Impact of intensive rehabilitation on long-term prognosis after stroke
A Korean nationwide retrospective cohort study
Dong-Yup Yoo, OT, MS, Jung-Kyu Choi, PhD, Chang-Yoon Baek, PT, MS, Jung-Bin Shin, MD, PhD

Abstract
An increasing number of patients are receiving rehabilitation after stroke. But the impact of intensive rehabilitation on the long-term prognosis of patients with stroke remains to be elucidated. The purpose of this study was to identify the impact of intensive rehabilitation on the long-term prognosis of patients with stroke using data from the National Health Insurance Service database. This is a register-based, retrospective cohort study. Using data from the National Health Insurance Service database, we included the patients who received rehabilitation for stroke from 2006 to 2013. Of the 14,984 patients diagnosed with stroke, 2483 died within 1 year, and 2866 did not receive rehabilitation; hence, they were also excluded. The final sample included 9635 (49.2% men, 50.8% women) patients. After correcting for covariates, the Cox model was used to evaluate the effects of physical therapy (PT) and occupational therapy (OT) on survival. We estimated the independent contribution of each factor to the risk of death from the initiation of rehabilitation. Significant differences in mortality were observed according to age, Charlson comorbidity index (CCI), income level, and stroke type. Patients with stroke who received both PT and OT had a better long-term prognosis than those who received either treatment alone. Therapy performed by a physical therapist with more than 120 hours of training effectively improved the patients’ long-term prognosis. Intensive PT and OT will help improve the long-term prognosis of patients with stroke. This study emphasizes the importance of intensive rehabilitation in these patients.

Keywords: mortality, occupational therapy, physical therapy, rehabilitation, stroke

1. Introduction
Stroke is attributed to an acute local damage to the central nervous system caused by cerebral blood vessel problems such as cerebral infarction, cerebral hemorrhage, and subarachnoid hemorrhage. It is becoming a health problem worldwide due to increasing elderly population and poor air quality. In 2019, stroke was the third most common major disease and the fifth most common cause of death worldwide. The incidence of degenerative brain disease and stroke in people aged 60 years is 14.4%. Cerebrovascular disease is the fourth most common cause of death worldwide, accounting for 7.3% of all deaths (42 deaths/100,000 people). In 2015, the socioeconomic cost of stroke in Korea was approximately 1.5 billion, resulting in an increased socioeconomic burden.

Advances in stroke treatment have significantly reduced the overall mortality but increased survivors with complications and disabilities. For example, epilepsy is a very important sequelae that can affect the quality of life of stroke survivors. In addition, patients with stroke initially experience loss of consciousness and functional decline. Subsequently, various functions, including physical disability, cognitive impairment, memory loss, and swallowing, are impaired. Accordingly, many studies on post-stroke treatment are in progress. The effectiveness of such treatment has been proven. Endovascular treatment or intravenous thrombolysis not only can improve physical and cognitive functions, but also can improve quality of life. However, rehabilitation also plays an important role in restoring functions after stroke. Prolonged hospitalization in the intensive care unit promotes immobility, and thus, contributes to functional decline. Therefore, intensive rehabilitation rather than traditional bed rest might help prevent complications and promote recovery of bodily functions, including speech and swallowing functions.
With the increasing importance of post-stroke rehabilitation, more patients are receiving intensive rehabilitation after stroke than earlier. According to the Korea Disease Control and Prevention Agency, patients not transferred to rehabilitation medicine (RM) centers had higher 1-year post-stroke mortality rates than those transferred to RM centers. However, the effects of physical therapy (PT) and occupational therapy (OT) performed at an RM center on long-term post-stroke prognosis have not been studied.

The mortality rate of patients with stroke is affected by demographic and sociological characteristics. For example, sex, increasing age, presence of comorbidities, and differences in income level affect stroke mortality. These have been studied in patients with stroke, but not in patients who received rehabilitation.

In Korea, data related to insurance claims across the country can be easily obtained; thus, research on stroke using large data is currently in progress. Therefore, using National Health Insurance Corporation (NHIS)-cohort (NSC) data, this study aims to objectively analyze the effects of the demographic and sociological characteristics of patients with stroke who received rehabilitation and whether they received intensive rehabilitation on their long-term prognosis.

2. Methods

2.1. Data extraction and study population

The NHIS established a nationwide recording system containing medical care claims and medical evaluation data in 2002, which was the baseline year for this study. The NHIS cohort was followed up annually until 2015 and consisted of 1025,340 participants, accounting for nearly 2% of the Korean population. Patients were stratified by sex, age, and income level.

We used International Classification of Diseases, 10th revision (ICD-10) codes to identify patients diagnosed with stroke (I60–64) who received rehabilitation between 2006 and 2013. Patients from 2002 to 2005 and those from 2014 to 2015 were excluded to target newly diagnosed patients and establish a minimum follow-up period of 2 years or longer, respectively. Of the 14,984 patients diagnosed with stroke between 2006 and 2013, 2,483 died within 1 year, and 2,866 did not receive rehabilitation, and they were excluded. Patients with missing information were excluded from the study. The final sample included 9,635 patients. The mean follow-up period was 70.84 ± 27.74 months for non-survivors and 46.81 ± 25.54 months for survivors.

All study components and procedures were approved by the Institutional Review Board of the National Health Insurance Medical Center (approval No. 2021-01-004). We used the National Sample Cohort Data (data No.: NHIS-2021-2-052) provided by the NHIS. Because this study uses standardized data, consent requirements are exempted.

2.2. Study variables

Stroke was defined using the following ICD-10 codes: I60 (sub-arachnoid hemorrhage), I61 (intracerebral hemorrhage), I62 (other non-traumatic intracranial hemorrhage), I63 (ischemic stroke), and I64 (stroke, not specified). Only the initial data points from 2006 to 2013 were used. All patients who received rehabilitation after stroke were enrolled. Patients who received PT/OT > 10 times a month after starting rehabilitation were considered to have received intensive treatment, and those who received PT/OT < 10 times a month were considered to not have received intensive treatment. As for the characteristics, the stroke diagnosis date of the participants was considered as the baseline. The participants were grouped according to sex, age, and income level. The baseline year for this study was 2002, which was the baseline year for this study. The NHIS cohort was established in 2002, and medical care claims and medical evaluation data in 2002 were used. All patients who received rehabilitation between 2006 and 2013 were considered to have received intensive treatment. As for the characteristics, the stroke diagnosis date of the participants was considered as the baseline. The participants were grouped according to age (>40 years, 40–49 years, 50–59 years, 60–69 years, and ≥70 years). The Charlson comorbidity index (CCI) score, a tool for assessing comorbidities, was used to evaluate the health status of patients with stroke. The CCI score was calculated for each disease using medical claim data from 1 year before the stroke diagnosis date, and it was classified as 0, 1, or ≥ 2. The income level was divided into quartiles, with the first and fourth quartiles corresponding to the low-income and high-income groups, respectively.

In Korea, the treatment prescribed to patients is billed to the Korean Health Insurance Review & Assessment Service. Claim data is recorded in the database at the NHIS and can be accessed after requesting to view the records. The following PT and OT codes were used:

- PT: disorder of the central nervous system (DCNS) (claim code: MM105), mattress or mobilization training (MMT) (claim code: MM301), and gait training (GT) (claim code: MM302).

Disorder of the central nervous system treatment was used when a rehabilitation specialist or physical therapist with >120 hour of training in treatment techniques such as Vojta or Bobath therapy for treating muscle paralysis and stiffness due to central nervous system disorders conducted a one-on-one session for ≥30 minutes. MMT was used when patients with limited mobility, including those with amputation, hemiplegia, paraplegia, quadriplegia, or cerebral palsy, received mat, mobility, ramp, and chair training for >30 minutes. GT was used when patients with gait impairments due to central nervous system diseases, including hemiplegia, paraplegia, quadriplegia, or cerebral palsy, received gait training for >30 minutes.

OT: complex OT (CO) (claim code: MM112), special OT (SO) (claim code: MM113), activities of daily living training (ADLT) (claim code: MM114), and rehabilitative dysphagia therapy (RDT) (claim code: MX141). CO was used when an occupational therapist provided one-on-one treatment for ≥10 minutes. SO was used when an occupational therapist provided one-on-one treatment for >30 minutes. ADLT was used when an occupational therapist provided one-on-one ADL training for >20 minutes. RDT was used when an occupational therapist provided one-on-one training for >30 minutes to patients with dysphagia due to diseases of the central nervous system, esophagus, and airways.

PT and OT were classified based on the codes claimed during rehabilitation. DCNS may only be claimed by a physical therapist who has been trained in Vojta or Bobath treatment techniques for >120 hour. There is a limited number of physical therapists who can claim DCNS. Therefore, the long-term prognosis of patients who received Few physical therapists can claim DCNS as analyzed. The long-term prognostic factors of patients who received Few physical therapists can claim DCNS as analyzed. We analyzed the treatment effects of PT, OT, and Few physical therapists can claim DCNS as analyzed. The survival of patients who received Few physical therapists can claim DCNS as analyzed. The survival of patients who received the following treatment combinations:

1. PT whole: DCNS, MMT, and GT or OT whole: CO, SO, ADLT, and RDT
2. PT: MMT and GT + OT whole
3. PT whole + OT whole
4. PT: DCNS and GT + OT whole

The primary outcome variable in this study was death. The data on the date of death and the presence or absence of death were used for analysis.

2.3. Statistical analysis

The t test and chi-square test were used to analyze the differences in medical expenditure and demographic characteristics, sociological characteristics, and systemic disease status, respectively, according to treatment type. After correcting for covariates (sex, age, income level, CCI score), the Cox model was used...
to evaluate the effects of the PT and OT on survival. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina). We analyzed the effect of post-stroke rehabilitation on long-term prognosis. The survival duration without recurrence was calculated from the time of initiating rehabilitation. We estimated the independent contribution of each factor to the risk of death from the time of initiation of rehabilitation using a Cox proportional risk model. The level of significance was set at \( P < .05 \).

3. Results

Table 1 summarizes the patients' demographic and sociological characteristics. A total of 9635 patients with stroke (male, 4745 [49.2%]; female, 4890 [50.8%]) received rehabilitation, and 86.5% did not receive intensive rehabilitation treatment. Of all the participants, 2373 (24.6%) died. The number of patients receiving rehabilitation increased with age, and the mortality rate increased from 4.5% in patients under the age of 40 years to 38.7% in those older than 70 years. Most of the patients experienced an ischemic stroke (I63), and those with nonspecific stroke had the highest mortality rate. The mortality rate increased with the CCI score. The low- and high-income groups had significantly higher mortality rates than the other groups. Among all the treatment groups, the Few physical therapists can claim DCNS and GT + OT whole group (12.7%) had the lowest mortality rate.

Table 2 summarizes the rehabilitation services used by the patients with stroke. Non-survivors had a higher average number of hospitalizations and a lower average number of outpatient visits than survivors (both \( P = .001 \)).

Table 3 summarizes the treatment prescriptions received by patients and the results of the Cox univariate and multivariate analyses of factors affecting survival. Fewer women died than men (hazard ratio [HR]: 0.613, 95% confidence interval [CI]: 0.564–0.667), and the mortality rate increased by 8.2% with every 1-year increase in age (HR: 1.082, 95% CI: 1.077–1.087). Patients with an income in the first quartile had a higher mortality rate than those with an income in the second (HR: 0.810, 95% CI: 0.716–0.917), third (HR: 0.743, 95% CI: 0.666–0.831), or fourth (HR: 0.756, 95% CI: 0.681–0.839) quartile. Patients with CCI scores of 1 and \( \geq 2 \) had 19% and 46% greater mortality, respectively, than those with a CCI score of 0 (HR: 1.191, 95% CI: 1.084–1.308 and HR: 1.458, 95% CI: 1.315–1.616, respectively). The mortality rate increased with the number of hospitalizations (HR: 1.009, 95% CI: 1.002–1.015) but decreased as the number of outpatient visits increased (HR: 0.995, 95% CI: 0.994–0.996). Patients who received >10 sessions of DCNS per month for 3 months had significantly lower mortality rates than those who did not (HR: 0.709, 95% CI: 0.564–0.891).

Table 4 summarizes the results of the Cox multivariate analysis of survival according to the treatment received. Patients who received CO, SO, ADLT, and RDT in addition to DCNS and GT had a lower mortality rate (HR: 0.361, 95% CI: 0.169–0.769) than those who did not receive intensive treatment.

Table 5 shows the results of the Cox multivariate analysis of the effectiveness of DCNS for improving survival. Patients who received >10 sessions of DCNS per month had significantly lower mortality rates at 3 (HR: 0.709, 95% CI: 0.564–0.891) and 6 months (HR: 0.752, 95% CI: 0.587–0.962) post-stroke than those who received <10 treatment sessions per month.

4. Discussion

This study used the NHIS-NSC database to objectively analyze the effects of the existing rehabilitation treatment on the survival rate in patients with stroke, considering the demographic and sociological characteristics.
Demographic and sociological characteristics affected long-term prognosis in patients with stroke who received rehabilitation. Age, sex, and degree of comorbidity had a significant effect on the mortality rate. Stroke occurred more frequently in men than in women, and the risk of stroke increased by 8.2% each year. CCI scores were also associated with mortality, which was consistent with the results of the previous studies.[2,4,5]

The low-income group had a significantly higher mortality rate than the other groups ($P = .0001$). Similar findings were reported by Jeong et al.[18] Patients with low income might
encounter difficulties in paying for both rehabilitation and primary medical treatment. Additionally, treatments such as robot-assisted gait and upper-limb therapy, cognitive therapy, and certain types of speech therapy have not yet been approved by the NHIS and are more expensive than approved treatments. Consequently, high- and low-income groups may receive treatment of different quality, thus highlighting the need for support programs for patients with low income.

Rehabilitation of stroke patients is one of the promising methods used for function recovery after stroke. It can minimize motor and cognitive impairment. However, specific approaches such as rehabilitation initiation time and intensity have not yet been thoroughly investigated. Inflammation plays an important role in the pathogenesis of ischemic stroke and other forms of ischemic brain injury. Inflammatory responses not only can cause brain damage in the acute phase of stroke, but also can contribute to brain recovery beneficially[20,21]. Post-stroke exercise, if too early, may result in elevated levels of cell stress and increased expression of pro-inflammatory cytokines, which may amplify tissue damage associated with cerebral ischemia/reperfusion injury.[22] However, active rehabilitation is also important for stroke patients to recover their physical functions to the maximum and ultimately lead an independent life.[23] According to the Korea Disease Control and Prevention Agency, patients transferred to an RM center after the stroke had a lower 1-year mortality rate than those who were not,[4] indicating that there is a significant difference in the mortality rate after intensive rehabilitation in patients with stroke who require rehabilitation. Physical and occupational therapists claim a prescription code suitable for the purpose of treatment for complications such as physical disability, dysphagia, and reduced quality of life (QOL) due to restriction of daily activities.[10,24] The GT and DCNS codes are claimed for the same treatment goals, but the primary difference is whether the physical therapist has >120 hours of training in neuro-developmental treatment concepts such as Bobath or Voita therapy.[17] A physical therapist claiming DCNS can be considered more skilled than those claiming GT. Mixed opinions exist regarding the neuro-developmental treatment concept.[25–28]

This study examined whether the long-term prognosis, excluding the treatment effect, was good when patients with stroke received intensive therapy from an experienced physical therapist. We reported that 3 to 6 months of intensive DCNS effectively improved long-term prognosis after stroke (HR: 0.752, 95% CI: 0.587–0.962). Therefore, the intensive participation of skilled physical therapists in rehabilitation is important and can improve the long-term prognosis of patients with stroke. However, the Bobath course costs USD 1450[29] and requires >120 hours of training; therefore, not all patients receive this treatment. To systematically nurture skilled physical therapists, an institutional plan is needed.

The results of our study indicated that DCNS-centered intensive care increased the long-term prognosis of patients with stroke who received rehabilitation. Therefore, the long-term prognosis of PT and OT was analyzed by combining prescriptions focusing on the presence or absence of DCNS. We reported that patients who received intensive PT (DCNS, GT) and OT (CO, SO, ADLT, RDT), excluding MMT, for 3 months had a significantly higher survival rate than those who did not (HR: 0.361, 95% CI: 0.169–0.769). Previous reports indicate that gait, physical function, and ADL training improved patient independence. Post-stroke ADL independence was significantly associated with stroke recurrence and exercise capacity.[30] Rehabilitation led to improved ADL independence and QOL in patients with stroke.[31-33] Therefore, ADL training should be provided to improve the survival of patients with stroke.[34] Chippala and Sharma[35] reported that gait training was associated with improved Barthel index scores. Nakayama et al[36] reported that the recovery of swallowing function in patients with acute stroke led to improvements in ADL independence measured using the Functional Independence Measure. Thus, the long-term prognosis of patients with stroke may be improved by providing intensive PT, including gait, muscle strength and function training, and subsequently providing ADL and swallowing training to improve QOL.

Intensive rehabilitation improves ADL independence and QOL through treatment effects. However, the optimal time to start treatment for each disease was not determined. The average duration of hospitalization after stroke was longer in Korea than in Western countries,[37-39] which was because of the differences in health insurance systems and medical services. Although the NHIS has formulated rehabilitation prescriptions for Korean patients with stroke, the treatment period and prescription are not based on the stroke type and severity. Regardless of stroke severity, 2 sessions per day of treatment are covered for up to 2 years. However, in this study, intensive DCNS treatment for >6 months did not significantly affect long-term prognostic outcomes (HR: 0.886, 95% CI: 0.670–1.172). Many patients received long-term inpatient rehabilitation (duration of hospitalization in non-survivors: 644.0 ± 1312.9 days) and did not return to their homes or communities, increasing the socioeconomic burden.[40] Despite rehabilitation techniques being increasingly studied, few follow-up studies exist on the effect of each technique on patients with stroke. Studies have reported that it is important to obtain objective data regarding the duration of rehabilitation and disease severity, establish medical systems and hospital policies for rehabilitation, and provide intensive rehabilitation, aiming to return the patients to the community.

Using data from the NHIS-NSC, which represents a national population with a unified health insurance system, we observed that intensive rehabilitation improved the long-term prognosis of patients with stroke. Previous studies[40,41] analyzed long-term prognosis using indirect data sources, including telephone or mail surveys and medical records, while we analyzed it accurately using actual billing data. Based on these findings, we observed that PT and OT had positive effects on long-term prognosis. Future cohort studies on the effects of intensive rehabilitation should be conducted in other countries to confirm our results.

5. Study limitations
First, since this study only included Korean patients with stroke, our results may not be generalizable to other countries with different cultures. Second, stroke severity was not determined because the NHIS-NSC data did not contain information regarding the patients’ blood pressure, National Institute of Health Stroke Scale score, consciousness level, and level of physical functioning. Instead, we analyzed the number of inpatient and outpatient treatments to indirectly gauge the stroke severity. Third, the effect of rehabilitation treatment code was analyzed by sampling all stroke patients based on the ICD-10 code without classifying the stroke. Therefore, in future studies using NHIS-NSC data, it

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**Table 5**

Results of the Cox multivariate analysis of survival according to the treatment period.*

| Parameter       | HR (95% CI)       | P value |
|-----------------|-------------------|---------|
| DCNS NIT        | 0.986 (0.670–1.172) | .3958   |
| Three months    | 0.709 (0.959–1.896) | .0032   |
| Six months      | 0.752 (0.587–0.962) | .0232   |
| One year        | 0.886 (0.670–1.172) | .0032   |

*These results were obtained after correcting for sex, age, income level, CCI score, duration of hospitalization, and number of hospitalizations and outpatient visits.

CD = Charlson comorbidity index, CI = confidence interval, DCNS = disorder of the central nervous system, HR = hazard ratio, NIT = no intensive treatment (<10 treatment sessions per month).

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is necessary to investigate the effect of rehabilitation treatment codes for each stroke through a stroke classification method such as Trial of Org 10172 in Acute Stroke Treatment.[12]

In conclusion, we analyzed the survival rates of patients with stroke based on the rehabilitation treatment received and observed that receiving both PT and OT improved the survival rate, and long-term rehabilitation treatment did not significantly affect survival. Survival rates were also improved in patients receiving treatment from a physical therapist who could claim DCNS and those receiving intensive rehabilitation. Further research is needed to determine the optimal number and combination of treatments to improve the survival of patients with stroke.

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