Peer Review File

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First Round of Review Comments

Comment 1: Lines 106-107 mention an interval duration of days to months between embolization and microsurgery in the multistage group. Can you please include comment or discussion on factors that may determine the duration of this interval, and if you observed any trends in patient outcomes associated with shorter or longer intervals between embolization and microsurgery?

Reply 1: In fact, there was no standard for the shorter or longer intervals between embolization and microsurgery. The HO/MO modalities were grouped following the real-world study design, while not following an interventional study design. The duration of treatment intervals mainly based on the level of tolerance in bAVM patients and the objective conditions in different medical centers.

Changes in the text: N/A

Comment 2: Lines 168-170 might suggest that patients that underwent the hybrid procedure presented with more severe pathology (were "more likely to present with poor mRS… and larger AVM volume"). Can you please include discussion on why patients with more severe pathology might have been more likely to receive the hybrid procedure?

Reply 2: In the multicenter prospective cohort study, bAVM patients who received the MO treatment were derived from sub-centers, where might not have the conditions to be eligible for the one-staged hybrid operation, and were enrolled in the early stage of the construction of hybrid operation. Considering the limited objective conditions, the patient selection in the MO group were relatively conservative. Therefore, the proportion of severe pathology were lower in the MO group.

In addition, the HO modality (endovascular embolization + surgical resection) was capable of curing the bAVMs in one session. It is likely that patients with high difficulty in the MO modality would be cured under the HO modality in one session, without the risk of hemorrhage during intervals. Therefore, patients in HO group were more likely to present with poor mRS and larger AVM volume as compared to the MO group. Consequently, a 1:1 matched analysis was adopted to reduce the heterogeneity and bias in baseline characteristics between groups.

Changes in the text: N/A

Comment 3: I would recommend some clarification in the wording in lines 209 to 213. As it reads now, it seems to say that the hybrid approach is correlated with short-term neurological deficits. However, based on the odds ratio (0.110), it seems to in fact be negatively correlated with short-term neurological deficits. Can you please make this wording clearer?

Reply 3: Thank you for your careful review. We are very sorry for the unclear expression. The variables of poor neurological status (OR, 7.612; 95% CI, 1.633-35.486; p=0.010) and bAVM maximum diameter (OR, 2.010; 95% CI, 1.167-3.461; p=0.012) were risk factors for short-term NDs, and HO modality (OR, 0.110; 95% CI, 0.017-0.737; p=0.023) was the protective factor for short-term NDs. Considering reviewer's suggestion, we've made the description of predictors clearer in *Results*.

Changes in the text: After adjusting for age, sex, eloquence and deep venous drainage, poor neurological status (OR, 7.612; 95% CI, 1.633-35.486; p=0.010) and bAVM maximum diameter (OR, 2.010; 95% CI, 1.167-3.461; p=0.012) were confirmed as risk factors for short-term NDs. HO modality (OR, 0.110; 95% CI, 0.017-0.737; p=0.023) was confirmed as the protective factor for short-term NDs (Table 3) (Page 11, line 220-225).

Comment 4: Lines 258-259. You mention Pandey et al. and Kocer et al. reporting morbidities of neurological deficits to be 4.5%-5.0% in bAVMs treated with multimodal treatments. Can you please clarify at what time point these morbidities were calculated? I believe this would be helpful for comparison, as you specify the time periods (3 and 6 months) in the following sentence when referring to your own data.

Reply 4: Thank you for your careful review. We are very sorry for the unclear expression. Considering reviewer's suggestion, we've modified the description of the referenced follow-up period in *Discussion*. The 6-month NDs was 4.5% in bAVMs treated with multimodal treatments reported by Kocer et al., which were comparable to our data.

Changes in the text: Kocer et al. reported morbidities of 6-month NDs to be 4.5% in bAVMs treated with multimodal treatments (33). In our study, NDs at 6 months occurred in 5.3% of cases, conforming to the result of the previous study (Page 14, line 273-275).

Comment 5: Figure 1 shows patients drawn from a "pilot study" and "prospective cohort study". I don't see pilot study described in the methods and how this differs from the prospective cohort study. Can you please introduce or clarify what these different study populations are in the methods section?

Reply 5: Thank you for your careful review. We are very sorry for the mistake in Figure 1. Patients were all retrieved and reviewed from the database of the prospective cohort study (NCT03774017). We've made the correction of Figure 1.
Changes in the text: Please refer to Figure 1.

Second Round of Review Comments

Comment 1: Line 61 (abstract) - I think it should be clarified here that HO is a protective factor. The word "predictor" could be replaced with "protective factor".
Reply 1: Thank you for your careful review. Considering reviewer's suggestion, we've modified the description in *Abstract*.
Changes in the text: The HO modality (OR, 0.110; 95% CI, 0.017-0.737; p=0.023) was confirmed as the protective factor for short-term NDs (Page 4, Line 60).

Comment 2: Lines 198-202 - Can the P values for these comparisons be included in the text? Additionally, Lines 200-202 is difficult to understand. It could instead read "...the difference between pre and post-operative neurological function was similar between MO and HO groups at 3 months (81.8% versus 90.9% with improved or unchanged neurological function respectively, **add P value**), and at 6 months (86.4% versus 92.4% with improved or unchanged neurological function respectively, **add P value** Figure 2).
Reply 2: Thank you for your careful review. We are very sorry for the unclear expression. Considering reviewer's suggestion, we've modified the description in *Results*.
Changes in the text: the difference between pre- and post-operative neurological function was similar between MO and HO groups at 3 months (81.8% *versus* 90.9% with improved or unchanged neurological function respectively, p=0.128), and at 6 months (86.4% *versus* 92.4% with improved or unchanged neurological function respectively, p=0.258, Figure 2) (Page 11, Line 200-204).

Comment 3: Line 276 - You compare rates in your study to rates from microsurgery. Is this comparison to microsurgery without embolization? If so, please make this clear to eliminate confusion. You could simply write "...which were similar to the outcomes reported in the literature of microsurgery without embolization."
Reply 3: Thank you for your careful review. We are very sorry for the unclear expression. Considering reviewer's suggestion, we've modified the description in *Discussion*.
Changes in the text: which were similar to the outcomes reported in the literature of

microsurgery without embolization (≈96%) (Page 14, Line 278-279).