

**Wardlaw D, Cummings SR, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Lancet 2009; 373: 1016–24.**

Design: Randomized clinical trial

Population/sample size/setting:

- 300 patients (232 women, 68 men, mean age 73) treated for vertebral compression fractures at 21 sites in 8 countries, including the US, UK, Germany, and Belgium
- Eligibility based on having 1 to 3 vertebral compression fractures from T5 through L5
  - o Fractures could be attributable to osteoporosis, multiple myeloma, or metastatic osteolytic tumor
  - o Fractures had to have MRI signal changes, progressive height loss, or pseudarthrosis
  - o Pain had to be at least 4 points on a 10 point scale
- Exclusion criteria included age < 21, estimated fracture age > 3 months, pedicle fracture, previous vertebroplasty, neurological deficit, radicular pain, spinal cord compression, canal narrowing, dementia, contraindications to MRI, and inability to walk
  - o Fracture could not be attributable to osteoblastic metastatic tumor, primary bone tumor, or high energy trauma

Main outcome measures:

- Randomization was to either balloon kyphoplasty (n=149) or non-surgical care (n=151)
  - o Randomization was stratified on sex, etiology, corticosteroid treatment, and bisphosphonate treatment within 12 months
- More than 95% of fractures were from primary osteoporosis; only 4 patients had fractures from metastatic disease or from multiple myeloma
- Kyphoplasty was done mostly under general anesthesia using one of several anatomical approaches
- Nonsurgical treatment, administered according to standard practices in the participating hospitals, was given to patients in both groups, and included analgesics, bed rest, back braces, physiotherapy, rehabilitation programs, and walking aids
- Outcome assessments were taken at 1, 3, 6, and 12 months after randomization
- Primary outcome was the difference after 1 month in the physical component summary of the SF-36 (PCS)
  - o Several secondary outcomes were measured; these included other subscales of the SF-36, the EuroQol-5D quality of life questionnaire, self rated back pain, back function by the Roland-Morris scale, and activity restrictions due to back pain

- In addition, standing lateral spine x-rays were done at baseline, 3 months, and 12 months and reviewed by 2 radiologists for evidence of new or worsening fracture
- The kyphoplasty group improved its SF-36 PCS score in the first month by 5.2 points more than the nonsurgical group
  - This advantage of kyphoplasty over nonsurgical treatment diminished over time; at 3, 6, and 12 months the kyphoplasty advantage was 4.0 points, 3.2 points, and 1.5 points
- Several secondary outcomes (EuroQol-5-D, Roland-Morris, and back pain) also showed greater improvements in the kyphoplasty than the nonoperative group in the first month of the trial
  - The kyphoplasty group reported 2.9 fewer days of restricted activity per 2 weeks at the 1 month assessment, but the difference between groups was no longer significant at 12 months
- Plain x-rays were available for nearly all patients at baseline, but for only 115 kyphoplasty and 95 control patients at 12 months
  - There was a statistically non-significant difference in new or worsening fracture frequency between the kyphoplasty group (33%) and the control group (25%)
- 2 serious adverse events were attributed to kyphoplasty; one patient had a soft tissue hematoma at the surgical site and one had a postoperative urinary tract infection
- The groups received similar amounts of osteoporosis treatment (bisphosphonate, Vitamin D, calcium, etc), but the control group had more analgesic use (91%) than the kyphoplasty group (71%)
  - Neither group had much physical therapy in the first month; this was done in 10% of the kyphoplasty group and 18% of the control group
- Cement extravasation occurred in 27% of the operated vertebrae; none were symptomatic, and no emboli were reported

Authors' conclusions:

- Balloon kyphoplasty improved quality of life, function, mobility, and pain more than nonoperative treatment in the first month of treatment of painful vertebral compression fractures
- Because of fracture healing, the differences between groups diminished over the course of the first year after the fracture, and most of the advantage of kyphoplasty occurred early
- It was estimated that the kyphoplasty group had on average 60 fewer days of pain-related activity restriction during the year of observation than the control group
- The intervention was not blinded, and nonsurgical treatment was not standardized, which may be limitations of the study

Comments:

- The nonsurgical treatment was given according to the practice patterns of the community in which treatment took place, but it is likely that the full set of

nonoperative interventions was used to the extent possible, with analgesics being the predominant intervention for that group

- For example, in the first month of the study, only 18% of the nonoperative group had physical therapy
- The results of the control group therefore may not represent what is possible with a multidisciplinary, coordinated care intervention with emphasis on activity
- Information on analgesic use in the first month is missing for a significant fraction of patients in both groups; it is reported for 114 kyphoplasty patients (138 completed the 1 month follow-up) and for 115 control patients (128 completed the 1 month follow-up)
  - However, the consumption of analgesics classified as “combination” of opioid and non-opioid plus analgesics classified as “strong opioid” appears to have been lower in the kyphoplasty group (53/114) than for the control group (74/115)
- The authors did report results with an intention to treat analysis, which provides some protection against bias when attrition is fairly high (17% of the kyphoplasty group and 26% of the control group)
- The analysis of group differences by repeated measures analysis of variance also provides some protection from biases which can arise from baseline imbalances and missing data

Assessment: Adequate for some evidence that kyphoplasty provides symptomatic and functional improvements greater than for care which relies principally on analgesics, and that the advantage of kyphoplasty is seen early in the course of treatment