Author's response to reviews

Title: Efficacy of intravitreal ranibizumab combined with Ahmed glaucoma valve implantation for the treatment of neovascular glaucoma

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Author's response to reviews: see over
Dear April Rada
Thank you very much for your letter and the comments from the referees about our manuscript (MS: 1586084483169159). We have checked the manuscript and revised it according to the comments.

Yours
Min Tang

Response to Angeline M Nguyen:
Thanks for your comments.

Major compulsory revisions:
1) Ranibizumab was allowed to be used in Ophthalmological clinic in China from 2012, just before the beginning of our study. Chinese Medical Care dose not afford this therapy, patients should pay by themselves, and it belongs to off-label use in NVG here. So it was difficult to enroll subjects by random. Every NVG patient in our hospital would be educated about IVR (effect, side-effect, risks, price, and so on), then they chose to take this therapy and signed an informed consent or not. From my point of view, the patients made their decisions mainly according to their economic base. As a non-randomized study, to certain extent, bias would be inevitable between groups.

2) IVR was used in picnic just before the beginning of our study, and mainly in AMD or PCV. No subject in our study had used Ranibizumab before. Our original intention was to exclude those who had intravitreal cortical hormone inside three months. We added this content to table 1 of revised MS.

3) We found many subjects here had done incomplete PRP or even none pre-surgery, and it might be the cause of NVG occurrence. We would try to do PRP for subjects before IVR or AGV if possible, and 2 weeks after that we evaluated again whether they needed IVR or AGV or could be enrolled. As to those who could not accept PRP due to very high IOP or corneal edema pre-surgery, we applied this therapy just after surgery, usually 1 or 2 weeks later. Our study did not take PRP as a criterion for exclusion or dropout. We added this content to table 1 of revised MS.

4) Prior injection, PRP and NVI/NVG degree and angle-closure degree were added in table 1 of revised MS.

Minor essential revisions:
1）Revised
2）Revised /line 27-30
3）We add survival analysis in revised MS
4）Revised (Inclusion criteria were reorganized in revised MS.)
5）Revised (We made explanation in method of revised MS.) / line 57-59
6）PRP is a routine therapy for severe DR or CRVO or BRVO. Even a complete PRP pre-surgery could be insufficient during follow-up to a patient. Some patients may need additional laser therapy if their retinal conditions go worse. And we believe whether PRP will affect the IOP after AGV differs from man to man. So we did not take PRP as a criterion for dropout.
7）Revised (Added in discussion of revised MS.) / line 252-254
8）Revised
Response to Pradeep Ramulu:
Thanks very much for your comments.
1) Ranibizumab was allowed to be used in Ophthalmological clinic in China from 2012, just before the beginning of our study. Chinese Medical Care do not afford this therapy, patients should pay by themselves, and it belongs to off-label use in NVG here. So it was difficult to enroll subjects by random. Every NVG patient in our hospital would be educated about IVR (effect, side-effect, risks, price, and so on), then they chose to take this therapy and signed an informed consent or not. So the anti-VEGF treatment was assigned at the discretion of the subjects. From my point of view, the patients made their decisions mainly according to their economic base. As a non-randomized study, to certain extent, bias would be inevitable between groups.
2) Revised (We added contents about NVI/NVA in table 1.)
3) Revised (We added contents about PRP in table 1.)
4) Revised (We added survival analysis in revised MS.)
5) We believe several relative high IOPs affect the results. For example: at 12 months, in control group, IOP: 12 18 18.5 19.5 19.5 19.5 20 20 20.5 20.5 21 21 25 26.5 28 29 29.5 30 mean: 22.1 std: 4.7 min: 12 max: 30 success rate: 13/19
6) We provided the follow-up time points were 2w ± 1d, 1m ± 3d, 3m ± 5d, 6m ± 7d, 12m ± 14d, we would remind every subject when the date was coming, and if subjects could not finish follow-up in time, they would be regarded as dropout cases. / line 82-83
7) We believe “mildly ligating” has two functions: Firstly, it can fix the tube on the surface of sclera; secondly, it can limit the aqueous outflow in the early stage (1~2 weeks after AGV), and it will not affect long time outflow, for we use 8-0 absorbable suture. It is a frequently-used surgical skill in AGV in China now.
8) Revised (We used LogMAR in Revised MS.)
9) Revised
10) Revised (We added Kaplan-Meier graph.)
11) Revised
12) We defined $6 \leq IOP \leq 21$ as a criterion for success, as this criterion has broadly used. But in our study, no IOP<6 was found during follow-up.
13) 3 patients in injection group and 4 patients in control group
14) The effect of using MMC in AGV for NVG is still doubted. As we know, most surgeons in China still tend to use MMC here. Really, we can not tell it is helpful or not.