Is the frequency of metabolic syndrome higher in South Korean women with rheumatoid arthritis than in healthy subjects?

Seung-Geun Lee1, Ji-Min Kim1, Sun-Hee Lee1, Kye-Hyung Kim1, Ji-Hye Kim1, Ji-Won Yi1, Woo-Jin Jung1, Young-Eun Park2, Seong-Hu Park1, Joung-Wook Lee1, Seung-Hoon Baek1, Jun-Hee Lee1, and Geun-Tae Kim6

1Department of Internal Medicine, Pusan National University School of Medicine, Busan; 2Department of Internal Medicine, Malgeunsem Hospital, Changwon; 3Department of Internal Medicine, Young Do Hospital, Busan; 4Department of Internal Medicine, Busan St. Mary’s Medical Center, Busan; 5Department of Internal Medicine, Ilsin Christian Hospital, Busan; 6Division of Rheumatology, Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea

Background/Aims: To compare the frequency of metabolic syndrome (MetS) and magnitude of insulin resistance, measured by the homeostatic model assessment of insulin resistance (HOMA-IR), between South Korean women with rheumatoid arthritis (RA) and healthy subjects, and to evaluate risk factors for MetS and increased HOMA-IR in patients with RA.

Methods: In a cross-sectional setting, 84 female patients with RA and 109 age-matched healthy female subjects were consecutively recruited at a university-affiliated rheumatology center in South Korea. MetS was defined according to the Third Report of the National Cholesterol Education Program’s Adult Treatment Panel (NCEP-ATP III) 2004 criteria.

Results: The frequency of MetS did not differ significantly between patients with RA (19%) and healthy subjects (15.6%, \( p = 0.566 \)), although patients with RA had a higher HOMA-IR compared with healthy subjects (\( p < 0.001 \)). Patients with RA met the NCEP-ATP III 2004 criteria for high blood pressure more often than healthy subjects (44% vs. 19.3%, \( p < 0.001 \)), and low high density lipoprotein cholesterol was more prevalent in healthy subjects (33%) than in patients with RA (14.3%, \( p = 0.004 \)). Although no obvious risk factors for the presence of MetS were identified in patients with RA, higher serum C-reactive protein and disease activity score assessed using the 28-joint count for swelling and tenderness-erythrocyte sedimentation rate significantly contributed to a higher HOMA-IR.

Conclusions: Despite their increased insulin resistance, South Korean women with RA did not have a significantly higher frequency of MetS compared with that in healthy subjects.

Keywords: Arthritis, rheumatoid; Metabolic syndrome X; Insulin resistance; Cardiovascular diseases

INTRODUCTION

Metabolic syndrome (MetS), also known as syndrome X or insulin resistance syndrome, comprises obesity, insulin resistance, impaired glucose tolerance or diabetes, hypertension, and dyslipidemia, all of which are known risk factors for atherosclerosis [1]. Among these factors, insulin resistance is recognized as the key pathophysiological factor for MetS. Moreover, insulin resistance per se increases the risk for cardiovascular
diseases (CVDs) and contributes to the association between MetS and coronary atherosclerosis [2,3]. Although the value of MetS as a predictor of cardiovascular risk has been much debated, a recent meta-analysis showed that MetS is associated with a 2-fold increase in cardiovascular outcome and a 1.5-fold increase in all-cause mortality [4]. Hence, MetS has grown in importance in light of its contribution to the burden of cardiovascular morbidity and mortality in recent years.

Recent studies have demonstrated that in addition to insulin resistance, inflammation is closely associated with the pathogenesis of MetS [1,5,6]. A rise in acute-phase reactants such as C-reactive protein (CRP) and proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), promote insulin resistance [1,7,8]. Inflammatory biomarkers are frequently elevated in subjects with MetS, and conversely, MetS is prevalent in patients with chronic inflammatory status such as rheumatic diseases [6].

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by articular and extra-articular involvement. Patients with RA have an increased risk for CVDs due to accelerated atherosclerosis as a result of both increased inflammatory cytokines and a higher prevalence of traditional risk factors such as type 2 diabetes mellitus (DM) and hypertension [9,10]. MetS may provide an additional connection between accelerated atherosclerosis and inflammation in RA [7]. MetS is a common manifestation in patients with RA, but previously reported frequencies of MetS among patients with RA vary widely, from 14% to 56% [11-24]. This diversity may be attributable to differences in the definition of MetS, ethnicity, geographic area, study design, and study population characteristics. Moreover, some studies have demonstrated a higher prevalence of MetS in patients with RA than in the general population [14,19,21], whereas others have not [12,13,22-24]. This discrepancy warrants further exploration. In addition, the prevalence of MetS in South Korean women with RA has not been investigated to date.

The objectives of the present study were to compare the frequency of MetS between South Korean female patients with RA and healthy subjects and to evaluate factors associated with the presence of MetS in patients with RA. Additionally, insulin resistance was measured by the homeostatic model assessment of insulin resistance (HOMA-IR) and compared between patients with RA and healthy subjects.

**METHODS**

**Study design and subjects**

We designed a cross-sectional study that included 84 female patients with RA and 109 age-matched female healthy subjects (± 2 years) (age range, 22 to 76). The entire study population was consecutively recruited at a university-affiliated rheumatology center in South Korea from January 2008 to December 2009. All patients with RA fulfilled the American College of Rheumatology 1987 revised classification criteria for RA [25]. Patients with rheumatic diseases other than RA or who refused to participate in this study were excluded. Healthy subjects were selected randomly from among applicants undergoing an annual health check in the same center and had no history of taking any medications such as glucocorticoids (GCs) or oral contraceptives that would affect insulin resistance and no current autoimmune or rheumatic diseases. Written informed consent was obtained from each subject based on the Declaration of Helsinki. This study was approved by the Research and Ethics Review Board of the Pusan National University Hospital, Busan, South Korea.

**Assessments**

All information was collected during an interview and by reviewing medical records. Anthropometric parameters, including height, weight, body mass index (BMI), waist circumference, and blood pressure, were measured in all study subjects. BMI was calculated by dividing body weight by the square of height in meters (kg/m^2), and waist circumference was measured using a tape at the midpoint between the lower part of the lowest rib and the highest point of the iliac crest on the mid-axillary line. Blood pressure was determined as the mean of two measurements taken at an interval of 5 minutes using a TM-2655P apparatus (A&D Company Ltd., Tokyo, Japan). Hypertension was defined as blood pressure ≥ 140/90 mmHg or requiring antihypertensive treatment.