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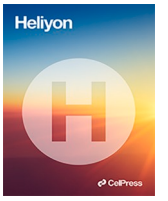

Research article

Analysis of readmission and hospitalization expenditures of patients with ischemic stroke suffering from different comorbidities

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A B S T R A C T

Background: The comorbidities of ischemic stroke (IS) are increasing worldwide. This study aimed to quantitatively assess the effect of different types of comorbidity on readmission and hospitalization expenditures of patients with IS.

Methods: A retrospective observational study was conducted from the basic insurance claims database of a large city in China, between January 1, 2018, and May 31, 2022. We identified patients with IS aged 18 years and over, who experienced the first episode of IS and had one-year follow-up records. This study divided eighteen different comorbid conditions into two categories (concordant comorbidity and discordant comorbidity) and the IS patients were further categorized into four groups. Multivariable logistic regression models and generalized linear models with log-link and gamma distribution were to estimate the effect of different comorbidity groups on one-year readmission rates and annual hospitalization expenditures.

Results: In total, 99,649 adult patients with IS were identified. Approximately 94.0 % of patients with IS had at least one comorbidity, and 63.8 % reported concordant comorbidity only. Patients with IS had a readmission rate of 26.7 %, and the mean of annual hospitalization expenditure and annual hospitalization out-of-pocket expenditure (OOPE) were 28086.6 Chinese Yuan (CNY) and 8267.3 CNY, respectively. After adjustment for covariates, the concordant comorbidity-only group had the highest readmission rate, annual hospitalization expenditure, and OOPE compared with the other groups, furthermore, these results increased as the number of comorbidity increased and had statistically significant positive associations.

Conclusions: The readmission and annual hospitalization expenditures of patients with IS were associated with different comorbidities. Concordant comorbidity increased hospital readmission risk and health expenditures. To better manage the comorbidities of patients with IS, especially concordant comorbidities, it is necessary to establish a routine care strategy specifically for comorbid conditions.

Abbreviations: CA, cardiac arrhythmia; CCI, Charlson Comorbidity Index; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; CLD, chronic liver disease; CNY, Chinese Yuan; CPD, chronic pulmonary disease; GBD, Global Burden of Disease; HD, heart disease; *ICD-10*, *International Classification of Diseases,* 10th *edition*; ID, identification number; IS, ischemic stroke; LOS, length of stay; MCCs, multiple chronic conditions; NIH ICs, National Institutes of Health Institutes and Centers; OOPE, out-of-pocket expenditure; PUD, peptic ulcer disease; PVD, peripheral vascular diseases; UEBMI, Urban Employee Basic Medical Insurance; URRBMI, Urban and Rural Resident Basic Medical Insurance; VIF, variance inflation factor.

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1. Introduction

Ischemic stroke (IS) is a major subtype of stroke and the leading cause of disease burden worldwide. The Global Burden of Disease (GBD) 2019 estimates showed that over 77 million people worldwide and 24.18 million in China experienced IS [1–3]. The prevalence of IS has been predicted to significantly increase owing to improved life expectancy. Patients with IS commonly have chronic comorbidities that directly or indirectly influence readmission and health expenditures [4–6]; thus, it is important to identify the comorbidities. A series of prospective cohort studies used the Charlson Comorbidity Index (CCI) and multiple chronic conditions (MCCs) index to predict the effect of comorbid conditions on the outcome of IS [7–9]. These indexes are limited by poor clinical specificity and potential recall and social desirability biases. Furthermore, the concept of concordant and discordant comorbidities was introduced by the National Institutes of Health Institutes and Centers (NIH ICs) [10] to understand the effect of comorbid conditions better. Concordant comorbidities usually bring the same care goals and risk management, while discordant comorbidities are not often directly related to either their etiology or risk factors [10,11]. To date, the concept of concordant and discordant comorbidities has been used to study diabetes and chronic kidney disease analysis but not for studying IS [11–13]. These studies suggest that distinguishing the type of comorbidity can improve the efficacy of comorbidity management. The relationship between different types of comorbidity and IS is still unknown.

Meanwhile, most studies on the outcome of IS focused on function and mortality using two logistic regression and Cox logistic regression models rather than readmission and health expenditures [6,7,14–16]. As a measure of clinical outcome, readmission rate is a more sensitive indicator for the outcome of IS and can help capture the secondary damage associated with chronic comorbidities, as not all patients die after IS. Hospitalization expenditures account for 90 % of the total health expenditure of patients with IS [17]; thus, their hospitalization expenditures can reflect the disease burden. Currently, the annual readmission and hospitalization expenditures of patients with IS receive less attention than the function and mortality of these patients [7,18]. To address this knowledge gap, our research question was which types of comorbidities have higher readmission rates and expenditures among IS patients? We also estimated the number of different types of comorbidities that affected readmission and hospitalization expenditures. The research hypothesis was as follows: there is no difference in readmission rates for IS patients with different types of comorbidities.

2. Methods

2.1. Data source

Between January 1, 2018, and May 31, 2022, this retrospective observational study was conducted using data from the basic

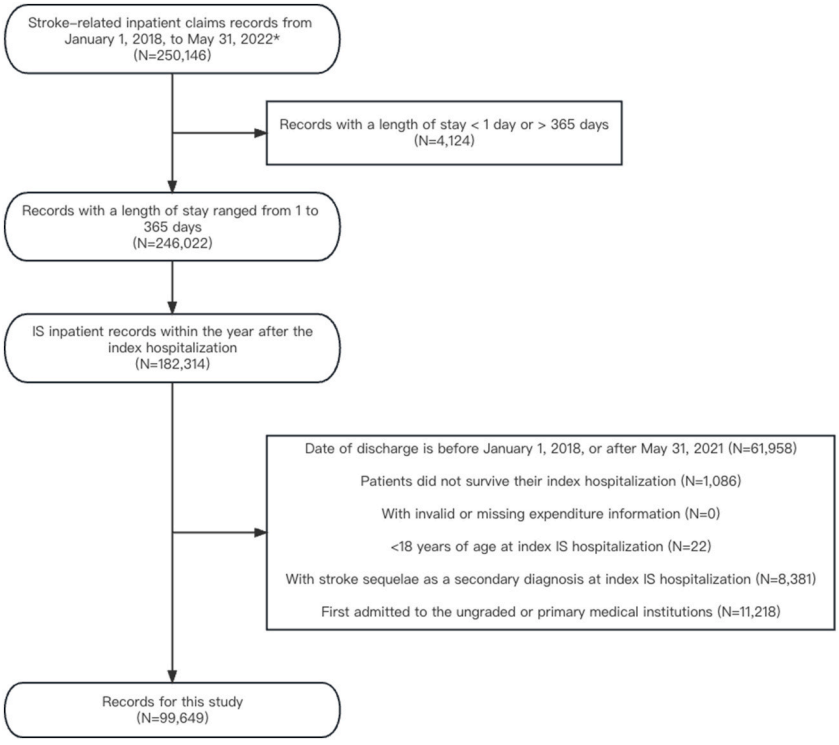

Fig. 1. Patients' selection. *Stroke-related records were identified by primary diagnosis codes (*ICD-10*: I63 for IS, I69 for stroke sequelae, I60, I61 and I62 for other stroke subtypes). Abbreviation: IS = ischemic stroke.

medical insurance database in a large city with 20 million people in southern China's Guangdong province. The claims data were standardized by the National Healthcare Security Administration in China, which continuously and regularly collects medical institutions information on demographic information, medical diagnoses, and expenditure information for inpatient services [19]. Since 2018, China's basic health insurance coverage has been above 95 % [20] and includes the two major health insurance types: the Urban Employee Basic Medical Insurance (UEBMI) and Urban and Rural Resident Basic Medical Insurance (URRBMI). The UEBMI scheme covers urban employees and those retired, and the URRBMI scheme covers urban residents, including the unemployed and the elderly, children, and students [21]. We collected data on identification, age, gender, grade of admitting hospital, date of admission and discharge, primary diagnosis code, and secondary diagnoses codes of admission (classified according to *International Classification of Diseases,* 10th *edition* (*ICD-10*)), and expenditure. The expenditure information included the total medical cost and the compensation fee for each hospitalization in Chinese Yuan (CNY). Every stroke inpatient's unique identification number (ID) was converted into a new pseudo-ID that did not expose personal information to identify unique patients before the study team had access to the data.

2.2. Study population

We enrolled all participants with local social basic health insurance who experienced and survived IS hospitalization from January 1, 2018, to May 31, 2021. Participants were identified based on primary diagnosis codes (*ICD-10:* I63 for IS, I69 for stroke sequelae) [22–24]. We recognized the index IS hospitalization record of insured patients as their first episode of acute IS and extracted their inpatient records related to stroke within one year after his/her first discharge.

We first excluded the hospitalization records with a length of stay (LOS) of less than one day or more than 365 days. We also excluded the following patients: 1) those with invalid or missing expenditure information; 2) those younger than 18 years of age at index IS hospitalization; 3) those with stroke sequelae as a secondary diagnosis at index IS hospitalization; and 4) those who were first admitted to ungraded or primary medical institutions. Fig. 1 shows the flowchart of the patient selection process.

2.3. Comorbid conditions

Based on previous studies on similar topics and the prevalence of comorbidity in our study, 18 different chronic conditions were chosen and divided into two types [22,25]. The concordant comorbidities include other cerebrovascular diseases, hypertension, hyperuricemia, gout, hyperlipemia, diabetes, heart diseases (HD), congestive heart failure (CHF), cardiac arrhythmia (CA), peripheral vascular diseases (PVD) [26–28], chronic kidney diseases (CKD) [11], dementia [29] and brain cancer [30]. The discordant comorbidities include cancer except for brain cancer, mental disorders, osteoporosis, chronic liver disease (CLD), chronic pulmonary disease

Table 1
Comorbidities assigned International Classification of Disease version 10 (*ICD-10*) codes and comorbid condition types.

Comorbidity diseases group	*ICD-10* codes	Type of comorbidity
Cerebrovascular Disease	G45, H34, I65, I66, I67, R90	Concordant
Hypertension	I10, I11, I12, I13, I15	Concordant
Hyperuricemia & Gout	E79.0, M10	Concordant
Hyperlipemia	E78.0-E78.5	Concordant
Diabetes	E10, E11, E12, E13, E14	Concordant
Heart diseases[a]	I05, I06, I07, I08, I09, I20, I21, I22, I23, I25, I24	Concordant
Congestive heart failure	I42.0, I42.5-I42.9, I43, I50	Concordant
Cardiac arrhythmia	I44, I45, I46, I47, I48, I49	Concordant
Peripheral vascular disease	I70, I71, I72, I73.1, I73.8, I73.9, I74, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9	Concordant
Dementia	F00-F03, F05.1, G30, G31	Concordant
Chronic kidney diseases	N03.2-N03.7, N05.2-N05.7, N18, N19, N25.0, Z49.0-Z49.2, Z94.0, Z99.2	Concordant
Brain cancer	C70.0, C70.9, C71, C79.3	Concordant
Cancer (except for brain cancer)	C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C85, C88, C90-C97	Discordant
Mental disorders[b]	F10, F17, F20, F21, F40, F41, F32, F33	Discordant
Osteoporosis	M80, M81, M82	Discordant
Chronic liver diseases	B18, K70, K71, K72, K73, K74, K76, Z94.4, I85, I86.4, I98.2	Discordant
Chronic pulmonary diseases	J40-J47, J60-J67, J68.4, J70.1, J70.3	Discordant
Peptic ulcer diseases	K25-K28	Discordant

[a]Heart disease included chronic rheumatic heart disease and coronary heart disease.
[b]Mental disorders included substance abuse, depression, anxiety, and schizophrenia.

(CPD), and peptic ulcer disease (PUD). Secondary diagnoses with *ICD-10* codes were applied to define comorbid conditions in this study. The full list of 18 types of comorbidities selected for this study, with corresponding *ICD-10* codes and comorbid condition types, is provided in Table 1.

According to the concordant and discordant comorbid conditions, four exclusive study groups of interest were considered: (1) IS only; (2) IS with one or more concordant comorbidities only; (3) IS with one or more discordant comorbidities only; (4) IS with both concordant and discordant comorbidities [12]. In addition, similar studies have shown the substantial effect of the number of comorbidities on the health expenditures of patients with IS [12,22,31]. The number of comorbid conditions (0, 1, 2, or ≥3) was also used to measure the status of comorbidity.

2.4. Definition of outcomes

One-year readmission rate, annual inpatient expenditure, and annual inpatient out-of-pocket expenditure (OOPE) were the outcomes of interest in this study. One-year readmission was defined as any inpatient admission within one year after the first discharge. Readmissions were identified by matching the pseudo-IDs [23,32]. OOPE of hospitalization was calculated as the total hospitalization cost minus the medical insurance reimbursement. The annual inpatient expenditure of each patient was defined as the total medical cost of hospitalization within one year after the first discharge. Annual inpatient OOPE was defined as the OOPE of hospitalization within one year after the first discharge [22].

2.5. Covariates

We considered several covariates in this study, including age (18–59, 60–79, and >80 years), gender (male/female), basic medical insurance status (Urban Employee Basic Medical Insurance (UEBMI)/Urban and Rural Resident Basic Medical Insurance (URRBMI)), grade of the hospital at index IS hospitalization (secondary/tertiary), year of index IS hospitalization (2018, 2019, 2020, 2021), and annual LOS (day) [22,23]. Annual LOS was defined as the total LOS of hospitalization within the year after the first discharge.

Table 2
Characteristics of patients by types of comorbidity.

Characteristics	Overall	IS only	With discordant comorbidities only	With concordant comorbidities only	With both type of comorbidities	*P*-value
N (%)	99649 (100)	5995 (6.0)	1667 (1.7)	63566 (63.8)	28421 (28.5)	
Age group, N (%)						<0.001
18-59	19281 (19.3)	1954 (32.6)	510 (30.6)	11804 (18.7)	5014 (17.6)	
60-79	53379 (53.6)	2766 (46.1)	810 (48.6)	34837 (54.8)	14966 (52.7)	
≥80	26989(27.1)	1275 (21.3)	347(20.8)	16926 (26.6)	8441 (29.7)	
Gender N (%)						<0.01
Male	52147 (52.3)	3062 (51.1)	831 (49.9)	33177 (52.2)	15077 (53.0)	
Female	47502 (47.7)	2933 (48.9)	836 (50.1)	30389(47.8)	13344 (47.0)	
Insurance status, N (%)						<0.001
UEBMI	66043 (66.3)	4157 (69.3)	1216 (72.9)	41274 (64.9)	19396 (68.2)	
URRBMI	33606 (33.7)	1838 (30.7)	451 (27.1)	22292(35.1)	9025 (31.8)	
Hospital grade N (%)						<0.001
Secondary	20307 (20.4)	1184 (19.7)	372 (22.3)	12358 (19.4)	6393 (22.5)	
Tertiary	79342 (79.6)	4811 (80.3)	1295 (77.7)	51208(80.6)	22028 (77.5)	
Year of index IS hospitalization, N (%)						<0.001
2018	31038 (31.2)	2295 (38.3)	512 (30.7)	19723 (31.0)	8508 (29.9)	
2019	30609 (30.7)	1605 (26.8)	519 (31.1)	19842 (31.2)	8643 (30.4)	
2020	25525 (25.6)	1214 (20.2)	439 (26.3)	16335 (25.7)	7537 (26.5)	
2021	12477 (12.5)	881 (14.7)	197 (11.8)	7666 (12.1)	3733 (13.1)	
No. comorbidities, N (%)						
0	5995 (6.0)	5995 (100)	-	-	-	
1	14333 (14.4)	-	1431 (85.8)	12902 (20.3)	-	
2	22502 (22.6)	-	221 (13.3)	18146 (28.5)	4135 (14.5)	
3+	56819 (57.0)	-	15 (0.9)	32518 (51.2)	24286 (85.5)	
Annual LOS, day	21.2 (20.9, 21.5)	19.8 (18.7, 20.8)	18.0 (16.1, 19.8)	21.8 (21.5, 22.2)	20.3 (19.9, 20.8)	<0.001
Readmissions rate, %	26.7 (26.4, 27.0)	23.8 (22.8, 24.9)	20.2 (18.3, 22.2)	27.8 (27.5, 28.2)	25.1 (24.6, 25.6)	<0.001
Annual inpatient expenditure, CNY	28086.6 (27802.7, 28370.4)	24401.0 (23356.9, 25445.1)	22921.0 (20952.1, 24889.9)	29301.9 (28932.5, 29671.4)	26448.7 (25954.3, 26943.1)	<0.001
Annual inpatient OOPE, CNY	8267.3 (8180.3, 8354.3)	7342.6. (7009.5, 7675.7)	6994.7 (6234.4, 7755.0)	8646.4 (8533.4, 8759.4)	7689.2 (7540.3, 7838.0)	<0.001

Readmission rate was given as frequency with 95% confidence intervals in parentheses.
For annual LOS, annual inpatient expenditure and annual inpatient OOPE, data were given as mean with 95% confidence intervals in parentheses.
Abbreviation: IS = ischemic stroke; UEBMI = Urban Employee Basic Medical Insurance; URRBMI = Urban and Rural Resident Basic Medical Insurance; LOS = length of stay; OOPE = out-of-pocket expenditure; CNY = Chinese Yuan.

2.6. Statistical analysis

Descriptive statistics were used to summarize patients' demographic data and clinical information by comorbidity groups. The crude mean with 95 % confidence intervals (CIs) was measured for annual LOS, one-year readmission rate, annual inpatient expenditure, and annual inpatient OOPE. The frequency was calculated for other categorical variables. Differences in continuous and categorical variables between comorbidity groups were assessed using the Kruskal–Wallis test and the Chi-squared test, respectively. Multivariable logistic regression models were used to measure the effect and interaction of different comorbidity groups on readmission rates. Generalized linear models with log-link and gamma distribution were conducted to estimate the effect and interaction of different comorbidity groups on annual inpatient expenditure and annual inpatient OOPE.

Subgroup analyses were used for individuals with only one additional comorbidity, two comorbidities, and three or more comorbidities. We also evaluated the multicollinearity of covariates adjusted in our analysis using the variance inflation factor (VIF). The results of VIFs were all less than five, indicating that the assumption of reasonable independence among predictor was met.

Furthermore, sensitivity analyses were conducted based on the patients whose index hospitalization was in 2018 to ensure the robustness of our results.

Statistical analyses were performed using R 4.2.1. A two-sided P value < 0.05 was considered statistically significant.

3. Results

3.1. Basic characteristics

There were 99,649 adult patients with IS in the insurance claims database between January 2018 and May 2021 (Table 2). Of them, 52.3 % were male, and the median age of all patients was 70.1 years (IQR 62.0–80.0). Most of the patients were covered by UEBMI (66.3 %) and first admitted to a tertiary hospital (79.6 %). In total, 94.0 % of patients with IS reported comorbid conditions, among which 1.7 % had discordant comorbidity only, 63.8 % reported concordant comorbidity only, and 28.5 % had both discordant and concordant comorbidities. The most common concordant comorbidities among patients with IS were hypertension (69.5 %) and cerebrovascular diseases (37.3 %). The most common discordant comorbidities were CLD (18.6 %) and CPD (7.8 %) (Fig. 2).

3.2. Readmission rate and inpatient expenditure

Overall, patients with IS reported a readmission rate of 26.7 % (95 % CI 26.4–27.0) (Table 2). The mean of annual inpatient expenditure and OOPE were 28086.6 CNY (95 % CI 27802.7–28370.4) and 8267.3 CNY (95 % CI 8180.3–8354.3), respectively. After adjusting for covariates, having discordant comorbidity only was significantly associated with decreased readmission rate; having concordant comorbidity only was significantly associated with increased readmission rate, annual inpatient expenditure, and annual inpatient OOPE; having both types of comorbidities was significantly associated with increased annual inpatient expenditure and annual inpatient OOPE (Table 3).

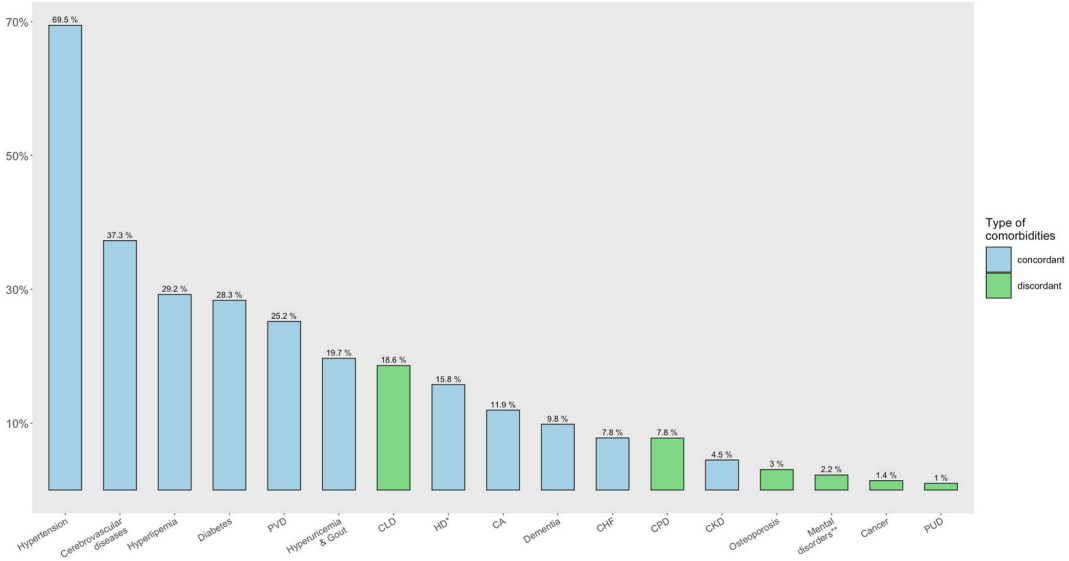

Fig. 2. Prevalence of concordant and discordant comorbidities of patients with IS. *Heart disease included chronic rheumatic heart disease and coronary heart disease. **Mental disorders include substance abuse, depression, anxiety, and schizophrenia. Abbreviation: CA = cardiac arrhythmia; CHF = congestive heart failure; CKD = chronic kidney disease; CLD = chronic liver disease; CPD = chronic pulmonary disease; HD = heart disease; IS = ischemic stroke; PUD = peptic ulcer disease; PVD = peripheral vascular diseases.

Table 3
Adjusted effects by multivariable analyses.

	Readmission rate				Annual inpatient expenditure				Annual inpatient OOPE			
	β	*z*	95% CI		*β*	*t*	95% CI		*β*	*t*	95% CI	
(Constant)	-1.323***	-36.374	-1.395	-1.252	9.453***	654.531	9.425	9.481	8.240***	489.565	8.207	8.273
Age group (Ref. = 18-59)												
60-79	0.212***	10.476	0.172	0.252	-0.039***	-4.701	-0.053	-0.022	-0.294***	-31.562	-0.312	-0.276
≥80	0.496***	22.186	0.453	0.540	-0.058**	-6.396	-0.076	-0.040	-0.403***	-37.901	-0.424	-0.382
Gender (Ref. = Male)	0.239***	16.120	0.210	0.268	0.144***	23.833	0.132	0.156	0.181***	25.602	0.167	0.194
Insurance type (Ref. = UEBMI)	-0.220***	-13.941	-0.251	-0.189	-0.089***	-13.976	-0.102	-0.077	0.808***	108.325	0.793	0.822
Hospital grade (Ref= Tertiary)	0.132***	7.391	0.097	0.167	-0.524***	-70.239	-0.539	-0.509	-0.698***	-80.37	-0.715	-0.681
Year of index IS hospitalization (Ref. = 2018)												
2019	-0.231***	-12.676	-0.267	-0.195	0.081***	10.741	0.066	0.096	0.074***	8.459	0.057	0.091
2020	-0.185***	-9.675	-0.222	-0.147	0.138***	17.423	0.122	0.153	0.292***	31.641	0.273	0.310
2021	-0.283***	-11.554	-0.330	-0.235	0.179***	18.008	0.159	0.198	0.303***	26.251	0.280	0.326
Annual LOS	-	-	-	-	0.019***	263.009	0.018	0.019	0.014***	175.720	0.014	0.015
Type of Comorbidities (Ref. = IS only)												
With discordant comorbidities only	-0.215**	-3.134	-0.349	-0.081	-0.019	-0.073	-0.053	0.049	0.003	0.100	-0.056	0.062
With concordant comorbidities only	0.188***	5.903	0.126	0.251	0.133***	10.496	0.108	0.158	0.121***	8.22	0.092	0.150
With both type of comorbidities	0.026	0.771	-0.040	0.092	0.092***	6.898	0.066	0.118	0.073***	4.649	0.042	0.103

* $P< 0.05$, ** $P< 0.01$; *** $P< 0.001$.
Coefficients were estimated after adjusting for study variables, (Logistic regression model for readmission rate; Generalized linear models with log-link and gamma distribution for expenditure).
Abbreviation: Ref. = control group; IS = ischemic stroke; CI = confidence interval; OOPE = out-of-pocket expenditure; UEBMI = Urban Employee Basic Medical Insurance; URRBMI = Urban and Rural Resident Basic Medical Insurance; LOS = length of stay.

The estimated differences in readmission rate and hospitalization expenditure between the study groups are presented in Table 4. The estimated incremental readmission rate of IS patients with concordant comorbidity only was 9.7 % (95%CI 6.3–13.3, P < 0.001) compared with patients with IS only. The estimated decremental readmission rate of IS patients with discordant comorbidity only was 8.7 % (95 % CI 3.4–13.3, P < 0.01), compared with IS only.

The estimated incremental inpatient expenditures and OOPE between IS patients with concordant comorbidity only and patients with IS only were 2099.8 CNY (95 % CI 1701.6–2505.2, P < 0.001) and 453.5 CNY (95 % CI 346.6–562.7 P < 0.001), respectively. The differences in the incremental expenditure and OOPE between IS patients with both types of comorbidities and patients with IS only were 1452.2 CNY (95%CI, 1050.5–1862.3, <0.001) and 275.8 CNY (95%CI, 168.7–385.4, P < 0.001), respectively. Besides, IS patients with concordant comorbidity only had a higher annual inpatient expenditure and OOPE than IS patients with discordant comorbidity only and IS patients with both types of comorbidities (Table 4).

Moreover, we conducted other multivariable analyses including the same covariates, to assess the potential interaction effect between concordant and discordant comorbidities regarding readmission rate and expenditure. The results showed that the interaction effect was not significant (for details, see Supplemental Material Table A1).

3.3. Results of subgroup analyses

The estimated differences in the subgroup analysis are reported in Table 4. The estimated incremental readmission rate of IS patients with concordant comorbidity only relative to patients with IS only was 7.9 % (95%CI 4.1–11.9, P < 0.001) and 13.0 % (95%CI 9.5–16.9, P < 0.001) for patients with two and three or more comorbidities, respectively. However, the difference between these two groups was not statistically significant in the presence of only one comorbidity. In the presence of only one comorbidity, IS patients with discordant comorbidity only had a significantly lower readmission rate than patients with IS only (9.6 %, 95 % CI 3.5–15.0, P < 0.01), while the difference was not statistically significant among patients with two comorbidities.

The estimated incremental inpatient expenditure of IS patients with concordant comorbidity only relative to patients with IS only was 438.9 CNY (95%CI 48.6–839.0, P < 0.05), 1774.9 CNY (95%CI 1337.8–2222.4, P < 0.001) and 3038.9 CNY (95%CI 2597.4–3489.2, P < 0.001) in the presence of one, two, and three or more comorbidities, respectively. Meanwhile, the estimated incremental inpatient OOPE of these two groups were 117.6 CNY (95%CI 4.6–233.9, P < 0.05), 413.0 CNY (95%CI 289.2–540.3, P < 0.001), and 656.0 CNY (95%CI 537.9–776.9 P < 0.001) in the presence of one, two, and three or more comorbidities, respectively. The difference in annual inpatient expenditure and OOPE between IS patients with both types of comorbidities and patients with IS only

Table 4
Difference of readmission rate and expenditure between types of comorbidity.

	Overall	One comorbidity	Two comorbidities	Three or more comorbidities
Readmission rate, %				
IS with concordant comorbidity only vs IS only	9.7 (6.3, 13.3) ***	3.2 (-0.5, 7.1)	7.9 (4.1, 11.9) ***	13.0 (9.5, 16.9) ***
IS with discordant comorbidity only vs IS only	-8.7 (-13.3, -3.4) **	-9.6 (-15.0, -3.5) **	-7.8 (-19.6, 7.7)	-
IS with concordant comorbidity only vs with discordant comorbidity only	18.3 (12.1, 25.6) ***	12.8 (6.1, 20.6) ***	15.6 (0.3, 38.3)	-
IS with both type of comorbidities vs IS only	1.5 (-1.5, 4.6)	-	-3.9 (-8.0, 0.5)	2.4 (-0.6, 5.6)
IS with both type of comorbidities vs with discordant comorbidity only	10.1 (4.7, 16.4) ***	-	3.9 (-8.5, 22.1)	-
IS with both type of comorbidities vs with concordant comorbidity only	-8.2 (-9.7, -6.7) ***	-	-11.8 (-15.3, -8.1) ***	-10.7 (-12.4, -8.9) ***
Annual inpatient expenditure, CNY				
IS with concordant comorbidity only vs IS only	2099.8 (1701.6, 2505.2) ***	438.9 (48.6, 839.0) *	1774.9 (1337.8, 2222.4) ***	3038.9 (2597.4, 3489.2) ***
IS with discordant comorbidity only vs IS only	49.0 (-643.9, 784.9)	48.3 (-648.0, 790.9)	600.0 (-1110.3, 2621.5)	-
IS with concordant comorbidity only vs with discordant comorbidity only	2050.8 (1329.2, 2795.1) ***	390.6 (-296.4, 1103.5)	1174.9 (-722.6, 3240.5)	-
IS with both type of comorbidities vs IS only	1452.2 (1050.5, 1862.3) ***	-	13.9 (-504.4, 553.4)	1750.7 (1332.9, 2177.6) ***
IS with both type of comorbidities vs with discordant comorbidity only	1403.2 (700.1, 2129.5) ***	-	-586.2 (-2300.6, 1289.5)	-
IS with both type of comorbidities vs with concordant comorbidity only	-647.6 (-848.6, -443.6) ***	-	-1761.0 (-2200.9, -1303.7) ***	—1288.2 (-1531.2, -1041.1) ***

	Overall	One comorbidity	Two comorbidities	Three or more comorbidities
Annual inpatient OOPE, CNY				
IS with concordant comorbidity only vs IS only	453.5 (346.6, 562.7) ***	117.6 (4.6, 233.9) *	413.0 (289.2, 540.3) ***	656.0 (537.9, 776.9) ***
IS with discordant comorbidity only vs IS only	32.9 (-155.3, 234.6)	23.0 (-177.7, 239.5)	236.4 (-255.1, 835.7)	-
IS with concordant comorbidity only vs with discordant comorbidity only	420.6 (227.5, 620.9) ***	94.6 (-103.7, 301.8)	176.6 (-356.2, 765.9)	-
IS with both type of comorbidities vs IS only	275.8 (168.7, 385.4) ***	-	-16.8 (-162.8, 136.2)	340.5 (229.3, 454.4) ***
IS with both type of comorbidities vs with discordant comorbidity only	242.9 (56.2, 436.8) **	-	-253.3 (-733.1, 280.6)	-
IS with both type of comorbidities vs with concordant comorbidity only	-177.7 (-231.2, -123.3) ***	-	-429.8 (-553.5, —300.3) ***	-315.5 (-380.0, -249.8) ***

* $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$.
Mean of difference with 95% confidence intervals in parentheses were derived from multivariable models.
Abbreviation: IS = ischemic stroke; CNY = Chinses Yuna; OOPE = out-of-pocket expenditure

was not statistically significant in the presence of two comorbidities, whereas in the presence of three or more comorbidities, the former group had a significantly higher inpatient expenditure and OOPE. The estimated increments were 1750.7 CNY (95%CI 1332.9–2177.6, P < 0.001) and 340.5 CNY (95%CI 229.3–454.4, P < 0.001), respectively. In addition, IS patients with concordant comorbidity only had a significantly higher annual inpatient expenditure and OOPE than IS patients with both types of comorbidities in the presence of two and three or more comorbidities.

Age and gender are treated as covariates in the statistical analysis. However, they are well-known confounders that can skew the estimation of an association. The analysis of subgroups by age revealed statistically significant differences in the impact of comorbidities among younger patients with IS on readmission rates. Concordant comorbidities were found to increase the risk of readmission. Furthermore, there was an interaction effect between age and types of comorbidities (P for interaction <0.001), indicating that the relationship between types of comorbidities and readmission rates varies significantly across different age groups. (The result table was added in the Supplemental Table A3.

3.4. Results of sensitivity analysis

By analyzing data from patients who were first admitted in 2018, we found that the estimates were closely similar to the estimates of the main analyses (for details, see Supplemental Material Table A2). These findings showed the robustness of our results while excluding the effects of the COVID-19 pandemic.

4. Discussion

Our study provides a comprehensive analysis of the readmission risk and related hospitalization expenditures attributable to different types of comorbidities co-existing with IS. For the first time, this study distinguished the comorbidities of IS patients. The proportion of comorbidities was very high, and concordant comorbidities accounted for the highest proportion. Readmission rates and expenditures associated with concordant comorbidity were higher than those associated with discordant comorbidity. The average annual expenditures of patients with IS only were lower than those of IS patients with concordant comorbidity. Notably, the incremental hospitalization expenditure of IS patients with concordant comorbidity increased with the number of comorbidities, while IS patients with discordant comorbidity did not show this trend. To our knowledge, there is no report in the literature showing that concordant or discordant comorbidity is associated with the readmission rate and health expenditure of patients with IS.

To address the gap of single-disease-focused multimorbidity research, we used a new conceptual model and research framework—concordant and discordant comorbidity from the committee of NIH IC to analyze various comorbidity with IS [10]. Our findings lay the foundation for developing new prevention and treatment strategies for comorbidities of IS. Before developing this research framework for multimorbidity, a considerable number of studies focused on the management of demonstrated concordant comorbidities [33–35]. Recently, research on discordant comorbidities, such as hypertension and depression [36,37], strokes and depression [38–40], has also received increasing attention [41–43]. The NIH IC committee also plans to identify future directions of research and evaluate single diseases with serious sequelae. We found that hypertension and cerebrovascular diseases were concordant comorbidities with the highest prevalence among patients with IS, and chronic liver diseases and chronic pulmonary diseases were the most common discordant comorbidities.

Elderly people with IS have a higher risk of comorbidities and receive more medications for treating these comorbidities [8,44]. A few systematic reviews have shown that some drugs may increase the risk of developing vascular events and lead to IS [45–48]. Due to the aging population and increasing prevalence of comorbidities [44], patients with IS are left with disability and suffer from low quality of life. The burden of IS will grow in the future in our country. This study emphasizes that managing the comorbidities of patients with IS is a key factor that should always be considered. These comorbidities were documented at the first stroke admission, and a causal relationship could not be demonstrated. However, previous studies indicated that such hypertension and cerebrovascular diseases, as concordant comorbidities, are the cause of stroke [1–3,49,50], and managing these comorbidities can promote health quality after stroke.

Concerning readmission rate, Australian studies have used multiple datasets linked with code to analyze all-cause readmission rates in different periods after acute stroke and found that readmission is related to comorbidities [51]. In addition, we also found that different types of comorbidities are significantly different in terms of readmission. Concordant comorbidities showed the highest rate, and discordant comorbidities showed the lowest rate of readmission. After controlling other factors (eg., age, gender, insurance type, hospital grade, and year of the first admission) related to readmission, there were increasing trends in readmission hospital burden associated with concordant comorbidities, but readmission was negatively correlated with discordant comorbidities during the study period. Our study not only demonstrated that readmission rates were associated with the type of comorbidities but also found a positive correlation with the number of concordant comorbidities. In subgroup analysis, different types of comorbidities affected the readmission of IS patients, suggesting a response relationship. The same relationship between comorbidity number and health status was observed in a nationally representative study [12].

A cross-sectional study using the claims data examined the relationship between comorbidity and health costs of stroke and found that the presence of comorbidities increased the healthcare burden of stroke patients in China [22]. Many factors influence stroke expenditures. A retrospective cohort study revealed that older age, comorbidities, and lower socioeconomic status increase stroke expenditures, and comorbidity plays an indispensable role not only in quantity but also in the category [52–54]. Our study found a positive association between concordant comorbidity and inpatient annual total expenditure and OOPE. In addition, we found that the number of concordant comorbidities has a greater impact on hospitalization expenditure compared with IS only and both types of

comorbidities. Most of the previous studies focused on the relationship between the number of comorbidities and mortality, disability, function, and costs. However, several studies measured the relationship between concordant and discordant comorbidities, including CKD and diabetes [11–13]. CKD and diabetes have a high number of comorbidities, and their proportion of discordant comorbidity is higher than that of IS. Discordant comorbidities of diabetes adversely affected the outcomes of patients, but discordant comorbidities of IS did not affect health expenditure. Further studies are needed to explore the exact mechanisms. Notably, disease-specific guidelines should consider concordant and discordant comorbidities of IS patients and modify health care to improve the management of comorbidities.

4.1. Strengths and limitations

Our study has several strengths. For instance, we used high-quality data with good representation from the health insurance claims dataset, and the health insurance coverage of the city was almost 98 %. We defined different types of comorbidities and quantitatively analyzed the readmission and health expenditure of IS patients. However, there are some important limitations to this study. Only acute IS was assessed, and different IS subtypes were not included in the final analyses, which can increase the heterogeneity of results. The claims dataset is limited to part of patient information, including disease diagnosis and basic characteristics of patients, without mentioning disease severity, treatment modality, patient's socioeconomic status, and education. Thus, this study did not investigate how specific medical interventions increase expenditures. Our study did not consider emergency room visits, outpatient visits, and regular drug use, which may have underestimated the burden of IS. This study used the data from 2018 to 2022, and the COVID-19 pandemic may have altered the results, but we did not analyze the impact of post-COVID conditions.

5. Conclusions

In this study, discrepancies between readmission and health expenditure were associated with concordant and discordant comorbidities of IS. Concordant comorbidity was associated with increased hospital readmission risk and higher health expenditures of IS. Routine care for people with IS should include the recognition of different types of comorbidities, and treatment guidelines should encourage clinicians to do so, avoiding therapeutic interactions that can worsen the outcomes.

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Ethics approval and consent to participate

This study was exempt from the purview of the Institutional Review Board by Sun Yet-Sen University and did not require participant patient consent as it was collected for administrative purposes no contact with patients was conducted and patient anonymity was assured.

Additional information

No additional information is available for this paper.

Data availability statement

The claims data from China Basic Medical Insurance in a large city analyzed in this study are regulated by governmental policies and cannot be made available to the public. Restrictions apply to the availability of these data, which were used under a license for studies. The authors do not have permission to share data.

CRediT authorship contribution statement

Honghong Feng: Writing – review & editing, Writing – original draft, Visualization, Resources, Formal analysis, Data curation, Conceptualization. **Jiachi Zhang:** Writing – review & editing, Writing – original draft, Software, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Zhenhua Qin:** Writing – review & editing, Writing – original draft, Validation, Supervision, Formal analysis, Data curation, Conceptualization. **Yi Zhu:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Data curation. **Xiaodi Zhu:** Writing – review & editing, Writing – original draft, Validation, Data curation. **Lijin Chen:** Writing – review & editing, Writing – original draft, Resources, Project administration, Data curation. **Zhengqi Lu:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Yixiang Huang:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

influence the work reported in this paper.

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Appendix A. Supplementary data

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