Review Comments for original version-Reviewer A

1) First, the title needs to indicate "vs. grafting materials alone".

   Reply 1): Thanks you for the helpful suggestion. We have revised the title.

   Changes in the text: Page 1, Line 3-5

2) Second, the abstract needs some revisions. The background did not explain why meta-analysis is suitable to address the clinical controversy. The methods did not describe the inclusion criteria according to the PICOS principles and the instrument for assessing the risk of bias of included studies. The results did not describe the sample sizes of the combination and grafting materials alone groups and the levels of risk of bias of included studies. The conclusion needs detailed comments for the clinical implications of the findings.

   Reply 2): We appreciate the reviewer's suggestion. The background has been rewritten to explain why this meta-analysis was performed. The methods has been described for inclusion criteria according to the PICOS principle, and the Cochrane bias risk assessment tool has been mentioned. The results has added the sample sizes of test and control groups, and the levels of risk of bias of included studies have been shown. The conclusion has updated the clinical implications of the findings.

   Changes in the text: Page 1-2, Line 27-67

3) Third, the introduction of the main text needs to provide detailed examples to support the clinical controversy regarding the efficacy of CGF+ grafting materials vs. grafting materials alone, did not analyze the potential reasons for the controversy, and did not explain why a meta-analysis is suitable to address this controversy.

   Reply 3): We thank the reviewer for this important comment. We have updated the detailed examples in the introduction to support the clinical controversy, have analyzed the potential reasons for the controversy, and have illustrated the need for conducting this meta-analysis.

   Changes in the text: Page 4-5, Line 115-127

4) Fourth, in the methodology of the main text, please describe the Cochrane RoB 2.0 in detail including the criteria for high, low, and unclear risk of bias. In statistics, please describe the funnel plot for publication bias, the test of the level of RoB on the pooled results, and ensure $P<0.05$ is two-sided. In general, the number of included studies is 8 only, so statistical test for publication bias is not necessary.

   Reply 4): We have added details of the Cochrane RoB 2.0 in the methodology as request; after referring to your recommendations, we have canceled publication bias due to fewer articles included than published bias requirements.

Changes in the text: Page 7, Line 189-198; Page 8, Line 226-234; Page 9, Line 227-282

1) First, the title needs to indicate "efficacy".

   Reply 1): Thanks you for the helpful suggestion. We have revised the title.

   Changes in the text: Page 1, Line 3

2) Comment 2: Second, the abstract and the main text needs to tone down the current conclusion since 7 of the 8 included studies are of unclear risk of bias and 1 of high risk of bias. The current conclusion is not convincing.

   Reply 2): Thanks again for your comments. Although 7 articles did not specify the random sequence generation, they were still randomized; but it cannot be denied that one article was at high risk of bias due to the loss of follow-up. In the abstract and text, we have gently mentioned that the current conclusions are unconvincing.

   Changes in the text: Page 2, Line 61-66; Page 10, Line 310-313

3) Comment 3: Third, in the introduction of the main text, detailed examples on the controversy were not provided and the authors did not analyze the potential reasons to indicate meta-analysis is suitable to address the controversy. In fact, meta-analysis cannot address all clinical controversy.

   Reply 3): Thanks again for your comments. A growing number of clinicians are choosing to use CGF in combination with grafting materials to promote tissue regeneration. There are currently no evidence-based analyses of relevant clinical practices, so we performed this meta-analysis to further explore the efficacy of combination therapy compared to conventional monotherapy with grafting materials to guide future clinical practice. The controversy we mentioned in the first manuscripts may not be accurate. We have corrected in the abstract and introduction of the main text. As a novel treatment, the efficacy of combination vs. traditional therapy needs to be evaluated with evidence-based analyses, which is the intent and purpose of our study.

   Changes in the text: Page 1, Line 27-30; Page 4, Line 117-123

4) Comment 4: In statistics, please ensure P<0.05 is two-sided. The authors need to explain why they did not test publication bias. The purpose of sensitivity analysis needs to be specified, which can not address sources of heterogeneity.

   Reply 4): In statistics, we ensure $P<0.05$ is two-sided. Since the number of included studies was 8 only, we did not conduct the publication bias. We've explained it in

the appropriate places. The purpose of sensitivity analysis is to evaluate the stability and reliability of the merged results, which we corrected in statistics and results.

Changes in the text: Page 7, Line 208-213; Page 9, Line 282-286

1. Your abstract is too long. The abstract should be 200-350 words, but you have 395. Please revise.

Reply 1: Revised. The abstract has 331 words now. Thanks

Changes in the text: Page 1, line 27-61

2. Please check if any more references need to be added in the below 4 sentences since you mentioned "Studies", but only one reference was cited. If not, "studies" should be changed to "a study/a previous study".

116	promote true tissue regeneration. Previous studies have proved that CGF have a role
117	in promoting differentiation and growth of cells involved in the periodontal healing
118	(15). However, it has also been claimed that adding CGF has no greater benefits in the
296	variable velocities (2,400 to 3,000 rpm) (32). Several studies have shown that CGF
297	has greater tensile strength and induces the growth of osteoblasts and gingival
298	fibroblasts than second generation PRF (33). Previous studies have found that CGF
304	efficiency, some studies have indicated that CGF has no clinical advantage in
305	promoting periodontal tissue recovery (38). After all, the use of CGF increases the
332	number of bone walls (46,47). Studies have shown that only 1－wall defects respond
333	well to tissue regeneration surgery, whereas 2－ and 3－wall defects do not have
334	such high tissue regeneration due to excessive tissue collapse (48). The study included

Reply 2: Revised. Thanks

Changes in the text: Page 4, line 111; Page 10, line 294,302; Page 11, line 330

3. The name of Weipu database should be "VIP". Please revise it in your manuscript and your Figure 1.

Reply 3: Revised. Thanks

Changes in the text: Page 2, line 38; Page 5, line 140

4. Table 1:
1) Please indicate how the data are presented in Age. For example, mean ± standard deviation or interquartile range.

Reply 4.1): Revised. Some articles showed mean ± standard deviation, but others

gave only age ranges, such as 20-60. Thanks

Changes in the text: Page 17, line 552

2) Should "(T/C)" be added in Follow-up?

Table 1 Characteristics of the included studies

Study	Sample size (female/male)	Age (years)	Intervention		Site (T/C)	Follow-up (months)	Outcome indicator
			T	C			
Xu 2019, (21)	58 (32/26)	55.2±8.3	CGF + Bio-Oss®	Bio-Oss®	30/30	6/12	PD, CAL

Reply 4.2): We apologize for the confusion, but 6 / 12 actually means twice follow-up at 6 and 12 months. We've changed them to 6, 12.

Changes in the text: Page 17, line 551

5. Figure 1:
1) The data is inconsistent.

Studies included in meta-analysis (n = 12)
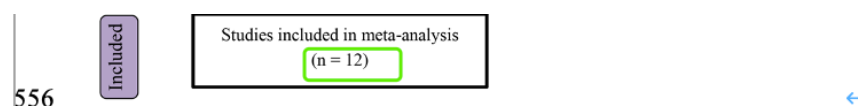
Included

556

557 **Figure 1** PRISMA diagram for the selection of literature search. After removing
558 duplicate literature and excluding literature that did not meet the inclusion criteria, 8
559 studies were included in this meta‐analysis finally. PRISMA, Preferred Reporting

Reply 5.1): We apologize for using an inappropriate diagram. We've revised it and sent you a new docx. diagram.
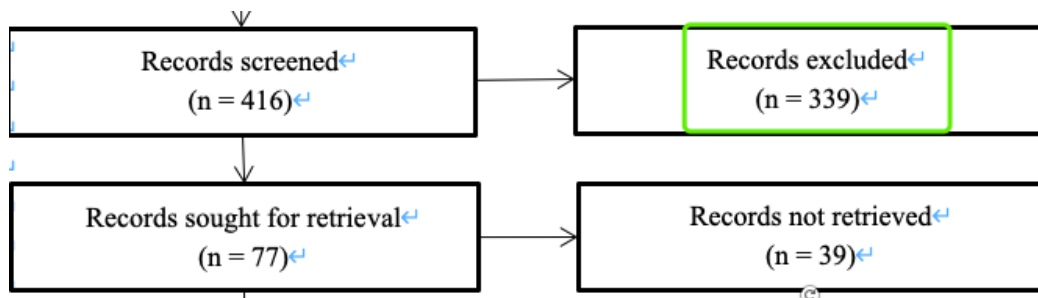
Changes in the text: Page 18, line 560

2) The data in your main text is inconsistent with Figure 1.

246 Through screening titles and abstracts, 57 articles remained, and after full‐texts
247 screening, 8 studies were finally included. There were 303 intrabony defect sites in
248 252 patients. Figure 1 depicts the literature screening process, and Table 1 depicts the

Reply 5.2): We apologize for using an inappropriate diagram. The main text is correct. We've revised the diagram.

Changes in the text: Page 18, line 560

3) Please indicate the specific reason for excluded studies in below box.

Reply 5.3): We've identified specific reasons for excluded studies and modified it in Figure 1.

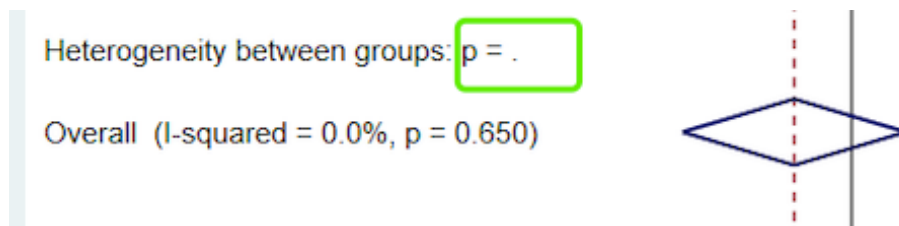**Changes in the text:** Page 18, line 560

6. Figure 2:

Figure 2 is not clear enough. Please provided it in higher resolution.

Reply 6: We've provided a higher resolution Figure 2 in the main text. Thanks.

Changes in the text: Page 19, line 569

7. Figure 5:

There is a missing data. Please complete. If it's no information, please fill "NA".

Reply 7: The REC only shows follow-up for 12 months and should not be divided into subgroups. Modified operations resulted in a new Figure 6 showing complete and revised data.

Changes in the text: Page 21, line 589

8. Figure 7:

1) There is a missing data. Please complete. If it's no information, please fill "NA".
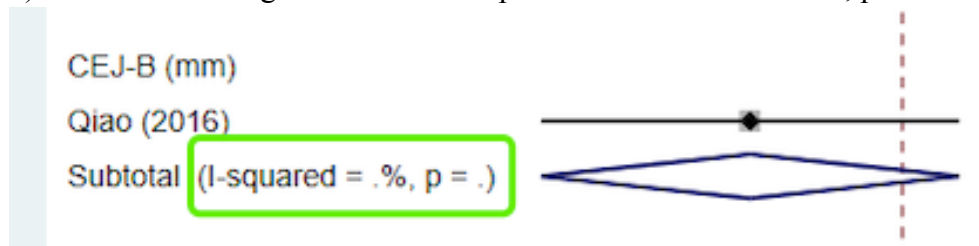
Reply 8.1): In the Figure 7, since it is done in Stata 15.0, there is only one piece of data in the subgroup, and there is no way to combine the statistics without also being able to calculate heterogeneity, so it is not possible to show this set of data. Thanks.

Changes in the text: No revised.

2) The numbers are too close. Please modify the spaces.

	%
WMD (95% CI)	Weight

-0.86 (-1.48, -0.24) 12.93

-1.00 (-2.02, 0.02) 4.68

-0.29 (-1.04, 0.46) 8.75

-0.70 (-1.13, -0.26) 26.36

Reply 8.2): We've modified the font and resubmitted figure 8 in tiff format. Thanks.

Changes in the text: Page 22, line 595