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치의학석사 학위논문

Association between obesity and flow rate of unstimulated whole saliva among elderly Koreans.

한국 노인에서 비만과 비자극성 전타액 분비율의 연관성

2013 년 2 월

서울대학교 치의학대학원 치의학과 문 선 희 Association between obesity and flow rate of unstimulated whole saliva among elderly Koreans.

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Abstract

Association between obesity and flow rate of unstimulated whole saliva among elderly Koreans.

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1. Objectives

The prevalence of obesity continue to increase in all ages and ethnicities worldwide. Obesity is associated with increased risk of chronic inflammatory diseases such as tvpe diabet. atherosclerosis, cancer, and respiratory disorders. In addition, several studies have reported that obesity is related to several aspects of oral health, such as caries, periodontitis and dry mouth. There have been few studies on the relationship between obesity and hyposalivation. Moreover, very few studies on old ages have been found in the literature. Dry mouth is a common symptom in the older people that can produce serious negative effects on the patient's quality of life. Although the increased prevalence of hyposalivation caused by diseases and intake of drugs in aged patients is well known, it is possible that obesity is also a determinant of dry mouth. Therefore, we performed this study to provide additional evidence of an association between obesity and salivary flow rate among Korean adults.

2. Methods

In Korea, the Sun-Chang longevity cohort started in 2009. All 514 subjects (177 males and 337 females), selected from the Sun-Chang longevity cohort at baseline survey, participated voluntarily and provided written informed consent. Their ages ranged from 48 to 93 years, with a mean of 70.5 years. Unstimulated saliva was collected in a relaxed position and was passively drained for 10min into a test tube. We classify into 3 groups; those with very low SFR (UWSFR < 0.1 ml/min); those with low SFR (UWSFR = 0.1-0.19ml/min); and those who have normal SFR (UWSFR ≥ 0.2 ml/min). For evaluating obesity, trained examiners measured weight, height, hip circumference and waist circumference. Obesity was defined as a BMI $\geq 25 \text{kg/m}^2$ and overweight was defined as a BMI between 23 and 25 kg/m². Regarding WC, obesity was defined as a WC≥90cm for men and ≥85cm for women. Considering WHR, obesity was defined as a WHR \geq 0.90 for men and \geq 0.80 for women. In order to obtain information about socio-demographic status, general healthrelated behaviors, the subjects were interviewed by a trained interviewer using structured questionnaires. To determine the strength of association and the dose-effect relationship between the salivary flow rate and the obesity indicator scores, analysis of covariance (ANCOVA) was performed. To determine the association between obesity and salivary flow rate, odds ratios with 95% confidence intervals were estimated by logistic regression analysis adjusting for age, gender, smoking, drinking, physical activity, number of teeth, denture wearing state, interaction of gender and obesity.

3. Results

Unstimulated salivary flow rate ranged from 0.001ml/min to 0.968ml/min, with a mean of 0.13ml/min. Obesity is significantly correlated with age, gender, smoking, number of remained teeth, denture wearing state. We found that salivary flow rate significantly decreased with age and females had a lower flow rate than males. The people who smokes present and drinks 1-5 times monthly presented a significant higher salivary flow rate than non-smoker and non-drinking patients respectively. Physical activity, remained teeth and denture wearing state were not significantly correlated with salivary flow rate.

In the analysis of covariance adjusted for age, gender, smoking, drinking, physical activity, number of teeth, denture wearing, none of the BMI, WC and WHR did not significantly correlated with salivary flow rate.

In the multivariate logistic regression model adjusted for age, gender, smoking, drinking, physical activity, number of teeth, denture wearing, and interaction of obesity indices and gender, the prevalence of very low salivary flow rate in obese group was 11.5

times significantly higher than that of normal group (OR=11.54, 95%

CI: 1.04-128.02). However, WC and WHR did not show the

significant association with salivary flow rate.

In conclusion, it is suggested that obesity may play a significant

role in the control of salivary secretion, but the population bias to

some of the rural elderly and obesity and salivary flow has been

limited to less overall significant association. Further studies are

needed to reappraise the interaction obesity and salivary flow rate

in large and diverse population.

Keywords : obesity, salivary flow rate, hyposalivation

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I. Introduction

The prevalence of obesity continue to increase in all ages and ethnicities worldwide (Ogden et al., 2002). The Korean National Health and Nutrition Survey (KNHANES) showed that the prevalence of obesity[body mass index (BMI) ≥25kg/m²] has increase among the adults from 26% in 1998(Korea Ministry of Health and Welfare, 1999) to 30.8% in 2010(Korea Ministry of Health and Welfare, 2011). Obesity and in particular abdominal obesity is associated with increased risk of chronic inflammatory diseases such as type 2 diabetes, atherosclerosis, cancer, and respiratory disorders (Fontaine et al., 2003).

Dry mouth is a common symptom in the older people that can produce serious negative effects on the patient's quality of life (Gupta et al., 2006). Although the increased prevalence of hyposalivation caused by diseases and intake of drugs in aged patients is well known (Ship et al., 2002), it is possible that obesity is also a determinant of dry mouth. In addition, several studies have suggested that obesity is related to some aspects of oral health, such as caries, periodontitis and dry mouth. Several studies showed a positive association between overweight and/or obesity and periodontits (Dalla Vecchia et al., 2005; Han et al., 2010; Saito et al., 2001; Saito et al., 2005; Wood and Johnson, 2008). But very few

studies have examined the relationship between obesity and hyposalivation. Although very low saliva flow rate has been demonstrated to be associated with younger adults (<50 years) only BMI >25 (Flink et al., 2008) there is limited knowledge concerning saliva flow rate in obese subjects in relation to healthy controls. Some studies based on limited number of obese subjects show normal salivary pattern compared with normal—weight individuals (Epstein et al., 1996; Powers et al., 1982).

Moreover, there are no data concerning the association between obesity and salivation among Korean adults. Therefore, we performed this study to provide additional evidence of an association between obesity and salivary flow rate (SFR) among Korean adults.

II. Material & Method

1. Study population

In Korea, the Sunchang longevity cohort started in 2009, focusing on longevity, lifestyle and systemic diseases. The dental health area covers several topics, including investigation about association of obesity and salivation.

This cross-sectional study was approved by the IRB of SNUSOD(#S-D20090003). All 514 subjects (177 males and 337 females), selected from the Sunchang longevity cohort(SLC) at baseline survey, participated voluntarily and provided written informed consent. Their ages ranged from 48 to 93 years, with a mean of 70.8 years. This survey included oral examination, saliva sampling for laboratory procedures, and questionnaires for confounders.

2. Determination of salivary flow rate

The saliva collection procedure was performed in the morning and food restriction was given to the subjects.

Unstimulated whole saliva was collected, with the participant in a relaxed position leaning slightly forward. After swallowing, saliva

was passively drained for 10min into a test tube. The amount of saliva was determined after collection and unstimulated whole salivary flow rate (UWSFR) rate was expressed as ml/min. There is no general agreement about UWSFR that distinguishes normal patients from those with hyposalivation; the value has ranged between 0.1 and 0.2 ml/min(Fenoll-Palomares et al., 2004; Longman et al., 1995; Marton et al., 2008; Navazesh et al., 1992; Sreebny and Valdini, 1987). As a result, we followed previous classification of SFR: very low SFR (UWSFR <0.1 ml/min); low SFR (UWSFR = 0.1-0.19 ml/min); and normal SFR (UWSFR \geq 0.2 ml/min) (Flink et al., 2008).

3. Assessment of obesity

For evaluating weight, height, hip circumference (HC) and waist circumference (WC), trained examiners measured the subjects wearing light clothing and no shoes. BMI was calculated as the weight (kg) divided by the square of height (m^2). Waist hip ratio (WHR) was calculated as the ratio of WC to HC (WHR=WC/HC). Obesity was defined as a BMI $\geq 25 \text{kg/m}^2$ and overweight was defined as a BMI between 23 and 25 kg/m² (WHO Expert consultation, 2004). Regarding WC, obesity was defined as a WC \geq 90cm for men and \geq 85cm for women (Lee et al., 2006).

Considering WHR, obesity was defined as a WHR \geq 0.90 for men and \geq 0.80 for women (Suk et al., 2003).

4. Assessment of confounders

Demographic status and general health-related behaviors, dental status were selected as confounders. Age, gender were selected as demographic factors. General health-related behaviors included smoking, drinking, physical activity. Dental status including the number of teeth, denture wearing state was evaluated by dentists using the oral examination. In order to obtain information regarding other potential confounders, the subjects were interviewed by a trained interviewer using structured questionnaires.

5. Statistical analysis

Salivary flow rate was an outcome variable, and obesity was a main explanatory variable. Confounders such as age, gender, smoking, drinking, the frequency of physical activity, number of teeth and denture wearing state were placed into models.

The distribution of obesity and SFR were described according to the characteristic variables. To determine the dose-effect relationship between the salivary flow rate (continuous variable) and the obesity indicator scores (continuous variable), correlation analysis and analysis of covariance (ANCOVA) were performed. Multivariable norminal logistic regression analysis was also used to evaluate the adjusted odds ratio (AOR) between hyposalivation (category with two groups) and the obesity indicators (category with three groups). Statistical analysis was performed using SPSS for Windows release 19.0 (SPSS Inc., Chicago, IL, USA).

III. Results

UWSFR of subjects ranged from 0.001ml/min to 0.97ml/min, with a mean of 0.13ml/min. BMI score is significantly correlated with age, gender, smoking, number of remained teeth, denture wearing state (Table 1). We found that salivary flow rate significantly decrease with age(p=0.001) and females had a lower flow rate than did males(p=0.006). The people who smokes present and drinks one to five times monthly presented a significant higher salivary flow rate than non-smoker and non-drinking patients respectively (p=0.003, 0.025). Physical activity, remained teeth and denture wearing state did not show the difference in SFR.

All the obesity indices significantly correlated each other: In Pearson's correlation coefficient (r) was 0.664 (p<0.01) between BMI and WC, 0.261 (p<0.01) between BMI and WHR, 0.739 (p<0.01) between WC and WHR. In crude association of UWSFR with BMI, WC and WHR, UWSFR was not significantly associated with any of the obesity indicators (Fig. 1). Although UWSFR fluctuated according to the severity of obesity defined by BMI, ANCOVA did not reveal any significant influence of obesity on the salivary flow rate after adjusting for age, gender, smoking, drinking, physical activity, number of teeth and denture wearing status (Table 2). In the multivariable norminal logistic regression model adjusted for

age, gender, smoking, drinking, physical activity, number of remained teeth, denture wearing and interaction term between obesity and gender, the prevalence of very low salivary flow rate in obese group was 11.5 times significantly higher than that of controls (OR=11.54, 95% CI: 1.04-128.02). The tendency toward a higher odds ratio(OR) for very low salivary flow rate or low salivary flow rate with increasing BMI was observed. But this was not statistically significant. In the analysis according to WHR, there were similar association between obesity and SFR, however the associations were not statistically significant. Interestingly, obese group analyzed by WC had a preventive association both for very low flow rate and low flow rate than normal group, which were not statistically significant.

IV. Discussion

The association between obesity and salivary pattern is still controversial. Several studies showed an association between salivary flow rate and obesity (Flink et al., 2008; Sawair et al., 2009; Yamamoto et al., 2009), although other studies showed no such association (Epstein et al., 1996; Powers et al., 1982). Hence present study was aimed to investigate whether obesity is associated with SFR in elderly Koreans.

For evaluating the association between obesity and salivary flow rate, we used both visceral adiposity (WC, WHR) and total body adiposity (BMI) as indicators of obesity. We also included several demographic factors, general health-related behaviors and dental status in the models. The results from the present study showing that obese people has higher risk for very low salivary flow rate. The link between obesity and salivary secretion rate is correspond well with the finding of an association between overweight and prevalence of very low salivary flow rate previous reported among adults (Flink et al., 2008). These results may be explained by the effect of inflammation. Most salivary gland inflammatory diseases have in common an associated salivary hypofunction (Beale and Madani, 2006; Dawson et al., 2006).

Obese subjects have been reported to exhibit enlargement of

parotid gland probably by an increased storage of adipocyte in the parotid parenchyma, while the submandibular glands show no signs of enlargement (Bozzato et al., 2008; Heo et al., 2001). There are several signaling pathways involved in the control of secretion that can be affected by proinflammatory cytokines (IL- β_1 , IL-6, TNF- α) and prostaglandins (Tanda et al., 1998 Weinstein et al. 2000; Yamakawa et al., 2000; Yu, 1986) Based on that, proinflammatory cytokines derived from adipocytes as well as macrophages, accumulated in adipose tissue (Weisberg et al., 2003) may negatively affect the function of salivary glands due to chronic low-grade inflammation in the gland.

Obesity is linked to chronic inflammation and a number of adipose—related proinflammatory cytokines, so called adipokines, are enhanced in plasma from obese subjects contributing to enhanced inflammatory response in many body organs (Lyon et al., 2003). The immune system modulates central nervous system function particular by cytokines and the hypothalamic—pituitary—adrenal axis is reported to be dysregulated in subjects with abdominal obesity (Pasquali et al., 2006). Altered function of the hypothalamic—pituitary—adrenal axis may affect the neuroendocrine regulation of salivary glands which seems to be the case in Sjogren's syndrome, characterized by diminished salivary gland secretion (Johnson et al., 2006).

Unstimulated salivary flow is produced primarily by the submandibular glands (65-70%), with the parotid and sublingual glands providing 20% and 7% to the flow, respectively (de Almeida Pdel et al., 2008). In contrast to parotid gland, submandibular gland is not affected by the obesity as was shown by some investigators (Bozzato et al., 2008; Heo et al., 2001). This may be one reason for the weak association between obesity and hyposalivation.

Limitation of this study included the lack of specific information about the medications that are the most common cause of hyposalivation. The use of medications increases with age, with more than 75% of people aged 65 and older taking at least 1 prescription medication (Chrischilles et al., 1992); therefore, the prevalence of medication—induced xerostomia is high in the elderly (Narhi). Another limitation was the population biases that our subjects were localized in Sunchang county. The cross—sectional design of the study makes it impossible to determine a direction of causality. In addition, the influence of residual and unmeasured confounding cannot be excluded in observational studies. Therefore, some of the confounders may be imprecisely measured, and there might be additional confounders that are not accounted for in the observed relationship between obesity and salivary secretion.

V. Conclusion

In conclusion, this novel finding is that old age obesity (BMI \geq 25) is associated with reduced flow rate of unstimulated whole saliva. However, WC and WHR did not show the significant association with salivary flow rate. Further longitudinal studies including the status of diseases and drug use in large and diverse population are needed to increase our understanding of the hyposalivation.

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Table 1. Distribution of obesity and salivary flow rate according to demographic, behavioral and oral factors

	Total	BMI	p	salivary flow	p
	N	$Mean \pm SD$		$Mean \pm SD$	
Age(years)			<0.001 [†]		0.001 [†]
45-64	103	24.28 ± 3.54^a		$0.15\!\pm\!0.12^a$	
65 - 74	268	23.33 ± 3.06^{b}		0.14 ± 0.12^a	
≥75	143	22.20 ± 2.48^{c}		0.10 ± 0.07^{b}	
Gender			0.02^{*}		0.006*
Male	177	22.77 ± 2.62		0.15 ± 0.13	
Female	337	23.44 ± 3.30		0.12 ± 0.10	
Smoking			0.005^{\dagger}		0.003^{\dagger}
no	327	23.52 ± 3.29^a		$0.12\!\pm\!0.10^a$	
past smoking	131	$22.80\!\pm\!2.65^{ab}$		0.14 ± 0.11^{b}	
present smoking	56	22.30 ± 2.64^{b}		0.17 ± 0.16^{b}	
Alcohol drinking	(drinks/	month)	0.207^{+}		0.025^{\dagger}
no	372	23.35 ± 3.21		0.12 ± 0.10	
1-5	102	22.92 ± 2.94		0.15 ± 0.15	
≥6	40	22.61 ± 2.28		0.12 ± 0.11	
Physical activity			0.251^{+}		0.551^{\dagger}
no	394	23.08 ± 0.98		0.13 ± 0.11	
1 - 4	40	23.55 ± 3.71		0.13 ± 0.10	
daily	80	23.65 ± 03.09		0.14 ± 0.12	
Remained teeth			<0.001*		0.096^{*}
<20	345	22.85 ± 2.89		0.12 ± 0.11	
≥20	169	23.94 ± 3.37		0.14 ± 0.11	
denture wearing			0.025^{*}		0.863*
no	229	23.55 ± 3.30		0.13 ± 0.10	
yes	285	22.93 ± 2.90		0.13 ± 0.12	

^{*} p-values are calculated by independent t-test. † p-values are calculated by one-way ANOVA.

Superscripts denote the same group in post hoc multiple comparison test of Scheffe at p=0.05.

SD denotes standard deviation.

Table 2. Distribution of salivary flow rates according to obesity indicators

Indicator of obesity		salivary flow rate			
_	N	Crude mean±SD	p [†]	Adjusted mean*± SE	p [†]
BMI			0.285		0.07
normal	260	0.130 ± 0.113		0.133 ± 0.007	
overweight	118	0.114 ± 0.102		0.108 ± 0.010	
obese	136	0.136 ± 0.117		0.128 ± 0.010	
WC			0.593		0.177
normal	308	0.126 ± 0.114		0.123 ± 0.006	
obese	206	0.131 ± 0.108		0.131 ± 0.008	
WHR			0.780		0.434
normal	91	0.131 ± 0.113		0.121 ± 0.015	
obese	423	0.127 ± 0.112		0.130 ± 0.005	

^{*} Obtained from ANCOVA adjusted for age, gender, smoking, alcohol drinking, physical activity, remained teeth, denture wearing.

[†] p-values are calculated by one-way ANOVA.

[†] p-values are calculated by ANCOVA.

SD denotes standard deviation.

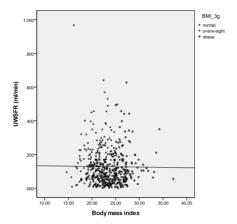
SE denotes standard error.

Table 3. Adjusted associations between obesity and salivary flow rate by multivariable norminal logistic regression model

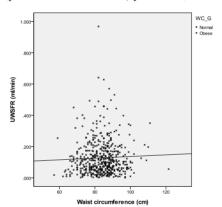
Indicator of N(%)		OR (95% CI)*			
obesity		very low (<0.1ml/min)	low (0.1-0.19ml/min)		
BMI					
normal	260 (50.6)	1	1		
overweight	118 (23.0)	1.16 (0.17-7.88)	1.55 (0.19-12.54)		
obese	136 (26.5)	11.54 (1.04-128.02)	3.76 (0.26-52.94)		
Trend p-valu	ıe		0.994		
WC					
normal	206 (40.1)	1	1		
obese	308 (59.9)	0.43 (0.14-1.35)	0.27 (0.08-0.88)		
WHR					
normal	423 (82.3)	1	1		
obese	91 (17.7)	1.80 (0.47-6.89)	1.77 (0.40-7.86)		

^{*} OR: very low=2 vs. low=1 vs. normal =0, adjusted for age, gender, smoking, alcohol drinking, physical activity, remained teeth, denture wearing and interaction between each obesity indicator and gender.

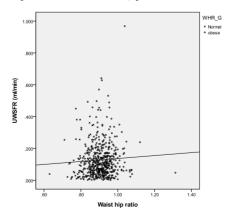
Figure 1. Crude association of obesity indicators and unstimulated whole salivary flow rates



(pearson r = -0.010, p=0.822)



(pearson r = 0.041, p=0.353)



(pearson r = 0.055, p=0.213)

초 록

1. 연구목적

비만은 전세계적으로 증가 추세에 있으며 제2형 당뇨와 동맥경화, 암, 호흡기 질환 등 만성 염증성 질환의 발병에 중요한 역할을 한다. 뿐만 아니라 치아우식, 치주질환 그리고 구강건조와 같은 구강질환과도 관련이 있음이 밝혀졌다. 비만과 타액분비율의 관련성에 대해서는 비교적적은 연구들이 진행되어 있으며 노인을 대상으로 한 연구는 더욱더 제한되어 있다. 구강건조는 높은 비율의 노령인구가 겪고 있는 구강 질환으로 삶의 질에도 많은 영향을 끼치는 질환이다. 노인의 구강건조는 주로전신적 질환과 약물 복용성의 증가 때문인 것으로 설명되고 있으나 비만과의 관련성도 생각해볼 수 있다. 따라서 본 연구에서는 한국 노인을 대상으로 비만과 타액분비의 관계를 파악하고자 한다.

2. 연구대상 및 방법

2009년 시작 된 순창 장수코호트(longevity cohort) 대상자 중 2009년과 2010년에 조사한 순창주민 514명을 대상으로 연구를 수행하였다. 대상자는 남자 177명, 여자 337명으로 구성되어 있으며 조사 대상자의 연령은 48세에서 93세에 분포하였고, 평균 연령은 70.47세이었다. 타액분비율은 편안한 상태에서 저자극성 전타액을 10분간 conical tube에 수집하여 기록하였고, 0.1ml 이상 0.2ml/min 미만을 저타액증, 0.1ml/min 미만을 최저타액증으로 진단하였다. 비만도 분석을 위해 신장, 체중, 허리둘레와 엉덩이둘레를 측정하였다. 비만은 BMI 25kg/m²이상, 과체중은 23-25kg/m²으로 각각 정의한다. 허리둘레(WC)에 대해서는 남성 90cm이상, 여성은 85cm 이상을 허리/엉덩이둘레 비율(WHR)은 남성 0.90 이상, 여성 0.80 이상을 각각 비만으로 정의하였다. 사회

인구학적인 요인, 건강관련 행동요인, 구강 상태, 전신건강 등에 관한 정보는 규격화된 설문지를 이용한 면접조사법을 통하여 확보하였다. 비만지수와 타액분비율 간의 양-반응 관계를 분석하기 위해 나이, 성별, 흡연, 음주, 운동량, 현존 영구치 수, 의치 장착 여부를 보정하여 공분산분석을 시행하였다. 비만 유무와 저타액증 유무의 연관성은 나이, 성별, 흡연, 음주, 운동량, 현존 영구치 수, 의치 장착 여부를 보정한 로지스틱회귀분석을 시행하여 odds ratio(OR) 및 95% confidence interval(95% CI)을 통해 평가하였다.

3. 결론

비자극성 타액분비율의 평균은 0.13ml/min이었고 분포는 최소 0.001ml/min, 최대 0.97ml/min이었다. 타액분비율은 연령이 증가할수록 감소하였으며 남성에 비해 여성에서 0.03ml/min 낮았으며, 현재 흡연자는 비흡연자보다 타액분비율이 높게 나타났으며 월 1-5회의 음주를 하는 사람이 음주를 하지 않는 사람에 비해 높은 타액분비율을 보였다. 육체적 활동, 잔존치아수, 의치장착여부와 타액분비율은 연관성이 나타나지 않았다. BMI로 분석한 비만도는 연령이 증가할수록 감소하였으며 남성에 비해 여성이 높았으며 흡연자에 비해 비흡연자가 높았고, 현존 영구치가 20개 이상인 사람과 의치를 장착한 사람이 각각 영구치가 20개 미만인 사람과 의치를 장착하지 않은 사람에 비해 높았다. 음주와운동량은 비만과 연관성이 나타나지 않았다.

나이, 성별, 흡연, 음주, 운동량, 현존 영구치 수, 의치 장착 여부를 보정한 공분산 분석에서 비만 지수인 BMI, WC, WHR와 비자극성 타액 분비율의 연관관계는 나타나지 않았다.

나이, 성별, 흡연, 음주, 운동량, 현존 영구치 수, 의치 장착 여부 그리고 성별과 BMI의 상관관계를 보정한 다변량 로지스틱 회귀분석 결과,

최저타액분비율(<0.1ml/min)과 정상타액분비율(≥0.2ml/min) 비교 모형에서 BMI로 분석된 비만군은 정상군에 비해 최저타액분비율자가 될 가능성이 11.5배 높았다(OR=11.54 95% CI: 1.04-128.02). 그러나 WC와 WHR로 분석된 비만군에서는 유의한 연관성을 보이지 못하였다. 특히 저타액분비율(0.1ml/min-0.19ml/min)과 정상 타액분비율의 비교에서는 BMI, WC, WHR로 분석한 모든 비만군에서 유의한 연관성을 보이지 못하였다.

총괄적으로 보아 비만과 타액분비량은 유의한 연관성을 보였으나, 본 연구의 대상자가 일부 농촌 노인층으로 제한되었으며 유의한 연관성 이 전반적이지 못한 한계를 가지고 있으므로 추후 보다 많은 대상자를 대상으로 한 연구로 재평가할 필요가 있다고 검토되었다.

주 요 어 : 비만, 타액분비율, 저타액증

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