Long-Term Follow-Up Results in Patients With Cervical Disk Disease Treated by Cervical Anterior Fusion Using Titanium Cage Implants

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Abstract

This study is a retrospective analysis of 146 patients, 85 males and 61 females aged 21–80 years (mean 52 years), with cervical disk disease who underwent anterior fusion and titanium cage implantation with follow-up periods of no less than 72 months after surgery. All patients underwent the conventional anterior cervical approach. After removing the protruded disk and osteophyte, cylindrical titanium cages were placed. Single, two, and three level fusion was performed in 76 (52%), 64 (44%), and 6 (4%) patients, respectively. Functional assessment used the Neurosurgical Cervical Spine Scale (NCSS). The curvature index and range of motion were evaluated pre- and postoperatively. The clinical outcomes were satisfactory and there were no significant complications. The mean NCSS was 9.7 before and 12.7 at 1 year after the operation, and 12.1 at final examination. No postoperative cage extrusion or pseudarthrosis occurred, but the cages descended in 10 patients (7%) although alignment was satisfactory. At 5 years after the operation, 140 of the 146 patients (96%) had solid fusion. The long-term results of anterior fusion with titanium cage implantation in patients with cervical disk disease were satisfactory. Titanium cage placement is a highly useful alternative to the conventional treatment method in these patients.

Key words: anterior fusion, cervical disk disease, titanium cage, long-term follow up

Introduction

Anterior interbody fusion of the cervical spine has become the gold standard for treating cervical disk disease,^{8,32,37)} and various anterior fusion methods have been developed.^{3,7,9,18,22–24,26,29,30,45)} The anterior approach has several advantages in the operative treatment of degenerative disease in the cervical region, i.e. direct decompression of the spinal cord and roots, better alignment, and less invasiveness compared to posterior decompression.^{8,32,37)} Several technical modifications have been developed, but there is currently no consensus regarding the optimal technique. However, the anterior approach using autologous iliac crest bone has numerous problems such as persistent donor-site pain, graft bone collapse, pseudoarthrosis, and kyphotic deformity.^{2,5,9,11,14,36,41)} To overcome these problems, various implants using ceramic,^{23,24,29,35)}

titanium,^{1,6,10,12–16,26–28,31,34,39,40,43,44,46)} and carbon cages⁷⁾ have been developed.⁴⁵⁾ Titanium cages are widely used because of the immediate good stabilization without donor site-related complications.^{1,6,10,12,13,15,16,26,28,31,34,39,40,43,44,46)} However, most evaluations involved short or intermediate follow-up periods, none exceeding 5 years.

This retrospective study of a series of patients treated by cervical anterior interbody fusion with titanium cage placement evaluated the surgical results, cervical alignment, bony fusion, and cage subsidence at follow-up periods of not less than 6 years after the operation.

Materials and Methods

We retrospectively reviewed the medical records and radiographs of 146 consecutive patients, 85 males and 61 females aged 21–80 years (mean 52 years), who underwent anterior interbody fusion and titanium placement at our institute or affiliated

Table 1 Scoring system for neurological status in degenerative cervical spine disease*

Lower extremity motor function:	
1 total disability	chair bound or bedridden
2 severe disability	needs support in walking on flat surface, unable to ascend or descend stairs
3 moderate disability	difficulty in walking on flat surface, needs support in ascending or descending stairs
4 mild disability	no difficulty in walking on flat surface, but mild difficulty in ascending or descending stairs
5 normal	normal walking, with or without abnormal reflexes
Upper extremity motor function:	
1 total disability	totally unable to perform daily activities
2 severe disability	severe difficulty in daily activities with motor weakness
3 moderate disability	moderate difficulty in daily activities with hand and/or finger clumsiness
4 mild disability	no difficulty in daily activities, but mild hand and/or finger clumsiness
5 normal	normal daily activities with or without abnormal reflexes
Sensory function and/or pain:	
1 severe disability	severe difficulty in daily activities with incapacitating sensory disturbance
2 moderate disability	moderate difficulty in daily activities with sensory disturbance and/or pain
3 mild disability	normal daily activities, but mild sensory disturbance and/or pain
4 normal	no sensory disturbance or pain

*According to Kadoya, Japanese Society of Spinal Surgery, 1992.²¹⁾

hospitals between November 1997 and April 2000. All patients had clinical symptoms of cervical myelopathy or radiculopathy. The indications for surgery included the medical history, clinical examination, imaging studies, and inadequate or no response to conservative treatment. Anterior fusion was performed in patients with local compression caused by protruded disk, osteophytes, or hypertrophic posterior longitudinal ligament generally involving 2 levels, although exceptionally up to 3 levels were involved. Laminoplasty was performed in patients with narrow spinal canal.

The neurological state of the patients was evaluated according to the Neurosurgical Cervical Spine Scale (NCSS), an official scoring system defined by the Japanese Society of Spinal Surgery.²¹⁾ The NCSS scores the motor function of the upper and lower extremities and sensory deficits (Table 1). The maximum and minimum scores are 14 and 3, respectively. All patients were evaluated at 1, 3, 6, and 12 months after the operation and at annual follow-up visits thereafter. Follow-up period in this series ranged from 72–101 months (mean 86 months).

After the induction of general endotracheal anesthesia, the patient was placed in the supine position with mild neck extension. A right-sided approach was used primarily via a transverse or longitudinal incision. The operative levels were confirmed using fluoroscopy. All patients underwent anterior cervical microdiscectomy and/or osteophylectomy under the operating microscope. After sufficient decompression of the root and spinal cord, 2 titanium cages with appropriate diameter were inserted in each intervertebral space.

The titanium cages were hollow, threaded, and cylindrical types (BAK/C; Sulzer Spine-Tech, Minneapolis, Minn., U.S.A. and CCM cage; Advanced Spine Technology Inc., Oakland, Calif., U.S.A.), with 12 mm length and 6–7 or 8 mm diameter. A bone tip from an osteophyte or β -tricalcium phosphate (OSferion; Olympus Biomaterial, Tokyo) was packed in the titanium cage with fibrin glue (Boh-heal; Chemo-Sero Therapeutic Research Institute, Kumamoto).

The patients were restricted to their hospital beds only on the day after surgery, and most were discharged within 10 days. All patients were instructed to wear a soft cervical collar for 3–4 weeks after the operation.

Preoperative radiography, magnetic resonance imaging, and computed tomography were performed in all cases. Cervical alignment was assessed on radiographs obtained immediately after surgery, at 3, 6, and 12 months, and annually thereafter. Pre- and postoperative sagittal alignment of the cervical spine was evaluated on lateral radiographs acquired in the neutral position. The Ishihara Cervical Curvature Index¹⁷⁾ was used to assess cervical alignment, with positive and negative indices indicating lordotic and kyphotic alignment, respectively. Range of motion, body fusion, and cage subsidence were also assessed. Postoperative bony fusion was categorized as non-fusion, partial fusion, and solid fusion. Partial fusion was defined as incomplete bony fusion in the absence of instability, and solid fusion as continuous and complete fusion without radiological lucidity (Fig. 1). Radiographs were obtained in the flexion, neutral, and extension positions in all

Fig. 1 A: Radiograph (lateral view) of the cervical spine showing solid fusion. B: Radiograph (anteroposterior view) of the cervical spine showing two cages inserted in parallel.

Fig. 2 Cage subsidence. A: Grade 1, implant has subsided slightly into the lower vertebral body. B: Grade 2, implant has subsided moderately into the vertebral body. C: Grade 3, implant has subsided markedly with collapse of the vertebral body.

patients. Cage subsidence was classified into 3 grades as shown in Fig. 2.

Differences were compared using the two-tailed paired samples t-test. A p value of less than 0.05 was considered statistically significant.

Results

Single, two, and three level fusion was performed in 76 (52%), 64 (44%), and 6 (4%) of the 146 patients, respectively. In patients undergoing 3 level fusion, titanium cages were introduced at 2 levels and iliac bone was used at one level. C5-6 was the most common cervical level involved. Among the 216 disk levels addressed in 146 patients, 6% ($n = 14$) involved C3-4, 18% ($n = 39$) involved C4-5, 47% ($n = 102$) involved C5-6, and 28% ($n = 61$) involved C6-7.

The mean preoperative NCSS score was 9.7 ± 1.3

Table 2 Pre- and postoperative final range of motion of the cervical spine in 77 patients who underwent titanium cylinder cage placement

	Range	Mean $\pm$ SD	
Preoperative	0–70	37.6 ± 14.1	] NS]
Postoperative	10–62	34.6 ± 11.8	
1 level	10–62	36 ± 13	
2 levels	15–53	33 ± 9.4	

NS: not significant, SD: standard deviation.

(standard deviation), the mean postoperative score at 1 year after the operation was 12.7 ± 1.3 , and the mean final score no less than 6 years postoperatively was 12.1 ± 2.2 . Our study population showed a significant difference between pre- and postoperative scores ($p < 0.001$), but scores obtained at 1 year after the operation and at final examination did not differ significantly ($p = 0.4713$). Perioperative transient Horner syndrome due to sympathetic nerve disturbance at lower cervical regions developed in 2 patients, and infection and intensive care unit syndrome in one patient each. No cases with cage extrusion or displacement occurred.

Radiological studies to compare preoperative findings and postoperative results at more than 5 years after the operation were possible in 81 patients. The rate of lordosis increased from 32% (26/81) to 57% (46/81), whereas the rate of straight alignment decreased from 54% (44/81) to 38% (31/81), and the rate of kyphotic alignment decreased from 14% (11/81) to 5% (4/81). The pre- and postoperative Ishihara Cervical Curvature Index in these 81 patients showed significant improvement from 5.6 ± 11.2 (range -19 to 30) to 11.2 ± 12.2 (range -20 to 35) ($p = 0.0124$). The range of motion assessed in 77 patients showed no significant effect of anterior fusion (Table 2). There was no significant difference between 1 level and 2 level anterior fusion.

Radiographs obtained 6 and 12 months after the operation revealed the formation of bridging bone (Fig. 3C). Sequential postoperative changes showed bony fusion proceeded rapidly at 2 years after anterior fusion (Fig. 3D). At 5 years after the operation, 140 of the 146 patients (96%) had solid fusion (Fig. 4).

Cage subsidence was observed in 10 of the 146 patients (7%). Six cases were grade 1, 2 cases were grade 2, and 2 cases were grade 3. Subsidence was moderate or severe in 4 of 146 cases (3%), but the patients did not manifest pseudoarthrosis and alignment was considered satisfactory.

Fig. 3 Serial changes in fusion after anterior fusion. **A:** Preoperative radiograph (lateral view) revealing narrowing of the C5-6 intervertebral space and kyphotic alignment. **B:** Radiograph (lateral view) obtained 3 months after the operation showing good alignment. **C:** Cervical tomogram obtained 12 months after the operation showing the formation of bridging bone from adjacent vertebral bodies. **D:** Cervical tomogram obtained 24 months after the operation revealing solid bony fusion.

Fig. 4 Serial changes in fusion after anterior fusion. **Open columns:** non-fusion, **shaded columns:** partial fusion, **closed columns:** solid fusion.

Four (2.7%) of the 146 patients required a second operation. One patient developed delayed infection leading to cage removal and posterior fusion 4 months after the initial operation. One patient manifested cage subsidence with radiculopathy and underwent anterior foraminotomy 18 months after the first operation. One patient required laminoplasty 2 years after anterior fusion. One patient developed an adjacent lesion and underwent anterior fusion 7 years after the first operation.

Discussion

Conventionally, autologous iliac bone grafts were used to achieve interbody fusion, resulting in solid fusion in 83–97% of cases.^{5,32,39,40} However, so-called “donor-site morbidity” was common, with a morbidity rate of 25.3%, manifesting as pain, hematoma, fracture, and meralgia paresthetica.³³ Donor-site pain continued for more than 6 months in 22% of patients,^{39,40} and chronic pain and functional impairment were present in 26.1% and >10% of patients, respectively, at 48 months after undergoing iliac crest autografts.³⁶

Only decompression alone, i.e. “discectomy without bone graft,” may be adequate in patients undergoing anterior cervical discectomy.^{4,14,45} However, microdiscectomy reportedly produces a short-term increase in pain, long-term narrowing of the decompressed intervertebral foramen, and increased stress on the adjacent disk levels.⁴¹ Treatment variations that do not employ implants in patients treated via the anterior approach include the William method¹⁸ and anterior foraminotomy.^{19,20} However, these methods cannot correct kyphotic alignment. Most spinal surgeons favor the placement of an intervertebral implant to correct the alignment.

Different materials have been developed for artificial implants. For example, ceramics²⁹ and hydroxyapatite ceramics^{23,24,29,35} have been effective. Subsequently, the anterior cervical plate was introduced to treat patients with cervical spondylosis.^{9,22,25,30,38,42} Placement of an anterior cervical plate with allografting is the favored method in the U.S.A., but the use of allografts is prohibited in Japan. The implantation of titanium cages was introduced in the late 1990s^{26,46} and it is currently one of the most common procedures in Japan. The aim is to create adequate decompression with restoration of disk height and subsequent fusion.⁴³ The greatest advantage of titanium cage implantation is quick stabilization after anterior fusion. Another advantage is that interbody fusion stops spur formation, preventing buckling of the ligamentum flavum and resulting in less postoperative pain.⁴³ However, the placement of titanium cages is expensive and carries the risk of subsidence and associated future complications.

Table 3 summarizes previous reports on titanium cage implantation to treat patients with cervical disk disease.^{1,6,10,12,13,15,16,26–28,31,34,39,40,43,44} Most of these patients were followed for periods not exceeding 24 months. The fusion ratio was between 74% and 100%, but greater than 95% in most cases.^{6,13,15,26,28,31,34,43,44} Cage subsidence occurred in

Table 3 Clinical summary of published patients with cervical disk disease treated by anterior fusion with titanium cylinder cage placement

Author (Year)	Follow up (mean)	Fusion ratio	Subsidence	Second surgery
Matge (1998) ²⁶⁾	12 mos	100% (40/40)	ND	3% (2/80)
al-Hami (1999) ¹⁾	12 mos	ND	ND	none
Hacker et al. (2000) ¹³⁾	12–24 mos	98% (60/61)	ND	none
Hacker (2000) ¹²⁾	24–48 mos	87% (39/45)	ND	3% (1/37)
Profeta et al. (2000) ³¹⁾	4–26 (16) mos	100% (52/52)	6% (3/52)	none
Matge (2002) ²⁷⁾	12 mos	ND	ND	8% (19/250)
Cauthen et al. (2003) ⁶⁾	1–5.6 (2.7) yrs	97% (29/30)	ND	3% (1/30)
Gercek et al. (2003) ¹⁰⁾	12–18 (15) mos	ND	56% (5/9)	13% (1/8)
Tureyen (2003) ⁴³⁾	12–32 (18) mos	98% (42/43)	ND	none
Hwang et al. (2004) ¹⁶⁾	13–28 (17.2) mos	91% (29/32)	6% (2/32)	none
Moreland et al. (2004) ²⁸⁾	6 mos	95%	22%	none
Thome et al. (2004) ³⁹⁾	12 mos	87% (20/23)	35% (8/23)	none
Hwang et al. (2005) ¹⁵⁾	18–35 (24.9) mos	95% (38/40)	4% (3/78)	none
van Jonberge et al. (2005) ⁴⁴⁾	6 mos	100%	9%	none
Schmieder et al. (2006) ³⁴⁾	24 mos	98%	45% (30/67)	none
Thome et al. (2006) ⁴⁰⁾	12 mos	74%	18%	none

ND: not described.

4–56% of cases. A high incidence of cage subsidence was reported (5 of 9, 56%) in patients treated by anterior interbody fusion,¹⁰⁾ but the rate was much lower in other series.^{15,16,31,44)} We found that 10 of our 146 patients (7%) suffered subsidence. Among them, moderate or severe cases were found in 4 patients (3%). To prevent cage subsidence, we suggest that as much of the intervertebral cortical bone as possible should be preserved, that the cage be inserted slightly anterior because the anterior cortical bone is stronger than the posterior cortical bone, and that the implanted cage be appropriately sized.

The long-term results of anterior fusion using titanium cages in patients with cervical disk disease were satisfactory. We conclude that titanium cage implantation is a highly useful alternative to the conventional treatment method.

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Commentary

In this article, the authors have provided us with important data based on their retrospective review of 146 patients who underwent anterior cervical fusion (ACDF) using titanium cage implants in patients with cervical disk disease. The majority of their patients underwent single or two-level ACDF. The follow-up periods were no less than 72 months with a mean of 86 months. Functional assessments were evaluated at

preoperative, postoperative, and final follow-up examination. There was a significant improvement between pre- and postoperative scores. 140 of 146 patients (96%) achieved radiological solid fusion over 5 year period. However, cage subsidence was observed in 7% of patients, and in one of these patients reoperative anterior foraminotomy was required for radiculopathy 18 months after the ACDF.

Titanium cage implantation for ACDF is one of the common procedures in Japan, because the use of allograft implants is prohibited in their country. The advantages of titanium cage implantation include quick stabilization, which prevents spur formation and buckling of the ligamentum flavum.

This scholarly article adds materially to our surgical knowledge by documenting the long-term follow-up results of an already popularized procedure. It confirms the feasibility and safety of ACDF using titanium cage implantation. We agree that ACDF using titanium cage implantation is a novel alternative procedure to the conventional plate and allograft ACDF, or, as in our practice, carbon fiber spacers filled with allograft bone putty, followed by plating.

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