Need for Education on the Differential Diagnosis between Chronic Glomerulonephritis and Nephrosclerosis, and Treatment of both Conditions to Reduce the Number of Patients Requiring Hemodialysis in Wakayama

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Abstract

Objective We investigated the present state of, and trends in, hemodialysis therapy in Wakayama, with the aim of identifying present and future problems.

Methods We compared the number of patients on maintenance hemodialysis, patients newly commencing hemodialysis each year, and proportion of diseases prompting the initiation of hemodialysis, between Wakayama and all Japan from 2002 to 2009, using the CD-ROM, “An overview of dialysis treatment in Japan,” published by the Japanese Society for Dialysis Therapy.

Results The number of patients on maintenance hemodialysis per head of population was higher in Wakayama than in all Japan throughout the study period. The number of patients newly commencing hemodialysis per head of population was higher in Wakayama than in all Japan from 2002 to 2004, but no significant difference was seen after 2005. The proportion of patients with chronic glomerulonephritis as the causative disease for hemodialysis initiation was higher in Wakayama than in all Japan. However, nephrosclerosis was less common as the causative condition in Wakayama than in all Japan. The proportions of the different causative diseases were similar in all patients on maintenance hemodialysis in Wakayama as in the newly initiated patients. Accordingly, some patients diagnosed with chronic glomerulonephritis might actually have nephrosclerosis, or treatment may be inadequate.

Conclusion In order to reduce the number of patients requiring maintenance hemodialysis, it is important to accurately differentiate between chronic glomerulonephritis and nephrosclerosis, and also to treat patients with either disease appropriately.

Key words: chronic kidney disease, community medicine, diabetic nephropathy, hemodialysis therapy

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Introduction

One of the most brilliant successes in medicine has been hemodialysis treatment for patients with end-stage renal diseases (ESRD), a life threatening condition. This treatment not only rescues patients with ESRD from death, but also raises their quality of life to a high level, near that of healthy individuals. On the other hand, the increasing number of patients requiring maintenance hemodialysis represents an enormous drain on the Japanese medical economy. Recently, the cost of dialysis has reached 1,300 billion yen...
each year (nearly 4% of all medical costs). Further increases in the number of patients on maintenance hemodialysis could cause the collapse of the Japanese medical economy. To prevent this, we need to hold down the increasing number of patients requiring maintenance hemodialysis. On the other hand, we also need to minimize deaths in patients on maintenance hemodialysis, and improve the quality of dialysis treatment. To decrease the number of patients on maintenance hemodialysis, we must reduce the number of patients newly commencing hemodialysis throughout Japan. However, in a symposium at the 2005 annual meeting of Japanese Society for Dialysis Therapy, it was reported that there are differences in the quality of hemodialysis treatment and the treatment of chronic kidney disease (CKD) patients among the regions of Japan. For us, it is an important issue whether the quality of treatment of CKD patients and dialysis treatment in Wakayama attains the average level in all Japan. To clarify these issues, we need to compare data related to dialysis treatment between Wakayama and other regions. For this purpose, dialysis-related data are made available by the Japanese Society for Dialysis Therapy every year, including data from each prefecture (1-8). Using this database, we can conduct regional analyses and time course analyses. In this way, we aimed to identify problems with hemodialysis treatment in Wakayama through comparison of data from Wakayama and all Japan, and investigate factors related to the identified problems.

In this study, we analyzed the number of patients on maintenance hemodialysis in terms of medical fees, and both the number of the patients newly commencing hemodialysis each year and the proportions of causative diseases for hemodialysis initiation in terms of the quality of treatment for CKD. Moreover, we analyzed the proportions of causative diseases for hemodialysis initiation on maintenance hemodialysis in terms of the quality of hemodialysis. To determine whether correction for age was necessary, we analyzed the average age of both patients on maintenance hemodialysis and newly initiated patients.

Data extraction
In this study, the factors examined included the number of patients on maintenance hemodialysis at the end of the year, the number of hemodialysis patients per million head of population, the proportions of causative diseases in these patients, and their average age. We also examined the number of patients newly commencing hemodialysis during the year, the number of new patients per million head of population, the proportions of causative diseases for hemodialysis initiation in these patients, and their mean age. Data were extracted from the database, “An overview of dialysis treatment in Japan” from 2002 to 2009. The causative diseases analyzed in this study were diabetic nephropathy, chronic glomerulonephritis and nephrosclerosis. We compared these factors between Wakayama and all Japan.

Permission was obtained from the Statistical Committee of the Japanese Society for Dialysis Therapy to use their data in this study.

Statistical analysis
Data were analyzed using the Z-test and the statistical software in Excel 2010. In this study, p<0.05 was considered to indicate statistical significance. Population figures for both Wakayama and all Japan were obtained from the “Current Population Estimates as of October 1st Each Year” databases produced by the Japanese Ministry of Internal Affairs and Communication (9).

Results

Changes in the number of the patients on maintenance hemodialysis in Wakayama
The number of patients on maintenance hemodialysis in Wakayama was 2,229 at the end of 2002, and 2,727 at the end of 2009, a 22% increase (Fig. 1). On the other hand, the number of patients on maintenance hemodialysis in all Japan was 229,600 at the end of 2002 and 290,661 at the end of 2009, a 27% increase. The number of patients on maintenance hemodialysis per million head of population in Wakayama was significantly higher than that in all Japan from 2002 to 2009 (Fig. 1).

Changes in the number of patients newly commencing hemodialysis in Wakayama
The number of patients newly commencing hemodialysis in Wakayama was 330 in 2002, and 309 in 2009 (Fig. 2), with no significant change seen over the period 2002 to 2009. On the other hand, the number of patients newly commencing hemodialysis in all Japan was 33,710 in 2002 and 37,566 in 2009, representing a gradual increase. The number of new hemodialysis patients per million head of population in Wakayama was higher than that in all Japan from 2002 to 2004. However, no significant difference was seen between Wakayama and all Japan after 2005 (Fig. 2).
Changes in proportions of causative diseases for hemodialysis initiation in patients on maintenance hemodialysis in Wakayama

Over the study period, the proportion of patients on maintenance hemodialysis with diabetic nephropathy as the causative disease increased, and the proportion of chronic glomerulonephritis decreased, in Wakayama as well as in all Japan (Fig. 3). No significant difference was seen between Wakayama and all Japan in the proportion of diabetic nephropathy causing hemodialysis initiation. However, the proportion of patients with chronic glomerulonephritis as the causative disease was higher in Wakayama than in all Japan (mean ± SD 54.8±3.08% Wakayama, 42.8±3.74% all Japan, p<0.01). On the other hand, the proportion of nephrosclerosis as the causative disease was lower in Wakayama than in all Japan (1.6±0.24% Wakayama, 6.1±0.71% all Japan, p<0.01).

Figure 1. Changes in the number of patients on maintenance hemodialysis in Wakayama and all Japan. The number of patients on maintenance hemodialysis per one million head of population was significantly higher in Wakayama than in all Japan throughout the study period (p<0.01). Closed bar: number of patients on maintenance hemodialysis in Wakayama, Closed circle: number of patients on maintenance hemodialysis per one million population in Wakayama, closed square: number of patients on maintenance hemodialysis per one million head of population in all Japan, **: p<0.01.

Figure 2. Changes in the number of patients newly commencing hemodialysis in Wakayama and all Japan. The number of patients newly commencing hemodialysis per one million head of population was significantly higher in Wakayama than in all Japan from 2002 to 2004 (p<0.05). After 2005, no significant difference was seen in the number of patients newly commencing hemodialysis between Wakayama and all Japan. Closed bar: number of patients newly commencing hemodialysis in Wakayama, closed circle: number of patients newly commencing hemodialysis per one million head of population in Wakayama, closed square: number of patients newly commencing hemodialysis per one million head of population in Japan, *: p<0.05.
Changes in proportions of causative diseases in patients newly commencing hemodialysis in Wakayama

The proportion of patients newly commencing hemodialysis with diabetic nephropathy as the causative disease for hemodialysis initiation increased, and the proportion of chronic glomerulonephritis decreased, in Wakayama as well as all Japan (Fig. 4). No significant difference was seen between Wakayama and all Japan in the proportion of diabetic nephropathy as the causative disease for hemodialysis initiation in new patients. However, the proportion of patients with chronic glomerulonephritis as the causative disease in new patients was higher in Wakayama than in all Japan (40.0±4.7% Wakayama, 26.4±3.4% all Japan, p<0.01). On the other hand, the proportion of nephrosclerosis as the causative disease in new patients was lower in Wakayama than in all Japan (2.5±0.89% Wakayama, 9.3±1.0% all Japan, p<0.01).

Average age of patients on maintenance hemodialysis and newly commencing hemodialysis in Wakayama

Only in 2008, the average age of patients on maintenance hemodialysis was greater in Wakayama than in all Japan (p<0.05). In the rest of the study period, no significant difference was seen in average age between Wakayama and all Japan (Fig. 5A). No significant difference was seen in the average age of patients newly commencing hemodialysis between Wakayama and all Japan throughout the study period (Fig. 5B).

Discussion

In this study, we demonstrated that the number of patients on maintenance hemodialysis in Wakayama increased, and the number of patients on maintenance hemodialysis per head of population was higher in Wakayama than in all Japan over the study period. This suggests regional differences in hemodialysis treatment. Indeed, “An overview of dialysis treatment in Japan” (1-8) reported the regional differences in the number of patients on maintenance hemodialysis per million head of population. There are two major possible reasons. One may be the different numbers of patients newly commencing hemodialysis per year between Japanese prefectures. The other may be differences in outcomes for patients on maintenance hemodialysis between prefectures. Differences in the number of patients newly commencing hemodialysis could be due to different incidences of renal diseases, and levels of treatment for nephritis between prefectures. Differences in outcomes could be caused by differences in average lifespan between prefectures, either too many or too few institutions providing hemodialysis, and varying quality of hemodialysis treatment. Masakane and Arizono reported that of these reasons, the number of new hemodialysis patients contributed most to increased numbers of patients on maintenance hemodialysis (10). In Wakayama, the number of newly commencing hemodialysis patients was higher than the average for all Japan from 2002 to 2004. Accordingly, the number of patients on maintenance hemodialysis in Wakayama could be proportionally higher than that in all Japan during the same period. After 2005, one possible reason for the high number of pa-
tion in prefectures with a temperate climate, such as Kyushu, and fewer in cold areas, such as the Tohoku region.

Another reason for the high number of patients on maintenance hemodialysis in Wakayama might be its temperate climate.

The number of patients newly commencing hemodialysis in all Japan increased over the study period, but not in Wakayama. There are known to be regional differences in the incidence of hemodialysis initiation in Japan (11, 12). Hidai (13) reported that the following two factors greatly influence this incidence. One is the degree of preparedness of patients on maintenance hemodialysis in Wakayama might be this greater number of newly initiated patients in Wakayama than in all Japan up until 2004, as the average duration of hemodialysis in Wakayama in 2009 was 7.27 years. Therefore, the number of patients on maintenance hemodialysis will be similar to that in all Japan. Moreover, there are more patients on maintenance hemodialysis per head of population in prefectures with a temperate climate, such as Kyushu, and fewer in cold areas, such as the Tohoku region.
the medical infrastructure in the region, including the number of hospitals, incidence of admissions, and doctor numbers. The other is how well general practitioners play the role of gatekeepers for renal disease (10, 13). Moreover, Imazawa and Nakazato reported that increased numbers of renal physicians decrease the incidence of hemodialysis initiation (14). In Wakayama, the reason for the high incidence of hemodialysis initiation is unlikely to be insufficient numbers of renal physicians, as there were more per million head of population than the average for all Japan between 2004 and 2008 (31.5±3.0 Wakayama, 21.4±1.3 all Japan) (14). The incidence of hemodialysis initiation in Wakayama has been similar to that in all Japan since 2005. This may be attributable to improved maintenance treatment for patients with CKD in Wakayama. If this is so, we can anticipate a slowing in the increase in the number of patients on maintenance hemodialysis in the near future.

In Wakayama, the proportion of chronic glomerulonephritis as the causative disease for hemodialysis initiation was higher, and that of nephrosclerosis lower, than those for all Japan. Usami et al. reported regional differences in both the incidence and rate of increase in patients ESRD caused by chronic glomerulonephritis, and factors related not to the incidence of chronic glomerulonephritis, but to the onset of ESRD, induce regional differences in hemodialysis initiation in patients with chronic glomerulonephritis, as they found the incidence of hemodialysis initiation correlated more significantly to the rate of increase in patients with ESRD than the incidence of ESRD (11). Therefore, it appears that the proportion of chronic glomerulonephritis as the causative disease for hemodialysis initiation was high in Wakayama due to lost opportunities for treatments related to delayed diagnosis or inadequate treatment following diagnosis. Another possible reason for the high incidence of chronic glomerulonephritis in Wakayama is that some patients with nephrosclerosis have been misdiagnosed as chronic glomerulonephritis. To confirm this, we investigated the causative diseases for initiation of hemodialysis in the 211 patients newly initiated hemodialysis in Division of Nephrology and Blood Purification Medicine, Wakayama Medical University from 2006 to 2009, according to the Table. Two of seven patients referred to us as chronic glomerulonephritis diagnosed by previous medical institutes were classified as nephrosclerosis. Another 34 patients were referred without expected diagnosis of causative disease, 9 of these patients were classified as nephrosclerosis, 9 patients as chronic glomerulonephritis, and 16 patients could not be classified into any group. These findings suggested that it was important to make the differential diagnosis between those diseases by gatekeeper doctors, and also treat each disease appropriately. Therefore, there is a need for education regarding the differential diagnosis between chronic glomerulonephritis and nephrosclerosis for the gatekeeper doctors using the Table.

There may be no difference in the prognosis between each causative disease for hemodialysis initiation in patients on maintenance hemodialysis in Wakayama owing to a similarity between the proportion of patients on maintenance hemodialysis and patients newly commencing hemodialysis, even though the prognosis of each causative disease could not be precisely compared using the database.

In Japan, patients on maintenance hemodialysis become older year after year, and Wakayama is no exception. No significant difference was seen in the average age of patients on maintenance hemodialysis between Japan and Wakayama throughout the study period. Age was therefore not considered a significant factor in the greater numbers of patients on maintenance hemodialysis and newly initiated in Wakayama than in all Japan.

This study had several limitations. First, we did not examine the levels of usage of either angiotensin-converting enzyme (ACE) inhibitors or erythropoietin (EPO), although there have been reports of lower incidences of ESRD in regions with higher levels of usage of ACE inhibitors, and a lower incidence of commencing hemodialysis with higher levels of usage of EPO (15, 16). Second, we did not investigate the causative disease for initiation of hemodialysis in all institutes of Wakayama, but only in the Division of Nephrology and Blood Purification Medicine, Wakayama Medical University. Third, we did not investigate the exact prognosis of causative diseases for hemodialysis initiation in patients on maintenance hemodialysis in Wakayama.

Table. Criterion of Differential Diagnosis between Nephrosclerosis and Chronic Glomerulonephritis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Nephrosclerosis</th>
<th>Chronic glomerulonephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematuria</td>
<td>Negative or minimal</td>
<td>Moderate – Severe</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(macrohematuria)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Mild ( &lt;1g/day )</td>
<td>Moderate – Severe</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(nephrosis)</td>
</tr>
<tr>
<td>Urinary sediment</td>
<td>Normal</td>
<td>Positive for cellular cast</td>
</tr>
<tr>
<td>Age</td>
<td>Middle – Old</td>
<td>Young – Middle</td>
</tr>
<tr>
<td>Other features</td>
<td>Previous long history of hypertension</td>
<td>Family history of urinary abnormality or renal disease</td>
</tr>
<tr>
<td></td>
<td>Arteriosclerosis in the eyebone</td>
<td>Complication of autoimmune disease or hepatic disease</td>
</tr>
<tr>
<td></td>
<td>Atrophic kidney with a granular surface on CT or US</td>
<td></td>
</tr>
</tbody>
</table>

Table showed a criterion of differential diagnosis between nephrosclerosis and chronic glomerulonephritis using in this study. US: ultrasonography, CT: computerized tomography.
In this study, we elucidated the present state and trends in hemodialysis treatment in Wakayama, in particular the number of patients on maintenance hemodialysis, the incidence of initiation, the proportions of causative diseases for hemodialysis initiation, average ages of both patients on maintenance hemodialysis and newly initiated patients in Wakayama. We also clarified problems with dialysis treatment in Wakayama through comparisons of data related to dialysis treatment between Wakayama and all Japan. To solve these problems, we believe it is important to improve the accuracy of the diagnosis of nephrosclerosis, and the treatment of chronic glomerulonephritis through education of the staff engaged in hemodialysis treatment. Addressing these problems should make it possible to 1) delay the initiation of hemodialysis treatment for patients with CKD disease and also to 2) moderate the huge medical costs associated with hemodialysis treatment in Japan.

**Conclusion**

The number of patients on maintenance hemodialysis per head of population was higher in Wakayama than in all Japan throughout the study period. The number of patients newly commencing hemodialysis was also higher in Wakayama than in all Japan prior to 2005, although the difference was not significant after 2005. These findings indicated that the incidence of hemodialysis initiation in Wakayama has improved. Regarding the causative disease for hemodialysis initiation, the proportion of chronic glomerulonephritis was higher, and that of nephrosclerosis lower, in Wakayama. We also identified the potential for further improvements with more accuracy in differentiating between glomerulonephritis and nephrosclerosis, and better treatment for both diseases.

**The authors state that they have no Conflict of Interest (COI).**

**Acknowledgement**

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**References**


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