Combined Association of Multiple Chronic Diseases and Social Isolation With Functional Disability in Elderly Stroke Patients: A Multicentre Cross-sectional Study in China

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Abstract

Background

Multiple chronic diseases (MCDs) and social isolation are independent risk factors related with stroke and disability, but it is unknown whether the combination of these two conditions resulted from ageing related to functional disability in stroke patients. The purpose of this study was to probe the relationship between combination of MCDs, social isolation and functional disability in elderly stroke patients.

Methods

A multicentre and cross-sectional study was conducted in the Departments of Rehabilitation Medicine of 103 hospitals located in 23 cities across China. Stroke patients aged over 60 years were selected as participants. Demographic characteristics, lifestyles and clinical information were investigated by questionnaire and medical records. Multi-nominal logistic regression model was used to explore the association of MCDs, social isolation and their combination with functional disability assessed by Barthel Index Scale.

Results

A total of 4281 elderly stroke patients were included in the final analysis. The proportion of social isolation and MCDs (>1) increased by the severity of functional disability. Social isolation was associated with increased risks for mild (33%), moderate (175%), and severe (833%) functional disability significantly in their comparisons with those without social isolation and MCDs. The intragroup odds ratio (OR) of MCDs increased by its number and the intergroup of OR increased by the severity of functional disability significantly. Social isolation and ≥3 MCDs associated the highest risk for severe (OR= 38.24, 95%CI: 14.76-99.07) and moderate (OR = 9.74, 95%CI: 3.62-26.22) functional disability, but not significant for mild group.

Conclusions

MCDs, social isolation, and their combination were associated with functional disability in Chinese elderly stroke patients. Future secondary prevention and rehabilitation for functional disability in this population should underscore both social activity and the combined treatments of MCDs.

Clinical Trial Registration NO

ChiCTR2000034067.

Background

In 2013, stroke, as the leading cause of death in China, affected over 12 million Chinese residents [1]. It was estimated that over 2 million newly diagnosed stroke patients annually, and the incidence was projected to increase continuously [2]. Over 70% of patients after stroke struggle to perform activities of daily living (ADL) and require substantial household and medical care [3]. A long-term cohort study (a mean of 13-year follow-up) described the disability trajectories and found a steep decrease in post-stroke functional ability [4]. Many studies have reported that the recurrence rate of stroke was approximately 10% within one year [5], and with an increase to 12% over five years [6]. The disability was more serious in recurrent stroke patients, two times higher than that of their first-ever counterparts in one year [7]. Some cost-effectiveness analyses have that indicated that functional disability was one of the strong determinants of the medical costs of stroke patients independent of its subtype and severity [8, 9], while the recovery of functional ability can effectively decrease the medical costs and improve the quality of life of stroke patients.

Epidemiological evidence has shown that ageing is the strongest nonmodifiable risk factor for the morbidity of stroke and disability [10, 11]. The 2013 Global Burden of Disease study in China has shown that geriatric patients accounted for over 70% of stroke deaths [12]. In general, the biological ageing process is embedded with the interaction of multiple chronic diseases (MCDs) to form the pathogenesis of stroke [13]. A systematic review indicated that the prevalence of MCDs ranged from 55–98% in the elderly population [14]. In older stroke patients, the most prevalent chronic disease was hypertension (80%); diabetes accounted for over 23%[10]. Atrial fibrillation and chronic kidney disease were also associated with an increased risk of stroke [15, 16]. Furthermore, ageing itself and its resulting MCDs have been shown to accelerate the simultaneous occurrence of stroke and functional disability [14]. Given that population ageing continues to increase in China [17], studies addressing functional disability in elderly stroke patients are warranted.

In addition to MCDs, social activity is a potential pathway linking the ageing process with stroke and functional disability. Commonly, social activity reflects the participation of activities that can enable connection and communication with other persons broadly, in the social milieu [18]. It has been found that over 40% of the geriatric population suffer from social isolation (absence of social activity) due to the shifts in social relationships, including the geographic migration and death of family members [19]. Emerging evidence has shown that the presence of social isolation is associated with an increase in the risk of stroke [20] and disability [21]. Furthermore, it was found that either pre-stroke or post-stroke social activity was a robust predictor of stroke outcomes: pre-stroke social isolation was linked to a 40% increase in adverse outcomes (including myocardial infarction, stroke recurrence, or death) after stroke [22], while Jansen's study reported that 1-year post-stroke social isolation is still strongly associated with 3-year post-stroke disability [23].

Despite the independent association of MCDs and social isolation with stroke and disability [20, 21], little is known about whether the combination of these two conditions resulted from ageing related to functional disability in stroke patients. These two conditions reflected two aspects at the individual level: MCDs are a general indicator of physical health [14], while social activity reflects healthy social engagement and is strongly linked with mental health [20], but they interact with each other and cannot be treated separately. Based on a previous finding that social activity decreased the risk of MCDs in a European macro-regional study [24], we hypothesised that the combination of MCDs and social isolation can increase functional disability more than a single condition alone in elderly stroke patients. Importantly, assessing the combination of these risk factors may suggest that earlier screening and interventions can improve rehabilitation strategies in stroke patients. Thus, the objective of this study was to test the hypothesis in stroke patients aged over 60 years using data from the Departments of Rehabilitation Medicine in hospitals in China.

Methods

Study design and setting

This multicentre cross-sectional study was conducted between September 2018 and December 2019 in the Departments of Rehabilitation Medicine of 103 hospitals located in 23 cities around China. Originally, this study was designed to assess the reliability and validity of a pictorial scale (Longshi Scale) for disability assessment, which was constructed to reduce the time of disability evaluation in non-professional evaluation [25]. Subsequently, Longshi Scale was widely popularized at a national level to ensure its good application as the Barthel Index (BI), which is always regarded as the gold standard for assessing functional disability [26]. This study was approved by the Medical Ethics Committees of First Affiliated Hospital of Shenzhen University (Project identification code: 2017070605). Written informed consent was obtained from all the inpatients or their proxies who agreed to participate in the study.

Participants

This study recruited a total of 11898 consecutive inpatients from the Departments of Rehabilitation Medicine. Among them, 1191 (10.0%), 3426 (28.8%), and 7281 (61.2% patients were recruited from primary, secondary primary, and tertiary hospitals respectively. For the purposes of this study, we only selected stroke patients aged over 60 years for further analysis. The diagnosis of stroke was based on the 10th Reversion of the International Classification of Diseases (I60.x and I61.x for the haemorrhagic subtype; H34.1, I63.x, and I64.x for the ischemic subtype) [27]. For inclusion, patients were required be conscious and able to read and answer questions. Those who suffered from deformities, mental illnesses, aphasias, and cognitive dysfunction were excluded. Additionally, patients who were participating simultaneously in other clinical studies were also excluded.

Data collection

The sociodemographic characteristics, lifestyles, and clinical information of the participants were collected using questionnaires and medical records. Functional disability was assessed by trained health-care practitioners (registered physicians, nurses, and therapists) at each collaborating hospital. All the data were recorded on electronic forms and uploaded to a specialised online system. Missing information was completed by requesting that the practitioner to re-interview the participants.

Measurement

Multiple chronic diseases: Our study considered five common chronic diseases: 1) hypertension, 2) diabetes, 3) hyperlipidaemia, 4) heart disease, and 5) chronic kidney disease. Participants were asked “Were you diagnosed with any specific chronic disease by a physician in your lifetime?” and with only answer two options, “yes or no”. This question was widely used to assess MCDs [28]. Additionally, medical histories which reported any chronic disease, or treatment with related drugs or other therapies, was also recorded as “yes”. Eventually, self-report, medical history, and their combination were used to define chronic disease. MCDs were classified based on the sum of categories: 0, 1, 2, and ≥ 3.

Social activity: Participants were asked to report their social activities engagement during the last month before stroke, involving four dimensions: 1) communication included deep conversations with relatives and friends by face-to-face or email; 2) leisure activities included chess and card entertainment, engaging in community clubs for singing and dancing together, playing outdoor exercise, fishing, hiking, and exercising with friends; 3) social affairs included voluntary or charitable work; and 4) education included some courses for health management and interest training. The investigation of social activity followed that used in a nationally representative longitudinal study [29]. Similarly, social activity was dichotomised by coding as “0” for no to indicate social isolation, “≥ 1” for yes to indicate social activity engagement.

Functional disability: The Barthel index (BI) was used to assess functional disability. It consisted of 10 aspects of ADL and showed high reliability and validity in the Chinese population: [26] 1) feeding, 2) moving from wheelchair to bed and return, 3) personal toilet, 4) getting on and off the toilet, 5) self-bathing, 6) walking on level surface, 7) ascending and descending on stairs, 8) dressing, 9) controlling bowel movements, and 10) controlling the bladder. Items 8 and 9 included four levels and were marked as 15, 10, 5, and 0 according to the independence of ADL, the items of 1, 4–7, and 10 included three levels and were marked as 10, 5, and 0, while items 2 and 3 only included two levels and were marked as 5 and 0, respectively. The total score ranged from to 0–100, with a higher score indicating a higher functional ability. Based on previous studies, we divided participants into four groups: severe (BI ≤ 55), moderate (BI: 60–85), mild (BI: 90–95), and no disability (BI = 100) [26, 30].

Statistical analysis

The demographic characteristics, current lifestyle, and clinical information were presented as numbers (%). Demographic characteristics included age (60 70–80 *years*), gender (male and female), ethnicity (Han and Minority), marital status (married and single including widowed and unmarried), annual household income (~ 50,000, 50,000–100,000, 100,000–150,000, and 15,000–*yuan*), and education level (primary and lower, middle school, high school, college, and higher). Current lifestyles which included drinking, smoking, and social activity were coded as “yes” and “no”, respectively. Clinical information included fall experience (none, fall without hurt, fall with light hurt, and fall with heavy hurt), stroke occurrence (first, second, and three or more), and MCDs.

Initially, an ordinal regression model was used to perform the association analysis; however, the parallel hypothesis test did not meet the requirement. Therefore, the independent associations of social activity and MCDs as well as their combination with functional disability, were examined using multi-nominal logistic regression models. Model 1 was the crude model, Model 2 adjusted the demographic information, lifestyles, and hospital levels, and further adjusted the clinical information in Model 3. A multiple imputation method was used to handle the missing data with the imputation of five datasets. All analyses were conducted using SPSS software (Version 24.0. Armonk, NY: IBM Corp). A *P*-value of less than 0.05 was considered statistically significant. Given that falls with heavy hurt directly influenced mobility [31] and could suppress the impact of MCDs and social isolation on functional ability, a sensitivity analysis was conducted to exclude participants with heavy hurt fall experience and subsequently repeat the multi-nominal logistic regression model.

Results

A total of 4281 elderly stroke patients aged 75.6 ± 9.3 years were included in this study, and their characteristics based on the categories of functional disability, are summarised in Table 1. Patients with a severe functional disability accounted for 71.5% of the patients (n = 3061), while mild and no functional disability accounted for only about 6%. Although the number of patients with no, mild, or moderate disability decreased with increasing age, the severity of disability presented a contrary trend. Among the total participants, 2326 (54.3%) were male, 57 patients (1%) were the minority, and over half were recruited from tertiary hospitals.

Table 1

Descriptive characteristics of elderly stroke patients according to functional disability †

Characteristics, n (%)	No disability 265 (%)	Mild disability 213 (%)	Moderate disability 742 (%)	Severe disability 3061(%)
Demographic				
Age (years)				
60~	123 (46.4)	81 (38.0)	307 (41.4)	808 (26.4)
70~	101 (38.1)	67 (31.5)	234 (31.5)	964 (31.5)
80~	41 (15.5)	65 (30.5)	201 (27.1)	1289 (42.1)
Gender				
Male	157 (59.2)	131 (61.5)	448 (60.4)	1590 (51.9)
Female	108 (40.8)	82 (38.5)	294 (39.6)	1471 (48.1)
Ethnicity				
Han	262 (98.9)	208 (97.7)	731 (98.5)	3023 (98.8)
Minority	3 (1.1)	5 (2.3)	11 (1.5)	38 (1.2)
Marital status				
Married	242 (91.3)	193 (90.6)	640 (86.3)	2577 (84.2)
Single (Widowed, Divorced, and Unmarried)	23 (8.7)	20 (9.4)	102 (13.7)	484 (15.8)
Annual Household Income (yuan)*				
< 50,000	85 (32.1)	51 (23.9)	238 (32.1)	949 (31.0)
50,000 ~ 100,000	105 (39.6)	84 (39.4)	273 (36.8)	1219 (39.8)
100,000 ~ 150,000	52 (19.6)	54 (25.4)	134 (18.1)	546 (17.8)
150,000~	20 (7.5%)	24 (11.3)	97 (13.1)	341 (11.1)
Education Level *				
Primary school and lower	73 (27.5)	61 (28.6)	220 (29.6)	1069 (34.9)
Middle school	95 (35.8)	60 (28.2)	215 (29.0)	856 (28.0)
High school	55 (20.8)	48 (22.5)	189 (25.5)	657 (21.5)
College and higher	36 (13.6)	38 (17.8)	85 (11.5)	308 (10.1)

Characteristics, n (%)	No disability 265 (%)	Mild disability 213 (%)	Moderate disability 742 (%)	Severe disability 3061(%)
Hospital Level *				
Primary	9 (3.4)	23 (10.8)	47 (6.3%)	340 (11.1)
Second	70 (26.4)	64 (30.0)	268 (36.1%)	1123 (36.7)
Tertiary	185 (69.8)	123 (57.7)	410 (55.3%)	1516 (49.5)
Drinking *				
No	232 (87.5)	185 (86.9)	663 (89.4)	2881 (94.1)
Yes	32 (12.1)	27 (12.7)	76 (10.2)	172 (5.6)
Smoking *				
No	202 (76.2)	159 (74.6)	554 (74.7)	2502 (81.7)
Yes	62 (23.4)	53 (24.9)	183 (24.7)	550 (18.0)
Social isolation				
Yes	54 (20.4)	60 (28.2)	310 (41.8)	2164 (70.7)
No	211 (79.6)	153 (71.8)	432 (58.2)	897 (29.3)
Clinical				
Fall				
No	238 (89.8)	185 (86.9)	616 (83.0)	2590 (84.6)
Fall without hurt	4 (1.5)	3 (1.4)	44 (5.9)	68 (2.2)
Fall with light hurt	10 (3.8)	2 (0.9)	46 (6.2)	119 (3.9)
Fall with heavy hurt	0	4 (1.9)	13 (1.8)	166 (5.4)
Stroke Occurrence				
First time	203 (76.6)	163 (76.5)	570 (76.8)	2258 (73.8)
Two times	48 (18.1)	37 (17.4)	133 (17.9)	573 (18.7)
Three and more times	14 (5.3)	12 (5.6)	38 (5.1)	216 (7.1)
Hypertension				
No	101 (38.1)	58 (27.2)	173 (23.3)	673 (22.0)
Yes	164 (61.9)	155 (72.8)	569 (76.7)	2388 (78.0)

Characteristics, n (%)	No disability 265 (%)	Mild disability 213 (%)	Moderate disability 742 (%)	Severe disability 3061(%)
Diabetes				
No	204 (77.0)	157 (73.7)	501 (67.5)	2043 (66.7)
Yes	61 (23.0)	56 (26.3)	241 (32.5)	1018 (33.3)
Hyperlipidemia				
No	246 (92.8)	188 (88.3)	660 (88.9)	2784 (91.0)
Yes	19 (7.2)	25 (11.7)	82 (11.1)	277 (9.0)
Heart Diseases				
No	207 (78.1)	162 (76.1)	539 (72.6)	1993 (65.1)
Yes	58 (21.9)	51 (23.9)	203 (27.4)	1068 (34.9)
Kidney Diseases				
No	263 (99.2)	208 (97.7)	708 (95.4)	2885 (94.3)
Yes	2 (0.8)	5 (2.3)	34 (4.6)	176 (5.7)
Multiple chronic disease				
0	71 (26.8)	36 (16.9)	103 (13.9)	331 (10.8)
1	105 (39.6)	87 (40.8)	288 (38.8)	1176 (38.4)
2	70 (26.4)	66 (31.0)	235 (31.7)	1022 (33.4)
3 and more	19 (7.2)	24 (11.3)	116 (15.6)	532 (17.4)

* Has missing value. Annual household, 9 (0.2%); Education level, 216 (5.0%); Hospital level, 203 (2.4%); Drinking, 13 (0.3%); Smoking, 16 (0.4%); Fall, 173 (4.0%); Stroke occurrence, 16 (0.4%).

† Measured by Barthel Index: severe disability (BI < 55), moderate disability (BI: 60–85), mild disability (BI: 90–95), and no disability (BI = 100).

Patients who are currently drinking accounted for 7.2%, and smoking accounted for 19.8%. Importantly, patients who reported social isolation increased with the severity of disability. Initially, social activity engagement far outweighed social isolation; however, the difference between them shrunk gradually from the no to moderate disability group. Nonetheless, social isolation surpassed social activity (20.7% vs. 29.3%) in the severe disability group (Table 1). About 15.2% of the patients had a fall experience and 183 (28.1%) fell with heavy hurt. Additionally, the first-ever stroke was twice as high as the recurrent stroke (75% vs. 25%). The distribution of stroke occurrence was almost the same in the no, mild, and moderate disability groups, while the average of recurrent stroke was slightly lower than that in the severe disability group. Importantly, hypertension was the most common (over 70%) in elderly stroke patients, followed by diabetes and heart disease. MCDs (2 and more) accounted for nearly half and increased with the severity of disability (Table 1).

We found a positive association between social isolation and MCDs independently with disability (Table 2). In addition, the crude and adjusted odds ratio (OR) was increased by the severity of disability. After adjusting for demographic characteristics, current lifestyles, and clinical information, the association of elderly stroke patients with social isolation for the risk of severe disability increased by 33% (OR = 1.33, 95% CI: 0.98–1.80, $P = 0.069$), for the risk of mild disability, 175% (OR = 2.75, 95% CI: 2.18–3.47, $P < 0.001$) for the risk of moderate disability, and 833% (OR = 9.33, 95% CI: 7.54–11.54, $P < 0.001$), compared with those with social activity engagement and without disability. Furthermore, in the three comparison conditions, the crude and adjusted OR increased by the sum of MCDs. In the severe group compared with the no disability group, participants with three or more MCDs had the highest risk for severe disability (OR = 4.31, 95% CI: 3.07–6.06, $P < 0.001$).

Table 2
The independent association of social isolation and multiple chronic diseases with functional disability in elderly stroke patients

	Model 1			Model 2			Model 3		
	OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Severe vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	10.09	(8.21, 12.39)	< 0.001	8.93	(7.24, 11.02)	< 0.001	9.33	(7.54, 11.54)	< 0.001
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	2.53	(2.06, 3.1)	< 0.001	2.30	(1.86, 2.84)	< 0.001	2.44	(1.97, 3.02)	< 0.001
2	3.11	(2.47, 3.92)	< 0.001	2.50	(1.96, 3.17)	< 0.001	2.73	(2.14, 3.48)	< 0.001
3 and more	4.53	(3.27, 6.28)	< 0.001	3.69	(2.64, 5.16)	< 0.001	4.31	(3.07, 6.06)	< 0.001
Moderate vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	2.88	(2.30, 3.62)	< 0.001	2.68	(2.13, 3.37)	< 0.001	2.75	(2.18, 3.47)	< 0.001
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	1.83	(1.45, 2.29)	< 0.001	1.73	(1.38, 2.18)	< 0.001	1.81	(1.44, 2.29)	< 0.001
2	2.37	(1.84, 3.06)	< 0.001	2.10	(1.62, 2.73)	< 0.001	2.24	(1.72, 2.91)	< 0.001
3 and more	3.19	(2.24, 4.53)	< 0.001	2.85	(1.99, 4.09)	< 0.001	3.24	(2.25, 4.66)	< 0.001
Mild vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	1.40	(1.04, 1.89)	0.026	1.32	(0.98, 1.79)	0.072	1.33	(0.98, 1.80)	0.069

	Model 1			Model 2			Model 3		
	OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	1.68	(1.25, 2.26)	0.001	1.61	(1.19, 2.17)	0.002	1.62	(1.20, 2.18)	0.002
2	2.32	(1.68, 3.20)	< 0.001	2.00	(1.44, 2.78)	< 0.001	2.00	(1.44, 2.79)	< 0.001
3 and more	2.28	(1.45, 3.60)	< 0.001	1.98	(1.25, 3.15)	0.004	2.03	(1.28, 3.24)	0.003

* Model 1 was the crude model;

† Model 2 adjusted for age group, gender, ethnicity, marital status, annual household income, education level, hospital level, drinking and smoking;

‡ Model 3 added to adjusted for fall and stroke occurrence.

Table 3 displays the combined association of social activity and MCDs with disability. The ORs of those with social isolation and ≥ 3 MCDs increased to 38.24 (95% CI: 14.76–99.07, $P < 0.001$) for severe disability, and 9.74 (95% CI: 3.62–26.22, $P < 0.001$) for moderate disability, but not significant for mild disability compared with those with social activity engagement and without any chronic disease.

Table 3
The combined association of social isolation and multiple chronic diseases with functional disability in elderly stroke patients

Social isolation	Multiple chronic diseases	Model 1			Model 2			Model 3		
		OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Severe vs. no disability										
No	0	Ref			Ref			Ref		
	1	3.16	(2.11, 4.73)	< 0.001	3.03	(2.01, 4.58)	< 0.001	3.11	(2.06, 4.71)	< 0.001
	2	3.39	(2.21, 5.22)	< 0.001	2.88	(1.85, 4.48)	< 0.001	2.92	(1.87, 4.56)	< 0.001
	3 and more	7.37	(3.9, 13.9)	< 0.001	6.06	(3.17, 11.58)	< 0.001	6.46	(3.37, 12.39)	< 0.001
Yes	0	17.90	(8.54, 37.48)	< 0.001	13.93	(10.91, 17.79)	< 0.001	13.76	(6.48, 29.2)	< 0.001
	1	20.89	(12.59, 34.66)	< 0.001	16.71	(9.96, 28.03)	< 0.001	17.03	(10.13, 28.66)	< 0.001
	2	35.62	(19.18, 66.16)	< 0.001	26.19	(13.95, 49.17)	< 0.001	26.79	(14.23, 50.44)	< 0.001
	3 and more	51.08	(19.97, 130.67)	< 0.001	36.65	(14.18, 94.72)	< 0.001	38.24	(14.76, 99.07)	< 0.001
Moderate vs. no disability										
No	0	Ref			Ref			Ref		
	1	2.15	(1.39, 3.33)	0.001	2.13	(1.37, 3.32)	0.001	2.18	(1.39, 3.40)	0.001
	2	2.25	(1.41, 3.59)	0.001	2.05	(1.27, 3.30)	0.003	2.06	(1.28, 3.34)	0.003
	3 and more	3.88	(1.97, 7.67)	< 0.001	3.56	(1.79, 7.09)	< 0.001	3.81	(1.90, 7.64)	< 0.001
Yes	0	4.03	(1.80, 9.01)	0.001	3.37	(1.49, 7.59)	0.003	3.35	(1.48, 7.58)	0.004
	1	4.04	(2.33, 7.00)	< 0.001	3.54	(2.02, 6.21)	< 0.001	3.64	(2.07, 6.41)	< 0.001
	2	7.02	(3.64, 13.55)	< 0.001	6.05	(3.1, 11.81)	< 0.001	6.21	(3.17, 12.16)	< 0.001
	3 and more	11.26	(4.24, 29.9)	< 0.001	9.27	(3.46, 24.88)	< 0.001	9.74	(3.62, 26.22)	< 0.001
Mild vs. no disability										
No	0	Ref			Ref			Ref		

Social isolation	Multiple chronic diseases	Model 1			Model 2			Model 3		
		OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
	1	2.04	(1.16, 3.60)	0.014	2.06	(1.16, 3.66)	0.014	2.03	(1.14, 3.63)	0.016
	2	1.99	(1.09, 3.66)	0.026	1.78	(0.96, 3.30)	0.068	1.77	(0.95, 3.29)	0.073
	3 and more	3.19	(1.38, 7.38)	0.007	2.89	(1.23, 6.76)	0.014	2.96	(1.26, 6.96)	0.013
Yes	0	3.03	(1.12, 8.21)	0.029	2.54	(0.93, 6.98)	0.070	2.44	(0.89, 6.73)	0.084
	1	2.10	(1.01, 4.37)	0.048	1.77	(0.84, 3.74)	0.135	1.76	(0.83, 3.73)	0.140
	2	3.72	(1.64, 8.45)	0.002	2.91	(1.26, 6.73)	0.012	2.89	(1.25, 6.69)	0.013
	3 and more	2.98	(0.83, 10.64)	0.093	2.31	(0.64, 8.37)	0.203	2.35	(0.65, 8.54)	0.195

* Model 1 was the crude model;

† Model 2 adjusted for age group, gender, ethnicity, marital status, annual household income, education level, hospital level, drinking and smoking;

‡ Model 3 added to adjusted for fall and stroke occurrence.

Results from the sensitivity analysis indicated that social isolation and MCDs were robustly associated with an increased risk of disability after excluding patients who had a fall experience with heavy hurt. Note that the adjusted OR of social isolation decreased and that of MCDs increased slightly. Besides, in the comparison between mild and no disability, social isolation was no longer significantly associated with mild disability (Table 4). The combined relationship of these two risk factors with functional disability was almost the same (Table 5).

Table 4
The independent association of social isolation and multiple chronic diseases with functional disability in elderly stroke patients without fall with heavy hurt

	Model 1			Model 2			Model 3		
	OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Severe vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	9.00	(6.59, 12.29)	< 0.001	7.55	(5.49, 10.39)	< 0.001	7.62	(5.54, 10.49)	< 0.001
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	2.50	(1.77, 3.53)	< 0.001	2.45	(1.73, 3.48)	< 0.001	2.47	(1.74, 3.51)	< 0.001
2	2.97	(2.05, 4.3)	< 0.001	2.59	(1.77, 3.79)	< 0.001	2.62	(1.79, 3.84)	< 0.001
3 and more	5.74	(3.35, 9.86)	< 0.001	4.94	(2.85, 8.57)	< 0.001	5.07	(2.92, 8.82)	< 0.001
Moderate vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	2.74	(1.96, 3.83)	< 0.001	2.44	(1.73, 3.43)	< 0.001	2.46	(1.74, 3.47)	< 0.001
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	1.94	(1.33, 2.84)	0.001	1.93	(1.32, 2.84)	0.001	1.96	(1.33, 2.89)	0.001
2	2.22	(1.47, 3.34)	< 0.001	2.08	(1.37, 3.15)	0.001	2.10	(1.39, 3.2)	< 0.001
3 and more	4.09	(2.3, 7.28)	< 0.001	3.79	(2.11, 6.8)	< 0.001	3.97	(2.21, 7.16)	< 0.001
Mild vs. no disability									
Social isolation									
No	Ref			Ref			Ref		
Yes	1.46	(0.95, 2.24)	0.085	1.24	(0.8, 1.92)	0.340	1.23	(0.79, 1.92)	0.350

	Model 1			Model 2			Model 3		
	OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Multiple chronic diseases									
0	Ref			Ref			Ref		
1	1.64	(0.99, 2.7)	0.054	1.64	(0.99, 2.71)	0.056	1.62	(0.97, 2.68)	0.063
2	1.82	(1.07, 3.1)	0.027	1.63	(0.95, 2.8)	0.075	1.63	(0.95, 2.8)	0.078
3 and more	2.52	(1.22, 5.22)	0.013	2.28	(1.09, 4.75)	0.029	2.30	(1.1, 4.83)	0.027

* Model 1 was the crude model;

† Model 2 adjusted for age group, gender, ethnicity, marital status, annual household income, education level, hospital level, drinking and smoking;

‡ Model 3 added to adjusted for fall and stroke occurrence.

Table 5
The combined association of social isolation and multiple chronic diseases with functional disability in elderly stroke patients without fall with heavy hurt

Social isolation	Multiple chronic diseases	Model 1			Model 2			Model 3		
		OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
Severe vs. no disability										
No	0	Ref			Ref			Ref		
	1	3.21	(2.13, 4.82)	< 0.001	3.08	(2.03, 4.67)	< 0.001	3.09	(2.04, 4.69)	< 0.001
	2	3.43	(2.22, 5.29)	< 0.001	2.92	(1.87, 4.55)	< 0.001	2.95	(1.89, 4.61)	< 0.001
	3 and more	7.55	(3.99, 14.29)	< 0.001	6.30	(3.29, 12.06)	< 0.001	6.45	(3.36, 12.38)	< 0.001
Yes	0	17.47	(8.32, 36.71)	< 0.001	13.67	(6.43, 29.03)	< 0.001	13.69	(6.44, 29.10)	< 0.001
	1	20.53	(12.34, 34.17)	< 0.001	16.69	(9.98, 27.94)	< 0.001	17.03	(10.11, 28.66)	< 0.001
	2	35.39	(19.00, 65.89)	< 0.001	26.30	(13.97, 49.48)	< 0.001	26.79	(14.22, 50.45)	< 0.001
	3 and more	50.86	(19.85, 130.34)	< 0.001	37.21	(14.37, 96.37)	< 0.001	38.33	(14.78, 99.41)	< 0.001
Moderate vs. no disability										
No	0	Ref			Ref			Ref		
	1	2.18	(1.41, 3.39)	0.001	2.15	(1.38, 3.37)	0.001	2.19	(1.40, 3.42)	0.001
	2	2.19	(1.36, 3.50)	0.001	1.98	(1.22, 3.20)	0.005	1.99	(1.23, 3.23)	0.005
	3 and more	3.93	(1.99, 7.77)	< 0.001	3.60	(1.80, 7.18)	< 0.001	3.80	(1.89, 7.61)	< 0.001
Yes	0	3.98	(1.77, 8.94)	0.001	3.32	(1.46, 7.51)	0.004	3.32	(1.46, 7.54)	0.004
	1	4.02	(2.31, 7.00)	< 0.001	3.53	(2.01, 6.21)	< 0.001	3.63	(2.06, 6.39)	< 0.001
	2	6.99	(3.61, 13.52)	< 0.001	6.00	(3.07, 11.74)	< 0.001	6.16	(3.14, 12.08)	< 0.001
	3 and more	11.04	(4.15, 29.40)	< 0.001	9.11	(3.38, 24.50)	< 0.001	9.50	(3.52, 25.63)	< 0.001
Mild vs. no disability										
No	0	Ref			Ref			Ref		

Social isolation	Multiple chronic diseases	Model 1			Model 2			Model 3		
		OR	95% CI	P *	OR	95% CI	P †	OR	95% CI	P ‡
	1	2.10	(1.17, 3.76)	0.012	2.11	(1.17, 3.80)	0.013	2.07	(1.14, 3.73)	0.016
	2	2.01	(1.08, 3.73)	0.028	1.79	(0.95, 3.35)	0.071	1.77	(0.94, 3.33)	0.076
	3 and more	3.29	(1.41, 7.66)	0.006	2.97	(1.26, 7.00)	0.013	2.98	(1.26, 7.05)	0.013
Yes	0	3.12	(1.15, 8.51)	0.026	2.62	(0.95, 7.24)	0.064	2.54	(0.92, 7.03)	0.074
	1	1.97	(0.93, 4.18)	0.079	1.68	(0.78, 3.63)	0.183	1.66	(0.77, 3.59)	0.196
	2	3.65	(1.59, 8.40)	0.002	2.86	(1.22, 6.70)	0.015	2.83	(1.20, 6.64)	0.017
	3 and more	3.07	(0.85, 11.02)	0.086	2.40	(0.66, 8.73)	0.186	2.41	(0.66, 8.82)	0.183

* Model 1 was the crude model;

† Model 2 adjusted for age group, gender, ethnicity, marital status, annual household income, education level, hospital level, drinking and smoking;

‡ Model 3 added to adjusted for fall and stroke occurrence.

Discussion

Results from our study indicated that both social isolation and MCDs were independent risk factors for functional disability in elderly stroke patients. Moreover, the hypothesis that a combination of these factors was associated with a greater extent of risk for functional disability than single factors alone, was successfully assessed. The coexistence of social isolation and MCDs ≥ 3 was associated with a 38 times higher risk for severe disability, a nearly 10 times higher risk for moderate disability than the counterparts.

This study, including 4281 elderly stroke patients from 103 clinical settings of 23 cities, was a nationally representative study with a large sample size. To the best of our knowledge, our study is the first to address the combined association of social isolation and MCDs with functional disability in this special population in China. We believe that these findings will provide insights that future prevention and intervention strategies for functional disability may integrate the social content with combined treatments of MCDs to achieve more effectiveness. However, the interpretation of these results also needs to consider the following limitations. First, the cross-sectional design of this study was restricted to drawing associations between the causal relationships among the variables. Second, the sampling method was non-random, and included hospitals that collaborated with our departments. Nonetheless, the inherent bias may have been avoided since our study covered over 100 hospitals in 23 sites to ensure its generalisability. Moreover, our study only selected stroke patients aged over 60 years, therefore our results may not be applicable to other aged populations. Third, the majority of variables were self-reported; we invited experienced investigators to assess functional disability and combine their assessments with the medical records to reduce recall bias as much as possible. Moreover, considering that this study covered a large sample size and many organisations, the investigation

of lifestyles selected only smoking and drinking as confounders [32] ; presented as a simple question to facilitate easy answering by the participants which resulted in the loss of information, including diet, physical activity, and ex-smokers. Fourth, our study included both first-ever and recurrent stroke, and social isolation could not be differentiated into pre-stroke or post-stroke social isolation. Thus, long-term prospective studies are needed to identify the differences between these aspects to provide more precise intervention strategies.

BI is the most popular method to measure functional disability in stroke patients [33]. Although the BI cut-off point for categorising stroke patients with an unfavourable outcome was different from study to study, each study stressed the fact that the prevalence of functional disability was severe in stroke patients [33, 34]. There is a paucity of studies that consider geriatric stroke patients in China. To the best of our knowledge, only Li et al. used the same classification criterion of BI (severe disability ≤ 55) in disabled elderly stroke patients with a small sample size (n = 158) and showed that the prevalence of severe disability was more than half [26]. Our study's results, similar to Li's research, was 71.5% scaled up to 76.2% after excluding patients without disability. Additionally, the prevalence of severe disability in our study was more than double that of a Brazilian study of 260 middle-aged and elderly stroke survivors (31.5%) [35], more than six times that of the Northern Manhattan Stroke Study of 340 elderly stroke patients [36]. Although the difference in the prevalence of severe disability was potentially attributed to ethnicity [33], the prevention of functional disability is important in Chinese elderly stroke patients.

The identification of risk factors for functional disability is key to the formulation of intervention strategies in elderly stroke patients. In our study, MCD status was found to be a risk factor for functional disability. Studies focusing on elderly stroke patients were limited, and we found some similar findings in a population with a single condition (geriatric or stroke) [37]. A recent systematic review of 3339 stroke patients from seven hospital-based cohort studies, indicated that MCDs are longitudinally associated with an 11% increase in the risk of functional disability after stroke, irrespective of the different methods used for assessing MCDs and functional disability [37]. Meanwhile, a large cohort study including a general geriatric population also showed that MCDs significantly increased the risk of functional disability by 117% [38]. In contrast, another cohort study with a small sample size but with a mean age over 85 years found no significant association between them [39]. We speculated that the inconsistency was attributed to age. On the one hand, based on trajectory analysis [4], functional disability tended to be stable beyond the age of 80 years; on the other hand, the combination of MCDs and the age over 80 years had a high probability of leading to death [38]. In fact, MCD status was inevitable to some extent in the ageing process, [14] and nearly half of the participants in our study suffered from two and more chronic diseases, which is consistent with a recent systematic review [14]. Many possible explanations have addressed this issue. Sharing similar risk factors, including genetic, environmental, social, physiological, and psychosocial factors, was the common one [14, 40]. For example, chronic inflammation and oxidative stress played an important role in the initiation and progression of MCDs related to ageing [40, 41]. Besides, the shared risk factors were more likely to be the mechanisms by which MCDs synergistically increased the functional disability [41]. Furthermore, another systematic review proposed that certain chronic disease clusters were internally and highly correlated [28]. As for stroke, we found that hypertension (77%), diabetes (32%), and heart diseases (33%) were more common in stoke patients than other two chronic diseases. A review similarly indicated that hypertension was the most important risk factor for stroke and sustained the highest population-attributable risk (34.6%) among obesity, several classic chronic diseases (diabetes, hyperlipidaemia, coronary artery disease, and arterial fibrillation) and lifestyles (smoking and physical inactivity).[42] Thus, the prevention of post-stroke functional disability requires the control and management of hypertension, diabetes, and heart diseases.

Another strong risk factor for functional disability in our study was social isolation, which has been well documented in many cohort studies. [43–45] Although these studies were conducted in older adults without referring to stroke, they consistently indicated that social activity can reduce or delay the decline of functional disability caused by ageing [43–

45]. Social isolation may have a deleterious effect on neural networks and decreased musculoskeletal function, accelerating the functional disability related to ageing [21]. In addition, many other behavioural and psychosocial pathways underlined the improvement in depression and cognitive decline associations with social activity; they all are important psychological risk factors for functional disability and stroke [22, 44]. Social networks change to smaller and close-knit ones during ageing [19] and after stroke. [46] A clinical study has reported that baseline social isolation robustly predicted the stroke and prognosis outcome. [46] Thus, both primary prevention and secondary therapies for stroke and functional disability should consider the promotion of social engagement among older adults.

Importantly, the novel finding of our study is that the combination of social isolation and MCDs is associated with a much higher risk for functional disability than a single condition. Although the exact mechanisms regarding the relationship of their combination with functional disability have yet to be explained sufficiently, we can understand its plausibility from several dimensions: 1) both ageing and stroke are the common risk factors for them [4, 7, 14, 20], although they represent social and biological levels, respectively; 2) social isolation may interact with MCDs through biological, behavioural, and neurological links. A previous study reported that a series of downstream biological changes, including abnormalities in cortisol secretion and a deterioration in immune and anti-oxidative stress functions, was easy to detect in people with social isolation [47–49]. From a behavioural point of review, social isolation constantly leads to the development of many unhealthy lifestyles, which accordingly increases the risk for MCDs [48]. As for the neurology aspect, a recent review synthesised the evidence and found that social isolation combined with other mental disorders (depression and anxiety) to accelerate the activation of the hypothalamic pituitary adrenocortical axis and subsequently moderates the biological process [49]. Additionally, we observed that the OR of social isolation reduced slightly after excluding patients with heavy hurt fall. Obviously, since many factors can directly influence social activity [50], future studies related to social activity should consider more potential mediators. It should be noted that the OR of social isolation in the comparison between the no disability and severe group was still much higher than that of the other two comparisons. Given that the intervention on social isolation through encouraging the participation of social activities was much more available than MCD management, future interventions aiming to increase functional ability and quality of life of elderly stroke patients should pay more attention to social activity.

Conclusions

The findings of this study indicated that social isolation and MCDs were associated with functional disability in elderly Chinese stroke patients. In addition, the combination of these two risk factors is related to a much higher risk for functional disability than a single condition. Future secondary prevention and rehabilitation for functional disability in elderly stroke patients should underscore both social activity and the combined treatments of MCDs.

Abbreviations

MCDs: Multiple Chronic Diseases; BI: Barthel Index; ADL: Activities of Daily Living; OR: Odds Ratio; CI: Confidence Interval.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committees of First Affiliated Hospital of Shenzhen University (Project identification code: 2017070605). All inpatients or their proxies were invited to participate in this study after obtaining the informed consent.

Consent for publication

All inpatients or their proxies consent to publish this study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. And all the authors confirmed that all methods were carried out in accordance with relevant guidelines and regulations.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

X.L. and Y.W. contributed to the conception and design of the study. X.L. and H.Y. accomplished the surveys and edited the manuscript. H.Y., L.W. and Y.G. contributed to the statistical analyses and drafted the tables and Figures. M.Z. and J.Z. contributed to acquisition, analysis and interpretation of data. Q.H., F.X., J.Z. and X.L. reviewed and revised the manuscript. All authors reviewed and approved the final manuscript.

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