Clinical Markers Associated with Metabolic Syndrome Among Military Aviators

Chulwoo Rhee; Jinho Kim; Ji-young Kim; Eunsuk Chang; Se-young Park; Wooyoung Lee; Hohyung Kang

BACKGROUND: Due to the recent increase of metabolic syndrome (MetS) in the Korean population, this study was performed to investigate the prevalence of MetS among Republic of Korea (ROK) Air Force military aviators and its relationship with clinical markers.

METHODS: A cross-sectional study was performed among 911 aviators who filled out the lifestyle questionnaire and underwent medical examinations at the ROK Air Force Aerospace Medical Center. Clinical markers of aviators with MetS were investigated and odds ratios were calculated.

RESULTS: Among the 911 aviators, 90 (9.9%) were found to have MetS and the prevalence of subcomponents were: 31.7% elevated blood pressure, 25.3% elevated waist circumference, 19.0% impaired glucose tolerance, 16.6% elevated triglycerides, 7.9% reduced high density lipoprotein (HDL) cholesterol. Among aviators, a significant statistical association was found between the diagnosis of MetS with the highest quartile of uric acid, white blood cell (WBC) count, and alanine transaminase (ALT) level. Adjusted odds ratio of MetS was 8.88 (3.16 ~24.99) if all three clinical markers were at highest quartile range.

DISCUSSION: Despite the relatively low prevalence of MetS in ROK Air Force aviators, further preventive measures are required as the prevalence is expected to increase in the future. Aviators with high levels of WBC count, uric acid, and ALT should be examined for MetS. Further comprehensive cohort study is required to link the elevation of clinical markers and development of MetS.

KEYWORDS: metabolic syndrome, clinical marker, military aviator.

Rhee C, Kim J, Kim J-Y, Chang E, Park S, Lee W, Kang H. *Clinical markers associated with metabolic syndrome among military aviators.* Aerosp Med Hum Perform. 2015; 86(11):970–975.

Metabolic syndrome (MetS) is a cluster of risk factors which often arises from insulin resistance followed by abnormal adipose deposition and function that increase the risk of cardiovascular diseases.[10,22] Due to the evidence suggesting MetS is responsible for increased incidence and mortality related to numerous health problems, recent increase of its prevalence has become a major public health issue worldwide.[30] The exact pathophysiology of MetS is very complex and only partially demonstrated; however, a combination of aging, central obesity, diet, and physical inactivity have been suggested as the cause.[22]

Prevalence of metabolic syndrome (MetS) is increasing worldwide and Korea is no exception.[14] The age-standardized prevalence of MetS in Korea was 29.2% in 2001 but it increased to 31.3% in 2007 and this rise in prevalence is expected to continue.[18] It is reported that 73.7% of Korean adults have at least one of five MetS components.[28]

Due to the nature of their work, Republic of Korea Air Force (ROKAF) aviators are held to stringent physical standards in order to be considered qualified for flight. As a result of this combined with the selection process, Air Force aviators are relatively healthy compared to the general population. However, due to their unique duties, special consideration and rigorous medical examinations are continually required. It is reported

From the Armed Forces Medical Command, and Aerospace Medical Center, and Aerospace Medical Division, Air Force, Ministry of National Defense, Republic of Korea; and National Evidence-based Healthcare Collaborating Agency, Ministry of Health and Welfare, Republic of Korea.

This manuscript was received for review in May 2015. It was accepted for publication in August 2015.

Address correspondence to: Dr. Chulwoo Rhee, Preventive Medicine Division, Armed Forces Medical Command, Saemaulro 177-81 Bundangu Seongnamsi Gyongido, Republic of Korea; rhee275@gmail.com.

DOI: 10.3357/AMHP.4362.2015

that the prevalence of obesity and diabetes is becoming a bigger concern within the aviation community.[23]

Considering the time and resources put into each individual military aviator, it is extremely important that all necessary precautions be taken to maintain their flight status. While MetS itself is not a medical condition which causes flight disqualification, aviators with MetS should be routinely checked with regard to aerospace medical concerns that might arise.[6]

There have been several clinical markers established which indicate a high risk group for developing metabolic syndrome. These include: serum uric acid, white blood cell (WBC) count, and alanine aminotransferase (ALT).[9,12] Even within the normal range, a person with the high-normal level of any one of the three markers has a higher risk of developing MetS.[3,15,17] However, these findings were never reported among aviators. We hypothesized that these findings should also be found among aviators. Therefore, we performed a cross-sectional study to identify a prevalence of MetS and its subcomponents, and evaluate the association between the three clinical markers and MetS among ROKAF male aviators.

METHODS

Subjects

The study protocol was approved in advance by the ROKAF Aerospace Medical Center Institutional Review Board. With the explanation of study objectives and protocol by Air Force flight surgeons, each subject provided written informed consent before participating in the questionnaire survey. Only male aviators were considered in this study due to the small number of female aviators in ROKAF.

ROKAF aviators are required to undergo routine medical examination annually at the Fighter Wing medical treatment facilities and biannually at the Air Force Aerospace Medical Center with a more in depth health check-up. A cross sectional survey was completed by each aviator and was merged with their laboratory measurements from the Aerospace Medical Center Aviator Health Examination. Study subjects consisted of ROKAF aviators who received a biannual medical examination at the Aerospace Medical Center from April 1 to December 31, 2014.

Procedure and Questionnaire

Data were collected via subjects' medical history, health related questionnaire, anthropometric measurements, and laboratory results. The aviator health related lifestyle questionnaire was adapted from a previously developed questionnaire by the Korea National Health and Nutrition Examination Survey (KNHANES)[16] and modified after reviews by ROKAF flight surgeons. During the survey, flight surgeons were present with the study subjects for a full response rate.

Current Smoker was defined as a person who is currently smoking with a lifetime total of more than 100 cigarettes and Past Smoker was defined as a person who is not currently smoking but has exceeded the lifetime total of 100 cigarettes. Questions regarding drinking included frequency and amount of different types of alcohol. Based upon the response, number of days in a week with high risk alcohol consumption was defined as the number of days in a week that the subject consumed alcohol in excess of 7 glasses with respect to their alcohol type. Also assessed were the number of days in a week in which the subject engaged in high intensity exercise that produced perspiration.

Laboratory measurements from ROKAF aviators who visited the ROKAF Aerospace Medical Center for routine health examination were utilized. Trained military nurses obtained height, weight, and blood pressure, and calculated body mass index using the formula: weight (kg) divided by the height squared (m^2). Blood samples were collected from an antecubital vein after more than 12 h of fasting. Lab results including complete blood count (CBC), serum level of ALT, and uric acid were extracted from the database.

The definition of metabolic syndrome according to the revised National Cholesterol Education Program criteria was applied.[5] A subject was diagnosed as having MetS if he had any three of following five components: 1) waist circumference $>$ 90 cm; 2) triglycerides $\geq$ 150 mg $\cdot$ dl^{-1}; 3) high-density lipoprotein (HDL) cholesterol $<$ 40 mg $\cdot$ dl^{-1}; 4) blood pressure $\geq$ 130/85 mmHg or hypertension medication use; 5) fasting glucose $\geq$ 100 mg $\cdot$ dl^{-1} or diabetes mellitus medication use.

Statistical Analysis

Data were expressed as means (SD) for continuous variables and frequency (percentage) for categorical variables. Student *t*-test and Chi-square test were used for continuous and categorical variables respectively for statistical analyses. Multiple logistic regression was used for calculating the odds ratio (OR) and its 95% confidence interval (CI). Serum uric acid, WBC, and ALT level were categorized to quartile groups and the highest quartile was used as the reference group in relation to the other three quartiles. For multivariate analyses, variables used for adjustment were considered initially if there was a statistical difference (P-value $>$ 0.1) in means or percentages between the normal and MetS group and adjusting variables were selected through the stepwise selection. All statistical analyses were performed using SAS 9.4 (SAS Inc., Cary, NC).

RESULTS

Baseline characteristics of study subjects are shown in **Table I**. Out of 911 total study subjects, 90 (9.88%) were diagnosed as positive for MetS. Age group, BMI, smoking status, alcohol consumption, and exercise frequency were statistically associated with a diagnosis of MetS. Average serum uric acid level, WBC count and ALT were also statistically higher among the MetS group.

Table II shows the prevalence of metabolic syndrome and its subcomponents according to the age group. Prevalence of MetS

Table I. Baseline Characteristics of Study Subjects.

VARIABLES		NORMAL (821)	METABOLIC SYNDROME (90)	*P*-VALUE
Age	24-29	304 (90.5%)	32 (9.5%)	
	30-39	467 (90.9%)	47 (9.1%)	
	40-49	50 (82.0%)	11 (18.0%)	0.09
Height	Mean (SD)	174.7(5.11)	175.9(5.04)	<0.05
Weight	Mean (SD)	74.06(8.40)	83.14(9.09)	<0.05
Body Mass Index (kg/m^2)	<23	239 (98.8%)	3 (1.24%)	
	23~24.9	298 (95.2%)	15 (4.8%)	
	≥25	284 (79.8%)	72 (20.2%)	<0.05
Smoking	Never	266 (79.2%)	70 (20.8%)	
	Former	381 (74.1%)	133 (25.9%)	
	Current	37 (60.7%)	24 (39.3%)	<0.05
Alcohol consumption	<1/wk	289(86.0%)	47(14.0%)	
	1/wk	415 (80.7%)	99 (19.3%)	
	≥2/wk	33 (54.1%)	28 (45.9%)	<0.05
Exercise	<2/wk	170 (50.6%)	166 (49.4%)	
	2~4/wk	289 (56.2%)	225 (43.8%)	
	≥5/wk	26 (42.6%)	35 (57.4%)	<0.05
White Blood Cell count	Mean (SD)	5.72 (1.27)	6.29 (1.21)	<0.05
Uric acid	Mean (SD)	5.98 (1.19)	6.79 (1.16)	<0.05
Aspartate Transaminase (AST)	Mean (SD)	23.89 (9.97)	28.21 (12.67)	<0.05
Alanine Transaminase (ALT)	Mean (SD)	24.10 (14.60)	37.57 (28.44)	<0.05
AST/ALT	Mean (SD)	1.12(0.38)	0.87 (0.28)	<0.05
Gamma-glutamyl transpeptidase (GTP)	Mean (SD)	28.87 (33.46)	40.22 (27.32)	<0.05
Alkaline Phosphatase (ALP)	Mean (SD)	70.99 (35.72)	82.76 (42.10)	<0.05

in subjects in their 20s and 30s was 9.5% and 9.1%, respectively, but among subjects in their 40s, it was 18.0%. Among the subcomponents of MetS, elevated blood pressure had the highest prevalence at 31.7%, followed by elevated waist circumference (25.3%) and impaired glucose tolerance (19.0%). A statistically significant trend with regard to the age was observed with elevated triglycerides and impaired glucose tolerance.

Relationships between mean values of three clinical markers and components of metabolic syndrome are shown in **Table III**. All three clinical markers were statistically higher among subjects with elevated waist circumference and elevated triglycerides. Serum uric acid and ALT were higher among subjects with impaired glucose tolerance and elevated blood pressure, while serum uric acid only showed significance among reduced HDL cholesterol. Serum uric acid level was the only clinical marker that showed significance in all subcomponents.

Multiple logistic regression analysis was performed to calculate the OR of MetS among the subjects with the highest quartile of clinical markers (**Table IV**). Subjects within the other three quartiles were used as the reference group. Cut-off value for the highest quartiles were 6.9 for serum uric acid, 6.48 for WBC and 26 for ALT. Subjects with the highest quartile of all three clinical markers were statistically associated with the diagnosis of MetS. Adjusted OR of MetS for elevated uric acid, WBC, and ALT level were 1.73 (95% CI: 1.07~2.81), 1.75 (95% CI: 1.08~2.83) and 2.60 (95% CI: 1.62~4.17), respectively.

Table V shows the multiple logistic regression analysis for metabolic syndrome according to the number of clinical markers with the highest quartile. Prevalence of MetS increased as the numbers of the highest quartile clinical markers increased, and 39.1% were diagnosed with MetS when all three markers were within the highest quartile. Adjusted OR of MetS for an aviator with all three clinical markers at the highest quartile, compared to none, was 8.88 (3.16~24.99).

DISCUSSION

In our study, we investigated the prevalence of MetS and its subcomponents among ROKAF military aviators and its relationship with three clinical markers: serum uric acid, WBC, and ALT level. Prevalence of the MetS was 9.9% overall, and subjects with the highest quartiles of serum uric acid, WBC count, and ALT level were at increased risk of the MetS diagnosis. Positive correlation was found between the prevalence of MetS and the number of clinical markers within the highest quartile.

The prevalence of MetS in the general Korean population has increased from 29.2% in 2001 to 30.4% in 2005 and 31.3% in 2007.[18] Prevalence of MetS in Korean adult men was 29% in

Table II. Prevalence of Metabolic Syndrome and Its Subcomponents According to Age Group.

DIAGNOSIS	AGE 24~29 N	AGE 24~29 %	AGE 30~39 N	AGE 30~39 %	AGE 40~49 N	AGE 40~49 %	ALL AGES N	ALL AGES %	*P* FOR TREND
Waist Circumference > 90 cm	79	23.5	130	23.3	21	34.4	230	25.3	0.14
Triglycerides ≥ 150 mg · dl^{-1}	38	11.3	96	18.7	17	27.9	151	16.6	<0.05
HDL Cholesterol* < 40m150 mg · dl^{-1}	21	6.3	45	8.8	6	9.8	72	7.9	0.16
Fasting Glucose ≥ 100 mg · dl^{-1}	58	17.3	95	18.5	20	32.8	173	19.0	<0.05
Systolic Blood Pressure ≥ 130 or Diastolic ≥ 85 mmHg	99	29.5	163	31.7	27	44.3	289	31.7	0.06
Metabolic Syndrome	32	9.5	47	9.1	11	18.0	90	9.9	0.24

* High-Density Lipoprotein Cholesterol.

Table III. Relationship Between Mean Values of Three Clinical Markers and Components of Metabolic Syndrome.

DIAGNOSIS		URIC ACID MEAN (SD)	*P*-VALUE	WHITE BLOOD CELL COUNT MEAN (SD)	*P*-VALUE	ALANINE TRANSAMINASE MEAN (SD)	*P*-VALUE
Waist Circumference	≤90cm	5.88 (1.12)		5.68 (1.23)		22.6 (13.46)	
	>90cm	6.58 (1.30)	<0.05	6.08 (1.37)	<0.05	33.6 (22.55)	<0.05
Triglycerides	$<150\ mg \cdot dL^{-1}$	5.99 (1.19)		5.68 (1.28)		23.5 (14.61)	
	$\geq150\ mg \cdot dL^{-1}$	6.41 (1.25)	<0.05	6.29 (1.11)	<0.05	35.1 (23.46)	<0.05
HDL Cholesterol*	$\geq40\ mg \cdot dL^{-1}$	6.02 (1.21)		5.76 (1.27)		25.1 (16.93)	
	$<40\ mg \cdot dL^{-1}$	6.52 (1.05)	<0.05	6.00 (1.39)	0.24	28.9 (16.92)	0.9
Fasting Glucose	$<100\ mg \cdot dL^{-1}$	6.00 (1.18)		5.74 (1.25)		24.7 (16.5)	
	$\geq100\ mg \cdot dL^{-1}$	6.30 (1.27)	<0.05	5.94 (1.39)	0.07	28.5 (18.59)	<0.05
Blood Pressure	Systolic < 130 and Diastolic < 85	6.00 (1.22)		5.71 (1.24)		24.5 (14.66)	
	Systolic ≥ 130 or Diastolic ≥ 85	6.18 (1.17)	<0.05	5.94 (1.34)	0.14	27.4 (20.94)	<0.05

* High-Density Lipoprotein Cholesterol.

2007 and stratified by age group, 25% in 20–29 yr olds and 32% in 30–39 yr olds. This is significantly higher than the prevalence of MetS among Air Force aviators and the prevalence of all five MetS components was higher in Korean adult men as well. MetS prevalence in the United States was 22.9% in 2010 according to the National Health and Nutrition Examination Survey,[4] however the prevalence among military and civilian aviators was also significantly lower compared to the general population.[8] This can be interpreted as the "healthy-worker effect" because soldiers and aviators have strict standards for physical status and unusual training exercises compared to the general population.

The prevalence of MetS among ROKAF aviators increased from 5.1% in 2008 to 9.9% in 2014, and the prevalence of all five components of MetS also increased.[2] This indicates that the trend of increasing MetS in Asian countries due to westernized lifestyle can also be observed within the ROKAF aviators.[25] A study that assessed the age adjusted prevalence of MetS among the Royal Jordanian Air Force pilots reported it as 18.0%.[13] Another study that examined the prevalence of MetS among civilian airline pilots in Spain reported the prevalence as 14.8%.[1] Our prevalence is considered to be lower than other countries because of the strict medical standards for Air Force aviators and a healthy dietary pattern. However, we expect the prevalence of MetS in ROK AF aviators will likely increase in next 5 yr, while the U.S. military is observing a decreasing trend in the prevalence.[7]

We found that relative elevation of serum uric acid, ALT, and WBC count (even within the normal range) was statistically associated with the prevalence of MetS. Uric acid, the end product of purine metabolism, has been reported to be linked with hypertension, insulin resistance, and atherosclerosis.[24] A cohort study that evaluated the serum uric acid level and the incidence of MetS after 5 yr of follow-up period among Korean men reported a hazard ratio of 1.48 (95% CI 1.26 ~1.73).[17] Possible mechanisms linking elevated serum uric acid level and MetS were proposed as oxidative stress, endothelial dysfunction, and inflammation.[26] These possible suggestions are parallel with the previous studies that reported uric acid level is associated with hypertension, diabetes mellitus, and dyslipidemia.[11,21]

ALT, a typical marker for liver injury, is elevated in patients with nonalcoholic fatty liver disease, which can be frequently observed among the patients with MetS.[29] Two meta-analysis studies were performed previously to quantify the risk of MetS when elevation of ALT is observed and they both reported the risk of MetS increasing by 13–14% for every $5\ U \cdot L^{-1}$.[15,19] In the present study, the cut off value for ALT was $26\ U \cdot L^{-1}$ while another study used $27\ U \cdot L^{-1}$.[9] These data indicate that even with the reference range, mild elevation of ALT reflects the presence of nonalcoholic fatty liver disease.

Elevated WBC count, which indicates subclinical systemic chronic inflammation, has also been shown to have close relationship with MetS and cardiovascular disease.[27] A cross sectional study in Thai men has shown that subjects with elevated WBC had met the diagnostic criteria for MetS at a rate 2.98 times higher than those in the normal range.[20] Another prospective study concluded the subjects within the upper quartile of WBC had an odds ratio of 2.47 (95% CI 2.03 ~2.99).[3] In our study, elevated WBC was closely associated with elevated waist circumference and triglycerides with a cut off value of 6.48. Other reported cut off values ranged from 5.99 ~7.50 in men.[3,9,20]

We observed that uric acid, ALT, and WBC were all associated with MetS and also there was a linear correlation with the number of clinical markers within the highest quartile and MetS. This indicates that all three clinical markers might play a

Table IV. Multiple Logistic Regression Analysis for Metabolic Syndrome in the Highest Quartile of Clinical Markers Compared with the Other Three Quartiles as the Reference Group.

CLINICAL MARKER	HIGHEST QUARTILE CUT-OFF VALUE	NUMBER OF SUBJECTS WITH HIGHEST QUARTILES	NUMBER OF METABOLIC SYNDROME	CRUDE ODDS RATIO (95% CI)	ADJUSTED* ODDS RATIO (95% CI)
Uric Acid	6.9	197	35	2.89 (1.64~4.09)	1.73 (1.07~2.81)
White Blood Cell count	6.48	225	34	2.00 (1.27~3.16)	1.75 (1.08~2.83)
Alanine Transaminase	26	217	46	3.97 (2.54~6.21)	2.60 (1.62~4.17)

* Adjusted for age, body mass index, smoking and drinking status.

Table V. Multiple Logistic Regression Analysis for Metabolic Syndrome According to Their Number of Clinical Markers with the Highest Quartile.

NUMBER OF CLINICAL MARKERS* WITH THE HIGHEST QUARTILE	NORMAL (821)	METABOLIC SYNDROME (90)	CRUDE OR	ADJUSTED† OR
0	437 (96.3%)	17 (3.7%)	ref	ref
1	258 (86.6%)	40 (13.4%)	3.99 (2.21∼7.18)	3.10 (1.69∼5.68)
2	112 (82.4%)	24 (17.7%)	5.51 (2.86∼10.61)	3.24 (1.63∼6.41)
3	14 (60.9%)	9 (39.1%)	16.53 (6.28∼43.48)	8.88 (3.16 ∼24.99)

* Clinical Markers include Uric acid, White Blood Cell count and Alanine Transaminase level.
† Adjusted for age, body mass index, smoking and drinking.

role in the causation of MetS or that elevated levels might be a clinical pathway for developing a diagnostic component of MetS. However the exact mechanism for how these clinical markers interact with each other is still unclear. Special factors to which aviators are prone, such as shift work, stress, altitude change, and radiation, add further complexity. As we continue to monitor those diagnosed with MetS or at high risk for MetS based on their blood profile, future follow-up on their cardiovascular disease will be rigorously checked.

The major strengths of our study are the large sample size to generalize our findings to the entire population of ROK Air Force aviators and the low possibility of information bias due to the protocol developed by the Air Force Aerospace Medical Center. However, before interpreting our results, the following limitations should be considered: First, due to cross sectional study design, we cannot rule out reverse causality in our findings. However, due to the strict medical standards for initial military aviator recruitment, any person with MetS or hyperuricemia would have been excluded. Second, dietary patterns were not investigated. Due to their mission, military aviators tend to stay on-post and eat at the military dining facility that offers the same menu for everyone each day. Finally, we did not obtain detailed information about the severity of fatty liver disease assessed by abdominal ultrasonography, results of glucose tolerance tests, levels of C-reactive protein, procalcitonin, 24 h Holter monitoring, and markers regarding adipokine metabolism, such as serum level of adiponectin and leptin. A further longitudinal cohort study with a questionnaire that includes dietary pattern is currently under development.

Prevention is critical in dealing with chronic disease in both the military and the civilian population. Upon the results of this study, the ROKAF has implemented more intensive weight control and smoking cessation programs, as well as reviewing possible ways to detect early signs of metabolic syndrome for primary prevention. Even though the prevalence of MetS among ROKAF aviators is considerably lower than the general population, the recent increase in the prevalence could be a possible threat to mission accomplishment and current status evaluation suggests more close observations and preventive public health actions are necessary.

ACKNOWLEDGMENTS

This study was funded by Republic of Korea Air Force Aerospace Medical Center. We would like to express sincere gratitude to all Republic of Korea Air Force military flight surgeons who participated and supported this study during the questionnaire development and survey. We would also like to extend our appreciation to Suzanne A. Stewart for English editing.

Authors and affiliations: Chulwoo Rhee, M.D., M.Sc., and Jinho Kim, M.D., M.Sc., Armed Forces Medical Command, Ministry of National Defense; Ji-young Kim, M.D., M.P.H., National Evidence-based Healthcare Collaborating Agency, Ministry of Health and Welfare; Eunsuk Chang, M.D., and Se-young Park, M.D., Aerospace Medical Center, Air Force, Ministry of National Defense; and Wooyoung Lee, M.D., and Hohyung Kang, M.D., M.P.H., Aerospace Medical Division, Air Force, Ministry of National Defense, Republic of Korea.

REFERENCES

1. Alonso-Rodríguez C, Medina-Font J. High sensitivity C-reactive protein in airline pilots with metabolic syndrome. Aviat Space Environ Med. 2012; 83(5):504–508.
2. An CH, Hwang SH, Chung KY. Prevalence and charateristics of metabolic syndrome in ROKAF pilots. J Aerospace Med ROKAF. 2008; 55(2):49–59 (Korean).
3. Babio N, Ibarrola-Jurado N, Bulló M, Martínez-González MÁ, Wärnberg J, et al. White blood cell counts as risk markers of developing metabolic syndrome and its components in the PREDIMED study. PLoS One. 2013; 8(3):e58354.
4. Beltrán-Sánchez H, Harhay MO, Harhay MM, McElligott S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999-2010. J Am Coll Cardiol. 2013; 62(8):697–703.
5. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285(19):2486–2497.
6. Fornoni A, Raij L. Metabolic syndrome and endothelial dysfunction. Curr Hypertens Rep. 2005; 7(2):88–95.
7. Herzog CM, Chao SY, Eilerman PA, Luce BK, Carnahan DH. Metabolic syndrome in the Military Health System based on electronic health data, 2009-2012. Mil Med. 2015; 180(1):83–90.
8. Kalff KG, Maya-Pelzer P, Andexer A, Deuber HJ. Prevalence of the metabolic syndrome in military and civilian flying personnel. Aviat Space Environ Med. 1999; 70(12):1223–1226.
9. Kang YH, Min HG, Kim IJ, Kim YK, Son SM. Comparison of alanine aminotransferase, white blood cell count, and uric acid in their association with metabolic syndrome: a study of Korean adults. Endocr J. 2008; 55(6):1093–1102.
10. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med. 2011 May 9:48.
11. Katsiki N, Papanas N, Fonseca VA, Maltezos E, Mikhailidis DP. Uric acid and diabetes: Is there a link? Curr Pharm Des. 2013; 19(27):4930–4937.
12. Kawada T. Insulin-related biomarkers to predict the risk of metabolic syndrome. Int J Endocrinol Metab. 2013; 11(4):e10418.
13. Khazale NS, Haddad F. Prevalence and characteristics of metabolic syndrome in 111 Royal Jordanian Air Force pilots. Aviat Space Environ Med. 2007; 78(10):968–972.

14. Kolovou GD, Anagnostopoulou KK, Salpea KD, Mikhailidis DP. The prevalence of metabolic syndrome in various populations. Am J Med Sci. 2007; 333(6):362–371.
15. Kunutsor SK, Seddoh D. Alanine aminotransferase and risk of the metabolic syndrome: a linear dose-response relationship. PLoS One. 2014; 9(4):e96068.
16. Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol. 2014; 43(1):69–77.
17. Lee JM, Kim HC, Cho HM, Oh SM, Choi DP, Suh I. Association between serum uric acid level and metabolic syndrome. J Prev Med Public Health. 2012; 45(3):181–187.
18. Lim S, Shin H, Song JH, Kwak SH, Kang SM, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998-2007. Diabetes Care. 2011; 34(6):1323–1328.
19. Liu Z, Que S, Ning H, Wang L, Peng T. Elevated alanine aminotransferase is strongly associated with incident metabolic syndrome: a meta-analysis of prospective studies. PLoS One. 2013; 8(12):e80596.
20. Lohsoonthorn V, Dhanamun B, Williams MA. Prevalence of metabolic syndrome and its relationship to white blood cell count in a population of Thai men and women receiving routine health examinations. Am J Hypertens. 2006; 19(4):339–345.
21. Osgood K, Krakoff J, Thearle M. Serum uric acid predicts both current and future components of the metabolic syndrome. Metab Syndr Relat Disord. 2013; 11(3):157–162.
22. Reynolds K, He J. Epidemiology of the metabolic syndrome. Am J Med Sci. 2005; 330(6):273–279.
23. Steinkraus LW, Cayce W, Golding A. Diabetes mellitus type 2 in aviators: a preventable disease. Aviat Space Environ Med. 2003; 74(10): 1091–1100.
24. Strazzullo P, Puig JG. Uric acid and oxidative stress: relative impact on cardiovascular risk? Nutr Metab Cardiovasc Dis. 2007; 17(6):409–414.
25. Tan DA. Changing disease trends in the Asia-Pacific. Climacteric. 2011; 14(5):529–534.
26. Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: an active component or an innocent bystander? Metabolism. 2006; 55(10):1293–1301.
27. Vozarova B, Weyer C, Lindsay RS, Pratley RE, Bogardus C, Tataranni PA. High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes. 2002; 51(2):455–461.
28. Yoon NH, Yoo S, Kim H. Composition of metabolic syndrome among Korean adults in a lifestyle modification intervention. Osong Public Health Res Perspect. 2014; 5(6):370–377.
29. Zhang X, Mu Y, Yan W, Ba J, Li H. Alanine aminotransferase within reference range is associated with metabolic syndrome in middle-aged and elderly Chinese men and women. Int J Environ Res Public Health. 2014; 11(12):12767–12776.
30. Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb. 2005; 12(6):295–300.