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ARTICLE

Factors affecting long-term mortality rate after diagnosis of syringomyelia in disabled spinal cord injury patients: a population-based study

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Abstract

Study design A retrospective, population-based study.

Objectives To identify factors affecting long-term mortality and medical resources use in disabled spinal cord injury (SCI) patients after syringomyelia diagnosis.

Setting A National Health Insurance Research Database containing 10,374 patients with SCI.

Methods Data recorded between 1997 and 2012 for 376 disabled SCI patients with syringomyelia and 376 characteristics-matched disabled SCI patients without syringomyelia were collected. The index date was the date of syringomyelia diagnosis. Cox proportional hazards regression model was used to investigate the factors affecting 10-year mortality in these patients. Medical resources use was compared for 1 year before and after index date.

Results The survival rate at 10-year follow-up after syringomyelia diagnosis was estimated at 68.6%. The 10-year survival rate was comparable between the two groups. Age ≥ 60 (adjusted hazard ratios (aHR) 4.21, 95% confidence interval (CI) 2.97 to 5.96) and < 30 years (aHR 0.25, 95% CI 0.10 to 0.62), spinal cord or spinal canal operations within 1 year after the index date (aHR 1.84, 95% CI 1.19 to 2.84), history of pneumonia (aHR 1.55, 95% CI 1.07 to 2.26), and history of coronary heart disease (CHD) (aHR 1.85, 95% CI 1.18 to 2.89) were significantly associated with long-term mortality. Outpatient prescription costs were higher during 1 year after the diagnosis than those of 1 year before the diagnosis.

Conclusion Age, spinal operations, history of pneumonia, and history of CHD are associated with 10-year mortality in disabled SCI patients with syringomyelia.

Introduction

Spinal cord injury (SCI) is a traumatic incident with lesion at spinal cord leading to motor deficits, sensory impairments, and bowel and bladder dysfunction [1]. The national incidence of SCI ranges from 8 to 49.1 per million throughout the world [2]. Post-traumatic syringomyelia is a disorder involving syrinx (cyst or cavity) formation within the spinal cord in patients with SCI. Most post-traumatic syringomyelia develops within 5 years after SCI, usually within 6 months to 25 years [3]. Although in radiological studies 28% of patients with SCI had a syrinx formation [4], only 3.43% of patients had symptomatic syringomyelia [5]. The most common symptom of post-traumatic syringomyelia is deterioration of motor and sensory function, followed in order of occurrence by pain, deterioration of motor function, increased spasticity, and dysesthesia/paresthesia [6].

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The 10-year cumulative death rate was estimated to be 31.3% in patients with traumatic SCI [7]. Most cases of post-traumatic syringomyelia occur in patients with severity (as classified by the American Spinal Injury Association Impairment Scale) A (81.3%), B (7.5%), and C (2.5%) [6]; majority of cases involve the cervical–thoracic spine (42.0%) or thoracic spine (36.2%) [6]. In reviewing past literature, minimal information regarding outcome of post-traumatic syringomyelia in disabled SCI patients could be found. This study aimed to determine the long-term outcome, including survival, of disabled SCI patients with syringomyelia, and what factors most affect long-term survival. Additionally, we investigated whether patients changed their use of medical resources after syringomyelia diagnosis. Using the National Health Insurance Research Database (NHIRD), we conducted a 10-year, nationwide, retrospective study to examine the factors influencing long-term mortality in disabled SCI patients after diagnosis of syringomyelia. An additional aim was to compare their use of medical resources 1 year before and 1 year after syringomyelia diagnosis.

Methods

Source of data

NHIRD contained nationwide health insurance data with de-identified personal information for research purposes. The Registry of Catastrophic Illness Patient Database (RCIPD)—a part of NHIRD—included all patients with catastrophic illness. We applied the legal use of RCIPD to the National Health Research Institutes in 2015 and were provided approval for the use of RCIPD from 2015 to 2020 (by extension). Catastrophic illness in the National Health Insurance (NHI) system was designed for caring more for patients with 30 severe diseases. A patient with catastrophic illness was exempt from copayment when utilizing inpatient or outpatient medical resources that were related to the diagnosis of catastrophic illness and was provided with additional social welfare resources. Patients with a physical disability were eligible to apply for status of catastrophic illness. A patient with SCI was considered to meet the criteria for a physical disability to apply for the status of catastrophic illness when a grade of ≤ 3 was observed in at least two of the four limbs on manual muscle testing for all key muscles. This application form for catastrophic illness status was completed by a physician and sent from the hospital to the Central Health Insurance Agency of the Ministry of Health and Welfare Certification of Catastrophic Illness for approval. After approval, the patient's catastrophic illness was registered in the NHI system.

Patient selection

In this study, only traumatic SCI patients, not non-traumatic SCI patients, were included. The data from 1997 to 2012 of disabled post-traumatic SCI patients were collected from the RCIPD, including their longitudinal inpatient and outpatient data (1997–2013), as per the International Classification of Diseases 9th Revision Clinical Modifications (ICD-9-CM) diagnostic code 806 (also including 806X and 806XX) or 952 (also including 952X and 952XX). Patients with syringomyelia were identified by the ICD-9-CM code 3360 from longitudinal inpatient and outpatient data of the disabled post-traumatic SCI patients. The ICD-9 code of NHIRD is valid and accurate in Taiwan because they are required in the claims data. Fraudulent coding discovered by the audit of Bureau of NHI results in the imposition of an expensive fine or even termination of the NHI contract. Previous studies have shown high validity and accuracy of the ICD-9 diagnosis included in the NHIRD [8] and RCIPD [9]. The index date (syringomyelia diagnosis) was defined as the date when ICD-9-CM code 3360 first appeared in a patient's longitudinal inpatient or outpatient claims, whichever came first. To eliminate syringomyelia that was not related to SCI, patients whose index date of syringomyelia diagnosis was earlier than the date of registration for SCI catastrophic illness were excluded. Based on similar characteristics, disabled SCI patients without a diagnosis of syringomyelia between 1997 and 2012 were randomly selected using propensity score matching with 1:1 ratio of case/control. Figure 1 shows the flow diagram of patient selection for this study.

This research involved secondary data analysis, and the Institutional Review Board for Human Studies of the Chang Gung Medical Foundation had carefully examined and approved the project (approval no. 201900205B1).

Collections of factors

Patient characteristics, including age (< 30, 30–59, and ≥ 60 years) at the index date, sex (men and women), urbanization residency level (urban, suburban, and rural), insured amount per month (< USD $695 and ≥ USD $695), operations on the spinal cord or spinal canal structures performed during first year after syringomyelia diagnosis, history of urinary tract infection (UTI), history of pressure ulcer, history of pneumonia, and history of coronary heart disease (CHD) in the disabled SCI patients with syringomyelia were recorded. The above-mentioned characteristics were used for propensity score matching a control group that included disabled SCI patients without syringomyelia. Age-based matching was done by pairing patients with and without syringomyelia of the same age at the index date. Patient

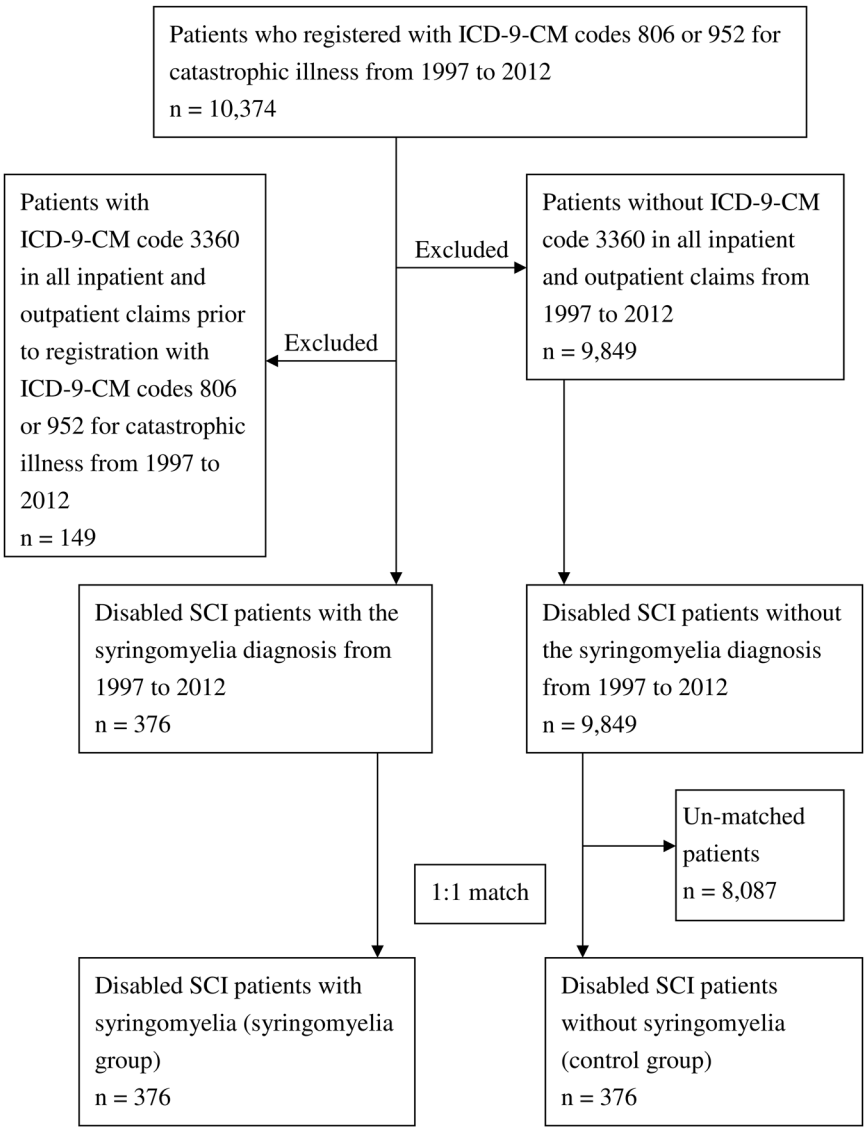

Fig. 1 Flow diagram of patient selection for the study

characteristics were also used to examine their associations with long-term mortality of these disabled SCI patients.

The seven levels of urbanization in national administrative divisions [10] were used to determine a patient's level of urbanization residency. "Urban" contained urbanization levels 1 and 2, "suburban" contained urbanization levels 3 and 4, and "rural" contained urbanization levels 5, 6 and 7. Operations on the spinal cord or spinal canal performed during the first year after the diagnosis of syringomyelia were defined as operations performed on patients with ICD-9-CM procedure code beginning with the number 03 as recorded in inpatient claims during the first year after the index date. Outpatient medication costs during the first year after syringomyelia diagnosis was defined as the sum of the cost for medications in the outpatient claims during the first year after the index date.

History of UTI (ICD-9-CM: 5990), pressure ulcer (ICD-9-CM: 707, 707X, and 707XX), pneumonia (ICD-9-CM: 480–486, 480X –486X , and 480XX–486XX), and CHD (ICD-9-CM codes 410–414, 410X–414X, 410XX–414XX, and 4292) was defined as patients with corresponding ICD-9-CM diagnosis codes in inpatient and outpatient claims before the index date.

Information about the number of outpatient visits/4 weeks, outpatient medication costs, number of hospitalizations, and number of all surgeries during the 1 year before and 1 year after syringomyelia diagnosis were recorded, and used for the comparison of differences in medical resources' use 1 year before and after syringomyelia diagnosis.

Definition of endpoint and mortality

All study patients were followed up from the index date to the endpoint. The endpoint was defined as the date of all-cause mortality or the date of last follow-up (31 December, 2013). All-cause mortality was defined as a condition

when a patient matched any one of the following criteria in their longitudinal database: discharge status recorded to be death, discharge status recorded to be a critical condition without any subsequent medical record to the end of the study follow-up, and withdrawal from the NHI programs without any subsequent medical record to the end of study follow-up. In Taiwan, if a patient with catastrophic illness withdrew from the NHI program, it meant he/she was dead.

Statistical analysis

Statistical analyses were performed using SAS® software, version Studio 3.71 (SAS Institute, Cary, NC, USA). Chi-square test and independent *t*-test were used to check the differences in the categorical and continuous variables of the groups. Paired *t* was used to compare the difference of medical resource use in patients with syringomyelia during 1 year before and 1 year after diagnosis. A life table method was used to calculate the 10-year survival rate of patients with post-traumatic syringomyelia and patients of control group. Kaplan–Meier survival curves were plotted for the comparison of 10-year survival rates of the two groups, and log-rank test was used to test their difference. Cox proportional hazards regression model [11] was adjusted for variables to assess their effects on the mortality of patients. A $p < 0.05$ was considered statistically significant.

Results

The data of 376 disabled SCI patients with syringomyelia and 376 disabled SCI patients without syringomyelia were collected for the final analysis. Table 1 shows the characteristics of disabled SCI patients with syringomyelia and the matched controls. The average age of syringomyelia diagnosis of the 376 patients was 47.9 (standard deviation (SD) 16.7) years. Table 2 represents medical resource use before and after syringomyelia diagnosis. The number of outpatient visits (mean 3.3 (SD 2.6) vs. mean 3.0 (SD 2.6); $p = 0.004$) and outpatient medication costs (mean 624.3 (SD 820.7) vs. mean 558.4 (SD 631.0) USD; $p = 0.032$) were higher during the first year after diagnosis than during the year before diagnosis.

Table 3 shows the survival rate and cumulative risk of death of the 376 patients with and without syringomyelia during the follow-up period from 1997 to 2013. The cumulative risk of death at 10-year follow-up was 31.37% in the syringomyelia group and 28.11% in the control group. The Kaplan–Meier survival curves (Fig. 2) showed no significant differences between the patients with and without syringomyelia ($p = 0.988$).

Table 1 Characteristics of patients with or without syringomyelia following spinal cord injury

Characteristics	Syringomyelia group ($n = 376$) Number (%)	Control group ($n = 376$) Number (%)	*p*
Age			0.983
<30 years	63 (16.8%)	62 (16.5%)	
30–59 years	231 (61.4%)	230 (61.2%)	
≥60 years	82 (21.8%)	84 (22.3%)	
Mean (SD)	47.9 (16.7)	48.0 (15.9)	0.918
Sex			0.316
Men	274 (72.9%)	286 (76.1%)	
Women	102 (27.1%)	90 (23.9%)	
Urbanization residency level			0.931
Urban	207 (55.1%)	207 (55.1%)	
Suburban	126 (33.5%)	129 (34.3%)	
Rural	43 (11.4%)	40 (10.6%)	
Insured amount per month			0.680
<USD $695	319 (84.8%)	323 (85.9%)	
≥USD $695	57 (15.2%)	53 (14.1%)	
Operations on spinal cord or spinal canal during first year after index date			>0.999
No	322 (85.6%)	322 (85.6%)	
Yes	54 (14.4%)	54 (14.4%)	
History of urinary tract infection			>0.999
No	121 (32.2%)	121 (32.2%)	
Yes	255 (67.8%)	255 (67.8%)	
History of pressure ulcer			0.585
No	251 (66.8%)	258 (68.6%)	
Yes	125 (33.2%)	118 (31.4%)	
History of pneumonia			0.647
No	299 (79.5%)	304 (80.9%)	
Yes	77 (20.5%)	72 (19.1%)	
History of coronary heart disease			0.705
No	343 (91.2%)	340 (90.4%)	
Yes	33 (8.8%)	36 (9.6%)	

SD standard deviation, *USD* United States dollar

Table 4 represents the hazard ratio (HR) of mortality in relation to the variables in disabled SCI patients. The proportional hazards assumption in the Cox model was tested for these variables, and none of the time-dependent variables were found to be significant. Patients aged ≥ 60 years had a higher mortality rate than those aged 30–59 years

Table 2 Use of medical resources by the disabled SCI patients with syringomyelia

	One-year pre-diagnosis[a], Mean (SD)	One-year post-diagnosis[a], Mean (SD)	*p*
Number of outpatient visits, per 4 weeks	3.0 (2.6)	3.3 (2.6)	0.004
Outpatient medication prescriptions costs, in $USD	558.4 (631.0)	624.3 (820.7)	0.032
Number of hospitalizations	2.1 (2.8)	2.2 (3.0)	0.236
Number of all surgeries	1.1 (2.1)	1.0 (2.4)	0.690

SCI spinal cord injury, *SD* standard deviation, *USD* United States Dollar

[a]Comparison of 358 patients with spinal cord injury with ICD-9-CM code 3360 between 1998 and 2012

Table 3 Survival rate and cumulative risk of death in the disabled SCI patients with and without syringomyelia during 10 years of follow-up

Years after index date	Cumulative number censored	Number at risk	Deaths	Cumulated-eaths	Survival rate (%)	Risk of death (%)	Cumulative risk of death (%)
Control							
0–1	16	368	10	10	97.28	2.72	2.72
1–2	29	343.5	13	23	93.60	3.78	6.40
2–3	49	314	15	38	89.13	4.78	10.87
3–4	65	281	15	53	84.37	5.34	15.63
4–5	112	234.5	9	62	81.13	3.84	18.87
5–6	145	185.5	0	62	81.13	0.00	18.87
6–7	174	154.5	4	66	79.03	2.59	20.97
7–8	201	122.5	7	73	74.52	5.71	25.48
8–9	219	93	2	75	72.91	2.15	27.09
9–10	241	71	1	76	71.89	1.41	28.11
Syringomyelia							
0–1	16	368	15	15	95.92	4.08	4.08
1–2	34	336	8	23	93.64	2.38	6.36
2–3	60	306	8	31	91.19	2.61	8.81
3–4	82	274	5	36	89.53	1.82	10.47
4–5	115	241.5	11	47	85.45	4.55	14.55
5–6	152	195.5	7	54	82.39	3.58	17.61
6–7	181	155.5	9	63	77.62	5.79	22.38
7–8	209	118	7	70	73.02	5.93	26.98
8–9	227	88	4	74	69.70	4.55	30.30
9–10	246	65.5	1	75	68.63	1.53	31.37

SCI spinal cord injury

(adjusted HR 4.21, 95% CI 2.97 to 5.96, $p < 0.01$). Patients aged < 30 years had a lower mortality rate than those aged 30–59 years (adjusted HR 0.25, 95% CI 0.10 to 0.62, $p < 0.01$). Patients who received underwent operations on the spinal cord or spinal canal during first year after diagnosis had a higher mortality rate than those who did not undergo such operations (adjusted HR 1.84, 95% CI 1.19 to 2.84, $p < 0.01$). Patients with history of pneumonia had a higher mortality rate than those without history of pneumonia (adjusted HR 1.55, 95% CI 1.07 to 2.26, $p < 0.05$). Patients with history of CHD had a higher mortality rate than those without history of CHD (adjusted HR 1.85, 95% CI 1.18 to 2.89, $p < 0.01$).

Discussion

This is the first article discussing the long-term mortality and changes in the use of medical resources in patients with post-traumatic syringomyelia. Although the 10-year survival rate of the disabled SCI patients with syringomyelia and without syringomyelia were not different, the major factors that influenced the long-term mortality in these patients were age, operations of the spinal cord or spinal canal performed during the first year after syringomyelia diagnosis, history of pneumonia, and history of CHD. Age has been reported to be independently associated with 12-year mortality in patients with SCI [12]. In addition, it has also

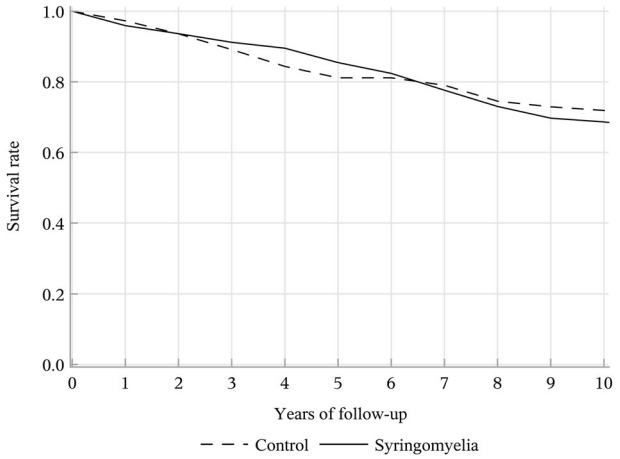

Fig. 2 Comparison of the Kaplan–Meier survival curves of the two groups. The *p*-value for log-rank test, 0.988

been reported that patients with traumatic SCI, aged < 60 years at the time of onset of the injury have higher overall survival among those with traumatic SCI [13]. It may be for the reason that older patients with SCI tend to have higher rates of complications, such as respiratory insufficiency, gastrointestinal bleeding, and renal stones [14], resulting in higher chances of mortality.

Surgeons opt for surgery in patients with syringomyelia in the following situations: worsening in their neurological condition with simultaneous pronounced cord compression, a positive correlation observed between the syrinx length and their neurological deterioration, and high risk of deterioration due to spinal structure [15]. Although performing surgery of the spinal cord or spinal canal may reduce symptoms in patients with post-traumatic syringomyelia, it was estimated that only 52% of patients showed symptom reduction, and 48% of the patients required two or more operations [16]. Our present study showed that in disabled SCI patients, with or without syringomyelia, who underwent operations of the spinal cord or spinal canal during the first year after index date, there could be an increase in the 10-year mortality rate. We believe that the possible reasons for this could be a high risk of complications, such as infection or cardiovascular compromise, with repeated surgical operations. However, we could not perform the analysis for the causes of death in these disabled SCI patients owing to the limitation of our database. These patients who underwent operations of the spinal cord or spinal canal during the first year after the index date and died earlier may not because of the surgery but owing to previous frailty. We believe that current operations may not be the ultimate method to resolve symptoms of syringomyelia. One article reported clinical improvement after injecting autologous bone marrow-derived mesenchymal stromal cells in the syrinx in patients with post-traumatic syringomyelia [17]. This could possibly be an alternative method for treating syringomyelia in the future.

Our present study reveals that disabled SCI patients with a history of pneumonia have a 1.55 times higher risk of long-term mortality than those without history of pneumonia. An article reported in the study by Leite et al. [18] followed 434 patients with traumatic SCI for a mean 4.8 years and they found that pneumonia was the most frequent cause (35.7%) of death. Kopp et al. [19] in their study showed that pneumonia acquired during acute medical care or inpatient rehabilitation was associated with lower gain in functional outcome for up to 5 years and increased 10-year mortality rate after SCI [19]. We considered that patients with history of pneumonia could have worse functional status, including swallowing and physical function, providing more opportunities for undesired events, such as choking and fall, leading to new episodes of pneumonia or to fracture, causing subsequent mortality. Patients with post-traumatic syringomyelia with history of pneumonia may need more surveillance and a prevention program after acquiring pneumonia.

Mean age for syringomyelia diagnosis in the 376 patients was 47.9 years in our present study; however, 8.8% of patients had a history of CHD. One previous article reported that patients with SCI had earlier occurrence, higher prevalence, and greater degree of CHD than did the matched general population [20]. Yekutiel et al. [21] in their study compared participants with and without SCI, and those with SCI had higher prevalence of hypertension, which was associated with increased risk of CHD. When CHD occurs, it might not show apparent prodromal signs and could be fatal. Patients with post-traumatic syringomyelia who had hypertension and metabolic abnormalities, including diabetes mellitus and high cholesterol, should be recognized earlier and require special consideration regarding therapeutic intervention.

Our study demonstrates that number of outpatient medication costs increased 1 year after syringomyelia diagnosis compared to 1 year before syringomyelia diagnosis. More than one half of patients with post-traumatic syringomyelia had sensory-associated symptoms [6]. If an operation was not an option or did not relieve patient symptoms, relieving his/her sensory symptoms could mainly depend on medications. Cohodarevic et al. [22] in their study illustrated that for those patients with post-traumatic syringomyelia choosing nonsurgical treatments, 74% of patients were on combinations of different medications, which included tricyclics, benzodiazepines, antiepileptics, baclofen, and narcotic analgesics. However, the effect of medications seemed to be modest, with only a reported 20–30% reduction of pain [22]. It seems that patients with post-traumatic syringomyelia need more pharmacological treatment after diagnosis to relieve their sensory-associated symptoms;

Table 4 Hazard ratio of mortality in relation to the variables in disabled SCI patients

Variables	Death rate (per 1000 person-years)	Unadjusted		Adjusted[a]	
		Hazard ratio	95% CI	Hazard ratio	95% CI
Group					
Control	33.2	1.00		1.00	
Syringomyelia	33	1.00	0.73–1.38	1.04	0.75–1.44
Age at index date					
<30 years	5.6	0.23[c]	0.09–0.58	0.25[c]	0.10–0.62
30–59 years	23.8	1.00		1.00	
≥60 years	92.8	4.13[c]	2.98–5.72	4.21[c]	2.97–5.96
Sex					
Men	33.8	1.00		1.00	
Women	31.1	0.93	0.64–1.35	0.68	0.46–1.01
Urbanization residency level					
Urban	34.8	1.00		1.00	
Suburban	25.2	0.72	0.49–1.04	0.81	0.56–1.19
Rural	51.9	1.51	0.96–2.38	1.26	0.79–1.99
Insured amount per month					
<USD $695	35.3	1.00		1.00	
≥USD $695	20.7	0.59	0.34–1.02	0.72	0.41–1.27
Operations on spinal cord or spinal canal during first year after index date					
No	31.9	1.00		1.00	
Yes	40.5	1.26	0.83–1.92	1.84[c]	1.19–2.84
History of urinary tract infection					
No	25.2	1.00		1.00	
Yes	37.7	1.55[b]	1.08–2.22	1.43	0.98–2.08
History of pressure ulcer					
No	33	1.00		1.00	
Yes	33.5	1.03	0.73–1.45	1.15	0.80–1.66
History of pneumonia					
No	27.7	1.00		1.00	
Yes	59.8	2.24[c]	1.58–3.17	1.55[b]	1.07–2.26
History of coronary heart disease					
No	28.8	1.00		1.00	
Yes	87.9	3.17[c]	2.12–4.76	1.85[c]	1.18–2.89

SCI spinal cord injury, *CI* confidence interval, *USD* United States Dollar

[a]Adjusted for group, age, sex, urbanization residency level, insured amount, operations on spinal cord or spinal canal, history of urinary tract infection, history of pressure ulcer, history of pneumonia, and history of coronary heart disease

[b]$p < 0.01$

[c]$p < 0.05$

nevertheless, they may have negligible improvement with medications.

The survival and mortality rates as well as the use of medical resources illustrated in this study only represent those of the disabled post-traumatic SCI patients with syringomyelia who were covered under the government's health insurance scheme. We believe that in the world, there are many disabled SCI patients with syringomyelia who do not have medical insurances, may not receive adequate medical services, and thus struggle with their symptoms, health problems, and survival. The impact of insufficient medical treatment for disabled SCI patients with syringomyelia on their survival rate could be a future research topic.

There are some limitations in this study. Firstly, the diagnoses of traumatic SCI, syringomyelia, and comorbidities are based on a retrospective database, which is less accurate than enrolling these patients in a prospective

manner. Secondly, we did not include mild post-traumatic SCI patients; thus, the survival and mortality rates after syringomyelia reported in this study may not represent the post-traumatic SCI population with syringomyelia. Thirdly, owing to the lack of medical charts in the NHIRD, we cannot collect the SCI severity and injury level from the NHIRD; this may affect the long-term mortality in patients with syringomyelia. Moreover, the etiologies of traumatic SCI are unclear; this limits further analyses in specific traumatic SCI patient population. Despite these limitations, our present study comprehensively demonstrates the factors associated with the 10-year mortality rate and the changing status of medical resources' use after syringomyelia diagnosis in a nationwide population of disabled post-traumatic SCI patients.

Conclusion

The long-term risk of mortality was similar in disabled SCI patients with and without syringomyelia. The survival rate at 10 years was about 68.6% after the syringomyelia diagnosis in disabled SCI patients. Age ≥ 60 and < 30 years, operations of the spinal cord or spinal canal performed during 1 year after diagnosis, history of pneumonia, and history of CHD were identified as factors associated with the 10-year mortality. These patients with any of these factors related to long-term mortality may require more intensive care, as well as prevention and early detection for associated diseases to improve long-term mortality. Outpatient visits and expenditure for medication significantly increased during the first year after the diagnosis of syringomyelia. The results of this study provide clinicians with more information about the important factors impacting long-term mortality in disabled SCI patients after syringomyelia and their use of medical resources.

Data archiving

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions CMC was responsible for study design, data collection, data interpretation, manuscript writing, and manuscript editing. WCH was responsible for study design, data collection, and data interpretation. YHY was responsible for data collection, data analysis, and data interpretation. SSH was responsible for the study design and data collection. KYL was responsible for the study design and data collection.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of ethics We certify that all applicable institutional and governmental regulations concerning the ethical use of data collection were followed during the course of this research.

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