Autograft versus interbody fusion cage without plate fixation in the cervical spine: a randomized clinical study using radiostereometry

Bengt I. Lind · Björn Zoega · Hans Rosén

Received: 17 November 2005 / Revised: 28 February 2006 / Accepted: 11 February 2007 / Published online: 7 March 2007
© Springer-Verlag 2007

Abstract A primary object with a fusion cage is avoidance of graft collapse with subsequent subsidence and malalignment of the cervical spine that is observed after bone grafting alone. No randomized studies exist that demonstrate the difference between these two methods in terms of graft subsidence and angulation of the fused segment. The size of the study population was calculated to be 24 patients to reach a significant difference at the 95% CI level. Patients with one-level cervical radiculopathy scheduled for surgery were randomized to anterior discectomy and fusion (ACDF) with autograft or to fusion cage, both without plate fixation. Tantalum markers were inserted in the two adjacent vertebrae at the end of surgery. Radiostereometry was performed immediately postoperatively and at regular intervals for 2 years. Questionnaires were used to evaluate the clinical outcome and an unbiased observer graded the outcome after 2 years. No significant differences were found between the two methods after 2 years in regard of narrowing of the disc space (mean 1.7 and 1.4 mm, respectively) or deformation of the fused segment into flexion (mean 7.7° and 4.6°, respectively). Patients in the cage group had a significantly better clinical outcome. The findings of subsidence and flexion defor-

mation of the fused segment after 2 years seem to be of no clinical importance after one-level cervical disc surgery. However, in multi-level surgery using the same methods, an additive effect of the deformations of the fused segments may affect the clinical outcome.

Keywords Cervical discectomy · Fusion · Cage · Randomization · Radiostereometry

Introduction

Non-fusion alternatives like artificial disc prosthesis have gained an increased interest amongst cervical spine surgeons over the last years in surgical treatment of patients with degenerative disc disease and radiculopathy [13, 21]. However, due to lack of evidence for an increased clinical efficacy with the methods, anterior cervical discectomy and fusion (ACDF), with or without plate fixation, still remains the gold standard of treatment [4, 8, 9, 14, 25]. Fusion is usually carried out with an intervertebral bone graft to restore disc height and to ensure primary stability of the motion segment. Discectomy alone may lead to inferior clinical results due to loss of disc height, narrowing of the neural foramen and to malalignment of the cervical spine because of the resulting kyphosis of the motion segment [10, 11, 22]. The same problems will appear in some patients with ACDFs in whom the bone graft collapses, autologous as well as allogenic [3, 31]. To avoid problems with malalignment (kyphosis) and donor site morbidity, fusion cages of different designs have been employed over the last decade, both in the lumbar and the cervical spine [32, 1, 5]. Biomechanical in vitro tests have shown a difference in stabilizing effect with these cages and that some cages will penetrate into the adjacent vertebrae more easily

B. I. Lind (✉)
Department of Orthopaedics, Sahlgrenska University Hospital,
Gröna stråket 8, 41345 Göteborg, Sweden
e-mail: bengt.lind@orthop.gu.se

B. Zoega
Department of Orthopaedics, Landspítali University Hospital,
Reykjavik, Iceland

H. Rosén
Department of Neurology, Sahlgrenska University Hospital,
Göteborg, Sweden

than others [29, 30]. However, despite an extensive clinical use of these cages the numbers of randomized studies comparing clinical outcome measures are limited [6, 16, 27].

Also, there are no prospective randomized studies on patients with cervical radiculopathy comparing cervical interbody fusion cages and ACDF in which the stability of the adjacent vertebrae in terms of maintenance of disc height restoration and development of kyphosis over the fused segment was studied (migration). The current study was carried out in order to evaluate this issue by using radiostereometry (RSA), a radiographic measuring technique that still is regarded as the most precise for studies of motion and migrations in vivo [18, 23, 33–35].

Materials and methods

From November 1997 to August 1999, 24 consecutive patients referred to the Department of Orthopaedics at our hospital were recruited for the study and randomized into two treatment groups (Table 1). Thirteen patients were women and the age range was 29–57 years (mean 42 years). All patients had radiculopathy corresponding to a MRI verified cervical disc herniation and/or spondylosis at one level between C4 and C7. Patients with myelopathy were excluded from the study. The duration of preoperative symptoms ranged from 2 to 60 months (mean 13 months) and all but one patient had a period of at least 8 weeks of non-surgical treatment before surgery. The number of patients needed for the study was calculated using the results from previous similar studies [33]. The power was based on a significant difference of migration between the vertebrae at the 95% confidence level (CI) using radiostereometry (RSA). These calculations indicated that a minimum of ten patients were required in each group. All patients except one used analgesics every day. Five patients in each group were smokers. Preoperatively, one patient

was working, one was retired and all other patients were on sick leave.

Prior to surgery, the patients were randomized to surgery using either autologous bone from the iliac crest as a Smith-Robinson procedure [25] or to fixation with a fusion cage. No additional plate fixation was used. Randomization was performed in the operating room on the day of surgery using sealed envelopes. A cylindrical threaded titanium cage (10 mm Ø, BAKTM/C, Centerpulse, Spine-Tech Inc, Minneapolis, MN, USA) was placed centrally in the disc space. The cage was filled with bone taken from the end plates during preparation. After discectomy and decompression of the nerve root, 4–7 tantalum markers (Ø 0.5 mm) were inserted with a small tool in each of the two adjacent vertebrae after pre-drilling the anterior cortex. These markers were spread apart in all three dimensions. The graft or the cage was placed and the wound was closed. A soft collar was prescribed to be used 6 weeks postoperatively in both groups. RSA films were taken with the patient positioned supine immediately postoperatively, after 2, 6, 12 weeks and after 6, 12 and 24 months. The films were digitized and the data were computerized. A specifically made software program (RSA Biomedical Innovations, Umeå, Sweden) was utilized to calculate any migration of the upper vertebra in relation to the lower vertebra that was nominated reference vertebra, by using three of the markers in each vertebra. This gave us the rotations and/or the translations of the upper vertebra that occurred between the different investigations in all three dimensions. The program detected if any of the markers were unstable in the vertebra between examinations, which allowed us to choose another marker instead. The reproducibility of the method was examined by repeated examinations with an interval of 5–10 min in 13 of the patients. Based on these double examinations the 99% CI was calculated using the difference and adding 2.96 times the SD. This was in rotation 0.7°–0.9° and in translation 0.1–0.3 mm (Table 2). Before surgery and at the clinical

Table 1 Preoperative demographic data

	Cage	Bone
Age (mean, range)	42 29–58	41 28–56
Sex (females)	7	6
Preoperative VAS arm (mean, range)	7.0 2.3–8.9	5.2 0.5–9.3
Preoperative VAS cervical (mean, range)	7.2 3.3–9.8	5.9 3.9–9.5
Smokers	5	5
Durations of symptoms, months (mean, range)	15.3 1.5–50	11.4 0.5–60

Table 2 99% confidence limits in 23 double examinations

	99% confidence limits
Translations (mm)	
Anterior–posterior	0.347
Proximal–distal	0.098
Medial–lateral	0.286
Rotations (degrees)	
Transverse axis	0.851
Longitudinal axis	0.797
Sagittal axis	0.939

follow-ups the patients filled out questionnaires in which the pain in the neck and arm was stated on visual analogue scales (VAS). The difference in the grading of pain between the different examinations, Δ VAS, was calculated. At 24 months an unbiased observer (a neurologist) examined the patient, unaware of which group the patient belonged to, and graded the outcome according to Odom's criteria [20].

The data were analyzed statistically using the Mann–Whitney *U*-test.

All patients gave informed consent to participate in the study and the study was approved by the Local Ethics Committee.

Results

No significant differences ($p = 0.07$ – 0.94) in migration of the upper vertebra in any of the three planes at any time during the follow-up were found between the two groups (Fig. 1a, b). Most of the migration occurred during the first 2 weeks in the cage group, whereas in the group with bone graft this occurred gradually during the first 3 months. After 3 months there was very little further migration in both groups. However, in a few patients a small but significant migration was seen up to 1 year after surgery but not between 1 and 2 years (Table 3). Thus, all patients fused uneventfully.

At the 2 years clinical follow-up, two patients, one in each group, refused to come for the clinical examination but filled in the questionnaires by mail. At this follow-up, 10/11 patients (93%) were graded excellent–good according to the Odom's criteria in the cage group compared to 7/11 patients (67%) in the group with bone graft. No patient was graded poor. A significant difference was found in Δ VAS for arm pain between the two groups at 24 months with less pain in the cage group ($p = 0.03$) (Fig. 2 a). However, no significant difference between the two groups

was found regarding Δ VAS for neck pain ($p = 0.15$) (Fig. 2b). Twenty patients were totally free from analgesics and two reduced their intake of analgesics. Six of the 12 patients with bone grafts had constant (three patients) or casual pain (three patients) from the graft site at the iliac crest. There was no difference in the clinical outcome between smokers or non-smokers. One patient, in the cage group, had a Horner's syndrome after surgery that partially resolved during the follow-up. No other complications were encountered in the study.

Discussion

The alignment of the cervical spine after ACDF has been emphasized as one important factor in the clinical outcome [34]. To reduce the risks of bone graft collapse with subsidence and subsequent malalignment, fusion cages have been used with or without plate fixation. In the current study, ACDF with a Smith–Robinson autograft and a cylindrical titanium cage, both without additional plate fixation, were compared in a randomized fashion. The results did not show any significant difference between the two in regards of subsidence or migration into kyphosis of the fused segment after 2 years.

Fusion cages were first introduced to fuse unstable motion segments in horses with “wobblers” syndrome” in 1980s. During the last decade there has been an increasing interest for their use in humans, not only in the lumbar spine but also in the cervical spine [32]. The early used cages were cylindrical and made of titanium which allowed osteoconduction [1], but over the years other shapes and materials have been designed and used [32, 5]. A fusion cage should not only ensure primary stability between the vertebrae but also allow bone ingrowth to achieve secondary stability without losing the structural integrity of the segment. The mechanical strength of each different cage has been extensively tested by the manufacturer [5, 2]

Table 3 Transverse rotations and proximal–distal translations over the follow-up period

	2 weeks		6 weeks		12 weeks		6 months		1 year		2 years	
	Cage	Bone	Cage	Bone	Cage	Bone	Cage	Bone	Cage	Bone	Cage	Bone
Transverse rotations (degrees)	3.0	2.7	3.3	3.5	4.4	1.5	2.4	3.1	4.6	6.6	4.6	7.7
	2.7	3.9	2.5	7.7	4.0	10.0	4.2	9.9	3.1	6.9	2.9	7.3
	(−.7 to 7.9)	(−1.3 to 10.4)	(0.4 to 8.8)	(−5.0 to 17.7)	(−3.8 to 7.8)	(−17.5 to 22.6)	(−5.7 to 6.9)	(−17.7 to 22.1)	(.64 to 9.7)	(−1.6 to 22.6)	(.75 to 8.8)	(−1.8 to 22.6)
Proximal–distal translations (mm)	−1.2	−.7	−1.2	−.9	−1.3	−.7	−0.9	−1.0	−1.4	−1.9	−1.4	−1.7
	.8	.8	1.0	1.5	1.1	2.3	1.0	2.1	.9	1.2	.9	1.4
	(−3.1 to −.4)	(−2.0 to .6)	(−3.6 to −.3)	(−3.2 to .8)	(−3.1 to 1.2)	(−4.2 to 3.7)	(−2.3 to 1.3)	(−4.2 to 3.7)	(−3.7 to −.3)	(−4.1 to −1.0)	(−3.5 to −.3)	(−4.1 to .3)

Mean, SD and (range)

Fig. 1 **a** Mean rotations around the transverse axis. **b** Mean compression of the disc segment (proximal–distal translation)

Fig. 2 **a** Mean Δ VAS arm and SEM (standard error of the mean) on a 10° centimetre (cm) scale. **b** Mean Δ VAS neck and SEM (standard error of the mean) on a 10° centimetre (cm) scale

and there exist a limited number of in vitro studies of the different cages used in the cervical spine comparing their primary stability of the motion segment [29, 12, 15, 17, 26]. Wilke and co-workers used human cervical specimens and compared the in vitro primary strength for flexion tests

of cages with three different designs and bone cement. In their tests, they found that the cylindrical cage provided the least primary stability of the four constructs and concluded that this was caused by the shape of the cage and the smaller distraction height achieved during surgery [29]. This initially poor stability of a cylindrical cage may account for the rapid deformation of the vertebral segment seen in the current study, where approximately 65–85% of the migration occurred during the first 2 weeks. A similar narrowing of the disc space after surgery with a dowel cage was also reported in a series of 43 patients with a follow-up time longer than 13 months [26]. Another reason for subsidence with cylindrical shaped fusion cages is probably that, like a Cloward procedure, both endplates are partially violated during preparation for the screw and that parts of the screw will rest only on spongy bone [8].

The fact that most of the rotatory deformation occurs around the transverse axis into kyphosis is not fully understood. There may be two different explanations. The first is that most of the load in all day activities on the neck probably is in flexion, i.e. reading, working at a desk, etc., putting most of the compression forces over the motion segment anterior between the vertebrae. Second, most of the preparation for the screw is anterior in the disc space which sometimes may leave some structural bone support postero-laterally between the vertebrae intact. It could also be claimed that a soft collar is not sufficient as an external support in the postoperative 6 weeks period in patients with only bone grafting and that this may account for the deformation seen in these patients. However, even with a more stable collar like a Philadelphia collar, a similar deformation is seen as shown in the current study [33]. In both of these series the cortical endplates were left intact and a Smith–Robinson tricortical bone graft was used [25]. This type of bone graft has been biomechanically tested and has the highest compression strength in comparison with other commonly used anterior bone graft constructs [28]. The quality of the bone is of course an important factor but has not been examined specifically in the patients in this study. A variation of the bone quality would probably affect the two patient groups equally. To avoid any flexion deformation in these patients, a bone graft has to be supplemented with an anterior plate fixation [33]. Does the small deformation of the fused segment shown in this study have any major impact on the clinical outcome? Probably not for one-level surgery, but it may have if more than one level is addressed with the same technique [34].

The primary intention with the study was not to study the clinical outcome, but there was a significant difference in the clinical outcome with less arm pain amongst patients with a fusion cage. However, these results have to be taken with some caution due to the limited number of patients in the study. Even if the number of patients in the series was small,

the results are in accordance with a few other series in which the same cage was used [6, 19]. Hacker et al. [16] compared cage fixation and ACDF in a multicenter randomized study including both one- and two-level degenerative disc disease with radiculopathy but found no significant difference in clinical outcome between the two groups. In another non-randomized single level study, a stand-alone cage was compared to ACDF with plate fixation and a similar result between the two groups was demonstrated [7]. All these studies show that the clinical outcome is at least as favourable after cervical discectomy and fixation with a dowel cage as after traditional ACDF with autologous bone grafting.

One of the problems using iliac crest autografts has been the remaining chronic donor site pain. Major or minor donor site pain affected 6 out of 12 patients in the current study. This is higher than reported in most previous studies [24]. In a retrospective study on donor site morbidity was found that 26.1% had continued pain at the bone harvest site, 15.7% had local numbness and 5.2% discomforts with clothing [24]. Certainly, this is a major problem in surgery with autologous bone grafting that could be avoided by using a fusion cage.

Radiostereometry (RSA) has become the golden standard for testing and comparing stability of new implants in hip and knee arthroplasty because of its high accuracy in detecting small motions and loosening of implants in comparison with other radiological techniques [18]. This radiographic technique has been used for almost 30 years and for the last 10 years also in spine surgery [23, 33–35]. It is a perfect tool to evaluate fusion and for studying migration of implants and motion also in small study groups, e.g. of artificial discs [13]. The accuracy is dependent on many factors. One of the most important is probably the technique of inserting the markers to achieve as large spread as possible of the markers in each vertebra. This together with a refinement of the analyzing technique and the computer software program has lead to an improved accuracy in evaluating one-level cervical disc surgery [33]. Because of its high accuracy comparisons of small series of patients are possible. However, the technique is not fit to be used in regular clinical practice but we strongly believe that it should be used more often in research to evaluate new spinal implants.

Conclusions

By using radiostereometry (RSA) to study migrations between vertebrae, ACDF with Smith–Robinson autografts was compared with a fusion cage (BAK/C) in a prospective, randomized series of patients with one-level radiculopathy. No significant differences were found between the two surgical techniques after 2 years in regard of narrowing of

the disc space (mean 1.7 and 1.4 mm) or deformation of the fused segment into flexion (kyphosis) (mean 7.7° and 4.6°). The cage group could have a significantly better clinical outcome in terms of pain reduction in both neck and arm as well as in a better Odom's score 2 years after surgery.

References

1. Bagby G (1998) Arthrodesis by the distraction-compression method using a stainless steel implant. *Orthopaedics* 11:931–934
2. Beynon B, Krag M, Pope M, et al. (1988) Fatigue evaluation of a new spinal implant. *Proceedings of the ASME* 56–57
3. Bishop RC, Moore KA, Hadley MN (1996) Anterior interbody fusion using autogenic and allogenic bone graft substrate: a prospective comparative analysis. *J Neurosurg* 85(2):206–210
4. Bohlmann H, Emery SE, Goodfellow DB, Jones PK (1993) Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. *J Bone Joint Surg (Am)* 75:1298–1307
5. Brantigan J, Steffee A, Geiger J (1991) A carbon fiber implant to aid interbody lumbar fusion. *Mechanical testing. Spine* 16:S277–S282
6. Bärlocher CB, Barth A, Krauss JK, Binggeli R, Seiler RW (2002) Comparative evaluation of microdiscectomy only, autograft fusion, polymethylmethacrylate interposition, and threaded titanium cage fusion for treatment of single-level cervical disc disease: a prospective randomized study in 125 patients. *Neurosurg Focus* 12:1–7
7. Cauthen JC, Theis RP, Allen AT (2003) Anterior cervical fusion: a comparison of cage, dowel and dowel-plate constructs. *Spine* 2:106–117
8. Cloward RB (1958) The anterior approach for removal of ruptured cervical disks. *J Neurosurg* 15:602–614
9. Connolly PJ, Esses SI, Kostuik JP (1996) Anterior cervical fusion: outcome analysis of patients fused with and without anterior cervical plates. *J Spinal Disord* 3:202–206
10. Dan NG (2000) Spinal angulation after anterior discectomy and graftless fusion. *J Clin Neurosci* 7(2):124
11. Dowd GC, Wirth FP (1999) Anterior cervical discectomy: is fusion necessary? *J Neurosurg* 90(1 suppl):8–12
12. Eysel P, Furderer S, Rompe JD, Zollner J (2000) Initial instability of different cages for fusion of the cervical spine. *Zentralbl Neurochir* 4:171–176
13. Goffin J, Van Calenbergh F, Van Loon J, Casey A, Kehr P, Liebig K, Lind B, Logroscino C, Sgrambaglia R, Pointillart V (2003) Intermediate follow-up after treatment of degenerative disc disease with the Bryan cervical disc prosthesis: Single-level and bi-level. *Spine* 24:2673–2678
14. Gore DR, Sepic SB (1998) Anterior discectomy and fusion for painful cervical disc disease. A report of 50 patients with an average follow-up of 21 years. *Spine* 23(19):2047–2051
15. Greene DL, Crawford NR, Chamberlain RH, Park SC, Crandall D (2003) Biomechanical comparison of cervical interbody cage versus structural bone graft. *Spine* 4:262–269
16. Hacker RJ, Cauthen JC, Gilbert TJ, Griffith SL (2000) A prospective randomized multicenter clinical evaluation of an anterior cervical fusion cage. *Spine* 20:2646–2654
17. Kandziora F, Pflugmacher R, Schafer J, Born C, Duda G, Haas NP, Mittlmeier T (2001) Biomechanical comparison of cervical spine interbody fusion cages. *Spine* 17:1850–1857
18. Kärrholm J, Herberts P, Hultmark P, Malchau H, Nivbrant B, Thanner J (1997) Radiostereometry of hip prostheses. Review of methodology and clinical results. *Clin Orthop* 344:94–110

19. Lopez-Olivia Munoz F, Garcia de las Heras B, Concejero Lopez V, Asenjo Siguero JJ (1998) Comparison of three techniques of anterior fusion in single-level cervical disc herniation. *Eur Spine J* 6:512–516
20. Odom GL, Finney W, Woodhall B (1958) Cervical disc lesions. *JAMA* 166:23–28
21. Phillips FM, Garfin SR (2005) Cervical disc replacement. *Spine* 17(Suppl):S27–S33
22. Savolainen S, Rinne J, Hernesniemi J (1998) A prospective randomized study of anterior single-level cervical disc options with long-term follow-up: surgical fusion is unnecessary. *Neurosurgery* 1:51–55
23. Selvik G (1989) Roentgen stereophotogrammetry. A method for the study of kinematics of the skeletal system. *Acta Orthop Scand* 60(Suppl 232)
24. Silber JS, Anderson DG, Daffner SD, Brislin BT, Leland JM, Hilibrand AS, Vaccaro AR, Albert TJ (2003) Donor site morbidity after anterior iliac crest bone harvest for single-level anterior cervical discectomy and fusion. *Spine* 2:134–139
25. Smith GW, Robinson RA (1958) The treatment of certain cervical spine disorders by anterior removal of the intervertebral disc and interbody fusion. *J Bone Joint Surg (Am)* 40:607–623
26. Tureyen K (2003) Disc height loss after anterior cervical microdiscectomy with titanium intervertebral cage fusion. *Acta Neurochir* 7:565–569
27. Vavrouch L, Hedlund R, Javid D, Leszniewski W, Shalabi A (2002) A prospective randomized comparison between the cloward procedure and a carbo fibre cage in the cervical spine. *Spine* 16:1694–1701
28. White AA, Jupiter J, Southwick WO, Panjabi MM (1973) An experimental study of the loadbearing capacity of three surgical constructions for the anterior spine fusions. *Clin Orthop* 91:21–28
29. Wilke HJ, Kettler A, Goetz C, Claes L (2000) Subsidence resulting from simulated postoperative neck movements: an in vitro investigation with a new cervical fusion cage. *Spine* 21:2762–2770
30. Wilke HJ, Kettler A, Claes L (2000) Primary stabilizing effect of interbody fusion devices for the cervical spine: an in vitro comparison between three different cage types and bone cement. *Eur Spine J* 9:410–416
31. Zdeblick TA, Hughes SS, Riew KD, Bohlman HH (1997) Failed anterior cervical discectomy and arthrodesis. *J Bone Joint Surg (Am)* 4:523–532
32. Zdeblick TA, Phillips FM (2003) Interbody cage devices. *Spine* 15S:S2–S7
33. Zoëga B, Kärrholm J, Lind B (1998) One-level cervical spine fusion. A randomized study, with or without plate fixation, using radiostereometry in 27 patients. *Acta Orthop Scand* 69:363–368
34. Zoëga B, Kärrholm J, Lind B (1998) Plate fixation adds stability to 2 level anterior fusion in the cervical spine: A randomized study using radiostereometry. *Eur Spine J* 7:302–307
35. Zoëga B, Kärrholm J, Lind B (2003) Mobility provocation radiostereometry in anterior cervical spine fusions. *Eur Spine J* 12(6):631–636