Clinical study

Association of Acute Myocardial Infarction with ankylosing Spondylitis: A nationwide longitudinal cohort study

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ABSTRACT

Pertaining to an association between Acute Myocardial Infarction (AMI) and Ankylosing Spondylitis (AS) is sparse. The purpose of this nationwide longitudinal study was to investigate the prevalence of AMI in newly diagnosed AS patients.

A total of 12,988 patients were enrolled in the AS group from January 1, 2010 to December 31, 2014 from the Korean National Health Insurance Service (NHIS). The control group consisted of 64,940 subjects according to 1:5 age-sex stratified matching. The AMI incidence rates in AS and control group were compared using the Kaplan-Meier method. The hazard ratio of AMI and the control group was estimated by Cox proportional hazards regression analyses.

During a 6 year follow up, 62 patients (0.48%) in the AS group and 157 persons (0.24%) in the control group developed AMI. The hazard ratio of AMI in the AS group was 1.99 (95% confidence interval [95% CI], 1.48–2.67) after adjusting for sex and age. The hazard ratio of AMI in the AS group was 1.81 (95% CI, 1.34–2.43) after adjusting for demographics and comorbid medical disorders.

The incidence rate of AMI increases in newly diagnosed AS patients.

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1. Introduction

Ankylosing Spondylitis (AS) is an autoimmune disease which involves chronic inflammation. Its extra-articular manifestations include uveitis, inflammatory bowel disease, osteoporosis, and issues related to the lungs and heart and kidneys [1].

The relationship between Acute Myocardial Infarction (AMI) and AS remains unclear. However, according to a recent meta-analysis conducted by Slyvain et al., AS patients appear to have a higher incidence risk of AMI [2]. There have been three nationwide longitudinal studies, with two showing no significant difference in AMI incidence rates between the AS and control groups [3–5]. However, these two studies did not control for confounding factors other than age and sex. Our nationwide longitudinal study was not only based on the largest amount of data made available thus far, but also adjusted for possible confounding factors including

hypertension and diabetes and dyslipidemia. The aim of this nationwide longitudinal study was to assess the incidence rate of AMI in the AS group compared to that in the control group.

2. Material and methods

2.1. Data source

The Korean National Health Insurance Service (NHIS) was used as the database for this study. It covers 97% of the population in South Korea. The NHIS database includes information pertaining to demographics, medical care, medical procedures, and disease diagnosis. Researchers can gain access to the database after being approved by an official review committee. The present study was approved by the institutional review boards at CHA University Bundang Medical Center (IRB No. 2017-08-015).

2.2. Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the

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institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The need for informed consent was waived because the data used consisted of de-identified secondary data released for research purposes and were analyzed anonymously.

2.3. Study design

This study used a 1:5 age-sex stratified matching cohort design to compare the risk of AMI in AS patients. The AS group consisted of subjects who received a diagnosis of AS (Reduction of Medical Expenses for Rare Complaints Code, V14.0) between January 1, 2010 and December 31, 2014. The AMI patients were defined by applying the following criteria: 1) ICD-10 codes (I21, I22), 2) hospitalization, and 3) brain CT or MRI [6]. The risk of AMI was evaluated using two Cox proportional hazards regression models. Model 1 evaluated the risk of AMI after adjusting for sex and age. Model 2 evaluated the risk of AMI after adjusting for sex, age, income, and comorbidities including hypertension and diabetes and dyslipidemia.

2.4. Establishment of study cohort

We extracted 15,547 AS subjects from January 1, 2010 to December 31, 2014 by using the database of NHIS. Subsequently, 1400 subjects with a previous history of ischemic stroke or AMI or congestive heart failure were excluded (Fig. 1). Another 1159 patients younger than 20 years old were excluded. Finally, 12,988 subjects constituted the AS group. Subsequently, 1:5 age- and sex- stratified matching was conducted using a Greedy digit match algorithm yielding 64,940 subjects in the control group. Subjects in both groups were followed up to December 31, 2015 (Fig. 1).

2.5. Statistical analysis

The Kaplan-Meier method was used to estimate the AMI-free survival probabilities in the AS and control groups. The mean differences in the demographic characteristics and comorbidities between the two groups were compared using the *Chi-square* test and Student's *t* test. The Wilcoxon's log rank test was used to evaluate the differences in disease-free survival in the two groups. Multivariate analyses in the Cox proportional hazard regression model were conducted to estimate the effect of AS on AMI. Two Cox proportional hazards regression models were used in this study. Model 1 estimated the AMI incidence after adjustment for sex and age. Hazard ratios were calculated after adjusting for sex, age, income, and other comorbidities in Model 2. The analyses were performed using SAS 9.2 software (for Windows, SAS Institute, Cary, NC).

3. Results

3.1. Characteristics of the AS and control group

The AS group consisted of 12,988 patients during the study period. The male/female sex ratio showed percentages of 72.54% to 27.46% respectively. The mean age of the patients was 40.19 ± 14.20 years old. There were significant differences between the two groups in terms of the prevalence rates of diabetes ($p = <0.0001$), hypertension ($p = <0.0001$), dyslipidemia ($p = <0.0001$) and AMI ($p = <0.0001$). Of the 12,988 subjects with AS, 62 (0.48%) developed AMI during the follow-up period compared to 157 (0.24%) of the 64,940 subjects in the control group (Table 1).

3.2. AMI in the AS and control group

The AMI incidence probability in the AS group was significantly higher than that in the control group ($p = <0.0001$, Fig. 2). The Kaplan-Meier curves with cumulative hazards of AMI showed that the AS group had a higher estimation of risk in developing AMI than the control group. In a multivariate analyses of Cox

Table 1
Characteristics of AS and Control group.

Variables	AS (n = 12,988)	Control (n = 64,940)	P
Female	3,566 (27.46%)	17,830 (27.46%)	
Age	40.186 ± 14.195	40.186 ± 14.194	
Diabetes	623 (4.80%)	2,447 (3.77%)	**<0.0001**
Hypertension	1,710 (13.17%)	6,199 (9.55%)	**<0.0001**
Dyslipidemia	1,135 (8.74%)	3,763 (5.79%)	**<0.0001**
AMI	62 (0.48%)	157 (0.24%)	**<0.0001**

Bold style indicates statistical significance.
Abbreviations: AS, ankylosing spondylitis; AMI, acute myocardial infarction.

Fig. 1. Flow of cohort establishment. This study was a 6-year longitudinal cohort study established from Korean nationwide health insurance claim data.
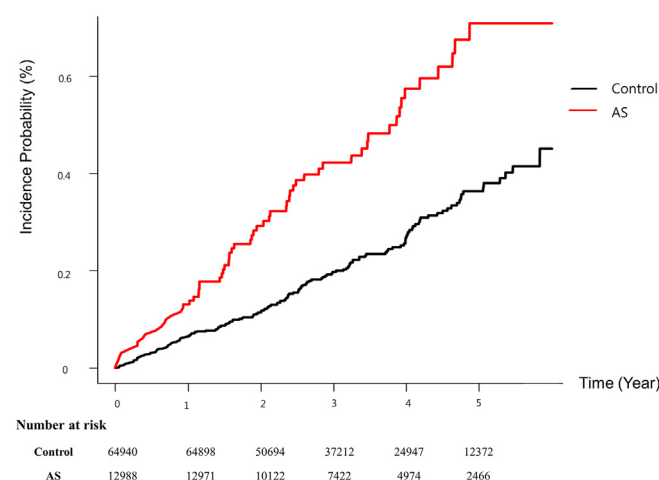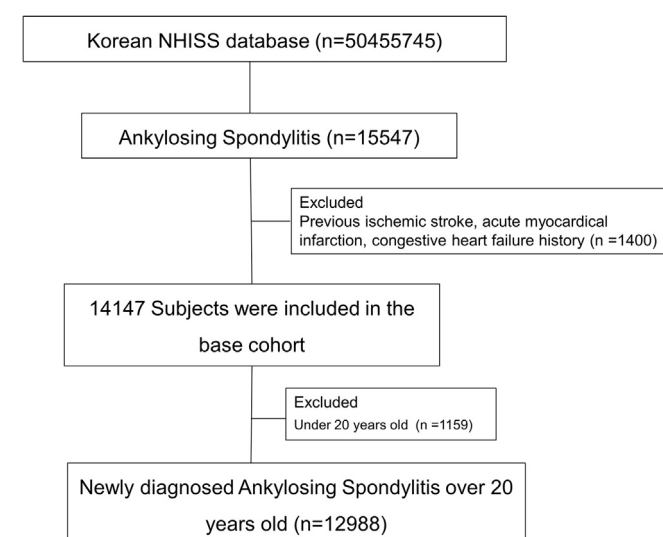

Fig. 2. Comparison of the cumulative incidence of AMI in the AS and control groups. The Kaplan-Meier curves with cumulative hazards of AMI were compared in the AS and control groups. The incidence probability of AMI in the AS group was significantly higher than that in the control group during the 6-year follow up (p = <0.0001).