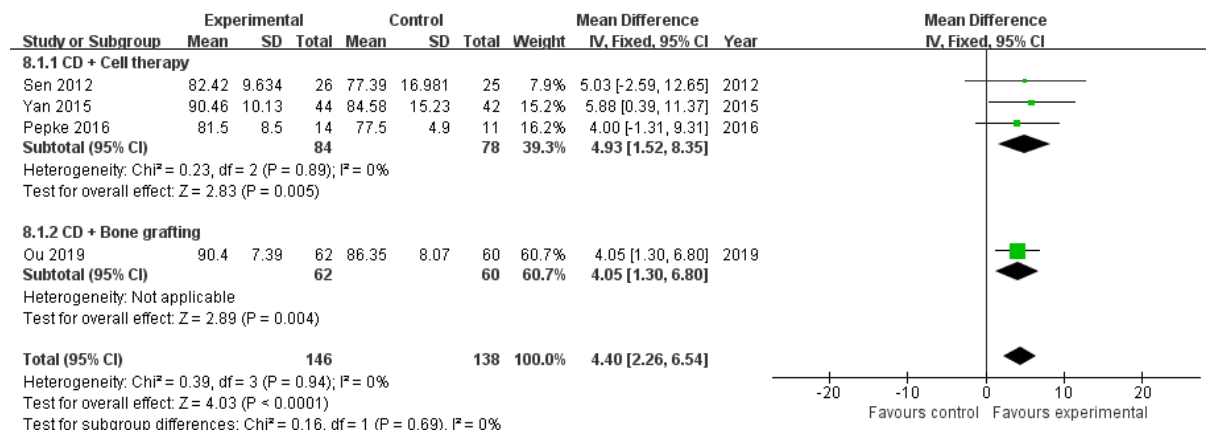


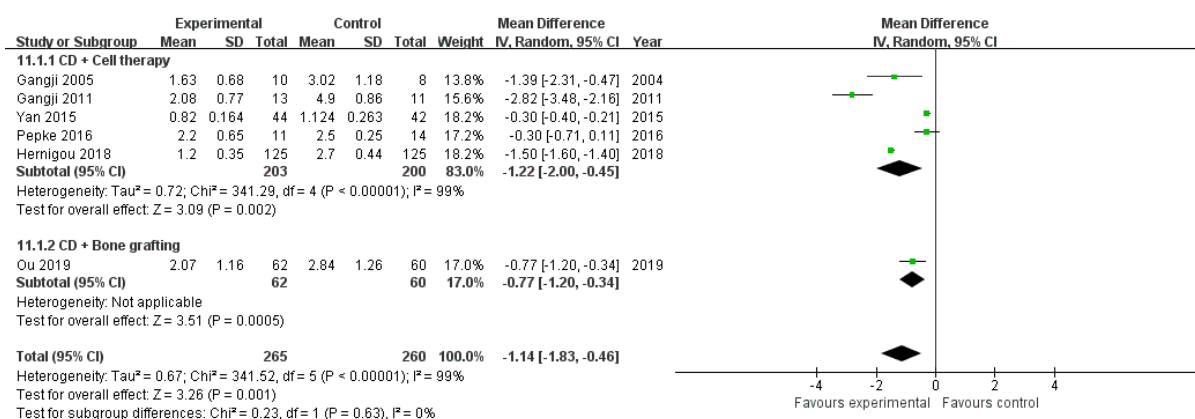


## Supplementary Material

10.1302/2046-3758.107.BJR-2020-0418.R1

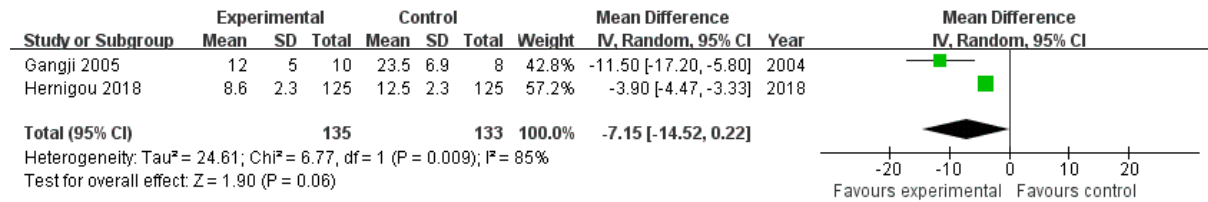


**Fig. a.** Subgroup analysis of stage I-II, Forest plot of Harris Hip Score (HHS). HHS was reported in three studies,<sup>33, 36, 43</sup> in which the intervention group was core decompression (CD) + cell therapy, and one study<sup>37</sup> in which the intervention group was CD + non-vascularized fibular graft (NVFG), and the results showed that both groups improved HHS in osteonecrosis of the femoral head (ONFH) patients compared to core decompression alone (cell therapy: mean difference (MD) = 4.93, 95% confidence interval (CI) 1.52 to 8.35, Z = 2.83, p = 0.005, chi-squared test) (NVFG: Z = 2.89, p < 0.004, chi-squared test).



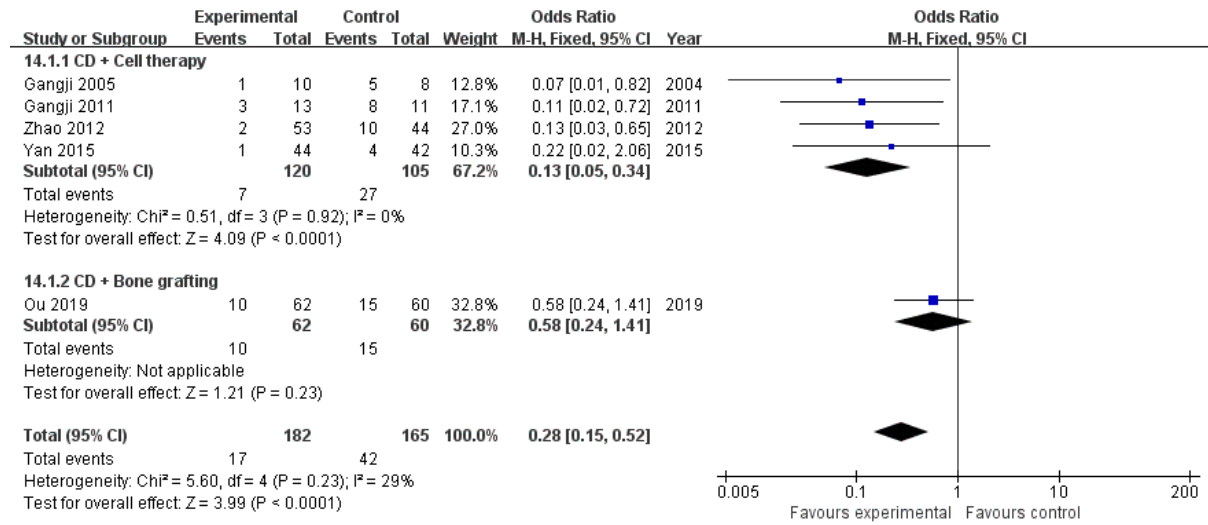
**Fig. b.** Subgroup analysis of stage I-II, Forest plot of visual analogue scale (VAS) score. VAS scores were reported in five studies,<sup>33, 38, 43, 44, 46</sup> with an intervention group of core decompression (CD) + cell therapy, and one study<sup>37</sup> with an intervention group of CD + non-vascularized fibular graft (NVFG). The results showed that both groups were able to reduce VAS scores in osteonecrosis of the femoral head (ONFH) patients compared to core decompression alone (cell therapy: mean difference (MD) -1.22, 95% confidence interval (CI) -2.00 to -0.45, Z = 3.09, p = 0.002, chi-squared test) (NVFG: Z = 3.51, p = 0.001, chi-squared test). However, greater heterogeneity existed between studies of cell therapy (I<sup>2</sup> = 99%, p < 0.001, chi-squared test), and therefore we performed sensitivity analysis by omission of each study but did not identify the source of heterogeneity.

**Fig. c.**

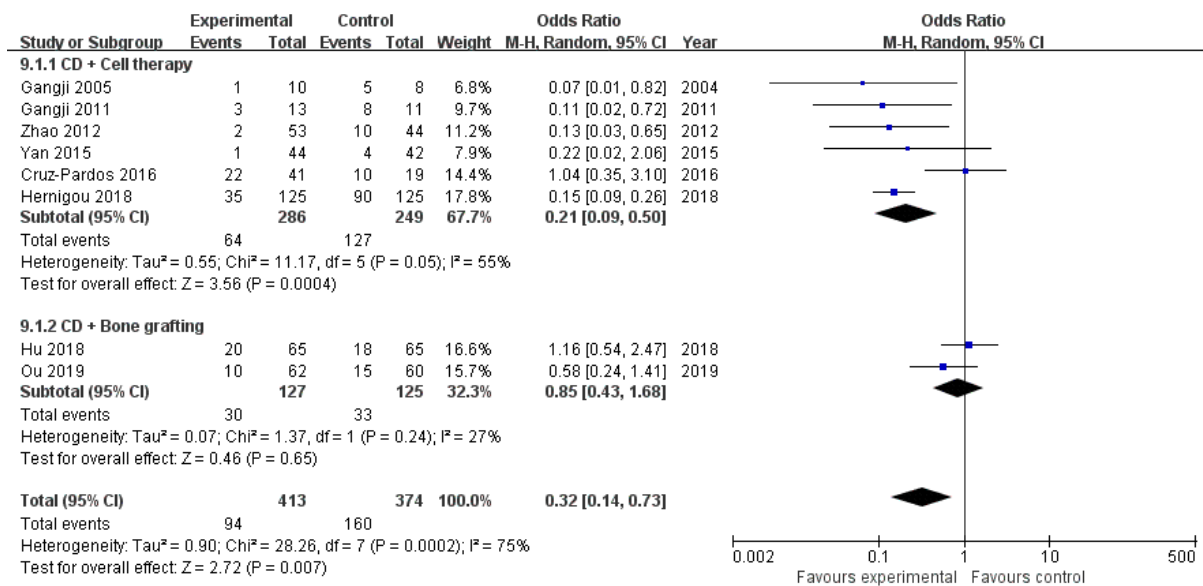


analysis of stage I-II, Forest plot of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. Two studies<sup>38, 46</sup> reported WOMAC scores, and their intervention group was core decompression (CD) + cell therapy. The overall estimate of effect size for WOMAC favoured the cell therapy group, although it reached only borderline significance levels in the presence of a huge degree of statistical heterogeneity (heterogeneity: I<sup>2</sup> = 85%, p = 0.009, chi-squared test) (significance: mean difference (MD) -7.15, 95% confidence interval (CI) -14.52 to 0.02, Z = 1.90, p = 0.060, chi-squared test).

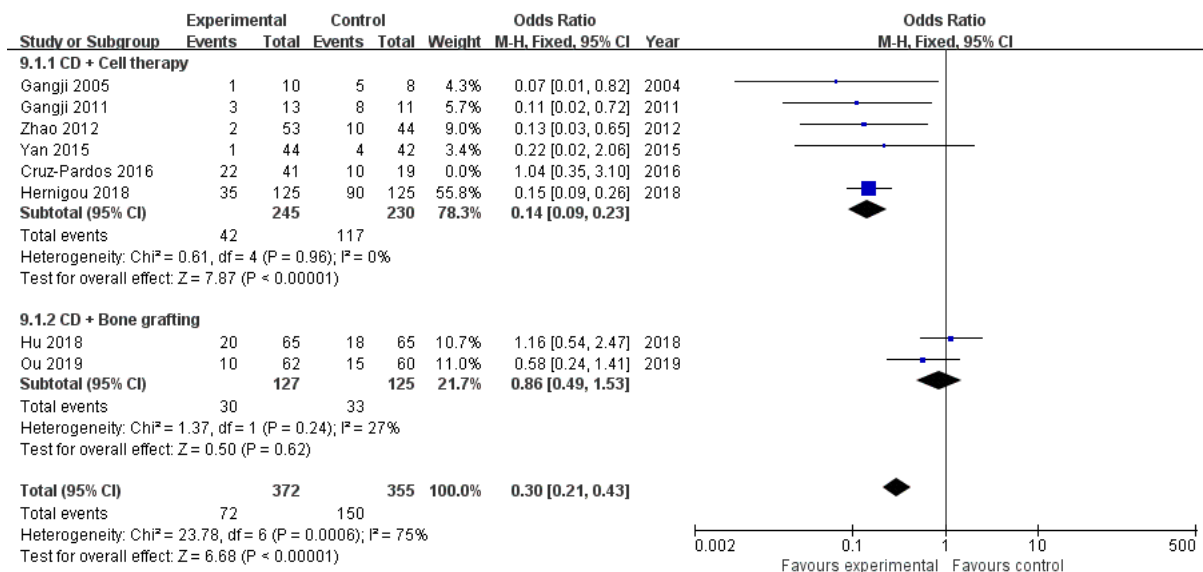
**Fig. d.**



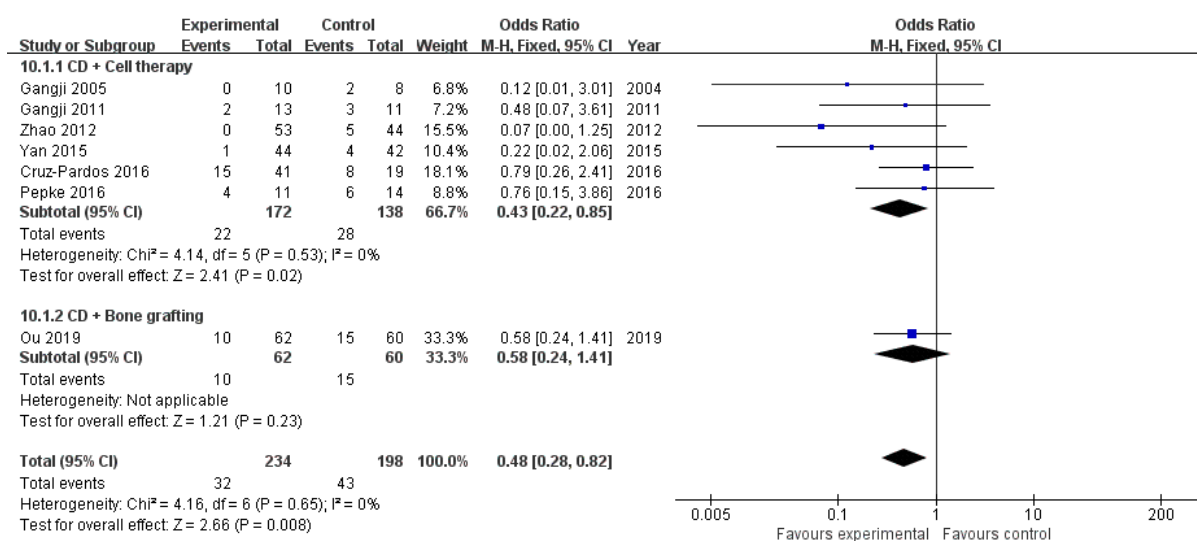
analysis of stage I-II, Forest plot of progression of osteonecrosis of the femoral head (ONFH) stage. Four studies<sup>35, 43, 44, 46</sup> with an intervention group of core decompression (CD) + cell therapy, and one study<sup>37</sup> with an intervention group of CD + non-vascularized fibular graft (NVFG) reported the progression of ONFH stage. The results showed that CD + cell therapy significantly delayed the progression of ONFH stage compared to core decompression alone (OR = 0.13, 95% confidence interval (CI) 0.05 to 0.34, Z = 4.09, p < 0.001, chi-squared test), while there was no statistical difference between CD + NVFG group and the control group (Z = 1.21, p = 0.230, chi-squared test).



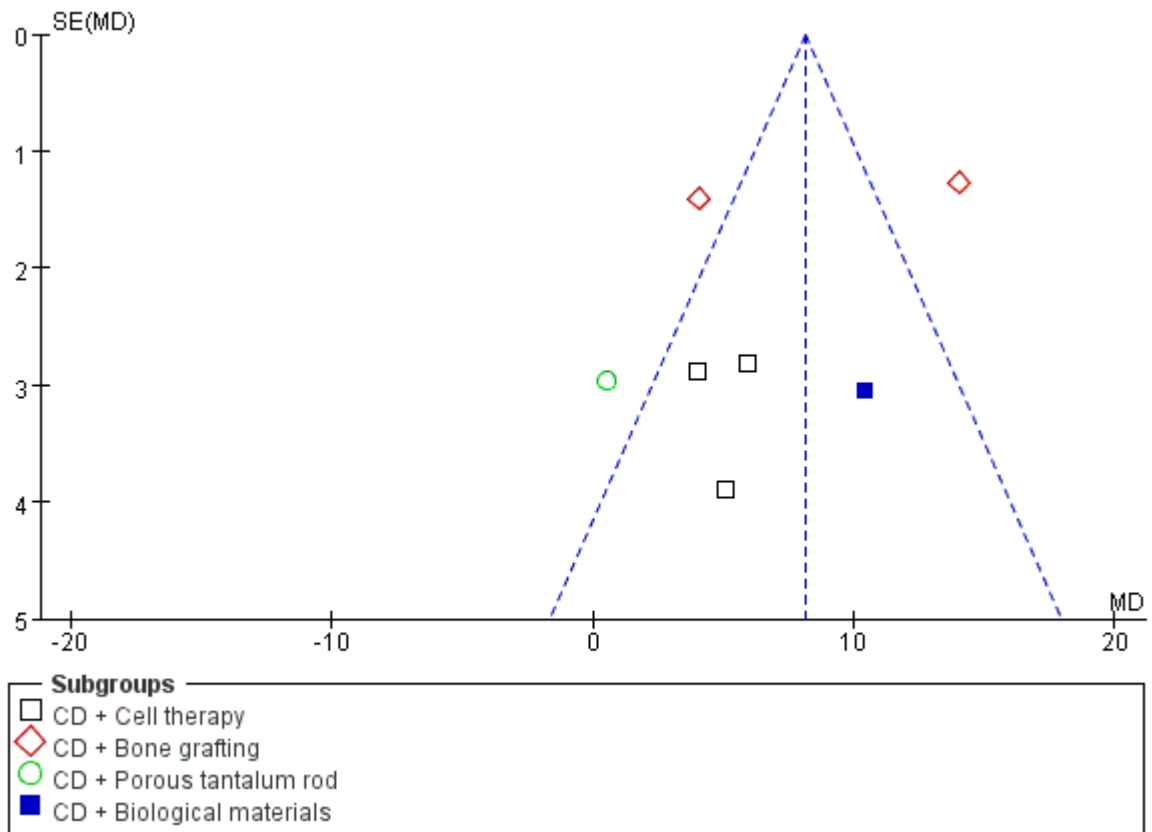
**Fig. ea.** Subgroup analysis of stage I-II, Forest plot of collapse of femoral head (Heterogeneity exists). Six studies<sup>35, 38, 41, 43, 44, 46</sup> in which the intervention group was core decompression (CD) + cell therapy, and two studies<sup>30, 37</sup> in which the intervention group was CD + non-vascularized fibular graft (NVFG) reported the collapse of femoral head. Due to the presence of slight heterogeneity between studies in the cell therapy group (I<sup>2</sup> = 55%, p = 0.050, chi-squared test), we performed sensitivity analysis by omission of each study to explore the source of heterogeneity and ultimately excluded the study by Cruz-Pardos et al<sup>41</sup> (see Supplementary Figure eb).



**Fig. eb.** Subgroup analysis of stage I-II, Forest plot of collapse of femoral head (Sensitive analysis). After excluding the study by Cruz-Pardos et al,<sup>41</sup> a fixed-effects model was used. Results showed that core decompression (CD) + cell therapy could significantly reduce the risk of femoral head collapse compared with core decompression alone (OR = 0.14, 95% confidence interval (CI) 0.09 to 0.23, Z = 7.87, p < 0.001, chi-squared test), while there was no statistical difference between CD + non-vascularized fibular graft (NVFG) group and the control group (Z = 0.50, p = 0.620, chi-squared test).

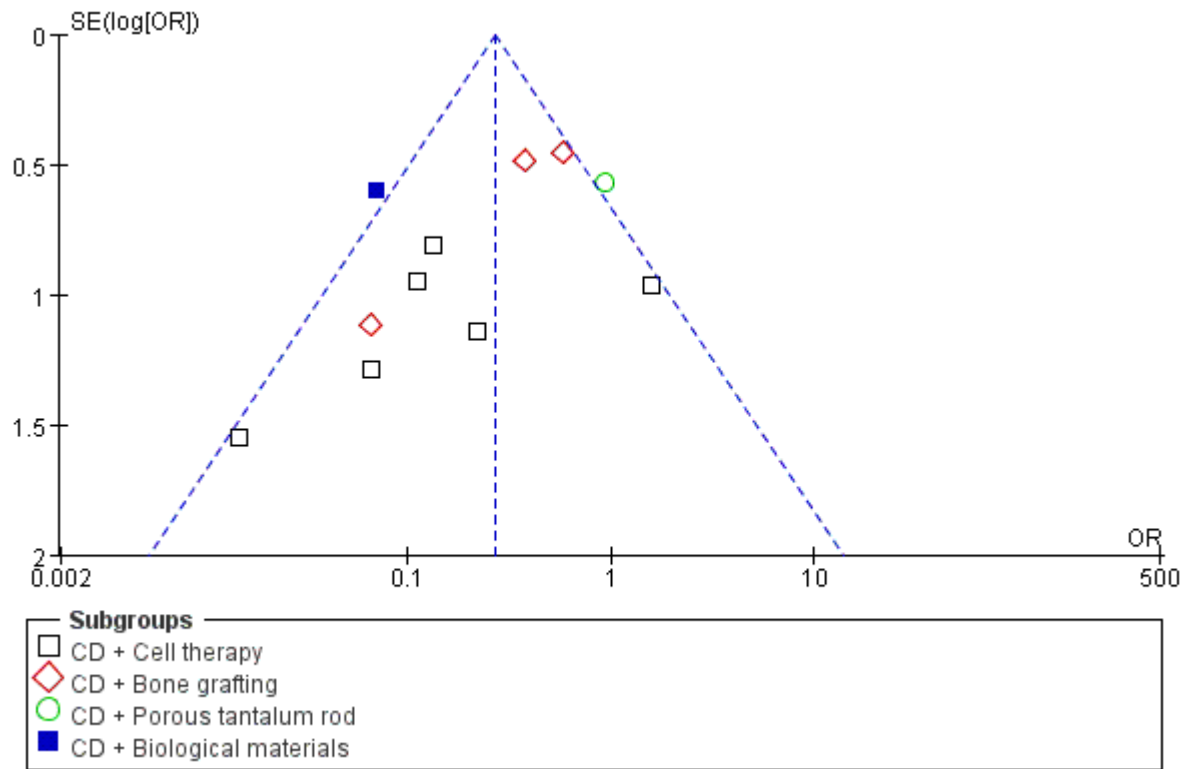


**Fig. f.** Subgroup analysis of stage I-II, Forest plot of conversion to total hip arthroplasty (THA). Seven studies<sup>33, 35, 38, 41, 43, 44, 46</sup> with an intervention group of core decompression (CD) + cell therapy, and one study<sup>37</sup> with an intervention group of CD + non-vascularized fibular graft (NVFG) reported the number of hips converted to THA. Results show that CD + cell therapy reduces the odds for conversion to THA by more than two-fold compared to CD alone (odds ratio (OR) = 0.43, 95% confidence interval (CI) 0.22 to 0.85, Z = 2.41, p = 0.020, chi-squared test), while there was no statistical difference between CD + NVFG group and the control group (Z = 1.21, p = 0.230, chi-squared test).



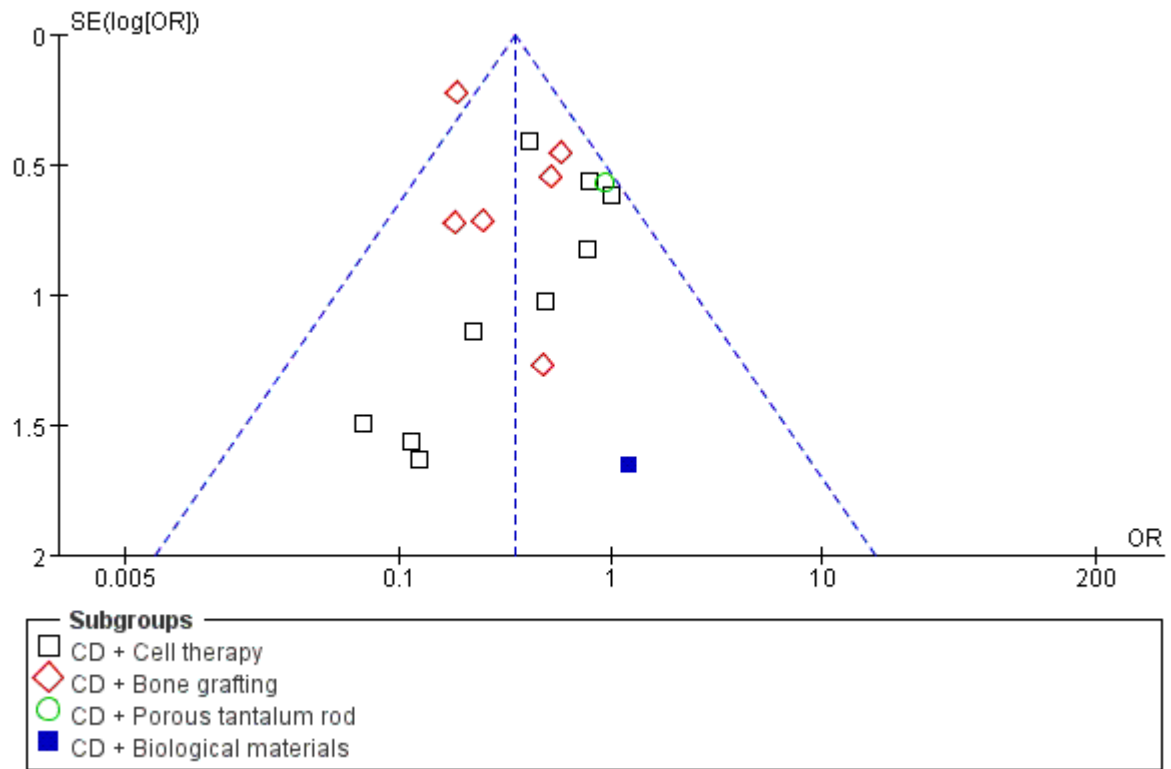
**Fig. ga.** Funnel plots for the Harris Hip Score (HHS). Publication bias was assessed by generating funnel plots for HHS. Symmetrical scatters were observed in the funnel plot, which shows that the publication bias is low.





**Fig. gb.** Funnel plots for the progression of osteonecrosis of the femoral head (ONFH) stage. Publication bias was assessed by generating funnel plots for progression of ONFH stage. Symmetrical scatters were observed in the funnel plot, which shows that the publication bias is low.





**Fig. gd.** Funnel plots for the conversion to total hip arthroplasty (THA). Publication bias was assessed by generating funnel plots for conversion to THA. Symmetrical scatters were observed in the funnel plot, which shows that the publication bias is low.

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