

Peer Review File

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Reviewer A

Global assessment:

Systematic review with a correct methodology, on a subject of general interest. Included studies cover more than 6,000 patients, making this the largest meta-analysis on the subject.

Studies of bronchial artery embolisation are often retrospective, with moderate levels of evidence, and prospective controlled studies are scarce. Because of the heterogeneity of studies in this field, it is difficult to carry out meta-analyses. This study increases the level of evidence on the value of bronchial artery embolisation.

However, the introduction and discussion could be better written, and the English (grammar and syntax) must be deeply improved. The comments below are non-exhaustive suggestions for English improvement.

Abstract:

It could be improved by making it more concise, especially the sub-group analysis section (line 26 to 38), and the conclusion.

Reply: We have modified our text as advised (see Page 1 to 2, line 16 to 28).

Introduction:

It would have been interesting to mention in the introduction Ishikawa et al national study (71), which involved more than 8,000 patients but did not include any patients treated with PVA or microsphere (because it was not licensed for Japanese public health insurance), even though this is the reference treatment in Europe (CIRSE 2022).

Reply: Thanks very much for your suggestion. We have modified our text as advised (see Page 5, line 92 to 97).

Line 57 to 64: Whilst it is true that the main causes of haemoptysis vary from region to region, it is preferable to cite national or observational studies, that include all incident cases like this one Abdulmalak C, Cottenet J, Beltramo G, Georges M, Camus P, Bonniaud P, Quantin C. Haemoptysis in adults: a 5-year study using the French nationwide hospital administrative database. *Eur Respir J.* 2015 Aug;46(2):503-11. doi: 10.1183/09031936.00218214. Epub 2015 May 28. PMID: 26022949, rather than studies that only include patients who have undergone BAE, such as citations 11 and 12.

Reply: We express our sincere appreciation to you for your invaluable feedback and illustrative example. We have modified our text as advised (see Page 3, line 56 to 65).

Line 65 to 71: Should be in Methods section.

Reply: We have modified our text as advised (see Page 7, line 133 to 138).

Line 75 to 78: « Conservative treatment carried the potential for relapse and negatively impacts both patient quality of life and long-term survival and in patients with massive hemoptysis, the

mortality rate even exceeds 50% with conservative treatment » Unclear, please rewrite.

Reply: We are very sorry for our unclear writing and we have rewritten the sentence as advised (see Page 4, line 69 to 73).

Line 79: Typo.

Reply: We feel sorry for our carelessness. In our resubmitted manuscript, the typo is revised. Thanks for your correction.

Line 79 and 80: Bronchoscopy is useful because it can also provide a histological diagnosis, for example to prove that haemoptysis is secondary to cancer or infection. However, in cases of excessive bleeding, bronchoscopy may not be appropriate.

Reply: We have modified our text as advised (see Page 4, line 73 to 77).

Methods:

Good.

Reply: We are grateful for your positive feedback.

Results:

The figures are interesting and clear.

Reply: We are grateful for your positive feedback.

The text would benefit from being more concise.

Reply: Thank you for your feedback. We have modified our text as advised (see Page 10, line 212 to 216).

The classification in subgroups with regard to the type of embolisation material is not clear. For example, table 1 shows only one study using exclusively NBCA and only one using exclusively gelfoam, but the S5 supplement shows that 3 studies were classified in the NBCA subgroup and 2 studies in the gelfoam subgroup.

Reply: Thank you for your comments. Table 1 of this paper presents three articles discussing the use of NBCA as an embolization material for treating hemoptysis (Lee (2022), Woo (2013), Jurado (2023)). Jurado et al.'s study exclusively used NBCA, while Lee (2022) and Woo (2013) divided patients into NBCA and PVA groups. Subgroup analysis specifically focusing on NBCA was conducted for these three groups, as detailed in Tables S1 to S5.

Table 1 also includes seven articles discussing the use of GS as an embolic material in the treatment of hemoptysis (Yan(2023), Han(2019), Pei(2014), Chen(2014), Racil (2013), Anuradha(2012), Hahn(2010)). Pei(2014) specifically focused on the use of GS for treatment, while Hahn(2010) compared outcomes between patients treated with GS and PVA. The remaining five studies did not observe the effects of BAE treatment with GS alone. Subgroup analysis specifically focusing on GS was conducted for Pei (2014) and Hahn (2010)' study, as detailed in Tables S1 to S5.

Discussion:

Line 229: Please delete « so we undertook this study ».

Reply: We have modified our text as advised.

Line 229 to 233: Unclear, please rewrite.

Reply: We are very sorry for our unclear writing and we have rewritten the sentence as advised (see Page 11 to 12, line 239-245).

Line 254: Unclear; did they really embolized subclavian artery ? Or Just it's branches ?

Reply: We are very sorry for our unclear writing. We have corrected “embolized 97.9% of the subclavian artery or its branches through the radial artery approach” into “Research indicated that the radial or brachial artery approach could be viable options for culprit arteries originating from the subclavian or axillary arteries” (see Page 12, line256 to 258).

Line 240 to 270: This section seems to be out of topic, and does not analyse the results of the study.

Reply: Thank you for your comments. In this section, we have elucidated the reasons behind the enhanced technical success and reduced recurrence rates of BAE after 2017. According to suggestions, we have modified our text to make this part more concise (see Page 12, line250 to 260).

The rest of the discussion is more interesting but deserves to be way more concise.

Reply: Thank you for your feedback. We have modified our text as advised. Additionally, we have enlisted the help of a native English speaker from the USA to further polish our article.

Line 259 and 416: Please replace interventional physicians by interventional radiologists.

Reply: We have corrected the “interventional physicians” into “interventional radiologists” (Page 2, line 44; Page 19, line 415; Page 21, line 447).

Line 334: Please replace « one-year hemoptysis free survival » by « one-year survival ».

Reply: We sincerely thank the reviewer for careful reading. As suggested by the reviewer, we have corrected the “one-year hemoptysis free survival” into “one-year survival” (Page 15, line 324).

Line 368: The article quoted does not mention which embolisation material was used, and does not justify the statement that precedes it (this statement should be removed, it is strange to promote the use of a combination of GS and non-absorbable material, without explaining it scientifically).

Reply: Thank you for your suggestions. We have modified our text as advised (see Page 17, line 354 to 355).

Line 370: Price may not be the main argument, as some pushable coils are cheaper than microspheres.

Reply: Thank you for your suggestions. We have modified our text as advised (see Page 17, line 356 to 359).

Line 381: It would have been interesting to explain why the Japanese mainly use coils (as PVA and microspheres have only recently been authorised).

Reply: Thank you for your suggestions. We have modified our text. (see Page 17, line 368 to 369).

Please delete line 413.

Reply: We have modified our text as advised.

Line 433 to 444: Instead of talking about renal and uterine embolisation, it would have been interesting to talk about the new studies on NBCA embolisation in haemoptysis, which could not be included in the analysis of the study because they were published after August 2023.

Reply: Thank you for your suggestions. We have modified our text as advised (see Page 19, line 397 to 416).

Conclusion:

Please rewrite more concisely, mentioning BAE's safety.

Reply: Thank you for your suggestions. We have modified our text as advised (see Page 21, line 442 to 447).

Please remove the sentence about SA-PF.

Reply: We have modified our text as advised.

Tables, Figures and Supplementary:

Please add NOS score values in Table 1.

Reply: We have modified the table1 as advised (see table1).

Please replace Orkun with Sarioglu (table 1 and Figures) and Thomas with Le Tat (table 1, Figures and line 334).

Reply: We have modified the text, table 1 and Figures (see Page 15, line 323; table 1 and Figure 2-6).

Reviewer B

Another meta-analysis concerning BAE without surprising results, but with subgroup-analysis. This is the notable difference when compared to other meta-analysis, so "subgroup-analysis" should be mentioned already in the title.

Reply: Thank you very much for your kindness comment, we have modified the title as advised (see Page 1, line 1 to 2).

Text needs linguistic and grammatical improvement.

Reply: Thank you for your feedback. We have modified our text as advised. Additionally, we have enlisted the help of a native English speaker from the USA to further polish our article.

Content-related comments, mainly to the discussion:

In general: The CIRSE-guideline should be mentioned (CIRSE Standards of Practice on Bronchial Artery Embolisation - see below) at any point.

Reply: Thanks very much for your suggestions. We have modified our text as advised (see Page 5, line 89 to 90; Page 19, line 404 to 406).

line 226: Current metaanalysis do exist (for example: Karlafti, Zheng - see below), they should be mentioned.

Reply: We have modified our text as advised (see Page 11 to 12, line 242 to 243).

line 247: BAE ain't a surgical procedure.

Reply: We apologize for our oversight. We have revised the statement "reduced surgical duration" to "reduced the BAE procedure time and X-ray exposure" (see Page 12, line 252).

Thank you for pointing out the error.

line 250: What is meant by "non-bronchial systemic arteries (NBSAs)? Are these "non-bronchial systemic collaterals" or "systemic-artery-to-pulmonary(-artery) fistula" (SA-P(A)F). Unfortunately, in general there is much confusion concerning appropriate terminology/nomenclature for the same pathological change. I would call it SA-PAF or SA-PF.

Reply: Thank you very much for your kindness comment, we have revised the statement "non-bronchial systemic arteries (NBSAs)" to "non-bronchial systemic collaterals" (see Page 3, line 54).

line 251: What is an "abnormal bronchial artery" (AbBA)? Just a dilated BAE with tortuous hypertrophy or an aberrant, ectopic BAE? The abbreviation AbBA is a bit unusual and also used for "aberrant bronchial arteries" and should be avoided.

Reply: Thank you very much for your kindness comment, we have revised the statement "abnormal bronchial artery (AbBA)" to "ectopic bronchial arteries" (see Page 12, line 259).

line 407, 408: The statements of Woo et al. (14) already in 2013 "BAE with NBCA provided higher hemoptysis-free survival rates compared with PVA particles without increasing complication rates" and Lee et al. (32) in 2022 "BAE using NBCA showed significantly superior initial hemostasis with longer haemoptysis-free survival, shorter procedure time, and reduced radiation dose than BAE using PVA particles" are clear: NBCA is superior to PVA for BAE. Unfortunately, this is not sufficiently reflected in the actual CIRSE-Standards of Practice ("NBCA is not recommended for the treatment of haemoptysis until the provider has gained significant familiarity with its behaviour in other settings") and even not in your conclusion. Please explain this.

Reply: The comments provided by you have been greatly appreciated and have helped enhance the quality of our manuscript. Woo and Lee et al. have demonstrated that NBCA has advantages over PVA in the treatment of hemoptysis in their research. However, compared with other embolic materials, the application of NBCA in the treatment of hemoptysis is still limited. The main reason for this limitation is that the skilled application of NBCA requires a long learning curve to avoid potential risks such as premature polymerization, microcatheter tip adhesion, reflux, and ectopic embolism. As described in the CIRSE standards of Practice, NBCA is not recommended for the treatment of hemoptysis by operators who are not experienced in its use. Nevertheless, NBCA remains a promising embolic material for the treatment of hemoptysis, and further evidence-based research is needed to confirm its effectiveness. Additionally,

standardized training protocols for interventional radiologists should be established. We have revised our text (see Page 19, line 400 to 416).

line 461: The conclusion concerning NBCA should be modified (see above).

Reply: We have modified our text as advised (see Page 21, line 444 to 447).

Additional references:

Kettenbach, J., Ittrich, H., Gaubert, J.Y. et al. CIRSE Standards of Practice on Bronchial Artery Embolisation. *Cardiovasc Intervent Radiol* 45, 721–732 (2022).

Karlafti E, Tsavdaris D, Kotzakioulafi E, Koungias L, Tagarakis G, Kaiafa G, Netta S, Savopoulos C, Michalopoulos A, Paramythiotis D. Which Is the Best Way to Treat Massive Hemoptysis? A Systematic Review and Meta-Analysis of Observational Studies. *J Pers Med*. 2023 Nov 26;13(12):1649. doi: 10.3390/jpm13121649. PMID: 38138876; PMCID: PMC10744930.

Zhiyuan Zheng, Zhiquan Zhuang, Minjie Yang, Jianjun Luo, Wen Zhang, Zhiping Yan, Xiaolin Wang, Bronchial artery embolization for hemoptysis: A systematic review and meta-analysis, *Journal of Interventional Medicine*, Volume 4, Issue 4, 2021, Pages 172-180, ISSN 2096-3602

Reply: Thanks very much for your suggestions. We have added these references as advised (see Page 24, line 520 to 521; Page 29, line 619 to 623).

Reviewer C

In the manuscript entitled Efficacy, Safety and Related Factors of Bronchial Artery Embolization for Hemoptysis: A Systematic Review and Meta-Analysis, authors comprehensively review the literature. Their meta-analysis identifies technical, clinical success rates as well as failures, recurrences, and mortality over the 13-year period of published studies. Finally, they perform specific subgroup analyses to further dissect the factors that contribute to success and recurrence.

The study is well-designed and the manuscript is well-written. I learned quite a bit and look forward to using the manuscript in my practice.

I have no major recommendations for the authors.

Reply: We are grateful for your positive feedback.

I have minor recommendations:

Table 1 - this is jumbled in my version of the manuscript and may require some editing

Reply: Thanks very much for your suggestions. We have modified table 1 as advised (see table1).

Figure 7 Funnel plots - the text is extremely small and hard to read - please consider making these larger. Also, I cannot find the related figure legend. Perhaps consider labeling the specific

outcome that is being evaluated in the funnel plot for ease of reading.

Reply: Thanks very much for your suggestions. We have modified our text and Figures as advised (see Page 33, line 733 to 737; Figure 7-11).