Metabolic Syndrome and Periodontal Disease Among Civilian Pilots

Xi Chen; Lu Xie; Yang Liu; Duanjing Chen; Qing Yu; Xueqi Gan; Haiyang Yu

BACKGROUND: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that can affect civilian pilots' health. Its prevalence and the correlation with periodontal disease (PD) among pilots had not been previously reported. The aim of the study was to determine MetS and PD status, and to reveal their relationship in a representative sample of Chinese civilian pilots.

METHODS: We investigated 303 civilian pilots (mean age 34.92 ± 7.66 yr). General information as well as blood and saliva samples were collected. Diagnostic criteria for MetS were based on the joint interim statements of several medical organizations. Periodontal status was evaluated by Community Periodontal Index (CPI). Measurements included body mass index (BMI), waist circumference (WC), blood pressure (BP), concentration of serum high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting plasma glucose (FPG), saliva matrix metalloproteinase-8, and tissue inhibitors of matrix metalloproteinase-1 (TIMP-1).

RESULTS: Of the subjects, 38.28% showed MetS and 23.10% showed periodontitis. Significant differences were found between the MetS and non-MetS pilots in total flying hours, CPI, WC, BP, TG, HDL-C, FPG, BMI, and TIMP-1. Significant relationships were found between MetS and CPI, BMI, and TIMP-1. The odds ratios were 3.378 (95%CI: 1.889–5924) for CPI, 1.269 (95%CI: 1.101–1.463) for BMI, and 0.600 (95%CI: 0.399–0.904) for TIMP-1.

CONCLUSION: The prevalence of MetS was sufficiently high to be a matter of medical concern, and was associated with PD among civilian pilots.

KEYWORDS: body mass index, tissue inhibitor of metalloproteinase-1, community periodontal index.

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Periodontal disease (PD) is a common chronic dental disease characterized by the gingival inflammatory response against pathogenic bacterial microfloras, resulting in alveolar bone and tooth loss. Matrix metalloproteinases (MMPs) and tissue inhibitor of metalloproteinases (TIMPs) are found in low levels in normal tissues and play a role in many biological processes. A continuous balance exists between MMPs and TIMPs activity in the maintenance of physiological events in an organism. It was documented that MMP activity is regulated by TIMPs, and MMPs are directly responsible for pathogenesis of PD.[17]

It is generally accepted that periodontitis is associated with many systemic diseases. Diabetes mellitus is a risk factor of periodontitis, as well as obesity, high blood pressure, cardiovascular disease (CVD), and so on. According to Chaffee,[2] a higher prevalence of periodontal disease should be expected among obese adults. In a study of 182 adults, severe periodontitis was associated with high blood pressure.[19] Moreover, periodontitis also contributes to atherosclerosis.

Metabolic syndrome (MetS) is an aggregation of multiple pathologic alterations in metabolism accompanied by hemodynamic disorders, including hypertension, dyslipidemia, glucose disorders, and central obesity. In recent years, several epidemiological studies have documented MetS as an aggregated risk factor for cardiovascular disease (CVD), type 2 diabetes mellitus, abnormal chronic inflammatory response, and other systemic diseases. With a prevalence rate of anywhere from 7 to 57%, depending on the definition and study group,[4] MetS can profoundly affect people's health.

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According to the reports, PD shares common risk factors with MetS related to smoking tobacco, poor diet, and lack of physical exercise.[16] A Korean study found that the number of positive parameters of MetS showed significant positive correlation with gingivitis among adolescents.[12] An early U.S. nationwide cross-sectional survey[3] found that severe periodontitis was associated with MetS in middle-aged individuals. It is also reported that MetS may be a risk factor for PD in an older Japanese population, based on data from a 3-yr longitudinal study.[9]

Civilian pilots undergo regular medical examinations to ensure they are healthy enough to fly safely. To the best of our knowledge, few studies have reported on pilots' MetS prevalence, periodontal status, and the association between MetS and PD. To determine MetS and PD status and to reveal their relationship among civilian pilots, we conducted a cross-sectional study.

METHODS

Subjects

The project was approved by the Human Research Ethics Committee of Sichuan University (2011090), and informed consent was obtained from each subject. There were 303 Chinese civilian pilots on duty from Shenzhen Airline who enrolled in the study. All subjects were male, between 23 and 58 yr of age, average 34.92 ($\pm$ 7.66) yr. All the subjects had passed their mandatory annual physical examination. Foreign and retired pilots, as well as those who failed to undergo the requisite examination or questionnaire, were excluded.

Procedure

Subjects were asked to finish the questionnaire and then have the medical examination, including blood test, saliva test, periodontal examination, blood pressure (BP), body mass index (BMI), and waist circumference (WC) measurement.

In the questionnaire, general information, including age, total flying hours, and flight hours for the previous year, was collected. Oral health behavioral information, including toothbrushing frequency, tobacco consumption, and alcohol intake, was obtained. Frequency of brushing teeth was evaluated by six grades: 1 = never or less than once per month, 2 = 1–3 times per month, 3 = once a week, 4 = 2–6 times a week, 5 = once per day, 6 = twice a day or more. Tobacco and alcohol consumption were evaluated by five grades: 1 = every day, 2 = every week, 3 = rarely, 4 = never, 5 = former user. The questionnaire was designed in accordance with the Third National Epidemiological Survey of Oral Health.[18] All questionnaires were reclaimed and checked by a trained investigator.

A blood sample was collected from the antecubital vein after an overnight fast. The serum was separated by centrifugation and stored at $-80°C$. Avoiding strenuous activities, BP was measured three times, and the mean was recorded. BMI was calculated according to the Chinese criteria,[25] obesity was defined by BMI $\geq 28\ kg \cdot m^{-2}$, while overweight was associated with a BMI between 24 and 28. WC was measured at the level of the umbilicus.

Prior to any oral manipulation, saliva samples were collected. Subjects rinsed their mouths with distilled water prior to the collection of unstimulated saliva by passively dripping into a centrifuge tube.[15] Periodontal status was evaluated by the Community Periodontal Index (CPI) according to the WHO criteria.[23] A trained dentist examined the periodontal status of each permanent tooth using the CPI probe (KOU SHEN®, China).Periodontitis was defined as CPI score greater than 2. Duplicate examinations were carried out on 10% of examined subjects about halfway through the survey (kappa value = 0.91) and at the end of the survey (kappa value = 0.88), respectively.

According to the Joint Interim Statements,[1] the diagnostic criteria for Chinese males for MetS include: 1) abdominal obesity (AO) (WC $\geq$ 85 cm); 2) hypertriglyceridemia [triglycerides (TG) $\geq 1.7\ mmol \cdot L^{-1}$]; 3) low level high-density lipoprotein cholesterol (HDL-C) ($< 1.03\ mmol \cdot L^{-1}$ for men); 4) high BP (systolic $\geq$ 130 mmHg or diastolic $\geq$ 85 mmHg); and 5) high level fasting plasma glucose (FPG) ($\geq 5.6\ mmol \cdot L^{-1}$). Subjects were considered to have MetS if they presented more than two of the above factors.

Concentrations of serum HDL-C, TG, and FPG were measured using an automatic biochemical analyzer (Advia 1650, Siemens, USA). The saliva MMP-8 and TIMP-1 were measured with relevant human enzyme-linked immunosorbent assay kits (BlueGene, Shanghai, China) using specific antibodies. Assays were performed according to the manufacturers' recommendations. Absorbance was recorded at 450 nm by a microplate reader (Bio-Tek, ELx800, San Jose, CA). Each sample was measured in triplicate and the average was recorded. The intra-assay and interassay coefficients of variation were maintained lower than 10%.

Statistical Analysis

The SPSS software package (Statistical Package for Social Sciences version 19) (IBM Inc., Chicago, IL) was used for the statistical analysis. First, the mean value, frequency, and percentages of general information, oral health behaviors, and tested parameters were calculated. Second, participants were divided into two groups: the MetS group and the non-MetS group, according to the diagnostic criteria. Rank-sum test, Chi-squared test, and *t*-test were used to investigate the differences between the two groups. Meanwhile, Spearman's correlation was used to reveal the correlation between MetS components and tested factors. The multivariate logistic regression model was used to examine the relationships between the investigated parameters and MetS. $P < 0.05$ was considered statistically significant.

RESULTS

Among the 303 subjects, 116 (38.28%) showed MetS. According to the Joint Interim Statements criteria, 195 (64.36%) subjects had an elevated WC, 140 (46.20%) subjects had a decreased level in HDL-C, 92 (30.36%) subjects had increased FPG level, 86 (28.38%) subjects had high systolic blood pressure (SBP), 84 (27.72%) subjects had increased TG concentration, and 51 (16.83%) subjects had high diastolic blood pressure (DBP). Among the MetS subjects, enlarged WC was the most prevalent (87.93%), followed by decreased HDL-C (74.14%), high TG (56.03%), high SBP (56.03%), high FPG (52.59%), and high DBP (38.79%) (**Fig. 1**).

The prevalence of periodontitis was 23.10% (70/303); 46.55% (54/116) of subjects had periodontitis in the MetS group while 8.56% (16/187) had periodontitis in the non-MetS group. Oral health behavioral characteristics of subjects in both the Mets and non-MetS groups are presented in **Table I**. The MetS group had significantly higher total flying hours, CPI, WC, BP, TG, FPG, and BMI, and lower HDL-C and TIMP-1 than the non-MetS group. No other differences were found.

The relationship between MetS components and tested parameters were also analyzed. Significant results are detailed in **Table II**. It shows that the CPI and BMI were related to each component, while TIMP-1 was related to three of them (FPG, WC, and TG), and total flying hours was related to BP, FPG, and WC.

Those four parameters (total flying hours, CPI, BMI, and TIMP-1) were included in the multivariate logistic regression model to determine their relationship with MetS. Significant results were found with CPI, BMI, and TIMP-1. The odds ratios (ORs) were 3.378 (95%CI: 1.889–5924, $P < 0.01$) for CPI, 1.269 (95%CI: 1.101–1.463, $P < 0.02$) for BMI, and 0.600 (95%CI: 0.399–0.904, $P < 0.001$) for TIMP-1.

DISCUSSION

According to the Joint Interim Statements, 35–41% of adults are reported to have MetS in the United States.[24] Camille et al. reported that the prevalence of MetS was 18.9% in French men.[11] In the Chinese population, a former study in Shanghai reported a 12.1% prevalence among those 32–45 yr of age using the same criteria.[22] In this study, 38.28% of subjects showed MetS, higher than the general population in previous studies. It suggests that civilian pilots are at a considerable risk of MetS, warranting prompt attention.

Based on the questionnaire and oral examination, subjects showed good oral health behavior: the majority of them brushed their teeth twice a day and never consumed tobacco or alcohol. The prevalence of periodontitis (23.10%) was lower compared with the national average.[18] It suggested that most of the subjects showed relatively good oral hygiene and better periodontal status than the entire nation. It is possible that physical screening during pilot enrollment excludes individuals with severe periodontal disease.

Studies reported a significant relationship between MetS and PD. Timonen et al. found that metabolic syndrome and its components were associated with periodontal infection in a large Finnish population.[21] A systematic review of case-controlled, cross-sectional cohort studies and population surveys in patients with MetS and PD showed a positive association between MetS and periodontitis.[16] Han et al. examined the significant relationship between MetS and periodontitis among 167 cases with MetS and 166 healthy controls in a Korean population, and found that the OR of periodontitis (CPI $\geq$ 3) for MetS was 1.76.[8] Kwon et al. also reported a significant association between MetS and periodontitis among 7178 subjects, and revealed that the adjusted OR of periodontitis was 1.55.[10] In the current study, the result shows agreement with former studies that associations do exist between MetS and PD. The study also revealed a stronger association between periodontitis and MetS than those former studies.

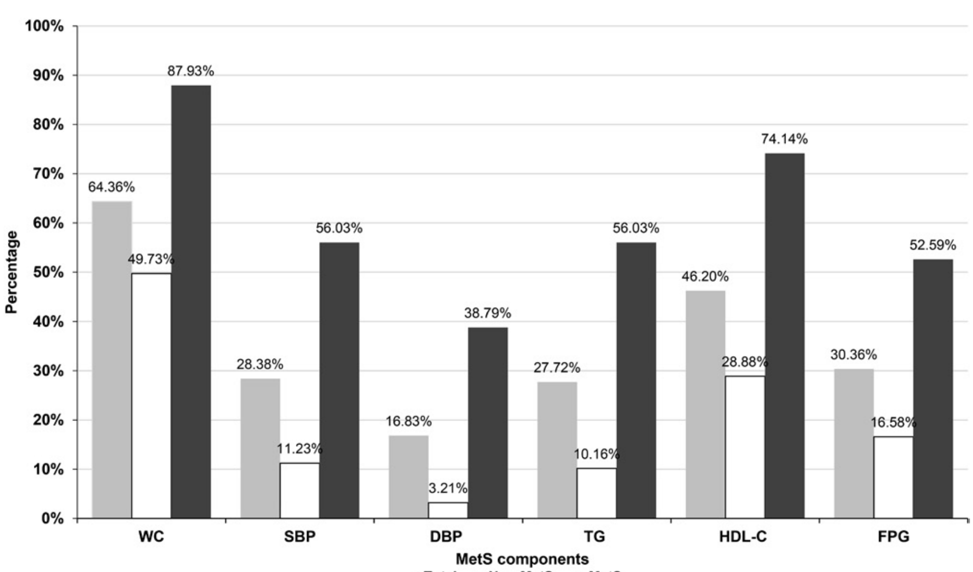

Fig. 1. Comparison of MetS components between the MetS and non-MetS group. The figure shows the percentage of subjects that surpass the diagnosis critera. The diagnosis of MetS is according to the Joint Interim Statements [Waist Circumference (WC) $\geq$ 85cm, Systolic Blood Pressure (SBP) $\geq$ 130 mmHg, Diastolic Blood Pressure (DBP) $\geq$ 85 mmHg, Triglycerides (TG) $\geq$ 1.7 mmol $\cdot$ L^{-1}, HDL-C $<$ 1.03 mmol $\cdot$ L^{-1}, Fasting Plasma Glucose (FPG) $\geq$ 5.6 mmol $\cdot$ L^{-1}].

Our results also showed association between TIMP-1 and MetS. TIMP-1 is found in most tissues and body fluids, but the saliva TIMP-1 was different from plasma TIMP-1, and TIMP-1 in saliva does not originate from plasma. Studies found higher circulating TIMP-1 levels in MetS patients compared with healthy controls.[6] A study suggested that periodontal treatment increased TIMP-1 expression and decreased the ratio of MMP to TIMP-1 in chronic periodontitis patients.[14] A study also reported that substantial reductions in TIMP-1 were found in periodontitis as compared to healthy subjects.[17] This shows a negative relationship between TIMP-1 and PD. According to our results, a negative relationship between TIMP-1

Table I. Comparison of Baseline Characteristics Between the MetS and Non-MetS Groups.

	MetS ($N = 116$)	NON-MetS ($N = 187$)
Age (yr)	35.14 ± 8.23	34.72 ± 7.31
BMI (kg/m^2)	24.78 ± 2.32*	22.89 ± 2.45
Total flying hours	5345.90 ± 3000.00*	3718.48 ± 1953.00
Last-year flight hours	689.00 ± 276.77	677.07 ± 263.20
Tooth-brushing frequency, *N* (%)		
At least twice a day	87(75.00)	126(67.38)
Once a day	24(20.69)	58(31.02)
Hardly ever	5(4.31)	3(1.60)
Tobacco consumption frequency, *N* (%)		
Current smoker	35(33.75)	59(31.55)
Former smoker	13(11.21)	14(7.49)
Never smoker	68(58.75)	114(60.96)
Alcohol consumption frequency, *N* (%)		
Current drinker	26(22.41)	32(17.11)
Former drinker	3(2.59)	4(2.14)
Never drinker	87(75.00)	151(80.75)
WC (cm)	89.21 ± 11.24*	86.56 ± 5.99
SBP (mmHg)	130.00 ± 9.75*	119.42 ± 9.82
DBP (mmHg)	81.48 ± 6.40*	77.83 ± 6.10
HDL-C (mmol · L^{-1})	0.93 ± 0.15*	1.29 ± 2.49
TG (mmol · L^{-1})	2.06 ± 0.82*	1.22 ± 0.62
FPG (mmol · L^{-1})	5.56 ± 0.41*	5.24 ± 0.63
CPI	2.61 ± 0.73*	2.10 ± 0.42
MMP-8 (ng · ml^{-1})	1.45 ± 0.39	1.46 ± 0.36
TIMP-1 (ng · ml^{-1})	1.35 ± 1.28*	2.50 ± 1.47

*Significant difference found between the MetS and non-MetS groups ($P < 0.05$).
BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; TG: triglycerides; FPG: fasting plasma glucose; CPI: Community Periodontal Index; MMP-8: saliva matrix metalloproteinase-8; TIMP-1: matrix metalloproteinase-1.

and MetS was also found. From this perspective, we can deduce that PD may have a possible correlation with MetS. To the best of our knowledge, there have been no studies regarding the relationship between saliva TIMP-1 and MetS (including their components), and their molecular mechanisms will require further research.

A large waist circumference is a sensitive indicator of abdominal obesity. It was often used to evaluate abdominal visceral fat.[5] In the current study, a large WC was the most common symptom among subjects. Abdominal obesity (defined as WC ≥ 85 cm) was present in 195 subjects, among whom only 130 subjects manifested general obesity or overweight (BMI ≥ 24 kg · m^{-2}); 65 AO subjects were not generally obese or overweight and had a normal BMI. This finding indicates that not just generally obese pilots, but even those with normal BMI levels may develop abdominal obesity. BMI represents the severity of obesity without showing the distribution of body fat while WC indicated an increase in visceral fat. Several studies have examined the predictive value of BMI and WC for hypertension, dyslipidemia, and CVD. An Austrian study found that youths with high BMI or high WC were more likely to have abnormal lipid profiles and elevated systolic and diastolic blood pressure compared with normal youths.[7] The current study showed that BMI was associated with MetS and WC is possibly a sensitive indicator of obese status. Pilot's health status should receive due attention when the WC is beyond the cutoff point, even while BMI is still normal.

Table II. Relationship Between MetS Components and Tested Parameters.[†]

COMPONENTS	CPI	TIMP-1	TOTAL FLYING HOURS	BMI
BP	0.420*	-0.014	0.134*	0.188*
FPG	0.245*	-0.135*	0.196*	0.161*
WC	0.248*	-0.182*	0.284*	0.566*
TG	0.336*	-0.143*	0.102	0.191*
HDL-C	0.369*	-0.077	0.044	0.142*

[†] Values are Spearman rank correlation coefficients.
* Significant correlation found between MetS components and tested parameters ($P < 0.05$).
BP: blood pressure; FPG: fasting plasma glucose; WC: waist circumference; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; CPI: Community Periodontal Index; TIMP-1: matrix metalloproteinase-1; BMI: body mass index.

Flying is a unique occupational feature for pilots. To the best of our knowledge, no data has been found to reveal the relationship between flying time and MetS. In our study, significant difference was found between the MetS and non-MetS groups in total flying hours, and flying hours have positive correlation with BP, FPG, and WC, but no significant association with MetS. It indicated that hypertension, hyperglycemia, or abdominal obesity had a tendency to occur with the cumulating of total flying hours. This might be because of the circadian disruption caused by flying. According to recent studies, disruption of diurnal rhythms due to shift work or frequent time zone traveling could regulate the gut microbiota populations, which is related to obesity, insulin resistance, and so on.[13,20] Our results also showed that flying may have direct effects on the human body as well, though it makes no significant contribution to MetS. This might be because pilots are working in a special environment in which pressure, temperature, oxygen, or humidity inside chambers is different from the ground. Besides, in-flight noises, radiation, hyper-gravity, or hypogravity might be possible risk factors of the above symptom as well. However, the exact etiology are still remaining to be further elucidated.

One limitation of this study was the cross-sectional survey design, which does not allow confirmation of conclusions. Despite the assurance that the results of this study would not affect a pilot's career, we believe that some pilots may have exaggerated the number of daily tooth-brushing and under-reported their smoking or drinking habits. Further follow-up research is expected to confirm the results observed and the follow-up outcomes should be used for further evaluation of the related factors.

In conclusion, the prevalence of MetS was sufficiently high to be a matter of medical concern, and MetS was associated with PD among civilian pilots.

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Authors X. Chen and L. Xie contributed equally to this work.

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