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OUTCOME OF CEREBRAL REPERFUSION PROCEDURE IN PATIENTS WITH CEREBROVASCULAR INSUFFICIENCY

By

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ABSTRACT

Background: Stroke continues to be the third leading cause of death in many countries in addition to being responsible for major disability among survivors. Therefore, stroke is actually a major health care problem and the economic burden of stroke is enormous and rapidly escalating in terms of both health care costs and lost productivity.

Objective: To assess the outcome of neurosurgical management of patients with cerebrovascular insufficiency.

Patient and Methods: A number of 43 patients with carotid artery stenosis were divided into two groups: group A 27 patients doing carotid endarterectomy (CEA) procedure and group B 16 patients doing carotid artery stenting (CAS) procedure. The patients had been recruited from inpatient hospital admission and outpatient clinics at Kafr Elsheikh University Hospital, Al-Azhar University Hospitals, Ain Shams University Hospital and Nasser institute hospital during the period from March 2018 to March 2020.

Results: Outcome was assessed postoperatively via neurologic status together with National Institute of Health Stroke Scale (NIHSS) and mini mental state examination (MMSE). At follow-ups, NIHSS and MMSE values were very similar in both groups. There was no obvious difference between the two studied groups in the postoperative complications. This study showed no statistically significant difference between groups according to both MMSE and NIHSS changes.

Conclusions: Cerebral reperfusion via carotid endarterectomy and carotid artery stenting improve the neurological state and cognitive function in addition to its well established rule in prevention in recurrent stroke.

Keywords: Atherosclerotic Carotid Artery Stenosis, Carotid Endarterectomy, Carotid Artery Stenting.

INTRODUCTION

Stroke is the third leading cause of death worldwide, and probably the most important cause of long-term disability. Approximately, 15 million people have a stroke annually, of which 5 million of die as a result of the event and another 5 million remain disabled *(Mozaffarian et al., 2016)*.

There is no widely accepted method of shielding the brain from injury during ischemic events or promoting neuronal regeneration in damaged areas. Stroke prevention, therefore, is the only available avenue for stroke treatment. Carotid

endarterectomy reduces the reported incidence of stroke alone and stroke and death in symptomatic patients with high-grade ≥70% stenoses. In addition, data presented by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) had confirmed the efficacy of CEA for ≥ 50% carotid stenosis *(Morris et al., 2017).*

Carotid artery stenting (CAS) had become widely used as an alternative to carotid endarterectomy (CEA) in revascularization therapy of carotid artery stenosis, especially in some high risk patients for surgical intervention. Long term follow up data showed that there is no significant difference in the outcome between the two procedures *(Flaherty et al., 2013).*

Carotid stenting has been established as one of the most effective procedures for the prevention of stroke in patients with carotid artery stenosis. A major concern during carotid artery stent placement is the potential for cerebral embolism. Cerebral protection devices have been developed in the last years. Preliminary results have shown that these devices can significantly reduce thromboembolic complication during CAS. However, concerns have been raised regarding these protection devices, because they add further manipulation, cost, and risk to the procedure. Diminishing the number of device manipulations across the lesion might reduce procedural stroke risk *(Altinbas et al., 2014).*

With widespread MRA, CTA, DUPLEX and DSA use, an increasing number of patients are diagnosed with carotid artery stenosis. The failure of best medical treatment (BMT) encourages doctor for the discovery of different techniques for cerebral revascularization. Carotid endarterectomy has been the gold standard treatment for carotid artery stenosis. Subsequently, less invasive technique has been used, i.e., Carotid artery stenting *(Saxena et al., 2019).*

The aim of this work was to assess the outcome of neurosurgical management of patients with cerebrovascular insufficiency.

PATIENTS AND METHODS

This study was a prospective study conducted on consecutive 43 patients with atherosclerotic carotid artery stenosis. Diagnosis was based on clinical symptoms and signs and confirmed radiologically.

The patients had been recruited from inpatient hospital admission and outpatient clinics at Kafr El-Sheikh University Hospital, Al-Azhar University Hospitals, Ain Shams University Hospital and Nasser institute hospital at the period from March 2018 to March 2020.

Preoperatively, conservative therapy for 3 to 6 months failed to improve symptoms for all cases were included.

Intervention was done for patient with the following criteria:

1. ≥ 60 % stenosis of the ICA in symptomatic patients.
2. ≥ 70 % stenosis of the ICA in asymptomatic patients.
3. ≥ 60 % stenosis of the ICA in asymptomatic patients pre-Coronary Artery Bypass Grafting (CABG) surgery.

Patients with the previous criteria were divided into 2 groups:

Group A (CAS 27 patients): included patients with one of the following criteria:

1. Age ≥ 70 years.
2. <2mm width of the lumen.
3. Visible intramural thrombus.
4. Sever tortuosity of the vessels.
5. Heavily calcified vessels.
6. Renal impairment.

Group B (CEA 16 Patients): included patients with one of the following criteria:

1. Carotid artery stenosis at or above C2.
2. Carotid artery stenosis below the clavicle.
3. With contralateral laryngeal nerve palsy.
4. With Contralateral ICA occlusion.
5. Previous Neck surgery.

All patients in this study were subjected to:

1. History taking: e.g., (age, gender, DM, smoking, hypertension, TIAs, cardiac disease, obesity).
2. Clinical examination: Clinical assessments, mini-mental-state-examination (MMSE) and National Institute of Health Stroke Scale (NIHSS) before, immediately after the procedure and after one month follow up visit.
3. Investigation: Routine laboratory investigation, brain CT or MRI to exclude other diseases, specific investigation: Doppler ultrasound or Angiography (CTA-MRA-DSA) and cerebral circulation time (CCT) affection was evaluated via DSA by counting the frames between the first and the last arterial phase pre and post intervention
4. Treatment: Medical, Endovascular (CAS) and surgical (CEA).

The patient preference was considered, after discussing the advantage and disadvantages of each procedure with the patient (unless one of these procedures was contraindicated).

For both groups of patients, an analysis was carried out on risk factors, degree of stenosis, cognitive function affection, NIHSS changes and complications that occurred (eg.stroke). Neurological examinations were performed preoperatively and during follow-up assessed NIHSS and MMSE.

An approval of the study was obtained from Al-Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis:

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data, qualitative were represented as number and percentage, quantitative was represented by Mean±SD. The following tests were used to test

differences for significance; difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent groups by t test. P value was set at <0.05 for significant results.

RESULTS

The first group (CEA) consisted of 11 males and 5 females with an average age of 65.19 years (range: 60 to 70 years). The second group (CAS) consisted of 18 males and 9 females with an average age of 62.85 years (range: 39 to 75 years) **(Table 1)**.

Table (1): Demographic data

Procedure Type / Demographic data	CAS (n=27)		CEA (n=16)	
	No.	%	No.	%
Gender				
Female	9	33.3%	5	31.3%
Male	18	66.7%	11	68.8%
Age (years)				
Range	39-75		60-70	
Mean±SD	62.85±7.20		65.19±2.69	

Regarding the risk factors in both groups, there was no statistically significant difference between them. While, there was highly statistically significant difference in the percentage of stenosis among those patients with more risk factors compared to those with less risk factors **(Table 2)**.

Table (2): Comparison between carotid duplex stenosis according to risk factors

Carotid duplex stenosis / Risk factors		<70%		≥70%		p-value
		No.	%	No.	%	
Smoking		2	9.1%	20	90.9%	<0.001
DM		6	20.0%	24	80.0%	<0.001
HTN		8	24.2%	25	75.8%	<0.001
ISHD		3	11.5%	23	88.5%	<0.001
Dyslipidemia		4	13.8%	25	86.2%	<0.001
Total risk factors	1	1	100.0%	0	0.0%	0.944
	2	3	30.0%	7	70.0%	0.179
	3	4	25.0%	12	75.0%	0.013
	4	1	11.1%	8	88.9%	0.005
	5	0	0.0%	7	100.0%	0.002

Regarding the clinical presentation of patients in both groups, it could be described. Duplex was the preferred screening test for carotid stenosis detection with the degree of stenosis **(Table 3)**.

Table (3): Clinical presentation of cases and Comparison between CAS and CEA according to carotid duplex stenosis

Procedure Type	CAS (n=27)		CEA (n=16)	
	No.	%	No.	%
Clinical presentation: Asymptomatic	7	25.9%	4	25.0%
Hemispheric	16	59.3%	9	56.3%
TIA	4	14.8%	3	18.8%
Cognitive function affection	11	40.7%	11	68.8%
Carotid duplex stenosis: <70%	5	18.5%	4	25.0%
≥70%	22	81.5%	12	75.0%

The outcome was analyzed in all patients by NIHSS an MMSE. Regarding to the NIHSS there was no statistical significant difference between the two groups pre and post intervention **(Table 4)**.

Table (4): Comparison between CAS and CEA according to NIHSS

Procedure Type / NIHSS	CAS (n=27)		CEA (n=16)	
	No.	%	No.	%
Initial NIHSS				
Zero	11	40.7%	7	43.8%
1-4 (Mild Stroke)	7	25.9%	4	25.0%
5-15 (Moderate Stroke)	8	29.6%	5	31.3%
>15 (Severe Stroke)	1	3.7%	0	0.0%
NIHSS immediately After procedure				
Zero	11	40.7%	7	43.8%
1-4 (Mild Stroke)	5	18.5%	3	18.8%
5-15 (Moderate Stroke)	10	37.0%	6	37.5%
>15 (Severe Stroke)	1	3.7%	0	0.0%
NIHSS after 1 Month	n=25		n=16	
Zero	12	40.7%	8	50.0%
1-4 (Mild Stroke)	8	29.6%	4	25.0%
5-15 (Moderate Stroke)	5	18.5%	4	25.0%

Regarding the cerebral circulation time ,it was assessed in the second group with shortness of the cerebral circulation time immediately post procedure in 100% of the cases with 33.3% improvement in the cognitive function and 55.6% shows no change in the cognitive function after one month ,which represent statistically significant relation between cerebral circulation time shortness after the procedure (as compared to pre intervention) with cognitive function after 1 month as compared to pre intervention. regarding the cognitive function 8 patients (50%) of the first group and 9 patients (33.3%) of the second group had better cognitive function ,7 patients (43.8%) of the first group and 15 patients 55.6% of the second group had same cognitive function while only one patient (6.3%) of the first group patients and one patient (3.7%) of the second group had a worse cognitive function. this shows no statistically significant difference between

CAS and CEA group of cases according to cognitive function after 1 month as compared to pre intervention *(Tables 6, 7)*.

Table (6): Comparison between NIHSS change at one month follow up in both groups

NIHSS / Procedure	No change		Improvement		Deterioration		p-value
	No.	%	No.	%	No.	%	
CAS	13	52%	11	44%	1	4%	0.855
CEA	7	43.8%	8	50%	1	6.2%	

Table (7): Comparison between CAS and CEA according to cognitive function after 1 month as compared to pre intervention

Cognitive function / Procedure	Better		Same		Worse		p-value
	No.	%	No.	%	No.	%	
CAS (n=25)	9	33.3%	15	55.6%	1	3.7%	0.593
CEA (n=16)	8	50.0%	7	43.8%	1	6.3%	

There was no obvious difference between the two studied groups in the postoperative complications. This study shows no statistically significant difference between groups according to both MMSE and NIHSS changes in both groups.

DISCUSSION

The study was conducted on 43 patients at the period from March 2018 to March 2020, and underwent either CEA or CAS procedure. Males were more frequent in our samples which were similar to what was reported in previous studies *(Werner et al., 2012* and *Ovbiagele et al., 2013)*. The mean age of our patients was 61.84±6.44 years. This coincided with *De Weerd et al. (2011)* who correlated this to the fact that with aging there is much more possibility of increase in atherosclerotic plaques in the vessel wall.

Twenty two patients in the study were cigarette smokers (51.2%). Cigarette smoking clearly confers increased stroke risk in all ages and in both sexes *(Brott et al., 2016)*. Twenty nine patients had dyslipidemia (29/43). This was in line with the fact that there is a strong relationship between total cholesterol, low-density lipoprotein cholesterol, and the extent of extra cranial carotid artery atherosclerosis and wall thickness *(Aronow et al., 2010)*.

Kernan et al. (2014) mentioned that the degree and progression of carotid atherosclerosis are directly related to lipid abnormalities. In the current study; 26 cases (26/43) had ischemic heart disease. In cardiac patients, a high prevalence of combined aortic and carotid plaques was detected *(Naylor and Bown, 2011)*. Hypertension was the most prevalent risk factor in our sample (33/43). *Newman et al. (2017)* found that hypertension accelerates the progression of atherosclerosis. Diabetes mellitus was the second most prevalent risk factor in our

sample (30/43). Diabetics are at three times risk to develop carotid stenosis than the non-diabetics *(Brasiliense et al., 2014)*.

In our study, regarding the mode of clinical presentation, thirty two cases (32/43) were symptomatic (25 cases had hemispheric weakness, 7 cases had TIA and 22 cases had cognitive affection). On the other hand, eleven cases (11 /43) had asymptomatic carotid stenosis. Transient ischemic attack is a powerful indicator of subsequent stroke. It increases stroke risk by 5-10 times. In this work, 19.3% had previous TIAs. Most of Asymptomatic carotid stenosis patients were discovered during preoperative assessment for CABG, and underwent either CAS or CEA. Studies suggested that 64% of patients with a cerebrovascular event develop dementia *(Feliziani et al., 2010)*, with fourfold increase in the risk of dementia in older patients after an ischemic stroke *(Wang et al., 2013)*.

In our study, all patients were assessed with mini mental state examination (MMSE). Among those patients only 22/43 had mild cognitive impairment according to MMSE. Carotid revascularization makes cerebral blood flow better leading to better CF *(Capoccia et al., 2010)*. Augmentation of cerebral blood flow (CBF) is thought to be achieved via cerebral revascularization a procedure which also improves the metabolism of cerebral oxygen leading to better cognitive function. Cerebral revascularization could be achieved by CAS, CEA or bypass surgery such as superficial temporal artery (STA) and middle cerebral artery (MCA) bypass in cases with proximal MCA occlusion. Other studies showed that 60% of CEA operated patients had a better cognitive function after carotid revascularization *(Gupta et al., 2011)*.

This was parallel to our study where (17/22) patients with mild cognitive impairment were improved after cerebral revascularization through CAS or CEA. The remaining 5 cases still have mild CF impairment; three of them had been operated with CEA, while the other two had been operated with CAS. In the current study, all patients were assessed with a base line initial NIHSS. Eighty cases (18/43) had Zero score, eleven cases (11/43) had mild stroke, thirteen cases (13/43) had moderate stroke and 1 case (1/43) had severe stroke according to the NIHSS. Patients eligible for study underwent noninvasive screening of the cervical carotid artery using duplex ultrasonography. A prospective study of consecutive cerebral arteriography revealed a 2.6% incidence of neurologic complications *(Karlsson et al., 2016)*. All patients were assessed by carotid duplex according to the NASCET criteria. Twenty five cases (25/43) had unilateral stenosis; eighteen cases (18/43) had bilateral stenosis. The degree of stenosis was then categorized, 9 cases (9/43) had stenosis less than 70% and 34 cases (34/43) had stenosis equal or more than 70%.

The main determinants (age, males/ females ratio, DM, HTN, dyslipidemia, ISHD, smoking, symptomatic/ asymptomatic ratio, laterality and degree of stenosis) were compared between patients of the two groups to make sure that both groups were homogenous with no selection bias. There was no significant

difference between the two groups. The patients were informed about the advantage and the disadvantage of each procedure and why this procedure is recommended for this case before intervention. The indications of endartecotmy in this work was parallel with that of *Tadros et al. (2013)*, while that of carotid artery stenting in this work was parallel with that of *Kernan et al. (2014)* and *Meschia et al. (2014)* studies. The deterioration according to NIHSS in our study was low, only in 4 cases (4/43).

The use of better tools such as the shunt in CEA cases with general anesthesia and on the other hand in CAS cases, the exchange system and the use of flexible guiding catheters instead of the long sheath together with the most important factor which is the avoidance of pre-stenting balloon dilation which was not routinely done. It was selectively done in cases with tight stenotic lesions, to allow passage of the stent across the lesion under filter protection device. Another explanation might be the younger age range of our sample. In the current study the frequency of NIHSS deterioration in CAS cases was more common on stenting of the left carotid artery versus the right carotid artery (2/1).

This finding was in accordance with what is reported by *Naggara et al. (2011)* who found that CAS performed for left ICA stenosis was associated with higher 30-day stroke and/or death rates 7.5% versus 6.0% in patients with CAS for the right carotid artery stenosis, although. In the current study, the frequency of periprocedureal clinical strokes occurred more among patients with symptomatic carotid stenosis than asymptomatic carotid stenosis. This finding was similar to the study of *Silver et al. (2011)*.

CONCLUSION

Cerebral reperfusion via carotid endarterectomy and carotid artery stenting improved the neurological state and cognitive function in addition to its well established rule in prevention in recurrent stroke with no significant difference in the outcome between both procedures. Both carotid artery stenting and carotid endarterectomy were not competitors, but different tools or weapons by which the surgeon should be armed with in the management of carotid artery stenosis.

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نتيجة إجراء إعادة التروية الدماغية في المرضى الذين يعانون من قصور الدورة الدموية الدماغية

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خلفية البحث: تعد السكتة الدماغية (الأزمة المخية) أحد الأسباب الرئيسية التي تؤدي إلى الإعاقة والموت في مصر والعالم، ويمثل ضيق الشريان السباتي بالرقبة حوالي عشرين بالمائة من أسباب السكتة الدماغية. ويمكن أن يكون ضيق الشريان السباتي بالرقبة غير مصحوبا بأعراض أومصحوبا بأعراض تتراوح مابين قصور مؤقت بالدورة الدموية المخية إلى حدوث الأزمة المخية.

الهدف من البحث: تقييم الطرق المختلفة لمواجهة قصور الدورة الدموية المخية من خلال إجراء التدخل الجراحي (استئصال سدة الشريان الثباتي العنقي) أو عن طريق القسطرة التداخلية المخية والدعامة.

المرضي وطرق البحث: تم تقسيم 43 مريضًا يعانون من ضيق في الشريان السباتي إلى مجموعتين: المجموعة أ (27 مريضا) حيث يتم إجراء إستئصال باطنة الشريان السباتي والمجموعة ب (16 مريضا) حيث يتم إجراء دعامة للشريان السباتي. وتم تنفيذ هذا البحث في مستشفى الأزهر الجامعي ومستشفى كفر الشيخ الجامعي ومستشفى عين شمس الجامعي ومستشفى معهد ناصر في الفترة من 2018مارس إلى مارس 2020.

نتائج البحث: خضع ستة عشر مريضا لجراحة إستئصال سدة الشريان الثباتي العنقي. وتم استخدام قسطرة تحويل مجرى الدم أثناء الجراحة لكل المرضى الذين خضعوا للتخدير الكلي، بينما تم إستخدام قسطرة تحويل مجرى الدم أثناء الجراحة في حاله واحده من المرضى الذين خضعوا لهذه الجراحه تحت تاثير التخدير الموضعي بسبب وجود تضيق الشريان السباتي المقابل. وقد تم رأب الشريان بواسطة رقعة صناعية في 7 حالات. تم الغلق الاساسي الأولي في 9 حالات. خضع سبعة وعشرون مريضا لتركيب دعامه مع التوسيع ببالون بواسطة القسطره التداخليه. لم تسجل وفيات في هذه الدراسه. أصيبت أربع حالات بسكتة

دماغيـــة بعـــد العمليـــة الجراحيـــة (9.8٪)، احـــداها تـــم اجـــراء تـــدخل لهـــا عـــن طريـــق القســـطره التداخليـــه ولكنهـــا تلقـــت العـــلاج الطبـــي بعـــد ذلـــك وتحســـنت. فـــي حـــين أن حـــالتين (احـــداها بعـــد القســـطره التداخليـــه والاخـــري بعـــد الجراحـــه) لا تـــزال تعـــاني مـــن تـــدهور علـــى الـــرغم مـــن تلقـــي العـــلاج الطبـــي. وقـــد تعـــذر الوصـــول إلـــى آخـــر حالـــة تدهورت للمتابعة بعد شهر.

الإســـتنتاج: ضـــخ الـــدم الـــدماغي عـــن طريـــق استئصـــال باطنـــة الشـــريان الســـباتي ودعامـــات الشـــريان الســـباتي يحســـن الحالـــة العصـــبية والوظيفـــة المعرفيـــة, بالإضـــافة إلـــى قاعدتـــه الراســـخة فـــي الوقايـــة مـــن الســـكتة الدماغيـــة المتكـــررة مـــع عـــدم وجـــود فـــرق كبير يمكن إظهاره في النتيجة بين كليهما.