Correlations between the properties of saliva and metabolic syndrome

A prospective observational study

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Abstract
Saliva tests, which are easy to perform and non-invasive, can be used to monitor both oral disease (especially periodontal disease) and physical conditions, including metabolic syndrome (MetS). Therefore, in the present study the associations between saliva test results and MetS were investigated based on medical health check-up data for a large population. In total, 1,888 and 2,296 individuals underwent medical check-ups for MetS and simultaneous saliva tests in 2017 and 2018, respectively. In the saliva tests, the buffer capacity of saliva, salivary pH, the salivary white blood cell count, the number of cariogenic bacteria in saliva, salivary occult blood, protein, and ammonia levels were tested using a commercially available kit. The relationships between the results of the saliva tests and MetS components were examined in cross-sectional and longitudinal multivariate analyses. Significant relationships were detected between salivary protein levels and serum HbA1c levels or blood pressure levels and between the buffer capacity of saliva and serum triglyceride levels. In addition, salivary pH was increased irreversibly by impaired renal function. This study suggested that saliva tests conducted during health check-ups of large populations might be a useful screening tool for periodontal disease and MetS/MetS components.

Abbreviations: CKD = chronic kidney disease, DM = diabetes mellitus, HDL-C = high-density lipoprotein cholesterol, MetS = metabolic syndrome, SMT = salivary Multi Test, WBC = white blood cell.

Keywords: saliva test, metabolic syndrome, medical check-up, blood pressure, screening, periodontal disease

1. Introduction
Metabolic syndrome (MetS) is a complex medical disorder, which is defined as the presence of three out of five interrelated conditions attributed to visceral fat-type obesity, including hypertension and abnormal glucose and lipid metabolism.[1–2] MetS was reported to increase the risk of cardiovascular disease, including atherosclerotic cardiovascular disease, and type 2 diabetes mellitus (DM).[3–4] The prevalence of MetS has increased worldwide.[5] In 2011–2012, the estimated prevalence of MetS in the USA was 34.7% and increased with age; that is, it was 18.3% in adults aged 20 to 39 years and 46.7% in those aged ≥60 years.[6] In middle-aged Japanese individuals, the prevalence of MetS was reported to be 14.9%.[7]

Periodontitis is a pathological infectious inflammatory disease, which causes the destruction of periodontal tissue and can lead to tooth loss.[9] In previous studies,[7–9,11] a close correlation was detected between periodontitis and MetS, and individuals with MetS have been reported to present with a worse periodontal status, including a higher prevalence of periodontitis, more severe periodontitis, and more wide-ranging periodontitis.[10] Many chronic diseases, including periodontitis, hypertension, and DM, are influenced by common risk factors including diet, smoking, alcohol, a lack of exercise, and stress.[12,13] It has been reported that chronic systemic inflammation might predispose individuals with periodontal disease to develop components of MetS or vice versa.[14] Therefore, investigations and health public policies targeting MetS and periodontitis are important for promoting public health.

Saliva tests are easy to conduct and non-invasive, and it has been reported that such tests can produce clinically significant information relating to both systemic and oral disease.[15–21] Many researchers have reported that saliva-based screening tests are useful for diagnosing periodontitis.[15–21] As stated above,
periodontitis and MetS are closely related and influenced by the same common risk factors\[22\]. Previously, we reported the effectiveness of incorporating dental check-ups into health check-ups and detected a significant association between periodontitis and MetS.\[11\] These results suggested that saliva tests could be used to monitor not only periodontal conditions, but also physical conditions related to MetS. Therefore, the purpose of the present study was to investigate the associations between the results of saliva tests and MetS based on medical health check-up data for a large population.

2. Materials and methods

The protocol of the present study was approved by the Committee on Medical Research of Shinshu University (2775). Individuals who underwent specific health check-ups (health check-ups for MetS) in the Japanese cities Azumino and Shiojiri between 2017 and 2018 were invited to participate in the study. All of the subjects, which included self-employed workers, farmers, and the elderly, were insured by the Japanese national health insurance system and were aged ≥25 years. They all provided written informed consent before participating in this study. The subjects underwent saliva tests during their health check-ups. The health check-ups were conducted according to the standard program provided by the Ministry of Health, Labour and Welfare of Japan (2013).\[23\] They included an interview on lifestyle and systemic disease treatment status (including on medication for hypertension, lipid abnormalities, or hyperglycemia); height, weight, abdominal circumference, and blood pressure measurements; and blood tests (of triglyceride, high-density lipoprotein cholesterol [HDL-C], blood sugar, hemoglobin A1c [HbA1c], and creatinine levels).

Regarding the saliva tests, each saliva sample was collected with 3 ml of mouthwash and was immediately evaluated using a commercially available test kit [Salivary Multi Test [SMT]; LION Dental Products Co., Ltd., Tokyo, Japan]. The saliva tests were performed according to the manufacturer’s protocols and were used to evaluate the buffer capacity of saliva; the number of cariogenic bacteria present in saliva; salivary pH; salivary occult blood, protein, and ammonia levels; and the salivary white blood cell (WBC) count. The test kit consisted of test strips and a measuring device. In this test, the color changes that occur in each pad of the test strip are assessed by measuring reflectance at a specific wavelength. Specifically, the number of cariogenic bacteria present in saliva is evaluated based on the reduction of resazurin sodium by Gram-positive bacteria. The salivary pH is assessed based on the color change exhibited by a pH indicator. The buffer capacity is determined based on the color change exhibited a compound pH indicator in the presence of a fixed quantity of acid. The salivary occult blood level is assessed by measuring pseudo-peroxidase activity in hemoglobin. The WBC count is evaluated by measuring leukocyte esterase activity, the salivary protein level is determined based on the “protein error of indicators” phenomenon. The salivary ammonia level is assessed based the color change seen after the addition of bromocresol green. The principles underlying the measurement of each parameter are summarized in Figure 1. The results of the saliva tests are expressed as percentages (0–100) and were classified into three categories (high, moderate, and low), according to the values established by the manufacturer.\[24\] Individuals who had been eating/drinking, had brushed their teeth, or had gargled within 2 two hours before the salivary test were excluded from the study because these might have affected the test results. The dental examination also included assessments of dental and periodontal conditions by well-trained dentists. The grade of

| Test item               | Measurement principle                                                                 | Detection range       |
|------------------------|----------------------------------------------------------------------------------------|-----------------------|
| **Cariogenic bacteria**| Resazurin reduction by bacteria                                                        | Resorufin (magenta)   | 10⁶ - 10⁹ cfu/mL |
| **Acidity**            | pH indicator                                                                            | pH 6.0 - 8.0          |
| **Buffer capacity**    | Combined pH indicator                                                                  | pH 2.8 - 6.0          |
| **Blood**              | CHP + TMBZ                                                                             | H₂O+Cumene+Oxidized TMBZ (blue) | 0 - 0.50 mg/dL |
| **Leukocyte**          | TAI Leukocyte esterase Hydrolysis                                                       | Indoxyl               | 0 - 200 U/L     |
| **Protein**            | Protein + TCTIF (light pink) Acid Complex formation (red)                               | 0 - 60 mg/dL          |
| **Ammonia**            | Ammonium ion Alkaline                                                                  | Ammonia gas + BCG     | 1 - 10,000 N-µg/dL |

**Figure 1.** Detection principle of the Salivary Multi Test. □: Detected substance [□] Ingredient in test strip. CHP: cumene hydroperoxide, TMBZ: 3,3’5,5’- tetramethylbenzidine, TAI: 3-[4-(touene-4-sulfonyl]-L- alanine-indole, MMIB: 2-methoxy-4-[4-(morpholino)benzenediazonium, TCTIF: 4,5,5,7-tetrachloro-2’,4’,6’,7’-tetrachlorofluorescin disodium salt, BCG: bromocresol green, cfu: colony forming unit.
periodontal disease was assessed according to the World Health Organization (WHO) Community Periodontal Index (CPI) criteria. PD was measured using standard WHO probes. Periodontal disease was diagnosed according to the CPI code: Code 0 (healthy periodontal condition) was judged as healthy, Codes 1 and 2 (with gingival bleeding on probing, BOP) as gingivitis, and Codes 3 and 4 (PD ≥ 4 mm) as periodontitis.

The results of the salivary test were compared with the results of the health check-up in the cross-sectional analysis. In addition, in the longitudinal analysis, the relationships between the changes in the salivary test results and the changes in the health check-up results were analyzed in the individuals who underwent examinations in both 2017 and 2018. In this study, the interyear changes in the salivary test results that occurred between 2017 and 2018 were classified into the four following categories:

- Remained high: “high” in both 2017 and 2018
- Increased: “moderate/low” in 2017 and “high” in 2018
- Decreased: “high” in 2017 and “moderate/low” in 2018
- Remained low: “moderate/low” in both 2017 and 2018

Statistical analyses were performed using JMP ver.13 (SAS Institute Inc., NC). In the cross-sectional analysis, the correlations between the results of the salivary test and the health check-up results were examined using univariate analyses (Spearman’s rank correlation coefficient) and multivariate analysis involving common risk (confounding) factors. In the longitudinal analysis, the correlations between the interyear changes in the results of the salivary test and the interyear changes in the health check-up parameters (the value obtained in 2018 minus the value obtained in 2017) were evaluated using univariate analyses (including the Tukey-Kramer HSD test) and multivariate analysis of common risk factors (sex, age in 2017, change in BMI, and change in smoking habits). P values of < .05 were considered to indicate statistical significance.

3. Results

Among the individuals who underwent the health check-up, 1,887 (24.0%) out of the 7,848 individuals who underwent the health check-up in 2017 and 2,279 (32.2%) out of the 7,084 individuals who underwent the health check-up in 2018 consented to saliva tests and participated in the study. The subjects’ characteristics and the results of the salivary tests are summarized in Table 1.

3.1. The results of the cross-sectional analysis

The correlations between systolic or diastolic blood pressure and the results of the salivary test are shown in Tables 2 and 3. This analysis included the data from the subjects who were not taking antihypertensive medication (n=1,374). Although in the univariate analyses weak but significant correlations were observed between systolic or diastolic blood pressure and the buffer capacity of saliva (diastolic blood pressure: P < .05), the salivary levels of occult blood (systolic blood pressure: P < .05; diastolic blood pressure: P < .05), protein (systolic blood pressure: P < .01; diastolic blood pressure: P < .05), or ammonia (systolic blood pressure: P < .01; diastolic blood pressure: P < .01), the multivariate analysis did not reveal any significant correlations between these parameters. The only significant correlation found in the multivariate analysis was between systolic blood pressure and the number of cariogenic bacteria in saliva (P < .05), even though no such correlation was detected in the univariate analysis.

### Table 1

| Characteristics of studied subjects. | 2017 Number (%) | 2018 Number (%) |
|--------------------------------------|-----------------|-----------------|
| Number of subjects received the specific health check-ups | 7,848 | 7,084 |
| Number of subjects received salivary examination | 1,887 (24.0) | 2,279 (32.2) |
| Gender | | |
| Male | 875 (46.3) | 1,119 (49.1) |
| Female | 1,012 (53.7) | 1,160 (50.9) |
| Age | | |
| Average ±SD | 64.8 ±12.9 | 67.6 ±11.7 |
| Range | 25-95 | 29-96 |
| Results of the salivary examination using SMT | 1,887 | 2,279 |
| Cariologenic bacteria | | |
| Much | 994 (52.7%) | 1,051 (46.1%) |
| Average | 495 (26.2%) | 542 (23.8%) |
| Little | 399 (21.1%) | 686 (30.1%) |
| Acidity | | |
| Much | 1,239 (65.3%) | 1,571 (69.9%) |
| Average | 430 (22.8%) | 485 (21.3%) |
| Little | 219 (11.6%) | 223 (9.8%) |
| Buffer capacity | | |
| Much | 757 (40.1%) | 921 (40.4%) |
| Average | 640 (33.9%) | 788 (34.6%) |
| Little | 491 (26.0%) | 570 (25.0%) |
| Occult blood | | |
| Much | 941 (49.9) | 1,253 (55.0) |
| Average | 506 (31.6) | 693 (30.4) |
| Little | 350 (18.5) | 333 (14.6) |
| White blood cell | | |
| Much | 1,050 (55.6) | 1,253 (55.0) |
| Average | 546 (28.9) | 708 (31.1) |
| Little | 291 (15.4) | 318 (14.0) |
| Protein | | |
| Much | 1,253 (66.4) | 1,463 (64.2) |
| Average | 395 (20.9) | 528 (23.2) |
| Little | 239 (12.7) | 288 (12.6) |
| Ammonium | | |
| Much | 1,541 (81.7) | 1,658 (81.5) |
| Average | 253 (13.6) | 312 (13.7) |
| Little | 93 (4.9) | 109 (4.8) |

SD: standard deviation.

The correlations between serum triglyceride or HDL-C levels and the results of the salivary test are shown in Tables 4 and 5. This analysis included the data for the subjects who were not taking antihyperlipidemic medication (n=1,345). The weak but significant or nearly significant correlations were observed between serum triglyceride or HDL-C levels and salivary buffer capacity (serum HDL-C level: P < .05), the salivary levels of occult blood (serum triglyceride level: P = .053) or HDL-C level: P = .05) and between the serum HDL-C level and the salivary WBC count (serum triglyceride level: P < .05; serum HDL-C level: P = .058) in the univariate analyses. However, the multivariate analysis only showed nearly significant correlations between the serum triglyceride (P = .053) or HDL-C (P = .091) level and the salivary WBC count. In addition, the multivariate analysis revealed significant correlations between the serum triglyceride level and salivary buffer capacity (P < .05) and between the serum HDL-C level and salivary pH (P < .05) or the salivary ammonia level (P < .01); however, no significant correlations were observed between these parameters in the univariate analyses.
### Table 2

**Correlation between systolic blood pressure and results of salivary multi test in those who had no antihypertensive medication (n = 1,374).**

| Level       | n   | Average | SE  | 95% CI        | r   | P value | Estimate | SE   | t value | P value |
|-------------|-----|---------|-----|---------------|-----|---------|----------|-------|---------|---------|
| **Systolic blood pressure** |     |         |     |               |     |         |          |       |         |         |
| Cariogenic bacteria | Much | 703     | 122.0 | 0.62 | 120.8 – 123.2 | -0.005 | .853    |          |       |         |         |
| Average      | 362  | 122.2   | 0.86  | 120.5 – 123.9 |       |         |          |       |         |         |
| Little       | 309  | 122.6   | 0.93  | 120.8 – 124.4 |       |         |          |       |         |         |
| **Acidity**  |     |         |     |               |     |         |          |       |         |         |
| Much         | 912  | 121.9   | 0.5   | 120.9 – 123.0 | -0.026 | .342    |          |       |         |         |
| Average      | 310  | 122.6   | 0.9   | 120.7 – 124.4 |       |         |          |       |         |         |
| Little       | 152  | 123.1   | 1.3   | 120.5 – 125.7 |       |         |          |       |         |         |
| **Buffer capacity** |     |         |     |               |     |         |          |       |         |         |
| Much         | 508  | 123.5   | 0.7   | 122.1 – 125.0 | -0.026 | .342    |          |       |         |         |
| Average      | 471  | 122.6   | 0.8   | 121.1 – 124.1 |       |         |          |       |         |         |
| Little       | 395  | 120.0   | 0.8   | 118.4 – 121.6 |       |         |          |       |         |         |
| **Occult Blood** |     |         |     |               |     |         |          |       |         |         |
| Much         | 638  | 123.5   | 0.6   | 122.2 – 124.8 | 0.117 | <.01    |          |       |         |         |
| Average      | 460  | 122.1   | 0.8   | 120.6 – 123.6 |       |         |          |       |         |         |
| Little       | 276  | 119.4   | 1.0   | 117.5 – 121.3 |       |         |          |       |         |         |
| **Protein**  |     |         |     |               |     |         |          |       |         |         |
| Much         | 854  | 123.4   | 0.6   | 122.3 – 124.5 | 0.111 | <.01    |          |       |         |         |
| Average      | 321  | 121.2   | 0.9   | 119.4 – 122.9 |       |         |          |       |         |         |
| Little       | 199  | 118.6   | 1.2   | 116.4 – 120.9 |       |         |          |       |         |         |
| **Leukocyte** |     |         |     |               |     |         |          |       |         |         |
| Much         | 734  | 122.5   | 0.6   | 121.3 – 123.7 | 0.031 | .252    |          |       |         |         |
| Average      | 411  | 122.3   | 0.8   | 120.7 – 123.9 |       |         |          |       |         |         |
| Little       | 229  | 121.0   | 1.1   | 118.9 – 123.1 |       |         |          |       |         |         |
| **Ammonia**  |     |         |     |               |     |         |          |       |         |         |
| Much         | 1088 | 123.1   | 0.5   | 122.1 – 124.0 | 0.111 | <.01    |          |       |         |         |
| Average      | 209  | 119.9   | 1.1   | 117.7 – 122.1 |       |         |          |       |         |         |
| Little       | 77   | 116.2   | 1.9   | 112.6 – 119.8 |       |         |          |       |         |         |

**Univariate analysis**

**Spearman’s rank correlation**

**Multivariate analysis**

SE: standard error; CI: confidence interval.

### Table 3

**Correlation between diastolic blood pressure and results of salivary multi test in those who had no antihypertensive medication (n = 1,374).**

| Level       | n   | Average | SE  | 95% CI        | r   | P value | Estimate | SE   | t value | P value |
|-------------|-----|---------|-----|---------------|-----|---------|----------|-------|---------|---------|
| **Diastolic blood pressure** |     |         |     |               |     |         |          |       |         |         |
| Cariogenic bacteria | Much | 703     | 73.9 | 0.41 | 73.1 – 74.7 | -0.004 | .880    |          |       |         |         |
| Average      | 362  | 74.1    | 0.57 | 73.0 – 75.3 |       |         |          |       |         |         |
| Little       | 309  | 74.3    | 0.62 | 73.1 – 75.5 |       |         |          |       |         |         |
| **Acidity**  |     |         |     |               |     |         |          |       |         |         |
| Much         | 912  | 73.9    | 0.36 | 73.2 – 74.6 | -0.024 | .380    |          |       |         |         |
| Average      | 310  | 74.2    | 0.62 | 73.0 – 75.4 |       |         |          |       |         |         |
| Little       | 152  | 74.8    | 0.88 | 73.0 – 76.5 |       |         |          |       |         |         |
| **Buffer capacity** |     |         |     |               |     |         |          |       |         |         |
| Much         | 508  | 74.8    | 0.48 | 73.8 – 75.7 | 0.06  | <.05    |          |       |         |         |
| Average      | 471  | 74.3    | 0.50 | 73.3 – 75.2 |       |         |          |       |         |         |
| Little       | 395  | 72.9    | 0.55 | 71.8 – 74.0 |       |         |          |       |         |         |
| **Occult Blood** |     |         |     |               |     |         |          |       |         |         |
| Much         | 638  | 74.6    | 0.43 | 73.7 – 75.4 | 0.065 | <.05    |          |       |         |         |

**Univariate analysis**

**Spearman’s rank correlation**

**Multivariate analysis**

(continued)
### Table 3 (continued)

| Univariate analysis | Multivariate analysis |
|---------------------|-----------------------|
| **Diastolic blood pressure** | **Spearman’s rank correlation** | **Estimate** | **SE** | **t value** | **P value** |
| Level | n | Average | SE | 95% CI | r | P value | | | | | |
| **Leukocyte Much** | 854 | 74.5 | 0.37 | 73.8 | 75.2 | 0.069 | <.05 | | | | |
| Average | 321 | 74.0 | 0.61 | 72.8 | 75.2 | | | | | | |
| Little | 199 | 72.3 | 0.77 | 70.8 | 73.8 | | | | | | |
| **Ammonia Much** | 1088 | 74.5 | 0.33 | 73.9 | 75.2 | 0.086 | <.01 | | | | |
| Average | 226 | 72.9 | 0.75 | 71.4 | 74.3 | | | | | | |
| Protein Much | 842 | 116.1 | 2.44 | 111.3 | 117.9 | 0.036 | .156 | | | | |
| Average | 226 | 111.0 | 4.71 | 101.8 | 120.3 | | | | | | |
| Little | 84 | 100.1 | 7.73 | 84.9 | 115.2 | | | | | | |

SE: standard error; CI: confidence interval.

### Table 4

**Correlation between triglyceride and results of salivary multi test in those who had no antihyperlipidemic medication (n = 1,545).**

| Univariate analysis | Multivariate analysis |
|---------------------|-----------------------|
| **Triglyceride** | **Spearman’s rank correlation** | **Estimate** | **SE** | **t value** | **P value** |
| Level | n | Average | SE | 95% CI | r | P value | | | | | |
| **Cariogenic bacteria Much** | 797 | 110.3 | 2.51 | 105.4 | 115.2 | −0.011 | .680 | | | | |
| Average | 414 | 116.0 | 3.48 | 109.2 | 122.9 | | | | | | |
| Little | 334 | 114.6 | 3.88 | 107.0 | 122.2 | | | | | | |
| **Acidity** | 1033 | 113.9 | 2.21 | 109.6 | 118.3 | 0.013 | .696 | | | | |
| Average | 336 | 110.9 | 3.87 | 103.4 | 118.5 | | | | | | |
| Little | 176 | 109.3 | 5.35 | 98.8 | 119.8 | | | | | | |
| **Buffer capacity** | 506 | 113.3 | 2.91 | 107.6 | 119.0 | 0.016 | .527 | | | | |
| Average | 517 | 111.8 | 3.12 | 105.7 | 117.9 | | | | | | |
| Little | 452 | 113.2 | 3.41 | 106.5 | 119.9 | | | | | | |
| **Occult Blood** | 755 | 117.5 | 2.57 | 112.5 | 122.5 | 0.087 | <.01 | | | | |
| Average | 488 | 113.1 | 3.20 | 106.8 | 119.4 | | | | | | |
| Little | 302 | 100.4 | 4.07 | 92.4 | 108.4 | | | | | | |
| **Protein Much** | 992 | 116.8 | 2.25 | 112.4 | 121.2 | 0.083 | <.01 | | | | |
| Average | 324 | 107.8 | 3.87 | 100.3 | 115.4 | | | | | | |
| Little | 219 | 102.2 | 4.78 | 92.9 | 111.5 | | | | | | |
| **Leukocyte Much** | 842 | 116.1 | 2.44 | 111.3 | 120.9 | 0.054 | <.05 | | | | |
| Average | 226 | 111.0 | 4.71 | 101.8 | 117.9 | | | | | | |
| Little | 84 | 100.1 | 7.73 | 84.9 | 115.2 | | | | | | |
| **Ammonia Much** | 1235 | 113.9 | 2.02 | 110.0 | 117.9 | 0.036 | .156 | | | | |
| Average | 226 | 111.0 | 4.71 | 101.8 | 120.3 | | | | | | |
| Little | 84 | 100.1 | 7.73 | 84.9 | 115.2 | | | | | | |

SE: standard error; CI: confidence interval.
Table 5
Correlation between HDL-cholesterol and results of salivary multi test in those who had no antihyperlipidemic medication (n=1,545).

| Level          | n   | Average | SE  | 95%CI  | r    | P value | Estimate | SE    | t value | P value |
|----------------|-----|---------|-----|--------|------|---------|----------|-------|---------|---------|
| HDL-cholesterol|     |         |     |        |      |         |          |       |         |         |
| Cariogenic bacteria | Much | 797    | 63.6 | 0.58  | 62.4 - 64.7 | -0.014 | .580   | 0.174    | 0.460 | 0.38   | .706    |
|                | Average | 414    | 63.8 | 0.80  | 62.2 - 65.4 |      |         | 4.260    | 0.387 | 11     | <.01    |
|                | Little   | 334    | 63.8 | 0.89  | 62.1 - 65.6 |      |         | -0.067   | 0.028 | -2.03  | <.05    |
|                |          |        |      |        |        |        |          |       |         |         |
| Acidity        | Much    | 1033   | 63.5 | 0.51  | 62.5 - 64.5 | -0.009 | .723   | -1.096   | 0.536 | -2.04  | <.05    |
|                | Average  | 336    | 64.2 | 0.89  | 62.5 - 66.0 |      |         | 3.344    | 0.389 | 11.17  | <.01    |
|                | Little   | 176    | 63.9 | 1.22  | 61.5 - 66.3 |      |         | -0.060   | 0.028 | -2.13  | <.05    |
|                |          |        |      |        |        |        |          |       |         |         |
| Protein        | Much    | 596    | 62.7 | 0.66  | 61.4 - 64.0 | -0.002 | <.05   | 0.563    | 0.487 | 1.16   | .247    |
|                | Average  | 517    | 63.8 | 0.71  | 62.4 - 65.2 |      |         | 3.339    | 0.393 | 11.04  | <.01    |
|                | Little   | 432    | 64.8 | 0.78  | 63.3 - 66.4 |      |         | -0.067   | 0.030 | -2.26  | <.05    |
|                |          |        |      |        |        |        |          |       |         |         |
| Occult Blood   | Much    | 755    | 62.2 | 0.59  | 61.1 - 63.4 | -0.107 | <.01   | -0.785   | 0.489 | -1.61  | .109    |
|                | Average  | 488    | 64.3 | 0.73  | 62.8 - 65.7 |      |         | 4.256    | 0.387 | 10.94  | <.01    |
|                | Little   | 302    | 66.4 | 0.93  | 64.6 - 68.3 |      |         | -0.045   | 0.029 | -1.58  | <.15    |
|                |          |        |      |        |        |        |          |       |         |         |
| Leukocyte      | Much    | 842    | 63.1 | 0.56  | 62.0 - 64.2 | -0.048 | .058   | -0.834   | 0.493 | -1.69  | .091    |
|                | Average  | 449    | 63.9 | 0.77  | 62.4 - 65.4 |      |         | 4.275    | 0.387 | 11.05  | <.01    |
|                | Little   | 254    | 65.3 | 1.02  | 63.3 - 67.2 |      |         | -0.048   | 0.028 | -1.7   | .089    |
|                |          |        |      |        |        |        |          |       |         |         |
| Ammonia        | Much    | 1235   | 63.8 | 0.46  | 62.9 - 64.7 | 0.008  | .766   | 1.984    | 0.699 | 2.84   | <.01    |
|                | Average  | 226    | 63.6 | 1.08  | 61.4 - 65.7 |      |         | 4.347    | 0.387 | 11.22  | <.01    |
|                | Little   | 84     | 62.8 | 1.77  | 59.3 - 66.3 |      |         | -0.079   | 0.029 | -2.71  | <.01    |
|                |          |        |      |        |        |        |          |       |         |         |

SE: standard error CI: confidence interval.

The correlations between the serum HbA1C level and the results of the salivary test are shown in Table 6. This analysis included the data for the subjects who were not taking antidiabetic medication (n=1,769). A significant correlation was found between the serum HbA1C level and salivary buffer capacity in both the univariate and multivariate analyses (univariate analysis: P<.01; multivariate analysis: P<.05). In addition, a significant correlation between the serum HbA1C level and the salivary protein level was detected in the univariate analysis (univariate analysis: pH: univariate analysis, P<.01, multivariate analysis, P<.01; buffer capacity: univariate analysis, P<.01, and multivariate analysis, P<.01). Although weak but significant correlations were observed between the serum creatinine level and the number of cariogenic bacteria in saliva (P<.05), the salivary occult blood level (P<.01), the salivary protein level (P<.01), and the salivary ammonia level (P<.01) in the univariate analyses, no such correlations between these parameters were detected in the multivariate analysis.

3.2. The results of the longitudinal analysis

The correlations between the interyear changes in systolic and diastolic blood pressure and the interyear changes in the salivary test results are shown in Tables 8 and 9. This analysis included the data for the subjects who were not taking antihypertensive medication in either 2017 or 2018 (n=539). The interyear change in systolic blood pressure was significantly correlated with the interyear changes in the salivary protein level (P<.01) and WBC count (P<.01), whereas diastolic blood pressure was significantly correlated with the interyear change in the salivary protein level (P<.01). The subjects that exhibited high salivary protein levels and WBC counts in both 2017 and 2018 had elevated blood pressure, while those with low salivary protein levels and WBC counts displayed decreased blood pressure in both years.
### Table 6
Correlation between HbA1c and results of salivary multi test in those who had no antidiabetic medication (n = 1,769).

| Level                  | Average | SE    | 95% CI | Spearman's rank correlation r | P value | Estimate | SE    | t value | P value |
|------------------------|---------|-------|--------|-------------------------------|---------|----------|-------|---------|---------|
| Cariogenic bacteria    |         |       |        | Cariogenic bacteria            | 0.001   | 0.13     | 0.17  | .895    |         |
| Mean                   | 926     | 0.72  | 0.02   | 5.69 – 5.75                   | 0.017   | .483     |       |         |         |
| Acidity                |         |       |        | Acidity                        |         |          |       |         |         |
| Mean                   | 1156    | 0.72  | 0.01   | 5.69 – 5.74                   | –0.018  | .451     |       |         |         |
| Buffer capacity        |         |       |        |                                |         |          |       |         |         |
| Mean                   | 1156    | 0.72  | 0.01   | 5.69 – 5.74                   | –0.018  | .451     |       |         |         |
| Leukocyte              |         |       |        |                                |         |          |       |         |         |
| Mean                   | 980     | 5.74  | 0.03   | 5.63 – 5.76                   | 0.129 . | <.01     |       |         |         |
| Occult Blood           |         |       |        |                                |         |          |       |         |         |
| Mean                   | 870     | 5.74  | 0.02   | 5.71 – 5.77                   | 0.079 . | <.01     |       |         |         |
| Protein                |         |       |        |                                |         |          |       |         |         |
| Mean                   | 1427    | 5.74  | 0.01   | 5.71 – 5.76                   | 0.157 . | <.01     |       |         |         |
| Leukocyte              |         |       |        |                                |         |          |       |         |         |
| Mean                   | 980     | 5.74  | 0.02   | 5.71 – 5.77                   | 0.061 . | <.05     |       |         |         |
| Ammonia                |         |       |        |                                |         |          |       |         |         |
| Mean                   | 1427    | 5.74  | 0.01   | 5.71 – 5.76                   | 0.135 . | <.01     |       |         |         |

SE: standard error, CI: confidence interval.

### Table 7
Correlation between serum creatinine and results of salivary multi test (n = 1,888).

| Level                  | Average | SE    | 95% CI | Spearman's rank correlation r | P value | Estimate | SE    | t value | P value |
|------------------------|---------|-------|--------|-------------------------------|---------|----------|-------|---------|---------|
| Acidity                |         |       |        |                                |         |          |       |         |         |
| Mean                   | 1239    | 0.71  | 0.01   | 0.69 – 0.72                   | –0.160  | <.01     |       |         |         |
| Buffer capacity        |         |       |        |                                |         |          |       |         |         |
| Mean                   | 757     | 0.78  | 0.01   | 0.76 – 0.80                   | 0.209 . | <.01     |       |         |         |

(continued)
Table 7
(continued).

| Univariate analysis | Multivariate analysis |
|---------------------|-----------------------|
| Level               | n | Average | SE  | 95% CI | r   | P value | Estimate | SE  | t value | P value |
| occult blood        |   |         |     |        |    |         |          |     |         |         |
| Much                | 940| 0.75    | 0.01| 0.73  | -  | 0.76    | 0.080    |     | <.01    |         |
| age (years)         |   |          |     |        |    |         |          |     |         |         |
| BMI (kg/m2)         |   |          |     |        |    |         |          |     |         |         |
| Smoking (no/yes)    |   |          |     |        |    |         |          |     |         |         |
| protein             |   |          |     |        |    |         |          |     |         |         |
| Much                | 1254| 0.74    | 0.01| 0.73  | -  | 0.76    | 0.067    |     | <.01    |         |
| age (years)         |   |          |     |        |    |         |          |     |         |         |
| BMI (kg/m2)         |   |          |     |        |    |         |          |     |         |         |
| Smoking (no/yes)    |   |          |     |        |    |         |          |     |         |         |
| leukocyte           |   |          |     |        |    |         |          |     |         |         |
| Much                | 1050| 0.73    | 0.01| 0.71  | -  | 0.74    | 0.001    |     | .959    |         |
| age (years)         |   |          |     |        |    |         |          |     |         |         |
| BMI (kg/m2)         |   |          |     |        |    |         |          |     |         |         |
| Smoking (no/yes)    |   |          |     |        |    |         |          |     |         |         |
| ammonia             |   |          |     |        |    |         |          |     |         |         |
| Much                | 1539| 0.74    | 0.01| 0.73  | -  | 0.75    | 0.114    |     | <.01    |         |
| age (years)         |   |          |     |        |    |         |          |     |         |         |
| BMI (kg/m2)         |   |          |     |        |    |         |          |     |         |         |
| Smoking (no/yes)    |   |          |     |        |    |         |          |     |         |         |

SE: standard error, CI: confidence interval.

Table 8
Correlation between the interval change of systolic blood pressure and that of salivary multi test in those who had no antihypertensive medication (n = 539).

| Univariate analysis | Multivariate analysis |
|---------------------|-----------------------|
| Interval change of Systolic blood pressure | Tukey-Kramer HSD |
| n | Average | SE  | 95% CI | P value | Estimate | SE  | t value | P value |
| calorie             |          |     |        |         |          |     |         |         |
| increased           | 136      | 1.169| 1.079 | −0.950  | 3.288    | NS  |         |         |
| change in smoking habit |          |     |        |         |          |     |         |         |
| sex (woman/man)     |          |     |        |         |          |     |         |         |
| age (years)         |          |     |        |         |          |     |         |         |
| BMI (kg/m2)         |          |     |        |         |          |     |         |         |
| smoking (no/yes)    |          |     |        |         |          |     |         |         |
| buffer capacity     |          |     |        |         |          |     |         |         |
| increased           | 77       | −0.558| 1.435 | −3.378  | 2.261    | NS  |         |         |
| change in Battery   |          |     |        |         |          |     |         |         |
| sex (woman/man)     |          |     |        |         |          |     |         |         |
| age (years)         |          |     |        |         |          |     |         |         |
| BMI (kg/m2)         |          |     |        |         |          |     |         |         |
| smoking (no/yes)    |          |     |        |         |          |     |         |         |
| occult blood        |          |     |        |         |          |     |         |         |
| increased           | 168      | 0.881| 0.968 | −1.021  | 2.783    | NS  |         |         |
| change in occult     |          |     |        |         |          |     |         |         |
| sex (woman/man)     |          |     |        |         |          |     |         |         |
| age (years)         |          |     |        |         |          |     |         |         |
| BMI (kg/m2)         |          |     |        |         |          |     |         |         |
| smoking (no/yes)    |          |     |        |         |          |     |         |         |
| protein             |          |     |        |         |          |     |         |         |
| increased           | 233      | 2.498| 0.815 | 0.898   | 4.098    | <.01|         |         |
| change in protein   |          |     |        |         |          |     |         |         |
| sex (woman/man)     |          |     |        |         |          |     |         |         |
| age (years)         |          |     |        |         |          |     |         |         |
| BMI (kg/m2)         |          |     |        |         |          |     |         |         |
| smoking (no/yes)    |          |     |        |         |          |     |         |         |
| leukocyte           |          |     |        |         |          |     |         |         |
| increased           | 93       | 1.538| 1.296 | −1.008  | 4.083    | <.05|         |         |
| change in leucocyte  |          |     |        |         |          |     |         |         |
| sex (woman/man)     |          |     |        |         |          |     |         |         |

(continued)
The correlations between the interyear changes in the serum levels of triglycerides or HDL-C and the interyear changes in the saliva test results are shown in Tables 10 and 11. This analysis included the data for the subjects who were not taking antihyperlipidemic medication in either 2017 or 2018 (n=608).

A significant inverse correlation was found between the interyear change in the serum triglyceride level and the interyear change in the buffer capacity of saliva in the multivariate analysis (P < .05), even though no significant correlation between these parameters was detected in the univariate analysis.
### Table 10
Correlation between the interval change of triglyceride and that of salivary multi test in those who had no antihyperlipidemic medication (n=608).

| Univariate analysis | Interval change of triglyceride | Tukey-Kramer HSD | Multivariate analysis |
|---------------------|---------------------------------|------------------|----------------------|
|                      | n  | Average | SE | 95%CI | P value | Estimate | SE | t value | P value |
| Carriogenic bacteria | Remain high | 157 | 3.02 | 4.50 | –5.82 | –11.85 | NS | | |
|                      | Increased | 100 | 2.34 | 5.64 | –8.73 | –13.41 | | | |
|                      | Decreased | 150 | 8.43 | 4.60 | –0.61 | –17.47 | | | |
|                      | Remain low | 201 | 1.53 | 3.98 | –9.14 | –6.47 | | | |
|                    | Acidity | Remain high | 300 | 3.24 | 3.62 | –3.16 | –9.64 | NS | |
|                      | Increased | 111 | 0.84 | 5.36 | –9.69 | –11.36 | | | |
|                      | Decreased | 86  | 6.44 | 6.09 | –5.51 | –18.40 | | | |
|                      | Remain low | 111 | 0.77 | 5.36 | –9.76 | –11.29 | | | |
|                    | Buffer capacity | Remain high | 85 | –8.35 | 6.10 | –20.34 | –3.63 | NS | |
|                      | Increased | 83  | 6.40 | 6.17 | –5.73 | –18.52 | | | |
|                      | Decreased | 95  | 0.73 | 5.77 | –12.06 | –10.61 | | | |
|                      | Remain low | 345 | 5.66 | 3.03 | –0.29 | –11.61 | | | |
|                    | Occult Blood | Remain high | 214 | 1.21 | 3.84 | –6.34 | –8.76 | NS | |
|                      | Increased | 106 | 1.80 | 5.46 | –12.53 | –8.93 | | | |
|                      | Decreased | 68  | 17.21 | 6.82 | 3.81 | –30.60 | | | |
|                      | Remain low | 220 | 2.12 | 3.79 | –5.32 | –9.57 | | | |
|                    | Protein | Remain high | 287 | 3.42 | 3.33 | –3.12 | –9.96 | NS | |
|                      | Increased | 60  | 7.27 | 7.28 | –7.03 | –21.56 | | | |
|                      | Decreased | 77  | 7.42 | 6.43 | –5.21 | –20.04 | | | |
|                      | Remain low | 182 | 1.54 | 4.16 | –9.70 | –6.63 | | | |
|                    | Leukocyte | Remain high | 228 | 4.04 | 3.73 | –3.30 | –11.37 | NS | |
|                      | Increased | 99  | 7.80 | 5.67 | –3.33 | –18.93 | | | |
|                      | Decreased | 99  | 3.11 | 5.67 | –8.02 | –14.24 | | | |
|                      | Remain low | 182 | 1.63 | 4.18 | –9.04 | –6.58 | | | |
|                    | Ammonia | Remain high | 416 | 3.71 | 2.77 | –1.72 | –9.15 | NS | |
|                      | Increased | 65  | 0.12 | 7.00 | –13.63 | –13.88 | | | |
|                      | Decreased | 65  | 3.12 | 7.00 | –10.63 | –16.88 | | | |
|                      | Remain low | 62  | 0.82 | 7.17 | –14.90 | –13.26 | | | |

SE: standard error CI: confidence interval, NS: not significant HSD: honestly significant difference

4. Discussion

Saliva is widely used for diagnostic purposes, monitoring systemic disease status, and predicting disease progression. The purpose of this study was to investigate the associations between the results of saliva tests and MetS based on medical health check-up data for a large population. Both the longitudinal and cross-sectional studies showed a significant relationship between salivary protein levels and serum HbA1c levels. The subjects with higher serum HbA1c levels had higher salivary protein levels. The SMT was used to measure three items (the salivary levels of occult blood and protein and the salivary WBC count) as markers of periodontal disease. In a study involving the SMT, periodontal pocket depth, bleeding on probing, and the Community Periodontal Index were reported to be correlated with salivary occult blood and protein levels as well as the salivary WBC count. Salivary occult blood and protein levels and the salivary WBC count are considered to be markers of inflammation in periodontal tissue. Salivary protein levels and the salivary WBC count are considered to be markers of inflammation in periodontal tissue.

[26] Suzuki et al. Medicine (2020) 99:51
Table 11
Correlation between the interval change of HDL-cholesterol and that of salivary multi test in those who had no antihyperlipidemic medication (n=608).

| Protein | Remain high | 157 | -0.09 | 0.89 | -1.83 | - | 1.65 | NS | Change in cariogenic bacteria |
|---------|-------------|-----|-------|-------|--------|---|--------|---|-----------------------------|
|         | Increased   | 100 | -0.62 | 1.11 | -2.80 | - | 1.56 | NS | Sex (woman/man) |
|         | Decreased   | 150 | -0.56 | 0.91 | -2.34 | - | 1.22 | NS | age (2017) |
|         | Remain low  | 201 | 1.03  | 0.78 | -0.51 | - | 2.57 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Ammonia | Remain high | 300 | 0.36  | 0.64 | -0.90 | - | 1.62 | NS | Change in acidity |
|         | Increased   | 111 | 0.08  | 1.06 | -1.99 | - | 2.16 | NS | Sex (woman/man) |
|         | Decreased   | 86  | -0.33 | 1.20 | -2.68 | - | 2.03 | NS | age (2017) |
|         | Remain low  | 111 | -0.57 | 1.06 | -2.45 | - | 1.71 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Leukocyte | Remain high | 85  | 0.11  | 1.21 | -2.27 | - | 2.48 | NS | Change in Buffer capacity |
|         | Increased   | 83  | 0.10  | 1.22 | -2.30 | - | 2.50 | NS | Sex (woman/man) |
|         | Decreased   | 95  | 0.56  | 1.14 | -1.69 | - | 2.80 | NS | age (2017) |
|         | Remain low  | 345 | -0.06 | 0.60 | -1.14 | - | 1.11 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Occult Blood | Remain high | 214 | 0.49  | 0.76 | -1.00 | - | 1.98 | NS | Change in occult blood |
|         | Increased   | 106 | -0.84 | 1.08 | -2.96 | - | 1.28 | NS | Sex (woman/man) |
|         | Decreased   | 68  | -0.51 | 1.35 | -3.16 | - | 2.14 | NS | age (2017) |
|         | Remain low  | 220 | 0.30  | 0.75 | -1.17 | - | 1.78 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Protein | Remain high | 287 | -0.36 | 0.65 | -1.64 | - | 0.93 | NS | Change in protein |
|         | Increased   | 60  | 0.58  | 1.43 | -2.23 | - | 3.40 | NS | Sex (woman/man) |
|         | Decreased   | 77  | 2.58  | 1.26 | 0.10  | - | 5.07 | NS | age (2017) |
|         | Remain low  | 184 | -0.46 | 0.82 | -2.06 | - | 1.15 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Leukocyte | Remain high | 228 | 0.00  | 0.74 | -1.45 | - | 1.44 | NS | Change in leukocyte |
|         | Increased   | 99  | -0.45 | 1.12 | -2.65 | - | 1.74 | NS | Sex (woman/man) |
|         | Decreased   | 99  | 0.90  | 1.12 | -1.30 | - | 3.10 | NS | age (2017) |
|         | Remain low  | 182 | 0.03  | 0.83 | -1.59 | - | 1.65 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |
| Ammonia | Remain high | 416 | -0.32 | 0.54 | -1.39 | - | 0.75 | NS | Change in ammonia |
|         | Increased   | 65  | 3.37  | 1.37 | 0.67  | - | 6.07 | NS | Sex (woman/man) |
|         | Decreased   | 65  | -0.48 | 1.37 | -3.18 | - | 2.22 | NS | age (2017) |
|         | Remain low  | 62  | -0.11 | 1.41 | -2.88 | - | 2.65 | NS | Change in BMI |
|         |             |     |       |       |        |   |       |   | Change in smoking habit |

CI = confidence interval, HSD = honestly significant difference, NS = not significant, SE = standard error.

In addition, many investigators have suggested that a two-way relationship exists between DM and periodontal disease. Previously, it was reported that salivary protein concentration was higher in DM patients with HbA1c levels of >0.7% than in those with HbA1c levels of <0.7%. It was also stated that the increase in the salivary protein concentration was due to a reduction in salivary secretion and inflammatory oral conditions, including periodontitis. In a prospective Japanese cohort study conducted over three years, it was suggested that the progression of periodontal disease might be associated with blood pressure in the univariate analyses. These findings suggested that a causal relationship exists between higher salivary protein levels and increased blood pressure/hypertension. As stated above, the salivary protein level is a marker of periodontal disease.

In this study, the longitudinal analysis revealed significant correlations between the interyear change in systolic blood pressure and the interyear changes in the salivary protein level and WBC count, and between the interyear change in diastolic blood pressure and the interyear change in the salivary protein level. In the cross-sectional analysis, significant relationships were observed between the salivary levels of protein or occult blood and blood pressure in the univariate analyses. These findings suggested that a causal relationship exists between higher salivary protein levels and increased blood pressure/hypertension. It was also suggested that a two-way relationship exists between DM and periodontal disease. A few previous studies have investigated the associations among hypertension, blood pressure, and periodontal disease. In a prospective Japanese cohort study conducted over three years, it was suggested that the progression of periodontal disease might be associated with blood pressure. In another four-year longitudinal study involving Japanese employees, the worsening of hypertension was also reported to be correlated with the presence of periodontal pockets. On the other hand, it was reported that there was no association between periodontal measurements and hypertension in a cohort study of middle-aged health-professionals. Although the precise mechanism responsible for the association between hypertension and periodontal disease remains uncertain, increased levels of C-reactive protein,
A significant relationship was observed between salivary protein level and the serum triglyceride level in both the cross-sectional and longitudinal analyses. The buffer capacity of saliva was also lower in the subjects with higher levels of triglycerides.

The salivary protein level was found to be inversely correlated with the salivary pH levels. This finding is consistent with the literature, which suggests that saliva with a higher protein content has a lower pH.

Buffer capacity is an important parameter that reflects the buffering capacity of saliva. Increased buffer capacity is associated with reduced pH changes, which could be beneficial in maintaining oral health.

The correlation between salivary protein level and systolic blood pressure was also noted, indicating that a high protein level might be related to higher blood pressure.

Furthermore, the salivary protein level, which is affected by age, smoking habits, and medications, was found to be correlated with changes in systolic and diastolic blood pressure.

The results of this study suggested that the salivary protein level, the salivary occult blood level, and WBC count are important parameters that can be used to monitor inflammatory processes and metabolic conditions.

In conclusion, the measurement of salivary protein level and other markers can provide valuable information about the systemic health status, which is important for the early detection and management of various diseases.

### Table 12

| Parameter          | Baseline | Change | Estimate | SE | P value |
|--------------------|----------|--------|----------|----|---------|
| Protein            | Decreased| 98     | 0.03     | 0.03| 0.03    |
| Blood pressure     | Decreased| 79     | 0.03     | 0.03| 0.03    |
| Acidosis           | Increased| 124    | 0.02     | 0.02| 0.02    |
| Acidity            | Increased| 135    | 0.02     | 0.02| 0.02    |
| Carbohydrates      | Increased| 117    | 0.02     | 0.02| 0.02    |

**Note:**
- Decreased indicates a decrease in the parameter from baseline.
- Increased indicates an increase in the parameter from baseline.
- NS indicates not significant.
- P value indicates the significance level of the change from baseline.
association between salivary and serum urea levels was reported in previous studies. A significant relationship between creatinine level and the pH or buffer capacity of saliva. Both salivary pH and buffer capacity were higher in the CKD patients. In one study, which was based on health check-up data for a large population, is the first to demonstrate the utility of saliva tests for screening individuals for MetS/MetS components as well as periodontal disease. However, it had some limitations. Another limitation was the cut-off values used for each test item in the SMT. In the SMT, the detection for salivary components. Another limitation was the standard error.

CI = confidence interval, HSD = honestly significant difference, NS = not significant, SE = standard error.

and serum lipid levels. These results indicate that associations exist between serum triglyceride levels and the salivary flow rate/ salivary pH.

In the present study, the cross-sectional analysis (multivariate analysis) revealed a significant relationship between the serum creatinine level and the pH or buffer capacity of saliva. Both salivary pH and salivary buffer capacity were higher in the subjects with higher serum creatinine levels/decreased renal function. Previous studies have assessed salivary flow, pH, and buffer capacity in chronic kidney disease (CKD) patients. In one study, the CKD patients exhibited hypoalimentation and increased salivary pH and buffer capacity. Our results were consistent with the latter study. In CKD patients, the blood tends to become acidic (due to metabolic acidosis) as renal function degrades, and metabolic acidosis is a common finding. Therefore, we speculated that the salivary pH might decrease as the serum creatinine level increases. However, our results showed the opposite, as was demonstrated in previous studies. A significant association between salivary and serum urea levels was reported to exist in pre-dialysis patients. The hydrolysis of nitrogen compounds by bacterial urease has been reported to result in the production of carbon dioxide and ammonium ions, leading to increased alkalizing potential. Impaired renal function might also affect salivary flow and salivary properties, which can result in saliva becoming alkaline.

The present study, which was based on health check-up data for a large population, is the first to demonstrate the utility of saliva tests for screening individuals for MetS/MetS components as well as periodontal disease. However, it had some limitations. For example, we used a commercially available saliva test kit. The test kit had a limited analytical ability and limited ranges of detection for salivary components. Another limitation was the cut-off values used for each test item in the SMT. In the SMT, the salivary WBC count and the salivary levels of occult blood, protein, and ammonia were classified into three grades. Further studies involving more sophisticated methods are required.

In conclusion, correlations between the results of saliva tests and the results of health check-ups for MetS were revealed in a large population study. A longitudinal study revealed significant correlations between salivary protein levels and serum HbA1c
levels or blood pressure. In addition, a significant correlation was detected between the buffer capacity of saliva and the serum triglyceride level. Salivary pH increased irreversibly in subjects detected between the buffer capacity of saliva and the serum levels or blood pressure. In addition, a significant correlation was detected between the buffer capacity of saliva and the serum triglyceride level. Salivary pH increased irreversibly in subjects detected between the buffer capacity of saliva and the serum levels or blood pressure. In addition, a significant correlation was detected between the buffer capacity of saliva and the serum levels or blood pressure.
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