

## Evaluation of the Effect of Ramadan Fasting on Parotid and Submandibular Gland Elasticity with Shear Wave Elastography

Ramazan Orucunun Parotis ve Submandibular Bez Üzerindeki Etkisinin Shear Wave Elastografi ile Değerlendirilmesi

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### Abstract

**Background:** The changes in eating-drinking and sleeping habits during Ramadan cause also changes in daily routines. It was aimed to evaluate the effect of Ramadan fast on parotid and submandibular gland elasticity with shear wave elastography.

**Materials and Methods:** The anthropometric measurements of the volunteers such as age, gender, height, and weight, and the elastography values of the bilateral parotid and submandibular glands measured on the day before and on the last day of Ramadan were obtained. Five 2D-SWE (Two-dimensional shear wave elastography) measurements were taken at the same depth. The average of these was calculated. In this way, the accuracy of the numerical data obtained was increased. The mean value of five 2D-SWE measurements was used for the statistical analysis. This procedure was repeated for both parotid and submandibular glands. Data obtained in the study were analyzed statistically. A value of  $p < 0.05$  was accepted as statistically significant.

**Results:** There was a statistically significant difference between the mean BMI values measured on the day before Ramadan and the last day of Ramadan fasting ( $p < 0.001$ ). No significant difference of elastography values was found between the bilateral parotid and submandibular glands on the day before Ramadan and on the last day of Ramadan.

**Conclusions:** The intermittent fasting during Ramadan had no effect on the elasticity of the salivary glands, as determined by our studied.

**Keywords:** Intermittent fasting, Elastography, Parotid gland, Submandibular gland

### ÖZ

**Amaç:** Ramazan ayında yeme-içme ve uyku alışkanlıklarında meydana gelen değişiklikler, günlük rutinlerde de değişikliklere neden olmaktadır. Bu çalışmada, Ramazan orucunun parotis ve submandibular bez elastikiyeti üzerine etkisinin shear wave elastografi ile değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Gönüllülerin yaş, cinsiyet, boy ve kilo gibi antropometrik ölçümleri ile bilateral parotis ve submandibular bezlerin Ramazan'dan bir gün önce ve Ramazan'ın son günü ölçülen elastografi değerleri elde edilmiştir. Aynı derinlikte beş adet 2D-SWE (Two-dimensional shear wave elastography) ölçümü alındı. Bunların ortalaması hesaplandı. Bu şekilde elde edilen sayısal verilerin doğruluğu artırıldı. İstatistiksel analiz için beş 2D-SWE ölçümünün ortalama değeri kullanılmıştır. Bu prosedür hem parotis hem de submandibular bezler için tekrarlandı. Çalışmada elde edilen veriler istatistiksel olarak analiz edilmiştir.  $P < 0.05$  değeri istatistiksel olarak anlamlı kabul edildi.

**Bulgular:** Ramazan'dan önceki gün ve Ramazan orucunun son gününde ölçülen ortalama vücut kitle indeksi (VKİ) değerleri arasında istatistiksel olarak anlamlı bir fark vardı ( $p < 0.001$ ). Bilateral parotis ve submandibular bezlerin Ramazan'dan önceki gün ve Ramazan'ın son günündeki elastografi değerleri arasında anlamlı bir fark bulunmamıştır.

**Sonuç:** Ramazan ayında aralıklı olarak tutulan orucun, çalışmamızda belirlendiği üzere tükürük bezlerinin esnekliği üzerinde herhangi bir etkisi olmamıştır.

**Anahtar kelimeler:** Aralıklı açlık, Elastografi, Parotis bezi, Submandibular bez

### Highlights

- The effect of Ramadan fasting on the elasticity of the parotid and submandibular glands using shear wave elastography.
- What are the effects of dehydration, which occurs intermittently during Ramadan, on the elasticity of the parotid and submandibular glands?
- Elastography is a US-based imaging technique used to evaluate the stiffness of tissues

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## Introduction

Fasting in Ramadan is one of the five pillars of Islam. Ramadan is the 9th month of the lunar calendar and moves forward about 11 days each year. Muslims abstain from eating any food, drinking any liquids, from dawn to sunset and fasten. Smoking, parenteral feeding and sexual intercourse are also prohibited during this period. The duration of fasting changes between 9 and 21 hours depending on the geographical situation. Ramadan lasts 29 or 30 days. The changes in eating-drinking and sleeping habits during Ramadan cause also changes in daily routines (1). Several studies have been conducted to demonstrate the effects of fasting on human physiology and the potential impact on the existing diseases (2-4). It has been reported that dehydration occurring during Ramadan fasting can increase the risk of developing acute sialadenitis (5). In another study, it was found that salivary levels of sIgA were elevated during the fasting period, while statherin levels were higher after fasting. These biomarkers are essential for oral health, as they help defend against microbial invasions and regulate the balance of calcium and phosphate ions in saliva (6).

The parotid glands are the largest salivary glands and contribute about 25% of the total saliva production. They secrete a serous fluid rich in electrolytes and enzymes. The submandibular glands, which produce approximately 70% of daily saliva, secrete a mixture of electrolytes, enzymes, and mucins. The sublingual glands, producing a mucus-rich fluid containing antigens and antibodies, drain either directly into the oral cavity or into the submandibular duct (7). Ultrasonography (US) is a non-invasive, inexpensive, repeatable, and portable imaging method (8). It is commonly used in the examination of the parotid and submandibular glands. Elastography is a US-based imaging technique used to evaluate the stiffness of tissues (9). It is a promising tool regarding the diagnosis of several benign and malignant disorders, particularly fibrosis. There are two types of US elastography: Strain Elastography (SE) and Shear Wave Elastography (SWE). In SE, external pressure with the help of a US probe is implemented to create mechanical stimulation. In SWE, mechanical stimulation is created with shear waves produced by the imaging device. In both methods, the elasticity properties of the tissues are evaluated according to the response to the implemented mechanic stimulation (10). The tissue elasticity is measured in kilopascal units or with shear wave velocity (SWV). The real-time quantitative measurement of the tissue elasticity, repeatability, and non-dependence to an operator (as no pressure is implemented), are the advantages of SWE (11).

In this study, it was aimed to investigate with SWE the effects of hunger and thirst, which occur in intermittent durations through Ramadan, on the elasticity of the parotid and submandibular glands.

## Material and Methods

### Study design

This study approval was obtained from the Harran University Faculty of Medicine, Ethics Committee (number: HRÜ/19.03.43. date: 11.03.2019). Informed consent was obtained from all patients. Healthy male volunteers, who were fasting in Ramadan (between May and June 2019) and working in our institute, were included in our study. Females were not included, because they could not fasten during the menstruation period. This single-center, prospective study had two phases. The first phase was defined as the day before the first day of Ramadan and the second phase was defined as the last day of Ramadan fasting. On the day before the first day of Ramadan and the last day of the Ramadan fasting, the body mass indexes, and the elastography values of the parotid and submandibular glands were measured. In both phases, the measurements were carried out at 12:00 am in order to get the measurement values at the near 8th hour of fasting. Body mass index (BMI) was calculated by dividing the weight (in kilograms) by the height (in square meters) ( $\text{kg}/\text{m}^2$ ).

### Ultrasound and 2D-SWE

The examinations were performed by using the Siemens ACUSON S2000 US system (Siemens Medical System Solution, CA, USA) with a 9L4 probe. First, the gray-scale US examination of both parotid and submandibular glands was performed, while the volunteers were in the supine position (**Figure 1**). After the gray-scale ultrasonography showed normal and healthy glands, the US probe was placed on the right parotid gland at the transverse plane following sufficient gel application. In this study, 2D-SWE (Two-dimensional shear wave elastography), the most novel elastography method using acoustic radiation force, was used. Elastography images were obtained by gently placing the US probe in the parotid and submandibular gland. Any pressure was avoided. Patients were instructed not to move to avoid artifacts. Values obtained from moving images were not considered in the analyses. SWE values were measured at the longest longitudinal measurements. A square

region of interest (ROI) was used as the plane. The ROI was placed at a depth of 0.5 cm. Quantitative elasticity values were measured in meters per second (m/s). Tissue elasticity was determined in a color range between dark blue (lowest stiffness) and red (highest stiffness) (**Figure 2 and 3**). Five 2D-SWE measurements were taken at the same depth. The average of these was calculated. In this way, the accuracy of the numerical data obtained was increased. The mean value of five 2D-SWE measurements was used for the statistical analysis. This procedure was repeated for both parotid and submandibular glands.

### Statistical analyses

Statistical analyses were performed using the SPSS 24.0 version (SPSS Inc, Chicago, IL) package program. Descriptive statistics were summarized as a number, percentage, mean and standard deviation. The suitability of the variables to the normal distribution was investigated using visual (histogram and probability charts) and analytical methods (Shapiro-Wilk test). When the repeat measurement of the groups was compared, the data with normal distribution (differences between them) were analyzed by paired sample t test. The relationship between normally distributed data was evaluated by Pearson correlation analysis and correlation coefficient ( $r$ ) was specified. Statistical significance level was accepted as  $p < 0.05$  in all statistical analyses.

### Results

Twenty-six cases, who were included in the study, were males. The mean age of the subjects was  $33.69 \pm 8.12$  years (min-max: 23-50 years). The mean BMI on the day before the first day of Ramadan was  $26.88 \pm 3.35$  (min- max: 19.23-36.14), while the same value on the last day of the Ramadan fasting was  $26.15 \pm 3.25$  (min-max: 18- 92-35.43). There was a statistically significant difference between the mean BMI values measured on the day before the first day of Ramadan and the last day of Ramadan fasting (Table 1;  $p < 0.001$ ). There was no statistically significant difference between the mean SWE values of both parotid glands on the day before the first day of Ramadan and the last day of Ramadan fasting were for the right side ( $p = 0.234$ ) and left side ( $p = 0.261$ ) (**Table 1**). There was also no statistically significant difference between the mean SWE values of both submandibular glands on the day before the first day of Ramadan and on the last day of Ramadan fasting were for the right side ( $p = 0.108$ ) and left side ( $p = 0.868$ ) (**Table 1**).

The Pearson's correlation analysis did not reveal any significant relationship between the age of the subjects and the SWE values of the right parotid ( $r = 0.049$ ,  $p = 0.813$ ), left parotid ( $r = 0.012$ ,  $p = 0.953$ ), right submandibular ( $r = 0.133$ ,  $p = 0.516$ ), and left submandibular ( $r = 0.003$ ,  $p = 0.987$ ) glands measured on the day before the first day of Ramadan. The Pearson's correlation analysis did also not show any significant relationship between the BMI values measured on the day before the first day of Ramadan and the SWE values of the right parotid ( $r = 0.267$ ,  $p = 0.187$ ), left parotid ( $r = -0.358$ ,  $p = 0.073$ ), right submandibular ( $r = 0.266$ ,  $p = 0.189$ ), and left submandibular ( $r = 0.008$ ,  $p = 0.967$ ) glands.

**Table 1. Comparison of body mass index and shear wave elastography values measured one day before and on the last day of Ramadan fast**

Variables	One day before ramadan fast Mean $\pm$ SD	Last day of ramadan fast Mean $\pm$ SD	$p^*$
BMI (kg/m <sup>2</sup> )	26.88 $\pm$ 3.35	26.15 $\pm$ 3.25	<0.001
Left parotid (kPa)	2.75 $\pm$ 0.26	2.7 $\pm$ 0.3	0.261
Right parotid (kPa)	2.94 $\pm$ 0.36	2.88 $\pm$ 0.36	0.234
Left submandibular (kPa)	2.72 $\pm$ 0.31	2.75 $\pm$ 0.36	0.868
Right submandibular (kPa)	2.82 $\pm$ 0.32	2.73 $\pm$ 0.28	0.108

Abbreviations: \*: Paired sample t test; BMI: Body mass index; SWE: shear wave elastography; SD: Standard deviation

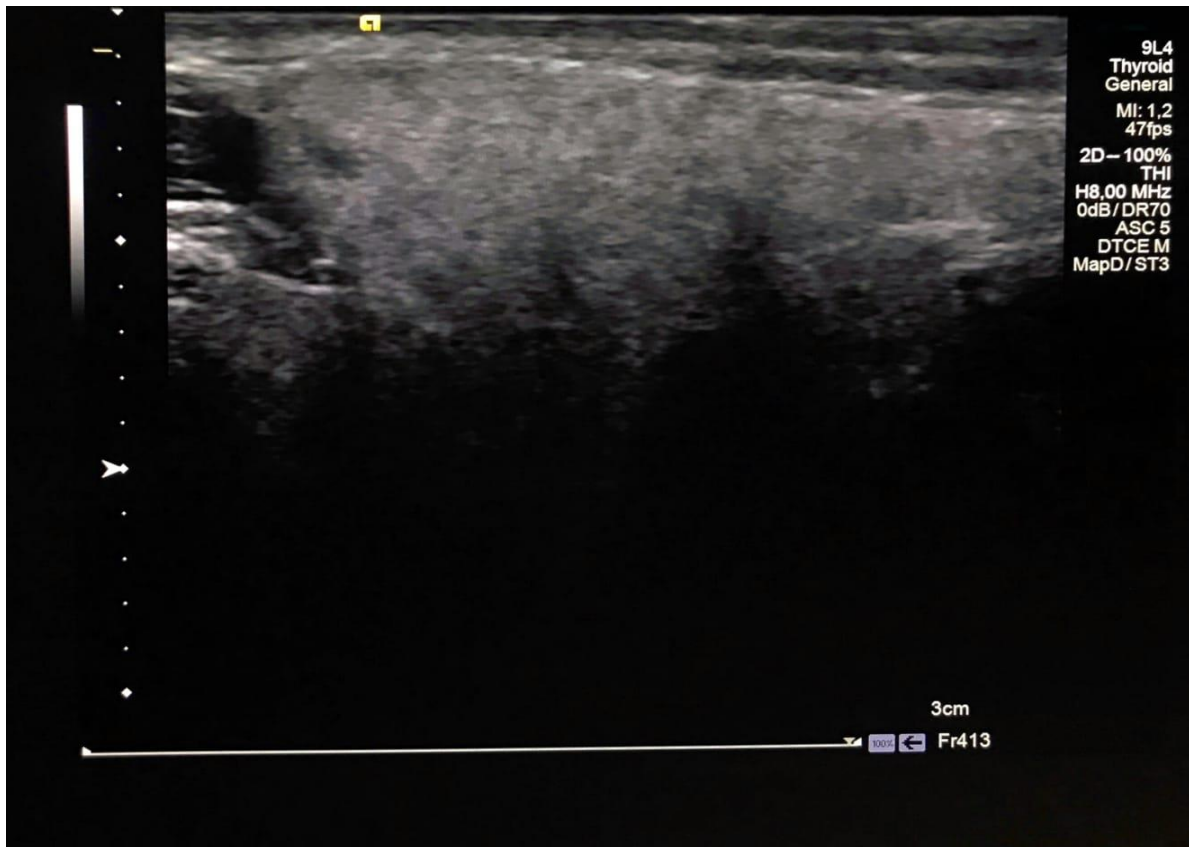


Figure 1. Healthy right parotid gland gray scale examination of a 27-year-old male patient

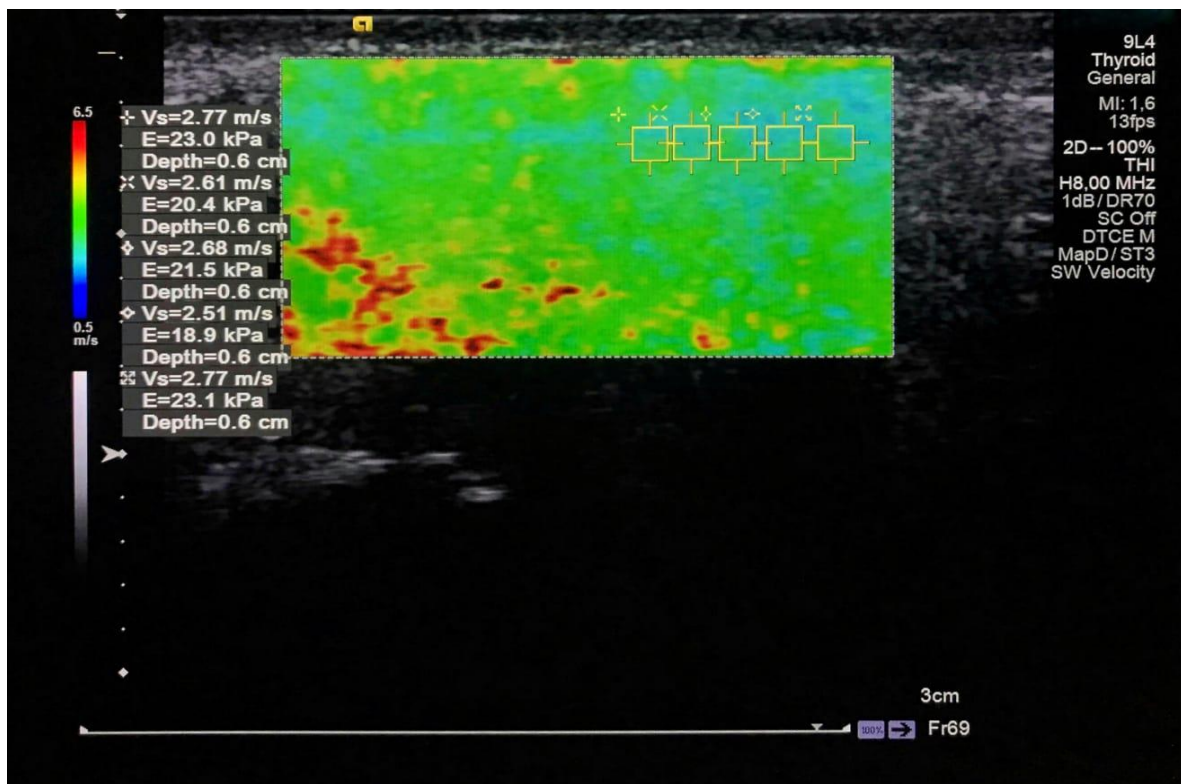


Figure 2. Elasticity values from the right parotid gland in elastography images obtained the day before Ramadan.



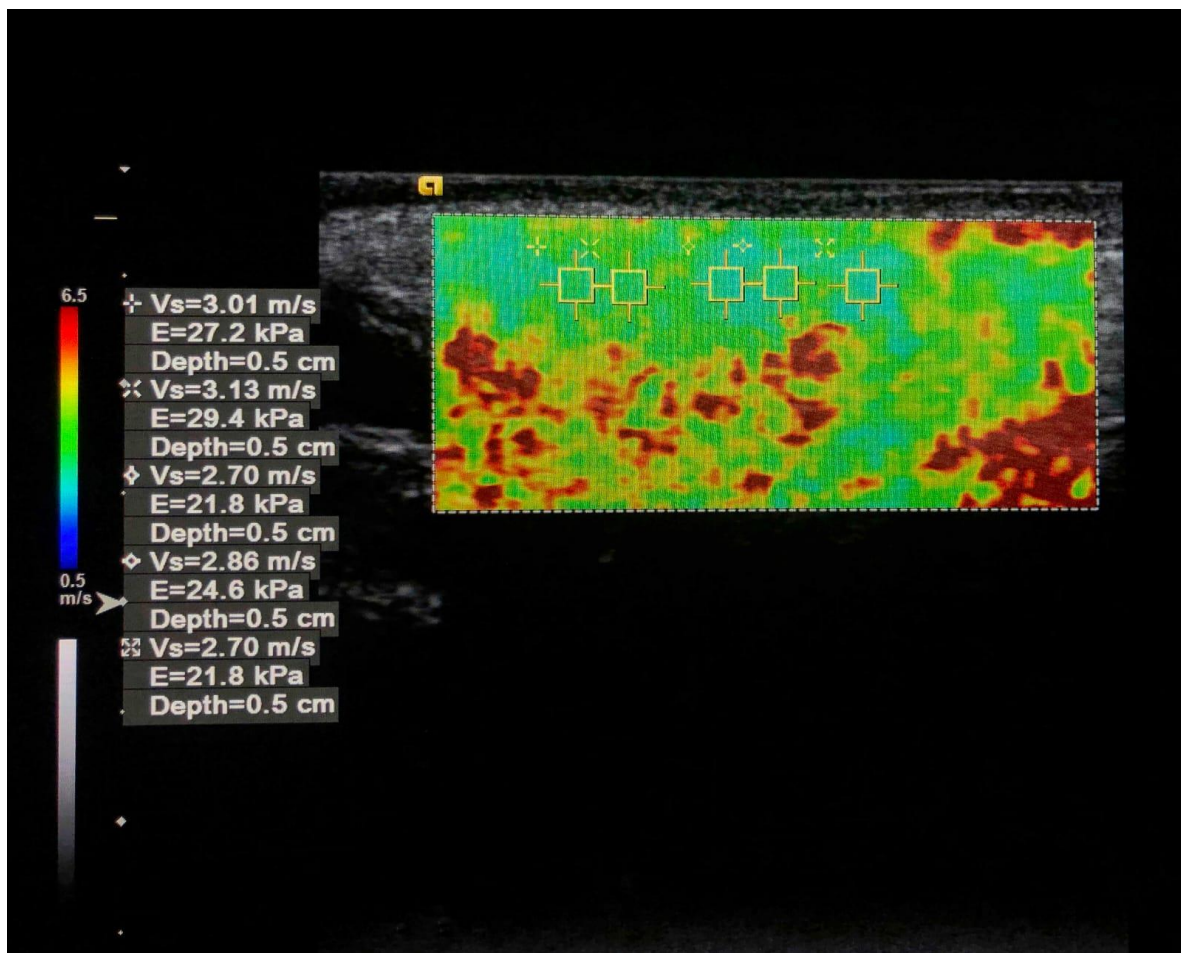


Figure 3. Elasticity values from the right parotid gland in elastography images on the last day of Ramadan

### Discussion

During Ramadan fasting, Muslims are prohibited to eat and drink from dawn to sunset, and they are allowed to eat and drink from sunset to dawn. Therefore, fasting Muslims experience intermittent hunger and thirst throughout Ramadan. In this study, we investigated the cumulative effect of Ramadan fasting on the elasticity of both parotid and submandibular glands.

Like in previous studies, we determined a decrease in BMI values of the participating volunteers at the end of Ramadan (12, 13). This decrease in the BMI values might be a result of the reduced calorie intake. The previous studies had been focused rather on the changes in the biochemical and immunological components in the salivary secretion, which might emerge as a result of fasting, instead of the effects on the structural characteristics. Develioğlu et al. (13) investigated the effects of Ramadan fasting on the concentrations of serum IgG, IgM, and salivary IgA and they found that IgG values declined but remained within the normal limits and the serum IgM levels were not affected. They also determined that there was a statistically significant decrease in the levels of salivary IgA. Sariri et al. (14) conducted a study to investigate the possible changes in the salivary glucose levels during Ramadan fasting and detected a drop in the mean salivary glucose concentration during Ramadan fasting compared to the concentrations before Ramadan. Khaleghifar et al. (15) investigated the effects of Ramadan fasting on the biochemical analysis of the salivary fluid and measured the uric acid concentration, alkaline phosphatase (ALP) and aspartate aminotransferase (AST) activity before, during, and after fasting. They reported a significant decline in the salivary uric acid and AST concentrations and a significant elevation in the ALP activity. In a study on the effect of Ramadan fasting on sleep patterns conducted by Bahaham et al., it was found that melatonin levels obtained from saliva samples declined significantly below basal levels, despite the fact that the circadian pattern was retained during Ramadan (16). Another study by Joachim et al. demonstrated that sialadenitis developed more than twice as frequently in patients who fasted during Ramadan than in non-fasting months. According to the researchers, this situation occurred as a result of dehydration (17).

US elastography is increasingly being utilized to diagnose both benign and malignant diseases of the salivary

glands. Elastography studies reveal promising outcomes, particularly in diseases that involve inflammatory alterations and fibrosis in the major salivary glands, such as primary Sjögren's syndrome (pSS) (18-20). In a study on pSS, sicca syndrome, and a healthy control group, Dejaco et al. found that patients with pSS had higher elastography scores (21). Wierzbicka et al. observed that parotid gland stiffness increased in all patient groups compared to the control group in patients with pSS, sialolitis, Stensen's duct stenosis, and chronic inflammation (22). Similarly, in another study utilizing the acoustic radiation force imaging method, Turnaoğlu et al. reported that mean SWV values in pSS patients were higher than in the control group (23). In a study performed by Arslan et al., higher SWE and elastic modulus values were obtained in patients with pSS compared to the control group (24).

Our aim in this study was to investigate the physiological changes that intermittent hunger and thirst may cause in salivary secretion during the month of Ramadan and the reflections of its possible effects on the elasticity of the tissue on the major salivary glands. To the best of our knowledge, this is the first study demonstrating the effects of Ramadan fasting on the elasticity of the salivary glands. Ratchataseetkul et al. (25) conducted a study to investigate the effects of food intake on liver stiffness and measured the hepatic elasticity in the 15th, 30th, 45th, 60th, and 120th minutes after overnight fasting. The measurements were repeated after the overnight fasting every 30 minutes until they returned to the basal level. The liver elasticity returned to baseline by 150 minutes. Mederacke et al. (26) performed a similar study to show the effects of food intake on liver stiffness in patients with chronic or resolved hepatitis C virus infection. Researchers found that liver stiffness significantly increased immediately after food intake for up to 60 min and normalizing after 180 min. In our current study, no similar changes were detected in the salivary glands.

As the measurements were performed on the day before the first day of Ramadan and after 8-hour fasting on the last day of Ramadan in our study, we believe that the elasticity of the parotid and submandibular glands was probably returned to baseline values. According to the results of this study, intermittent hunger, and thirst like in Ramadan fasting did not have any effect on the elasticity of the parotid and submandibular glands.

### Study limitations

One of the limitations of our study is that comparing the control group not only at the beginning and end of the Ramadan month, but also during other periods, could have added further value to our paper. The second limitation is the small number of voluntary participants. The third limitation is that, since the study sample consisted solely of healthy young men, the results cannot be generalized to other age groups.

### Conclusion

The intermittent fasting during Ramadan had no effect on the elasticity of the salivary glands, as determined by our studied. Further multicenter clinical studies with larger sample sizes are needed to demonstrate to confirm these findings.

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**Ethical Approval:** This Study approval was obtained from the Harran University Faculty of Medicine, Ethics Committee (number: HRÜ/19.03.43. date: 11.03.2019). Informed consent was obtained from all patients.

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