Peer Review File

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Reviewer A

Comment 1: One exclusion criterion was "survival less than 18 months". Is it better to use "median duration of follow up" as a better definition? (even though it did not mention any article was excluded using this criteria)

Reply 1: Thank you, we accepted your advice.

Comment 2 Another exclusion criterion, "without pathology". CNS GCT with raised serum/CSF AFP and/or HCG is widely accepted to treat without pathology. 6 articles were excluded, did they have diagnostic information such as raised serum / CSF markers?

Reply 2: In these articles, they used radiosensititcity testing or chemosensitivity testing to make a germinoma diagnosis for marker negative patients while they used raised serum/CSF AFP and/or HCG to make diagnosis of secreting GCT, but marker thresholds vary in these articles. Therefore, we did not include these articles.

Comment 3: 70 articles were excluded as "no treatment information". This is a high proportion indeed. Did they have "absolutely no treatment information"? e.g. chemo vs chemo+RT, or RT field for CNS GCT etc. It may be still useful to give a wide picture.

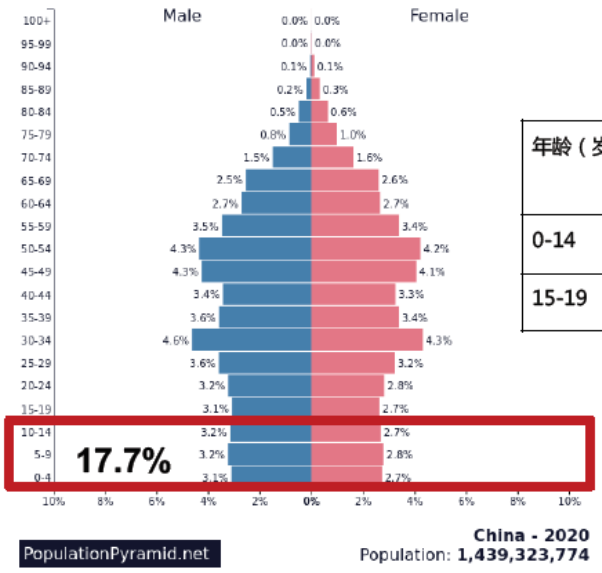
Reply 3: These articles gave very vague picture of treatment information, such as “Some patients received chemotherapy, some patients received radiotherapy, some received both.” They did not describe how many and which patients received which treatment, nor the dosing or the radiotherapy field. Therefore, we did not include these articles.

Comment 4 What is the 3yr-OS for CNS NGGCT?

Reply 4: The prognosis of the CNS NGGCT is relatively poor, patients in china tend to give up and lose contact when disease relapse or progress. So many articles in china did not give OS, just PFS for CNS NGGCT. We lose contact with these patients.

Commet 5 Line 208-209, any reference to support the number 531, and number 288/20 years? (or typo?)

Reply 5: The population in china was about 1439,323,774 according to the official data. (http://www.populationpyramid.net) We referred to website of Hong Kong Cancer Registry for cancer incidence among children and adolescents with CNS tumors between 15-19 years old because short of data in China mainland. The incidence rate of NCS tumor was 23.6/10^6 among 0-14 years old, and 15.6/10^6 among 15-24 years old. And our data from several large centers showing that at least 7.27% (hospital-based) children were diagnosed as IGCT among CNS tumors. As blow calculation (6012+1302)*7.27%=531.



2020年中国儿童CNS肿瘤（估计）病例数

年龄（岁）	比例	绝对人口数	标化发病率（1/10⁶）	新发恶性肿瘤病（例数/年）
0-14	17.7%	254,760,307	23.6	6012
15-19	5.8%	83,480,778	15.6	1302

http://www.populationpyramid.net. Accessed:13 February 2021.

Figure1. numbers of CNS tumors in china in 2020.

Comment 6 Line 245, Limitations: other limitations include level of tumor markers, e.g. AFP <1000 ng/ml vs >1000 ng/ml; response to chemotherapy before radiotherapy; residual lesion with / without 2nd look surgery. However, afraid not mentioned in most of the articles being analysed.

Reply 6: Thank you for your reminder. It is true there were limitations as you mentioned, we have added it in our context.

Comment 7 Apart from MDTs, perhaps a national treatment protocol / study would also be useful to standardise treatment within China.

Reply 7: We agreed with your wonderful advice, and we added it in our context. Thank you.

Reviewer B

Comment 1 The exclusion criteria is somewhat concerning (Lines 31, 101-102) – (1) including only articles which have a pathological diagnosis may have excluded a significant number of articles as secreting germ cell tumours (non-germinomatous germ cell tumours) are frequently diagnosed through serum/CSF tumour markers; It is noted that authors took effort to explain the reason behind this exclusion criteria; (2) including only articles with long-term survival of at least 18 months may have excluded patients whose poor outcome would affect the true prognosis of this disease, which is one of the said aims of this meta-analysis. There was no explanation for this. It was also not indicated how many studies were excluded due to this exclusion clause.

Reply 1: First, Yes, we excluded a significant number of articles as secreting germ cell tumors diagnosed through serum/CSF tumor markers, because marker thresholds varied a lot in these articles, which were not comparable. Andy Also in these articles, they tend to use radiosensititcity testing or chemosensitivity testing to make a germinoma diagnosis for marker negative patients while they used raised serum/CSF AFP and/or HCG to make diagnosis of secreting GCT. So we excluded these articles.

Second, we may not explain it clearly. “18 months”, we mean some duration of follow up, not lose contact with patient immediately after treatment. We did not exclude those patients with poor outcome or relapse. When patient relapsed or progressed, this was an Event, it was of course within our review. We excluded those papers without follow up after treatment.

Comment 2 Regarding limitations (in lines 45 & 246) – do the authors mean that publication bias was present due to large heterogeneity in the included studies as indicated by high I2, which then weaken the evidence drawn from the results?

Reply2: Regarding the NGGCT, I think the answer is yes, because of few high-quality papers are reviewed. But regarding germinomas, I is not high. The evidence was convincing.

Comment 3 Is the meaning in Lines 83-84 better conveyed as such: “It was the same case in Korea, though according to the 4th International CNS germ cell tumour symposium, surgical biopsy is reserved for patients who are marker-negative.”

Reply 3: Thank you for your advice. I have revised it in the context.

Comment 4 It would be good to correct the following grammatical mistakes: Also, some spelling errors:

Reply 4: Thank you for help. I have revised the mistakes and spelling errors.