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Extended-Hours Hemodialysis without Dietary Restrictions Is Associated with Lower Risk for Developing of Dialysis-Related Amyloidosis

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Dialysis-related amyloidosis (DRA) is characterized by the deposition of amyloid consisting of beta2-microglobulin in the musculoskeletal system, causing carpal tunnel syndrome, destructive spondyloarthropathy, and/or bone cysts. Increased cystic radiolucency of the bones and tendon thickening due to inflammation are common findings in DRA. We have developed a new dialysis method, extended-hours hemodialysis without dietary restrictions for the aim of improving both hypertension and malnutrition. We retrospectively evaluated the clinical effects of dialysis time on the risk for developing of DRA. The study subjects were all of the 30 patients who had received this treatment for more than 11 years. They were divided into two groups according to the weekly dialysis hours: 15 patients ≥ 16.5 hours/week (L-group) and 15 patients ≤ 15.5 hours/week (S-group). Plain x-ray imaging and ultrasonography were used to assess cystic radiolucency of the bones and thickness/diameter of the soft tissues. The proportion of the carpal bone cystic radiolucency was lower in the L-group. The severity of median nerve compression at the wrist was significantly less in the L-group (right hand: $p = 0.0082$, left hand: $p = 0.0137$). Multivariate regression analysis showed that dialysis time was a predictor of median nerve compression ($\beta = -0.559$, $p = 0.005$). In conclusion, extended-hours hemodialysis without dietary restrictions contributes to lower the risk for developing of DRA at the wrist. We therefore propose that extended-hours hemodialysis without dietary restrictions is a preferred method which maintains the patients' quality of life compared with the conventional hemodialysis method.

Keywords: β2-microglobulin; cystic radiolucency; dialysis-related amyloidosis; extended-hours hemodialysis without dietary restrictions; median nerve compression
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Introduction

Long-term hemodialysis (HD) survivors tend to develop dialysis-related amyloidosis (DRA), which is caused by long-term exposure to the uremic toxins. It involves joints and tendons, especially at the wrist, shoulder, and spine (Charra et al. 1985). Accumulation of glycosylated beta2-microglobulin (β2-MG) is thought to play an important role in the pathophysiology of this complication (Yamamoto et al. 2009). The lesions include cystic radiolucency in the bony structures of the joints, increased thickness of synovial membranes, joint capsules, tendons, and ligaments. Cystic radiolucency originates from amyloid-related synovitis developing and spreading to the surrounding regions of the bone and cartilage. Amyloid substance deposits at the wrist joint on the synovial membrane of the flexor tendon sheath or flexor retinaculum cause tendovaginitis and increase the lesions invading the carpal tunnel. Consequently, the median nerve is compressed, and dialysis-related carpal tunnel syndrome develops. These conditions are frequently observed in patients on long-term HD. Recently, long-term HD patients for more than 25 years in Japan are increasing in number owing to the technological improvements such as the progress of biocompatible dialy-

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sis membranes, ultrapure dialysate, and the use of hemodiafiltration (Nitta et al. 2019). Furthermore, worse accessibility to kidney transplantation in Japan necessarily tends the dialysis patients to depend on the dialysis therapy alone for long-term period. Thus, DRA becomes a heavier burden in patients treated with long-term HD. However, the relationship between dialysis time and treatment of DRA has been poorly studied. Charra et al. (1992, 1998) reported that extended-hours HD provided excellent blood pressure control in dialysis patients with hypertension. Therefore, we implemented a new dialysis method, extended-hours HD without dietary restrictions for the aim of improving both hypertension and malnutrition. (Kaneda 2001, 2012; Nishiyama et al. 2012; Kaneda et al. 2013, 2014; Kaneda and Nishiyama 2019). We speculated that extended-hours HD may promote *β*2-MG removal and prevent DRA. In this report, we evaluated the clinical effects of two different dialysis time on the risk for developing of DRA in long-term HD survivors undergoing extended-hours HD without dietary restrictions. The aim of this study was to determine whether dialysis time would affect the risk for developing of DRA.

Patients and Methods

Study design

All of the 30 patients who had undergone extended-hours HD without dietary restrictions for 11 years or more and had provided informed consent were the subjects of this study. They were divided into two groups according to the total weekly hours of dialysis (Table 1). The long-time group (L-group) consisted of 15 patients with HD 3 times per week, with a total weekly dialysis duration of 16.5 hours or longer, and the short-time group (S-group) consisted of 15 patients with HD 3 times per week with a total weekly dialysis duration of 15.5 hours or less. Since the eligible patients had been on maintenance dialysis for a long period of time (≥ 11 years), it was expected that the weekly dialysis time in each patient would have varied slightly over time; therefore, we took the average of dialysis time of the three dialysis sessions weekly. This was a retrospective study, which was approved by the Institutional Review Board of Kamome Clinic where the study was conducted.

Hemodialysis therapy

We will describe the unique hemodialysis therapy used in this study. Hemodialysis patients are generally given strict dietary restrictions to avoid electrolyte abnormalities and excessive weight gain. However, such restrictions can cause a reduction in BMI and malnutrition (Rivara et al. 2016; Pérez-Torres et al. 2018). Some studies have linked extended-hours HD with several beneficial outcomes such as reduced mortality (Culleton et al. 2007), decreased left ventricular mass, and control of serum phosphorus and parathyroid hormone (Xiong et al. 2015). While most of these studies focus on substance removal, our dialysis facil-

Table 1. Dermographics of 30 patients.

	L-group (n = 15) ≥ 16.5 hr/week	S-group (n = 15) ≤ 15.5 hr/week	p value
Sex ; n (%)			
Male	7 (46.7)	4 (26.7)	0.256
Female	8 (53.3)	11 (73.3)	
Average age; year	57.7 ± 12.2	55.7 ± 13.2	0.263
Dialysis time; hour/week	17.4 ± 1.2	14.8 ± 0.7	**< 0.0001**
HD duration; year	20.7 ± 7.3	17.5 ± 5.7	0.103
Age at initial HD; year	36.2 ± 14.7	37.7 ± 15.1	0.398
Primary kidney diseases (%)			
Glomerulonephritis	13 (86.6)	12 (80.0)	0.385
Diabetic nephropathy	0 (0.0)	2 (13.3)	
Hypertensive disease	1 (6.7)	0 (0.0)	
Others	1 (6.7)	1 (6.7)	
Laboratory data			
*β*2-MG (mg/dl)	26.2 ± 4.5	29.4 ± 4.1	**0.028**
Types of dialysis membrane (%)			
PS	6 (40.0)	5 (33.3)	0.165
PES	4 (26.7)	8 (53.3)	
EVAL	5 (33.3)	1 (6.7)	
CTA	0 (0.0)	1 (6.7)	

Data are expressed as number (percentage) or mean ± standard deviation.
L-group, long-time group; S-group, short-time group; HD, Hemodialysis; *β*2MG, Beta2-microglobulin; PS, polysulfone ; PES, polyethersulfone ; EVAL, ethylene vinyl alcohol copolymer ; CTA, cellulose triacetate.

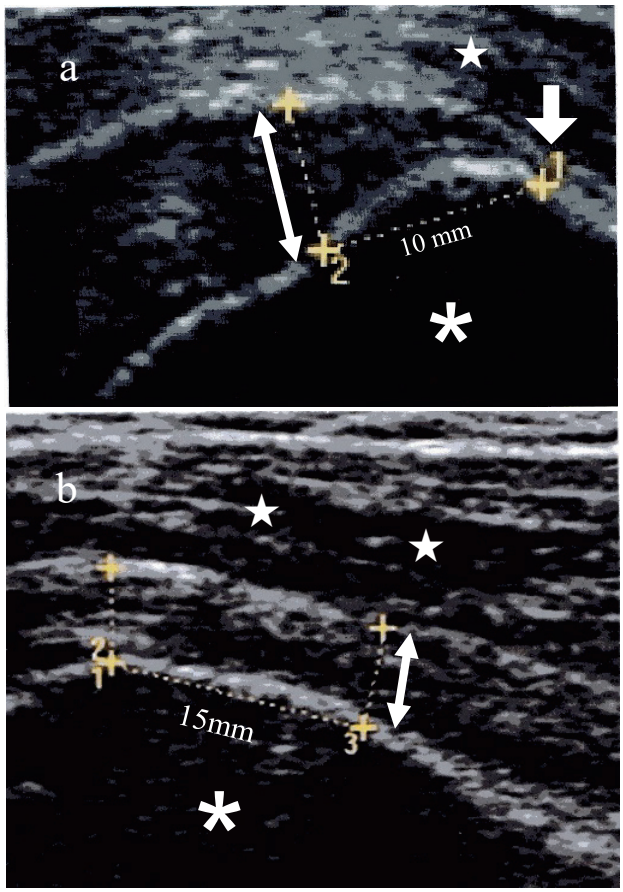

Fig. 1. Ultrasonography image of the shoulder joint.
(a) Thickness of the supraspinatus tendon. White arrow indicates the attachment site of the supraspinatus tendon. The white double arrow is thickness of the supraspinatus tendon. (b) Shoulder capsular distance. The white double arrow is shoulder capsular distance. White star is the Deltoid. Asterisk is the humeral head.

ity uniquely improves the patient's nutritional state by providing a combined therapy consisting of extended-hours HD without dietary restrictions. Under this policy, medical staff actively encourages patients to eat without restrictions and to gain weight. This treatment may be innovative because it not only contributes to the regulation of electrolyte levels and the stabilization of hemodynamics during treatment by slow and long ultrafiltration, but also to maintain proper nutrition.

Examination of cystic radiolucency and destructive spondyloarthropathy by plain x-rays

Plain x-ray images were obtained by the following protocols; the anteroposterior view of the wrist and the shoulder, and the lateral views of the cervical spine both in flexion and extension. In accordance with the classification of Homma et al. (1992), cystic radiolucency was defined as radiolucent area with a clear margin measuring 2 mm or larger in diameter for the carpal bones and 5 mm or larger in diameter for the humeral head, anatomical neck, or greater tuberosity. The proportion of the carpal bone cystic radiolucency was defined as the proportion of cyst-positive carpal bones among the 16 bones per patient. For cervical spine lesions, we used the classification of destructive spondyloarthropathy (DSA) (Nomura et al. 1991). In this study, we defined DSA when the cases were in stage 2 or 3, characterized by erosion of the vertebral body endplate or a diminished intervertebral disc space.

Shoulder examination by ultrasonography

For soft tissue assessment, we used ultrasonography. An ultrasonograph Logic book X-P (GE medical system, Waukesha, Wisconsin) was used in combination with a linear transducer 8L-RS 6.3 MHz. Patients who had undergone shoulder surgery or had had a cuff tear were excluded from the study. With the patient supine and the shoulder in neutral position, ultrasonography of the shoulder joint (transverse section) was performed to determine the thickness of the supraspinatus tendon (Fig. 1a) and the shoulder capsular distance (Fig. 1b). The supraspinatus tendon was measured using electronic calipers at a site located 10 mm towards the midline from the attachment site of the tendon. The right and left supraspinatus tendons were both measured. The shoulder capsular distance was determined according to Aoyagi's procedure (Aoyagi 1992) after observing transverse images of biceps brachii tendon connected to the long head. Longitudinal images were obtained with a transducer placed directly over the rotator interval in a position parallel to the biceps brachii tendon, and based on these images, we defined the shoulder capsular distance as the distance between the inferior border of the deltoid and the surface of the humeral head along the intertubercular groove, and measured it at the inward position 15 mm away towards the midline from the greater tuberosity of the humerus. Both right and left shoulder capsular distances were measured.

Carpal tunnel examination by ultrasonography

Since carpal tunnel syndrome is common in patients with dialysis amyloidosis, we determined the extent of median nerve compression by measuring the maximum anteroposterior diameters of the median nerve along the length at both proximal and distal part beneath the transverse carpal ligament. Measurement was performed with the wrist placed in a neutral and supinated position between flexion and extension. The anteroposterior diameters of the median nerve were measured at the vertices of the palmar eminence of both the distal radius and lunate bone using electronic calipers to determine the proximal maximum diameter, and the same measurements were performed at the vertices of the proximal and distal palmar eminence of the capitate bone to determine the distal maximum diameter (Fig. 2). The differences between the proximal and distal anteroposterior diameters were measured on both sides and reflected the importance on median nerve compression.

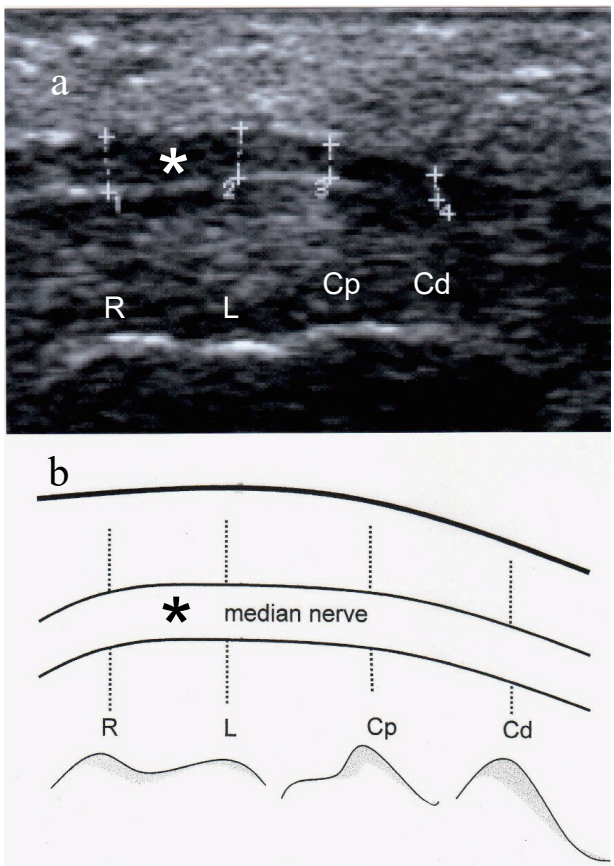

Fig. 2. Ultrasonography image of the median nerve in carpal tunnel.
(a) Ultrasonography image. (b) Schematic diagram. Asterisk is the median nerve.
R, Distal radius; L, Lunate; Cp, Proximal palmar of the capitate bone; Cd, Distal palmar eminence of the capitate bone.

Statistical analysis

Data were expressed as mean ± standard deviation, unless differently stated. Comparisons between the two groups were made using Student's t-test and Chi-square test. We performed univariate logistic regression and multivariate logistic regression models to identify the parameter that affects cystic radiolucency of the bones and DSA associated with DRA. We determined the proportion of cystic radiolucency by examining the carpal bone and shoulders of humeral head. In addition, simple regression and multiple regression analysis models were performed to identify the parameter that affects median nerve compression, thickness of the supraspinatus tendon and shoulder capsular distance, which is a factor related to DRA. We used the mean value of the left side and right side as the thickness and diameter of the soft tissue. The explanatory variables entered into the model included sex, average age, dialysis time, HD duration, age at initial HD, and β2-MG. Taking the number of patients (n = 30) into account, we selected three explanatory variables for multivariate logistic regression analysis and multiple regression analysis in order to prevent overfitting within the model. Variance Inflation Factor (VIF) was employed to eliminate multicollinearity. We considered VIF value of less than 10 as the absence of multicollinearity. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), and Statcel 4 software (OMS, Saitama, Japan). Statistical significance was set at p value < 0.05.

Results

As shown in Table 1, the average age of the subjects between the L-group and the S-group showed no significant difference (57.7 ± 12.2 years vs. 55.7 ± 13.2 years; p = 0.263). Hemodialysis durations in the two groups were both long-term dialysis cases (20.7 ± 7.3 years vs. 17.5 ± 5.7 years; p = 0.103). The age at initial HD in the two groups were both young (36.2 ± 14.7 years vs. 37.7 ± 15.1 years; p = 0.398). The β2-MG showed significant less in the L-group (26.2 ± 4.5 mg/dl vs. 29.4 ± 4.1 mg/dl; p = 0.028). As a primary renal disease, glomerulonephritis accounted for more than 80% in both groups. However, recently diabetic nephropathy has become the main primary renal disease, and glomerulonephritis has decreased to 26.8%, which is different from our study cases. The reason of this discrepancy is presumed to be because the analysis period of this study was 2007, and the subjects started HD in the 1980s when glomerulonephritis was predominant (Nitta et al. 2019).

In the whole 30 patients, the proportion of cystic radiolucency was 9.6% in the carpal bones and 20% in the shoulders (humeral head), respectively. Comparing the two groups, the proportion of carpal cystic radiolucency was 5.4% (13/240 carpal bones) in the L-group, and 9.6% (23/240 carpal bones) in the S-group (p = 0.055), respectively. The proportion of the shoulder joint cystic radiolucency was not significantly different between both groups, at 16.7% (5/30 shoulders) in the L-group, and 23.3% (7/30 shoulders) in the S-group. The proportion of DSA was 15.6% (7/45 vertebrae) in the L-group, and 8.9% (4/45 vertebrae) in the S-group (p = 0.170).

Table 2 shows the comparison between the L-group and the S-group in thickness of supraspinatus tendon, shoulder capsular distance and difference between proximal and distal maximal diameter of the median nerve. The thickness of the supraspinatus tendon was evaluated in 14 patients in each group because of shoulder surgery or cuff tear history in one patient in each group. There were no significant differences neither in the supraspinatus thickness nor in the shoulder capsular thickness between the two groups. However, median nerve compression was significantly less in the L- group. The maximum anteroposterior diameters proximal and distal to the median nerve in the L-group and the S- group was right hand (0.24 ± 0.30 mm vs. 0.55 ± 0.37 mm; p = 0.0082), and left hand (0.11 ± 0.39 mm vs. 0.42 ± 0.36 mm; p = 0.0137).

Table 2. Comparison of various parameters between the groups.

	L-group	S-group	p value
Thickness of the supraspinatus tendon			
Right side (mm)	6.7 ± 1.4	6.0 ± 1.2	0.117
Left side (mm)	5.9 ± 0.9	6.5 ± 1.5	0.133
Shoulder capsular distance			
Right side (mm)	5.1 ± 1.1	5.0 ± 1.2	0.446
Left side (mm)	4.6 ± 1.2	5.2 ± 1.5	0.170
Difference between the proximal and Distal maximal diameter of the median nerve			
Proximal/distal maximal diameter, right side (mm)	1.79 ± 0.23/1.54 ± 0.34	2.07 ± 0.41/1.52 ± 0.31	
Difference (mm)	0.24 ± 0.30	0.55 ± 0.37	**0.0082**
Proximal/distal maximal diameter, left side (mm)	1.94 ± 0.47/1.83 ± 0.55	2.00 ± 0.39/ 1.58 ± 0.47	
Difference (mm)	0.11 ± 0.39	0.42 ± 0.36	**0.0137**

L-group, long-time group; S-group, short-time group.

Table 3. Logistic regression for risk of developing cystic radiolucency and DSA.

Variables	Carpal bone				Shoulders (humeral head)				DSA			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Sex (female)	2.0 (0.25-16)	0.529			2.1 (0.34-12)	0.429			0.84 (0.12-6.0)	0.866		
Age	0.72 (0.16-3.3)	0.704			1.0 (0.93-1.1)	0.873			1.1 (0.98-1.2)	0.108		
HD duration	1.4 (0.33-6.2)	0.695	1.1 (0.74-1.6)	0.691	1.1 (0.99-1.3)	0.080	1.1 (0.96-1.3)	0.164	1.0 (0.89-1.2)	0.699	0.97 (0.82-1.1)	0.666
Dialysis time	1.0 (0.53-2.0)	0.993	0.69 (0.23-2.1)	0.513	1.1 (0.67-1.8)	0.733	0.89 (0.48-1.7)	0.710	1.3 (0.72-2.2)	0.431	1.0 (0.54-2.0)	0.927
Age at initial HD	1.4 (0.32-6.5)	0.640			0.97 (0.92-1.0)	0.362			1.0 (0.98-1.1)	0.213		
β2-MG	1.2 (0.70-2.0)	0.535	1.2 (0.62-2.2)	0.647	0.89 (0.74-1.1)	0.253	0.94 (0.73-1.2)	0.629	0.81 (0.60-1.1)	0.156	0.79 (0.56-1.1)	0.189

DSA, Destructive spondyloarthropathy; HD, Hemodialysis; β2-MG, Beta2-microglobulin.

The explanatory variables used in the multivariate regression were determined by the following methods. Firstly, we selected dialysis time which is the main focus in this study and β2-MG which is a major constituent protein of DRA (Gejyo et al. 1985). Secondly, we selected HD duration among the explanatory variables initially selected for the multivariate regression model after eliminating the VIF values for average age, HD duration and age at initial HD since they exceeded 10, indicating multicollinearity.

Table 3 shows the logistic regression for the risk of developing cystic radiolucency and DSA. No significant association was shown in univariate logistic regression and multivariate logistic regression.

Table 4 shows the regression analysis for soft tissue lesions. In multiple regression analysis, a significant association was demonstrated between median nerve compression and dialysis time ($\beta = -0.559$, $p = 0.005$). It was also shown in simple regression analysis for dialysis time ($r = -0.478$, $p = 0.007$). Multiple regression analysis showed that dialysis time was a predictor of median nerve compression.

Discussion

DRA in dialysis patients has not been an important issue to be solved in the US and Europe (Assenat et al. 1980, Schwalbe et al. 1997). The high mortality rate of patients in the US (Goodkin et al. 2004) may be an explanation. The progress in biocompatible hemodialysis membranes, ultrapure dialysate, and increased β2-MG removal may also explain the observed decline of DRA in Europe. In addition, an easier access to kidney transplantation in Western Europe has reduced the risk of amyloidosis. However, in countries like Japan with prolonged patient survival under dialysis treatment (Goodkin et al. 2004) and limited access to kidney transplantation, DRA remains a burden for dialysis patients.

Gejyo et al. (1985) showed that β2-microglobulin (β2-MG), an amyloid precursor protein, was present in high concentrations in the blood of patients with chronic renal failure, which might cause inflammatory changes in the motor apparatus through amyloid fibrosis, resulting in the development of DRA. Extended-hours HD increases β2-MG clearance and extraction (Eloot et al. 2008) and

Table 4. Regression analysis for soft tissue lesions.

Variables	Thickness of the supraspinatus tendon				Shoulder capsular distance				Median nerve compression			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	r	p value	β	p value	r	p value	β	p value	r	p value	β	p value
Sex (female)	0.019	0.921			0.181	0.340			0.229	0.223		
Age	0.272	0.145			0.347	0.061			−0.228	0.226		
HD duration	0.219	0.245	0.045	0.218	0.192	0.309	0.175	0.430	−0.106	0.577	−0.064	0.742
Dialysis time	0.190	0.314	0.180	0.325	−0.023	0.905	−0.114	0.591	−0.478	**0.007**	−0.559	**0.005**
Age at initial HD	0.150	0.428			0.228	0.226			−0.161	0.396		
β2-MG	0.014	0.940	0.069	0.321	−0.141	0.458	−0.103	0.657	0.013	0.994	−0.244	0.237

HD, Hemodialysis; β2-MG, Beta2-microglobulin.

decreases its level as found in the L-group of our study.

Cianciolo et al. (2007) reported that blood levels of β2-MG and the incidence of DRA do not always correlate. Age, genetic factors, advanced glycation end products (AGEs), chronic inflammation, and oxidative stress are known risk factors for the onset (Drüeke 2000; Gejyo and Narita 2003; Cruz et al. 2008). Therefore, it is likely to occur in HD patients with a long-term HD period.

Recently, Hishida et al. (2020) and Okazaki et al. (2020) had demonstrated that extended-hours HD without dietary restrictions provided body weight increase, favorable metabolic status, hemodynamic stability, increased dietary intake and better survival rate, especially in elderly maintenance HD patients (more than 70 years old). However, they did not refer to the effects of extended-hours HD without dietary restrictions on the risk for developing of DRA.

Fenves et al. (1986) were the first to report the relationship between dialysis-related carpal tunnel syndrome and cystic radiolucency. Among 7 patients with dialysis-related carpal tunnel syndrome, they found cystic radiolucency of the carpal bone in 6 patients, in addition to amyloid-positive synovitis at the lesion. Homma et al. (1992) reported that cystic radiolucency was observed in 28.8% of the patients who had undergone maintenance dialysis for 10 or more years, concluding that cystic radiolucency could be a useful indicator for making a diagnosis or evaluating the status of dialysis-related amyloid osteoarthrosis. Konishiike et al. (1994) reported that the detection of cystic radiolucency of the carpal bone in long-term dialysis patients could be used as an indicator to make the initial diagnosis of carpal tunnel syndrome. Maruyama (1998) compared patients who had undergone conventional HD (4 hours /session) for 10 years or less with those who had undergone dialysis for 11 years or more, and found that both long-term dialysis patients on maintenance dialysis and older age were associated with a higher rate of cystic radiolucency, which was 44.1% in the higher long-term dialysis patients. The proportion of cystic radiolucency in the carpal bones and humerus in the L-group were clearly lower than what was observed in their reports.

Regarding DSA and HD spondyloarthropathy, Kuntz et al. (1984) identified a class of lesions characterized by three kinds of radiographic changes in dialysis patients, which were designated as DSA. Kerr et al. (1988) proposed instability of the cervical spine as the underlying mechanism. Yokoyama et al. (2004) found that HD spondyloarthropathy developed sooner and progressed more rapidly when dialysis was initiated at an older age. In this study, median nerve compression was significantly lower in the L group, but the incidence of DSA was low in both groups with no difference. The reason may be the young average age at initial HD, which was in their 30s in both groups. Therefore, it was speculated that the progress of DSA was slower than carpal tunnel syndrome. Further studies are required to determine whether there is an association between the extended-hours HD and the incidence of DSA.

Shoulder lesions are frequent in long-standing dialysis patients. (Kurer et al. 1991) Shoulder pain is often seen in dialysis patients and also affects the quality of dialysis treatment, forcing sometimes dialysis discontinuation. Examination of the shoulders by ultrasonography and accurate assessment are important to detect the signs that precede these complications and manage the patient's quality of life and activities of daily living. The underlying mechanism of "supine shoulder pain" has not yet been clearly described in the literature. Research only suggests that amyloid deposition on the coracoacromial ligament, subacromial bursa, or rotator cuff tendon causes narrowing of the subacromial space, and then increases the internal pressure, leading to partial ischemia in the subacromial space. McMahon et al. (1991) reported an increased supraspinatus tendon thickness of 7.4 ± 0.7 mm in patients on long-term dialysis. This report described also that long-term dialysis was associated with thickening of the cuff, but did not mention the effect of dialysis time. Aoyagi (1992) demonstrated that shoulder capsular distance increases in dialysis patients due to thickening of the synovial membrane and retention of joint effusion. Jadoul et al. (1993) showed that the thickness of the supraspinatus and shoulder capsular distance were positively correlated with both the dialysis duration and age. Negi et al. (1995) observed a significant increase

of the shoulder capsular distance in patients who had undergone dialysis for 10 years or more, and concluded that the increase of shoulder capsular distance may indicate possible DRA. Our results are comparable to the literature description but do not allow us to conclude an effect of longer dialysis time on shoulder lesions.

Dialysis-related carpal tunnel syndrome has been demonstrated to involve the formation and deposition of β2-MG amyloid on the synovial membrane of the flexor tendon sheath, possibly causing tendinous synovitis. Amyloid deposition increases the volume of the lesions occupying the carpal tunnel, producing a relative constriction. Enlargement of the carpal tunnel may compromise the blood flow such as by the local edema to produce pressure symptoms of the median nerve. Buchberger et al. (1991) found that the median nerve was swollen inside the proximal part of the carpal tunnel and flattened in the distal part in patients with carpal tunnel syndrome attributable to median nerve compression. The changes observed in the ultrasonographic images of the median nerve trunk in patients with dialysis-related carpal tunnel syndrome may be attributable to the constriction caused by synovitis or degenerative changes in the surrounding tissues due to aging. In this study the severity of median nerve compression at the wrist was significantly less in the L-group compared to the S-group. Multiple regression analysis showed significant association between dialysis time and median nerve compression; longer dialysis time reduced median nerve severity. Furthermore, serum β2-MG levels were shown to be significantly lower in the L-group. From these results, we could argue that less median nerve compression in the L-group might be resulted from an increased removal of β2-MG and suppression of serum β2-MG to low levels by extended-hours HD without dietary restriction.

Our study has a couple of limitations. First, this was a retrospective study. However, considering that it takes several years to observe the onset of complications, it would be very difficult to plan a prospective study. Second, even the patients in the S-group were treated with HD over the standard dialysis time (14.5 vs. 12 hours), which might have obscured a preventive effect of extended-hours HD treatments on the other lesions. Despite these limitations, we were able to confirm our hypothesis.

In conclusion, patients treated with extended-hours hemodialysis without dietary restrictions presented with lower risk for developing of DRA. We therefore propose that extended-hours hemodialysis without dietary restrictions is a preferred method which maintains the patients' quality of life, compared with the conventional hemodialysis method.

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Conflict of Interest

The authors declare no conflict of interest.

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