

# Metabolic syndrome and risk of monoclonal gammopathy of undetermined significance: a large Korean cohort study

Ji Yun Lee,<sup>1</sup> Eun-Jung Jung,<sup>1</sup> Soyeon Kwon,<sup>2</sup> Sang-A Kim,<sup>1</sup> Jeong-Ok Lee,<sup>1</sup> Kyungdo Han<sup>3</sup> and Soo-Mee Bang<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam; <sup>2</sup>Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul and <sup>3</sup>Department of Statistics and Actuarial Science, Soongsil University, Seoul, Korea

**Correspondence:** S-M. Bang

[smbang7@snu.ac.kr](mailto:smbang7@snu.ac.kr)

K. Han

[hkd917@naver.com](mailto:hkd917@naver.com)

**Received:** October 13, 2025.

**Accepted:** January 12, 2026.

**Early view:** January 29, 2026.

<https://doi.org/10.3324/haematol.2025.300043>

©2026 Ferrata Storti Foundation

Published under a CC BY-NC license



# **Metabolic syndrome and risk of monoclonal gammopathy of undetermined significance: a large Korean cohort study**

Ji Yun Lee<sup>1</sup>, Eun-Jung Jung<sup>1</sup>, Soyeon Kwon<sup>2</sup>, Sang-A Kim<sup>1</sup>, Jeong-Ok Lee<sup>1</sup>, Kyungdo Han<sup>3†</sup>,  
Soo-Mee Bang<sup>1†</sup>

<sup>1</sup>Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

<sup>2</sup>Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Korea

<sup>3</sup>Department of Statistics and Actuarial Science, Soongsil University, Seoul, Korea

Running title: MGUS and Metabolic syndrome

## **Address for correspondence:**

**Soo-Mee Bang, MD, PhD**

Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam-Si, Gyeonggi-do 13620, Korea

Tel: +82-31-787-7039; Fax: +82-31-787-4098

E-mail: [smbang7@snu.ac.kr](mailto:smbang7@snu.ac.kr)

**Kyungdo Han, PhD**

Department of Statistics and Actuarial Science, Soongsil University, 369 Sangdo-ro, Dongjak-gu, Seoul 06978, Korea

Tel: +82-2-828-7025; Fax: +82-2-

E-mail: [hkd917@naver.com](mailto:hkd917@naver.com)

## **Supplementary methods**

### **Study Design**

This retrospective cohort study utilized data from the National Health Information Database (NHID), a comprehensive public health big data platform established and maintained by the National Health Insurance Service (NHIS). The NHID covers South Korea's entire population of over 50 million individuals.<sup>16</sup> The NHIS oversees South Korea's national health insurance system, reimbursing healthcare providers and pharmacies based on submitted claims.<sup>17</sup> The NHIS also conducts biennial health examinations for all employees, regardless of age, and for adults aged 40 years or older. These health checkups include anthropometric measurements, laboratory assessments (e.g., lipid profiles and blood glucose), and standardized questionnaires on lifestyle factors, such as smoking, alcohol use, and physical activity.<sup>16</sup>

The study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB No. X-2507-986-901). The requirement for informed consent was waived because the data were publicly available and de-identified prior to analysis.

### **Study Population**

The enrollment process for the study cohort is illustrated in *Online Supplementary Figures S1*. We included individuals who underwent NHIS health checkups between January 1, 2012, and December 31, 2012 (index year), and followed them until December 31, 2022, to identify new cases of MGUS. The cohort included 4,910,068 adults who completed NHIS health checkups in 2012, representing 40% of the eligible workplace/regional insurance adults aged  $\geq 20$  years. The exclusion criteria were as follows: individuals with incomplete data (e.g., misentered

questionnaire responses or aberrant lab values,  $n = 333,385$ ), those with a prior diagnosis of cancer or amyloidosis before the index date ( $n = 112,700$ ), and those diagnosed with MGUS within the 1-year lag period ( $n = 65$ ). Therefore, 4,453,504 individuals were included in the study population.

### **Definition of Metabolic Syndrome and MGUS**

MetS was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria.<sup>18</sup> It required at least three of the following: (1) waist circumference  $\geq 90$  cm (men) or  $\geq 85$  cm (women); (2) fasting glucose  $\geq 100$  mg/dL or use of antidiabetic medication; (3) blood pressure  $\geq 130/85$  mmHg or use of antihypertensive medication; (4) HDL cholesterol  $< 40$  mg/dL (men) or  $< 50$  mg/dL (women) or drug treatment for low HDL cholesterol; (5) triglycerides  $\geq 150$  mg/dL or drug treatment for elevated triglycerides.

MGUS cases were defined as individuals with at least two outpatient visits coded as MGUS (International Classification of Diseases [ICD-10] code D47.2) or registered under the V193 code (a special copayment reduction program for cancer patients in South Korea). This definition was chosen to enhance diagnostic specificity in claims data. Multiple outpatient visits minimize misclassification, and V193 registration reflects confirmed diagnoses, typically supported by laboratory evidence such as serum protein electrophoresis.<sup>19</sup> MGUS cases were incidentally diagnosed in clinical practice (e.g., during workups for comorbidities) rather than through a formal national screening program, which may introduce acquisition bias.

### **Data Collection and Covariates**

A standardized self-administered questionnaire was used to collect data on smoking status, alcohol consumption, and physical activity. Regular exercise was defined as moderate-intensity activity performed for at least 30 minutes, five or more times per week, or high-intensity activity performed for at least 20 minutes, three or more times per week. Low income was defined as being in the lowest income group (within the bottom 25% of the income distribution) or meeting the criteria for medical aid benefits.

For the longitudinal analysis of changes in MetS status and MGUS risk, 3,294,672 individuals who underwent both baseline and follow-up MetS assessments were included from the baseline cohort. These individuals were categorized into four groups based on MetS status changes: persistent absence of MetS (No→No), development of MetS (No→Yes), resolution of MetS (Yes→No), and persistent MetS (Yes→Yes). The study evaluated MGUS risk associated with MetS status changes, calculating hazard ratios using models adjusted for relevant covariates to assess the impact of MetS changes on MGUS incidence over time.

### **Statistical Analysis**

Statistical analyses evaluated baseline characteristics, incidence rates, and associations between MetS status changes and MGUS risk. Categorical variables were summarized with frequencies/percentages and continuous variables with means  $\pm$  SDs; comparisons used chi-square and t-tests, respectively. The large cohort size yielded significant differences in most variables by MGUS status. Incidence rates (IRs) were computed as MGUS cases per 1,000 person-years, with group differences assessed. Cox proportional hazards models estimated HRs and 95% CIs for MGUS risk by MetS changes (reference: No→No): Model 1 (unadjusted), Model 2 (age/sex-adjusted), Model 3 (further adjusted for smoking, alcohol, physical activity,

income, CKD). Robustness was evaluated via stratified Cox models by sex and age (20–39, 40–64,  $\geq 65$  years), including interaction p-values. Analyses used SAS 9.3; two-sided  $p < 0.05$  significant.

**Supplementary Table S1. Association of Metabolic Syndrome and Its Components with Monoclonal Gammopathy of Undetermined Significance: A Subgroup Analysis by Sex and Age**

		Hazard ratio (95% CI) for Subgroup (Model 3)						
		Male	Female	p inter	Age 20-39	Age 40-64	Age ≥ 65	p inter
MetS	No	1 (Ref.)	1 (Ref.)	0.152	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.053
	Yes	1.36 (1.18-1.57)	1.15 (0.95-1.39)		2.73 (1.447,5.156)	1.29 (1.10-1.50)	1.21 (1.01-1.44)	
Number of MetS Components	0	1 (Ref.)	1 (Ref.)	0.073	1 (Ref.)	1 (Ref.)	1 (Ref.)	< 0.001
	1	1.33 (1.01-1.76)	1.00 (0.73-1.39)		0.77 (0.34-1.77)	1.40 (1.08-1.82)	0.76 (0.52-1.13)	
	2	1.45 (1.10-1.91)	1.15 (0.84-1.58)		0.84 (0.32-2.16)	1.5 (1.15-1.96)	0.89 (0.61-1.29)	
	3	1.57 (1.19-2.09)	1.34 (0.98-1.84)		1.04 (0.35-3.15)	1.49 (1.13-1.97)	1.11 (0.77-1.60)	
	4	1.94 (1.45-2.60)	1.06 (0.75-1.50)		5.82 (2.54-13.32)	1.83 (1.36-2.46)	0.93 (0.64-1.36)	
	5	2.20 (1.55-3.10)	1.29 (0.86-1.94)		2.81 (0.37-21.31)	2.32 (1.61-3.34)	1.06 (0.69-1.62)	
Central obesity†	No	1 (Ref.)	1 (Ref.)	0.032	1 (Ref.)	1 (Ref.)	1 (Ref.)	< 0.001
	Yes	1.30 (1.12-1.52)	0.98 (0.80-1.21)		3.10 (1.69-5.68)	1.32 (1.11-1.56)	0.97 (0.80-1.16)	
Elevated glucose†	No	1 (Ref.)	1 (Ref.)	0.073	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.281
	Yes	1.19 (1.03,1.37)	0.96 (0.79-1.16)		1.82 (0.96-3.43)	1.07 (0.92-1.25)	1.08 (0.91-1.29)	
Hypertension†	No	1 (Ref.)	1 (Ref.)	0.051	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.014
	Yes	1.44 (1.30-1.69)	1.13 (0.93-1.38)		1.71 (0.94-3.11)	1.48 (1.26-1.73)	1.02 (0.82-1.26)	
Low HDL cholesterol†	No	1 (Ref.)	1 (Ref.)	0.271	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.317
	Yes	1.44 (1.25-1.67)	1.27 (1.05-1.53)		1.43 (0.71-2.89)	1.48 (1.27,1.72)	1.24 (1.04-1.47)	
Elevated triglycerides†	No	1 (Ref.)	1 (Ref.)	0.959	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.735
	Yes	1.07 (0.93-1.23)	1.08 (0.89-1.30)		1.08 (0.57-2.05)	1.02 (0.88-1.19)	1.12 (0.94-1.33)	

95% CI, 95% confidence interval; MetS, metabolic syndrome; p inter, p-values for interaction between the covariate (MetS status) and subgroup (sex or age); HDL, high-density lipoprotein

†Full criteria (NCEP-ATP III): waist circumference ≥ 90 cm (men) or ≥ 85 cm (women); fasting glucose ≥ 100 mg/dL or use of antidiabetic medication; blood pressure ≥

130/85 mmHg or use of antihypertensive medication; HDL cholesterol < 40 mg/dL (men) or < 50 mg/dL (women) or drug treatment for low HDL cholesterol; (5) triglycerides  $\geq$  150 mg/dL or drug treatment for elevated triglycerides.

Model 3: Adjusted for age, sex, smoking, alcohol consumption, and household income, physical activity, chronic kidney disease

**Supplementary Table S2. Monoclonal Gammopathy of Undetermined Significance by Longitudinal Changes in Metabolic Syndrome and Its Components Across Sex and Age Subgroups (Model 3)**

		Hazard ratio (95% CI) for Subgroup (Model 3)						
		Male	Female	p inter	Age 20-39	Age 40-64	Age ≥ 65	p inter
MetS	No→No	1 (Ref.)	1 (Ref.)	0.106	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.093
	No→Yes	1.43 (1.17-1.75)	0.97 (0.74-1.28)		3.55 (1.40-9.00)	1.21 (0.96-1.51)	1.21 (0.95-1.54)	
	Yes→No	1.06 (0.77-1.46)	0.88 (0.56-1.41)		1.58 (0.37-6.84)	0.91 (0.63-1.31)	1.06 (0.71-1.56)	
	Yes→Yes	1.39 (1.13-1.71)	1.03 (0.78-1.36)		4.48 (1.85-10.80)	1.21 (0.95-1.53)	1.19 (0.93-1.53)	
Central obesity†	No→No	1 (Ref.)	1 (Ref.)	0.087	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.006
	No→Yes	1.24 (0.94-1.65)	0.79 (0.52-1.18)		3.10 (1.04-9.20)	1.13 (0.82-1.56)	0.89 (0.63-1.28)	
	Yes→No	1.06 (0.79-1.44)	0.83 (0.56-1.25)		0.00 (0.00-2.33)	0.88 (0.61-1.28)	1.05 (0.76-1.45)	
	Yes→Yes	1.36 (1.11-1.66)	0.95 (0.72-1.26)		4.55 (2.13-9.72)	1.34 (1.07-1.69)	0.97 (0.76-1.25)	
Elevated glucose†	No→No	1 (Ref.)	1 (Ref.)	0.265	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.491
	No→Yes	1.17 (0.93-1.47)	0.81 (0.58-1.12)		2.14 (0.84-5.47)	0.97 (0.75-1.25)	1.02 (0.77-1.36)	
	Yes→No	1.00 (0.76-1.31)	0.90 (0.62-1.29)		2.04 (0.75-5.58)	0.90 (0.67-1.20)	0.93 (0.66-1.32)	
	Yes→Yes	1.198(0.99-1.45)	0.97 (0.74-1.26)		2.44 (0.89-6.66)	1.02 (0.82-1.26)	1.13 (0.90-1.43)	
Hypertension†	No→No	1 (Ref.)	1 (Ref.)	0.065	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.053
	No→Yes	1.53 (1.21-1.95)	1.41 (1.07-1.88)		1.83 (0.40-4.82)	1.72 (1.36-2.16)	1.09 (0.79-1.50)	
	Yes→No	1.16 (0.83-1.61)	1.09 (0.70-1.70)		0.65 (0.15-2.87)	1.05 (0.74-1.48)	1.20 (0.78-1.85)	
	Yes→Yes	1.54 (1.23-1.92)	1.01 (0.76,1.34)		2.66 (1.19-5.95)	1.40 (1.12-1.75)	1.07 (0.79-1.44)	
Low HDL cholesterol†	No→No	1 (Ref.)	1 (Ref.)	0.137	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.396
	No→Yes	1.62 (1.34-1.95)	1.20 (0.91-1.60)		2.82 (1.20-6.62)	1.51 (1.22-1.87)	1.34 (1.06-1.70)	
	Yes→No	0.98 (0.69-1.39)	1.28 (0.89-1.85)		1.47 (0.44-4.91)	1.29 (0.94-1.78)	0.90 (0.60-1.36)	
	Yes→Yes	1.50 (1.18-1.91)	1.35 (1.03-1.76)		0.43 (0.06-3.22)	1.53 (1.20-1.95)	1.37 (1.05-1.77)	
Elevated triglycerides†	No→No	1 (Ref.)	1 (Ref.)	0.502	1 (Ref.)	1 (Ref.)	1 (Ref.)	0.711

No→Yes	1.20 (0.97-1.48)	1.03 (0.79-1.34)	0.92 (0.27-3.15)	1.16 (0.92-1.45)	1.10 (0.87-1.40)
Yes→No	1.05 (0.80-1.37)	0.73 (0.47-1.12)	1.46 (0.49-4.37)	0.95 (0.70-1.29)	0.87 (0.60-1.25)
Yes→Yes	1.02 (0.83-1.25)	0.91 (0.68-1.22)	1.69 (0.75-3.83)	0.89 (0.71-1.12)	1.02 (0.79-1.31)

---

95% CI, 95% confidence interval; MetS, metabolic syndrome; p inter, p-values for interaction between the covariate (MetS status) and subgroup (sex or age); HLD, high-density lipoprotein

†Full criteria (NCEP-ATP III): waist circumference  $\geq 90$  cm (men) or  $\geq 85$  cm (women); fasting glucose  $\geq 100$  mg/dL or use of antidiabetic medication; blood pressure  $\geq 130/85$  mmHg or use of antihypertensive medication; HDL cholesterol  $< 40$  mg/dL (men) or  $< 50$  mg/dL (women) or drug treatment for low HDL cholesterol; (5) triglycerides  $\geq 150$  mg/dL or drug treatment for elevated triglycerides.

Model 3: Adjusted for age, sex, smoking, alcohol consumption, and household income, physical activity, chronic kidney disease

**Supplementary Figure S1.** Flowchart showing the enrollment process for the study cohort.

