Comparative Study of Renal Replacement Therapy in Korean Diabetic End-Stage Renal Disease Patients: a Single Center Study

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The number of diabetic ESRD patients has increased and death rates of diabetic patients on hemodialysis (HD), peritoneal dialysis (PD) and renal transplantation (RT) have remained higher than the death rate of non-diabetic patients. An attempt was made to compare the clinical characteristics, patients' cumulative survival, and technical survival among the three groups retrospectively according to the mode of renal replacement therapy (RRT), and to analyze the risk factors associated with mortality. A total of 229 diabetic ESRD patients diagnosed between 1986 and 1995 at the Severance Hospital who began dialysis or who underwent a kidney transplant were included and their medical charts were reviewed.

Hypertension was the most common co-morbid disease in all study groups. The prevalence of cardiovascular disease was the only co-morbid condition that was significantly different among the three groups, which was highest in the PD group (24.4%) and lowest in the RT group (8%). In the analysis of a patient's cumulative survival rate not adjusted for age and sex, the RT group had the highest survival rate, and the cumulative survival rate of the HD and PD group were similar. The 5-year survival rate of the patients treated with HD, PD and RT was 28.8%, 19.8%, and 72.0%, respectively. No differences were observed in the patient's cumulative survival rate between the HD and PD patients even when it was adjusted for age. When adjusted for age, sex and risk factors, the relative death rate of the RT group was significantly lower in male patients younger than 60 years of age. With the exception of male patients younger than 60 years of age, the PD group showed a slightly lower relative death rate although it was not significant. The multiple Cox regression analysis of patient survival showed that age, serum albumin, BUN, mean hospital days, the presence of cardiovascular disease at the initiation of RRT were associated with mortality. The analysis of the technique survival rate revealed a better result in the HD group compared to PD group, but a limitation in being able to investigate the AVF function disturbed the accuracy of the analysis of technical survival rate.

In conclusion, the survival rate between the PD and HD patients was not different and the RT group had the best survival rate. Therefore, kidney transplantation in diabetic ESRD patients should be considered positively if no other contraindicated condition for RT exit.

Key Words: Diabetic esrd, modality, patient's cumulative survival, technical survival

INTRODUCTION

Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD). It develops in 30 - 40% of type 1 diabetic patients and in 20 - 30% of type II diabetic patients. The number of diabetic ESRD patients has increased. The survival rates of diabetic patients on hemodialysis (HD), peritoneal dialysis (PD) and renal transplantation (RT) are still lower than that of non-diabetic ESRD patients even though the survival rates of diabetes have improved during the last decade, particularly in uremic type 1 diabetic patients and, to a lesser extent, in type 2 diabetic patients. The survival rate of ESRD patients is partly dependent on the type of renal replacement therapy (RRT) used.

In general, the patient’s survival after RT is markedly better than that observed with either
HD or PD. Transplantation is also associated with a better quality of life and a higher degree of rehabilitation. However, RT in diabetic ESRD patients had been usually avoided due to the side effects of steroids, combined disease and old age. Nevertheless, the outcome of RT in diabetic patients had been improved after the introduction of cyclosporin in the 1980’s. In addition, a similar treatment success rate was observed in diabetic and non-diabetic patients. A better outcome of transplantation than dialysis therapy are partly related to the patient selection bias particularly in diabetic patients, since dialysis patients with serious co-morbid conditions are usually not accepted on the transplant waiting list and hence remain in the dialysis group. Because of the rapid rise in the incidence of ESRD and the continued shortage of donor kidneys, most ESRD patients will need some form of dialysis during their lifetime. To date, no consensus regarding which form of dialysis (PD or HD) offers patients the best chance for survival has been reached. Moreover, a comparison of the survival rates of diabetic ESRD patients between the HD and PD showed some disparity in the results. For example, Bloembergen, et al. reported that, on average, patients treated with PD had a 19% higher adjusted mortality rate than the patients treated with HD (relative risk=1.19). In contrast, Fenton, et al. demonstrated a 27% lower adjusted mortality rate among patients treated with PD versus HD (relative risk=0.73). In addition, the outcome in elderly diabetic patients has not been specifically addressed and the optimal modality of treatment in this group is still disputed.

Therefore, we tried to compare the clinical characteristics, the patient’s cumulative survival, and technique survival among three groups (HD, PD, and RT) retrospectively according to the mode of renal replacement therapy, and to analyze the risk factors for mortality.

MATERIALS AND METHODS

Patient’s collection

Between 1 January 1986 and 31 December 1995, the data from 229 new diabetic ESRD patients who were started on dialysis therapy or had a kidney transplant at Yonsei University Severance Hospital, Seoul, Korea was retrieved in 31 December 2001. In these patients, the patients who were followed up at least 1 month were included. The patients were divided into three groups by the initially treated modalities as the HD group (75 cases), the PD group (128 cases) and the RT group (26 cases). In this paper, diabetic nephropathy was defined as a pathologic diagnosis proven by a renal biopsy or a clinical diagnosis by the duration of DM and the presence of diabetic retinopathy. The dialyzed patients who received RT were analyzed as the censoring data at the point of renal transplantation.

Clinical characteristics

All the patient’s medical charts were reviewed retrospectively, and the data obtained such as age, sex, type of DM, duration of DM and age, height, weight, laboratory data and co-morbid conditions at the beginning of RRT was collected. The co-morbid conditions included hypertension defined as previously diagnosed hypertension, medicated with antihypertensive drug or a blood pressure higher than 140/90 mmHg, cardiovascular disease defined as angina pectoris, myocardial infarction and congestive heart failure, cerebrovascular diseases defined as cerebral hemorrhage or infarction, B-viral or C-viral hepatitis, alcoholic or viral liver cirrhosis, tuberculosis and malignancy.

Patient’s cumulative survival

In this study, the endpoint was considered as following conditions: death, change to another modality, and the end of this study. The patient’s survival duration was measured from the start of the first RRT to death from any cause or the date of their last follow-up prior to death.

Technical survival

The technical survival duration was measured from the start of the first RRT to the technical failure. In the PD patients, technical failure included catheter removal from any cause. In the HD patients, technical failure included a change
to other modalities due to causes such as hypoten-
sion, heart failure, loss of the hemodialysis root. In the RT patients, technical failure included a change to dialysis therapy or receiving a second renal transplant. The dialyzed patients receiving renal transplantation were censored at the date of transplantation. Those who had died and were effective in the modality function were analyzed as being technically alive.

Statistical analysis

The results are presented as a mean ± SD. The data among the groups were compared using the analysis of variance (ANOVA). The Kaplan-Meier method was used to analyze the survival rate. Univariate and multivariate analysis of the survival rate was performed to identify the significant prognostic factors. Multivariate analysis was done using the Cox proportional hazard regression model. The SPSS package version 10.0 statistical software was used. A p value < 0.05 was used as the criterion for statistically significance.

RESULTS

Clinical characteristics at initiation of RRT

A total 229 new diabetic ESRD patients who were started on dialysis therapy or underwent kidney transplantation between 1986 and 1995 were divided into 3 groups by the initial treatment modalities. These groups were the HD group (75 cases), the PD group (128 cases) and the RT group (26 cases). The clinical characteristics of the patients in each group are summarized in Table 1.

The patient's clinical characteristics among the groups were similar, except for age and the serum BUN level at the beginning of RRT. The age of the RT patients was significantly lower than that of the dialysis patients (RT 47.9 ± 7.9 vs. HD 59.3 ± 8.9 vs. PD 57.0 ± 9.5 years, p=0.01). Of the HD patients, 44.6% were over than 61 years of age. Of the PD patients, 44.1% were in the 50-60 years of age range. Of the RT groups, only 1 case was over 60 years of age due to an avoidance of transplantation in old age. The serum BUN level in the RT group was significantly lower than that of the dialysis groups (RT 71.3 ± 26.4 vs. HD 87.7 ± 22.9 vs. PD 91.1 ± 32.9 mg/dL, p=0.02).

Comorbid conditions at the initiation of RRT

The co-morbid conditions at the initiation of RRT were revised in the medical records and are shown in Table 2. Hypertension was the most common co-morbid disease in all groups. Cardiovascular disease was the only co-morbid condition

| Table 1. Clinical Characteristics at the Initiation of Renal Replacement Therapy |
|---------------------------------|------|------|------|
|                                | HD   | PD   | RT   |
| Number (cases)                 | 75   | 128  | 26   |
| Sex (M/F)                      | 51/24| 79/49| 8/18 |
| Age (yrs)                      | 59.3 ± 8.9 | 57.0 ± 9.5 | 47.9 ± 7.9<sup>a</sup> |
| Height (cm)                    | 163.0 ± 8.2 | 162.9 ± 8.1 | 164.5 ± 7.3 |
| Weight (kg)                    | 59.8 ± 9.7 | 58.9 ± 9.1 | 60.5 ± 7.9 |
| BUN (mg/dL)                    | 87.7 ± 22.9 | 91.1 ± 32.9 | 71.3 ± 26.4<sup>b</sup> |
| Creatinine (mg/dL)             | 9.3 ± 3.2 | 10.1 ± 3.9 | 10.6 ± 2.9 |
| Ccr (ml/min/1.73 m<sup>3</sup>) | 7.6 ± 2.8 | 7.4 ± 3.3 | 7.3 ± 1.5 |
| Hemoglobin (g/dL)              | 7.8 ± 1.5 | 7.5 ± 1.4 | 8.4 ± 1.9 |
| Albumin (g/dL)                 | 3.2 ± 0.8 | 3.07 ± 0.5 | 3.4 ± 0.7 |
| Duration of DM (yrs)           | 15.7 ± 6.9 | 14.5 ± 5.9 | 15.7 ± 4.6 |
| HbA1c (%)                      | 7.6 ± 2.8 | 7.6 ± 3.2 | 7.3 ± 3.3 |

<sup>a</sup>p<0.05 vs. HD, <sup>b</sup>p<0.05 vs. PD.
<sup>a</sup>age at initiation of RRT, <sup>c</sup>creatinine clearance, <sup>d</sup>duration from diagnosis of DM to initiation of RRT.
that was significantly different among each group, and its prevalence was highest in the PD group (24.4%) and lowest in the RT group (8%). This result may be related to the fact that many clinicians prefer CAPD therapy for patients with cardiovascular problems. One patient treated with HD had rectal cancer and one patient treated with PD had lung cancer in a state of complete remission after cancer resection surgery.

Patient’s cumulative survival rates and risk factor for mortality

In an analysis of the patient’s cumulative survival rate not adjusted for age and sex, the RT group exhibited the lowest mortality rate ($p<0.05$). The HD patient survival rate was higher than that of PD patients although not significant ($p=0.44$) (Fig. 1). The one-year survival rate of the diabetic ESRD patients treated with HD, PD and RT was 76.3%, 77.8% 92.3%, respectively. The 5-year survival rate of the diabetic ESRD patients treated with HD, PD and RT was 28.8%, 19.8% and 72%, respectively.

In an analysis of the patient’s survival rate adjusted for age, patients younger than 60 years of age in the RT group showed significantly higher survival rate than the other two groups ($p<0.05$) (Fig. 2A). The survival rates between the HD and PD patients were similar even when adjusted for age (Fig. 2A and B).

The results of the multivariate analysis aimed at identifying the risk factors for mortality are listed in Table 3. The multiple Cox regression analysis of the patient survival showed that age (≥60 years vs. <60 years), serum albumin, BUN, mean hospital days, and a history of cardiovascular disease at the initiation of RRT were associated with mortality (Table 3).

The patients were divided into 4 subgroups
according to age and sex, and were adjusted for the risk factor for a comparison of the death rate. The death rate of the renal transplanted male patients younger than 60 year of age was significantly lower than the HD and PD patients (relative rate=0.34, \(p<0.05\)). With the exception of male patients younger than 60 year of age, the PD group showed a slightly better odds ratio although not significant (Fig. 3).

**Technical survival rates**

The HD patients showed significantly better outcomes in terms of technical survival rate than the PD patients (\(p<0.05\)), and showed slightly higher technical survival rates than the RT patients although not significant (\(p=0.059\)) (Fig. 4). The 5-years technical survival rate of the HD, PD and RT patients was 87.9%, 60.4%, and 74.6%, respectively.

**Cause-specific death rate by modalities**

There were no significant differences between the groups by the modalities. The most common cause of death was infection in the PD and RT patients (33.7 vs. 26.5 death/1000 patient-year), and cardiovascular disease in the HD patients (27.9 death/1000 patient-year). The second common cause of death was cardiovascular disease in the PD and RT patients (31.8 vs. 19.9 death/1000 patient-year), and infection in the HD patients (23.9 death/1000 patient-year) (Fig. 5).

**DISCUSSION**

Diabetic nephropathy is the leading cause of ESRD, and the number of diabetic ESRD patients has increased. Although gradually decreasing, the mortality rate in diabetic ESRD patients was

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**Table 3. Risk Factors of Mortality by Multiple Cox Regression Analysis**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds ratio</th>
<th>95% C.I.</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dL)</td>
<td>0.381</td>
<td>0.248-0.585</td>
<td>0.002</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>1.017</td>
<td>1.007-1.026</td>
<td>0.045</td>
</tr>
<tr>
<td>Hospital day (day/yr/patients)</td>
<td>1.02</td>
<td>1.014-1.026</td>
<td>0.001</td>
</tr>
<tr>
<td>Hx of cardiovascular dz.</td>
<td>2.376</td>
<td>1.324-4.264</td>
<td>0.02</td>
</tr>
<tr>
<td>Age ((\geq 60) vs. (&lt; 60) yrs)</td>
<td>3.788</td>
<td>2.354-6.094</td>
<td>0.001</td>
</tr>
</tbody>
</table>
higher than in the non-diabetic ESRD patients.\textsuperscript{14,15} Diabetic ESRD patients have many problems such as cardiovascular disease, intradialytic hypotension compared to non-diabetic patients. They also have limitations in performing HD therapy due to difficulties in vascular access, and have limitations in performing PD therapy due to diabetic retinopathy.

The ability of PD to control azotemia, hyperglycemia (with intraperitoneal insulin), and hypertension without sudden drastic changes in the body fluid make PD a preferable treatment modality for diabetic ESRD than HD.\textsuperscript{16-18} However, to date, no consensus has been reached regarding which form of dialysis, PD or HD, offers patients the best chance for survival. Several studies have reported conflicting results with respect to the survival benefits of one therapy over another. In early previous studies comparing survival, the survival rate of PD patients was reported to be higher than that of HD patients.\textsuperscript{14,19,20} Nelson, et al.\textsuperscript{(1992)} reported that the mortality rate of PD patients with diabetes was lower than HD patients and the relative ratio of death (PD/HD) was 0.4-0.7 and increasing with increasing age.\textsuperscript{14}

Subsequently, several studies reported a similar mortality rate between HD and PD patients. Marcelli, et al.\textsuperscript{(1995)} reported that the 5-year survival rate of dialyzed diabetic patients was 28%, and there was no difference between HD and PD patients.\textsuperscript{16} Serke, et al.\textsuperscript{(1990)} also reported no difference between the groups.\textsuperscript{21} Recent registry studies have reported conflicting results when comparing the mortality rate between PD and HD patients.\textsuperscript{22-25} Several studies have demonstrated that the mortality rate adjusted for age and sex was higher in PD patients compared to HD patients with diabetes. Held, et al.\textsuperscript{(1994)} reported by a reanalysis of USRDS data that the adjusted mortality for the two broadly defined age groups (< 50 years, ≥ 50 years) of diabetics suggest that an elevated mortality for PD relative to HD may be accentuated among older patients (RR=1.11 vs. 1.34), and suggested the need for further controlled studies of the mortality rate among PD.

\textbf{Fig. 3.} Relative risk of death (PD/HD or RT/HD) according to the subgroups, which are adjusted for age, sex and risk factors (risk factor defined as serum albumin, BUN, hospital day and the presence of cardiovascular disease). $p<0.05$.

\textbf{Fig. 4.} Technical survival rates by modalities of renal replacement therapy. $p=0.059$ HD vs. RT, $p<0.05$ HD vs. PD.

\textbf{Fig. 5.} Cause-specific death rates according to the modality. CVD: Cardiovascular disease, CVA: Cerebrovascular accident.
patients with diabetes. In a more recent report, Vonesh, et al. (1999) reported the relative mortality rate of diabetic ESRD patients adjusted for age and sex. They found that except for older diabetic patients, particularly older female diabetic patients, PD patients have a similar (non-diabetic patients) or better (younger diabetic patients) survival rate than HD patients.

We analyzed patient's cumulative survival rate with and without adjustment for age and sex among 3 groups in our study. In the analysis of patient's survival rate not adjusted for age and sex, the survival of RT patients was significantly better than that of HD and PD patients. The survival rate of HD patients was slightly higher than that of PD patients, but showed no significant difference (5-year survival rate was 28.8% in HD and 19.8% in PD). The RT patients showed similar 5-year survival rate (72.0%) compared with previous studies.

Thereafter, we analyzed the patient's survival rate with adjustment for age (<60 years, ≥60 years). In the patients younger than 60 years of age, the 5-year survival rate of HD patients was slightly higher than that of PD patients (40.0% vs. 21.0%), but there was no significant difference. The 5-year survival rate of RT patients was significantly higher (70%) than that of dialyzed patients. In the patients older than 60 years of age, the survival rate showed marked decrease compared with the patient younger than 60 years of age, but there was no difference in survival rate between HD and PD patient (17.2% vs. 17.9%).

In the analysis of risk factor influencing survival, multiple Cox regression analysis weighed serum albumin, BUN, mean hospital day, presence of cardiovascular disease, and age (older than 60) as a risk factor of death. Age (older than 60/younger than 60) was most powerful factor (Odds ratio=3.78), and the presence of cardiovascular disease (presence/absence) was secondary powerful factor (Odds ratio=2.38). Mean hospital day was risk factor that influence in the patient's cumulative survival rate. The patient's mortality rate increased 2% per hospital day, and the survival rate was fallen according to increment hospital day by various causes. Serum albumin was also risk factor of death (Odds ratio=0.38) as likely as previous reported results. The odds ratio of the serum BUN was 1.017. However, the serum BUN level was influenced by multiple factors such as the catabolic status of the protein, nutritional status, uremic status, and the significance of BUN influencing the survival rate was not clarified. Apolipoprotein A, fibrinogen, a history of cardiovascular disease and liver cirrhosis, which were reported as risk factors in previous studies, did not influence the mortality rate in this study.

The patient's relative risk of death adjusting for the risk factors (serum albumin, BUN, age, presence of cardiovascular disease) was compared. All patients were divided into 4 subgroups according to age and sex. The relative risk of death was similar in HD and PD patients. Except for male patients younger than 60 year of age, the PD patients, particularly female and those younger than 60 years, showed a slightly lower relative risk of death although not significant. This result contrasts with the data that was not adjusted for the risk factors that affected the survival, which showed that the survival rate of PD patients was poorer than that of HD patients. The suggestion was made because the prevalence of cardiovascular disease in PD patients was higher than the other modalities, as patients with cardiovascular disease were given PD therapy preferably. Therefore, in the condition of the adjusted for risk factors, the relative death ratio of the PD patients was lower than the HD patients except for male patients younger than 60 year of age. The relative risk of death in male RT patients young than 60 were lower than that in female RT patients young than 60. It was supposed due to higher combid disease of female RT patients such as cardiovascular disease in this study. But, the number of patients was small and more large scaled study was needed.

In an analysis of the technical survival rate, HD patients had a significantly higher technical survival rate than PD patients, but showed no difference with the RT patients. The technical failure of the PD patients was clearly clarified in their medical records because the patients required hospitalization for a CAPD catheter removal by peritonitis, metabolic disorders, malnutrition, and ultrafiltration failure. The technical failure of RT patients was also clearly identified.
in the patients' medical records such as acute and chronic rejection. However, the accuracy of the HD patient's technical survival rate is questionable because treatment was achieved mainly on the basis of outpatient care in case of AVF and catheter function loss. Therefore, the HD patient's technical failure was defined as a change in the modality to PD or RT therapy more than an AVF or catheter function loss in this study.

The most common cause of death was infection in PD and RT patients, and cardiovascular disease in HD patients. The cause of death could not be analyzed properly in many cases due to the poor medical records, and limitations because of the difficulty of obtaining information over the telephone. Cardiovascular disease was reported to be the most common cause of death in previous studies. In a recent study, 25 the most common cause of death was cardiac arrest apart from cardiovascular disease, but more a correct analysis was impossible in this study.

In conclusion, the risk factors influencing the survival rates were serum albumin, BUN, age (> 60 years), presence of cardiovascular disease, and the mean hospital day. The survival rate between the CAPD patient group and the HD patient group was similar, and the RT group had the best survival rate. Therefore, kidney transplantation in diabetic ESRD patients should be considered positively if no other contraindicated condition for RT exit.

REFERENCES


