Neurocognitive Improvement in Patients Undergoing Carotid Endarterectomy for Atherosclerotic Occlusive Carotid Artery Disease

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Objectives: To assess the improvement in neurocognitive functions after carotid endarterectomy (CEA) under local anesthesia (LA) in patients with carotid bifurcation occlusive disease.

Place and duration of study: Department of Vascular Surgery, Combined Military Hospital Lahore from January 2013 to January 2015.

Patients and Methods: A total of 79 patients with carotid artery occlusive disease, having no history of major stroke, depression, or dementia underwent CEA under LA. Cognitive functions were assessed 3 days before surgery and then 4 weeks and 12 weeks after the surgery using the Addenbrookes cognitive examination (ACE) score and General Practitioner Assessment of Cognition (GPCOG) Score.

Results: In ACE score, Attention, Memory, Fluency, Language, and Visuospatial orientation improved by 33.3%, 30.7%, 21.4%, 38.4%, and 31.2%, respectively, by the end of 12 weeks. An overall improvement in neurocognition was 32% (P = 0.03). In GPCOG score, Orientation, Recall, and Memory improved by 33%, 20%, and 100%, respectively, with an overall improvement of 33.3% at the end of 12 weeks (P = 0.02).

Conclusion: Both scoring systems show an overall improvement in neurocognition as well as improvements in all the subcategories in each system. Hence, we conclude statistically significant improvement in neurocognitive functions after CEA.

Keywords: cognition, endarterectomy, carotid, local anesthesia

Introduction

Occlusive disease of carotid artery can cause cerebral hypoperfusion and repeated embolic attacks. The multiple ischemic events in such patients can cause deterioration of the cognitive functions due to a major infarct or repeated smaller lacunar infarcts. In such patients, endarterectomy of the carotid vessels can help to restore the circulation to the brain and hence can improve the neurocognitive functions.1–3 A controversy still exists whether carotid endarterectomy (CEA) does significantly improve the cognition and whether this improvement is statistically significant or not? Certain studies suggest that there is no clinically significant improvement4 especially when permanent neurological damage has occurred.4–6 However, other studies recommend CEA as it results in improved neurocognition.5–8 This improvement in functions may be the result of reduction in the embolic showering9,10 or due to improvement in the blood supply to the brain.11–13 There is improvement in memory and learning as the brain recovers from chronic hypoperfusion.14–17

We aimed to answer the question whether CEA results in improvement of the neurocognition in our clinical setup. And if it does, is this improvement statistically significant to recommend the technique further?

Materials and Methods

All consecutive patients reporting to the department of Vascular Surgery in Combined Military Hospital, Lahore between January 2013 to January 2015, with documented narrowing of carotid artery occlusive disease (symptomatic and had ≥50% stenosis of carotid on duplex scan and asymptomatic patients with ≥70% stenosis) and undergoing CEA under local anesthesia (LA) were included in this study. Those patients, who had dementia, depression, 100% carotid stenosis, stenosis less than 50%, patients unwilling to participate in scoring system, and patients unwilling for surgical intervention at all, were all excluded. The demographic data
including age and gender were noted. Risk factors of atherosclerosis, that is, smoking, diabetes, and hypertension were also noted.

Patients who were already on oral aspirin and/or clopidogrel were continued on them preoperatively. LA was infiltrated using a mixture of 20 ml 2% lignocaine and 10 ml 0.5% bupivacaine diluted to a total of 50 ml. Standard approach anterior to sternocleidomastoid was used. Shunt was used selectively only in those patients who developed neurological signs on carotid clamping during the operation or have critical bilateral carotid stenosis of ≥90% on preoperative duplex scan. Neurological monitoring during cross clamping was done by observation of awake patient. Patient was asked to clinch fist and move toes on command to assess motor function. Patient was asked about his particulars and orientation to place and time to assess for confusion. Traditional CEA was performed as a routine but evasion endarterectomy was also performed in patients having long or kinking internal carotid artery. Postoperatively, patients were nursed in intensive care unit for 24 hours and then in ward till discharge. All patients received or continued on aspirin and clopidogrel postoperatively.

Cognitive functions of all patients were assessed using the standard Addenbrookes cognitive examination (ACE) Version 3 Score and General Practitioner Assessment of Cognition (GPCOG) score.\textsuperscript{18,19} Patient scores were recorded on a standard internationally predefined printed questionnaire. The preoperative and postoperative scores were compared. In ACE scoring system, points were awarded for “Attention” (18 points), “Memory” (26 points), “Fluency” (14 points), “Language” (26 points), and “Visuospatial” cognition (16 points). Patients were awarded a total numerical score out of a maximum of 100 points. Similarly in GPCOG scoring system, patients were awarded points for “Orientation” (3), “Memory” (1), and “Recall” (5), out of a total of 9. The scoring was done 3 days before the surgery, and then 4 weeks and 12 weeks after the operation by the same person.

A sample size (n) of 97 patients was calculated using 95% confidence interval (C), 10% margin of error (E), and response distribution (r) of 50%. Following formula was used.

\[ n = \frac{Nx}{(N - 1)E^2 + x} \]

where \( x = (c/100)^2 r(100 - r) \) and N is the population size.

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 20. The numerical outcomes, for example, age and cognitive score were calculated as mean. Gender was recorded as frequency and percentage. Chi-square test was applied to assess the association of various parameters. The results were considered statistically significant if the \( P \) value was found to be less than or equal to 0.05.

Results

A total of 97 patients were referred to Vascular Surgery Department for CEA in the study period. Out of these, 7.2\% (n = 7) patients had major stroke, 3\% (n = 3) had bilateral severe carotid artery stenosis (≥90\%), one (1\%) patient had complete blockade of carotid artery, 5.1\% (n = 5) were unwilling to undergo operation under LA, and 2\% (n = 2) were unwilling to participate in the study due to their remote residence and regular follow-up. Hence, these 18.6\% (n = 18) patients were excluded. The remaining 81.4\% (n = 79) patients fulfilling the inclusion criteria were included. The minimum age was 55 years and maximum was 79 years with mean age of 69 (standard deviation [SD] ± 6.4) years. In these, 87.3\% (n = 69) were males and 12.7\% (n = 10) were females with a male to female ratio of 7:1. Out of a total of 79 CEA, 83.5\% (n = 66) were performed on left side and 16.5\% (n = 13) were operated on right carotid artery. The atherosclerotic risk factors in our patients are described in Table 1. We performed 89.8\% (n = 71) conventional CEA while in 10.1\% (n = 8) patients, evasion CEA was performed due to tortuous anatomy of carotids. Shunt was used selectively in 6.3\% (n = 5) patients only; four patients developed neurological symptoms on cross clamping of carotids and one patient had severe bilateral carotid artery stenosis of more than 91\%.

In ACE scoring system (Table 2), the “Attention” span improved from 55.5\% (10 points) to 88.8\% (16 points), 4 weeks after the operation. No further improvement was recorded when it was re-assessed at 12 weeks after the operation. The overall improvement in “Attention” was 33.3\%. Similarly “Memory” improved from 61.5\% (16 points) before the operation to 84.6\% (22 points) and 92.3\% (24 points) at 4 and 12 weeks, respectively, after the operation. The overall improvement in “Memory” after 12 weeks of operation was 30.7\%. The “Fluency” also

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics and atherosclerotic risk factors</th>
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<tbody>
<tr>
<td>Total patients who had CEA (n)</td>
<td>79</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>69 (55–79)</td>
</tr>
<tr>
<td>Male gender</td>
<td>69 (87.3%)</td>
</tr>
<tr>
<td>Female gender</td>
<td>10 (12.7%)</td>
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<tr>
<td>Diabetes mellitus alone</td>
<td>40 (50.6%)</td>
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<tr>
<td>Hypertension alone</td>
<td>10 (12.6%)</td>
</tr>
<tr>
<td>Smoking alone</td>
<td>8 (10.1%)</td>
</tr>
<tr>
<td>Diabetes and hypertension</td>
<td>10 (12.6%)</td>
</tr>
<tr>
<td>Diabetes, hypertension, and smoking</td>
<td>11 (13.9%)</td>
</tr>
<tr>
<td>CEA: carotid endarterectomy</td>
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CEA: carotid endarterectomy

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Improved from 64.2% (9 points) before the operation to 85.7% (12 points) after 4 weeks of operation, with no further improvement over next 3 months, hence resulting in an overall improvement of 21.4%. Furthermore, an improvement in “Language” was also noted. It was 50% (13 points) before the operation, and it improved to 76.9% (20 points) and then to 88.4% (23 points) at 4 and 12 weeks, respectively, after the operation, giving an overall improvement of 38.4% after 12 weeks of operation. Similar trend was noted in “Visuospatial” orientation, with an improvement of score to 81.2% (13 points) and 93.7% (15 points) at 4 and 12 weeks, respectively, when compared to a preoperative score of 62.5% (10 points). The overall improvement stood at 31.2% at 12 weeks after the operation. The aggregate score was 58 before the operation and it improved by 25% to a total score of 83 after 4 weeks of operation. A further incremental improvement by 7% was noted to record a final score of 90 at 12 weeks after the operation (P = 0.03).

In GPCOG scoring system, the mean “Orientation” score was 33.3% (1 point) before the surgery and it doubled to 66.6% (2 points) after 4 weeks of operation. However, no further improvement was recorded at 12 weeks; hence, an overall improvement of 33.3% is noted. Similarly, “Recall” also improved from 60% (3 points) preoperatively to 80% (4 points) by 12 weeks after the operation. An improvement in “Memory” by 100% was recorded at 4 weeks after the operation. The overall improvement in GPCOG score at 12 weeks was 33.3% when compared to the score before the operation (P = 0.02).

Both the scoring systems show an overall improvement in neurocognition as well as improvements in all the subcategories in each system (Figs. 1 and 2).

Preoperative neurological deficit developed in 5% (n = 4) patients on cross clamping of carotids which resolved immediately on deployment of an intravascular shunt. The early postoperative complications included hematoma formation in 5% (n = 4) patients which was drained by opening the wound under LA. In all these cases, there was no bleeding from the major vessels or arteriotomy site. Local wound infection occurred in 5% (n = 4) and dropping of lower lip (temporary) in 1.2% (n = 1) cases. There was no mortality in this study.

**Discussion**

Ischemic event leading to cerebral hypoperfusion results in impairment of cognitive functions. This is due to showering of micro-emboli from the stenotic atherosclerotic carotid arteries. CEA prevents the showering of these embolic episodes and also restores adequate circulation to the brain; hence, it should improve the neurocognitive functions. However, this improvement in cognition related to CEA is still controversial.
Drinkwater et al.\textsuperscript{20} demonstrated no change in the neurocognition after CEA. Similarly, Pearson et al.\textsuperscript{13} also noted no change in the neurocognition after CEA. However, there were number of limitations in these studies such as a small group of patients, not using an internationally standardized cognition monitoring system and ill-defined exclusion criteria when selecting patients. Bossema et al.\textsuperscript{21} compared the study group with a control group. They failed to see any improvement in cognition and they concluded that the patients already had reduced neurocognition due to generalized atherosclerotic small vessels disease or other intracortical abnormalities unrelated to amendment by CEA.

On the contrary, Baracchini et al.\textsuperscript{22} showed improvement in neurocognition after CEA in elderly patients. However, the difference was not statistically significant.

Similarly, Migliara et al.\textsuperscript{23} in 7 out of 10 tests demonstrated a statistically significant improvement in the neurocognition after CEA. Lal et al.\textsuperscript{24} also concluded an overall improvement in neurocognition; however, no difference was observed when a comparison was done between CEA and carotid stenting.

Keeping in view the drawbacks in the study designs which failed to show any improvement in neurocognition, in our study, we increased the number of patients included. We also used standardized neurocognitive tests and predefined the exclusion criteria to critically assess the effect of CEA on neurocognition. The neurocognition was assessed across an array of seven different parameters in two sets of test. We were able to show statistical improvement in both sets of tests deployed. The results are comparable to international literature.

There were certain limitations in our study such as variable degree of carotid stenosis, absence of a control group, variable education level of the subjects, and small duration of follow-up. Certain confounding factors such as effects of learning during repetitive test may have influenced the outcome and must be kept in mind when assessing the end results.

**Conclusion**

CEA under LA improves cognitive functions in both symptomatic and asymptomatic patients. But keeping in view several limitations in our study, further studies with larger sample size, more specific cognitive test, and a longer follow-up are required to answer the issue of improvement in cognitive functions after CEA.

**Disclosure Statement**

All authors have no conflict of interest.

**Author’s Contributions**

Study conception: RU.
Data collection: RU and MJ.
Analysis: RU.
Investigation: IH and AAM.
Writing: RU and MJ.
Critical review and revision: IH and AAM.
Final approval of the article: RU, MJ, IH, and AAM.
Accountability for all aspects of the work: RU, MJ, IH, and AAM.

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