



The Association of Acute Myocardial Infarction with Pyogenic Spondylitis in Korea: A Nationwide Longitudinal Cohort Study

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Objective: The goal of this nationally matched longitudinal study was to investigate the relationship between acute myocardial infarction (AMI) and pyogenic spondylitis (PS) in Korea.

Methods: We collected patient data from the National Health Insurance Service Health Screening cohort from January 1, 2004 to December 31, 2015. PS was classified using the International Classification of Diseases codes M46.2 (osteomyelitis), M46.8 (inflammatory spondylopathy), M49.2 (enterobacterial spondylitis), and M49.3 (enterobacterial spondylitis) (spondylopathy in other infectious and parasitic diseases). The PS group had a total of 628 patients. The control group included 3,140 people. Utilizing the Kaplan-Meier technique, the groups' AMI rates were estimated. A Cox proportional-hazards regression analysis was used to compute the hazard ratio for AMI.

Results: After controlling for age and sex, the hazard ratio for AMI in the PS group was 2.241 (95% confidence interval [CI], 1.112–4.516). The adjusted hazard ratio in the PS group was 2.138 after controlling for demographics and concomitant medical conditions (95% CI, 1.056–4.318). In a subgroup analysis, the AMI percentages were substantially greater in the PS group in women over 65, those with diabetes, and in non-hypertension and non-dyslipidemia subgroups.

Conclusion: This nationwide longitudinal study found that PS patients had an elevated risk of AMI.

Keywords: Epidemiology; Myocardial infarction; Population; Spondylitis

INTRODUCTION

Recent research has found a substantial link between illnesses including pneumonia, urinary tract infections, dental infections and sudden myocardial infarction (acute myocar-

dial infarction [AMI])^{4,6,11,17,20,26-27}. Infectious spinal illnesses tend to be on the rise in older people as a result of chronic disabling diseases, more non-surgical treatments, and increased spine surgery^{8,21}. There are some studies that show pyogenic spondylodiscitis patients have high long-term

mortality due to cardiovascular diseases such as ischemic heart diseases^{1,2}). Given the paucity of studies demonstrating a link between infectious spinal illnesses and AMI, we undertook countrywide longitudinal research to inquire into how common AMI is in individuals with pyogenic spondylitis (PS).

MATERIALS AND METHODS

1. Data Source

For this investigation, results from the National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) data were gathered from 2004 to 2015. The NHIS is in charge of running a single-payer healthcare system^{3,18}). The NHIS performs health checks on non-employees and office workers over 40 once a year or every 2 years, respectively. The information gathered (for example, national health check-up results) is kept in the National Health Information Database (NHID)^{9,13}). The NHIS data is accessible to the public for research purposes. The Institutional Review Board (IRB) authorized our study (IRB No. 2020-01-011).

2. Study Design and Subjects

This sex- and age-matched research was aimed at determining the potential chances of AMI in individuals with PS. A PS and a control group were included in the research population. PS group participants were diagnosed using the International Classification of Diseases, Tenth Revision (ICD-10) codes M46.2-M46.8 and M49.2-M49.3. The NIHSS database contained 515,547 patients (about 10% of Koreans above age 40 who had national health check-ups between January 1, 2002 and December 31, 2003). The patients were followed for 12 years, ending in December 2015. The following criteria were used to identify AMI patients: 1) ICD-10 codes (I21, I22), 2) hospitalization^{18,19}). The NIHSS database was used to obtain information regarding pre-existing comorbidities.

The patients in this research were tracked from the time of their first AMI until they died or reached the end of their follow-up period. Duration refers to the time period from the first diagnosis of AMI to the death of the patient or reaching the end of the follow-up period. The duration of Table 1 shows the sum of follow-up period of all patients.

3. Establishment of the Study Cohort

From 515,547 diagnosed individuals in the NIHSS database, we retrieved 10,890 PS individuals. The 653 individuals hospitalized at least once a year were chosen to represent patients with higher disease activity. After excluding the 25 individuals with preexisting PS, 628 patients who have been newly diagnosed with PS stayed. The greedy matching algorithm of the 'Match IT' R package was used to choose 3,140 individuals as controls using 1:5 age- and gender-stratified matching (without replacement)^{12,14}). The batches were monitored until December 31, 2015 (Fig. 1).

4. Statistical Analysis

The distinctions in the means of demographic variables amid the PS and control batches were examined using the χ^2 and the Student's *t*-test. The Kaplan-Meier technique was used to evaluate the likelihood of survival without AMI in both groups. The differences in the rates of surviving disease-free between the batches were compared with the Wilcoxon's log-rank test. Multivariate studies employing a Cox proportional hazard regression model were used to evaluate the impact of PS on the following incidence of incidents. There were two Cox proportional-hazards regression models employed. Model 1 was modified to account for gender and age. Model 2 was adjusted for gender, age, DM, Hypertension, and Dyslipidemia. To adjust covariates, we conducted subgroup analyses. R software was used to conduct the analysis. (version 3.3.3; The R Foundation for Statistical Computing, Vienna, Austria).

Table 1. Adjusted hazard ratios for AMI in the PS and control groups

Group	Events	Duration (days)	Incidence rate (%)	HR (95% CI)	
				Model 1*	Model 2†
AMI					
Control (n = 3,140)	53	12,896,218	1.500	1	1
PS (n = 628)	10	931,034	3.920	2.241 (1.112, 4.516)	2.138 (1.056, 4.318)

AMI: acute myocardial infarction; PS: pyogenic spondylitis; HR: hazard ratio; CI: confidence interval.

*Model 1: adjusted for age and sex.

†Model 2: adjusted for age, sex, low income, diabetes, hypertension, and dyslipidemia.

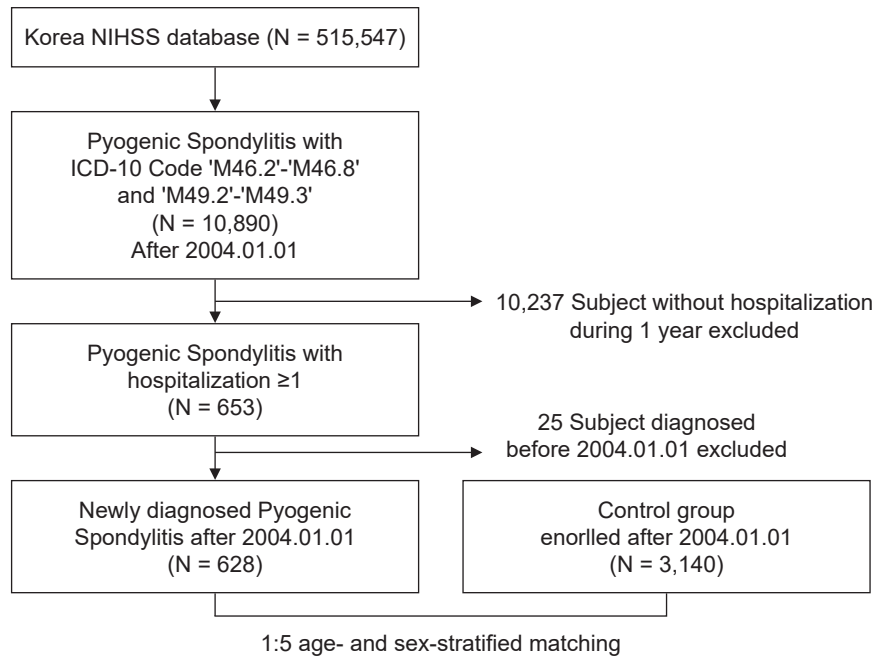


Fig. 1. The cohort formation process is depicted in a flow diagram. The National Health Insurance Service–Health Screening Cohort (NIHSS database) was used in this 12-year longitudinal cohort study.

RESULTS

1. Characteristics of the PS and Control Groups

There were 628 newly diagnosed PS patients. The average age was 59.09 ± 9.35 years, and most of the following were men (51.43 percent). Diabetes mellitus prevalence differed substantially between the two groups (p < 0.01; [Table 2](#)).

2. AMI in the PS and Control Groups

The PS group had a substantially greater incidence rate of AMI than the control batch (p = 0.003; [Fig. 2](#)). The Kaplan-Meier curves with accumulative AMI risks revealed that the PS batch was more likely than the control to develop AMI. A multivariate analysis of the Cox proportional-hazards regression model 1 revealed that the AMI hazard ratio in the PS group was 2.241 when juxtaposed with the control batch (95% confidence interval [CI], 1.112–4.516; [Table 1](#)). The hazard ratio of AMI in the PS batch was 2.138 in a multivariate analysis of model 2. (95% CI, 1.056–4.318; [Table 1](#)).

3. Subgroup Analysis of AMI Incidence Rate

The AMI rate in females differed substantially in both the PS and control batches (95% CI, 1.292–8.928; [Table 3](#)). AMI rate was substantially divergent amid the PS and control batches

Table 2. Characteristics of the PS and control groups

Variables	PS (n = 628)	Control (n = 3,140)	p-value
Sex (male)	323 (51.43%)	1,615 (51.43%)	1
Age	59.09 ± 9.35	59.09 ± 9.35	1
Age ≥ 65	199 (31.69%)	995 (31.69%)	1
Low income	161 (25.64%)	840 (26.75%)	0.6
Diabetes	83 (13.22%)	289 (9.20%)	<0.01*
Hypertension	268 (42.68%)	1,241 (39.52%)	0.15
Dyslipidemia	99 (15.76%)	486 (15.48%)	0.9

The data is presented as number (%) or mean ± standard deviation.

PS: pyogenic spondylitis.

*Statistical significance.

in the age <65 subgroup (95% CI, 1.549–9.166; [Table 3](#)), the diabetic subgroup (95% CI, 1.096–14.590), the non-hypertensive subgroup (95% CI, 1.024–9.827), and the non-dyslipidemia subgroup (95% CI, 1.006–4.795).

DISCUSSION

After controlling for age and gender, our countrywide longitudinal follow-up research found that the exposure to AMI was 2.241-fold greater in the PS group. After controlling for age, gender, wealth, and other comorbidities, the incidence of AMI rose by 2.138-fold in the PS batch. In female, age >65,

diabetic, non-hypertensive, and categories, the incidence of AMI was substantially greater in PS patients than in controls. Similar to our study, there have been several studies that the risk of cardiovascular disease was increased in PS^{1,2}.

Previous research has indicated an association between infection and heart-related events. Corrales-Medina et al.⁵

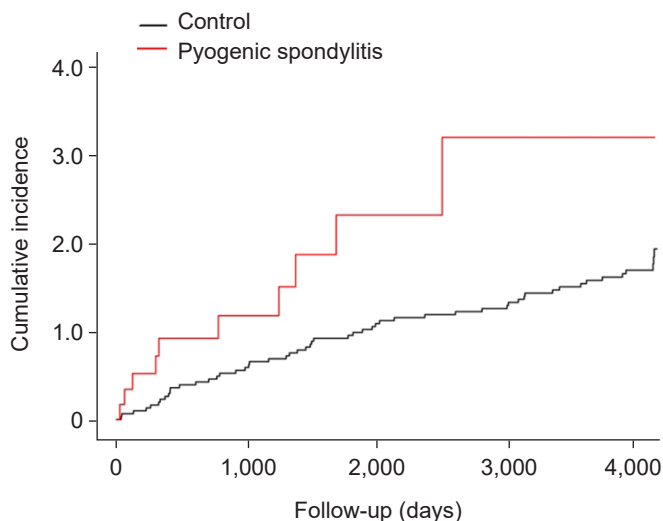


Fig. 2. The increasing incidence of acute myocardial infarction (AMI) in the pyogenic spondylitis (PS) and control groups was compared. The Kaplan-Meier curves for increasing AMI risk were contrasted between the PS and control groups.

reported a 7.8-fold increase in the odds of severe coronary conditions in patients with acute bacterial pneumonia. Kwong et al.¹¹ reported that AMI incidence ratios within 7 days after influenza B, influenza A, respiratory syncytial virus, and other virus infections were 10.11 (95% CI, 4.37–23.38), 5.17 (95% CI, 3.02–8.84), 3.51 (95% CI, 1.11–11.12), and 2.77 (95% CI, 1.23–6.24), respectively.

Several potential explanations for the connection between AMI and infection have been proposed. Atherosclerotic plaques contain inflammatory cells. Infections in other parts of the body release inflammatory cytokines into the bloodstream, which can trigger the inflammatory cells in atherosclerotic plaques^{15,17}. The coagulation-promoting state associated with acute infection raises the likelihood of coronary artery thrombosis at the site of plaque breakdown even more^{17,22,24}. Factors that contribute to coronary thrombosis include increased platelet activity, increased production of procoagulants, hypercoagulability, and endothelial dysfunction^{10,17,28-30}. AMI can also occur when the metabolic demands of myocardial cells exceed the capacity of the blood to supply oxygen. Fever and inflammation raise the metabolic requirements of outer tissues and organs. As a result of the increased heart rate, the filling time during diastole is shortened, limiting coronary perfusion^{7,17}.

There are a few imperfections to this study that should be mentioned. First, the pathogenesis of atherosclerosis and

Table 3. Acute myocardial infarction incidence rate in subgroup analyses between the PS and control groups

Variables	PS		Control		HR (95% CI)	p-value for difference
	n	Incidence rate (%)	n	Incidence rate (%)		
Sex						
Male	7	5.727	16	0.951	1.509 (0.522, 4.363)	0.456
Female	9	6.774	27	1.458	3.397 (1.292, 8.928)	0.013
Age						
<65	6	6.081	5	0.202	3.767 (1.549, 9.166)	0.004
≥65	10	12.130	38	3.640	1.133 (0.337, 3.805)	0.851
Diabetes						
N	3	5.900	9	0.973	1.681 (0.700, 4.034)	0.248
Y	13	6.827	34	1.600	3.999 (1.096, 14.590)	0.035
Hypertension						
N	9	1.370	21	0.280	3.172 (1.024, 9.827)	0.045
Y	7	36.087	22	10.724	1.808 (0.739, 4.423)	0.196
Dyslipidemia						
N	3	1.379	10	0.335	2.197 (1.006, 4.795)	0.048
Y	13	34.712	33	6.045	2.451 (0.499, 12.040)	

PS: pyogenic spondylitis; HR: hazard ratio; CI: confidence interval.

AMI can be associated with elevated inflammatory markers and chronic infectious burden^{16,23,25}. However, the NIHSS database is insufficient data on inflammatory markers. As a result, it is complicated to examine the possible impact of inflammatory markers on the relationship between PS and AMI. Second, variables of medical claims data may not accurately reflect a patient's health status^{13,14}.

Nonetheless, this is the first statewide longitudinal cohort research to indicate that PS patients have an elevated risk of AMI.

CONCLUSION

Our countrywide longitudinal cohort analysis showed an increased tendency of AMI in PS patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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