Author's response to reviews

Title: Clinical significance of retinal emboli during diagnostic and therapeutic cardiac catheterization in patient with coronary artery disease

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Author's response to reviews: see over
Dear Sir:

Thank you for your support and give us this chance to improve our article and also thank so much for the prosperous comments of reviewers which were so helpful. We corrected all required fields, we copy edited our article by native English speaker as editor again and also include every comments of reviewers point by point and highlighted the changes as green for reviewer No 1 and blue for reviewer No 2. Here are our changes

Reviewer, Professor CH Meyer:

1) We added every required changes by the reviewer in text and highlighted it in blue

2) Our statistic consultant insisted on the equality of the number in each group and patient enrollment started and every angioplasty and angiography patients were recorded till the number of samples reach to 150 in each group and as it is evident our angio group reached to 150 earlier and sampling from angioplasty patients continued till it reached to 150 too

3) Retinal examination and the required data was added and highlighted in blue (page 7 end of eye examination)

Reviewer professor J wilentz:

1) Sampling was clarified upper in number 1

2) All required changes in text were done and highlighted in green (P2,P3,P6,P14,and P15)

3) Exclusion and inclusion criteria were redefined in page 5-6 and highlighted in green. About not including patients with normal coronary, it seems that chance of emboli in these population is much lower due to minimal atherosclerosis process in these population and also we excluded any potential source for emboli like patients with AF and significant valvular hear disease and AS to reach a true estimation of rate of retinal emboli only as complication of cardiac cath. So as reviewer mentioned we changed title to significance of retinal emboli ….. in patients with significant CAD and highlighted it in green. However to compare rate of emboli in angioplasty patient with significant CAD we need to compare it with the same population undergoing cardiac cath with significant CAD

4) As reviewer mentioned the references were cited with some error in order, we corrected the order and for the time to loss of vision we added several refrences and added the recommended reference by the reviewer. Here is several other references changes:

A) In P4 about reference 11, we used following references:


The last one was a reference of an article by Thyer et al. (number 22 in the references’ list in the end of the article) about the incidence of retinal artery embolization.

B) We found some references about the irreversible retinal damage occurred about 97 minutes after Retinal Ischemia. You can see them below and also I attached the original articles – in the file named Attachment.


4. Steele EC, Guo Q, Namura S. Filamentous Middle Cerebral Artery Occlusion Causes Ischemic Damage to the Retina in Mice. Stroke. 2008; 39; 2099-2113.

In the last reference, the research was done on Mice and the tolerance time in them reported about 60 minutes.

In the first reference you can find the tolerance time in DISCUSSION, paragraph 3, line 10.

In the second one, you can find it in Discussion, Inner versus outer retinal layer cell death. Paragraph 2, line 9. However, it believed in 2 hours for irreversible retinal damage not 97 minutes. In the third, you can find the tolerance time between 97 to 240 minutes in Discussion, Paragraph 2, line 15.

As you see, the exact time of irreversible retinal damage because of Ischemia is controversial. But the majority of researches define this time less than 2 hours. I just saw 240 minutes in two researches, one of them is number 3 in the list and the other one is: Hayreh SS, Zimmerman MB, Kimura A, Sanon A. Central Retinal Artery Occlusion, Retinal survival time. Exp Eye Res. 2004; 78: 723-736.

You can find all the references mentioned about Ischemic Retinal Damage in the attachment or you can search them on the net.
5) In our study we had just one patient with Aortic Stenosis. A 61 y/o man with the valvular area about 0.8 cm$^2$, with the pressure gradient of 60 mm Hg. He was scheduled for AVR but before operation, he should be assessed for coronary artery disease by angiography. We excluded him, because chance of emboli is much higher in this patient and it is not comparable to those without significant valvular heart disease in angioplasty group. However our exclusion criteria was to exclude any patient with significant valvular heart disease (P5)

6) About the patient mentioned in the article diagnosed with no abnormality in the visual field by physical exam (P8):

We were testing the visual field by confrontation test, we didn't do nothing more like any complementary test or exam by instruments, if we did more accurate exam like Goldmann visual field exam, Humphrey field exam, and perimetry test, definitely we could find the abnormality in the visual field. As you know confrontation test often misses scotoma in the central 10 degree. This case undergone TEE and exact visual testing and reported elsewhere and you can see the report here:

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Herein, we describe 1 case of branch retinal artery embolism following coronary artery angiography and balloon angioplasty

**Key words:**

**Case presentation**

A 65 year old man came with some visual problem in his left eye. He gave history of this problem just after coronary artery angiography and balloon angioplasty that was done for him 3 months ago. Best corrected visual acuity was 20/20 in both eye. Intraocular pressure was 14mmHg, there was no relative afferent papillary defect. Slit lamp biomicroscopy revealed clear cornea lens and vitreous, no uveitis. Visual field was grossly normal. The patient insisted on his problem despite giving reassurance for several times by another physician. On fundoscopy a tiny Hollenhorst plaque was seen in a bifurcation area of a branch of superior temporal artery and some drusen in area temporal to macula (Figure-1).

A 65 year old man presented to emergency department with a visual problem in his left eye since 3 months ago. He has undergone balloon angioplasty with drug-eluting stent just before developing symptoms. Ocular examination of his left eye was as follows: His vision was 20/20. The ocular motility was normal. His pupils were symmetric and RAPD was negative. No restricted field of vision was found in manual confrontation test. Slit lamp examination was normal with IOP=14mmHg. The patient insisted on his problem despite giving reassurance for several times by another physician. On fundoscopy a tiny Hollenhorst plaque was seen in a bifurcation area of a branch of superior temporal artery and some drusen in area temporal to macula (Figure-1).
Cardiologic examination was normal except for a s4 in auscultation. TEE was done that was all normal but only showed a grade 5 atherosclerotic plaque in ascending aorta with mobile particle on it (Figure-2).

One of the treatment modalities for this problem is laser thromboablation, that was not done for this patient because the site was close to macula and the patient had minor complaints. The patient was followed and no decrease in visual acuity was detected in 3 months follow up.

Discussion

Retinal arterial circulation obstruction has serious complications. It may result in acute visual loss, but more significantly, it implies that the patient's systemic health needs further review and investigations in order to prevent severe and life-threatening consequences such as myocardial infarction and cerebrovascular accidents. Left eye is more reported as a target for embolization after intervention on carotid artery than the right eye and it may be due to its more straight arterial supply that is directly from aorta. Breaking of atheromatous plaque happens in the time of passing the angiography camula through the aorta.

We conclude that at least a trans-thoracic echocardiography should be done in all the patients under going coronary artery angiography in order to evaluate the presence of atheromatous plaque in the beginning portion of aorta. The suspicious patients may evaluate more precise with a trans-esophageal echocardiography as well.
We could not use Retinal Angiography, since many patients refused this procedure by awareness of the complications and also it was taking so much time and money (any procedure cost about 40 USD).

7) We changed operator expertise to fluoroscopy time as reviewer nicely mentioned, page 8-9 and highlighted it in green (P12)

8) For non categorical variables we did simple Student T-test, and we did not claim anything is significant unless P was less than 0.05 (P15), however statement about power was added to page 8 under risk factors and highlighted in yellow (P15)

9) We changed the conclusion as reviewer mentioned and highlighted it in green (P15)

10) We changed the discussion as reviewer recommended at the end of discussion and highlighted it in green (P15)