has shown that CEA is a safe, feasible, and advantageous procedure, as in patients in the non-CNO group, instead of follow-up with BMT in selected CNO patients. Therefore, considering these results in this patient group, we recommend a surgical approach to prevent neurological events. Our data are consistent with those reported by other groups, although our experience is limited to a small number of patients. Undeniably, these patients should be included in future randomized controlled trials to evaluate the best treatment.

Ethics Committee Approval: The study was approved by İzmir Katip Çelebi University Faculty of Medicine Local Ethics Committee (Decision Date: December 22, 2022, IRB: 0603).

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