Long-term follow up of surgical outcomes in patients with cervical disorders undergoing hemodialysis

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Object. As increasing numbers of patients receive long-term hemodialysis, the number of reports regarding hemodialysis-related cervical spine disorders has also increased. However, there have been few reports summarizing the surgical results in patients with these disorders. The objective of this study was to evaluate the long-term follow up and clinical results after surgical treatment of cervical disorders in patients undergoing hemodialysis.

Methods. Seventeen patients in whom surgery was performed for cervical spine disorders while they received long-term hemodialysis therapy were enrolled in this study. Of these, 15 underwent follow-up review for more than 3 years after surgery, and these represent the study population. The remaining two patients died of postoperative sepsis. The average follow-up period was 120 months. Five patients without spinal instability underwent spinal cord decompression in which bilateral open-door laminoplasty was performed. Ten patients with destructive spondylarthropathy (DSA) underwent reconstructive surgery involving pedicle screw (PS) fixation. In eight patients in whom posterior instrumentation was placed, anterior strut bone grafting was performed with autologous iliac bone to treat anterior-column destruction. Marked neurological recovery was obtained in all patients after the initial surgery. In the mobile segments adjacent to the site of previous spinal fusion, the authors observed progressive destructive changes with significant instability in four patients (40%) who underwent circumferential spinal fusion. No patients required a second surgery after laminoplasty for spinal canal stenosis without DSA changes.

Conclusions. Cervical PS-assisted reconstruction provided an excellent fusion rate and good spinal alignment. During the long-term follow-up period, however, some cases required extension of the spinal fusion due to the destructive changes in the adjacent vertebral levels. Guidelines or recommendations to overcome these problems should be produced to further increase the survival rates of patients undergoing hemodialysis.

Key Words • hemodialysis • cervical spine • surgical outcome

The survival of patients with end-stage chronic renal failure has been significantly prolonged by renal dialysis and transplantation regimens. The cervical spine is a tissue that is severely affected by long-term hemodialysis, which can lead to DSA or spinal canal stenosis due to hypertrophy of the ligamentum flavum, the formation of a calcified mass, or spinal amyloid deposition. The number of reports concerning these disorders in the cervical spine has steadily increased as the number of surviving patients receiving long-term hemodialysis has grown.

The radiological features of DSA were first described by Kuntz, et al. In that study, the characteristics of DSA were defined as a narrowing of the intervertebral disc space and the presence of erosion and cysts in the adjacent vertebral plates associated with minimal osteophyte formation. The subaxial cervical spine was the most frequently involved region. Beta-2-microglobulin amyloidosis is a major cause of DSA, and the discs in the midcervical region are most susceptible to Beta-2-microglobulin amyloid deposition. Risk factors for the development of DSA include the duration of renal failure, duration of hemodialysis therapy, and clinical variables.

The authors of several reports have described the pathological features and the pathogenesis of spinal disorders in patients undergoing long-term hemodialysis, yet there have been relatively few clinical studies detailing surgical follow-up results in these patients. The main purpose of the present study was to report in detail the precise long-term follow-up results after surgical treatment of cervical disorders in patients undergoing hemodialysis.

Clinical Material and Methods

Between April 1990 and September 2000, 17 patients (13 men and four women) who underwent surgery for cervical spine disorders while undergoing long-term hemodialysis were enrolled in this study. Of these, 15 underwent follow up for more than 3 years, and they represent the study population (Table 1). The remaining two patients died of postoperative sepsis. Of these two patients, one
underwent open-door C3–7 laminoplasty and died of sepsis 6 months after surgery. The other patient, who underwent circumferential spinal reconstruction, died of sepsis 2 months after surgery (Table 2).

The age range at surgery was 44 to 72 years (mean 56.1 years). The duration of hemodialysis therapy at the time of the initial operation ranged from 10 to 27 years (mean 18.6 years). The mean follow-up period was 120 months (range 36–185 months). The causes of renal failure were glomerulonephritis in 13 patients, polycystic kidney disease in one, and nephrosis in one. The pathological features seen in the cervical spines were spinal canal stenosis due to hypertrophy of the ligamentum flavum (five patients) or the presence of a calcified mass or amyloid deposition and DSA (10 patients). The compromised vertebral levels were in the middle and lower cervical spine below C3–4 in 11 patients and C-2 in three patients. The remaining patient had two noncontiguous lesions at the C1–2 segment and in the lower cervical spine. Neurological symptoms were radiculomyelopathy (one patient) or myelopathy (14 patients). The patient in whom radiculopathy was present experienced intolerable radiating pain in the right C-5 area. Ten of 14 patients with cervical myelopathy were unable to walk. Seven of 14 patients with myelopathy exhibited a disturbance in their precise finger motion.

Five patients without spinal instability underwent cord decompression involving bilateral open-door laminoplasty with or without the removal of the amyloid or calcified mass that had adhered well to the dural sac. All patients in this group had lordotic or neutral alignment. Ten patients in whom there was radiographic evidence of destructive changes and significant spinal instability underwent reconstructive surgery in which PS fixation was performed with or without bilateral open-door laminoplasty. An autologous iliac bone graft was used in all cases. Due to severe destruction of the anterior column or kyphotic deformity compressing the spinal cord, eight patients in whom posterior instrumentation was placed underwent anterior bone strut grafting (with autologous iliac bone) and/or anterior decompression. One patient with radiculopathy underwent unilateral foraminotomy and PS-assisted fusion. The number of surgically treated spinal segments ranged from one to five (mean 2.8). Patients who underwent reconstructive surgery wore a rigid cervical collar for 3 to 4 weeks after surgery.

### TABLE 1

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<th>Case No.</th>
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<th>Duration of Dialysis (yrs)</th>
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<th>Vertebral Level</th>
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<th>Surgery</th>
<th>JOA Preop</th>
<th>JOA Postop</th>
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<th>FU (mos)</th>
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* AF = anterior fusion; CCS = cervical canal stenosis; DM = diabetes mellitus; FU = follow up; LF = ligamentum flavum; PF = posterior fusion; RA = rheumatoid arthritis.
Anteroposterior and lateral flexion–extension radiographs were obtained to determine the fusion status, the presence of any late-onset implant or graft complications, and adjacent-level destructive changes. Preoperative and postoperative neurological status was assessed using the cervical myelopathy scoring system of the JOA (the highest possible score for normal well-being, 17). Because of the difficulty of evaluating patient bladder function, three points were universally deducted for JOA bladder function, and thus a JOA score of 14 represented the highest possible score in this study.

### Results

Neurological recovery occurred in all patients after surgery. Early postoperative complications were demonstrated in two patients—postoperative bleeding in one and pneumonia in another (Table 2). There were no neurovascular complications related to the placement of PSs. The mean preoperative JOA score of 6.9 (range 2–11) improved to 12.3 (range 6–14) after the initial surgery. The mean final follow-up JOA score was 10.4 (range 2–14). During the follow-up period, four patients died (Table 2). One patient who underwent circumferential fusion died after coronary bypass surgery, approximately 95 months after the initial spinal procedure. One patient who underwent circumferential spinal reconstruction died of intestinal necrosis due to abdominal angina 129 months after the initial surgery. The third patient who underwent combined anterior–posterior fusion died of acute heart failure 81 months after the first operation. The fourth patient who underwent circumferential spinal fusion died of an unknown cause at 36 months after the initial surgery. There was no association between the duration of hemodialysis treatment and postoperative complications.

Late-onset complications included pseudarthrosis in one patient (10%) who underwent circumferential spinal fusion (Case 13). In this case the circumferential fusion was extended 12 months after the initial surgery. Osseous fusion in this patient was completed by the final follow up (36 months after the initial surgery). Progressive destructive changes causing significant instability in the mobile segments adjacent to the previous fusion site were observed in four patients (40%) who underwent circumferential fusion. Two patients underwent extension of circumferential fusion—PSs and anterior iliac bone grafts were placed at 26 and 31 months after the initial surgery, respectively. Solid fusion was documented in both at the final follow-up examination after the second surgery. One patient underwent extension of posterior fusion alone at 75 months after the initial surgery; however, at 28 months after the second surgery we observed destructive change below the previous surgical sites, and these we followed conservatively. The remaining patient underwent conservative follow-up treatment because general anesthesia posed too high a risk. No patients required a second surgery after laminoplasty for spinal canal stenosis without DSA changes (Table 2).

### Illustrative Cases

#### Case 5

**History and Examination.** This 47-year-old man had been receiving maintenance hemodialysis for 20 years to treat end-stage renal failure caused by chronic glomerulonephritis; he presented with severe cervical myelopathy due to DSA. Plain lateral radiography showed C5–6 slippage (Fig. 1A). Sagittal T2-weighted MR imaging revealed a pseudotumor compressing the spinal cord at the C5–6 level (Fig. 1B).
Fig. 1. Case 5. A: Plain lateral radiograph showing DSA changes at the C5–6 level. B: Sagittal MR image demonstrating pseudotumor compression of the spinal cord. C: Anteroposterior and lateral radiographs obtained after the patient underwent circumferential spinal fusion. D: Lateral radiograph revealing subluxation at the C4–5 segment adjacent to the fusion site 75 months after the initial surgery. E: Sagittal MR image obtained 28 months after the second surgery revealing destructive changes at the C6–7 level, below the previous surgical sites.
First Operation. The patient underwent C5–6 posterior decompresison and PS fixation, followed by anterior decompresison and autologous iliac bone graft–augmented fusion (Fig. 1C). In cases of DSA, osteoporosis or bone fragility of VBs is especially accelerated, but the pedicle is the last structure to undergo destruction. Thus, the PS system is more reliable than anterior instrumentation. Therefore, in cases of DSA, the posterior route was choosen prior to the anterior approach. In addition to providing stability, resection of amyloid deposits around the intervertebral discs and autologous iliac crest bone graft were essential to achieve biological fusion. When we use the PS system to restore spinal alignment and provide stability, anterior implants are not necessary, and autologous bone grafting alone is sufficient." For the aforementioned reaons, the spine was realigned and stabilized via a posteri- or route, and the intervertebral discs were removed and bone grafts were placed.

First Postoperative Course and Follow Up. The patient was able to walk after surgery and his bilateral hand numbness had nearly resolved. At 75 months postoperatively, he experienced a gait disturbance characterized by lower-extremity spasticity and upper- and lower-extremity numbness. Plain lateral radiography showed C4–5 subluxation adjacent to the first surgically treated lesion (Fig. 1D).

Second Operation. Extension of posterior fusion was undertaken using the PS system at the C4–5 level. The myelopathy resolved after the second surgery. At 28 months after the second surgery, however, the patient gradually began experiencing ambulatory difficulty and complete paraplegia developed. Magnetic resonance imaging demonstrated destructive tissue changes compressing the spinal cord at the C6–7 level (Fig. 1E). The patient underwent conservative follow up because his general condition was very poor; at 54 months after the second surgery, he died of intestinal necrosis due to abdominal angina.

Commentary. The initial sagittal MR image showed existing hypertrophy of the ligamentum flavum at the C4–5 level; however, this was not associated with the patient’s clinical symptoms and, thus, we did not perform decompression at this level. The principle of this surgical method for patients with DSA hinges on minimal invasiveness to prevent perioperative complications related to a patient’s poor general condition. We have treated patients in whom progressive slippage developed at the decompression level several years after the surgery, and we have treated others in whom progression of DSA changes occurred at levels adjacent to prior fusion segments. Therefore, we cannot determine whether all affected segments should be included in the surgery. Further studies regarding the natural history of DSA and long-term large-scale clinical studies will be needed to answer this question.

Case 6

History and Examination. This 44-year-old man had been on maintenance hemodialysis for 21 years to treat chronic renal failure caused by chronic glomerulonephritis. He was unable to walk because of cervical myelopathy. Preoperative plain radiography demonstrated no destructive changes. A T2-weighted MR image revealed cervical canal stenosis compressing the spinal cord (Fig. 2A).

Operation and Postoperative Course. A bilateral C4–7 open-door laminoplasty was performed (Fig. 2B). After the treatment, the cervical myelopathy disappeared. An apparent complete neurological recovery was achieved, and the patient was able to walk.

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**FIG. 2.** Case 6. A: Sagittal MR image demonstrating cervical canal stenosis compressing the spinal cord. B: Lateral radiograph obtained after bilateral C4–7 open-door laminoplasty. C: Lateral radiograph revealing DSA changes at the C5–6 level 163 months after the initial surgery. The patient underwent a conservative follow-up course because little neurological deterioration was apparent.
Follow-Up Course. Plain radiography revealed DSA changes at the C5–6 level at 163 months after the initial surgery (Fig. 2C); however, the patient was undergoing conservative follow up because he experienced only limited neurological deterioration.

Discussion

The incidence of spinal DSA is approximately 20% in patients undergoing long-term hemodialysis treatment. In a 5-year radiological prospective study, Leone, et al., reported finding cervical spine DSA in 19% of patients. Although the pathogenesis of DSA is still unknown, accumulation of β2-microglobulin is one possible cause of DSA. Beta2-microglobulin is a normal blood protein; in patients with renal failure, its levels are elevated to 30 to 50 times the normal values. It has a predilection for deposition in cartilage, connective tissue, and synovial membranes, especially the collagen bundles of the anulus fibrosus. The suggested mechanism of amyloid fibril formation involves inflammatory processes that cause the partial proteolysis of β2-microglobulin into smaller fragments. The amyloid converted from β2-microglobulin has a particular affinity for collagen in intervertebral discs, specifically the peridiscal, periarticular, and perineural tissues. Such amyloid deposits in the VB and disc lead to damage and loss of structural integrity and to further erosive destruction of the spinal segment.

We have previously reported a distribution pattern of amyloid deposition in the facet joints, intervertebral discs, and VBs. Amyloid was densely deposited at the point where the collagen fibers enter the bone at the facet joints and in the peripheral tears of the anulus fibrosis (Fig. 3). The capsular and anular fibers, we found, were disrupted by amyloid deposition, which eventually may have led to laxity of posterior ligaments and spinal instability. In addition to ligament laxity, the vertebral endplates were also destroyed by amyloid granulation penetration into the adjacent VBs. These destructive changes to the spinal three-joint complex eventually led to subluxation at multiple levels and severe spinal instability. Besides these destructive changes, calcified masses or amyloid deposits have been detected in the spinal canal and hypertrophied liga-

When patients have neurological symptoms due to either destructive changes or intracanalicular amyloid deposition, surgical treatment should be considered. The specific treatment plan must be determined on an individual basis according to the state of neural compression, spinal instability, osteoporosis, and the general condition of the patient.

There have been few reports describing the long-term surgical follow-up results in hemodialysis patients with cervical disorders. In particular, there have been no reports of surgical outcomes of more than five years. Patients who undergo long-term hemodialysis may experience several types of spinal surgery-related difficulties because of their poor general condition, severe bone fragility, and low bone fusion rates. Consequently, a high postoperative mortality rate has been reported in these patients. Although the overall number of patients in the present study was small because of the high mortality rate, there are some important clinical topics to discuss. In this study, patients with spinal canal stenosis due to a calcified mass or amyloid deposition in the ligamentum flavum or epidural space without marked segmental spinal instability were successfully treated by posterior decompression alone. However, reconstructive surgery and instrumentation-augmented fixation were necessary in cases of DSA. Because of the severe destructive changes in the three-joint complex of the spinal column, circumferential spinal reconstruction comprising posterior fusion and replacement of the destroyed VBs was considered.

We have used the PS system for reconstructive surgery because the pedicle is maintained intact even after severe destruction of many other spinal components, such as the facet joint or lateral mass. Based on the surgical results of the present study, we believe that the cervical PS system

Fig. 3. Case 7. Magnetic resonance imaging and histopathological studies. The photomicrographs of the tissue samples resected at the time of surgery show destruction of the intervertebral disc and the vertebral endplate caused by penetration of amyloid deposits. ALL = anterior longitudinal ligament. H & E, original magnification × 100.
Cervical disorders in patients undergoing hemodialysis

is associated with an excellent fusion rate and maintenance of good spinal alignment during the long-term follow-up period. Moreover, circumferential or posterior fusion with PSs does not require rigid external fixation such as halo vest therapy after the operation, making either option advantageous in the treatment of patients in poor general condition who are undergoing hemodialysis. To improve the PS system further, we have recently used a computer-assisted surgical insertion navigation system to avoid difficulties with screw placement, which enables safer and more accurate PS placement in the cervical spine.  

Conversely, we found in the present study that 40% of patients who underwent circumferential spinal reconstruction required extension of spinal fusion due to destructive changes in the adjacent levels during the long-term follow-up. Because most DSA cases involving the cervical spine require circumferential fusion, the construct stiffness of the reconstructed segment is increased, which commonly leads to hypermobility and additional stresses in the adjacent segment(s). Ohashi, et al.,15 have reported that collagen degenerated after mechanical stress has a high affinity for β2-microglobulin. This phenomenon may accelerate the destructive changes in the adjacent mobile segment. Therefore, the surgeon must determine the most appropriate fusion level. Guidelines or recommendations to overcome these problems should be produced in the future to further increase the survival rates of patients undergoing hemodialysis.

Conclusions

As a possible strategy to manage cervical disorders in hemodialysis patients, spinal canal stenosis not associated with marked segmental spinal instability can be successfully treated using posterior decompression alone. In some patients who have undergone posterior decompression alone, DSA change may occur in the previously treated site as part of the natural course of long-term hemodialysis. In this study, DSA changes developed in one patient during the follow-up period, but the patient remains asymptomatic. Hence, patients undergoing hemodialysis must be properly treated according to the pathological conditions at the time they present with their symptoms, because their general condition is usually not ideal for invasive surgery.

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References