Metabolic Syndrome, Hyperlipidemias, and Associated Clinical Markers Among Military Airmen

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BACKGROUND: Due to the increased overweight and obesity prevalence in Colombia, the aim of this study is to determine the frequency of metabolic syndrome (MetS) among Colombian Air Force military aviators, crews, remote piloted aircraft operators, and air traffic controllers and relationships with clinical markers.

METHODS: Operationally active Columbian Air Force military personnel examined periodically at the Colombian Air Force Aerospace Medical Directorate were chosen for a cross-sectional study performed among 2179 subjects. Medical history, anthropometrics, and laboratory results were analyzed and frequencies, correlations, and odds ratios were calculated.

RESULTS: Overall prevalence of MetS was 21.7%; in subjects with BMI ≥25, frequency increased to 36% vs. those with BMI <25. Hypertriglyceridemia was present in 31%, impaired fasting glucose 12.5%, hypertension (≥130/85 mmHg) 14.4%, low HDL-C 35.2%, and increased waist circumference 46.2%. Those with three criteria were 14.6%, four criteria 5.8%, and five criteria 1.2%. Pilots had a significantly lower prevalence of MetS at 17.7% and an adjusted OR of 0.61 (0.49–0.76) than other crew; hyperuricemia was three times more likely (3.2–5.1) and hypercholesterolemia OR was 2.3 (1.9–2.9). Subjects with MetS had a significantly higher fat percentage, waist circumference, low-density lipoprotein, very low-density lipoprotein, non-high-density lipoprotein cholesterol, atherogenic index of plasma (AIP), uric acid, and white blood cell (leukocyte) count, and a lower estimated glomerular filtration rate. There is a linear relationship of the AIP and waist circumference, BMI, uric acid, and white blood cell count.

DISCUSSION: MetS prevalence among Colombian Air Force aviators is lower than the general population, higher than other countries, and displays worse lipid profiles that increase cardiovascular and diabetes mellitus risk within the military.

KEYWORDS: metabolic syndrome, aviation, military crew.

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Metabolic syndrome (MetS) is a constellation of abnormalities that increase the risk of coronary heart disease and diabetes mellitus (DM).[5] The diagnostic criteria is dictated by the International Diabetes Federation, the National Heart Lung Blood Institute, and the American Heart Association, among others. The prevalence is highly variable due to the different diagnostic criteria, but generally increases with age and is more frequent in men older than 20 yr with an estimated 17–40%, 30% in the age range from 40–50 yr, and 40–45% in those older than 50 yr in the general population. This condition is frequently tied to obesity in 38% of American Caucasians and 80% in Hispanics and constitutes a public health concern around the world. MetS is found in approximately 50% of patients with coronary heart disease, in 35% of patients younger than 45 yr old with myocardial infarction, and in 28% of adults without cardiovascular antecedents. Between 2005 and 2014, cardiovascular diseases were the most common cause of death in Colombia, with a frequency of 30%, and ischemic heart disease was responsible for 49% of mortality due to

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the cardiovascular system, representing a rate of 78.2 per 100.000 people-years. The frequency of hypertension (HTN) in the Colombian population is 23%, DM 2–7%, and prediabetes is found in 11% of people between 35 and 70 yr old.[15]

One study attempted to determine the frequency of risk factors for MetS in aircrews from Germany and obesity was found in 29% of cases, hyperlipidemia in 36%, and hypertension in 14.7%, with a similar distribution in the general population.[19] The prevalence of risk factors for MetS in U.S. Department of Defense personnel from 1976–2013 was found to be overweight in 53% of personnel, obesity in 21.7%, hyperlipidemia 33.5%, and HTN 21.4%[17] and a recent review from U.S Army databases in military pilots revealed that the incidence of hyperlipidemias in 2016 was 6.83 per 1000 person-years, and in 2017 was 4.47 per 1000 person-years.[14]

The prevalence of MetS in Korean military aircrews was 13%, central obesity 24%, altered fasting glucose 24.5%, hypertension 28%, hypertriglyceridemia 24%, and low high-density lipoprotein (HDL) 9.8%, with higher prevalence (21%) in maintenance personnel.[21] Colombian civilian pilots were included in a study to determine the frequency of cardiovascular risk factors and estimated that hypercholesterolemia was in 36% of the study population, hypertriglyceridemia 40%, low HDL 37%, high low-density lipoprotein (LDL) 33%, tobacco use 13%, HTN 7.8%, DM 1.3%, MetS 6%, and obesity 7%.[3]

There is evidence that several clinical markers are correlated with MetS, including uric acid and white blood cell count within the highest quartile among military aviators, and even reduced glomerular filtration rates and increased atherogenic index of plasma (AIP)[4,8,26] in people with MetS. The aim of this study was to determine the frequency of MetS and the correlation with hyperlipidemia, hyperuricemia, AIP, white blood cell count, and estimated glomerular filtration rate (eGFR) using the method for calculating the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) in the Colombian Air Force aircrews.

METHODS

Subjects

The study was a retrospective cross-sectional review of clinical records and laboratory measurements from the annual routine aeromedical examination at the Colombian Air Force Directorate of Aerospace Medicine from January 1st to December 31st, 2016. Study subjects included military pilots, remote piloted aircraft operators, air traffic controllers, and aircrew other than pilots who received an annual medical examination through Air Force Aeromedical Regulations. The study did not need informed consent from the subjects since this was a retrospective design according to Colombian Resolution 008,430 of 1993, Article 11, Category A, "Research with no risk", and Article 16, the privacy of clinical records must be always maintained. Only authorized medical personnel from the Directorate of Aerospace Medicine had access to the information.

Procedure

Data was collected via subjects' operational medical history, which includes past medical history, tobacco use, and family and personal occupational history. The physical exam included blood pressure measurements taken by the flight surgeon, fat percentage measured with the Ironman InnerScan BC-554 (Tanita, Tokyo, Japan), waist circumference, weight, height, and body mass index (BMI; $kg \cdot m^{-2}$) were taken with the examination technique recommended by the World Health Organization[30] by trained nurses at the Exercise Physiology Laboratory. Also collected were 12-h fasting blood samples from the median cubital or median antebrachial vein, which were processed with the Cobas C-501 (Roche Diagnostics, Indianapolis, IN, USA) on the same day of the exam to grant the aeromedical certificate. The laboratory results, including serum glucose, creatinine, cholesterol, HDL, triglycerides, LDL, complete blood count, and glomerular filtration rate, were calculated using CKD-EPI in $mL \cdot min^{-1}$.

The definition of MetS requires three or more of the following[1]: central obesity for the Hispanic population includes a waist circumference ≥90 cm in men and ≥80 cm in women; hypertriglyceridemia ≥150 $mg \cdot dL^{-1}$ or specific medication; low HDL <40 $mg \cdot dL^{-1}$ in men and <50 $mg \cdot dL^{-1}$ in women or specific medication; systolic blood pressure ≥130 mmHg or diastolic ≥85 mmHg or specific medication; fasting blood glucose ≥100 $mg \cdot dL^{-1}$ or specific medication; or current diagnosis of DM.

Statistical Analysis

Central tendency and dispersion measures were applied to the dataset, including frequencies, Chi-squared and Mantel-Haenszel tests for nominal variables, Pearson correlations and Fisher exact tests, ANOVA, and the robust Welch test when homogeneity of variance was not achieved. Prevalence odds ratios with 95% confidence intervals were calculated, and lineal regression analysis for quantitative variables and receiver operator characteristic curve to estimate the area under the curve were used for AIP for the diagnosis of MetS and Youden's J index. The study had a power of 80% and alpha was defined as 0.05 for bilateral statistical significance. All statistical analyses were performed using the trial period of MedCalc statistical software (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

The clinical records of 2516 study subjects were collected during the annual exams for aeromedical certification, and it was found that some aircrews underwent the same procedure twice in the same year for a more in-depth health check-up related to internal administrative purposes and 337 cases were excluded from the analysis. The description of the variables included in this study are shown in **Table I**.

This analysis included 2179 subjects who consisted of 960 pilots, 986 aircrew, 96 parachutists, and 96 air traffic controllers.

Table I. Characteristics of the Study Subjects.

VARIABLE	METABOLIC SYNDROME MEAN (SD) NO ($N = 1707$)	YES ($N = 472$)	*P*-VALUE
Age (yr)	30 (6.4)	35 (6.2)	<0.001
sBP (mmHg)[*]	114 (9.8)	122 (12.1)	<0.001
dBP (mmHg)[†]	70.2 (8.4)	77 (9.5)	<0.001
BMI (kg · m^{-2})[‡]	24.7 (2.7)	27.8 (2.5)	<0.001
Fat (%)	21.1 (5.1)	26.2 (4.1)	<0.001
Waist circumference (cm)	86.2 (8)	95.7 (6.1)	<0.001
Fasting blood glucose (mg · dL^{-1})	90.8 (6.3)	95.7 (7.7)	<0.001
Total cholesterol (mg · dL^{-1})	187.1 (35.3)	203 (38.2)	<0.001
HDL (mg · dL^{-1})[§]	48.3 (10.6)	35.7 (6.9)	<0.001
Triglycerides (mg · dL^{-1})	110.2 (56.5)	235.51 (134.6)	<0.001
LDL (mg · dL^{-1})[¶]	116.4 (31.1)	122.1 (35.1)	0.001
VLDL (mg · dL^{-1})[**]	22.7 (14.4)	43 (19.1)	<0.001
no-HDL cholesterol (mg · dL^{-1})	138.7 (35.4)	167.2 (36.8)	<0.001
AIP[††]	−0.035 (0.24)	0.42 (0.24)	<0.001
Uric acid (mg · dL^{-1})	5.7 (1.16)	6.6 (1.11)	<0.001
Leukocytes (mm^3)	6825 (1415.5)	7175 (1508)	<0.001
Creatinine (mg · dL^{-1})	0.97 (0.11)	0.99 (0.10)	<0.039
eGFR × CKD-EPI (mL · min^{-1})[‡‡]	104 (12.9)	99 (12.1)	<0.001

[*]Systolic blood pressure, [†]diastolic blood pressure, [‡]body mass index, [§]high density lipoprotein, [¶]low density lipoprotein, [**]very low density lipoprotein, [††]atherogenic index of plasma, [‡‡]estimated glomerular filtration rate calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

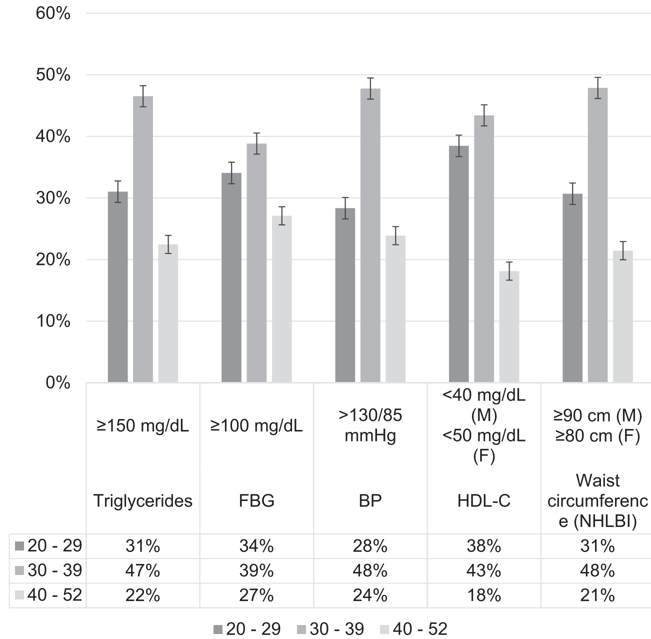

Fig. 1. MetS criteria distribution in age groups.

The prevalence of MetS was 21.7%. The prevalence of MetS in pilots was 17.7%, while in aircrews it was 26% ($P < 0.001$). In the air traffic control population, this frequency was 25%, and in the group of parachutists, it was 16.1%. The prevalence of MetS increases with age, with the lowest counts in the 20–29 yr age group, followed by 26.4% from 30–39 yr of age and 42.6% in older aircrews. The OR for MetS in this population who are older than 30 yr is 3.55 (IC95% 2.81–4.48) and the frequency of hypertriglyceridemia, abdominal obesity, high HDL, high blood pressure, and altered fasting glucose among age groups is shown in **Fig. 1**.

Hypercholesterolemia was found in 36.5% of the study subjects, with an LDL ≥190 mg · dL^{-1} in 1.7% and very low density lipoprotein (V-LDL) >40 mg · dL^{-1} in 14.3%. Low HDL, defined as <40 mg · dL^{-1} in men and <50 mg · dL^{-1} in women, was found in 35.2% overall, and hypertriglyceridemia was 31.1%.

Subjects with MetS have higher mean values of body mass index, fat percentage, lipids, uric acid, leukocytes, and creatinine, and lower glomerular filtration rates than people without the diagnosis. The components of this syndrome tend to appear in the third decade of life, with higher frequencies of hypertriglyceridemia, fasting glycemia, blood pressure, waist circumference, and low HDL ($P < 0.0001$).

Odds ratio of the diagnostic criteria for MetS and other related clinical markers were calculated and the results are shown in **Table II**. There is a significant relationship between MetS and the elevation of uric acid, total cholesterol, LDL, V-LDL, and a lower eGFR using CKD-EPI estimation.

Table II. Odds Ratio of Metabolic Syndrome and Associated Clinical Markers.

VARIABLE	CATEGORIES	METABOLIC SYNDROME OR	95% IC	z STATISTIC
Triglycerides	≥150 mg · dL^{-1}	33.3	24.9–44.6	23.5
HDL[*]	Males <40 mg · dl^{-1} Females <50 mg · dL^{-1}	17.7	13.6–23.2	21.1
Fasting glucose	≥100 mg · dL^{-1}	7.5	5.7–9.8	14.6
Waist circumference	Males: ≥90 cm Females: ≥80 cm	36.6	24.2–55.5	16.9
BP[†]	≥130/85 mmHg	8.0	6.2–10.4	15.8
Uric acid	≥7 mg · dL^{-1}	4.0	3.2–5.1	11.9
eGFR CKD-EPI[‡]	<90 mL · min^{-1}	1.9	1.4–2.4	4.8
Total cholesterol	≥200 mg · dL^{-1}	2.3	1.9–2.9	8.0
LDL[§]	≥190 mg · dL^{-1}	2.3	1.2–4.5	2.4
V-LDL[¶]	>40 mg · dL^{-1}	14.4	10.9–19.0	19.0

[*]High-density lipoprotein cholesterol, [†]blood pressure, [‡]glomerular filtration rate calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, [§]low-density lipoprotein, [¶]very low-density lipoprotein.

Table III. Logistic Regression for MetS in the Highest Quartile of Clinical Markers Compared with the Other Three Quartiles as Reference Group.

VARIABLE	HIGHEST QUARTILE	FREQUENCY OF SUBJECTS WITH HIGHEST QUARTILE	FREQUENCY OF MetS	ADJUSTED* OR (95% CI)
Uric acid	$6.6\,mg \cdot dL^{-1}$	574	472	4.05 (3.26–5.03)
Leukocytes (mm^3)	7590 mm^3	138	472	1.31 (1.05–1.64)
LDL†	$137\,mg \cdot dL^{-1}$	550	443	1.57 (1.24–1.96)
V-LDL‡	$33\,mg \cdot dL^{-1}$	546	442	19.8 (15.3–25.6)
Total cholesterol	$214\,mg \cdot dL^{-1}$	546	472	2.15 (1.73–2.68)

*Adjusted for age and body mass index; †low-density lipoprotein; ‡very low-density lipoprotein.

A logistic regression analysis was performed to estimate the OR of the people with the highest quartile of clinical markers in MetS, which were compared with the other quartiles as a reference value as shown in **Table III**. Lipid profile characteristics such as LDL, V-LDL, and total cholesterol are significantly higher in subjects with MetS.

A negative correlation of uric acid and the glomerular filtration rate calculated with the CKD-EPI using a linear regression was found [$r = -0.306$, $R^2 = 0.094$ ($P < 0.0001$)], as well as a positive correlation with triglycerides [$r = 0.260$, $R^2 = 0.067$ ($P < 0.0001$)].

The receiver operating characteristics of the AIP as a sole marker to identify subjects with MetS has an area under the curve of 0.92. The Youden J Index was 0.73 (95%CI: 0.69–0.75), with a cutoff point ≥0.195, sensibility of 88.4%, specificity of 84.4%, positive predictive value for MetS of 61 (95%CI: 58.2–63.7), negative predictive value of 96.3 (95%CI: 95.3–97.1), positive likelihood ratio (LR) of 5.65 (95%CI: 5–6.3), and negative LR of 0.14 (95%CI: 0.1–0.2). When the AIP is >0.5, the LR is 18.8 (95%CI: 12.6–28.14), as shown in **Fig. 2**.

DISCUSSION

The prevalence of MetS in active military aircrews and air traffic controllers from the Colombian Air Force was 21.7% overall and pilots tend to have lower prevalence (17.7%) in contrast with the general population in Bogota (19.1%) diagnosed with the International Diabetes Federation criteria and 27% in South Americans.[16] The prevalence of MetS in Colombian Air Force pilots is similar compared to Jordanian Air Force pilots with 15.3% and commercial Spanish aircrews,[2,20] and higher than the Korean Air Force (9.9%)[27] and German aircrews.[29] The prevalence found in active parachutists was lower than that of the pilots, with 16.1%, and this is consistent with its counterparts in Iran, which was the lowest in the military and lower than reported in the general population.[29]

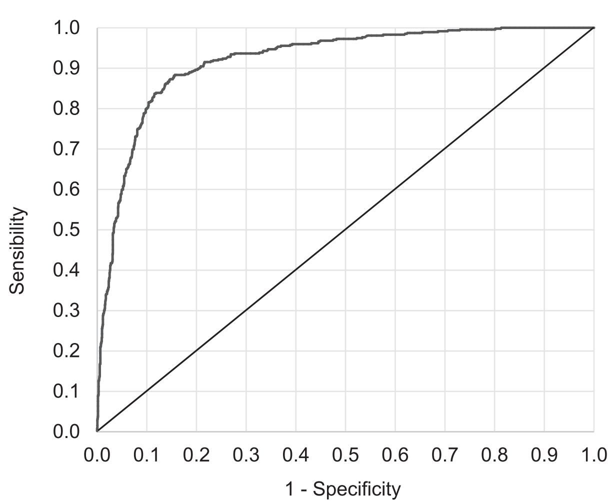

Fig. 2. Receiver operator characteristic curve of the AIP for identifying subjects with MetS.

Aircrews including technicians and maintenance personnel tend to show the highest number of MetS cases, with a frequency of 26%, which is more than other military operational personnel. Lower numbers are found in the Korean Air Force (21.3%),[27] but overall there is a higher count of cases in this population compared to pilots[21] and the same phenomenon can be found in air traffic controllers, who have a higher frequency of MetS in the Colombian Air Force, with 25% compared to the 21.8% of Italian air traffic controllers.[9] This may be attributed to some extent to the healthy worker effect, but many other factors converge, including socioeconomics, education, and income, as suggested by Kim et al.,[21] but more studies are needed to clarify this situation.

MetS frequency increases with age and similar trends have been found in military aircrews in India.[28] The National Health and Nutrition Examination Survey report in 2012 showed a frequency of MetS in Mexican Americans from 18–29 yr to be 12%, and 37% in people within 30–49 yr of age, which is higher than the 16.6% found in this study.[24] The prevalence of abdominal obesity within the subjects with MetS is one of the most frequent findings with 46.2%, followed by high triglycerides in 31%, low HDL in 35.2%, high blood pressure in 14.4%, and high fasting blood glucose in 12.5%, consistent with the frequency observed in a population of Andean Peruvians and Colombians with similar age groups.[15]

There is a significant association with overweight, hyperlipidemias, hyperuricemia, and elevated white blood cell count in this population, which are known contributors of cardiovascular disease[23] and DM. Clinical markers that include elevations of uric acid are found in 40% of personnel with MetS and are broadly found in people with insulin resistance due to its inverse relationship with the urate clearance by the kidneys,[12] and a direct relationship with the deleterious effects on the endothelium, platelet activation, and oxidative metabolism, worse lipid profiles, higher cardiovascular death risk with worse outcomes in both acute and chronic heart failure, overall higher risk for all-cause mortality, and reduction of the glomerular filtration rate.[7]

This study found that there is a negative linear correlation between eGFR calculated using CKD-EPI and serum uric acid, which is thought to contribute to kidney injury[11] and further decreases in glomerular filtration rate, although the current significance is not known in operational personnel because this condition is not expected to impact human performance significantly when kidney function remains within normal limits and, thus, aeromedical certification is not typically affected.

There is evidence that hyperlipidemias, diabetes, HTN, and proinflammatory characteristics are related to poor cognitive outcomes later in life. Declines in working memory, executive functions, visuospatial memory, and fluid intelligence have been shown to be related to MetS.[25] There is also an association between the number of total leukocytes and other white blood cells with MetS in previous research[27] that suggests proinflammatory characteristics of adiposity. This study describes an increase in the average white blood cell count in subjects with hyperlipidemias and MetS that needs to be elucidated in further research to clarify how the inflammatory process influences cognitive decline in older people or participates in the presence of comorbidities such as atherosclerotic cardiovascular disease.[18] Also, this topic needs to be addressed to understand how this process might affect military personnel as this has not been broadly quantified in critical tasks such as the combat pilot population, air traffic control, and unmanned aircraft system operators, although this is not expected to impact aeromedical certification because most operational personnel are younger than 50 yr.

The AIP has not been mentioned broadly in the aerospace medicine literature as a way to establish the presence of MetS, but this marker has been largely described as a predictor of atherosclerosis and an indirect measure for cholesterol esterification rates in apoB-lipoprotein-depleted plasma and lipoprotein particle size,[10] which has been described in people with low insulin sensitivity and has adequate performance in measuring MetS in healthy subjects. This study found that the AIP area under the curve (AUC) is similar to the 0.869 in men and 0.872 in women reported in a multicultural population.[13] The performance of the AIP for the identification of MetS was found to have an AUC of 0.92, a sensitivity of 88.4%, and specificity of 84.4%, with a cutoff point >0.195 and an LR of 18.8 when the AIP is >0.5, which has also been demonstrated in a 9 yr longitudinal study that highlights significant correlation of the AIP with MetS and DM in several multi-variate models[22] and its strong relationship with atherosclerosis in regression analyses in young people in India.[6] The cutoff values of AIP to predict MetS have been identified to be 0.488 in men and 0.332 in women, with a sensitivity of 85.3% in men and 87.2% in women, a specificity of 76% in men and 81.7% in women, and an AUC of 0.87 (CI95% 0.86–0.88) for men and 0.91 (CI95% 0.89–0.92) in women. In people younger than 39 yr, the AIP cutoff value is 0.42 and from 40–64 yr is 0.47 for predicting MetS.[22]

Hypercholesterolemia is a well-established risk factor for cardiovascular disease and the prevalence in this study was similar to the 36% of Colombian commercial pilots as reported by Arteaga-Arredondo et al.[3] and several other studies have found that this frequency varies between 40–70%. Hypertriglyceridemia was estimated to be in 31% of the study subjects compared to the 40% in commercial aviation in Colombia.

One strength of this study is the large subject size as all the aircrew, parachutists, and technicians had to do their annual and biannual aeromedical certification process that includes all these parameters on a yearly basis. Much of these results might change in the future due to the complex dynamics of the society that was largely affected by the COVID-19 pandemic that included lockdown, thus reduced physical exercise and increases in caloric intake. It is recommended to do a follow-up study to compare the frequencies after relaxing strict lockdown rules within the military and to get the whole population vaccinated.

The limitations of this design approach include those of any cross-sectional study and reverse causality cannot be ruled out; nevertheless, entry medical standards would have prevented this from happening. Due to complex operational scenarios, personnel usually do not keep a good record of dietary patterns and this contributor was not considered to explain many of the cases detected here. A prospective design study may reveal how specific proinflammatory markers interact or impact the frequency of comorbidities and possible associations with a slight decrease in cognitive performance in young pilots and its implications for aeromedical certification and operational safety.

The prevention strategies set up by the Colombian effort included a strict policy to recommend regular and moderate intensity physical exercise and follow-up of cardiometabolic measures such as the waist/height index and body mass index by the military operational physician. Even though metabolic profiles are taken every 5 yr in a low cardiovascular risk scenario, due to the high prevalence of MetS, the AIP must be taken into consideration as a marker for a clinical follow-up to evaluate the prevention strategies in place by the organization.

Every situation where there is a diagnosis in personnel with a critical role in aerospace safety must be taken seriously and followed up by a physician. The impact on human performance should include a risk management analysis for aeromedical certification in the decision-making process for declaring fitness for duty by an aerospace medicine specialist.

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