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Measuring the health outcomes of Chinese ischemic stroke patients based on the data from a longitudinal multi-center study

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Abstract

Purpose Faced with scarcity of large-scale health measurement study in China, the study aims to provide health outcomes evidence from ischemic stroke patients.

Methods Data were collected from a prospective multi-center real-world study held from March 2015 to December 2018. Health-related quality of life (HRQoL) was assessed at admission, hospital discharge, 90 ± 14 days after medication treatment, and 360 ± 28 days after medication treatment. Baseline characteristics of patients were summarized. Mean values and standard deviation (SD) of EQ-5D utility index scores, VAS values, and NIHSS scores were reported. Rank-sum test was applied to analyze the differences of HRQoL among patient groups. Mix-effects regression was used to investigate the impact factors.

Results At the baseline visit, a total of 9978 patients with a mean age of 64.0 years were included. The mean utility index scores recorded at admission, discharge, 90 ± 14 days after therapy initiated, and 360 ± 28 days after therapy initiated were 0.546 (SD = 0.327), 0.709 (SD = 0.306), 0.801 (SD = 0.259), and 0.846 (SD = 0.237), respectively. Differences among sex and TOAST classification subgroups were observed. The mean utility index scores stratified by mRS levels ranged from 0.983 (SD = 0.076) to 0.058 (SD = 0.167) for level 0 to level 5. The mean NIHSS scores were 5.3 (SD = 4.98) and 3.6 (SD = 4.24) at admission and discharge.

Conclusion The impact of ischemic stroke on patient's HRQoL is significant, particularly during the acute phase. Results from the study are well representative and can be utilized in health policy making, economic evaluations and other comparison studies.

The study was registered with ClinicalTrials.gov (NCT02470624) in October 2015.

Keywords Ischemic stroke · Health-related quality of life · EQ-5D-3L · mRS · Longitudinal study

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Plain English Summary

Ischemic stroke is a kind of cardiovascular diseases with significant clinical and economic burden to patients and society. Ischemic stroke can impair both physical and mental health of the patients, therefore, it is important to describe and understand the health-related quality of life (HRQoL) among these patients. So far, limited evidence related to health is available in China. In this study, we conducted a multicenter study to collect consecutive HRQoL data from Ischemic stroke patients for one year. We found that the health status of ischemic stroke patients was impaired especially during the acute phase of the disease. The results from this study can provide solid data for other health studies such as economic evaluation. Also, the results can help healthcare decision makers to understand patients' health status and improve disease management.

Introduction

As one of the primary cardiovascular afflictions in China, stroke imposes a substantial burden owing to its elevated prevalence, recurrence rates, mortality figures, and unfavorable prognoses [1]. The incidence of ischemic stroke (IS), constituting 69.0–70.8% of stroke cases in China [2] surged from 112 per 100,000 individuals in 2005 to 156 per 100,000 in 2017. Notably, the Chinese Health Statistics of 2020 revealed that the average direct medical expenditure for IS patients stands at Chinese Yuan (CNY) 9809, representing a third of the annual per capita disposable income recorded in 2019. With shifting lifestyles and an aging demographic, IS emerged as a significant health concern endangering the well-being of the Chinese populace.

Ischemic stroke can impair physical movements and trigger mental health challenges, significantly impacting the patient's health-related quality of life (HRQoL). Various assessment scales have been devised to evaluate the health outcomes of stroke patients, including the modified Rankin Scale (mRS) [3] and the National Institution of Health Stroke Scale (NIHSS) [4]. Additionally, multi-attribute utility instruments (MAUIs) such as EQ-5D and SF-6D are commonly employed to gauge the health outcomes of stroke patients. These scales are extensively utilized in both clinical trials and practice due to their ability to provide a comprehensive assessment of the patient's health status.

However, despite the crucial importance of generating evidence on HRQoL, there remains a need for more high-quality data from IS patients in China to bolster further research and inform healthcare decisions. Utility index scores measured using MAUIs could serve to compare different disease groups and aid in economic evaluations. Notably, the utility index scores of Chinese IS patients, as reported in current literature, exhibit considerable variation (range from 0.75 to 0.96) due to diverse study designs and patient characteristics [5–7]. Moreover, there is a scarcity of studies focusing on the changes in health outcomes following stroke onset in China. Capturing the progress of disease could significantly benefit patient outcomes by enhancing disease management strategies and expanding treatment options.

Therefore, the primary objective of this study is to analyze and present the utility index scores of Chinese IS patients assessed with EQ-5D-3L utilizing data from a multi-center prospective longitudinal registration study. The secondary objective is to provide the HRQoL data of Chinses IS patients using disease specific measurements such as mRS and NIHSS. The results from this study aim to furnish data for heath assessment and clinical evidence for health decision-making.

Materials and methods

Study design

We collected the data from the Chinese Acute Ischemic Stroke Treatment Outcome Registry (CASTOR), a prospective multi-center real-world study registered with ClinicalTrials.gov (NCT02470624). The study was proved by the Ethics Committee of Peking University First Hospital (No. 2015 [922]). The protocol for this study has been previously published [8]. Forty tertiary hospitals with over 100 admitted IS patients per year in China were involved and the planned enrollment of this trial was 10,000 patients with acute IS based on the resource available in this study to reflect the real-world setting. The convenient sampling method was applied to enroll patients willing to participate and sign the informed consent. The inclusion criteria included: (1) age $\geq$ 18 years, (2) acute ischemic stroke diagnosed according to the *Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke (2014)* [9], (3) admitted within 1 week after onset of stroke or within treatment time window for patients with thrombolysis therapy, (4) consent to participate in this study. The exclusion criteria included: (1) patients with cerebral hemorrhage confirmed by CT imaging or MRI, (2) patients complicated by serious systemic diseases with an expected survival of less than 3 months, (3) patients cannot provide continuous follow-up information [8]. A total of 5 visits (scheduled during the one-year follow-up period: at the time of admission, 7 ± 2 days after treatment initiated, at hospital discharge, 90 ± 14 days after medication treatment, and 360 ± 28 days after medication treatment. The data were collected from March 2015 to December 2018.

Information collected in the trial encompassed baseline demographic data, comorbidities, treatment strategies, adverse events, Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, recurrence, readmission, NIHSS assessment, mRS assessment, and EQ-5D assessment [8]. As the quality of life was evaluated only at recruitment (Visit A), hospital discharge (Visit B), 90 ± 14 days after medication treatment (Visit C), and 360 ± 28 days after medication treatment (Visit D), the data analyzed in this study were merely from the abovementioned visits.

Health-related quality of life assessment

Patients' health-related quality of life was measured with three health scales, EQ-5D-3L, NIHSS, and mRS. The EQ-5D-3L, introduced in 1990 by the EuroQol Group [10] is widely used as a preference-based generic tool in clinical trials, population surveys and real-world studies. Mobility, self-care, usual activity, pain/discomfort, and anxiety/depression are the 5 health dimensions within the scale. EQ-5D-3L measures patient-reported health utility ranging from -0.149 to 1 where 1 represents perfect health and 0 represents death. The validity and reliability of EQ-5D-3L for stroke patients was proved [11, 12]. The Chinese EQ-5D-3L value set established in 2014 [13] was applied for calculating health utilities in this study. NIHSS instrument is a widely used 15-item tool introduced in 1988 to measure neurologic defects [14]. A composite score ranging from 0 to 42 can be added up from the scores of each item with higher score indicating a worse state. The mRS evaluates the independence and activities of stroke patients [15] and is applied as an essential endpoint in clinical trials due to the satisfactory performance, brevity, and simplicity of use [3]. The mRS scale consists of 7 health levels running from 0 to 6 representing no symptoms to death, respectively. Both NIHSS and mRS assessments were reported by clinicians, while the EQ-5D-3L was reported by patients.

Statistical analysis

Given the primary objective of this study, patients with missing data in the EQ-5D-3L items and mRS levels were excluded from the main analysis sample. Additionally, patients who were lost to follow-up during the survey were excluded from subsequent analyses. Patient who died during the follow-up period were excluded from subsequent analyses, as they were unable to provide HRQoL. In the sensitivity analysis, patients with missing data in no more than half of the EQ-5D-3L and NIHSS items were included and the missing data for health items were imputed using the average results of patients with the same mRS levels. An additional sensitivity analysis included patients who did not respond to the EQ-5D-3L at Visit C but provide responses at Visit D. Differences in characteristics between the analytical and excluded samples were assessed using Chi-square test, Fisher's exact test or T-test. Descriptive statistical analysis was applied to summarize the baseline characteristics of patients at baseline and the health outcomes evaluated at following visits. Mean values and standard deviation (SD) of utility index scores, VAS values, and NIHSS scores as well as other continuous outcomes were reported. Frequencies and percentages of categorial outcomes were reported. Histograms, box plots, and line charts were applied to illustrate the distribution and change of the utility index scores, NIHSS scores, and mRS levels during the 1-year follow-up. Utility index scores stratified by mRS and NIHSS groups were reported as mean and SD based on the data pooled from different visits. Rank-sum test was applied to analyze the differences of utilities, NIHSS scores and mRS levels according to visits, TOAST classifications and genders. A mixed-effects linear model, indicated a suitable approach regardless of missing data in longitudinal study [16], was used to investigate the changes and the potential impact factors of the utility index scores across different visits. In mixed-effects model, baseline characteristics, different visits, and baseline NIHSS scores were defined as fixed effects, with a random intercept included for individuals. Additionally, mixed-effect logistic models were applied to analyze the EQ-5D health dimensions. Coefficients were considered statistically significant when p-values were less than 0.05. Statistical analysis was performed using STATA version 18. The study was presented according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines and the checklists are listed in Supplementary file 1.

Results

Characteristics of the participants

A total of 10,029 patients with IS were recruited and 10,002 patients fulfilled the inclusion and exclusion criteria were included into the CASTOR trial. Due to loss to follow-up, missing outcome data, death, misdiagnosis, withdrawal, 9978, 9944, 9162, and 8396 patients with IS were included in the main analytical datasets for Visit A, Visit B, Visit C, and Visit D, respectively. The average follow-up days of Visit B, Visit C, and Visit D were 13.0 days (SD = 8.5), 91.0 days (SD = 8.8), and 361.5 days (SD = 16.6). The inclusion process is listed in Fig. 1.

The patients were recruited from 19 provinces or municipalities across China with an average age of 64.0 upon admission. According to the sex assigned at birth based on examination of body characteristics, 34.2% of the included patients were female. Detailed demographic information is provided in Table 1. Hypertension was the most prevalent comorbidity, followed by diabetes and coronary heart disease. The average length of stay was 13.0 days. Regarding stroke therapy, only 4.3% of the patients received thrombolysis, while 76.2% of the patients received Traditional Chinese Medicine (TCM) as combination therapy. Significant differences in characteristics between included and excluded patients are also mentioned in Table 1 and Supplementary file 2 (Table S1).

EQ-5D

The mean utility index scores for IS patients were 0.546 (SD = 0.327), 0.709 (SD = 0.306), 0.801 (SD = 0.259), and 0.846 (SD = 0.237) at admission, discharge, 90 ± 14 days, and 360 ± 28 days after therapy initiated, respectively

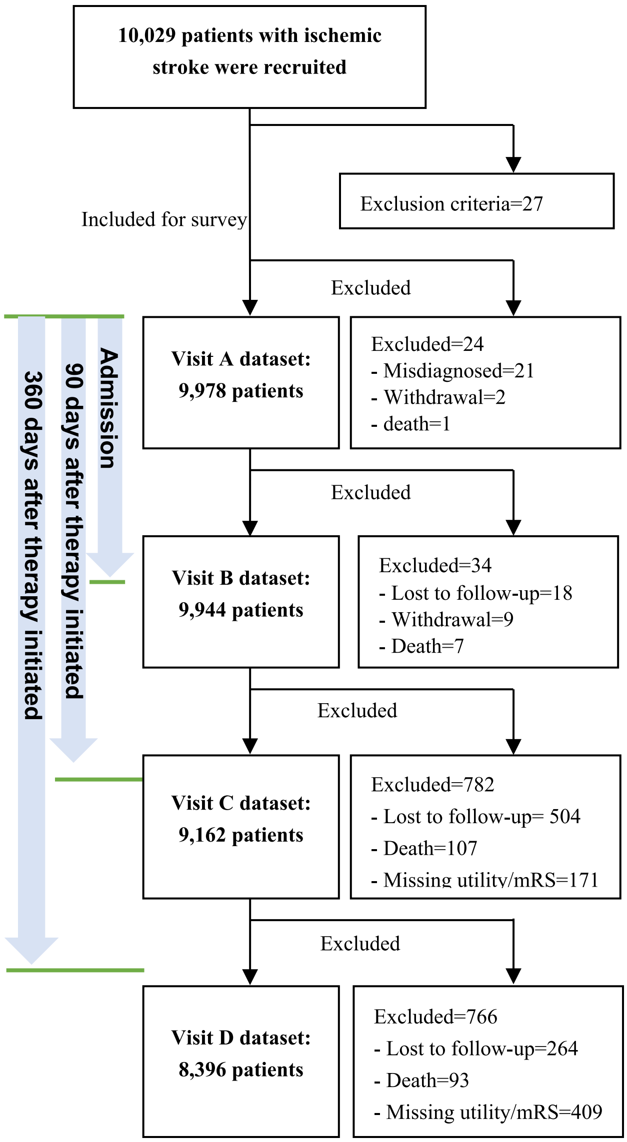

Fig. 1 Flow diagram. *Note* Visit A represents the visit at admission, Visit B represents the visit at discharge, Visit C represents the visit at 90 ± 14 days after medication treatment, and Visit D represents the visit at 360 ± 28 days after medication treatment

(results listed in Table 2). Figure 2 illustrates a rising trend in utility index scores, depicting a notable slope during the initial period after admission followed by a gradual increase, indicating obvious recovery during admission period. The mixed-effects regression results showed that different follow-up visits were significant within-patient factor for the repeated-measured utility index scores (results listed in Table 3). Additionally, Mann–Whitney test revealed significant differences in utility index scores across the measures and the mean change of the utility index scores between Visit C and Visit D was notably lower than those observed between earlier visits (see Supplementary file 2; Tables S2 and S3). The utility index scores within the one-year follow-up are presented as histograms in Supplementary file 2; Fig. S1, where a negatively skewed distribution could be observed. During the follow-up period, the proportions of patients who reported full health (with "no problem" for all the five dimensions) increased from 12.5% at admission to 57.3% at 360 days after therapy was initiated. No sensitivity analysis was performed for imputation of the missing EQ-5D-3L items, as those patients had missing data for more than 50% of the total items. However, a total of 154 patients who were excluded after Visit C due to missing data in more than half of the EQ-5D-3L items later responded to the survey at Visit D and were subsequently included in the sensitivity analysis. The sensitivity analysis results (see Supplementary file 2; Table S4) were nearly identical to the base case results.

Differences in health outcomes among sex and TOAST classification can be observed based on the information listed in Table 2. The mean utility value for females were lower than that for males. Results from Mann–Whitney test showed that the differences were significant in statistics. As for the TOAST classifications, utility index scores for patients with cardioembolic subtype were significantly lower compared with that of other subtypes. In order to provide detailed HRQoL data for further research, the utility index scores classified by different age and sex groups are summarized in Supplementary file 2; Tables S15 and S16.

When comparing the health levels of different dimensions within each visit, it was found that the proportions of the patients who reported no problem in Mobility and Usual Activities were lower than those reported in other health dimensions. Furthermore, the proportions of level 3 (the worst level) in Mobility, Self-care, and Usual Activities were higher than in Pain/Discomfort and Anxiety/Depression, indicating a severe impact on physical health. Differences in health aspects between sex were also noted. The reported levels for the five health dimensions are summarized and listed in Supplementary file 2; Table S5. The reported health levels for the five health dimensions are displayed in Fig. 3, demonstrating improvement in the five health aspects over the follow-up period. The EQ-VAS scores are presented in Supplementary file 2; Fig. S2. The mean EQ-VAS scores were estimated to be 64.9 (SD = 19.8), 78.1 (SD = 17.4), 83.1 (SD = 15.1) and 85.8 (SD = 14.2) at Visit A, Visit B, Visit C, and Visit D, respectively.

mRS

During the follow-up visits, the number of patients assessed with higher mRS levels decreased, indicating improvements in symptoms, mobility, and self-care abilities. Detailed proportions of mRS levels at each visit are listed in Supplementary file 2; Table S6. The significant differences in the mRS levels between the sex

Table 1 Social-demographic characteristics and clinical information

Patient characteristics	Visit A (n = 9978)	Visit B (n = 9944)	Visit C (n = 9162)	Visit D (n = 8396)
Age[a], mean (SD)	64.0 (11.9)	64.0 (11.9)	63.9 (11.9)	63.8 (11.8)
Sex[b]				
Male %(n)	65.8% (6564)	65.8% (6539)	66.1% (6055)	65.8% (5527)[d]
Female %(n)	34.2% (3414)	34.2% (3405)	33.9% (3107)	34.2% (2869)[d]
Medical insurance plan				
BMIW %(n)	39.5% (3943)	39.5% (3929)	40% (3667)[d]	40.7% (3417)[d]
BMIUR %(n)	19.5% (1944)	19.5% (1941)	18.9% (1729)[d]	18.6% (1560)
BMIRR %(n)	20.9% (2085)	20.9% (2080)	21.6% (1983)[d]	21.8% (1832)
FMC %(n)	0.9% (91)	0.9% (91)	0.9% (80)[d]	0.7% (56)[d]
BMI %(n)	1.6% (157)	1.6% (157)	1.7% (152)[d]	1.7% (141)[d]
Without insurance %(n)	17.5% (1747)	17.4% (1735)	16.8% (1543)[d]	16.5% (1384)[d]
Disease history in recent 3 months[a]				
Stroke %(n)	23.7% (2366)	23.7% (2358)	23.9% (2188)[d]	23.9% (2009)
Hypertension %(n)	64.4% (6428)	64.4% (6402)	64.3% (5895)	64.4% (5410)
Diabetes %(n)	25.8% (2573)	25.8% (2562)	25.7% (2352)	25.7% (2160)
Dyslipidemia %(n)	3.2% (317)	3.2% (317)	3.1% (287)	3% (255)
Coronary heart disease %(n)	13.8% (1376)	13.8% (1370)	13.8% (1267)[d]	14% (1175)[d]
Atrial fibrillation %(n)	4.3% (430)	4.3% (428)	4.1% (377)	4.1% (341)
Carotid plaque %(n)	0.7% (65)	0.7% (65)	0.7% (65)[d]	0.7% (60)
Cancer %(n)	2.4% (243)	2.4% (241)	2.4% (222)	2.5% (206)
TOAST classification[c]				
LAA %(n)	64.6% (2890)	64.6% (2880)	64.2% (2731)[d]	64.3% (2562)
CE %(n)	4.2% (190)	4.2% (189)	3.9% (167)[d]	3.8% (150)
SVD %(n)	25.3% (1131)	25.3% (1129)	26% (1107)[d]	26.3% (1048)
Other determined cause %(n)	2.3% (105)	2.4% (105)	2.3% (100)	2.3% (92)
Undetermined cause %(n)	3.6% (159)	3.5% (158)	3.5% (151)	3.4% (135)
Length of Stay, mean (SD)	–	13.0 (8.46)[d]	–	–
Families' Company %(n)	–	82.7% (8220)[d]	–	–
Thrombolysis %(n)	–	4.3% (431)	–	–
TCM therapy %(n)	–	76.2% (7578)[d]	–	–
ICU patients %(n)	–	3.7% (363)	–	–
Persistent adverse Reactions %(n)	–	24.1% (2396)	–	–
Recurrent rate %(n)	–	–	2.5% (225)	3.5% (295)
Readmission rate %(n)	–	–	9.9% (907)	8.1% (680)

SD Standard deviation, *BMIW* basic medical insurance for workers, *BMIUR* basic medical insurance for urban residents, *BMIRR* basic medical insurance for rural residents, *FM* free medical care, *BMS* business medical insurance, *TOAST* Trial of Org 10172 in acute stroke treatment, *LAA* large-artery atherosclerosis, *CE* cardioembolic stroke, *SVD* small-vessel disease, *TCM* Traditional Chinese Medicine, *ICU* intensive care unit

[a]Measured at admission

[b]Sex assigned at birth according to external examination of body characteristics

[c]The percentages were calculated based on patients with TOAST information (n = 4475, 4461, 4256, 3987 for visit A, visit B, visit C, and visit D, respectively)

[d]Significant differences ($P < 0.05$) were found between analytical samples and missing data or withdrawal or lost to follow-up samples

groups indicated the female patients' poorer health status. The mRS levels measured at each visit showed positively skewed distribution as presented in Supplementary file 2; Fig. S3. The distributions of the mRS levels for different TOAST classifications are presented in Supplementary file 2; Fig. S4 and worse mRS levels were found among patients with cardioembolic stroke. A total of 37,480 records pooled from the 4 visits were used to get the utility index scores stratified by mRS levels. The mean utility index scores were 0.983 (SD = 0.076), 0.894 (SD = 0.137), 0.679 (SD = 0.150), 0.556 (SD = 0.154), 0.270 (SD = 0.215), and 0.058 (SD = 0.167) for ischemic

Table 2 Utility index scores measured at the follow-up visit

Patient groups	Visit A (n = 9978)	Visit B (n = 9944)	Visit C (n = 9162)	Visit D (n = 8396)
Total patients, mean (SD)	0.546 (0.327)	0.709 (0.306)	0.801 (0.259)	0.846 (0.237)
Sex[a], mean (SD)				
Male	0.567 (0.324)	0.725 (0.301)	0.815 (0.250)	0.858 (0.226)
Female	0.507 (0.329)	0.678 (0.314)	0.772 (0.272)	0.822 (0.256)
Mann–Whitney test P	< 0.001	< 0.001	< 0.001	< 0.001
TOAST classification, mean (SD)				
LAA	0.533 (0.327)	0.693 (0.311)	0.783 (0.273)	0.837 (0.248)
CE	0.309 (0.366)	0.505 (0.370)	0.653 (0.352)	0.717 (0.332)
SVD	0.613 (0.288)	0.797 (0.238)	0.859 (0.210)	0.901 (0.188)
Other determined cause	0.528 (0.332)	0.782 (0.254)	0.851 (0.237)	0.886 (0.2)
Undetermined cause	0.565 (0.323)	0.763 (0.3)	0.839 (0.231)	0.876 (0.194)
Kruskal–Wallis rank test P	< 0.001	< 0.001	< 0.001	< 0.001

SD Standard deviation, *TOAST* Trial of Org 10172 in Acute Stroke Treatment, *LAA* large-artery atherosclerosis, *CE* cardioembolic stroke, *SVD* small-vessel disease

[a]Sex assigned at birth according to external examination of body characteristics

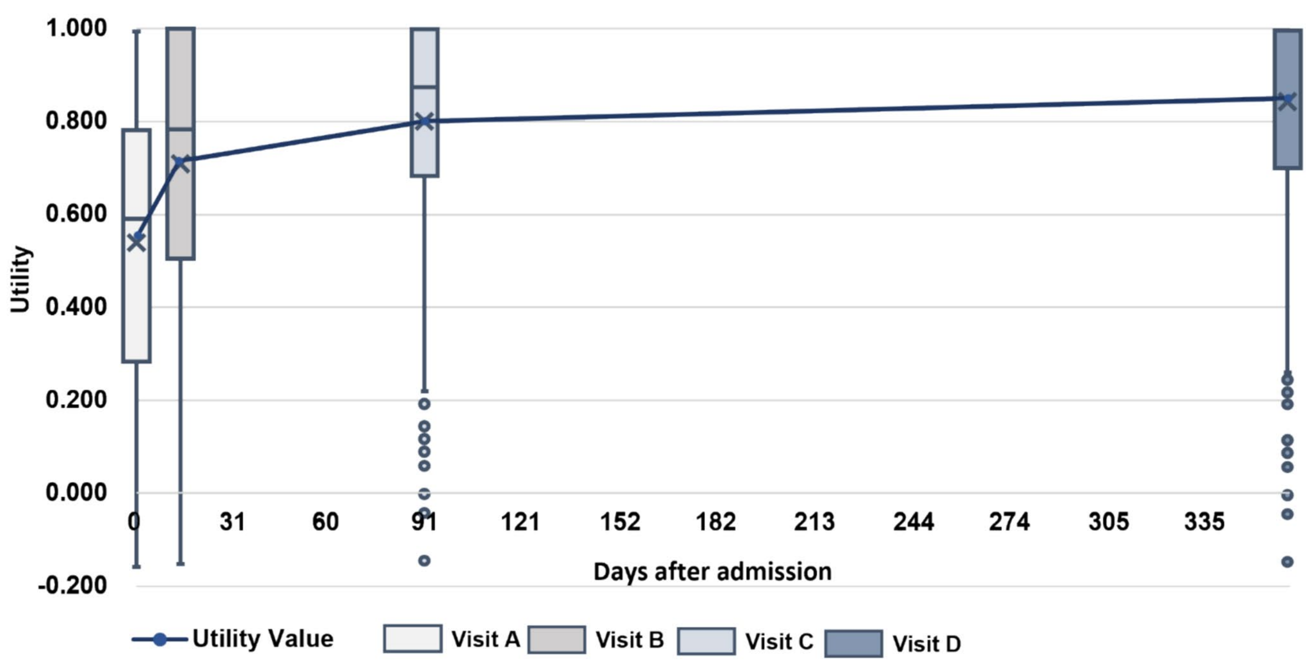

Fig. 2 Change of the utility index scores for ischemic stroke patients

patients with mRS levels at 0, 1, 2, 3, 4, 5 and 6, respectively (details provided in Supplementary file 2; Table S7).

NIHSS

NIHSS scores were assessed only at admission (Visit A) and discharge (Visit B). The distributions of the NIHSS scores are presented as histograms in Supplementary file 2; Fig. S5. The mean NHISS scores were 5.3 and 3.6 at Visit A and Visit B, respectively. According to the classification of NIHSS applied in China [17], patients were divided into five groups (severe stroke: NIHSS > 20, severe to moderate stroke: 20 ≥ NIHSS ≥ 16, moderate stroke: 15 ≥ NIHSS ≥ 5, mild stroke: 4 ≥ NIHSS ≥ 1, and normal: NIHSS = 0), and the proportions of patients in the five groups are listed in Supplementary file 2; Table S8. NIHSS scores for different TOAST classifications were analyzed, and a significant difference was found among the sub-groups ($P < 0.001$). Utility index scores stratified by NIHSS groups are listed in Table S9. The NIHSS scores

Table 3 Results of mixed-effects model regression

Variable	Coefficient	SE	95% Cis	*P*
Visit				
Visit A	Reference			
Visit B	0.162	0.0025	(0.157, 0.167)	< 0.001
Visit C	0.247	0.0026	(0.242, 0.252)	< 0.001
Visit D	0.287	0.0027	(0.282, 0.292)	< 0.001
Sex[a]				
Male	Reference			
Female	− 0.019	0.0041	(− 0.027, − 0.011)	< 0.001
Age	− 0.002	0.0002	(− 0.002, − 0.002)	< 0.001
Medical insurance plan				
BMIW	Reference			
BMIUR	− 0.018	0.0053	(− 0.029, − 0.008)	< 0.001
BMIRR	− 0.009	0.0052	(− 0.019, 0.001)	0.09
FMC	0.002	0.02	(− 0.037, 0.041)	0.923
BMI	0.033	0.0152	(0.003, 0.063)	0.029
Without insurance	− 0.012	0.0055	(− 0.022, − 0.001)	0.035
Disease history				
Stroke	− 0.022	0.0045	(− 0.031, − 0.013)	< 0.001
Hypertension	0.003	0.0041	(− 0.005, 0.011)	0.453
Diabetes	− 0.025	0.0044	(− 0.034, − 0.016)	< 0.001
Dyslipidemia	0.011	0.0109	(− 0.01, 0.032)	0.319
CHD	− 0.009	0.0057	(− 0.02, 0.003)	0.129
AF	− 0.008	0.0097	(− 0.027, 0.011)	0.428
CP	− 0.005	0.0232	(− 0.05, 0.04)	0.831
Cancer	− 0.011	0.0122	(− 0.035, 0.013)	0.359
Thrombolysis	− 0.003	0.0093	(− 0.022, 0.015)	0.71
TCM therapy	− 0.016	0.0045	(− 0.025, − 0.008)	< 0.001
Baseline NIHSS classification				
Normal	Reference			
Mild	− 0.074	0.0069	(− 0.088, − 0.061)	< 0.001
Moderate	− 0.305	0.007	(− 0.318, − 0.291)	< 0.001
Moderate to severe	− 0.567	0.0123	(− 0.591, − 0.543)	< 0.001
Severe	− 0.623	0.0163	(− 0.655, − 0.591)	< 0.001
Constant	0.903	0.0131	(0.878, 0.929)	< 0.001
Random effect parameter (patient individual)				
Constant	0.026	0.0005	(0.025, 0.027)	< 0.001
Residual	0.031	0.0003	(0.03, 0.032)	< 0.001

SE standard error, *BMIW* basic medical insurance for workers, *BMIUR* basic medical insurance for urban residents, *BMIRR* basic medical insurance for rural residents, *FM* free medical care, *BMS* Business Medical Insurance, *CHD* coronary heart disease, *AF* atrial fibrillation, *CP* carotid plaque, *TCM* Traditional Chinese Medicine

[a]Sex assigned at birth according to external examination of body characteristics

from the sensitivity analysis are listed in Supplementary file 2; Table S8.

Mixed-effects regression analysis

The results of mixed-effects regression analysis are listed in Table 3. Compared to the baseline Visit A, the follow-up visits demonstrated significant positive effects on the utility index scores. Age, sex, stroke history, diabetes, TCM therapy were indicated as significant negative factors affecting the utility index scores. Additionally, medical insurance plans were found to influence utility index scores with lower scores observed in Basic Medical Insurance for Urban Residents and Without Insurance groups, while the Business Medical Insurance group had higher scores compared to the Basic Medical Insurance for Workers group. The random-effects intercept for patients was also significant. The results for each health dimension in EQ-5D-5L are reported in Supplementary file 2; Table S10–S14. The impact factors varied slightly across health dimensions.

Discussion

This study examined the HRQoL of Chinese IS patients measured by EQ-5D-3L from admission to 1-year post-stroke, utilizing data from a prospective multi-center real-world study. Utility index scores, mRS levels, and NIHSS scores measured at each visit were analyzed and compared. Substantial impairment of HRQoL was observed at admission compared to Chinese general population [18], followed by significantly improvement thereafter. The gradual improvement was consistent with the findings reported in other studies [19, 20]. However, the average utility index score of 1-year post-stroke patients was still worse than general population [21], resulting from more problem reported in Mobility and Usual Activity. Compared to the 1-year post-stroke utility index scores (ranging from 0.33 to 0.83) reported by a systematic review [22], the score from the current study is slightly higher (0.846). This difference may be attributed to variations baseline clinical status [23] and differences in measurement properties across patients from different countries (e.g., the EQ-5D exhibits higher ceiling effect among the Chinese population) [24]. According to the NIHSS scores, majority of the patients exhibited moderate or mild stroke. Sex and TOAST classification were found to significantly impact HRQoL, with IS notably affecting the Mobility and Usual Activity dimensions. Results from the mixed-effects regression analysis suggested that age, sex, insurance types, IS and diabetes history were impact factors during the disease recovery. These findings will contribute to the understanding of health outcomes research in Chinese IS patients. Additionally, summarizing the utility index scores stratified by mRS levels provides valuable evidence that can be applied in further research, including economic evaluation.

The representativeness of the characteristics for patients in our study is comparable with those reported from official statistical reports. As mentioned in the *China Stroke Statistics 2019 Report*, the mean age for IS patients was

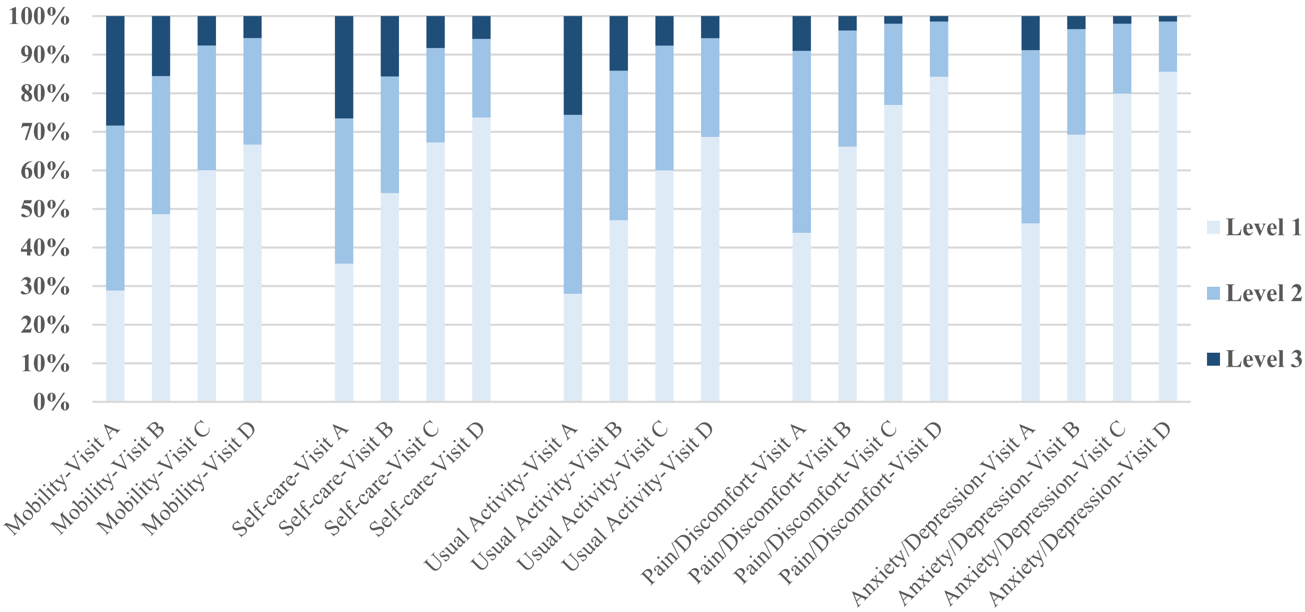

Fig. 3 Change of the reporting levels within EQ-5D dimensions at follow-up visits

67.3, and the proportion of males accounted for 59.2% [25]. Regarding medical insurance types, patients with Basic Medical insurance for Workers, Basic Medical insurance for Urban Residents, Basic Medical Insurance for Rural Residents accounted for 37.8, 22.9 and 15.4% [25], respectively. The demographic characteristics of patients in our study (in Table 3) are similar to those from the stroke reports. According to the registry data from 2015 to 2018 in *China Stroke Statistics 2019 Report*, proportions of patients with stroke history, diabetes history, high blood pressure history, dyslipidemia history, coronary heart disease, and atrial fibrillation are 23.9, 23.5, 63.0, 7.6, 10.5 and 6.9%, respectively [26]. Disease histories reported in the report and our study are similar. However, the proportion of patients with cardioembolic stroke varies from 10 to 26% in the *Brief Report on Stroke Prevention and Treatment in China (2019)* [1], while patients with cardioembolic stroke was reported to be 4.25% at admission in our study. The lack of records of TOAST classifications in this study may explain this difference, though bias related to this factor was likely limited due to the relatively low percentage of cardioembolic stroke patients. The average length of stay was similar to that reported from *China Stroke Statistics 2019 Report* [27] (11.3 ± 8.3 days). It should be acknowledged that significant differences were observed between analytical samples and those excluded due to loss to follow-up, missing outcome data, or withdrawal. However, the large sample size likely mitigated the impact of loss to follow-up, missing outcome data or withdrawals. Overall, the patients included in our study were representative of individuals with IS in China.

Currently, there exists a research gap regarding the examination of HRQoL in Chinese patients diagnosed with IS. She et al. [6] reported the HRQoL of IS patients using EQ-5D-3L within two weeks after admission. The results reported the average utility index and EQ-VAS scores as 0.746 and 72.7, similar to those reported at Visit B in the current study (utility = 0.714, EQ-VAS = 78.37). When conducting cost-utility analyses related to IS, careful consideration of the trend of utility index scores over time is crucial, especially since many analyses adopt a one-year cycle length [28, 29]. Therefore, selecting the appropriate utility value to represent the health state in the first year of analysis is of paramount importance. Another gap exists in the economic evaluation related to IS. According to the economic evaluations of IS published recent years, Markov health state classified by mRS levels were widely applied [30, 31]. However, high-quality evidence for economic evaluations specific to Chinese stroke patients remains limited. Consequently, most utility index scores for Chinese IS patients in the published literatures were derived from studies conducted in other countries [32–34]. For example, the utility index scores used by Pan et al. in their cost-effectiveness analysis conducted in a Chinese context were derived from patients in other countries [35]. These values differ from those estimated in current study (0.80 vs. 0.92 for mRS 0–1, 0.58 vs. 0.76 for mRS 2–3, 0.28 vs. 0.20 for mRS 4–5). The discrepancies in utility index scores may stem from different approaches for the measurement, and more importantly, diverse cultural backgrounds. In light of this difference, several guidelines for economic evaluation recommend using utility index scores from population within the same country or region

[36–38]. Therefore, summarizing the utility stratified by mRS from the representative study is valuable for future economic evaluation focus on the Chinese patients with IS.

As for health policy indications, firstly, sex differences significantly influence the utility index scores and mRS levels of patients, with female patients consistently experiencing worse outcomes than their male counterparts throughout the entire follow-up period. The disparities in the Mobility, Self-care, and Usual Activities dimensions were more pronounced. The cause of these differences may be attributed to the sex-specific differences in the recovery of body functions [39, 40]. Additionally, females generally exhibit lower health-related quality of life (HRQoL) compared to males in the general population [21]. These findings underscore the importance of considering sex-based heterogeneity in health outcomes and the unmet needs of cares for females during recovery. Secondly, the impact of TOAST classification on HRQoL suggests that cardioembolic stroke patients have the worst health status. *Brief Report on Stroke Prevention and Treatment in China (2019)* revealed that atrial fibrillation was a major risk factor for cardioembolic stroke [1]. Therefore, it is necessary to focus on preventing and screening for atrial fibrillation to reduce the prevalence of Cardioembolic stroke. Thirdly, as previously mentioned, IS affected various health dimensions differently, with Mobility and Usual Activities being the most impacted. Therefore, healthcare policies should be specifically designed to address the needs of physical function recovery. Furthermore, several impact factors were identified using the mix-effects models. Medical Insurance plans were found to significantly affect utility index scores and the five health dimensions. In general, people with BMIW, FMC, and BMI plans benefit from higher reimbursement rates and have better economic conditions. Thus, improving the medical insurance coverage could contribute to enhanced health outcomes. Patients with history of stroke or diabetes tended to report poorer HRQoL across all five health dimensions, and those with chronic heart disease (CHD) experienced severe status in Pain/Discomfort dimension. Consequently, disease management strategies should be strengthened for individuals with stroke, diabetes, or CHD history. Additionally, the mix-effect models revealed that TCM treatment showed negative impact on the HRQoL, particularly in the Usual Activity, Pain/Discomfort, and Anxiety/Depression dimensions. However, as information on other treatments received by patients was not included in this study, we are unable to account for the differences in HRQoL between patients receiving TCM treatment and those not receiving it. Future study could further investigate the impact of different treatments.

Despite the contribution of this study to the knowledge of IS and HRQoL, there remain some limitations. Firstly, this phase IV clinical trial relied on convenience sampling instead of random sampling, which may lead to sampling bias. Nevertheless, the comparison of patients' characteristics showed that the study's IS patients were representative. Secondly, the EQ-5D-3L was used instead of the EQ-5D-5L since EQ-5D-3L was more widely used when the study was initially designed in 2015. EQ-5D-5L could provide the advantage of reducing the ceiling effect observed in this study [41]. Given that there are studies reporting mapping algorithms from EQ-5D-3L to EQ-5D-5L [42–44], the results of our study can be transferred accordingly. However, as mentioned by Wailoo et al. [45], EQ-5D-3L and EQ-5D-5L are not interchangeable in cost-effectiveness analysis. Therefore, researchers should take caution when mapping EQ-5D-3L values to EQ-5D-5L. Thirdly, the study excluded patients who were lost to follow-up, had missing data or withdrew from the study. Nevertheless, based on the comparison of characteristics, the impact of these exclusions appears to be limited. The sensitivity analysis of utility index scores yielded results similar to those of the base case. For the NIHSS scores, the sensitivity analysis showed slightly higher scores compared to the base case, likely because more severe patients failed to complete the NIHSS assessment, leading to the missing data.

Conclusion

The impact of IS on a patient's HRQoL is significant, particularly during the acute phase. According to the study, utility index scores showed a rapid improvement in the patient's health status during hospitalization, with mild improvement three months post-stroke. Most patients in the study experienced mild or moderate strokes. The HRQoL data gathered in this study is representative and can be utilized in health policy making, economic evaluations and other comparison studies.

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Author contribution The study conception and design were complete by Hongchao Li, Xuejing Jin, Luying Wang and Xin Guan. Material preparation and data collection were performed by Hongchao Li, Yining Huang, Weiping Sun. Data analysis was performed by Luying Wang, Xin Guan, Jiting Zhou, Hongfei Hu, Wei Liu and Qiran Wei. The first draft of the manuscript was written by Luying Wang and Hongchao Li and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability Anonymized data may be made available from the corresponding author upon reasonable request, subject to institutional review board approval and a completed data sharing agreement.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Ethics Committee of Peking University First Hospital (No. 2015 [922]).

Consent to participate Informed consent was obtained from all individual participants included in the study.

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