

Jacobs W, Willems PC, et al. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease (Review). Cochrane Database of Systematic Reviews 2011, Issue 1, Art # CD004958.

Design: Meta-analysis of randomized clinical trials

PICOS:

- **Patient population:** Patients scheduled for cervical spine surgery for chronic degenerative disc disease at one or two levels for pain lasting at least 12 weeks
 - o Trials including patients with fractures, tumors, or disease at more than 2 levels were excluded
- **Interventions:** Single or double level anterior discectomy and interbody fusion (ACDF)
 - o Studies involving disc arthroplasty as an intervention were excluded
- **Comparison interventions:** Other anterior fusion techniques; comparisons were separated into several groups
 - o Discectomy alone versus human bone graft
 - o Discectomy alone versus cages or cement
 - o Discectomy alone versus iliac crest autograft with plates
 - o Iliac crest autograft vs human allograft or bone substitute
 - o Iliac crest autograft versus cages
 - o Iliac crest autograft vs iliac crest autograft with plates
 - o Different kinds of autograft
 - o Allograft vs cages
 - o Comparisons between different types of instrumentation
- **Outcomes:** Minimal duration of follow-up was 6 months for clinical, functional, and radiological outcomes
 - o Primary outcome was pain in arm and neck
 - o Secondary outcomes included clinical “success” (coded as excellent/good versus moderate/poor), neck disability, quality of life, daily tasks, work status, radiological measures (fusion, mobility, kyphosis), and serious complications
- **Study types:** Randomized clinical trials only; quasi-randomized designs such as birth data and alternating appointments were excluded

Study selection:

- Databases were MEDLINE, the Cochrane Library, EMBASE, and BIOSIS through May 2009

- Risk of bias was assessed with the 12 criteria of the Cochrane Back Review Group; studies meeting 6 or more criteria were classified as having a “low risk of bias”
- In addition to rating individual articles for risk of bias, the authors defined six domains to designate quality of evidence
 - o 75% of articles have low risk of bias
 - o Included studies have consistent findings
 - o Included patient populations reflect selection criteria of review
 - o Results are based on direct comparisons between interventions
 - o Estimate of effect is precise, having a narrow and conclusive confidence interval
 - o Analysis is free of publication bias, with more than 75% of studies contributing to the analysis
- Quality of evidence depended on how many of these six domains were met
 - o High quality=all domains are met; further research is unlikely to change confidence in the estimate of the treatment effect
 - o Moderate quality=all but one domain met; further research is likely to have an important impact in confidence in estimate of the effect
 - o Low quality=all but two domains met; further research is very likely to have an important impact in confidence in estimate of the effect
 - o Very low quality=all but three domains met; great uncertainty about the estimate of treatment effect
 - o No evidence=no RCTs identified for this outcome

Results:

- A total of 40 articles describing 33 studies were included in the review
- Risk of bias was often high due to problems involving method of randomization and failure of concealment of allocation; lack of blinding was also common but often not avoidable
- Most quality of evidence was low and very low for all comparisons due to risks of bias and lack of precision due to small sample sizes
- **Discectomy alone versus human bone graft**
 - o 7 small studies with 487 patients compared discectomy alone with discectomy plus one or another form of bone graft
 - o For pain, success, rates, return to work and alignment, there were no treatment differences between interventions, but the quality of evidence that the effects were equal was low or very low
 - o For radiological fusion, there was moderate quality evidence that bone graft was more effective than discectomy alone
 - The risk of failure of fusion with bone graft was only 0.22 times the risk of failure of fusion with discectomy alone

- For complication rates, there was moderate quality evidence that there was no difference between discectomy alone and bone graft
- **Discectomy alone versus cages or cement**
 - 4 small studies made this comparison
 - For no outcome (pain, recovery, complication rates, radiographic fusion) was there evidence of a difference between discectomy alone versus cages or bone substitute (cement)
- **Discectomy alone versus human bone graft with plates**
 - 3 small studies made this comparison, each using a different plate design
 - For no outcome (arm pain, fusion, complications) was there even low quality evidence that plates improved outcomes
 - There was very low quality evidence from one study that anterior plating resulted in better neck pain relief
- **Iliac crest autograft versus human allograft or bone substitute**
 - 4 small studies made this comparison
 - The risk of bias was high and the results were too heterogeneous to combine in a meta-analysis
 - One small (n=33) study comparing BMP with iliac crest autograft reported that BMP was a safe substitute for autograft
 - The risk of bias in the studies was high, and the authors did not infer evidence at any level from them
- **Iliac crest autograft versus cage**
 - 7 small studies made this comparison
 - All autograft studies used iliac crest as the source; the cages were filled with local autograft or bone substitute or were not filled at all
 - There was low quality evidence that autograft is more effective than a cage in achieving fusion
 - There was low quality evidence that a cage is more effective than autograft in preventing complications
 - This appears to refer mainly to re-operations, hematomas, and Horner syndrome, rather than to donor site pain
- **Iliac crest autograft versus iliac crest autograft with plates**
 - 3 small studies made this comparison
 - Differences in pain, fusion rates, and complication rates were not found
- **Different kinds of autograft**
 - 1 small study with a high risk of bias compared iliac crest with vertebral body autograft, and reported that the vertebral body graft was not superior
- **Different kinds of instrumentation**
 - 9 small studies with high risk of bias provided no level of evidence above “very low quality” for any comparison for any outcome

Authors' conclusions:

- No treatment was found to be superior for relief of pain in patients with cervical degenerative disc disease or disc herniation
- The only choice which was supported by evidence (low quality) was between iliac crest autograft and a cage
 - o Autograft had superior fusion rates
 - o Cages had fewer complications
 - o Since the relationship between fusion and clinical outcomes is weak, cages are a valid alternative over iliac crest autograft

Comments:

- Numerous comparisons were made but few conclusions could be drawn, due to high risks of bias in many small studies which were eligible for inclusion
- Discectomy alone is rarely done in current practice; since the evidence for its comparisons was of such low quality, further research is not likely to be done to strengthen the comparisons involved
- "Low quality" evidence in Cochrane reviews generally approximates to "some evidence" in the DOWC guideline system, and can be reasonably applied to the iliac crest autograft versus cage comparison
- The "complication" rate of iliac crest autograft did not include reports for donor site pain, suggesting that the comparison would likely to additionally favor cages if this pain were included in the analysis

Assessment: High quality systematic review and meta-analysis of a set of interventions with generally inadequate evidence; adequate for some evidence that in cervical fusion for degenerative disease, iliac crest autograft provides greater fusion rates, but cages are a valid alternative, since cages result in fewer complications of surgery