

Reviewer #1:

1.Four studies were included, the treatment time of fingolimod was after the patients were hospitalized, but the onset time of the patients during the treatment and the basic treatment methods of the patients, such as whether to undergo endovascular treatment, were not stated. This has a significant impact on the recovery of the patients.

Answering: Thank you for your question. It was our omission in writing “Inclusion and Exclusion Criteria” section of the manuscript that the onset time of the patients were less than 6 hours. And the basic treatment methods of the patients were standard treatment adhered to current American Heart Association guidelines. As far as we concerned, standard treatment included endovascular treatment. We strongly agree your comment that the onset time of the patients during the treatment and the basic treatment methods of the patients, such as whether to undergo endovascular treatment, had a significant impact on the recovery of the patients. Although only 4 studies were included, fortunately, onset time of the patients were all less than 6 hours, and all of patients received purely medical treatment in meta-analysis of fingolimod’s effect and safety. If more studies published were included, endovascular or neurosurgical treatment would be a special factor for us to perform subgroup analysis.

2.Only 4 studies were included in the article, and the author should explain the significance and necessity of making funnel plots.

Answering: Thank you for your question. Although only 4 studies were included, to perform a rigorous systemic review and meta-analysis as far as possible, we completed our study according to PRISMA 2009 Checklist strictly. Therefore, we still provided funnel plots.

3. For the clinical significance of this study, the article pointed out that "fingolimod as immunomodulator might involve the reduction of the migration of lymphocytes to central nervous system", the reference is a clinical study published on NEJM in 2018, but in fact this article did not raise this point of view, and the author should explain it.

Answering: Thank you for your question. In this clinical study published on NEJM in 2018, its "Discussion" section had showed that "A reduction in peripheral lymphocyte counts may increase the risk of infection, and infections that were reported as serious adverse events were more frequent with fingolimod than with interferon beta-1a." We considered that reduction in peripheral lymphocyte counts, which was the effect of fingolimod, might involve reduction of the migration of lymphocytes to central nervous system.

Reviewer #2:

1. Search terms in PubMed and Embase are different. Please attach syntax used in each database as supplementary.

Answering: Thank you for your question. In "Literature Search" section of our manuscript, we had provided the strategy of literature search in Embase.

2. As a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least ten study groups

Answering: Thank you for your question. Although only 4 studies were included, to perform a rigorous systemic review and meta-analysis as far as possible, we completed our study according to PRISMA 2009 Checklist strictly. Therefore, we still provided funnel plots.

3. Some revision of the english language is needed. There are some parts of the paper where it is quite difficult to make sense of some sentences English edit will help to improve the quality of the manuscript.

Answering: Thank you for your question. And we apologized that our poor level of writing in English brought out trouble to your reviewing. This time we had polished our article via native speakers of English editing.

4. Who are “two independent investigators”?

Answering: Thank you for your question. In our study, Qiang Zhang and Kai Zhao conceived the idea and designed the study. Kai Zhao and Yu Guo screened studies and extracted the data independently. Mingfei Yang and Yu Guo analysed and interpreted the data. Kai Zhao and Yu Guo wrote the first draft of the manuscript. Qiang Zhang proofread the manuscript before submission. All authors reviewed the manuscript and approved the final version.

5. It will be better to show kappa for the selection and data extraction. Please show the data of kappa of agreement during the systematic searches. How disagreements were solved during the systematic search among two independent reviewers?

Answering: Thank you for your question. We made the definition that the counts of studies selected or data extraction were positive events (+). The others were negative events (-). Kappa was calculated to test the agreement between Kai Zhao and Yu Guo. $Kappa > 0.6$ meant the high agreement. Or Qiang Zhang would make the final decision.

Agreement between Kai Zhao and Yu Guo in studies selected.

Kai Zhao		Yu Guo		Total
		+	-	

+	4	3	7
-	2	176	179
Total	6	179	185

Kappa=0.601, $p<0.001$

Agreement between Kai Zhao and Yu Guo in data extraction.

Kai Zhao	Yu Guo		Total
	+	-	
+	16	5	21
-	3	20	23
Total	19	25	44

Kappa=0.634, $p<0.001$