

Impact of Home-Based Rehabilitation on Renal Prognosis in Patients with Chronic Kidney Disease

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Background: The increasing prevalence of chronic kidney disease (CKD) requires effective preventive measures, particularly due to an aging population. This study aimed to assess the effectiveness of home visit rehabilitation in preventing renal function decline among patients with CKD.

Method: In this retrospective study, patients with non-dialysis CKD undergoing home visit rehabilitation were compared with those receiving outpatient care at the Nippon Medical School Hospital between August 2017 and August 2023. Patients' backgrounds were matched using propensity scores derived from a logistic regression model. The primary endpoint was the annual change in the estimated glomerular filtration rate (eGFR), and the secondary endpoint was the annual change in blood parameters (Δ blood urea nitrogen, Δ creatinine, Δ total protein, Δ albumin, Δ C-reactive protein, Δ hemoglobin, and Δ hematocrit). Furthermore, the incidence of clinical outcomes, including mortality, hospitalization rate, and dialysis initiation rate, were analyzed within the additional 1-year observation period.

Results: Overall, 128 patients (64 matched pairs) were analyzed. After a mean follow-up period of 12.7 ± 4.6 months, there was no significant difference in the eGFR between both groups (40.1 ± 13.7 vs. 37.8 ± 13.8 mL/min/1.73 m², $p = 0.36$), but the annual decline in eGFR (%/year) was significantly lower in the rehabilitation group ($-1.1 \pm 29.8\%$ vs. $-11.8 \pm 27.7\%$ /year, $p = 0.037$). The annual change in the level of each blood test parameter and clinical outcomes were not significantly different between the two groups.

Conclusion: Home-based rehabilitation interventions may mitigate the progression of renal impairment in patients with CKD. (J Nippon Med Sch 2024; 91: 439–445)

Key words: chronic kidney disease, home visit rehabilitation, renal rehabilitation, rehabilitation, renal prognosis

Introduction

The prevalence of chronic kidney disease (CKD) has been increasing worldwide and is attributed to an aging population. By 2018, Japan had 13.3 million cases of CKD, with approximately 350,000 patients undergoing dialysis¹. CKD progression imposes substantial healthcare burdens, encompassing the management of CKD, and initiation of renal replacement therapies. Furthermore, patients with CKD and end stage renal disease experience a markedly diminished quality of life (QOL) compared to the general

population^{2–4}. Therefore, preventing renal function decline has become an urgent global priority from medical, healthcare economics, and patient QOL perspectives.

In the 2018 revision of Japan's insurance reimbursement system, the upper limit of the estimated glomerular filtration rate (eGFR) as an eligible condition for insurance coverage was expanded to 45 mL/min/1.73 m², underscoring the importance of early intervention to prevent renal function decline. Previously, preventive strategies for CKD primarily revolved around medications and

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dietary restrictions, with exercise therapy often discouraged or prohibited for patients with CKD. However, the emerging concept of renal rehabilitation for addressing both the physical and psychological symptoms associated with CKD and dialysis is gaining recognition, thereby contributing to an extended life expectancy and enhanced psychosocial QOL for patients¹.

Home visit rehabilitation offers potential benefits to individuals who are unable to access outpatient facilities or face challenges in participating in autonomous exercise therapy. Moreover, this type of rehabilitation underscores the importance of home care, providing modern healthcare solutions with significant medical and psychosocial implications. This study aimed to assess the impact of home-based rehabilitation on the prognosis of renal dysfunction.

Methods

Study Population

The study participants consisted of patients diagnosed with CKD who underwent home-based rehabilitation at IKI KI SUN Visiting Nursing Rehabilitation Station between August 1, 2017 and August 31, 2023. Meanwhile, the control group included patients with CKD receiving care at the Department of Nephrology, Nippon Medical School Hospital outpatient clinics. Inclusion criteria for both groups were an eGFR of <60 mL/min/1.73 m², not being on maintenance dialysis, aged ≥ 54 years, and having had a follow-up duration of at least 6 months. Propensity scores for rehabilitation implementation were derived for both groups, and 1:1 matching based on these scores was performed for retrospective analysis.

Rehabilitation

Following home nursing instructions provided by primary care physicians, rehabilitation sessions were conducted at a frequency ranging from 1 to 6 times per month. Each session lasted 40-60 min, occurred 1-3 times per week, and was supervised by a physical therapist during home visits. Before rehabilitation started, the participants' primary doctors evaluated their degree of independence in daily living, and regraded their disabilities and cognitive functions. Initially, the patients underwent individual assessments of muscle strength, joint range of motion, walking ability, and activities of daily living (ADL). Subsequently, a program comprised of muscle strengthening exercises, joint range of motion exercises, stretching, basic movement exercises, walking exercises, and muscle relaxation massage was implemented. The target intensity for rehabilitation exercises was set to

range from 4 to 5 on the modified Borg scale.

Follow-Up and Endpoint

Patients undergoing home-based rehabilitation underwent regular follow-ups at their primary healthcare facilities, wherein blood test measurements, including blood urea nitrogen (BUN), creatinine (Cr), total protein (TP), albumin (Alb), C-reactive protein (CRP), hemoglobin (Hb), and hematocrit (Hct), were conducted every 1-6 months. The blood test results closest to the start date provided by the primary care physician were considered as the baseline blood test information. Furthermore, the control group receiving outpatient care at the Department of Nephrology, Nippon Medical School Hospital underwent follow-up blood testing according to the evidence-based clinical practice guidelines for CKD 2012⁵. In the control group, baseline data were defined as the earliest blood test information available within the study period. The primary outcome was the estimated annual change in eGFR, calculated in intervals of at least 6 months, and secondary outcomes included the annual change in BUN, Cr, TP, Alb, CRP, Hb, and Hct levels. Additionally, we evaluated clinical outcomes, including mortality, hospitalization rate, and initiation of dialysis rate, within 1 year after the follow-up period. In the rehabilitation group, changes in the degree of independence in daily living activities were also assessed from the initiation of the program to the final follow-up.

Statistical Analysis

Continuous variables are expressed as mean \pm standard deviation, while categorical variables are presented as proportions. Comparisons for continuous and categorical variables were conducted using t-tests and chi-squared tests, respectively. Levene's test was employed to assess the homogeneity of variance. This study considered factors that predicted rehabilitation implementation and those influencing renal function changes, including age, sex, eGFR, hypertension, and diabetes. Propensity score matching involved utilizing baseline information from both groups, with scores estimated using binary logistic regression rounded to the nearest first decimal place. Nearest neighbor matching without replacement was also conducted between the rehabilitation and non-rehabilitation groups. Post-matching, patient characteristics between the two groups were compared using t-tests for continuous variables and chi-squared tests for categorical variables. Group comparisons for the primary outcome were performed using t-tests. For the secondary outcome, the annual change in each level of blood parameters from baseline to follow-up was calculated and

Table 1 Baseline patient characteristics pre-matching

	Control (n=1,536)	Rehabilitation (n=69)	<i>p</i> value
Age (years)*	71.2 ± 9.8	81.3 ± 8.8	<0.001
eGFR* (mL/min/1.73 m ²)	29.7 ± 15.2	41.0 ± 10.7	<0.001
No. of patients (male %)	1,030 (67.1)	28 (40.6)	<0.001
No. with hypertension (%)	896 (58.3)	48 (69.6)	0.079
No. with diabetes mellitus (%)	884 (57.6)	24 (34.8)	<0.001

*Values are presented as mean ± SD.

eGFR: estimated glomerular filtration rate

Table 2 Baseline patient characteristics after propensity score matching

	Control (n=64)	Rehabilitation (n=64)	<i>p</i> value
Age-years*	78.8 ± 10.1	80.7 ± 8.7	0.26
eGFR-mL/min/1.73 m ² *	41.6 ± 12.2	40.4 ± 10.6	0.56
Sex-no. (male %)	31 (48.4)	28 (43.8)	0.72
Hypertension-no. (%)	41 (64.1)	43 (67.2)	0.85
Diabetes mellitus-no. (%)	28 (43.8)	24 (37.5)	0.59

*Values are presented as the mean±SD.

eGFR, estimated glomerular filtration rate

compared between groups using t-tests. Using chi-squared tests, mortality, hospitalization, and initiation of dialysis rates within 1 year after the follow-up period were compared between groups. Statistical significance was set at $p < 0.05$ (two-tailed). IBM SPSS Statistics software version 29.0 (IBM Corp, Armonk, NY) was employed for all statistical analyses.

Statement of Ethics

The study protocol was designed in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Nippon Medical School Hospital (approval number: B-2022-638), and an opt-out option was provided on the Clinical Research Center's website.

Results

Patient Characteristics

Between August 1, 2017 and August 31, 2023, 969 patients received home-based rehabilitation at IKI KI SUN Visiting Nursing Rehabilitation Station, with 69 patients meeting the inclusion criteria. Meanwhile, 1,536 patients attending the nephrology outpatient clinic at Nippon Medical School Hospital during the same period also met the inclusion criteria. Although there was no significant difference in the proportion of patients with hypertension between the two groups (rehabilitation group, 69.6% vs. control group, 58.3%, $p = 0.079$), the rehabilitation group was older (81.3 ± 8.8 vs. 71.2 ± 9.8 years, $p < 0.001$) and had a significantly lower proportion of men (40.6% vs.

67.1%, $p < 0.001$) and patients with diabetes (34.8% vs. 57.6%, $p < 0.001$) (Table 1). After matching, 128 patients (64 pairs) were analyzed. There were no significant differences in patient characteristics, including age (80.7 ± 8.7 vs. 78.8 ± 10.1 years), gender (43.8% vs. 48.4%), baseline eGFR (40.3 ± 10.6 vs. 41.6 ± 12.2 mL/min/1.73 m²), hypertension (67.2% vs. 64.1%), and diabetes (37.5% vs. 43.8%) between the two matched groups (all $p > 0.05$) (Table 2).

Primary Endpoint

The mean follow-up duration was 12.7 ± 4.4 and 12.7 ± 4.8 months for the rehabilitation and control groups, respectively; there was no significant difference ($p = 0.99$). At follow-up, the mean eGFRs were 40.1 ± 13.7 mL/min/1.73 m² and 37.8 ± 13.8 mL/min/1.73 m² for the rehabilitation and control groups, respectively; there was no significant difference ($p = 0.36$). Analysis of the annual eGFR change (%/year) between the two groups showed that the rehabilitation group experienced a significantly slower decline in eGFR compared to the control group ($-1.1 \pm 29.8\%/year$ vs. $-11.8 \pm 27.7\%/year$, $p = 0.037$) (Fig. 1).

Secondary Endpoint

The annual change in the levels of each blood test parameter were as follows: Δ BUN ($14.2\% \pm 41.8\%/year$ vs. $44.2\% \pm 141\%/year$, $p = 0.11$), Δ Cr ($6.33\% \pm 29.6\%/year$ vs. $27.0\% \pm 99.6\%/year$, $p = 0.11$), Δ TP ($1.49\% \pm 10.1\%/year$ vs. $2.04\% \pm 10.5\%/year$, $p = 0.81$), Δ Alb ($0.09\% \pm 12.7\%/year$ vs. $5.79\% \pm 27.2\%/year$, $p = 0.20$), Δ CRP

(39.0% \pm 271%/year vs. 773% \pm 4,799%/year, $p = 0.48$), Δ Hb (1.39% \pm 13.4%/year vs. 0.86% \pm 28.7%/year, $p = 0.90$), and Δ Hct (1.95% \pm 13.5%/year vs. 1.08% \pm 25.8%/year, $p = 0.82$); none of the differences between the two groups were statistically significant (Table 3). Additionally, regarding outcomes within 1 year after the follow-up period, there were no significant differences in the mortality rate (4.7% vs. 3.1%, $p = 0.99$), hospitalization rate (14.1% vs. 25.0%, $p = 0.18$), or initiation rate of dialy-

sis (1.6% vs. 4.7%, $p = 0.62$) between the two groups (Table 4).

In the rehabilitation group, changes in the degree of independence in daily living activities related to disabilities were observed as follows: improvement in 9 participants (15%), no change in 44 (72%), and worsening in 8 (13%). Additionally, changes in the degree of independence in daily living activities related to cognitive functions were recorded as follows: improvement in 4 participants (6%), no change in 49 participants (77%), and worsening in 11 participants (17%).

Discussion

This study is the first to validate the effects of home visit rehabilitation on renal prognosis in patients with CKD by utilizing propensity score matching to adjust for background factors. Among patients receiving regular follow-ups at healthcare facilities, those undergoing rehabilitation exhibited a significantly slower decline in eGFR compared to those not undergoing rehabilitation. Additionally, no significant differences were observed in the annual change in the levels of various blood test parameters between the two groups nor in clinical outcomes within the 1-year post-follow-up period.

Impact of Rehabilitation on Renal Outcomes

Renal rehabilitation includes dietary therapy, fluid management, medication adjustment, and patient and family education, with appropriate exercise therapy play-

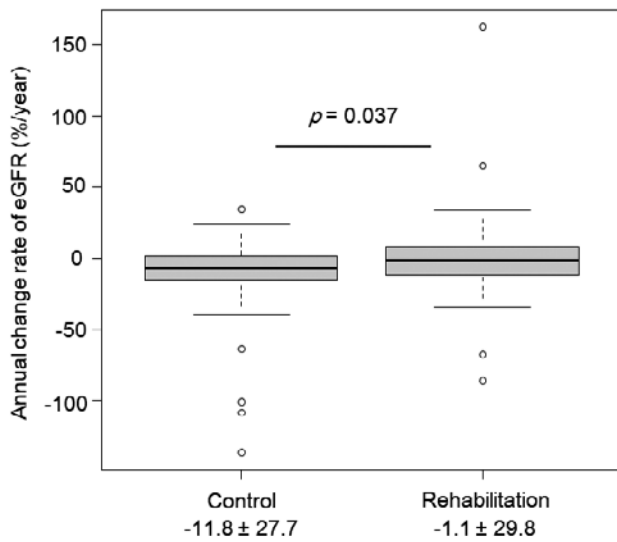


Fig. 1 Analysis of eGFR changes between the two groups
Abbreviations: eGFR, estimated glomerular filtration rate

Table 3 Annual change rates of blood test parameters (%/year)

	Control (n=64)	Rehabilitation (n=64)	<i>p</i> value
Δ BUN*	44.2 \pm 141	14.2 \pm 41.8	0.11
Δ Cr*	27.0 \pm 99.6	6.33 \pm 29.6	0.11
Δ TP*	2.04 \pm 10.5	1.49 \pm 10.1	0.81
Δ Alb*	5.79 \pm 27.2	0.09 \pm 12.7	0.20
Δ CRP*	773 \pm 4,799	39.0 \pm 271	0.48
Δ Hb*	0.86 \pm 28.7	1.39 \pm 13.4	0.90
Δ Hct*	1.08 \pm 25.8	1.95 \pm 13.5	0.82

*Values are presented as the mean \pm SD.

BUN, blood urea nitrogen, Cr, creatinine, TP, total protein, Alb, albumin, CRP, C-reactive protein, Hb, hemoglobin, Hct, hematocrit

Table 4 Incidence of clinical outcomes one year after the follow-up period

	Rehabilitation (n=64)	Control (n=64)	<i>p</i> value
Mortality-no. (%)	3 (4.7)	2 (3.1)	0.99
Hospitalization rate-no. (%)	9 (14.1)	16 (25.0)	0.18
Initiation of dialysis rate-no. (%)	1 (1.6)	3 (4.7)	0.62

ing an important role^{1,2}. In the early stages, physical activity in patients with CKD was reportedly insufficient, highlighting the potential preventive effects of exercise on renal function decline⁶. Studies have revealed the effects of exercise therapy in patients on hemodialysis, showing improvements in exercise tolerance as evidenced by parameters such as peak oxygen consumption and 6-min walking distance as well as enhancements in QOL⁷⁻⁹. Herein, physical therapy through home-based rehabilitation that targeted the musculoskeletal system in patients with non-dialysis CKD resulted in a more gradual decline in eGFR.

Previous research has shown the beneficial effects of exercise therapy on renal prognosis in CKD. Zhao et al.¹⁰ noted decreased serum Cr and BUN levels, alleviated renal fibrosis, reduced oxidative stress, and decreased expression of inflammatory cytokines in the kidneys of elderly rats following 12 weeks of swimming exercise. Heifets et al.¹¹ reported remarkably higher GFR, decreased proteinuria, and milder degrees of glomerulosclerosis in partially nephrectomized rats after 2 months of swimming exercise. Additionally, Yamakoshi et al.¹² reported improvements in collagen metabolism in the kidneys of partially nephrectomized rats and mitigation of renal renin-angiotensin-aldosterone system deterioration, resulting in improvements in hypertension, proteinuria, renal dysfunction, glomerulosclerosis, and interstitial fibrosis following treadmill running.

Several studies have explored the effects of exercise therapy on renal prognosis in patients with non-dialysis CKD. A secondary analysis of a phase 3 multi-center randomized clinical trial on health education programs showed that moderate exercise intervention of >2 years in older individuals with a median eGFR of 54 mL/min/1.73 m² improved the mean annual rate of eGFR decline⁴. Additionally, another meta-analysis of randomized controlled trials (RCTs) that included patients with CKD stages 3-4 showed a 2.16-mL/min/1.73 m² improvement in eGFR after an 8-month aerobic training program¹³. Similarly, a meta-analysis of RCTs that included patients with non-dialysis CKD revealed a significant increase in eGFR (+2.62 mL/min/1.73 m²) with exercise therapy¹⁴.

Meanwhile, home-based rehabilitation has several advantages over conventional outpatient rehabilitation. During the COVID-19 pandemic in 2019, the low infection risk resulted in the increased adoption of home-based rehabilitation. Furthermore, compared to outpatient rehabilitation, home-based rehabilitation does not incur facility maintenance costs¹⁵. Home-based rehabilita-

tion is reportedly effective in sustaining improvements in exercise function and QOL even after discontinuation of rehabilitation, as observed in cardiac rehabilitation studies¹⁶. Although limited, reports on the effectiveness of home-based rehabilitation in non-dialysis patients with CKD exist, with improvements observed in exercise function, QOL, and reduced urinary liver-type fatty acid-binding protein levels. One study involving 46 patients with stage 4 CKD demonstrated these improvements¹⁷. Hence, our findings on the renal protective effects of home-based rehabilitation suggests an additional benefit to the clinical management of patients with CKD.

Change in Laboratory Data

The annual rates of change in levels of various blood test parameters were not remarkably different between patients with CKD who underwent home-based rehabilitation and those that did not. A meta-analysis examining the impact of exercise on nutritional indices in patients with CKD showed significant reductions in body mass index and waist circumference post-exercise training, while no significant differences in serum albumin levels or body fat were noted between the exercise and usual care groups¹⁸. Although a significant difference in baseline serum Alb levels was observed between the rehabilitation and control groups, the annual change between the two groups was not significantly different, with both groups exhibiting an upward trend annually.

Regarding the impact of rehabilitation on inflammation, research has shown increased expression of the inflammatory cytokines interleukin (IL)-4 and IL-10 and decreased expression of IL-6 in exercised rats with CKD¹⁹. However, there are conflicting results regarding CRP levels in patients with CKD, with some reporting decreases in the exercise group compared to the sedentary group and others reporting no differences between the groups^{18,20}. Although there was a large deviation in baseline CRP levels in this study, no differences in the rate of change due to rehabilitation were observed.

A report assessing the relationship between anemia and rehabilitation showed no significant changes in red blood cell count, Hb level, or Hct value before and after exercise in patients with CKD and mild anemia²¹. Herein, both patient groups had mild anemia, and the rate of change for each parameter between the groups was also not significantly different.

Regarding serum Cr levels, a meta-analysis indicated that exercise therapy had no significant impact¹⁴. Similarly, our study showed no significant difference between the rehabilitation intervention and control groups in

terms of serum Cr levels. However, a significant difference was observed in the rate of change in eGFR between them. This discrepancy might be attributed to the increase in muscle mass due to exercise and the improvement in renal function, canceling out each other's effects on Cr levels.

Prognosis

In this study, home-based rehabilitation did not change the occurrence of death, hospitalization, or initiation of dialysis. However, long-term implementation of aquatic aerobic exercise in patients with non-dialysis CKD reportedly resulted in significantly lower mortality and initiation of dialysis rates compared to the control group²². Given the short follow-up period in this study in comparison to event occurrence rates, a longer observation period might reveal a potential suppression of events, considering the observed milder decline in eGFR.

Limitations

This study has several limitations. First, our study utilized eGFR based on serum Cr levels to assess renal function. Evaluating eGFR through cystatin C could have enhanced the scientific significance further, considering the potential elevation of Cr associated with increased muscle mass following rehabilitation. However, this study showed that the rate of decline in eGFR among patients in the rehabilitation intervention group was gradual, suggesting the efficacy of rehabilitation even after adjusting for muscle mass augmentation. Second, data on proteinuria were not recorded in this investigation. Given that proteinuria is associated with the progression of chronic kidney disease (CKD), further prospective research on the impact of rehabilitation on proteinuria is warranted. Third, there is the lack of information and adjustment for baseline mobility differences between the rehabilitation and control groups. Patients in the rehabilitation group may have lower mobility initially, with some relying on home medical care. Meanwhile, those in the control group, who have outpatient access, possibly maintained their mobility. Nevertheless, our findings suggest that exercise therapy potentially prevents progression of renal dysfunction as evidenced by the slower decline in eGFR in the rehabilitation intervention group. Future prospective studies are warranted to match the baseline mobility levels in both groups. Fourth, there are concerns regarding the nature of home-based rehabilitation, including the absence of supervision compromising safety, adherence to the program, and accurate assessment of exercise volume as well as the inability to sufficiently increase exercise intensity^{15,23}. However, this study revealed that the

presence of physical therapists providing supervised guidance during home visits may better facilitate the implementation of appropriate rehabilitation programs. Finally, the short follow-up period warrants future prospective studies with longer observation periods to better evaluate intervention effectiveness. We hope such studies will provide more extensive insights into the effectiveness of interventions.

Conclusion

In conclusion, the implementation of home visit rehabilitation in patients with non-dialysis CKD may potentially mitigate the progression of renal dysfunction. Given the challenges posed by an aging population, multidisciplinary home-based rehabilitation interventions may play a critical role in preserving patients' ADL performance and renal function.

Data Availability: All data generated or analyzed during this study are available from the corresponding author on request.

Authors' Contributions: AI wrote the first draft of the manuscript and collected the data. SW and YY collected the data. TK, and MI helped design the study. YS coordinated the study and helped revise the manuscript. All authors participated in discussions of the manuscript and read and approved the final manuscript.

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