



Hip Fracture and Risk of Acute Myocardial Infarction: A Nationwide Study



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Running head: Hip fracture and myocardial infarction
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Background

Osteoporotic fractures are associated with increased mortality risk. However, few data are available on the risk of acute myocardial infarction (AMI) following hip fracture. Therefore, we investigated whether hip fracture increased the risk of AMI in a large, nationwide cohort study.

Method

We obtained data from 8,758 patients diagnosed with hip fracture from 2000 to 2009 and from 4 matched controls for each patient from the Longitudinal Health Insurance Database (LHID 2000), Taiwan. Controls were matched for age, gender, comorbid disorders, and enrollment date. All subjects were followed up from the date of enrollment until AMI, death, or the end of data collection (2009). Cox's regression model adjusted for age, gender, comorbid disorders, and medication was used to assess independent factors determining the risk of development of AMI.

Results

We assessed data for 8,758 patients diagnosed with hip fracture and 35,032 controls without hip fracture. The mean age of the study subjects was 70 years (SD, 17.4), and the median follow-up duration was 3.2 years (interquartile range, 1.4–5.8 years), with a maximal follow-up period of 10 years. In total, 1,183 patients (2.7%) suffered from newly developed AMI during the follow-up period: 257 of the hip fracture patients (2.9%) and 926 of the controls (2.6%). **Table 1** shows the baseline characteristics and medications of the hip fracture patients and controls. Compared to controls, patients with hip fracture had a shorter follow-up duration (2.8 vs. 3.4 years, $P < 0.001$). Hip fracture patients also had more comorbid disorders, including chronic kidney disease, dyslipidemia, and chronic obstructive pulmonary disease (COPD), and they also took more medications, including aspirin, clopidogrel, warfarin, PPIs, statins, oral estrogen, oral steroids, and oral bisphosphonates. **Table 2** shows the baseline characteristics of patients with and without development of AMI during follow-up. The patients who developed AMI were older and had more comorbid disorders including hypertension, diabetes, CAD, chronic kidney disease, dyslipidemia, and COPD. Those who developed AMI also took more aspirin, clopidogrel, warfarin, and statins.

Figure 1 exhibits the results of the log-rank test and Kaplan-Meier survival analysis. During the maximal 10-year follow-up period, the cumulative incidence of AMI was significantly higher in patients with hip fracture than controls ($P = 0.001$ by log-rank test).

Table 3 shows the association between hip fracture and risk of subsequent AMI. The crude hazard ratio (HR) for AMI in hip fracture patients was 1.27 (95% confidence interval [CI], 1.10–1.45, $P = 0.001$). After adjustment for other confounders including age, sex, comorbid disorders, and medication, hip fracture remained associated with a 29% increase in AMI risk (HR: 1.29, 95% CI, 1.12–1.48, $P < 0.001$). **Figure 2** shows a stratified analysis of hip fracture and AMI risk among variable subgroups. Patients with hip fracture had a higher risk of AMI development, especially women, older patients, and patients with comorbid disorders including hypertension, diabetes, CAD, osteoporosis, and COPD.

Conclusions

We conclude that hip fracture is independently associated with a higher risk of subsequent AMI.

Disclosures

No conflicts

Table 1. Baseline characteristics and medication use of the study population

	Hip fracture		P value
	No n = 35,032	Yes n = 8,758	
Age, years	70.0 ± 17.4	70.0 ± 17.4	NS
Follow-up duration, years	3.4 (1.5–6.1)	2.8 (1.1–5.3)	<0.001
Male, n (%)	15,720 (44.9)	3,930 (44.9)	NS
Hypertension, n (%)	22,449 (64.1)	5,612 (64.1)	NS
Diabetes, n (%)	12,473 (35.6)	3,118 (35.6)	NS
CAD, n (%)	13,273 (37.9)	3,318 (37.9)	NS
Osteoporosis, n (%)	10,945 (31.2)	2,735 (31.2)	NS
Chronic kidney disease, n (%)	5,650 (16.1)	1,759 (20.1)	<0.001
Dyslipidemia, n (%)	10,995 (31.4)	2,374 (27.1)	<0.001
COPD, n (%)	12,282 (35.1)	3,350 (38.3)	<0.001
Medications, n (%)			
Aspirin			0.002
Clopidogrel	8,977 (25.6)	2,390 (27.3)	0.001
Warfarin	1,154 (3.3)	352 (4.0)	0.002
PPIs	530 (1.5)	173 (1.6)	<0.001
Statins	4,204 (12.0)	1,409 (16.1)	<0.001
Oral estrogen	4,898 (14.0)	911 (10.4)	<0.001
Oral steroids	950 (2.7)	381 (4.4)	<0.001
Oral bisphosphonates	5,902 (16.8)	1,836 (21.0)	<0.001

Data are mean ± SD or median (interquartile range); t test and chi-square test were used for evaluating continuous and categorical variables, respectively. NS, non-significant. CAD, coronary artery disease. COPD, chronic obstructive pulmonary disease

Table 2. Demographic data of the study population with or without acute myocardial infarction

Data are mean ± SD; t test and chi-square test were used for evaluating continuous and categorical variables, respectively. NS, non-significant; CAD, coronary artery disease; PPIs, proton pump inhibitors; COPD, chronic obstructive pulmonary disease

	Acute Myocardial Infarction		P value
	No (n = 42,607)	Yes (n = 1,183)	
Age, years	69.8 ± 17.5	76.6 ± 10.8	<0.001
Male, n (%)	19,148 (44.9)	502 (42.4)	NS
Hypertension, n (%)	27,122 (63.9)	939 (79.4)	<0.001
Diabetes, n (%)	15,033 (35.3)	558 (47.2)	<0.001
CAD, n (%)	16,022 (37.6)	568 (48.0)	<0.001
Osteoporosis, n (%)	13,287 (31.2)	393 (33.2)	NS
Chronic kidney disease, n (%)	7,168 (16.8)	241 (20.4)	0.001
Dyslipidemia, n (%)	12,958 (30.4)	411 (34.7)	0.002
COPD, n (%)	15,172 (35.6)	460 (35.7)	0.021
Medications, n (%)			
Aspirin			<0.001
Clopidogrel	10,872 (25.5)	495 (41.8)	<0.001
Warfarin	1,401 (3.3)	105 (8.9)	0.021
PPIs	674 (1.6)	29 (2.5)	NS
Statins	5,481 (12.9)	132 (11.2)	0.012
Oral estrogen	5,623 (13.2)	186 (15.7)	NS
Oral steroids	1,286(3.0)	45 (3.8)	NS
Oral bisphosphonates	7,527 (17.7)	211 (17.8)	NS

Table 3. Association between hip fracture and acute myocardial infarction

Patient groups	AMI, n (%)		Incidence (per 1000 person-years)	Hazard Ratio (95% CI)		
	Yes	No		Unadjusted HR	Adjusted HR	
				Model 1*	Model 2†	Model 3‡
Controls (n = 35,032)	926 (2.6)	34,106(97.4)	6.82	1.00	1.00	1.00
Hip fracture (n = 8,758)	257(2.9)	8,501(97.1)	8.70	1.27 (1.10–1.45)	1.30 (1.14–1.50)	1.28 (1.1–1.47)

* Model 1: Adjusted for age and gender

† Model 2: Adjusted for age, gender, and comorbid disorders (hypertension, diabetes, coronary artery disease, osteoporosis, chronic kidney disease, dyslipidemia, chronic obstructive pulmonary disease)

‡ Model 3: Adjusted for age, gender, comorbid disorders and medications (aspirin, clopidogrel, warfarin, proton pump inhibitors, statins, oral estrogen, oral steroids, oral bisphosphonates)

Figure Legends

Figure 1. Kaplan-Meier estimates of the cumulative incidence of acute myocardial infarction in subjects categorized by hip fracture. The cumulative incidence of acute myocardial infarction was significantly higher in patients with hip fracture ($P < 0.001$ by log-rank test).

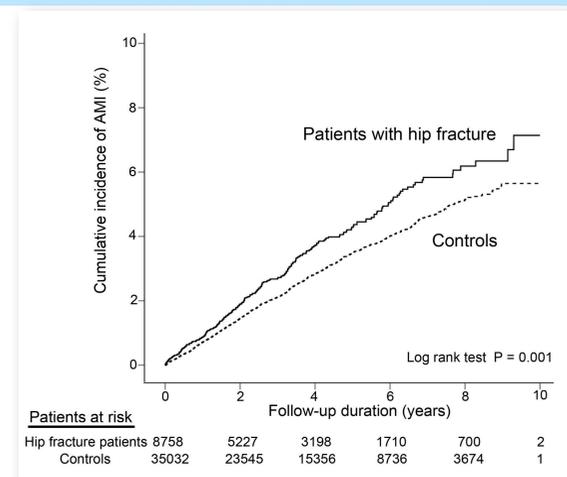


Figure 2. The association between hip fracture and acute myocardial infarction in specific subgroups identified by Cox regression analysis.

