

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript Title:** Evaluation of ischemic lesions after carotid artery stenting with diffusion-weighted imaging

**Manuscript Type:** RETROSPECTIVE STUDY

**Manuscript No.:** 53787

**Reviewer 1 Comments:**

1. What is the prognosis of the patients with these new cerebral ischemic lesions? Does the symptom disappear?

Response: After the CAS procedure, 15 cases were found to have new ischemic lesions without any neurological symptoms and were considered silent ischemias. Three of the symptomatic cases healed without sequel in their follow ups while sequelae (minimal muscle loss) was observed in two patients. The following addition has been made in the Results section of the manuscript: "In symptomatic patients, time to symptom development, neurological symptoms and prognosis were given in Table 6."

2. The background and INTRODUCTION section is well written and provides essential information's for the readers. However, the background section is relatively simple. What is the current determined status? How about other methods? Advantages of DWI? the author should explain more extensively the MRI basic principles of DWI, that they had subsequently analysed in their experience. Moreover, it is useful specify the difference between the standard MRI and the DWI. In this way the reader would have a clearer idea about the results that will be analysed later.

Response: Since the journal format allows no more than 100 words for background section, the following limited addition has been made to this section based on the suggestion: "Diffusion-weighted imaging is an effective method for detection of silent or symptomatic acute ischemic

lesions that may arise due to CAS or carotid endarterectomy.”

3. Manuscript needs an English editing, due to some errors. Such as: 1) In Core tip section: In this retrospective study, the numbers and volumes of new ischemic lesions, cerebral parenchymal and vascular distribution were investigated after carotid artery stenting (CAS) with diffusion-weighted imaging (DWI). After CAS, despite the detection of 39 newly arising ischemic lesions after the operation. Whether “After CAS ”and “after the operation” are duplicate? 2) INTRODUCTION section: .....Among the leading causes of ischemic strokes such as transient ischemic attacks or cerebral infarction is stenosis in the proximal carotid artery as a result of atherosclerosis. It is very difficult to understand, please reword it.....

Response: Revisions and corrections have been made. Besides, the whole manuscript has been revised by a colleague of ours who had Ph.D. degree in the United States, and some minor language revisions have been made.

4. In the background section: “DWI examinations were carried out by a 1.5 T MR device one hour before and after the operations. Ischemic lesions emerging in the first 24 hours following the operation were considered new lesions”. The duration is one hour before CAS, What is the time duration after CAS? one hour? first 24 hours? Whether the author observed the new lesions 1 hour or 24 hours after CAS? It was very confusing. This issue is also the core and important issue of this article.

Response: Ischemic lesions detected in the DWI taken in the first hour after the operation were considered new lesions. However, ischemic lesions detected in DWI carried out for symptomatic cases manifesting neurological finding during the follow-ups within 5-24 hours were assumed to emerge due to CAS, and they were considered new ischemia. No new lesions were observed in the patients due to CAS after the first 24 hours. An addition has been made in Radiologic Evaluation section.

5. In front of INTRODUCTION section: the sentence: Beyhan M, Acu B, Gokce E, Firat MM. Evaluation of ischemic lesions after carotid artery stenting with diffusion-weighted imaging. Should it be deleted? Please check it.

Response: That sentence were added since the journal format required it. But it has been removed based on the suggestion.

6. Carotid endarterectomy or carotid artery stenting (CAS) are the methods proposed to prevent ischemic strokes. At present, the main and effective treatment of carotid stenosis is carotid endarterectomy or CAS. How to choose carotid endarterectomy or CAS?

Response: Based on the suggestion, the following sentences have been added to Introduction section. "CE is still the best treatment modality for symptomatic patients and the patients with carotid stenosis of over 70% (NASCET). On the other hand, CAS should be used in patients with contralateral occlusion which poses high risk in surgery, patients with anatomical variations which cause technical difficulties in surgical accessing (such as high-placement ICA bulb, history of prior neck dissection, presence of tracheostomy and radiation injury) or patients with serious comorbidities."

7. Radiologic Evaluation section: The author writed: All cases had two DWI examinations, one hour before and an hour after the procedure using a 1.5 T MR machine (Signa Excite HDx12.0 M5B software; GE Healthcare, Milwaukee, WI, US.....Ischemic lesions detected in the first 24 hours after the procedure were considered as new. What is the duration after CAS? one hour? first 24 hours? Whether the author observed the new lesions 1 hour or 24 hours after CAS? It is confusing me.

Response: Ischemic lesions detected in the DWI taken in the first hour after the operation were considered new lesions. However, ischemic lesions detected in DWI carried out for symptomatic cases manifesting neurological finding during the follow-ups within 5-24 hours were

assumed to emerge due to CAS, and they were considered new ischemia. No new lesions were observed in the patients due to CAS after the first 24 hours. An addition has been made in Radiologic Evaluation section.

8. What is the shortest time for MRI to detect new ischemic lesions? Why the the author considers 1 hour or 24 hours?

Response: New ischemic lesions were detected in DWI taken in the first hour after CAS. This has been explained in detail in answers given for the Questions 4 and 7.

9. CAS operation time (duration)?

Response: CAS procedure takes about 30 minutes, and necessary information has been added to Material and Method section.

10. What are the causes of new ischemic focus? In general, the causes of new ischemic focus are plaque falling off during operation, or falling off from stent hole after stent placement. What are the reasons in this group, and how to avoid them?

Response: As the referee mentioned, the causes of new ischemic focus due to CAS procedure are plaque falling off during operation, or falling off from stent hole after stent placement. However, since our study is retrospective and data regarding the mechanisms for the occurrence of new ischemic lesions during the operation were not given in examination reports, exact causes were not mentioned in the manuscript. However, embolic protection device had been used to prevent the plaques to produce new ischemias during the procedure.

11. Current medical guidelines suggest the use of embolism protection devices during CAS to prevent periprocedural ischemic events. What is the reason that some cases do not use embolism protection devices during CAS?

Response: Dissection, vasospasm or unfavorable anatomy, such as the type and length of aortic arches and excessive tortuosity of the carotid

arteries were the factors limiting the use of embolic protection devices (EPDs). Therefore, EPD was not used in one case (case No: 4) who underwent CAS because of stenosis due to dissection in ICA bulb. In all other cases, "Angioguard RX (Cordis)" EPDs were used.

12. Picture: good.

We would like to thank for the positive comment.

13. Tables: please refer to the format of journal.

Response: Necessary revisions have been made in Tables based on the Journal format.

### **Reviewer 3 Comments:**

1. In RESULTS part of Abstract:" The volume of the lesions detected by the two observers was 1.10 cm<sup>3</sup>." What was the sentence used to express?

Response: The average volume of new ischemic lesions calculated by the two radiologists was 1.10 cm<sup>3</sup>. An addition has been made in the Results section of the manuscript.

2. In MATERIALS AND METHODS, please provide the definition for ulcerated plaques and Corresponding MR picture.

Response: The surface properties of plaques causing stenosis were also considered on diagnostic digital subtraction angiography (DSA). Ulcerated plaques were defined as extension of contrast media beyond the vascular lumen within the plaque. In order for the reader to comprehend this point better, Figure 1 has been added to the manuscript.

3. In RESULTS, Please specify statistical methods in the purple part of the text.

Response: Statistical methods used have been added in Results section based on the suggestion.

4. In DISCUSSION, what is the basis for conclusion in the last sentence ( the purple part of the text) of paragraph 2?

Response: The following revision has been made in Discussion section: "Since

ischemic lesions were observed in watershed areas in 28.1% of our cases, hemodynamic factors along with the microembolisms were also established as factors for the development of new ischemias.”

5. The syntax and expression of the paper need to be greatly improved. Please check in the red part of the text whether there are any spelling mistakes, improper use of words, incomplete expression and so on. Please refer to other reviewers' comments.

Response: Necessary revision has been made based on the suggestion. Besides, the whole manuscript has been revised by a colleague of ours who had Ph.D. degree in the United States, and some minor language revisions have been made.

**Reviewer 2 Comments:**

The study is interesting and facing a problem extremely debated to date. The main limitations of the study are that the study is retrospective and the lack of a control group subjected to operation instead of stenting. Indeed one of the to date problem is the choice between stenting and interventional procedure. Anyway the manuscript is well written and merit to be published.

Response: We would like to thank for the positive comments of the referee.