

## Outcomes of coronary artery bypass grafting in patients with inflammatory rheumatic diseases: An 11-year nationwide cohort study

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**Objective:** Patients with inflammatory rheumatic diseases have an increased risk of developing coronary atherosclerosis. However, outcomes of surgical revascularization in these patients have been rarely studied. We aimed to determine whether, or which, inflammatory rheumatic diseases may pose effects on mortality and adverse cardiac outcomes after coronary artery bypass grafting.

**Methods:** By using the National Health Insurance Research Database of Taiwan, we identified 40,639 adult patients who underwent first-time coronary artery bypass grafting between 2000 and 2010. Among these patients, 101 had rheumatoid arthritis, 56 had systemic lupus erythematosus, and 73 had ankylosing spondylitis. The odds ratios (ORs) of operative mortality and hazard ratios (HRs) of overall mortality and adverse cardiac outcomes after coronary artery bypass grafting (ie, myocardial infarction and repeat revascularization) in relation to rheumatoid arthritis, systemic lupus erythematosus, and ankylosing spondylitis were estimated.

**Results:** With adjustment for potential confounders including patient characteristics, hospital levels, and combined surgery, systemic lupus erythematosus was an independent predictor for operative mortality (adjusted OR, 2.63; 95% confidence interval [CI], 1.04-6.65;  $P = .04$ ) and ankylosing spondylitis was marginally associated with operative mortality (adjusted OR, 2.41; 95% CI, 0.99-5.88;  $P = .054$ ). Systemic lupus erythematosus was a significantly independent predictor for overall mortality during the follow-up period (adjusted HR, 2.23; 95% CI, 1.51-3.31;  $P < .0001$ ) and might increase the risk of repeat revascularization (adjusted HR, 1.89; 95% CI, 0.97-3.68;  $P = .06$ ). Neither rheumatoid arthritis nor ankylosing spondylitis was significantly associated with overall mortality and adverse cardiac outcomes.

**Conclusions:** Our study may help surgeons and physicians recognize the potential risks inherent to systemic lupus erythematosus and ankylosing spondylitis when conducting coronary artery bypass grafting and providing follow-up care. (*J Thorac Cardiovasc Surg* 2015;149:859-66)

See related commentary on pages 866-8.

Supplemental material is available online.

Despite recent advances in diagnostic procedures and therapeutic modalities, coronary artery disease (CAD) remains

the leading cause of death globally.<sup>1</sup> It is well established that several conventional risk factors (eg, age, male gender, diabetes, and hypertension) account for the development of CAD. Other novel risk factors have been implicated recently. Evidence suggests the essential role of chronic inflammation in the pathogenesis of coronary atherosclerosis.<sup>2-5</sup> Inflammatory rheumatic diseases, a group of disorders that primarily affect joints, may involve different organ systems with a wide spectrum of clinical manifestations. These inflammatory rheumatic disorders may result in chronic, relapsing, and systemic inflammatory responses and increase cardiovascular risks in affected patients.<sup>2-7</sup> Patients with inflammatory rheumatic diseases have a high burden of cardiovascular diseases that may cause increased morbidity and mortality.

Although patients with inflammatory rheumatic diseases seem to be more susceptible to coronary atherosclerosis, outcomes of patients who underwent surgery for coronary revascularization have not been well documented. Although several studies demonstrated single-hospital experiences of coronary artery bypass grafting (CABG) in patients with inflammatory rheumatic diseases, all except 1 were case

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**Abbreviations and Acronyms**

ASp	= ankylosing spondylitis
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
CI	= confidence interval
CKD	= chronic kidney disease
DM	= diabetes mellitus
ESRD	= end-stage renal disease
HR	= hazard ratio
IBD	= inflammatory bowel disease
ICD-9-CM	= <i>International Classification of Diseases, Ninth Revision, Clinical Modification</i>
NHIRD	= National Health Insurance Research Database
OR	= odds ratio
PCI	= percutaneous coronary intervention
PM-DM	= polymyositis-dermatomyositis
RA	= rheumatoid arthritis
SLE	= systemic lupus erythematosus
SSc	= systemic sclerosis

series/reports collecting 7 patients or less.<sup>8-12</sup> The largest among these series included 44 patients with inflammatory rheumatic diseases, composed mainly of patients with rheumatoid arthritis (RA).<sup>13</sup> Limited surgical experiences in any single center were probably due to the rarity of this special patient population. Thus, conducting investigations using a large database would be a reasonable and practical approach.<sup>13-15</sup>

The National Health Insurance Research Database (NHIRD) of Taiwan contains a large sample size and high validity of diagnosis for catastrophic illnesses (eg, inflammatory rheumatic diseases, cancers, and end-stage renal disease [ESRD]) in the claims data. This database may provide a valuable and real-world platform to review the outcomes of various surgical procedures in patients with certain rare diseases. Literature reviews indicate that a number of inflammatory rheumatic diseases, including RA, systemic lupus erythematosus (SLE), ankylosing spondylitis (ASp), systemic sclerosis (SSc), polymyositis-dermatomyositis (PM-DM), and inflammatory bowel diseases (IBDs), are risk factors for the development of CAD, myocardial infarction, and cardiovascular death.<sup>2-7</sup> Through the NHIRD of Taiwan, we attempted to describe the characteristics and outcomes of patients with inflammatory rheumatic diseases undergoing CABG and to conduct risk analysis to recognize whether, or which, inflammatory rheumatic diseases might be associated with increased risks of mortality and adverse cardiac outcomes during the perioperative period and long-term follow-up.

**PATIENTS AND METHODS****The Coronary Artery Bypass Grafting Cohort**

This retrospective cohort study was performed using the NHIRD of Taiwan. Our access to the NHIRD was approved by the Review Committee of the National Health Research Institutes. The whole study was approved by the Institutional Review Board of National Cheng Kung University Hospital (approval number A-EX-102-010). The details of the NHIRD of Taiwan are shown in [Appendix E1](#).

The procedures that established the study cohort are summarized in [Figure 1](#). We selected hospitalizations with the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) procedure codes for CABG from January 1, 2000, to December 31, 2010. Overall, there were 41,113 hospitalizations for CABG during the study period. Among these hospitalizations, we identified a total of 40,639 adult patients aged at least 18 years who underwent first-time CABG as the CABG cohort. By using the ICD-9-CM diagnosis codes, we extracted patients with RA, SLE, ASp, SSc, PM-DM, and IBD from the database. In the CABG cohort, the diagnosis of RA was preoperatively established in 101 patients (0.25%), SLE was preoperatively established in 56 patients (0.14%), and ASp was preoperatively established in 73 patients (0.18%). Patients with SSc (7 patients), PM-DM (7 patients), and IBD (2 patients) were few in number and thus were not included for further analysis.

**Comorbidities and Outcome Measurements**

On the basis of the hospital care data and prior hospitalizations of each patient, we recognized baseline medical comorbidities using ICD-9-CM codes, including hypertension, diabetes mellitus (DM), dyslipidemia, congestive heart failure, chronic kidney disease (CKD), peripheral artery disease, prior stroke, and chronic obstructive pulmonary disease. Patients with ESRD were further identified from the patients with CKD if they were registered with a dialysis catastrophic illness certificate. We also identified whether the patients were hospitalized with the diagnosis of acute coronary syndrome. In addition, we recorded the levels of hospitals (medical centers, regional hospitals, or district hospitals) where the CABG procedures were conducted. Concomitant procedures, such as valve procedures and thoracic aortic surgery, were also recorded.

Outcomes measured and analyzed in this study included operative mortality, overall mortality, and adverse cardiac outcomes, including myocardial infarction and repeat revascularization, after CABG surgery. All patients of this cohort were evaluated for any occurrence of myocardial infarction and hospitalization for repeat revascularization (defined as percutaneous coronary intervention [PCI] or re-CABG) until mortality, withdrawal from the insurance program, or December 31, 2010. For myocardial infarction and repeat revascularization, the date of the first episode would be counted if patients experienced it more than 1 time. The ICD-9-CM codes of procedures, diseases, and adverse outcomes described in this study are listed in [Table E1](#).

**Statistical Analysis**

The patients who did not have these inflammatory rheumatic diseases associated with CAD constituted the control group of this study. Patients with different inflammatory rheumatic diseases were compared separately with the control group to describe the differences in baseline characteristics and outcomes. Categorical variables, expressed as numbers and percentages, were compared by the chi-square test or Fisher exact test as necessary. Continuous variables, expressed as mean  $\pm$  standard deviation, were compared by the Student *t* test. Kaplan-Meier estimates of overall survival, freedom from myocardial infarction, and freedom from repeat revascularization were plotted. Logistic regression analysis was performed to estimate the odds ratios

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