

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comparison of Two Anterior Fusion Methods in Two level Cervical Spondylosis Myelopathy: A Meta-Analysis
AUTHORS	Huang, Zhe-Yu; Wu, Ai-Min; Li, Qing-Long; Lei, Tao; Wang, Kang-Yi; Xu, Hua-Zi; ni, wenfei

VERSION 1 - REVIEW

REVIEWER	Burkhardt, Jan Department of Neurosurgery, Zurich, Switzerland
REVIEW RETURNED	19-Jan-2014

- The reviewer completed the checklist but made no further comments.

REVIEWER	Dr Bernet Kato Medical Statistician IMPERIAL COLLEGE LONDON UNITED KINGDOM
REVIEW RETURNED	04-Feb-2014

GENERAL COMMENTS	<p>1. Major comments</p> <p>This paper reports the results of a meta-analysis to evaluate the efficacy and safety of two treatments for cervical spondylitis myelopathy (CSM) namely anterior cervical corpectomy and fusion (ACCF) and Anterior cervical discectomy and fusion (ACDF). The authors note that controversies still exist between ACCF and ACDF. This work would be of considerable interest in clinical practice as systematic reviews of the best available evidence for efficacy and safety of the two treatments can inform decision making.</p> <p>Strengths and limitations of the study</p> <p>Another limitation that should be added is that the number of studies used in the meta-analysis is small (9 studies). In fact for most of the outcomes the studies used in the meta-analyses are less than 5.</p> <p>Introduction</p> <p>Page 5: The authors mention that the aim of the meta-analysis is to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM. It is not clear in the paper how "efficacy" and "safety" were evaluated. The authors should clarify</p>
-------------------------	--

	<p>this.</p> <p>Page 5: It is worthwhile to mention that ACCF and ACDF are surgical procedures. Furthermore some references that highlight the controversies that exist between ACCF and ACDF should be provided.</p> <p>Materials and Methods</p> <p>Eligibility Criteria</p> <p>Page 6 – criteria for inclusion: criterion (3) is not clear.</p> <p>Page 6 – criteria for exclusion: criteria (1) and (2) are not clear.</p> <p>Data extraction</p> <p>It is not clear what types of research studies were looked at by the authors (randomized control studies, case control studies,) and what sort of data was extracted (means and standard deviations/standard errors, odds ratios,). The authors should shed more light on this.</p> <p>The authors use the term “parameters” in several places including tables S1, S2, S3a, S3b and S3c: for example intraoperative parameters, clinical parameters. I think that in this context the right word should be “outcomes”.</p> <p>Statistical Analysis</p> <p>Meta-analysis is a statistical procedure that pools the results of several independent studies considered by the analyst to be combinable. The authors mention that for continuous outcomes, means and standard deviations were pooled to generate a standardised mean difference (and 95% confidence intervals). Did they pool means or mean differences. If they pooled mean differences from each study, what were the mean differences in each study measuring? The authors should clarify these issues.</p> <p>Page 7, last sentence mentions that “The source of heterogeneity was investigated by subgroup analysis and sensitivity analysis”. Under results the authors do not show any results from the subgroup and sensitivity analyses.</p> <p>Results</p> <p>Risk of bias assessment - this section is not clear to a reader. It needs to be re-written. Furthermore, I could not find Tables 1, 2 and 3 which are referred to on page 9.</p> <p>Discussion</p> <p>Out of the 606 potential reports looked at during the search only 9 reports satisfied the inclusion criteria. On page 14 under the discussion it is mentioned that of the 9 studies used in the meta-analysis, there were just 3 studies that reported on randomization. If</p>
--	---

	<p>there was no randomization in the other 6 studies, were confounders adjusted for in the analyses to compare subjects who underwent ACCF to those who underwent ACDF? The authors should highlight this as it is a potential source of bias to the results in the original studies.</p> <p>Conclusion</p> <p>The first sentence states that “Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other ...”</p> <p>Subsequently the second sentence states “This information gives surgeons a deeper understanding of the difference between the two surgeries”. I think this is too strong a statement and should be toned down given that the authors have just mentioned that they could not draw any firm conclusions regarding the superiority of one treatment over the other. The results should be interpreted with caution as they are based on a rather small sample size (fewer than 10 studies).</p> <p>Author Contributions</p> <p>It is mentioned that ZYH, AMW and WFN conceived and designed the experiments. ZYH, AMW and WFN performed the experiments. I thought this was a meta-analysis. Therefore it is not clear to me what sorts of experiments were designed and performed. This needs to be clarified.</p> <p>2. Minor comments</p> <p>There are a number of grammatical errors in places – the authors should go through the paper again and make the necessary corrections. For example:</p> <p>Page 3: the last sentence under results in the abstract could read “We found that ACDF has significantly lower blood loss (SMD= 1.70, 95% CI: [0.62, 2.78]),...”</p> <p>Page 5: first sentence in the third paragraph should read “ACDF and ACCF are two widely used ...”</p> <p>Page 5: last sentence should read “The keywords used for the search were: “cervical spondylitis myelopathy”,</p>
--	---

REVIEWER	Ankit Mehta Johns Hopkins University USA
REVIEW RETURNED	10-Mar-2014

GENERAL COMMENTS	The paper provided a meta-analysis of ACDF compared to ACCF. The ACDF outcomes demonstrate an improvement compared to ACCF. However the pathological processes are not always the same an inherent limitation of the study.
-------------------------	---

REVIEWER	Mohammed F. Shamji Toronto Western Hospital, Toronto, Ontario, Canada I am the first author on a paper that explores this specific question of discectomy vs. corpectomy.
REVIEW RETURNED	27-Mar-2014

GENERAL COMMENTS	<p>The authors undertook defining the benefit of different procedures for cervical spondylotic myelopathy. This is a study of significance and the authors are to be applauded for undertaking this work. Several major revisions and explanations are necessary prior to being accepted for publication:</p> <p>Flaw - in the October 2013 issue of Spine, there is a systematic review and meta-analysis examining precisely this issue, about multilevel anterior cervical discectomy/corpectomy. It is not cited and the material here is similar. At the very least, that study must be cited. It is unclear what this study adds beyond that work.</p> <p>Flaw - as in the conclusion, the authors state that they "could not draw any firm conclusions regarding superiority of one treatment over the other". What is the contribution of this work to the broader literature? It is unclear that anything new is being contributed.</p> <p>Methods - the search strategy may be overly-limiting by indicating "single-level" or "two-level", whereby several useful papers drawing comparisons between multi-discectomy and corpectomy are regrettably missed. I would suggest redoing the search with more rigorous manual review of the manuscripts.</p> <p>Writing - this manuscript would benefit substantially from an English-language proofreader - many of the comments are colloquial, often confusing, and sometimes wrong as written.</p> <p>Discussion - do the authors truly feel that a randomized controlled trial of multi-discectomy versus corpectomy is warranted? They cite this, but do not recognize the feasibility, challenge with determining appropriate inclusion criteria. If no retro-vertebral disease, why do a corpectomy in the face of the data they and others have already shown? If there is retro-vertebral disease, why consider only a multi-discectomy? To say that RCT is required will require justification.</p> <p>Conclusion - the authors must clarify what new is added to the literature based on their contribution.</p>
-------------------------	---

VERSION 1 – AUTHOR RESPONSE

Replies to Reviewer Name Dr Bernet Kato:

Comment 01:

Strengths and limitations of the study:

Another limitation that should be added is that the number of studies used in the meta-analysis is small (9 studies). In fact for most of the outcomes the studies used in the meta-analyses are less than 5.

Answer: Thank you for your point out of this. We really appreciate it. In 1955, Robinson RA and Smith GW1 report the anterior procedures to treat cervical spondylosis myelopathy, the development of the two anterior methods is just more than 50 years, it is difficult for us get more studies into our work, especially for searching the studies which only focus on the two-adjacent-level CSM. After we search for PubMed (1966-2013), Cochrane Central Register of Controlled Trials (Issue 9 , 2013), ScienceDirect (1985-2013), CNKI(1996-2013), WANFANG DATA(1997-2013), CQVIP(1996-2013), there are only nine studies meeting our criteria. Thank you again.

Comment 02:

Introduction:

Page 5: The authors mention that the aim of the meta-analysis is to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM. It is not clear in the paper how “efficacy” and “safety” were evaluated. The authors should clarify this.

Answer: Thank you for your careful review. We compare the two surgical procedures of perioperative, clinical, radiographic and complications results. From perioperative and complications results, we can learn which surgery is more effective. The other two aspects explain that the safety of the ACCF and ACDF. The efficacy and safety between the two operations are still controversies. We learn that no significant difference was identified between the two groups regarding hospital stay, JOA, neck and arm pain VAS, total cervical ROM, fusion ROM, fusion rate, adjacent-level ossification, and complications. While ACDF has significantly less blood loss (SMD = 1.14, 95% CI: [0.74, 1.53]), shorter operative time (SMD =1.13, 95% CI: [0.82, 1.45]), greater cervical lordosis both total cervical (SMD= -2.95, 95% CI: [-4.79,-1.12]) and fused segment (SMD= -2.24, 95% CI: [-3.31,-1.17]), higher segmental height(SMD= -0.68, 95% CI: [-1.03,-0.34]), and less graft subsidence (SMD=0.40, 95% CI: [0.06,0.75]). Thank you again.

Page 5: It is worthwhile to mention that ACCF and ACDF are surgical procedures. Furthermore some references that highlight the controversies that exist between ACCF and ACDF should be provided.

Answer: Thank you for your advice. There is considerable controversy as to which procedure is more better for patient with cervical spondylosis myelopathy between ACCF and ACDF. Chang et al.2 support the treatment of choice for cervical disc herniation and spondylotic radiculopathy or myelopathy is ACDF. Lu et al.3 think ACCF is an effective surgical procedure for the treatment of multilevel cervical myelopathy because it can remove almost all pathology causing spinal cord compression like osteophytes, discs, and ossified PLL. As your suggestion, we added “Shamji et al.4 and Jiang et al.5 had reviewed the efficacy and safety of anterior procedures for patients with multilevel CSM, covering the patients with two-adjacent-level CSM, which both of them did not pay attention to. Chang et al.2 support the treatment of choice for cervical disc herniation and spondylotic radiculopathy or myelopathy is ACDF. Lu et al.3 think ACCF is an effective surgical procedure for the treatment of multilevel cervical myelopathy because it can remove almost all pathology causing spinal cord compression like osteophytes, discs, and ossified PLL. KAZUO et al.19 and Mamoru et al.20 think that ACDF and ACCF are both widely used anterior methods for CSM especially with two levels. And patients with two-adjacent-level CSM often can be seen in clinical practice, while controversies still exist between ACCF and ACDF for patients with two-adjacent-level CSM when comparing perioperative, clinical, radiographic and complications outcomes. This meta-analysis is to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM.” into

Introduction Part. Thank you.

Comment 03:

Eligibility Criteria

Page 6 – criteria for inclusion: criterion (3) is not clear.

Page 6 – criteria for exclusion: criteria (1) and (2) are not clear.

Answer: Thank you for your comment. As your suggestion, we clear the criteria for inclusion and criteria for exclusion.

Criteria for inclusion: 1) ACCF with titanium mesh, cage or autologous ilium bone grafting, ACDF with interbody cage devices or autologous ilium bone grafting, moreover the two surgeries both used anterior cervical plate and screw fixation. 2) All patients included with a confirmed CSM at two adjacent segments that recommended surgical intervention. 3) The trials have been followed up for more than 12 months. (Materials and Methods Part, Page 5 Line 13-21)

Criteria for exclusion: 1) The studies did not meet the inclusion criteria. 2) Do not extract the data what we compare. 3) The number of samples was less than 30 cases. 4) The patients evaluated come from the same hospital. (Materials and Methods Part, Page 6 Line 1-3) Thank you again.

Comment 04:

Data extraction

It is not clear what types of research studies were looked at by the authors (randomized control studies, case control studies,) and what sort of data was extracted (means and standard deviations/standard errors, odds ratios,). The authors should shed more light on this.

Answer: Thank you for your point out of this. The types of research studies include randomized control studies, non-randomized control studies, prospective studies and retrospective studies. As a result, Two studies are randomized controlled trials,^{6 7} one study is a quasi-RCT, in which patients were allocated according to sequence of hospitalization,⁸ the other six studies are all not randomized controlled trials.⁹⁻¹⁴ For continuous data, such as hospital stays, bleeding amounts and operation times, means and standard deviations were extracted. For dichotomous data, such as fusion rate, degeneration of the adjacent-level and complications, the risk ratio (RR) were extracted. (Data extraction Part) Thank you again.

authors use the term “parameters” in several places including tables S1, S2, S3a, S3b and S3c: for example intraoperative parameters, clinical parameters. I think that in this context the right word should be “outcomes”.

Answer: Thank you for your suggestion. Intraoperative outcomes, consisting of hospital stays, bleeding amounts, operation times. Clinical outcomes, including Japanese Orthopedic Association scores(JOA), Visual Analog Scale scores(VAS) for neck and arm pain. Radiologic outcomes, such as cervical lordosis for total cervical and fused segment, total cervical range of motion, segmental range of motion, graft collapse, segmental height, fusion rate, degeneration of the adjacent-level. AS your suggestion, we use the word “outcomes” instead of “parameters” in this context. Thank you again.

Comment 05:

Statistical Analysis

Meta-analysis is a statistical procedure that pools the results of several independent studies considered by the analyst to be combinable. The authors mention that for continuous outcomes, means and standard deviations were pooled to generate a standardised mean difference (and 95% confidence intervals). Did they pool means or mean differences. If they pooled mean differences from each study, what were the mean differences in each study measuring? The authors should clarify these issues.

Answer: Thank you for your suggestions. We extract the means and standard deviations of each studies in which continuous data are looked at. Using the Review Manager 5.2 software (Cochrane Collaboration, Oxford, UK), we obtain the corresponding standardised mean difference (SMD) and

95% confidence intervals (CI), for example the data of hospital stay in Oh 20096, the standardised mean difference (and 95% confidence intervals) is 0.2 (-0.51, 0.91)(Fig. 2a). (Statistical Analysis Part) Thank you again.

Page 7, last sentence mentions that "The source of heterogeneity was investigated by subgroup analysis and sensitivity analysis". Under results the authors do not show any results from the subgroup and sensitivity analyses.

Answer: When the test for heterogeneity was $P < 0.1$ or $I^2 > 50\%$ indicated very high heterogeneity, the source of heterogeneity was investigated by subgroup analysis and sensitivity analysis. In our meta-analysis, Four outcomes (bleeding amounts, operative time, fused segment height and graft collapse) have a high heterogeneity. Wu et al. summarized a method to deal with the heterogeneity in meta-analysis.²⁴ For bleeding amounts, we think that there exit a methodological heterogeneity because of different research types. From the sensitivity analysis(Fig.S1), we can easily learn that the result of Jia 2012¹⁷ has a significantly heterogeneity which should be removed. And we owe the heterogeneity to the operative ability of surgeons, and the subgroup SMD and 95%CI were adopted to represent the outcomes of bleeding amounts because of the clinical homogeneity, the results of subgroup analysis about bleeding amounts was showed in Fig.2b. About operative time, we think that there also exit a methodological heterogeneity because of different research types. From the sensitivity analysis(Fig.S2), we can easily learn that the result that ACDF has shorter operative time will not be reversed regardless of which study was removed. So we owe the heterogeneity to the operative ability of surgeons, and the total SMD and 95%CI were adopted to represent the outcomes of operative time because of the clinical homogeneity, the results of subgroup analysis about operative time was showed in Fig.3. As to fused segment height, there exit a clinical heterogeneity, Oh et al.¹¹ and Burkhardt et al.¹⁴ define the fused segment height as the distance between the midlines of involved cranial vertebral bodies and caudal vertebral bodies. Jia et al.¹⁷ did not describe the method to measure the fused segment height. While Liu et al.¹⁸ and Kim et al.¹⁹ reported the anterior and posterior height of involved vertebral bodies. In summary, for fused segment height, we pooled the data of Oh et al.¹¹ and Burkhardt et al.¹⁴, the outcome is displayed in Fig.6a. With regard to graft collapse, no significant clinical heterogeneity and methodological heterogeneity are found, we consider that there exit a statistical heterogeneity, so we also pooled the two studies.^{12 15} The result is showed in Fig.6b. (Statistical Analysis Part) Thank you again.

Comment 06:

Results

Risk of bias assessment - this section is not clear to a reader. It needs to be re-written. Furthermore, I could not find Tables 1, 2 and 3 which are referred to on page 9.

Answer: Thank you for your comment. As your suggestion, we have re-written the part of risk of bias assessment. For three randomized studies,⁶⁻⁹ two studies are randomized controlled trials,^{7 8} one of which did not provide the information of allocation concealment. One study is a quasi-RCT, in which patients were allocated according to sequence of hospitalization.⁹ Due to the informed consent right of procedures between patients and doctors, it was impossible to perform blinding of participants and personnel. All of the three studies did not reported blinding of outcome assessment. No patients were lost to follow-up except for Liu et al.,⁷ in which eight patients were excluded, since the missing data was small in number, which also balances in both arms, we considered it as low risk of bias of incomplete outcome data addressed. In the three trials, the outcomes were provided in detail, we regarded them as low risk of bias of selective reporting. Owing to insufficient information to assess whether an important risk of bias existed in a number of trials, we argued all trials had unclear risk of bias towards other potential sources of bias. The methodological quality assessment was summarized in Table 1a. For six non-randomized studies,⁹⁻¹⁴ according to the modified MINORS criteria,¹⁶ all of them did not report the unbiased assessment of the study endpoint, the same to the item of prospective calculation of the study size. With regard to prospective collection of data, three studies did not report the relevant information.^{10 12 14} Only one study reported the follow up rate.¹¹ The

other eight items were all reported definitely. In summary, scores ranged from 16 to 18, with a median value of 16.5. The methodological quality assessment was summarized in Table 1b. (Risk of bias assessment Part, Page 7 Line 21-22 and Page 8 Line 1-19) Thank you again.

Comment 07:

Discussion

Out of the 606 potential reports looked at during the search only 9 reports satisfied the inclusion criteria. On page 14 under the discussion it is mentioned that of the 9 studies used in the meta-analysis, there were just 3 studies that reported on randomization. If there was no randomization in the other 6 studies, were confounders adjusted for in the analyses to compare subjects who underwent ACCF to those who underwent ACDF? The authors should highlight this as it is a potential source of bias to the results in the original studies.

Answer: Thank you for your point out of this. In our meta-analysis, three randomized studies⁶⁻⁸ were assessed with the Cochrane Handbook for Systematic Reviews of Interventions, six non-randomized studies⁹⁻¹⁴ were evaluated according to the methodological index for non-randomized studies (MINORS) criteria, an established method for evaluating non-RCTs.¹⁶ As your suggestion, we rewrite the part of Risk of bias assessment. For three randomized studies,⁶⁻⁹ two studies are randomized controlled trials,^{7 8} one of which did not provide the information of allocation concealment. One study is a quasi-RCT, in which patients were allocated according to sequence of hospitalization.⁹ Due to the informed consent right of procedures between patients and doctors, it was impossible to perform blinding of participants and personnel. All of the three studies did not report blinding of outcome assessment. No patients were lost to follow-up except for Liu et al.,⁷ in which eight patients were excluded, since the missing data was small in number, which also balances in both arms, we considered it as low risk of bias of incomplete outcome data addressed. In the three trials, the outcomes were provided in detail, we regarded them as low risk of bias of selective reporting. Owing to insufficient information to assess whether an important risk of bias existed in a number of trials, we argued all trials had unclear risk of bias towards other potential sources of bias. The methodological quality assessment was summarized in Table 1a. For six non-randomized studies,⁹⁻¹⁴ according to the modified MINORS criteria,¹⁶ all of them did not report the unbiased assessment of the study endpoint, the same to the item of prospective calculation of the study size. With regard to prospective collection of data, three studies did not report the relevant information.^{10 12 14} Only one study reported the follow up rate.¹¹ The other eight items were all reported definitely. In summary, scores ranged from 16 to 18, with a median value of 16.5. The methodological quality assessment was summarized in Table 1b. (Risk of bias assessment Part, Page 7 Line 21-22 and Page 8 Line 1-19) Thank you again.

Comment 08:

Conclusion

The first sentence states that "Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other ..."

Subsequently the second sentence states "This information gives surgeons a deeper understanding of the difference between the two surgeries". I think this is too strong a statement and should be toned down given that the authors have just mentioned that they could not draw any firm conclusions regarding the superiority of one treatment over the other. The results should be interpreted with caution as they are based on a rather small sample size (fewer than 10 studies).

Answer: Thank you for your recommendation. In our meta-analysis, we found that ACDF was associated with significantly less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence. These information give surgeons a preliminary understanding of the difference between the two surgeries to treat two-adjacent-level CSM. Further high-quality RCT and longer follow-up duration are needed to assess the two treatments. As your suggestion, we revised the Conclusion Part. Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other, but

ACDF has some advantages such as less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence. These information give surgeons a preliminary understanding of the difference between the two surgeries to treat two-adjacent-level CSM and will be helpful to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. Further high-quality RCT and longer follow-up duration are needed to assess the two treatments.(Conclusion Part, Page 17 Line 12-20) Thank you again.

Comment 09:

Author Contributions

It is mentioned that ZYH, AMW and WFN conceived and designed the experiments. ZYH, AMW and WFN performed the experiments. I thought this was a meta-analysis. Therefore it is not clear to me what sorts of experiments were designed and performed. This needs to be clarified.

Answer: Thank you for your comment. The experiments refer to this meta-analysis, ZYH, AMW and WFN conceived the subject of this meta-analysis, search the related literature, arrange and analysis the data and so on. (Author Contributions Part)

Minor comments

There are a number of grammatical errors in places – the authors should go through the paper again and make the necessary corrections. For example:

Page 3: the last sentence under results in the abstract could read “We found that ACDF has significantly lower blood loss (SMD= 1.70, 95% CI: [0.62, 2.78]),...”

Page 5: first sentence in the third paragraph should read “ACDF and ACCF are two widely used ...”

Page 5: last sentence should read “The keywords used for the search were: “cervical spondylitis myelopathy”,

Answer: Thank you for your point out of these grammatical errors. The revised manuscript has been edited and proofread by a english teacher in Wenzhou university, wenzhou, China.

Replies to Reviewer Name Ankit Mehta:

Comment 01:

The paper provided a meta-analysis of ACDF compared to ACCF. The ACDF outcomes demonstrate an improvement compared to ACCF. However the pathological processes are not always the same an inherent limitation of the study.

Answer: Thank you for your careful review and positive comments. It is difficult for us to get enough studies in our meta-analysis with the patients having the same pathological process, this is an unavoidable limitation in our work. However, all patients had symptoms and signs of neural compression at the two adjacent segments that were refractory to conservative treatment. Thank you for your point out of this.

Replies to Reviewer Name Mohammed F. Shamji

Comment 01: In the October 2013 issue of Spine, there is a systematic review and meta-analysis examining precisely this issue, about multilevel anterior cervical discectomy/corpectomy. It is not cited and the material here is similar. At the very least, that study must be cited. It is unclear what this study adds beyond that work.

Answer: Thank you for your valuable suggestion. The systematic review published in the October 2013 issue of Spine is a well work, with whose points we agree very much, meanwhile we cite the points of that study in Introduction Part, however there are still differences between my study and that work. Our work focuses on two-adjacent-level CSM, about which we analyses more details, while the systematic review published in the October 2013 issue of Spine expresses the viewpoint of ACCF and ACDF to treat multilevel cervical spondylotic myelopathy.Thank you again.

Comment 02:

As in the conclusion, the authors state that they "could not draw any firm conclusions regarding superiority of one treatment over the other". What is the contribution of this work to the broader literature? It is unclear that anything new is being contributed.

Answer: Thank you for your point out of this. Although several aspects indicate that ACDF was associated with significantly less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence, our work is based on just 9 studies, we can not draw the conclusion sloppy that ACDF is more advantage than ACCF or ACCF is more better than ACDF. Our study offers several information to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. As your suggestion, we clear the Conclusion Part. Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other, but ACDF has some advantages such as less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence. These information give surgeons a preliminary understanding of the difference between the two surgeries to treat two-adjacent-level CSM and will be helpful to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. Further high-quality RCT and longer follow-up duration are needed to assess the two treatments.(Conclusion Part, Page 17 Line 12-20) Thank you again.

Comment 03:

Methods - the search strategy may be overly-limiting by indicating "single-level" or "two-level", whereby several useful papers drawing comparisons between multi-discectomy and corpectomy are regrettably missed. I would suggest redoing the search with more rigorous manual review of the manuscripts.

Answer: Thank you for your suggestion. Shamji et al.⁴ and Jiang et al.⁵ had reviewed the efficacy and safety of anterior procedures for patients with multilevel CSM, including the patients with two-adjacent-level CSM, about which both of them did not produce special studies. Patients with two-adjacent-level CSM often can be seen in clinical practice, while controversies still exist between ACCF and ACDF for patients with two-adjacent-level CSM when comparing perioperative, clinical, radiographic and complications outcomes. So we compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM. According to your suggestion, we redoing the search without the limitation of single-level or two-level, a total of 994 potential reports were retrieved with the new search strategy. 70 studies report the anterior surgeries to treat the patients with multilevel CSM, some of them involve the two-adjacent-level CSM, however we can not extracted the data to be compared from them.(Methods Part) Thank you again.

Comment 04:

Writing - this manuscript would benefit substantially from an English-language proofreader - many of the comments are colloquial, often confusing, and sometimes wrong as written.

Answer: Thank you for your point out of these grammatical errors. The revised manuscript has been edited and proofread by a english teacher in Wenzhou university, wenzhou, China.

Comment 05:

Discussion - do the authors truly feel that a randomized controlled trial of multi-discectomy versus corpectomy is warranted? They cite this, but do not recognize the feasibility, challenge with determining appropriate inclusion criteria. If no retro-vertebral disease, why do a corpectomy in the face of the data they and others have already shown? If there is retro-vertebral disease, why consider only a multi-discectomy? To say that RCT is required will require justification.

Answer: Thank you for your comment. The aim of our meta-analysis is to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM. As our work is based on just 9

studies, further high-quality RCT and longer follow-up duration are needed to assess the two treatments. Thank you again.

Comment 06:

Conclusion - the authors must clarify what new is added to the literature based on their contribution.

Answer: Thank you for your point out of this. As your suggestion, we clear the Conclusion Part. Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other, but ACDF has some advantages such as less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence. These information give surgeons a preliminary understanding of the difference between the two surgeries to treat two-adjacent-level CSM and will be helpful to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. Further high-quality RCT and longer follow-up duration are needed to assess the two treatments.(Conclusion Part, Page 17 Line 12-20) Thank you again.

Replies to Editor:

Comment 01:

Strengths and limitations need rewriting as they are not self critical enough nor provide enough detail.

Answer: Thank you for your comment. 1) ACCF and ACDF are both effective and safe for treating CSM in our study. 2) ACDF has more advantages than ACCF in some aspects. 3) The trials in our study are not the high-quality RCTs, and do not have long enough follow-up duration. 4) The number of studies used in the meta-analysis is small (9 studies). In fact for most of the outcomes the studies used in the meta-analyses are less than 5. 5) The pathological processes are not always the same for the patients studied.(Strengths and limitations Part, Page 3 Line 14-20) Thank you again.

Comment 02:

Introduction – this is too short with no references to any controversy. How does this review compare with say this one from 2012? (their ref 15) <http://www.ncbi.nlm.nih.gov/pubmed/21968573>

Answer: Thank you for your point out of this. We really appreciate it. As your suggestion, the Introduction Part has been revised as followed: Cervical spondylosis is a common disease and a progressive degenerative process of the cervical spine result in loss of disc height and formation of osteophyte. When it develops into cervical spondylosis myelopathy (CSM), motion abnormalities and sensory disturbances will follow, resulting in decreasing life quality of patients.¹⁷ Surgical intervention is recommended for these patients with severe symptoms.¹⁸

The choice between an anterior, posterior, or combined approach for decompression is based primarily on (1) the sagittal alignment of the spinal column, (2) the extent of disease, (3) the location of compressive abnormality, (4) the presence of preoperative neck pain, and (5) previous operations.¹⁸

Shamji et al.⁴ and Jiang et al.⁵ had reviewed the efficacy and safety of anterior procedures for patients with multilevel CSM, covering the patients with two-adjacent-level CSM, which both of them did not pay attention to. Chang et al.² support the treatment of choice for cervical disc herniation and spondylotic radiculopathy or myelopathy is ACDF. Lu et al.³ think ACCF is an effective surgical procedure for the treatment of multilevel cervical myelopathy because it can remove almost all pathology causing spinal cord compression like osteophytes, discs, and ossified PLL. KAZUO et al.¹⁹ and Mamoru et al.²⁰ think that ACDF and ACCF are both widely used anterior methods for CSM especially with two levels. And patients with two-adjacent-level CSM often can be seen in clinical practice, while controversies still exist between ACCF and ACDF for patients with two-adjacent-level CSM when comparing perioperative, clinical, radiographic and complications outcomes. This meta-analysis is to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM.(Introduction Part, Page 4 Line 3-22 and Page 4 Line 1-3) Thank you again.

Comment 03:

Many of the references are to Asian/ Chinese journals – what about the wider literature?

Answer: We searched electronic databases including PubMed (1966-2013), Cochrane Central Register of Controlled Trials (Issue 9 , 2013), ScienceDirect (1985-2013), CNKI(1996-2013), WANFANG DATA(1997-2013), CQVIP(1996-2013). Finally nine studies are included. Although some of them are come from Asian/ Chinese journals, they are all satisfied with our Eligibility Criteria. As to the other references, they are also helpful to compare the efficacy and safety of ACCF and ACDF for patients with two-adjacent-level CSM. Thank you again.

Comment 04:

We need more information on the methods and inclusion and exclusion criteria (can you provide the search?) and the choice of databases.

Answer: We searched electronic databases including PubMed (1966-2013), Cochrane Central Register of Controlled Trials (Issue 9 , 2013), ScienceDirect (1985-2013), CNKI(1996-2013), WANFANG DATA(1997-2013), CQVIP(1996-2013). The keywords used for the search were: "cervical spondylosis myelopathy", "anterior cervical discectomy and fusion", "anterior cervical corpectomy and fusion", "two level(s)", or "single-level"). The search strategy is showed in Fig.1. As your suggestion, we clear the inclusion and exclusion criteria. Criteria for inclusion: 1) ACCF with tatanium mesh, cage or autologous ilium bone grafting, ACDF with interbody cage devices or autologous ilium bone grafting, moreover the two surgeries both used anterior cervical plate and screw fixation. 2) All patients included with a confirmed CSM at two adjacent segments that recommended surgical intervention. 3) The trials have been followed up for more than 12 months. (Materials and Methods Part, Page 5 Line 13-21)

Criteria for exclusion: 1) The studies did not meet the inclusion criteria. 2) Do not extract the data what we compare. 3) The number of samples was less than 30 cases. 4) The patients evaluated come from the same hospital. (Materials and Methods Part, Page 6 Line 1-3) Thank you again.

Comment 05:

It's at least a search of more than one database, although searching Science Direct is unusual I think (this is the Elsevier platform can you explain this decision in the paper?).

Answer: Thank you for your comment. As our university has bought this database, we have access to it for searching the studies we wanted for free. Thank you again.

Comment 06:

You don't say how you resolved differences of opinion between yourselves.

Answer: Thank you for your point out of this. Although several aspects indicate that ACDF was associated with significantly less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence, our work is based on just 9 studies, we can not draw the conclusion sloppy that ACDF is more advantage than ACCF or ACCF is more better than ACDF. Our study offers several information to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. As your suggestion, we clear this content. Based on this meta-analysis, we could not draw any firm conclusions regarding the superiority of one treatment over the other, but ACDF has some advantages such as less blood loss, shorter operative time, greater cervical lordosis both total cervical and fused segment, higher segmental height, and less graft subsidence. These information give surgeons a preliminary understanding of the difference between the two surgeries to treat two-adjacent-level CSM and will be helpful to clinical surgeons for choosing the surgeries to treat the patients with two-adjacent-level CSM. Further high-quality RCT and longer follow-up duration are needed to assess the two treatments.(Conclusion Part, Page 17 Line 12-20) Thank you again.

Comment 07:

We were not sure about this: you included studies 'regardless of published and unpublished' but we know what you mean, we think (that you searched grey literature? but how?).

Answer: Thank you for your point out of this. We search the unpublished literature from the academic conference of spinal surgery and the peers I recognised. However, they all do not meet the eligibility criteria. I know that there are a lot of unpublished literature, and it is almost impossible for us to search all of them. So we revised this sentence as follow: We identified all comparative studies of adopting ACCF and ACDF to treat adjacent two-level cervical spondylosis, searched reference lists of articles, and included studies to identify other potentially eligible studies.(Eligibility Criteria Part, Page 5 Line 13-16) Thank you again.

Comment 08:

Please improve the English; you may need professional help with this

Answer: Thank you for your point out of these grammatical errors. The revised manuscript has been edited and proofread by a english teacher in Wenzhou university, wenzhou, China.

Comment 09:

We need a baseline table describing each study in the paper.

Answer: Thank you for your point out of this. The baseline table is displayed in Table 2 and 3.Thank you again.

Reference

1. Robinson RA, Smith GW. Anterolateral cervical disc removal and interbody fusion for cervical disc syndrome. *SAS Journal* 2010;4(1):34-35.
2. Chang WC, Tsou HK, Chen WS, Chen CC, Shen CC. Preliminary comparison of radiolucent cages containing either autogenous cancellous bone or hydroxyapatite graft in multilevel cervical fusion. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia* 2009;16(6):793-6.
3. Lu J, Wu X, Li Y, Kong X. Surgical results of anterior corpectomy in the aged patients with cervical myelopathy. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2008;17(1):129-35.
4. Shamji MF, Massicotte EM, Traynelis VC, Norvell DC, Hermsmeyer JT, Fehlings MG. Comparison of anterior surgical options for the treatment of multilevel cervical spondylotic myelopathy: a systematic review. *Spine* 2013;38(22 Suppl 1):S195-209.
5. Jiang SD, Jiang LS, Dai LY. Anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion for multilevel cervical spondylosis: a systematic review. *Archives of orthopaedic and trauma surgery* 2012;132(2):155-61.
6. Min Chul Oh M, Ho Yeol Zhang, MD, Jeong Yoon Park, MD, and Keun Su Kim, MD. Two-Level Anterior Cervical Discectomy versus one-level corpectomy in cervical spondylotic myelopathy. *Spine* 2009;34(7):692-96.
7. Yong Liu LC, Yong Gu, Yun Xu, Hui-Lin Yang, Tian-Si Tang. Comparison of two anterior decompression bone fusion treatments plus titanium plate implantation for two-level cervical spondylotic myelopathy. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2011;15(4):597-601.
8. You-Lai Yu W-CG, Bing Xin. The comparison of therapeutic eff icacy between two operative methods for the treatment of two-adjacent-level CSM. *Medical College Journal of Qiqihaer* 2007;28(23):2821-23.
9. Park Y, Maeda T, Cho W, Riew KD. Comparison of anterior cervical fusion after two-level discectomy or single-level corpectomy: sagittal alignment, cervical lordosis, graft collapse, and adjacent-level ossification. *The spine journal : official journal of the North American Spine Society* 2010;10(3):193-9.
10. Jeffrey C. Wang PWM, Kevin K. Endow, and Rick B. Delamarter. A Comparison of Fusion Rates Between Single-Level Cervical. *Journal of Spinal Disorders* 2001;14(3):222-25.

11. Burkhardt JK, Mannion AF, Marbacher S, et al. A comparative effectiveness study of patient-rated and radiographic outcome after 2 types of decompression with fusion for spondylotic myelopathy: anterior cervical discectomy versus corpectomy. *Neurosurgical focus* 2013;35(1):E4.
12. Feng-Bin Yu D-YC, Xin-Wei Wang, Xiao-Wei Liu. Radiographic comparison of anterior cervical fusion after two-level discectomy or single-level corpectomy for two-level cervical spondylotic myelopathy. *National Medical Journal of China* 2012;92(37):2636-40.
13. Xiao-Lin Jia Z-JT, Fu-Bin Yang, et al. Comparision between single-level cervical corpectomy and two-level discectomy in two-adjacent-level cervical spondylotic myelopathy. *Orthopedic Journal of China* 2012;20(21):1931-34.
14. Kim MK, Kim SM, Jeon KM, Kim TS. Radiographic Comparison of Four Anterior Fusion Methods in Two Level Cervical Disc Diseases : Autograft Plate Fixation versus Cage Plate Fixation versus Stand-Alone Cage Fusion versus Corpectomy and Plate Fixation. *Journal of Korean Neurosurgical Society* 2012;51(3):135-40.
15. Tai-xiang Wu G-jL, Jing Li. Some Risk of Affecting the Quality of Published Systematic Reviews. *Chinese J Evidence-Based Medicine* 2005;5(1):51-58.
16. KAREM SLIM EN, DAMIEN FORESTIER, FABRICE KWIATKOWSKI, YVES PANIS AND JACQUES CHIPPONI. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J. Surg.* 2003;73(9):712-16.
17. Joseph T. King J, M.D., M.S.C.E., Kathleen A. McGinnis, M.S., Mark S. Roberts, M.D., M.P.P. QUALITY OF LIFE ASSESSMENT WITH THE MEDICAL OUTCOMES STUDY SHORT FORM-36 AMONG PATIENTS WITH CERVICAL SPONDYLOTIC MYELOPATHY. *NEUROSURGERY* 2003;52(1):113-21.
18. Rao RD, Gourab K, David KS. Operative treatment of cervical spondylotic myelopathy. *The Journal of bone and joint surgery. American volume* 2006;88(7):1619-40.
19. KAZUO YONENOBU M, TAKESHI FUJI, MD, KEIRO ONO, MD, KOZO OKADA, MD, TOMIO YAMAMOTO, MD, and NORIMASA HARADA, MD. Choice of Surgical Treatment for Multisegmental Cervical Spondylotic Myelopathy. *CERVICAL SPONDYLOTIC MYELOPATHY* 1985;10(8):710-16.
20. Mamoru Kawakami MTT, MD; Hiroshi Iwasaki, MD; Munehito Yoshida, MD; Muneharu Ando, MD; and Hiroshi Yamada, MD. A Comparative Study of Surgical Approaches for Cervical Compressive Myelopathy. *CLINICAL ORTHOPAEDICS AND RELATED RESEARCH* 2000;381:129-36.

VERSION 2 – REVIEW

REVIEWER	Dr. BERNET KATO STATISTICIAN NATIONAL HEART AND LUNG INSTITUTE IMPERIAL COLLEGE LONDON UNITED KINGDOM
REVIEW RETURNED	28-May-2014

GENERAL COMMENTS	<p>The authors have addressed most of the issues I raised in the review.</p> <p>However, some outstanding issues remain. These are:</p> <p>Page 32, line 5: criteria for exclusion: criterion (2) is still not clear. Probably it is better to drop it all together.</p> <p>Page 33, line 15: It is mentioned that “Fixed effects model was used for data with homogeneity, while a random effects model was used for data with high heterogeneity”. The decision to use either a fixed effects or random effects model for the meta-analysis should be decided apriori rather than basing it on the results.</p> <p>Page 36: The authors refer to “subgroup analyses” and “sensitivity analyses” that were conducted for bleeding amounts and operative time. Please clarify the objective of the subgroup and sensitivity analyses and explain the results referring to the information in the</p>
-------------------------	--

	<p>corresponding tables and figures. For instance how do the sensitivity analyses for bleeding amounts and operative time confirm the stability of these outcomes (line 6 and 13)?</p> <p>Page 38, line 18: It is mentioned that "Fig 6b, no significant clinical heterogeneity and methodological heterogeneity are found, we consider that there exit a statistical heterogeneity, so we also pooled the studies". Please clarify what you mean by clinical, methodological and statistical heterogeneity and how you come to the conclusion above.</p> <p>Pages 58 and 59: Please clarify what these graphs are showing and what we learn from them.</p> <p>Author Contributions:</p> <p>It is mentioned that ZYH, AMW and WFN conceived and designed the experiments. ZYH, AMW and WFN performed the experiments. I thought this was a meta-analysis. Therefore it is not clear to me what sorts of experiments were designed and performed. Please clarify.</p>
--	--

REVIEWER	<p>Mohammed F. Shamji Toronto Western Hospital, University of Toronto, Canada</p>
REVIEW RETURNED	07-May-2014

GENERAL COMMENTS	<p>The authors have attempted to address several of the concerns introduced during the first review. There are still many shortcomings that require comment or revision:</p> <p>1) The authors repeatedly discuss "high quality RCT" but do they truly feel that a randomized controlled trial of multi-discectomy versus corpectomy is warranted? They cite this, but do not recognize the feasibility, challenge with determining appropriate inclusion criteria. If no retro-vertebral disease, why do a corpectomy in the face of the data they and others have already shown? If there is retro-vertebral disease, why consider only a multi-discectomy? To say that RCT is required will require justification.</p> <p>2) Conclusion - the authors must clarify what new is added to the literature based on their contribution.</p>
-------------------------	--

VERSION 2 – AUTHOR RESPONSE

Replies to Reviewer Name Mohammed F. Shamji

Comment 01:

The authors repeatedly discuss "high quality RCT" but do they truly feel that a randomized controlled trial of multi-discectomy versus corpectomy is warranted? They cite this, but do not recognize the feasibility, challenge with determining appropriate inclusion criteria. If no retro-vertebral disease, why do a corpectomy in the face of the data they and others have already shown? If there is retro-vertebral disease, why consider only a multi-discectomy? To say that RCT is required will require justification.

Answer: Thank you for your comment. We are very sorry for our unclear expression. As to those patients with severe congenital canal stenosis, such as serious ossification of posterior longitudinal ligament(OPLL), ACDF will not be adopted because the overall anteroposterior diameter of the canal

is not increased by the procedure.¹ While for those patients with no retro-vertebral disease or mild retro-vertebral disease, ACDF and ACCF are both suitable. In our meta-analysis, ACDF and ACCF are both appropriate to treat the patients with two-level-adjacent CSM, while controversies still exist between ACCF and ACDF for patients with two-adjacent-level CSM when comparing perioperative, clinical, radiographic and complications outcomes. Accordingly, further high-quality RCT and longer follow-up duration are needed. Thank you again.

Comment 02:

Conclusion - the authors must clarify what new is added to the literature based on their contribution.

Answer: Thank you for your suggestion. Shamji et al.² and Jiang et al.³ had reviewed the efficacy and safety of anterior procedures for patients with multilevel CSM. However, the focus of our work is on the two-adjacent-level CSM, which is different from Shamji et al.¹ and Jiang et al.²'s work, and this is also the major contribution of our work. In our meta-analysis, ACDF has some advantages such as less blood loss, a shorter operation time, greater cervical lordosis both in the total cervical and fused segments, a higher segmental height, and less graft subsidence. However, no significant differences in JOA, VAS, ROM, or complications were found. This information will provide surgeons a preliminary understanding of the differences between the two surgeries to treat two-adjacent-level CSM and will be helpful to clinical surgeons for choosing which surgical method to treat patients with two-adjacent-level CSM. Further high-quality RCTs and longer follow-up durations are needed to assess these two treatments. (Conclusion Part, Page 18 Line 12-22) Thank you again.

Replies to Reviewer Name Dr Bernet Kato:

Comment 01:

Page 32, line 5: criteria for exclusion: criterion (2) is still not clear. Probably it is better to drop it all together.

Answer: Thank you for your comment. As your and editor's suggestion, we clear the criteria for exclusion Part. Criteria for exclusion: 1) The studies did not meet the inclusion criteria. 2) The intraoperative outcome data (length of hospital stay, amount of bleeding, and operation time), clinical outcomes (Japanese Orthopedic Association (JOA) score and visual analog scale (VAS) score for neck and arm pain), radiological outcomes (cervical lordosis for total cervical and fused segments, total cervical range of motion (ROM), segmental ROM, graft collapse, segmental height, fusion rate, and degeneration of the adjacent-level), or complications (short-term and long-term complications) were not reported. 3) The number of samples was less than 30 cases. 4) The patients evaluated were treated at the same hospital. (Criteria for exclusion Part, Page 6 Line 5-13) Thank you again.

Comment 02:

Page 33, line 15: It is mentioned that "Fixed effects model was used for data with homogeneity, while a random effects model was used for data with high heterogeneity". The decision to use either a fixed effects or random effects model for the meta-analysis should be decided apriori rather than basing it on the results.

Answer: Thank you for your point out of this. As your suggestion, we clear the content as follow: A fixed effects model was used for homogeneous data, and a random effects model was used for data with high heterogeneity. As for the data with significant methodological heterogeneity, sensitivity analysis was adopted to find the source of the heterogeneity. With regard to the data with significant clinical heterogeneity, subgroup analyses were applied to identify the source of the heterogeneity. (Statistical Analysis Part, Page 7 Line 21-22 and Page 8 Line 1-5) Thank you again.

Comment 03:

Page 36: The authors refer to "subgroup analyses" and "sensitivity analyses" that were conducted for

bleeding amounts and operative time. Please clarify the objective of the subgroup and sensitivity analyses and explain the results referring to the information in the corresponding tables and figures. For instance how do the sensitivity analyses for bleeding amounts and operative time confirm the stability of these outcomes (line 6 and 13)?

Answer: Thank you for your recommendation. We have revised this part. For the bleeding amount, it was reasonable to perform sensitivity analysis (Fig. S1) because of the different research types. As shown in Fig. S1, the results of Jia 2012⁴ have significant heterogeneity, which should be removed. The bleeding amount results are shown in Fig. 2b. Regarding the operation time, sensitivity analysis was performed to analyze the data because of the different research types. As shown by the sensitivity analysis results (Fig. S2), ACDF had a shorter operation time that could not be reversed regardless of which study was removed. Therefore, the heterogeneity did not come from the methodological heterogeneity. Accordingly, there probably exists clinical heterogeneity. Due to the strict eligibility criteria, the patient data had a good homogeneity; thus, the heterogeneity was due to the ability of the surgeons. The subgroup analysis results regarding operation time are shown in Fig. 3. (Discussion Part, Page 17 Line 4-17) Thank you again.

Comment 04:

Page 38, line 18: It is mentioned that "Fig 6b, no significant clinical heterogeneity and methodological heterogeneity are found, we consider that there exist a statistical heterogeneity, so we also pooled the studies". Please clarify what you mean by clinical, methodological and statistical heterogeneity and how you come to the conclusion above.

Answer: Thank you for your point out of this. We clear this part as follow: With regard to graft collapse, as the two literature examples are both retrospective studies, it is believed that no methodological heterogeneity existed. Regarding the clinical heterogeneity, the patient data had a good homogeneity due to the strict eligibility criteria and the fact that the methods of measuring the graft collapse were the same. As a result, no significant clinical heterogeneity or methodological heterogeneity was found. However, statistical heterogeneity likely existed, so the studies were pooled. (Discussion Part, Page 18 Line 1-8) Thank you again.

Comment 05:

Pages 58 and 59: Please clarify what these graphs are showing and what we learn from them.

Answer: Thank you for your comment. As your suggestion, we have revised the Figure Legends Part. Fig. 1: The search strategy for our meta-analysis and reasons for exclusion.

Fig. 2: Perioperative parameters. a: Forest plot and tabulated data for length of hospital stay; no significant difference between the two types of surgery was observed. b: Forest plot and tabulated data for bleeding amount; the ACDF group had significantly less intraoperative bleeding than the ACCF group.

Fig. 3: Perioperative parameters. Forest plot and tabulated data for operation time; the ACDF group had a significantly shorter surgical time compared to the ACCF group.

Fig. 4: Clinical parameters. a: Forest plot and tabulated data for JOA; b: Forest plot and tabulated data for neck VAS; c: Forest plot and tabulated data for arm VAS. There were no significant differences in these parameters between the two types of surgery.

Fig. 5: Radiological parameters. a: Forest plot and tabulated data for C2-C7 Cobb; b: Forest plot and tabulated data for fusion Cobb; c: Forest plot and tabulated data for total cervical ROM; d: Forest plot and tabulated data for fusion ROM. The ACCF group had a significantly lower Cobb than the ACDF group. There was no significant difference in the cervical or fusion ROM between the two types of surgery.

Fig. 6: Radiological parameters. a: Forest plot and tabulated data for the fused segment height; the ACCF group had a significantly lower fused segment height than the ACDF group. b: Forest plot and tabulated data for graft collapse; the ACDF group had a significantly lower graft collapse than the ACCF group.

Fig. 7: a: Forest plot and tabulated data for fusion rate; b: Forest plot and tabulated data for degeneration of the adjacent level; c: Forest plot and tabulated data for complications. There was no significant difference in any of these parameters between the two types of surgery.

Fig. S1: The sensitivity analysis for bleeding amounts. Significant heterogeneity was found between the four studies.

Fig. S2: The sensitivity analysis for operation time. No significant heterogeneity was found between the four studies. (Figure Legends Part, Page 19 Line 18-22 and Page 20 Line 1-22) Thank you again.

Comment 06:

Author Contributions: It is mentioned that ZYH, AMW and WFN conceived and designed the experiments. ZYH, AMW and WFN performed the experiments. I thought this was a meta-analysis. Therefore it is not clear to me what sorts of experiments were designed and performed. Please clarify.
Answer: Thank you for your suggestion. We are very sorry for our unclear expression. We have re-written this part according to your suggestion. Conceived and designed the review: ZYH, AMW, and WFN. Performed the review: ZYH, AMW, and WFN. Analyzed the data: ZYH and AMW. Contributed reagents/materials/analysis tools: QLL, TL, KYW, and HZX. Wrote the paper: ZYH and AMW. (Author Contributions Part, Page 19 Line 10-12) Thank you again.

Reference

1. Rao RD, Gourab K, David KS. Operative treatment of cervical spondylotic myelopathy. The Journal of bone and joint surgery. American volume 2006;88(7):1619-40.
2. Shamji MF, Massicotte EM, Traynelis VC, et al. Comparison of anterior surgical options for the treatment of multilevel cervical spondylotic myelopathy: a systematic review. Spine 2013;38(22 Suppl 1):S195-209.
3. Jiang SD, Jiang LS, Dai LY. Anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion for multilevel cervical spondylosis: a systematic review. Archives of orthopaedic and trauma surgery 2012;132(2):155-61.
4. Xiao-Lin Jia Z-JT, Fu-Bin Yang, et al. Comparison between single-level cervical corpectomy and two-level discectomy in two-adjacent-level cervical spondylotic myelopathy. Orthopedic Journal of China 2012;20(21):1931-34.