Impact of Hemodialysis on Surgical Outcomes and Mortality Rate after Lumbar Spine Surgery: A Matched Cohort Study

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Abstract:

Introduction: Despite ongoing improvements in both dialysis and surgical techniques, spinal surgery in patients undergoing hemodialysis (HD) is a challenge to surgeons because of the high mortality rate. However, no previous studies have examined clinical outcomes after lumbar surgery in HD patients. The purpose of this study is to compare clinical outcomes and complication rates after lumbar spinal surgery in patients with or without hemodialysis.

Methods: This retrospective, matched cohort study was conducted to compare surgical outcomes between HD vs non-HD patients who underwent lumbar surgery at our hospital. Controls were individually matched to cases at a ratio of 1:2. Clinical outcomes, complications, and mortality rates were compared between the two groups.

Results: Twenty-nine patients in the HD group and 57 in the non-HD group were included in the current study. Five patients in the HD group died during the follow-up period, whereas no patients died in the non-HD group (mortality rate, 17.2% vs. 0%, $P = 0.003$). Japanese Orthopaedic Association (JOA) scores were significantly less improved in the HD group than in the non-HD group (11.9 vs. 14.2 preoperatively, $P = 0.001$; 19.9 vs. 25.1 at final follow-up, $P < 0.001$). Five patients underwent repeat surgery in the HD group, which was significantly higher than the non-HD group (17.2% vs. 3.5%, $P = 0.041$).

Conclusions: The current study indicates that patients undergoing HD had poor outcomes after lumbar spinal surgery. Moreover, 5 of 29 patients died within a mean 2.4-years follow-up. The indications for lumbar spine surgery in HD patients must be carefully considered because of poor surgical outcomes and high mortality rate.

Keywords:

lumbar spine, lumbar spinal stenosis, hemodialysis, surgery, mortality, end-stage renal disease

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Introduction

In Japan, there are many patients undergoing hemodialysis for end-stage renal disease who require spinal surgery. According to an international comparison system, Japan has the second highest prevalence of patients undergoing dialysis[1]. The Japanese Society for Dialysis Therapy[2] reported that the number of dialysis patients had increased to 304,856 in Japan as of the year 2011 and that this was due to the increase in the total population of patients over the age of 60 years.

Despite ongoing improvements in both dialysis and surgical techniques, spinal surgery in patients with hemodialysis (HD) is a challenge to surgeons because such patients have poor bone quality and sometimes experience destructive spondyloarthropathy (DSA), which is a typical HD-related spinal disorder[3,4]. Chronic renal failure causes abnormal bone turnover, coupling, and mineralization, which can result in delayed bone healing[5]. DSA is frequently seen in patients undergoing long-term HD and can develop into spinal instability and cause serious neurological symptoms[3].

Surgeons should pay attention to not only complications associated with spinal surgery but also systemic problems. Patients treated with dialysis usually have multiple comorbidities such as diabetes, cardiovascular disease, anemia, and malnutrition[6]. They also are at a high risk for infection because of weak self-defense mechanisms and comorbidities[7]. Moreover, high mortality rates have been reported in HD

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patients after orthopedic surgery[8-11]. There are, however, few studies that have assessed the impact of HD on spinal surgery, especially of the lumbar spine[12-16]. Some studies have reported good clinical outcomes, but others have reported more complications and higher mortality rates in HD patients[12-16]. Chikuda et al.[11] conducted a large retrospective analysis of a nationally representative inpatient database including 869 dialysis-dependent patients and reported that dialysis-dependent patients had a ten-fold higher risk of in-hospital death than did non-dialysis-dependent patients, and they were also more likely to have major complications such as cardiac events, sepsis, and respiratory complications. However, this study examined only inpatients' information, and clinical outcomes were not revealed. We therefore undertook this matched cohort study to compare the clinical outcomes and complication rates of lumbar spinal surgery in patients with or without hemodialysis.

Materials and Methods

This retrospective matched cohort study was conducted to compare surgical outcomes between HD and non-HD patients who underwent lumbar surgery at our hospital from January 2010 to December 2015. During this period, 791 patients underwent surgery for lumbar spinal stenosis. Decompression with or without fusion surgery was performed for these disorders. Of 791 patients, 36 patients were undergoing HD, and the majority of them had their cardiac function evaluated preoperatively. Patients who had a prior history of lumbar surgery or who could not be followed up for at least 1 year were excluded. Of the 36 enrolled patients, five had a history of lumbar surgery; two died within 1 year: one because of a cerebrovascular event and the other of an unknown cause; total 29 patients were registered as HD patients.

Controls were individually matched to cases at a ratio of 1:2. Matching criteria included the following well-established variables: age (≤5 years), sex, type of surgery (fusion or non-fusion), range of surgery (≤2 or ≥3 disc levels), and date of surgery (patients who underwent surgery with the closest date to control, within a year).

Postoperative antibiotic therapy was usually administrated with Sulbactam/Ampicillin (1.5 g every 8 hours for 72 hours) for fusion surgery and with Cefazolin (1 g every 8 hours for 24 hours) for non-fusion surgery. On the other hand, for the patients with HD or CKD (eGFR < 45 ml/min/1.73 m^2), half the dose of antibiotics was administrated.

Clinical outcomes were evaluated with the Japanese Orthopaedic Association (JOA) score and visual analog scale (VAS) of low back pain (LBP), leg pain, and leg numbness. We did not score bladder or bowel dysfunction in either group. Reoperation, surgical site infection (SSI), nonunion, and mortality during the follow-up period were evaluated as postoperative complications, and operation times and blood loss were compared.

Sample size calculations assumed 20% and 1% for the mortality rates in the HD group and the non-HD group, respectively. Accepting a two-sided type I error rate of 5%, we would achieve 80% power to detect a difference with 44 patients per arm. However, this study was performed with two unequal groups at a 1:2 ratio because the available number of patients for the study was limited. Individual sample sizes in the two groups were 31 and 62 patients[17].

The χ^2-test or Fisher's exact test was used for categorical variables and the paired *t*-test was used for continuous variables. When comparing clinical outcomes, analysis of covariance was used to adjust for covariates that included each preoperative outcome. A proportional odds model was used to compute the odds ratios (ORs) and 95% confidence intervals (CIs) of HD and HD duration for various surgical outcomes. An improvement in any category, classified into three levels (excellent, good or fair, or poor), was determined as the dependent variable of the model. Potential confounding factors considered in the multivariate analysis included age and sex. Testing for a dose-response trend over the duration of HD was estimated by fitting the ordinal exposure variable as the continuous term. Statistical tests were considered significant at $P < 0.05$. All P values were two-sided. All analyses were performed using SAS version 9.4 software (SAS Institute, Inc., Cary, NC).

Results

Thirty-one patients with HD underwent lumbar spinal surgery in the study period. However, two patients died within a year after the surgery. Therefore, 29 patients in the HD group and 57 in the non-HD group were included in the current study. A 69-year-old man who underwent six-level fusion surgery could be matched with only one adequate control. Patients' demographics are shown in Table 1, and they were similar with respect to the matching criteria: age (HD, 69.7 years; non-HD, 70.1), sex (HD, 17 men and 12 women; non-HD, 33 men and 24 women), types of surgery (HD, 21 decompressions, 8 fusions; non-HD, 42 decompressions, 15 fusions), and follow-up periods (both, mean 2.4 years). There were only two patients with CKD (eGFR < 45 ml/min/1.73 m^2) in the control group.

Comparisons of clinical outcomes and postoperative complications between patients in the HD and non-HD groups are shown in Table 2. Patients in the HD group presented a significantly worse JOA score (11.9 vs. 14.2, $P = 0.001$) and VAS of LBP (59.0 mm vs. 42.5 mm, $P = 0.019$). At final follow-up, the JOA score was significantly worse in the HD group (19.9 vs. 25.1, $P < 0.001$), whereas patients in the HD group complained stronger LBP (35.3 vs. 24.1, $P = 0.066$) and leg pain (31.8 vs. 20.9, $P = 0.078$) and numbness (38.2 vs. 29.9, $P = 0.247$), although the differences were not significant. The JOA score was significantly less improved in the HD group than in the non-HD group (8.0 vs. 10.9 change, $P < 0.001$). The improvement in VAS scores for LBP, leg pain, and numbness showed no difference between the HD and non-HD groups. There was no

Table 1. Baseline Characteristics of Patients in the HD and Non-HD Groups.

Characteristic	HD (*n*=29)	Non-HD (*n*=57)	*P**
	n (%) or mean (SD)	*n* (%) or mean (SD)	
Sex, male	17 (58.6)	33 (57.9)	0.949
Age, years	69.7 (6.8)	70.1 (6.7)	0.779
Follow-up period, years	2.4 (1.2)	2.4 (1.2)	0.933
ASA			
Class 1	0	4 (7.0)	
Class 2	0	52 (91.2)	
Class 3	29 (100)	1 (1.8)	<0.001
Surgery			
Fusion	8 (27.6)	15 (26.3)	0.900
Non-fusion	21 (72.4)	42 (73.7)	
Range of surgery (<3 levels)	25 (86.2)	50 (87.7)	0.843

HD: hemodialysis; SD: standard deviation; ASA: American Society of Anesthesiologists

* The *t*-test was used for continuous variables and χ^2-test or Fisher's exact test was used for categorical variables

Table 2. Comparison of Clinical Outcomes and Postoperative Complications between Patients in the HD and Non-HD Groups.

Characteristic	HD (*n*=29)	Non-HD (*n*=57)	*P*
	n (%) or mean (SD)	*n* (%) or mean (SD)	
Blood loss, mL	206.6 (237.2)	183.9 (274.1)	0.706*
Operative time, min	190.1 (63.5)	196.9 (72.1)	0.668*
JOA score			
Preoperatively	11.9 (3.6)	14.2 (3.9)	0.001*
At final follow-up	19.9 (6.0)	25.1 (3.1)	<0.001*
Change	8.0 (4.7)	11.4 (4.2)	<0.001†
Low back pain			
Preoperatively	59.0 (26.6)	42.5 (31.6)	0.019*
At final follow-up	35.3 (28.6)	24.1 (25.0)	0.066*
Change	23.7 (25.3)	18.4 (32.9)	0.367†
Leg pain			
Preoperatively	71.0 (24.2)	62.8 (28.1)	0.183*
At final follow-up	31.8 (29.9)	20.9 (24.9)	0.078*
Change	39.3 (26.3)	41.5 (36.6)	0.158†
Leg numbness			
Preoperatively	55.6 (30.5)	60.9 (26.6)	0.415*
At final follow-up	38.2 (32.1)	29.9 (30.8)	0.247*
Change	18.9 (29.2)	31.0 (33.2)	0.162†
Complications			
Death	5 (17.2)	0	0.003*
Infection	0	2 (3.5)	1.000*
Non-union	3/8 (37.5)	2/15 (13.3)	0.330*
Repeat surgery	5 (17.2)	2 (3.5)	0.041*

HD: hemodialysis; SD: standard deviation; JOA: Japanese Orthopaedic Association

*The *t*-test was used for continuous variables and Fisher's exact test was used for categorical variables

†Analysis of covariance was used to adjust for each preoperative outcome

significant difference in operation time (190.1 min vs. 196.9 min, $P = 0.668$) or blood loss (206.6 mL vs. 183.9 mL, $P = 0.706$).

Five patients in the HD group died during the follow-up period, whereas no patients died in the non-HD group; mortality rate was significantly higher in the HD group (17.2% vs. 0%, $P = 0.003$). Additionally, two patients undergoing HD died 1 month and 6 months after the surgery, respectively, and were not included in this study because of the insufficient follow-up period. Two of the five patients died of

Table 3. Characteristics of Patients who Died after Surgery.

Age (years)	Sex	Length of HD, years	Surgery	Cause of death	Period between surgery and death
82	Male	2	decompression	cardiac disease	5 years
53	Female	12	decompression	sepsis	14 months
65	Female	3	fusion	brain hemorrhage	12 months
79	Male	12	decompression	sepsis	5 years
71	Female	30	decompression	unknown	12 months

HD: hemodialysis

Table 4. Odds Ratios for Deterioration of Each Outcome Associated with HD (from Proportional Odds Model).

	JOA score Adjusted OR*	LBP Adjusted OR*	Leg pain Adjusted OR*	Leg numbness Adjusted OR*
HD	4.62 (1.73-12.49)	0.96 (0.42-2.21)	0.88 (0.36-2.20)	2.32 (0.99-5.39)
HD duration				
<10 years	Reference	Reference	Reference	Reference
10-19 years	0.40 (0.04-3.87)	0.82 (0.10-6.47)	NA	0.37 (0.04-3.36)
≥20 years	0.77 (0.12-4.83)	1.32 (0.24-7.25)	1.81 (0.25-12.90)	1.14 (0.20-6.45)
P for trend	0.767	0.718	0.488	0.897

HD: hemodialysis; JOA: Japanese Orthopaedic Association; LBP: low back pain; OR: Odds ratio

*Data expressed as OR (95% confidence interval), adjusted for age and sex

sepsis more than a year after surgery. Of the other two patients, one died of brain hemorrhage and the other of heart failure. The cause of death was unknown in one patient who did not undergo autopsy after sudden death (Table 3). SSI occurred in only two patients in the non-HD group, one of whom had severe renal failure staged as CKD G5. Both patients developed an infection that progressed only to the superficial layer and was treated with antibiotics. Among patients who underwent fusion surgery, the HD group experienced a high rate of nonunion, but there was no significant difference (37.5% vs. 13.3%, $P = 0.33$). Five patients underwent repeat surgery in the HD group, the rate of which was significantly higher in the HD group than in the non-HD group (17.2% vs. 3.5%, $P = 0.041$). Reasons for repeat surgery in the HD group were as follows: implant failure in two patients, adjacent segment disease, instability after decompression, and progression of stenosis at another level. On the other hand, two patients in the non-HD group underwent reoperation due to adjacent segment disease and a facet cyst at the surgical site.

The results of a multivariate analysis of the proportional odds model are listed in Table 4. Compared with non-HD patients, patients undergoing HD displayed a 4.6-fold increase only in the OR for poor improvement in JOA score (OR = 4.62; 95% CI, 1.73-12.49). Additionally, patients undergoing HD had an elevated OR for leg numbness compared with non-HD patients (OR = 2.32; 95% CI, 0.99-5.39). On the other hand, HD duration was not associated with poor outcomes after lumbar spine surgery.

Discussion

Patients established on dialysis therapy have among the highest mortality rates of all chronic conditions[18-20]. According to a large retrospective analysis from Japan, dialysis-dependent patients have a significantly higher in-hospital mortality rate (3.57%) than non-dialysis-dependent patients (0.35%), and dialysis-dependent patients have a 10-fold higher risk of in-hospital death after spinal surgery than non-dialysis-dependent patients[11]. Some long-term follow-up studies have indicated a high postoperative mortality rate in patients undergoing hemodialysis: 35.3% (6/17) over an average 10-year follow-up after surgical treatment of cervical disorders[21] and 50% (6/12) over an average 5.5-year follow-up after surgery for unstable cervical spondylolisthesis[9]. The current matched cohort study also indicates a higher mortality rate in hemodialysis patients. Five patients undergoing HD died during the follow-up period, whereas no patients died in the non-HD group. Moreover, two patients undergoing HD died within 1 year and were excluded from this study because of the insufficient follow-up period. Patients undergoing HD had a higher risk of mortality following spinal surgery, even though the surgery achieved better clinical outcomes than preoperatively.

Previous studies have reported high complication rates in HD patients after spinal surgeries, including infection, instrumentation failure, nonunion, and other systemic complications[11,12,16]. Our matched cohort study did not indicate a significant difference in infection and nonunion rates between HD and non-HD patients, whereas the reoperation rate was significantly higher in HD patients. Reoperation is

usually associated with poor results, and the rates of reoperation for lumbar spinal stenosis have been reported to be 2.1% to 6.1%[22-24]. In HD patients, Yamada T et al. reported that 8 of 29 patients (27.6%) needed revision surgery after lumbar fusion or decompression surgery[13], and Sasaki M et al. reported that 1 of 8 patients (12.5%) underwent reoperation after decompression surgery[14]. The reoperation rate for HD patients in the current study was 17.2%, which was significantly higher than that of non-HD patients.

On the other hand, there was no significant difference in the rates of infection and nonunion between the HD and non-HD groups. The current study presented a low infection rate (2.3%) compared with the previous study; the infection rate of spinal surgeries reported in the literature ranges from 0.7% to 11.9%[25-28]. In spite of weak self-defense mechanisms, in the current study, there was no patient who experienced SSI in the HD group, whereas two patients in the non-HD group were suffering from SSI, one of whom had severe renal dysfunction staged as CKD G5. Pseudarthrosis rates after spinal fusion in patients undergoing HD varies from 0% to 42.9% because of its different definition[12,13,16]. In the current study, the pseudarthrosis rate was relatively high in the HD group (37.5%), but there was no significant difference compared with that in the non-HD group (13.3%). Only eight patients who underwent fusion surgery in the HD group were enrolled in the current study; this number was too small to detect a statically significant difference. There might be a selection bias for indication of the surgery to the HD patients. Because patients undergoing HD often had many problems, such as cardiovascular disease, diabetes, anemia, weak self-defense, and poor bone quality, surgeons might hesitate to perform spinal surgery for severe cases, particularly fusion surgery.

Neurological and functional outcomes of HD patients who underwent lumbar surgery have been reported to be favorable. However, there are few studies comparing clinical outcomes between HD and non-HD patients. Yu et al. conducted a comparative study between an HD group and a matched cohort group who underwent posterior instrumented lumbar surgery and concluded that functional outcomes in uremic patients could be comparable with those in the normal population; however, they investigated only VAS and simple a 5-grade patient-centered general outcome assessment questionnaire in terms of “feel excellent,” “feel better,” “no change,” “feel worse,” and “feel terrible.”[12]. In the current study, clinical outcomes were assessed by the JOA and VAS scores for LBP, leg pain, and numbness; all of them improved at the final follow-up, even in patients undergoing HD. Although improvement in JOA scores of HD patients was comparable with previous reports[13,14], it was significantly worse than those in non-HD patients. One of the reasons might be the difference of preoperative conditions. In the current study, the preoperative JOA score was significantly worse in the HD group. Patients undergoing HD often visited spinal clinics after their symptom becomes sever. Longer duration of the symptom causes severe preoperative conditions and might lead to poorer surgical outcomes for lumbar spinal stenosis. VAS of LBP, leg pain, and numbness were relatively high in the HD group, but there was no significant difference. Multivariate analysis showed that patients undergoing HD had an elevated OR for leg numbness compared with non-HD patients, although the HD duration was not associated the improvement of leg numbness. This was contrary to our expectation as it was generally thought that the longer the dialysis period, the more the amyloid deposits. In the current study, approximately 50% dialysis patients had a dialysis history of 20 years or more (long-term); this might be the reason why the dialysis period did not become a significant risk factor.

This study has several limitations. First, the sample size was too small to demonstrate a significant difference in the complication rates, except for mortality and reoperation. However, our sample size was enough to prove the poor surgical outcomes as well as higher mortality and resurgery rates in the HD patients than in non-HD patients. Moreover, there are few studies with larger sample sizes to investigate the clinical outcomes of spinal surgery in HD patients. Second, the follow-up period was relatively short. If we had established the minimum follow-up period as 2 years, many patients in the HD group would have had been excluded because some of them died or dropped out because of admission to another hospital for treatment of other diseases. The mean follow-up period was 2.4 years, which was comparable with most previous reports. Third, we could not detect a specific risk factor leading to death after lumbar surgery. Fourth, the patient-based outcomes (ex. ODI, SF-36, COMI etc.) were not examined. We evaluated the clinical outcomes only using the JOA and VAS scores, which did not necessarily indicate whether the patient is satisfied with the current state. Despite these limitations, the current study demonstrates that patients with HD have poor surgical outcomes and a higher mortality rate after lumbar spine surgery. We hope these data contribute to decision-making for both surgeons and HD patients regarding the treatment for lumbar spinal stenosis.

The current study indicates that patients undergoing HD have poorer surgical outcomes after lumbar spine surgery than non-HD patients. Moreover, 5 of 29 patients died within a mean 2.4-year follow-up. The indications for lumbar spine surgery in HD patients must be carefully considered because of the risks of poor surgical outcomes and a high mortality rate.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

Author Contributions: Yusuke Hori wrote and prepared the manuscript, Shinji Takahashi designed and analyzed the data for the work, and all of the authors participated in the study design. All authors have read, reviewed, and approved the article.

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