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Evaluation of the Outcome of Carotid Endarterectomy Following Ischemic Stroke in Vali-e-Asr Hospital, Zanjan, 2016 to 2020

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ABSTRACT

Background & Objective: Carotid endarterectomy (CEA) is a method to reduce the risk of occurrence or recurrence of stroke in patients with cerebrovascular atherosclerosis. Patients should be followed up after this surgery to evaluate the neurological consequences. The aim of this study was to evaluate the short-term and long-term neurological consequences of CEA in terms of improvement of neurological complications, recurrent stroke, and recurrent stenosis after surgery based on technical conditions and specific patient characteristics.

Materials & Methods: Ischemic stroke patients admitted to the neurology ward of Zanjan Vali-e-Asr Hospital who underwent CEA by a single experienced vascular surgeon at the same center from 2016 to 2020 (n=45) were included in the study. Patients were asked to return for cervical color duplex ultrasonography (CDU) and clinical examination. Additional information was collected from the patient's medical records and follow-up results. MRS criterion was used to evaluate neurological outcomes, and CT angiography and CDU were used to grade carotid artery stenosis.

Results: No intraoperative complications were reported. At short-term follow-up (30 days), cardiovascular events occurred in 5% of patients, and surgical site hematoma was observed in 2.5%. At long-term follow-up (90 days), cerebrovascular events were reported in 7.5% of patients. Five patients were lost to follow-up. Both 30-day and 90-day postoperative mortality rates were 5%. No restenosis was detected among surviving patients who underwent CDU.

Conclusion: This study demonstrated a 15% complication rate for CEA in Zanjan Vali-e-Asr Hospital, which was not significantly affected by demographic factors and comorbidities. CEA showed low short-term and long-term mortality rates, with acceptable overall results. Compared to other studies conducted globally and nationally, CEA outcomes at this center appear relatively safe for eligible patients, with relatively low re-stroke rates.

Keywords: Stroke, Carotid Endarterectomy, Neurological Complications, Carotid Artery Stenosis

1. Introduction

Ischemic stroke is the most common type of stroke and is caused by thrombosis, embolism, or stenosis (1). It is one of the leading causes of disability and cost imposition in developed countries and one of the most common causes of mortality worldwide. Timely diagnosis and referral to care centers may be the key. In these centers, imaging and clinical evaluation are performed to assess the extent of ischemia and the condition of the carotid arteries, enabling selection of the

most appropriate treatment (medical or surgical) based on the time elapsed since the onset of symptoms (2).

Despite all the advances in prevention and treatment, re-stroke remains the most significant health threat to patients who survive a primary stroke (3).

The stroke recurrence rate in the first year is between 2.2% and 25.4%. Irreversible risk factors for recurrence include age, previous history of cerebrovascular events, and type of stroke. The strategic secondary prevention method is health education and managing risk factors through lifestyle interventions and treatment (4). Drug therapies to control dyslipidemia, hypertension, and blood sugar, as well as antiplatelet, anticoagulants, and anti-inflammatory therapies, are used in this regard, and sometimes invasive interventions (carotid endarterectomy (CEA) and carotid angioplasty and stenting (CAS)) are required (5, 6). Color duplex ultrasonography (CDU) is a promising imaging modality for determining stenosis greater than 70% (7). The surgery is recommended if the CDU reports more than 70% stenosis. However, for patients with 50-69% stenosis reported by CDU, it is necessary to use other modalities before making treatment plans.

Relative contraindications to CEA include contralateral carotid occlusion, prior neck radiation, prior neck lymph node dissection, prior left side esophagostomy, very high or very low carotid bifurcation, prior carotid endarterectomy, severe tortuosity of the carotid artery, cardiopulmonary comorbidity (8). For patients with symptomatic obstruction, surgery is preferred to be performed within two weeks of the onset of symptoms (delayed when the area of acute ischemia is large and associated with a risk of cerebral edema). Effectiveness will be reduced if it takes longer or if the patient shows a stable neurological defect. Symptomatic patients who cannot tolerate open surgery may be candidates for CAS (5). The two main methods of CEA are the classical method and eversion. In the classical method, the internal carotid artery is clamped at the proximal and distal plaques, and the plaque is separated from both ends and removed. The clamps are released, and a shunt bypass is placed. The artery is then repaired, and the shunt is removed with a vein patch that dilates the artery. The eversion method cuts the internal carotid artery at the origin. The vessel wall is turned upside down, and the plaque is removed. The artery is then repaired end-to-end by anastomosis (5).

Major complications of CEA include myocardial infarction, hyper-perfusion syndrome, nerve damage, postoperative stroke, restenosis, and death. Minor complications include transient ischemic attack, hemorrhage, infection, large nerve branch injury, and dysphagia (5). Frailty also plays a crucial role in the outcome after the CEA. Elderly patients are at increased risk of complications (9). CEA reduces the risk of stroke in well-selected patients; however, the occurrence or recurrence of stroke is a potential complication of CEA, and physicians should encourage the patient to use other secondary prevention methods as well (5). Predictors of quality of life in stroke patients undergoing CEA include stroke severity, general health status, other postoperative complications, treatment and rehabilitation, and socioeconomic factors (10).

All of the patients who underwent CEA in Vali-e-Asr Center of Zanjan after stroke care, according to the indication, were operated on by the same expert vascular surgeon using the classical method. The intraoperative shunt was used in all patients, and the autologous greater saphenous vein graft was used to patch the site of the artery incision. Aspirin and statins were prescribed for all patients in the postoperative period. The average ICU stay after CEA was two days.

This study aimed to evaluate the short-term (90 days) and long-term (more than 90 days) neurological consequences of CEA (in terms of improvement of neurological complications, recurrent stroke, and recurrent stenosis after surgery) based on technical conditions and specific patient characteristics.

2. Materials and Methods

This single-center cross-sectional study included all ischemic stroke patients admitted to the neurology ward of the Vali-e-Asr Hospital in Zanjan. Patients who underwent CEA at the exact center from 2016 to 2020 (n=40) were evaluated. They were asked to return to Vali-e-Asr Center in Zanjan for a clinical examination and CDU of the cervical arteries. Additional information was collected from medical records and follow-up results, and was recorded in the study information form (Table 1).

National Institutes of Health Stroke Scale (NIHSS) scores were used to assess the neurological consequences of stroke at admission. Modified Ranking scale (MRS) was used to follow up on and assess the response to treatment. The ASPECTS scoring criterion was used to interpret brain CT scans of patients to determine the extent of cerebral ischemia at admission.

Patient information was entered into the designed checklists. Statistical analysis of data was performed using SPSS 16 (SPSS Inc., Chicago, USA). Descriptive results are presented as: number, percent, mean, and SD. As the quantitative results were normally distributed, an independent samples t-test was used to compare quantitative data between groups; chi-square and Fisher's exact tests were used to compare qualitative data. The level of statistical significance was assumed to be 0.05. Due to the limited study population, this number was able to detect the occurrence of 1% complication rate with a 99% probability.

Table 1. CDU classification table used at Vali-e-Asr center.

Stenosis	Velocity	Grade
A	Normal velocities (<125cm/sec), No plaques	-
B	Normal velocities, Minimal plaque or mild intimal thickening	0-15%
C	Normal velocities, Plaque>2mm diameter thick, min spectral turbulence	16-49%
D	PSV>125cm/sec, wide spectral turbulence & plaque, ICA/CCA 2-3.99, EDV 40-99	50-69%
D1	PSV>230 cm/sec with: EDV>100 or ICA/CCA>4 w. spectral turbulence	>70%
D2	PSV>230 cm/sec, EDV>130, marked spectral turbulence & ICA/CCA >4	80-99%
E	No flow by spectral color, present plaque or thrombosis	100%

3. Result

In this study, 32 (71%) were male, and 13 (28.9%) were female. The mean age of the patients was 73.3 ±9.964 years, with a range of 50 to 90 years (median, 75 years). Among patients, 33 (73.3%) had hypertension, followed by diabetes (9 cases; 20%), hyperlipidemia (5; 11.1%), history of ischemic heart disease (9; 20%), history of previous cerebrovascular accident (15; 33.3%), history of recent bone fracture leading to surgery (5 cases; 11.1%) and history of smoking, opium usage or both (31; 68.9%).

The mean time interval between stroke and surgery was 34 days with a standard deviation of 43.968 (minimum three days and maximum 240 days). The mean interval between CEA and the study time was also determined to be 3.26 years, ranging from6 months to 5 years. Regarding the interval between surgery and the study, the mode and median were determined to be four years.

According to the information registered in the stroke unit of Vali-e-Asr Center in Zanjan, among the patients studied, the NIH stroke index at the time of hospitalization of 26 patients (61.9%) was less than 8, followed by greater than or equal to 8 in 16 patients (38.1%), (mean ± Standard deviation =6.17±4.213 with a minimum of 1 and a maximum of 19).

Based on the same data, the NIH stroke index before surgery or at the hospital discharge date was less than 8 in 19 patients (82.6%) and greater than 8 in 4 patients (17.4%). Based on the clinical evaluation at the time of admission, 23 patients (54.8%) had ischemia in the Anterior Right region and 19 patients (45.2%) in the Anterior Left region.

Based on the interpretation of a CT scan (without contrast) of the brain at the time of admission, the Astro Alberta Stroke Scale (ASPECTS) showed that the extent of acute cerebral ischemia in 18 patients (47.4%) was less than grade 3, and in 17 patients (58.1%) was rated greater than or equal to 3. Only cerebral small vessel disease (SVD) was reported for three patients.

The incidence of neurological complications (Ischemic symptoms in the carotid blood supply area) was not significantly related to sex and comorbidities such as hypertension, diabetes, ischemic heart disease, history of cerebrovascular events, unilateral or bilateral stenosis, smoking history, hemisphere involved in ischemia, and vertebral blood flow disorders; despite hyperlipidemia (Table 2). Notably, hyperlipidemia demonstrated a statistically significant association with neurological complications (P=0.043), as presented in Table 2.

Of the four patients who died due to cardiovascular events, two patients had one of the complications of CEA. Of the two patients who died following re-stroke, one was due to a complication of CEA.

The rate of neurological complications was not significantly related to NIHSS, MRS, carotid artery stenosis severity, carotid intima-media thickness, or the extent of acute cerebral ischemia (Table 3).

According to the study, there is no significant relationship between the degree of carotid artery stenosis in a surgery candidate as assessed by color Duplex ultrasound and the rate of surgical complications (Table 4).

Three re-strokes happened on the CEA side; two of them experienced the same neurologic symptoms, and the re-stroke led to their deterioration and death. One of these three patients had experienced a TIA and did not care about or follow the condition; more details are described in Table 5.

Overall, no intraoperative complications were observed. In the short-term follow-up, 5% of patients (2 people) experienced cardiovascular events, and 2.5% (1 patient) presented with a surgical site hematoma. In the long-term follow-up, a cerebrovascular event occurred in 7.5% of patients (3 people). Five patients were unavailable. Among 11 patients (27.5%) who died until the study date, the leading causes of death were cardiovascular incidents (4 patients), cerebrovascular accident (3 patients), bedsore-related sepsis (2 patients), and COPD exacerbation (2 patients). The 30-day surgical mortality rate was 5% (2 patients), and the 90-day mortality rate was 5% (2 patients). Among alive patients who underwent color Duplex ultrasound, no restenosis was observed. 24 patients (60%) had a satisfactory general condition until the study.

Table 2. Frequency of neurological complications based on quantitative and qualitative variables.

No.	Variable	Classification	Side effect (Death±stroke)		Total	*P*-value
			Yes	No		
1	Sex	Male	3(10 %)	27(90%)	30	1.000
		Female	1(10%)	9(90%)	10	
2	Hypertension	Yes	4(13.8%)	25(86.2%)	29	0.560
		No	0(0%)	11(100%)	11	
3	Diabetes	Yes	1(12.5 %)	7(87.5 %)	8	0.792
		No	3(9.4%)	29(90.6%)	32	
4	Hyperlipidemia	Yes	2(50%)	2(50%)	4	**0.043**
		No	2(5.6%)	34(94.4%)	36	
5	Ischemic heart disease	Yes	1(12.5%)	7(87.5%)	8	1.000
		No	3(9.4%)	29(90.6%)	32	
6	History of cerebrovascular accidents	Yes	3(23.1%)	10(76.9%)	13	0.092
		No	1(3.7%)	26(96.3%)	27	
7	Smoking	Yes	0(0%)	11(100%)	11	0.560
		No	4(13.8%)	25(86.2%)	29	
8	Stenosis	Unilateral	3(10.7%)	25(89.3%)	28	1.000
		Bilateral	1(8.3%)	11(91.7%)	12	
9	Ischemic hemisphere	Right	2(8.3%)	22(91.7%)	24	1.000
		Left	2(12.5%)	14(87.5%)	16	
10	Vertebral blood flow	Normal	3(9.1%)	30(90.9%)	33	0.677
		Disrupted	1(14.3%)	6(85.7%)	7	
Total			**4(10%)**	**36(90%)**	**40(100%)**	

Table 3. Frequency of neurological complications of surgery based on quantitative variables.

CEA side effect SD±Mean	Yes	No	*P*-Value
Age At the time of surgery	10.434±72.86	6.377±76	0.562
Stroke-Surgery interval (Day)	31.466±30.86	115.754±66.5	0.136
Surgery-Study interval (Year)	1.423±3.152	2.136±3.375	0.779
NIHSS at admission	4.442±6.21	2.217±3.25	0.201
NIHSS at discharge	4.485±2.67	0.000±0.000	0.326
MRS before stroke	0.710±0.31	1.000±0.50	0.620
MRS at admission	1.052±0.75	2.000±1.000	0.684
MRS after 3 months	1.436±1.38	2.217±2.25	0.286

Current MRS	1.575±1.54	0.000±2.000	0.774
Brain ASPECTS	1.822±1.68	1.5±2.5	0.642
Operated ICA stenosis based on CT angiography before CEA	14.713±71.29	21.360±76.25	0.589
The thickness of operated ICA intima media based on ultrasound before CEA	0.187±0.888	0.8	0.737

Table 4. Frequency of surgical complications based on the degree of carotid ultrasound stenosis on the operative side, P=0.091.

Stenosis grade on CEA side	Side effect (Death±Stroke)		Total
	Yes	No	
B (0-15)	0(0%)	3(100%)	3(100%)
C (16-49)	1(100%)	0(0%)	1(100%)
D (50-69)	0(0%)	10(100%)	10(100%)
D1 (70-79)	0(0%)	13(100%)	13(100%)
D2 (80-99)	2(16.7%)	10(83.3%)	12(100%)
E (100)	1(100%)	0(0%)	1(100%)
Total	**6(15%)**	**34(85%)**	**40(100%)**

Table 5. More details about patients with stroke recurrence.

No.	The first stroke symptom	Surgical side	The second stroke symptom	surgical-second stroke duration	Age At the time of surgery	The side of the second stroke	Cause of increased MRS	Death
1	Right Hemi Paresis	LICA	Right Hemi Paresis	3 years	82	LICA	Following second stroke	Yes
2	Right Hemi Paresis	Both arteries	Transient para paresis	3 years	82	Unknown	Following the first stroke	No
3	Transient left hand paresis	RICA	Right Hemi Paresis	1 year	70	LICA	Did not increase	Yes
4	Dysarthria	LICA	Dysarthria	3 months	71	LICA	Following second stroke	Yes

4. Discussions

The 30-day outcome of CEA in Vali-e-Asr Center in Zanjan was evaluated as follows: 5% death and no re-stroke. The 90-day outcome was 5% death and 7.5% re-stroke. No recurrent stenosis was observed in patients examined at the study date, and none developed intraoperative complications.

Compared to this study, the NASCET clinical trial reported 30-day follow-up results, including 1.1% death, 1.8% debilitating stroke, 3.7% non-debilitating stroke, and 90-day results included 1.1% death. 0.9% debilitating stroke and 4.5% non-debilitating stroke. At an 8-year postoperative follow-up, stroke risk has been reported to be 5.7%, and the risk of any stroke was 17.1% (11).

According to Iranian studies, Hemmati et al (12) reported the outcomes of CEA in a one-month study, with a 1.96% mortality rate and a 1.96% complication rate. In the study of Parsa et al (13), the complication rate was 27.5%. In a prospective observational study, the total early critical neurologic complications of CEA in high-risk patients were calculated to be 6% (14). In a retrospective study conducted by Ghandahari et al (15) at

five centers, mortality and morbidity were estimated to be at 6.4%.

The present study's highest death rate was due to cardiovascular and cerebrovascular events (P=0.003). Consistent with this study, TIA was found to be the most common outcome. MI was the second most common adverse surgical outcome (16).

According to this study, the mean age of patients who experienced one of the complications of CEA was not significantly different from those of the uncomplicated group. The effect of sex on complications was not statistically significant. Also, the difference in the rate of CEA complications in people with hypertension, diabetes mellitus, ischemic heart disease, history of cerebrovascular accident and smoking/opium use history were not statistically significant compared to other individuals, despite hyperlipidemia. Based on the NASCET and consistent with our study, the age and sex of the patient, the minor stroke, and the interval between surgery and the symptom of stenosis did not increase the risk of stroke or postoperative death. Also, none of the known risk factors for cerebrovascular events, such as diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and recent smoking history, have any statistically significant effect on the risk of postoperative complications. A history of recurrent cerebrovascular ischemic events in the last six months and the severity of carotid stenosis also did not affect postoperative risk (11). Consistent with our results, a study by M. Farooq et al. Stated that chronic hypertension might play an important role in postoperative complications (17).

In a Korean study, the incidence of major adverse events in the diabetic group was significantly higher than in non-diabetic individuals four years after CEA (18). These results are inconsistent with the findings of our study. Consistent with our study, a study by Dempsey et al. concluded that smoking was the only independent cardiovascular factor significantly increasing carotid plaque thickness in surgical patients (19).

In the present study, the mean NIHSS at the time of admission in patients who experienced one of the complications of CEA was not significantly different from those without complications. The mean NIHSS at the discharge time of these patients was not statistically significant when compared with uncomplicated individuals.

Inconsistent with our results, in the study of Capoccia et al (20) a more significant benefit in reducing neurological symptoms after CEA has been observed in patients with NIHSS scores greater than or equal to 8 before surgery (20).

Mean MRS before stroke, hospitalization time, three months after stroke hospitalization, and study time in patients with one of the complications of CEA were not significantly different from uncomplicated individuals.

Consistent with the present study, symptomatic or asymptomatic conditions (initial MRS and NIHSS conditions) of patients before surgery had no significant effect on NIHSS or MRS after surgery (21).

The mean interval between stroke and surgery in patients who experienced one of the complications of CEA was 48.5 days (standard deviation: 93.846), which was not statistically significant compared with individuals without complications.

Consistent with this result, a NASCET study reported that the time interval between surgery and the onset of stenosis did not significantly increase the risk of stroke or postoperative death (11).

The mean time interval between surgery and study in patients who experienced one of the complications of CEA was not statistically significantly different from those without complications. Inconsistent with our results, a study by Banning et al (9) showed that increasing the age of patients who underwent surgery increased the risk of complications and mortality.

According to our results findings, there was no statistically significant difference in surgical complications between people with right-hemisphere ischemic involvement compared to people with left-hemisphere ischemia. Consistent with this study, Alves-Ferreira et al (22) demonstrated that patients with left stenosis could experience poorer outcomes after CEA.

In this study, the mean extent of acute ischemia caused by stroke (based on a CT scan of the hospitalization time ASPECTS) in patients with complications of CEA was not significantly different from those without complications.

Inconsistent with our results, according to a study by Pini et al (23) patients with symptomatic ischemia caused by carotid stenosis who have ischemic lesions greater than 4000 mm3 experience a weaker prognosis.

Based on our results, the difference in the rate of surgical complications between people with vertebral blood flow disorders and others was not statistically significant. Consistent with our results, Yang et al (24) reported that occlusion and stenosis of vertebral arteries were not significantly associated with early surgical complications.

According to studies on stroke time, the difference in the rate of surgical complications did not differ based on the quantitative intima-media thickness (QIMT) in surgical candidates. Inconsistent with the present study, Mortimer et al (25) suggested that the intima-media thickness of the carotid artery can be used to classify at-risk patients (especially moderate-risk and elderly patients) (25). The difference in internal carotid artery stenosis of the candidate for surgery based on CT angiography in patients who experienced one of the complications of CEA was not statistically significant compared to patients without complications.

Based on carotid artery CT angiography of candidates for CEA, the degree of stenosis in people with CEA complications was not statistically significant compared

with other people. Consistent with our results, Ballotta et al (26) showed that CEA was more effective than the best non-surgical treatments for symptomatic patients with stenosis above 69% in carotid angiography. However, those with symptomatic stenosis less than 50% benefited the least from CEA (26).

According to the results of the present study, there was no statistically significant relationship between unilateral or bilateral stenosis and the incidence of complications of CEA. Consistent with our results, Kazantsev et al (16) reported that unstable plaque in the medial carotid artery (bilateral stenosis) was a risk factor for long-term complications of CEA.

Suggestions

Regarding the limited number of samples and the single-center nature of the study, it is suggested that long-term multi-center studies be performed to enhance the validity of the results when deciding on a treatment approach for patients with symptomatic carotid artery stenosis.

5. Conclusion

This study found a 15% complication rate for CEA at Zanjan Vali-e-Asr Hospital, which was not significantly influenced by demographic factors or comorbidities. CEA showed low short-term (30 days) and long-term (90 days) mortality rates, with acceptable overall results. As such, CEA can be recommended for eligible patients. Compared with other studies conducted nationally and globally, CEA outcomes at this center appear relatively safe, with relatively low re-stroke rates. This study's small sample size may lead to a higher long-term mortality percentage observed.

6. Declarations

6.1 Acknowledgments

This research was conducted without external funding or assistance.

6.2 Ethical Considerations

The researcher kept patients' personal information confidential, and no cost was imposed on patients. Ethics code: A-11-340-23

6.3 Authors' Contributions

Original draft preparation and edition, SPS; project administration and supervision, ARG; professional procedure, MRT; formal data analysis, KK; CDU performance and interpretation, SN.

6.4 Conflict of Interest

The authors declare no conflicts of interest.

6.5 Fund or Financial Support

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6.6 Using Artificial Intelligence Tools (AI Tools)

No artificial intelligence tools were used in the writing or editing of this manuscript.

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