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Original article

Combined association of oral and skeletal muscle health with type 2 diabetes mellitus among community-dwelling older adults in Japan: a cross-sectional study

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Abstract

Objective: Although oral health and skeletal muscle status are known to be risk factors for type 2 diabetes mellitus (T2DM), there is limited information on their combined effects among community-dwelling older adults. The purpose of this study was to investigate the association between oral health and skeletal muscle status among older adults with T2DM in Japan.
Participants and Methods: This cross-sectional study included data from individuals aged ≥60 years. T2DM was defined as a glycosylated hemoglobin A1c level ≥48 mmol/mol (≥6.5%) or the use of hypoglycemic agents. For oral health status, dental hygienists assessed the number of teeth (NT) and masticatory function (MF). Skeletal muscle status was assessed using skeletal muscle mass index (SMI) and handgrip strength (HGS). Logistic regression analysis examined T2DM in nine-category combinations of oral health status (each of the three categories in NT and MF) and skeletal status (each of the three categories in SMI and HGS).
Results: T2DM was prevalent in 83 participants (16.4%) and was significantly associated with low NT and SMI (odds ratio [OR] = 5.93, 95% confidence interval [CI]: 1.37–25.73) and low MF and SMI (OR = 4.48, 95% CI: 1.23–16.35) compared to high NT and SMI and high MF and SMI, respectively.
Conclusion: Our findings indicate that low muscle mass with tooth loss or masticatory dysfunction is associated with T2DM among community-dwelling older adults. This suggests that maintaining oral health and muscle mass may be an effective strategy for the prevention of T2DM.

Key words: teeth loss, oral health, mastication, health check-up, diabetes

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Introduction

Type 2 diabetes mellitus (T2DM) is one of the most pressing health issues affecting more than 500 million people worldwide[1]. It is an independent risk factor for cardiovascular disease[2], which is a major cause of mortality among patients with T2DM[3]. Therefore, preventing its onset is an important public health issue.

The literature shows that previous studies have reported that muscle mass and strength are associated with T2DM[4–7], and their loss with increasing age is regarded as one of the causes of chronic diseases. Because skeletal muscles play a key role in improving insulin sensitivity and preventing resistance[8, 9], maintaining muscle mass and strength may help prevent the development of T2DM in older adults.

In addition, periodontal disease and T2DM are known to have a potential and bidirectional association[10–12]. Periodontal disease causes a decrease in the number of teeth (NT)[13, 14], which may affect diabetic status if masticatory

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function (MF) is not maintained as its reduction has been reported to be associated with T2DM[15]. Moreover, worsening oral health has been independently associated with T2DM.

Although oral health and skeletal muscle health have been studied before in terms of their independent association with T2DM, to the best of our knowledge, the combined relationship among these three factors has not been examined in an older population. We hypothesized that older adults with poor oral health and skeletal muscle status are more likely to develop T2DM. There is a need to identify the relationship between these two combined factors and T2DM to provide information on the high-risk population for the benefit of public health practices. Therefore, this study aimed to examine whether there is a combined effect of oral and skeletal muscle health on the prevalence of T2DM among community-dwelling older adults in Japan.

Participants and Methods

Participants

This cross-sectional study was part of the cohort study (Shimane CoHRE Study) conducted by the Center for the Community-based Healthcare Research and Education, Shimane University. This study collected data from a health checkup conducted in June 2016 in Ohnan town, Shimane, Japan. In total, 732 older adults aged 60–74 years participated in the health checkup. We excluded participants with missing data on study variables (n=227), such as skeletal muscle status (n=93), oral health status (n=45), and education (n=79). The study protocol was approved by the Ethics Committee of Shimane University (approval number: 2888), and written informed consent was obtained from all participants before enrollment. This study was conducted in accordance with the Declaration of Helsinki.

Type 2 diabetes mellitus

T2DM screening was carried out by measuring serum glycosylated hemoglobin A1c (HbA1c) levels according to the recommendations of the Ministry of Health, Labour, and Welfare[16]. Trained nurses and public health practitioners assessed the use of hypoglycemic agents based on face-to-face interviews. In this study, T2DM was defined as an HbA1c level ≥6.5% or by the self-reported use of hypoglycemic agent(s).

Skeletal muscle status

Skeletal muscle mass index (SMI) was measured with a body composition meter using bioimpedance analysis (MC-780A; Tanita Corporation, Tokyo, Japan). The SMI was estimated based on the appendicular lean mass divided by height in meters squared. Handgrip strength (HGS) was measured twice for each hand, and the data used were based on the maximum HGS. SMI and HGS were divided into three groups according to the tertile cut-off points for each sex.

Oral health status

A trained dental hygienist examined the oral health status of the participants, with both the examiner and participant in a seated position. NT was counted, excluding the third molars and missing teeth. Participants were divided into three categories: NT-high (≥21 teeth), NT-middle (1–20 teeth), and NT-low (0 teeth), as per a previous study[17]. Objective MF was assessed using a gelatinous candy, where participants were instructed to chew with maximal effort. It was then collected after 15 sec and the number of pieces was counted[18, 19]. Participants were divided into three categories: MF-high (women: ≥26 pieces, men: ≥31 pieces), MF-middle (women: 16–25 pieces, men: 16–30 pieces), and MF-low (women and men: ≤15 pieces), according to the tertiles of each sex.

Additional data

Sex, age, current smoking status, alcohol consumption (assessed using the question "how often do you drink?"), and years of education (≥12 years or <12 years) were evaluated using a questionnaire. Body mass index (BMI) was calculated from the recorded height and weight (kg/m^2). Hypertension was defined as a systolic blood pressure of at least 140 mmHg, a diastolic blood pressure of at least 90 mmHg, or by the self-reported use of antihypertensive medications[20].

Statistical analyses

Descriptive data were analyzed to assess the differences in the prevalence of T2DM as a function of demographic characteristics using chi-square tests for categorical variables and the Mann–Whitney U test for continuous variables. We used combined analyses to evaluate the strength of the associations among skeletal muscle, oral health status, and T2DM. Multivariate adjusted logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for T2DM in the nine category combinations of SMI (high/middle/low), NT (high/middle/low), MF (high/middle/low), and HGS (high/middle/low). We used model 1, which was adjusted for sex, age, and BMI. Model 2 was further adjusted for smoking, alcohol intake, hypertension, and education. Before the logistic regression analysis was conducted, correlations among the variables were assessed to examine multicollinearity. All statistical analyses were conducted using IBM SPSS Statistics for Windows (version 24.0; IBM Corp., Armonk, NY, USA), and statistical significance was set at a *P*-value of <0.05.

Results

A total of 505 participants were included in the study. Table 1 shows the participant characteristics according to

T2DM status. Only 16.4% (n=83) of the participants had T2DM. There were significant differences in terms of sex (P<0.01), BMI (P<0.01), alcohol consumption (P=0.02), hypertension (P=0.02), and years of education (P=0.03). No differences in age, current smoking status, SMI, HGS, NT, and MF were observed. Individuals with missing data were significantly more likely to be younger than those without missing data (P<0.01). No other differences were found in terms of sex (P=0.84), BMI (P=0.16), or T2DM (P=0.05) (Table 1).

The combined associations between oral health status, SMI, and T2DM are shown in Table 2. After adjusting for sex, age, and BMI in model 1, T2DM was found to be associated with SMI-low in the NT-low group (OR=6.99, 95% CI: 1.65–29.72), compared to SMI-high in the NT-high group (standard reference). T2DM was found to be associated with SMI-low in the NT-low group even after adjusting for all confounders in model 2 (OR=5.93, 95% CI: 1.37–25.73). T2DM was associated with SMI-low in the MF-low group in model 1 (OR=5.09, 95% CI: 1.44–18.04), compared to the SMI-high in the MF-high group (standard reference). This association was significant in model 2 (OR=4.48, 95% CI: 1.23–16.35) (Table 2).

The combined associations between oral health status, HGS, and T2DM are shown in Table 3. After adjusting for sex, age, and BMI in model 1, T2DM was found to be associated with HGS-middle in the NT-high (OR=2.26, 95% CI: 1.02–4.99), HGS-middle in the NT-low (OR=5.38, 95% CI: 1.21–23.93), and HGS-low in the NT-low (OR=3.20, 95% CI: 1.14–9.02) groups, compared to SMI-high in the HGS-high group (standard reference). After adjusting for all confounders in model 2, T2DM was not found to be associated with any of the combined variables. There were no significant associations between the combined variables of HGS and MF (Table 3).

Table 1 Characteristics of participants included in the study

Variables[1] n (%)		Total	No T2DM	T2DM[2]	P-value[3]
		505 (100)	422 (83.6)	83 (16.4)	
Basic parameters					
Sex, n (%)	Female	291 (57.6)	256 (88.0)	35 (12.0)	<0.01
	Male	214 (42.4)	166 (77.6)	48 (22.4)	
Age	Years	69.9 (3.6)	69.8 (3.6)	70.5 (3.6)	0.12
BMI[4]	kg/m^2	22.7 (3.2)	22.5 (3.1)	23.7 (3.5)	<0.01
Current smoking, n (%)	No	459 (90.9)	388 (84.5)	71 (15.5)	0.06
	Yes	46 (9.1)	34 (73.9)	12 (26.1)	
Alcohol drinking, n (%)	Rarely/no	234 (46.3)	192 (82.1)	42 (17.9)	0.02
	Sometimes	106 (21.0)	98 (92.5)	8 (7.5)	
	Daily	165 (32.7)	132 (80.0)	33 (20.0)	
Hypertension, n (%)	No	248 (49.1)	217 (87.5)	31 (12.5)	0.02
	Yes	257 (50.9)	205 (79.8)	52 (20.2)	
Education, n (%)	≥12 years	376 (74.5)	322 (85.6)	54 (14.4)	0.03
	<12 years	129 (25.5)	100 (77.5)	29 (22.5)	
Skeletal muscle status, n (%)					
Skeletal muscle mass index	High	167 (33.1)	137 (82.0)	30 (18.0)	0.79
	Middle	170 (33.7)	144 (84.7)	26 (15.3)	
	Low	168 (33.3)	141 (83.9)	27 (16.1)	
Handgrip strength	High	162 (32.1)	144 (88.9)	18 (11.1)	0.07
	Middle	174 (34.5)	143 (82.2)	31 (17.8)	
	Low	169 (33.5)	135 (79.9)	34 (20.1)	
Oral health status, n (%)					
Number of teeth	High	316 (62.6)	268 (84.8)	48 (15.2)	0.21
	Middle	132 (26.1)	111 (84.1)	21 (15.9)	
	Low	57 (11.3)	43 (75.4)	14 (24.6)	
Masticatory function	High	159 (31.5)	140 (88.1)	19 (11.9)	0.08
	Middle	175 (34.7)	147 (84.0)	28 (16.0)	
	Low	171 (33.9)	135 (78.9)	36 (21.1)	

[1] Data shown as mean (standard deviation) for continuous and number (percentage) for categorical variables. [2] Type 2 diabetes, defined by HbA1c ≥6.5%, or taking hypoglycemic agents. [3] Statistical significance of the differences between those with and without T2DM was determined using Mann–Whitney U test for continuous data and χ^2-test for categorical data. P<0.05 shown in bold. [4] Body mass index.

Table 2 Combined associations of oral health status and skeletal muscle mass index with type 2 diabetes mellitus

			n	T2DM[1], %	Model 1[2]		Model 2[3]	
					OR	(95% CI)[4]	OR	(95% CI)
Number of Teeth[5]								
High								
	SMI[6]	High	105	17.1	1.00	(Reference)	1.00	(Reference)
		Middle	107	13.1	1.38	(0.58–3.30)	1.47	(0.61–3.52)
		Low	104	15.4	2.47	(0.91–6.67)	2.36	(0.86–6.47)
Middle								
	SMI	High	43	18.6	0.93	(0.36–2.44)	0.94	(0.36–2.47)
		Middle	40	17.5	1.64	(0.57–4.69)	1.55	(0.53–4.54)
		Low	49	12.2	1.57	(0.49–5.07)	1.46	(0.45–4.75)
Low								
	SMI	High	19	21.1	1.02	(0.29–3.61)	1.04	(0.29–3.75)
		Middle	23	21.7	1.91	(0.56–6.49)	1.59	(0.44–5.77)
		Low	15	33.3	**6.99**	**(1.65–29.72)**	**5.93**	(1.37–25.73)
Masticatory Function[7]								
High								
	SMI	High	42	14.3	1.00	(Reference)	1.00	(Reference)
		Middle	57	10.5	1.25	(0.34–4.61)	1.35	(0.36–5.04)
		Low	60	11.7	1.78	(0.45–6.96)	1.70	(0.42–6.88)
Middle								
	SMI	High	62	21.0	1.34	(0.44–4.05)	1.35	(0.44–4.15)
		Middle	61	16.4	1.81	(0.54–5.99)	1.76	(0.52–5.95)
		Low	52	9.6	1.52	(0.36–6.44)	1.50	(0.35–6.50)
Low								
	SMI	High	63	17.5	1.01	(0.33–3.15)	0.99	(0.31–3.15)
		Middle	52	19.2	1.98	(0.59–6.65)	1.85	(0.52–6.56)
		Low	56	26.8	**5.09**	**(1.44–18.04)**	**4.48**	(1.23–16.35)

[1] Type 2 diabetes, defined by HbA1c ≥6.5%, or taking hypoglycemic agents. [2] Adjusted for sex, age, and body mass index. [3] Adjusted for model 1, current smoking, alcohol drinking, hypertension, and education. [4] Odds ratios and 95% confidence intervals were estimated using logistic regression. P<0.05 shown in bold. [5] Categorized into high (≥21 teeth), middle (1–20 teeth), and low (0 teeth). [6] Skeletal muscle mass index. [7] Categorized into three groups by tertiles depending on sex.

Discussion

This study is the first to examine the combined effect of oral health and skeletal muscle status on T2DM among older adults in Japan. The analysis showed that low NT and SMI were associated with T2DM, as were low MF and SMI. However, HGS did not show this association. Our findings suggest that the maintenance of both SMI as skeletal muscle and NT or MF as oral health may be an effective strategy for the primary prevention of T2DM in older adults living in rural areas.

Previous studies have shown that skeletal muscles are involved in improving insulin sensitivity and preventing resistance[8, 9]. Loss of muscle mass, the tissue that stores glucose after intestinal absorption, causes glucose to remain in the blood, hence increasing postprandial blood levels[21, 22]. In older adults, the maintenance and improvement of muscle mass and strength through physical exercise may help to prevent the onset of T2DM. In cases of worsening oral health, such as loss of teeth and masticatory dysfunction, the surge in soft meals or glucose-rich meals and shortening of masticatory time increases postprandial blood glucose levels by promoting glucose absorption[23–26]. In addition, periodontal disease leads to decreased insulin sensitivity and impaired glucose tolerance, causing T2DM[27]. Although our results cannot be used to conclude a causal relationship, oral and skeletal muscle health may influence the onset of T2DM. Since older adults with poor oral and skeletal muscle health are at a high risk of T2DM, it is important to consider these factors in early prevention.

Although low HGS and poor oral health had relatively high ORs in terms of T2DM prevalence, no significant association was found after adjusting for all confounders. This may be due to the small sample size, which yielded a low statistical power. Moreover, HGS is a simple estimator for whole muscle strength, and upper limb strength might not

Table 3 Combined associations of oral health status and handgrip strength with type 2 diabetes mellitus

		n	T2DM[1], %	Model 1[2]		Model 2[3]	
				OR	(95% CI)[4]	OR	(95% CI)
Number of Teeth[5]							
High							
HGS[6]	High	109	11	1.00	(Reference)	1.00	(Reference)
	Middle	114	18.4	**2.26**	**(1.02–4.99)**	2.20	(0.98–4.96)
	Low	93	16.1	1.92	(0.82–4.48)	1.75	(0.73–4.21)
Middle							
HGS	High	37	13.5	1.33	(0.42–4.20)	1.24	(0.38–4.04)
	Middle	50	12	1.16	(0.40–3.37)	1.07	(0.36–3.18)
	Low	45	22.2	2.28	(0.87–5.95)	2.04	(0.77–5.42)
Low							
HGS	High	16	6.3	0.52	(0.06–4.34)	0.49	(0.06–4.17)
	Middle	10	40	**5.38**	**(1.21–23.93)**	4.34	(0.94–19.99)
	Low	31	29	**3.20**	**(1.14–9.02)**	2.72	(0.93–7.93)
Masticatory Function[7]							
High							
HGS	High	55	12.7	1.00	(Reference)	1.00	(Reference)
	Middle	58	12.1	0.89	(0.28–2.81)	0.82	(0.25–2.61)
	Low	46	10.9	0.71	(0.20–2.51)	0.61	(0.17–2.20)
Middle							
HGS	High	59	13.6	0.75	(0.25–2.33)	0.69	(0.22–2.18)
	Middle	63	17.5	1.19	(0.41–3.46)	1.11	(0.38–3.26)
	Low	53	17	1.30	(0.43–3.94)	1.07	(0.35–3.32)
Low							
HGS	High	48	6.3	0.31	(0.07–1.33)	0.26	(0.06–1.15)
	Middle	53	24.5	2.07	(0.72–5.89)	1.70	(0.58–5.02)
	Low	70	28.6	2.15	(0.79–5.82)	1.79	(0.65–5.00)

[1] Type 2 diabetes, defined by HbA1c ≥6.5%, or taking hypoglycemic agents. [2] Adjusted for sex, age, and body mass index. [3] Adjusted for model 1, current smoking, alcohol drinking, hypertension, and education. [4] Odds ratios and 95% confidence intervals were estimated using logistic regression. P<0.05 shown in bold. [5] Categorized into high (≥21 teeth), middle (1–20 teeth), and low (0 teeth). [6] Handgrip strength. [7] Categorized into three groups by tertiles depending on sex.

be a suitable predictor of SMI, leading to under- or overestimation of the muscle function of the whole body. Whether HGS is associated with T2DM remains controversial.

Our study had several limitations. First, this cross-sectional study cannot be used to draw any conclusions regarding the causal relationship between oral and skeletal muscle status and T2DM. Second, because our data do not allow the accurate typing of DM, the population of this study might include patients with type 1 DM (T1DM) or slowly progressive insulin-dependent DM (SPIDDM), which have different mechanisms of onset. However, considering the prevalence of T1DM or SPIDDM in the Japanese population[28, 29], the impact of this factor on the analysis results was considered to be very small and limited. Third, the study sample included participants who completed an annual health checkup across multiple centers within one town. This could lead to a selection bias, as individuals who did not have the means of transportation to come to a center were not included. Lastly, we could not account for the influence of any unmeasured variables that may impact the relationships between confounding factors and T2DM. However, it is important to note that the strength of our study was the clinical assessment of oral health status, as opposed to self-reporting.

Conclusion

This study found that the combination of SMI-low and low oral health status was associated with T2DM among community-dwelling older adults in Japan. Our findings suggest the need to consider SMI as skeletal muscle and NT or MF as oral health status to prevent T2DM among these participants. Future studies should consider longitudinal designs and larger sample sizes to better assess the role of oral and skeletal muscle health in T2DM.

Conflicts of interest: The authors declare that they have no conflicts of interest.

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References

1. Kaiser AB, Zhang N, Van Der Pluijm W. Global prevalence of type 2 diabetes over the next ten years (2018–2028). Diabetes 2018; 67: 202-LB. [CrossRef]
2. Bartnik M, Norhammar A, Rydén L. Hyperglycaemia and cardiovascular disease. J Intern Med 2007; 262: 145–156. [Medline] [CrossRef]
3. Einarson TR, Acs A, Ludwig C, *et al*. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. Cardiovasc Diabetol 2018; 17: 83. [Medline] [CrossRef]
4. Kim CR, Jeon YJ, Jeong T. Risk factors associated with low handgrip strength in the older Korean population. PLoS One 2019; 14: e0214612. [Medline] [CrossRef]
5. Larsen BA, Wassel CL, Kritchevsky SB, *et al*. Health ABC Study Association of muscle mass, area, and strength with incident diabetes in older adults: The Health ABC Study. J Clin Endocrinol Metab 2016; 101: 1847–1855. [Medline] [CrossRef]
6. Cuthbertson DJ, Bell JA, Ng SY, *et al*. Dynapenic obesity and the risk of incident Type 2 diabetes: the English Longitudinal Study of Ageing. Diabet Med 2016; 33: 1052–1059. [Medline] [CrossRef]
7. Kunutsor SK, Voutilainen A, Laukkanen JA. Handgrip strength improves prediction of type 2 diabetes: a prospective cohort study. Ann Med 2020; 52: 471–478. [Medline] [CrossRef]
8. Ryan AS, Hurlbut DE, Lott ME, *et al*. Insulin action after resistive training in insulin resistant older men and women. J Am Geriatr Soc 2001; 49: 247–253. [Medline] [CrossRef]
9. Shaibi GQ, Cruz ML, Ball GD, *et al*. Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. Med Sci Sports Exerc 2006; 38: 1208–1215. [Medline] [CrossRef]
10. Glurich I, Acharya A. Updates from the evidence base examining association between periodontal disease and type 2 diabetes mellitus: Current status and clinical relevance. Curr Diab Rep 2019; 19: 121. [Medline] [CrossRef]
11. Glavind L, Lund B, Löe H. The relationship between periodontal state and diabetes duration, insulin dosage and retinal changes. J Periodontol 1968; 39: 341–347. [Medline] [CrossRef]
12. Preshaw PM, Alba AL, Herrera D, *et al*. Periodontitis and diabetes: a two-way relationship. Diabetologia 2012; 55: 21–31. [Medline] [CrossRef]
13. Williams RC. Periodontal disease. N Engl J Med 1990; 322: 373–382. [Medline] [CrossRef]
14. Ramseier CA, Anerud A, Dulac M, *et al*. Natural history of periodontitis: disease progression and tooth loss over 40 years. J Clin Periodontol 2017; 44: 1182–1191. [Medline] [CrossRef]
15. Yamazaki T, Yamori M, Asai K, *et al*. Nagahama Study Collaboration Group Mastication and risk for diabetes in a Japanese population: a cross-sectional study. PLoS One 2013; 8: e64113. [Medline] [CrossRef]
16. Ministry of Health, Labor and Welfare. Specific Health Checkups and Specific Health Guidance. 2013; https://www.mhlw.go.jp/english/wp/wp-hw3/dl/2-007.pdf (Accessed: Jun. 30, 2021)
17. Ramsay SE, Papachristou E, Watt RG, *et al*. Influence of poor oral health on physical frailty: a population-based cohort study of older British men. J Am Geriatr Soc 2018; 66: 473–479. [Medline] [CrossRef]
18. Tominaga K, Ando Y. A study of the consistency between subjective and objective evaluation of mastication. J Dent Health 2007; 57: 166–175 (in Japanese).
19. Hamano T, Tominaga K, Takeda M, *et al*. Accessible transportation, geographic elevation, and masticatory ability among elderly residents of a rural area. Int J Environ Res Public Health 2015; 12: 7199–7207. [Medline] [CrossRef]
20. Chobanian AV, Bakris GL, Black HR, *et al*. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute National High Blood Pressure Education Program Coordinating Committee Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42: 1206–1252. [Medline] [CrossRef]
21. DeFronzo RA, Jacot E, Jequier E, *et al*. The effect of insulin on the disposal of intravenous glucose. Results from indirect calorimetry and hepatic and femoral venous catheterization. Diabetes 1981; 30: 1000–1007. [Medline] [CrossRef]
22. Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. J Clin Endocrinol Metab 2011; 96: 2898–2903. [Medline] [CrossRef]
23. Wakai K, Naito M, Naito T, *et al*. Tooth loss and intakes of nutrients and foods: a nationwide survey of Japanese dentists. Community Dent Oral Epidemiol 2010; 38: 43–49. [Medline] [CrossRef]
24. Suzuki H, Fukushima M, Okamoto S, *et al*. Effects of thorough mastication on postprandial plasma glucose concentrations in nonobese Japanese subjects. Metabolism 2005; 54: 1593–1599. [Medline] [CrossRef]
25. Zhu Y, Hsu WH, Hollis JH. Increasing the number of masticatory cycles is associated with reduced appetite and altered postprandial plasma concentrations of gut hormones, insulin and glucose. Br J Nutr 2013; 110: 384–390. [Medline] [CrossRef]
26. Zhu Y, Hsu WH, Hollis JH. Increased number of chews during a fixed-amount meal suppresses postprandial appetite and modulates glycemic response in older males. Physiol Behav 2014; 133: 136–140. [Medline] [CrossRef]
27. Bui FQ, Almeida-da-Silva CLC, Huynh B, *et al*. Association between periodontal pathogens and systemic disease. Biomed J 2019; 42: 27–35. [Medline] [CrossRef]
28. Kawasaki E, Matsuura N, Eguchi K. Type 1 diabetes in Japan. Diabetologia 2006; 49: 828–836. [Medline] [CrossRef]
29. Yasui J, Kawasaki E, Tanaka S, *et al*. Japan Diabetes Society Committee on Type 1 Diabetes Mellitus Research Clinical and genetic characteristics of non-insulin-requiring glutamic acid decarboxylase (GAD) autoantibody-positive diabetes: a nationwide survey in Japan. PLoS One 2016; 11: e0155643. [Medline] [CrossRef]