Injury, Int. J. Care Injured 50 (2019) 738–743

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Adults with polio are at risk of hip fracture from middle age: A nationwide population-based cohort study

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ARTICLE INFO

Keywords:
Femoral fracture
Hip
Physical disability
Polio

ABSTRACT

Background: Having motor impairment since childhood and being at risk of osteoporosis and falls, adults with polio would be more likely to suffer a hip fracture (HF) and may experience different epidemiological characteristics from the general population.
Objective: To estimate the risk and incidence of HF in adults with polio.
Design: Using a national database, we conducted a population-based cohort study. We identified patients with polio using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 138. For each patient with polio, we randomly selected five age- and sex-matched control subjects. Those subjects aged <40 years were excluded. We analyzed participants aged 4064 years (middle-aged) and subjects aged ≥65 years (elderly) separately and recognized subjects who had an HF (ICD-9-CM code, 820) only when they received hospitalization to care for the illness from January 1, 2003 to December 31, 2008.
Results: We identified 403 adults with polio (mean age ± standard deviation, 47.2 ± 8.6 years). Compared to the controls, patients with polio had a higher incidence of HF (all, 4.1 vs. 1.1/1000 person-years, $p = 0.002$; middle-aged, 2.3 vs. 0.3/1000 person-years, $p < 0.001$; male, 6.2 vs. 0.9/1000 person-years, $p < 0.001$); had a younger mean age (±standard deviation) of fracturing a hip (61.0±14.9 vs. 74.4±9.3 years, $p = 0.015$); had a lower cumulative HF-free probability (±standard error) before the age of 65 years (0.970±0.017 vs. 0.988±0.007, $p<0.001$) and throughout the study duration (0.415 ± 0.296 vs. 0.682 ± 0.158, $p<0.001$); and had a higher risk of HF, yielding an adjusted hazard ratio (95% confidence interval) of 3.58 (1.458.79, $p = 0.006$). Patients with polio aged >48.2 years were likely to experience an HF.
Conclusions: Adults with polio are at risk of HF. A customized HF prevention program is important for people with polio. The program should be started early in middle-age and should include men.

Introduction

Poliomyelitis (polio) is a common cause of early-onset physical disabilities. An epidemic of polio occurred in Taiwan during the 1950s and 1960s [1]. Subjects with sequelae of polio often contracted the illness before the age of 3 years, and it was the spinal type in Taiwan [2]. Most of them have abnormal gait patterns and require aids for walking because of motor impairments, such as muscular atrophy and weakness of the legs. Falling often occurs in persons who require aids for walking and have moderate gait impairment [3]. Patients with polio are hence at a greater risk of falls [4,5]. In addition, adults with polio tend to experience low bone mass by middle age [6,7]. Falls and osteoporosis are both major risk factors for bony fractures [8].

Osteoporotic fractures can result from a fall from a standing height or other low-impact trauma [9]. Compared to other common sites of osteoporotic fracture, people experiencing femoral neck or hip fracture (HF) may die within 1 year [10]. More than half of HF survivors have difficulty walking, and this

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https://doi.org/10.1016/j.injury.2019.02.006
0020-1383/

compromises their quality of life [11]. Being at risk of both osteoporosis and falls, adults with polio would be more likely to suffer an HF thus leading to a double disability. In addition, partly because of having had motor impairment since childhood, adults with polio who fracture a hip may experience different epidemiological characteristics from the general population. We hypothesized that adults with polio are at risk of HF early in their middle age. The starting time of HF prevention interventions is thus an important issue for people with polio. To our knowledge, few studies have measured differences in the incidence and risk of HF between adults with polio and matched controls in population-based cohorts.

The Taiwan National Health Insurance (NHI) Research Database (NHIRD) compiles all information on diagnoses and medical services for each participant in the NHI program which includes >22 million participants (97% of Taiwan's population). The database offers comprehensive, longitudinal medical information and is available for population-based cohort studies [12]. Using the Taiwan NHIRD, we attempted to clarify the contributions of polio to the risk of HF and estimate the incidences of HF in adults with polio. Personal identification data in the NHIRD were encoded for public access. Thus, this study was exempt from full review by the Taipei Medical University-Joint Institutional Review Board (TMU-JIRB No. 201501012).

Materials and methods

Using data of 1,055,705 randomly selected enrollees from the Taiwan NHIRD from January 1, 2003 to December 31, 2008 (Fig. 1), we conducted a nationwide population-based cohort study to estimate the incidence and risk of HF in adults with polio and the controls. This probability-sampling database consisted of all medical claims, including ambulatory care and hospital inpatient care, of those enrollees in the Taiwan NHI program. Every enrollee was selected with equal probability of 0.045 in the year 2005 [13].

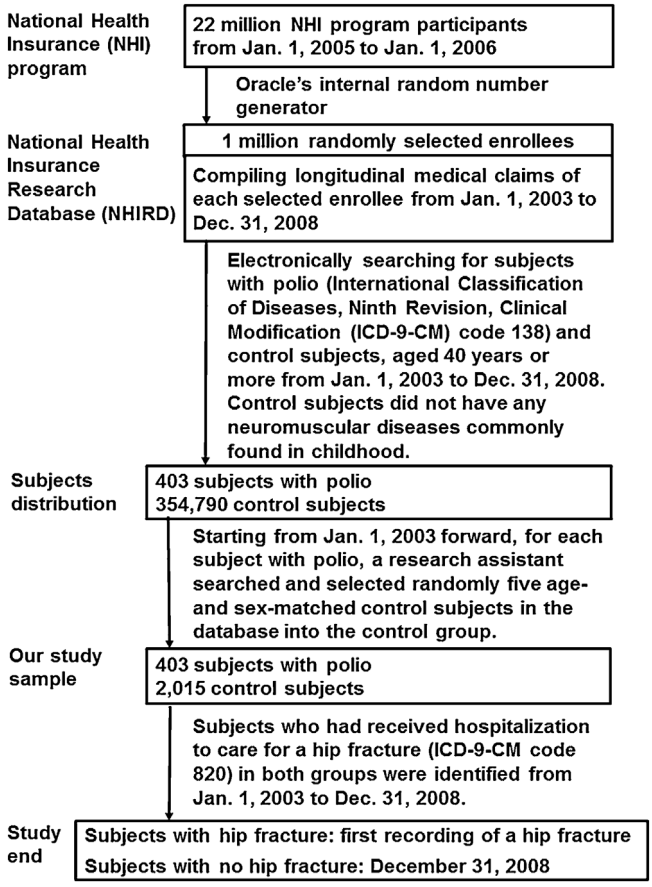

Fig. 1. Summary of the construction of Taiwan National Health Insurance Research Database and the processes of recruitment of adults with polio and the controls in this study.

Based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 138 [1], we identified subjects with polio in the database. Focusing on middle-aged subjects with polio, we needed a certain proportion of middle-aged participants. The study hence analyzed the NHIRD from 2003 to 2008 because an epidemic of polio occurred in Taiwan during the 1950s and 1960s [1]. For each subject with polio (polio group), we randomly selected five age- and sex-matched control subjects (control group). Control subjects did not have polio or any other diseases in childhood that usually lead to disabilities, such as delays in development (ICD-9-CM code 315), intellectual disabilities (317–319), cerebral degeneration (330), or cerebral palsy (343). The birthday of each control subject was <6 months before or after that of the matched polio subject. The age of each participant was calculated on the basis of January 1, 2003. Subjects under 40 years of age were excluded. Because an advanced age of ≥65 years is a risk factor for osteoporosis [14], we separately analyzed those participants aged 40–64 years (middle-aged) and subjects aged ≥65 years (elderly). For those participants who turned 65 years old during the study period, we separately calculated the duration of each participant before and after his/her age of 65 years. To elucidate the incidence difference in HF between sexes, we separately analyzed the incidences for women and men.

Searching for a new HF during the study period, we identified subjects who had an HF (ICD-9-CM code 820) [12] only when they received hospitalization to care for the illness. Subjects with diagnostic claims of an HF in records of ambulatory care only and those having records of ambulatory care 7 days or more before the first day of hospitalization to care for an HF were considered to have had a prior history of the illness and were excluded from the study. The start date for each participant in this study was January 1, 2003. The end of the study coincided with the date of the recording of an HF in the database. For subjects with no HF during the study period, the end of the study for both groups was December 31, 2008. Considering that HF may also result from conditions related to falls and osteoporosis [14–16], we calculated the frequencies of subjects with risk factors for falls, including arthropathies (ICD-9-CM codes 711716), alcoholism and dizziness (291, 303, or 386), and visual disorders (361366, 368371 or 377378) and those for osteoporosis, including malignancy (140205 or v10), endocrine disorders and malnutrition (240242, 255, 262269, or 579), chronic obstructive pulmonary disease (491492 or 496), chronic hepatic disease (571572), chronic renal disease (582 or 585586), scanty or absence of menstruation (626.1 or 626.0), postmenopausal disorders (627), and non-hip fractures. Non-hip fractures included fractures of the skull/face (801804), the axial bone (805809), the upper extremity (810816), and the lower extremity other than the hip (821827). We also calculated the frequencies of diabetes mellitus (250) and hypertension (401405) because both illnesses are related to a higher risk of HF.

Data analysis

We compared differences between the polio and control groups and between subjects with and those without an HF of each group using a Pearson Chi-squared test or Fisher's exact test for clinical characteristics, while using the Mann-Whitney *U* test for age. A finite population correction value of 0.9995 was used to adjust the variance estimation of our probability-sampling data. We used

univariate and multivariate Cox proportional hazard regression analyses with an entry method to assess risk factors for fracturing a hip. Variables entered into the multivariate analysis of model 1 included subject group and age, and those variables found to be significantly associated with HF in the univariate analyses. Variables entered into the model 2 analysis included subject group and age, and a more-detailed division of those significant variables in model 1. We used a receiver operating characteristic (ROC) curve to predict subjects of each group experiencing an HF for each age group. We also used a Kaplan-Meier curve to estimate the cumulative HF-free probability (CHFFP) of each group for years of the study and compared these two curves with a log-rank test. Data were analyzed using SAS software (vers. 9.1, SAS Institute, Cary, NC, USA). An alpha value of 0.05 was considered significant.

Results

We identified 403 subjects with polio between January 1, 2003 and December 31, 2008 in the Taiwan NHIRD. Their mean age (±standard deviation) was 47.2 (±8.6) years. The age difference between sexes was not significant (female, 46.9 ± 8.4 years; male, 47.5 ± 8.8 years; t=-0.64, p = 0.53). Distributions of age and sex were similar between the polio and control groups (Table 1). The mean study durations of the two groups before and after the age of 65 years were also similar. Ten subjects with polio (incidence, 4.1/1000 person-years) and 13 control subjects (1.1/1000 person-years, p = 0.002) experienced an HF during the study period. Compared to the controls, polio subjects had a higher incidence of HF if they were middle-aged or male (both $p < 0.001$, Fig. 2). Table 2 shows that polio subjects aged >48.2 years were likely to experience an HF. Control subjects had a higher cutoff value of age for predicting an HF. Compared to the mean age of fracturing a hip in the control group, that of the polio group was 13 years younger (t=-2.64, p = 0.015, Table 1). Subjects with an HF were significantly older than those without an HF in both groups. Except for age, frequencies of risk factors for falls and osteoporosis in polio subjects with and without HF were similar in this study.

Compared to the controls, adults with polio had a lower CHFFP before the age of 65 years and also throughout the study duration (both $p < 0.001$, Fig. 3). After adjusting for those significant variables identified in the univariate analyses, the polio group, age, and a prior history of non-hip fractures (model 1, Table 3) or an axial bone fracture (model 2) were significant risk factors for HF. The risk of an HF during the 6-year study was higher for subjects with polio compared to the controls, yielding an adjusted hazard ratio (95% confidence interval) of 3.58 (1.458.79, p = 0.006) for model 2.

Discussion

Using a population-based cohort study, we estimated the incidences and risks of HF in adults with polio and matched controls. This information is important for assessing the resources needed to implement an HF prevention program for subjects with

Table 1
Comparisons of clinical characteristics between the polio and control groups [a] and between subjects with and those without a hip fracture (HF) in each group.[b]

Variable, units	Polio			Control		
	All (n = 403)	HF, yes (n = 10)	HF, no (n = 393)	All (n = 2015)	HF, yes (n = 13)	HF, no (n = 2002)
Age, years						
On the start date [c]	47.2 ± 8.6	57.9 ± 15.2†	46.9 ± 8.2	47.2 ± 8.6	71.2 ± 8.7††	47.1 ± 8.4
On the fracture date	–	61.0 ± 14.9*	–	–	74.4 ± 9.3	–
Study duration, years/person						
Middle-aged period	5.7 ± 0.7	–	–	5.6 ± 0.8	–	–
Elderly period	5.2 ± 1.4	–	–	5.3 ± 1.2	–	–
Women	188 (46.7)	2 (20)	186 (47)	940 (46.7)	7 (54)	933 (47)
Non-hip fracture	96 (23.8) ***	5 (50)	91 (23)	221 (11)	5 (38) †	216 (11)
Fracture, skull/face	7 (1.7)	0 (0)	7 (2)	11 (0.5)	0 (0)	11 (0.5)
Fracture, axial bone	24 (6)	2 (20)	22 (6)	86 (4.3)	3 (23) †	83 (4)
Fracture, UE	12 (3)	0 (0)	12 (3)	84 (4.2)	1 (8)	83 (4)
Fracture, LE, non-hip	66 (16.4) ***	4 (40)	62 (16)	65 (3.2)	2 (15)	63 (3)
Risk factors for falls						
Positive item number	1.1 ± 0.9***	1.1 ± 1.0	1.1 ± 0.9	0.8 ± 0.8	1.6 ± 1.0††	0.8 ± 0.8
Arthropathy	219 (54.3) ***	5 (50)	214 (54)	667 (33.1)	11 (85) ††	656 (33)
Alcoholism/dizziness	72 (17.9)	2 (20)	70 (18)	288 (14.3)	4 (31)	284 (14)
Visual disorders	136 (33.7)	4 (40)	132 (34)	579 (28.7)	6 (46)	573 (29)
Risk factors for osteoporosis						
Positive item number	1.1 ± 1.1***	1.2 ± 1.2	1.1 ± 1.1	0.8 ± 0.9	1.9 ± 1.3††	0.8 ± 0.9
Malignancy	28 (6.9)	0 (0)	28 (7)	138 (6.8)	4 (31) †	134 (7)
Endo	37 (9.2) *	0 (0)	37 (9)	120 (6)	2 (15)	118 (6)
COPD	78 (19.4) ***	2 (20)	76 (19)	254 (12.6)	8 (62) ††	246 (12)
CHD	109 (27) *	3 (30)	106 (27)	424 (21)	3 (23)	421 (21)
Chronic renal disease	27 (6.7) **	2 (20)	25 (6)	64 (3.2)	2 (15)	62 (3)
Meno	73 (18.1)	0 (0)	73 (19)	318 (15.8)	1 (8)	317 (16)
Diabetes mellitus	82 (20.3) *	4 (40)	78 (20)	311 (15.4)	8 (62) ††	303 (15)
Hypertension	183 (45.4) ***	5 (50)	178 (45)	599 (29.7)	12 (92)††	587 (29)

NOTE. Values are the mean ± standard deviation or number (%).
Abbreviations, CHD, chronic hepatic disease; COPD, chronic obstructive pulmonary disease; Endo, endocrine disorder/malnutrition; LE, lower extremity; Meno, menopausal/postmenopausal disorders; UE, upper extremity.

[a] Comparisons between polio and the control groups in all subjects and subjects who fractured a hip (Mann-Whitney U test for continuous variables; Pearson Chi-squared test or Fisher's exact test for categorical variables. Bonferroni correction, * $p < 0.03$, ** $p < 0.005$, *** $p < 0.001$).

[b] Comparisons between subjects with vs. subjects without a hip fracture in each group (Mann-Whitney U test for age; Pearson Chi-squared test or Fisher's exact test for categorical variables. † $p < 0.05$, †† $p < 0.001$).

[c] Age calculated on the basis of January 1, 2003.

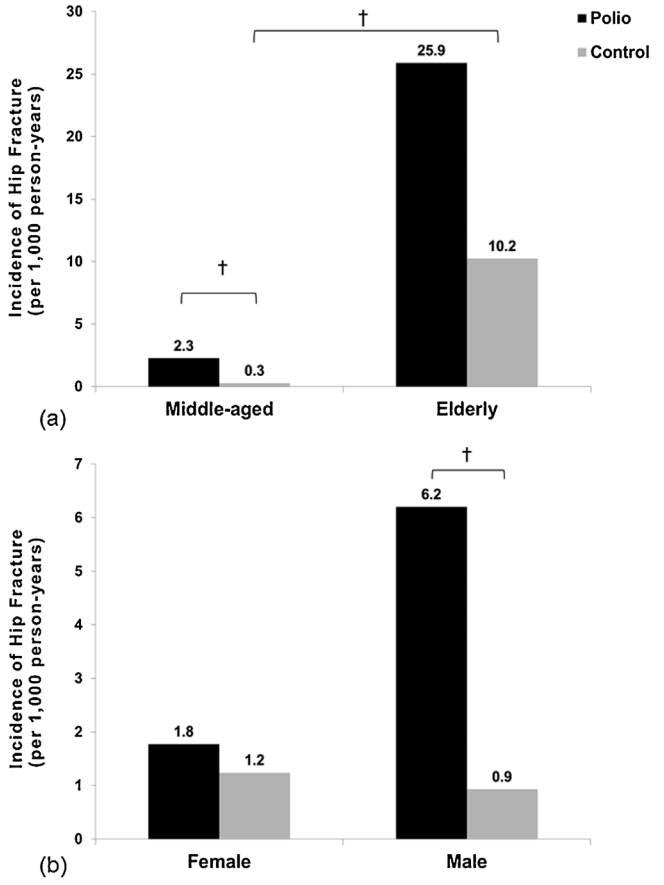

Fig. 2. Comparison of the incidences of hip fracture between the polio and control groups (a) among middle-aged (aged 4064 years) and elderly (aged ≥65 years) adults and (b) among women and men. The value shown at the top of each bar indicates the incidence per 1000 person-years. (a) The polio-to-control incidence rate ratio of hip fracture was 8.3 for middle-aged subjects ($p < 0.001$) and was 2.5 for the elderly ($p = 0.76$). The difference between middle-aged persons and the elderly was significant for the controls ($p < 0.001$), but was insignificant for subjects with polio ($p = 0.12$). (b) The polio-to-control incidence rate ratio of hip fracture was 6.9 for men ($p < 0.001$) and was 1.5 for women ($p = 0.65$). The male-to-female rate ratio was 3.5 for the polio group ($p = 0.11$) and was 0.7 for the control group (Chi-squared=0.27, $p = 0.60$). † $p < 0.001$ (by Pearson Chi-squared test or Fisher's exact test).

polio. The polio group had a higher incidence of HF than the control group when subjects were middle-aged and when they were male. After adjusting for those factors associated with falls and osteoporosis, the polio group, old age, and a prior history of an axial bone fracture were significant risk factors for HF. Adults with polio had a 2.58-fold higher risk of HF than the controls.

In addition to the increased incidence and risk of HF, adults with polio who fractured a hip had different epidemiological characteristics from the general population. First, subjects with polio had a younger mean age when fracturing a hip than the controls (Table 1). The incidence of HF often rises steeply after the age of 65 years in the general population [17]. But, subjects with polio were likely to experience an HF early from the age of 48.2 years (Table 2). Being similar to the general population [14], elderly subjects had a greater incidence of HF than middle-aged subjects in the study. However, middle-aged subjects with polio also experienced an increased incidence of HF. They had a 7.3-fold higher incidence of HF than the middle-aged controls (Fig. 2). Ray et al. reported that HF in middle-aged patients experiences a higher incidence of postoperative complications and mortality than elderly patients [18]. Those middle-aged patients often had concomitant conditions. Further study to compare mortality rates between subjects with polio having and not having an HF is hence important.

Second, the HF incidence for men was 2.5 times higher than for women in the polio group (Fig. 2). Contrarily, the incidence was greater for women in the general population [19]. Men with polio may suffer osteoporosis early during middle age [6,20]. Compared to women, men with polio also experience a greater decrease in leg muscle strength with age [21] and have a higher risk of falls [3,4]. Probably because of these features, men with polio had a higher incidence of HF than the controls (Fig. 2). Additionally, the experience of an HF in men often leads to compromised outcomes. One-third of them die within 1 year [22]. The mortality rate after fracturing a hip is higher in men than in women [23]. A cost–benefit analysis of fall prevention interventions for the elderly demonstrates a positive result [24]. Accordingly, a practical and useful program must be implemented for adults with polio to effectively prevent HFs. The program is especially important for men with polio and should begin early in middle age. A health-promoting program for increasing physical activities can reduce the risk of osteoporosis [25]. The program should include both weight-bearing exercise and resistance training to effectively reduce bone loss [25]. But, those exercise modes must be safe and accessible to persons with physical disability. Two-thirds of adults with polio had experienced a fall from a standing height over a 1-year period. One-third of those who fell had complications of a bony fracture [26]. It is hence essential for people with polio to customize their health-promoting programs to reduce the fall risks based on the degree of motor impairment. It may also be necessary to identify men at risk of osteoporotic fracture using a specific assessment method [27].

Strengths and limitations

This study had three strengths. First, the NHIRD offers comprehensive, longitudinal medical information of the Taiwanese population and consequently is available for conducting population-based cohort studies to estimate the incidence and risk of fracturing a hip in adults with polio [12]. Data of the NHIRD are also reliable because they are audited by the authority of the NHI program. Second, to reduce possible confounding, we matched for age and sex between the polio and control groups and confirmed that distributions of risk factors for falls and osteoporosis were similar between the two groups. And third, to elucidate the contribution of age and sex to the HF incidence in the polio and control groups, we separately analyzed the incidences for middle-aged and elderly subjects and also for women and men. This study also had four major limitations. First, it was difficult to determine

Table 2
Cutoff values of age for predicting hip fracture in the polio and control groups using receiver operating characteristic (ROC) analyses.

Group	Area under the curve (95% confidence interval)	Age cutoff value (years)	Sensitivity	Specificity
Polio	0.72 (0.510.92)*	48.2	0.70	0.78
Control	0.96 (0.940.98)**	61.2	0.92	0.92

* $p < 0.05$.
** $p < 0.001$.

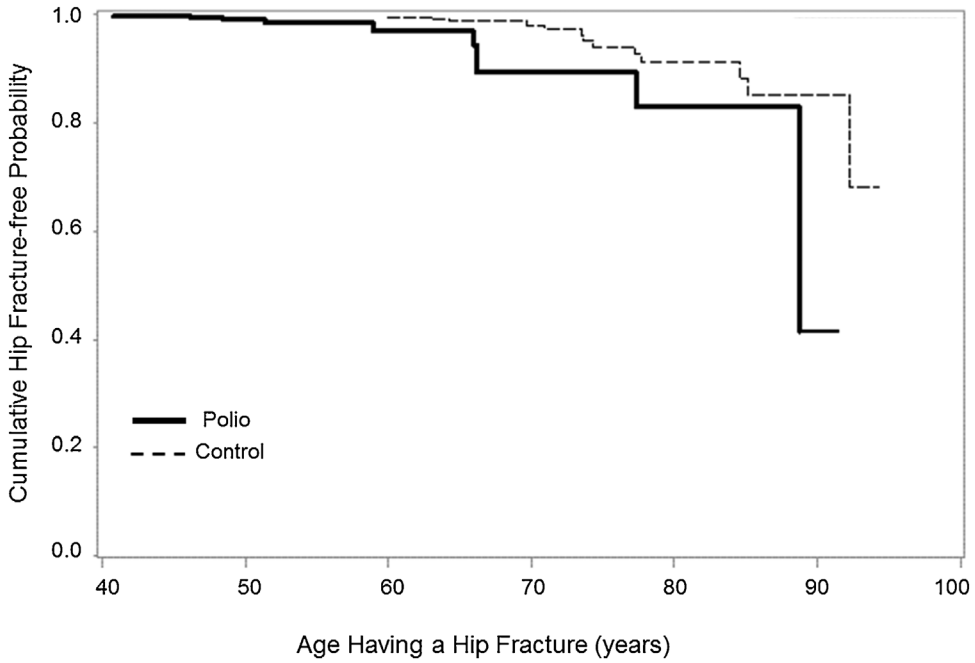

Fig. 3. The cumulative hip fracture-free probability (CHFFP) with age for having a first-ever hip fracture among adults with polio (thick line, $n = 403$) and the controls (dashed line, $n = 2015$). The estimated CHFFP (±standard error) of subjects with polio at the end of the study was 0.415 (±0.296), which was significantly lower than 0.682 (±0.158) of the controls (log rank test, $X^2 = 13.1$, $p < 0.001$). The estimated CHFFPs of the polio (0.970±0.017) and control groups (0.988±0.007) before the age of 65 years also significantly differed ($X^2 = 12.5$, $p < 0.001$).

the mobility status of participants from the NHIRD. Middle-aged adults with polio have a walking rate range of 86%94% [5,26,28,29]. The incidence of HF in ambulatory adults with polio hence could be higher than the study's estimates. Information about travelling history and mortality of our participants and the age of polio onset was also lacking. For those persons who were abroad or who died during the study period, the study duration could have been overestimated, and the incidence of HF would have been underestimated. Second, partly because of the participants' mean age (±standard deviation) of 47.2 (±8.6) years and partly because of the short study period of 6 years, the overall numbers of HF in both polio and control groups were low. The total number of HF often increases when the proportion of aged participants increases [17]. The HF incidence of 1.1/1000 person-years for our controls is similar to 1.6/1000 person-years for Japanese population aged ≥ 40 years [30], but is lower than those incidences for people aged ≥ 50 years in many western countries [31]. Further investigation with a longer data collection period to recruit a larger sample and up-to-date data is needed. Third, we could not determine the cause of the HF. HF could also have resulted from traffic accidents or falling from more than a standing height in subjects without osteoporosis. But, we excluded subjects aged <40 years. Osteoporotic fracture rarely occurs in people younger than that [14]. In addition, the association between HF and a prior history of axial bone fracture in

Table 3
Cox proportional hazards regression analyses of potential risk factors of hip fracture for patients aged >40 years ($n = 2418$).

Variable	Univariate analyses	Multivariate analyses Model 1	Model 2
Subject group, polio	3.78 (1.668.63) *	3.60 (1.548.42) *	3.58 (1.458.79) *
Age, unit = 10 years	3.13 (2.434.02) **	2.75 (2.033.71) **	3.03 (2.343.93) **
Sex, men	1.32 (0.612.84)	–	–
Fracture, non-hip, yes	6.07 (2.8512.93) **	3.13 (1.406.96) *	–
Fracture, skull/face, yes	4.93 (0.6736.33)	–	2.65 (0.3321.10)
Fracture, axial bone, yes	8.58 (3.7519.60) **	–	5.19 (2.2012.22) **
Fracture, upper extremity, yes	0.85 (0.126.29)	–	0.39 (0.053.06)
Fracture, lower extremity, non-hip, yes	6.32 (2.6714.94) **	–	2.56 (1.006.53)
Arthropathy, yes	3.71 (1.628.48) *	1.09 (0.442.71)	–
Alcoholism/dizziness, yes	2.16 (0.944.93)	–	–
Visual disorders, yes	2.08 (0.984.43)	–	–
Malignancy, yes	3.81 (1.549.43) *	2.10 (0.815.40)	–
Endocrine disorder/malnutrition, yes	1.07 (0.254.50)	–	–
Chronic obstructive pulmonary disease, yes	4.09 (1.908.82) **	1.17(0.512.69)	–
Chronic hepatic disease, yes	0.94 (0.382.33)	–	–
Chronic renal disease, yes	4.3 (1.4912.44)	0.91(0.302.80)	–
Diabetes mellitus, yes	4.44 (2.099.45) **	1.52(0.663.51)	–
Hypertension, yes	5.49 (2.3212.98) **	1.25(0.473.37)	–
Menopausal/postmenopausal disorder, yes	0.18 (0.021.32)	–	–

Values are hazard ratios (95% confidence intervals).
* $p < 0.006$.
** $p < 0.001$ (after the Bonferroni correction).

model 2 (Table 3) suggests osteoporotic HF [16]. Finally, participants who only received ambulatory care following an HF would have been missed in the study. But, most patients having a new HF are severely ill and hospitalized [32]. Thus, the underestimation of HF incidence may be acceptable.

Conclusions

Adults with polio are at risk of an HF. Those who are middle-aged or male had higher incidences of fracturing a hip than the age- and sex-matched controls. A customized HF prevention program is important for people with polio. The program should be begun early in middle age and include male adults.

Conflict of interest/disclosure

The authors report no conflicts of interest.

Funding

This study was supported by Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan [grant no. 103wf-eva-28 and 106TMU-WFH-02]. The funding source had no involvement in the study.

Acknowledgements

This study is based in part on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance, Department of Health and managed by the National Health Research Institutes. The interpretation and conclusions contained herein do not represent views of the Bureau of National Health Insurance, Department of Health, or National Health Research Institutes.

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