Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2023;48(1):227-233
DOI: 10.17826/cumj.1186009

RESEARCH

Evaluation of pancreas elastography in pediatric patients diagnosed with Celiac disease

Çölyak hastalığı tanılı çocuklarda pankreas elastografisinin değerlendirilmesi

Didem Gülcü Taşkın[1], Okan Dilek[2]

[1]Department of Pediatric Gastroenterology, Adana City Training and Research Hospital, Adana, Turkey
[2]Department of Radiology, Adana City Training and Research Hospital, Adana, Turkey

Abstract

Purpose: The goal of this study was to evaluate the pancreatic parenchyma in celiac patients with transabdominal ultrasonography (US) and ultrasound elastography (UE). The aim of this study is to identify the difference of pancreatic elastography values and pancreatic dimension between the different four pediatric coeliac patient groups with respect to their development curve standart deviation (SD) scores.

Materials and Methods: This study is single-center, prospective study. We included 5–18 years old patients diagnosed with Celiac Disease (CD). Pancreatic dimension and parenchymal elastography measurements of 106 patients eligible for the study were performed by a single radiologist. Height, weight, body mass index (BMI), fecal elastase values, age at diagnosis, duration of illness and medical history of the patients were evaluated. The patients were divided into four groups with respect to their development curve SD scores.

Results: Our study group included 106 CD patients, 72 female and 34 male children were included in our study. The age at diagnosis of the patients was 100.4±97.5 months, and the disease duration was 4.1±2.5 years. The patients were examined in 4 groups. There was no difference in pancreatic elastography values between four groups. There was no difference in the dimensions of the pancreatic head between these groups. It was observed that the anteroposterior diameters of the body and tail increased as SD values increased. There was no difference between fecal elastase values.

Conclusion: Pancreas dimensions were higher in celiac patients with a higher kilogram SD score. However, no significant difference in pancreatic elastography values was observed when the kilogram SD score was used.

Keywords: Celiac disease, child, pancreas, elastography, fecal elastase

Öz

Amaç: Çalışmamızda Çölyak Hastalarında (ÇH) pankreas parankimi transabdominal ultrasonografi (USG) ve elastografi ile değerlendirildi. Çalışmada ÇH'lerde pankreas elastografi ve pankreas boyutunun ölçümü ile hastaların gelişim eğrilerinin karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Çalışmamız tek merkezli, prospektif tasarlanmış olup Çölyak Hastalığı tanılı, 5-18 yaş arası hastalar dahil edilmiştir. Çalışmaya uygun olan 106 hastanın pankreas boyutları ve parankim elastografi ölçümleri tek radyolog tarafından yapıldı. Hastaların boy, kilo, vücut kitle indeksi (VKİ), fekal elastaz değerleri, tanı yaşları, hastalık süreleri ve özgeçmişleri değerlendirildi. Hastalar gelişim eğrileri standart deviasyon SD skoruna göre dört gruba ayrıldı.

Bulgular: Çalışmamıza 106 ÇH dahil edilmiş olup bunların 72'si kız, 34'ü erkek idi. Hastaların tanı yaşları ortalama 100,4±97,5 ay, tanı süreleri ise 4,1±2,5 yıl olarak hesaplandı. Hastalar gelişim eğrilerinin SD skorlarına göre (<-2SD, -1, -2SD, -1,0SD, >0 SD grupları) 4 grupta incelendi. Gruplar arasında pankreas elastografi değerleri arasında anlamlı farklılık saptanmadı. Yine bu gruplar arasında pankreas baş kısmı boyutlarında farklılık saptanmadı. Gözlemlendiği kadarıyla gövde ve kuyruk kısmı ön-arka çapları ile SD skoru arttıkça pozitif korelasyon izlendi (sırası ile pankreas gövde; 9,75±1,4, 8,9±1,5, 10,2±1,8, 10,7±1,9 mm, pankreas kuyruk; 7,75±0,9, 7,2±1,4, 8,14±1,4, 8,4±1,4 mm). Fekal elastaz değerleri arasında da bir fark saptanmadı.

Sonuç: Çölyak hastalarında kilogram SD skoruna göre yapılan değerlendirmede SD skoru yüksek olan hastaların pankreas boyutlarının daha büyük olduğu saptandı. Ancak kilogram SD skoruna göre pankreas elastografi değerleri arasında anlamlı bir faklılık saptanmadı.

Anahtar kelimeler: Çölyak hastalığı, çocuk, pankreas, elastografi, fekal elastaz

Address for Correspondence: Didem Gulcu Taşkın, Adana City Training and Research Hospital, Department of Pediatric Gastroenterology, Adana, Turkey E-mail: dgulcu@gmail.com
Received: 09.10.2022 Accepted: 06.02.2023

INTRODUCTION

Celiac disease (CD) is a systemic autoimmune disease characterized by both intestinal and extra-intestinal manifestations, resulting in the destruction of intestinal villi caused by antibodies produced against "gluten" in the diet of individuals[1]. CD prevalence is between 0.5% and 1% worldwide[2]. CD may be asymptomatic, oligosymptomatic or present with extraintestinal symptoms[3]. Exocrine pancreatic insufficiency (EPI) has been recorded in children with uncured CD[4]. Although the underlying pathophysiology is not fully understood, many factors are suspected. Disrupted excretion of pancreatic hormons, amino acid insufficiency due to malabsorption giving rise to a decrease in pancreatic enzyme production, and protein malnutrition reasoning textural changes in the pancreas are some of the physiopathological pathways[4]. Postmortem autopsy studies give definitive results to directly show the changes that occur in the pancreas of patients with CD. Furthermore, fecal elastase, which shows pancreatic exocrine function may help indirectly. Nevertheless, the last study using magnetic resonance imaging (MRI) to assess pancreatic parenchymal textural did not detect a morphological anomaly in EPI patients and therefore concluded that EPI is a functional default in pancreatic enzyme excretion[5]. On the other hand, there are endoscopic ultrasonography and ultrasound elastography (UE) studies trying to demonstrate the structural change of the pancreatic parenchyma[6]. In literature one of the other uses of elastography is chronic pancreatitis (CP). Chronic inflammation of the pancreas in CP with fibrosis is resulting in irreversible structural damage and impairment of exocrine and endocrine functions. The evaluation of tissue stiffness is the option to assess the diagnosis of CP[7]. And especially one of the studies conducted that elastography is not only a tool for diagnosing pancreatic diseases, it may also use for screening general population[8].

Some CD patients exhibit growth retardation. Not only diet, but also changes in the pancreas are thought to contribute to this condition in these patients. It is possible to demonstrate the structural changes in pancreas radiologically in CD. Structural changes, changes in pancreatic volume and stiffness can be evaluated by ultrasonography (US). US is a non-invasive test, would be appropriate for this purpose. It can be done in elastography along with US. Whether there is a change in the size and stiffness of the pancreas in celiac patients and the relationship between this change and growth parameters has not been evaluated before. Therefore, the goal of this study was to assess the pancreatic parenchyma in CD patients using transabdominal US and UE.

MATERIALS AND METHODS

Sample

In this study, patients diagnosed with CD who were followed up in Pediatric Gastroenterology outpatient clinic in Adana City Training and Research Hospital were evaluated. 148 patients, whose patient sample was determined by power analysis and selected by randomized sampling method, were included in the study. The study designed as prospectively. The patients selections were done by the pediatric gastroenterology specialist according to the exclusion and inclusion criteria of the study. Sixteen patients were excluded from the study because they were under 5 years old; nine patients were excluded because they did not comply during US, and 7 patients were excluded because they had pancreatic atrophy. The radiologist evaluating the measurements was blinded to the patients' medical history. Ten patients were excluded from the study because of the withdrawal of the consent. We exclude all the conditions that may affect the pancreas. A total of 106 patients were evaluated.

Procedure

Weight, height, BMI, age and duration of diagnosis, and fecal elastase values of each patient were recorded from the electronical files of each patient. All electronical files are reliable and accessible by id number. Ethical approval was obtained from Adana City Training and Research Hospital Ethic Committee (Date: 27.01.2021, Approval number: 1292/75). This study acted consistently with the ethical principles outlined in the Declaration of Helsinki. The study was explained in detail and the participants were included in the study after acquiring written informed consent from their families.

Ultrasonography and 2D shear wave elastography

Radiological evaluation and measurements were made by single radiologist, a radiologist with at least 10 years of experience. All the radiological

evaluations and measurements were analysed by the same radiologist and recorded. Pancreatic ultrasound scanning was performed on all participants using a high-resolution ultrasound device (Philips EPIQ7) and a 1-5 MHz high-resolution probe (Philips Health Care, Bothell, WA).

Elastography reveals the morphological changes in the tissue and contributes to the gray scale ultrasound examination findings in the differential diagnosis of tissue lesions. In some diseases, it provides additional information, such as revealing the severity of progression and evaluating response to medical treatment[9]. Elastography is becoming increasingly common in medical practice and its clinical value is increasing day by day. Furthermore, elastography has great potential in the field of research because it is a new method. The ElastPQ technique generates shear waves within the organ using a force impulse of acoustic radiation.

All participants were asked to be in a fasting state for at least 6-8 hours before the ultrasonographic examination. Those who could not hold their breath, had flatulence in the abdomen, whose pancreas could not be fully visualized or who were extremely obese were excluded from the study. First, the transabdominal US probe was placed in the epigastric region and the pancreas was visualized.

The pancreas was evaluated while the participants were in the supine position. Pancreatic echogenicity and anteroposterior lengths of the pancreatic head, body, and tail were measured by B-mode gray-scale ultrasound, which provides a clear view of the entire pancreas. Pancreatic echogenicity was considered normal in those with iso, or mild echogenicity compared to the liver parenchyma. Those more echogenic than liver were considered fatty changes and were not included in the study. Then, the participants were instructed to hold their breath, and measurements were taken from the pancreatic head with point share wave elastography (pSWE). A fixed Region of interest (ROI) of 5x5 millimeters was used in pSWE. The obtained data were recorded as m/sec. Five consecutive measurements were taken from the pancreatic head. The median value was considered a sample of the velocity in each part of the pancreas. Only procedures with a performance ratio of at least 60% were accepted dependable. The ROI selection region was chosen as the zone of the head, body or tail of the pancreas most clearly visualized in B-mode imaging that is not near to a gas or liquid components such as a blood vessel or stomach.

Statistical analysis

SPSS 23.0 package program was used in the analysis of the data. Categorical measures were presented as numbers and percentages, and continuous measures as mean and standard deviation (median and min-maxi, where appropriate). Chi-square and Fisher's exact tests were used to match categorical variables. For continuous measurements, compliance with the normal distribution was checked with the Shapiro-Wilk test. The Mann-Whitney U test was used to match the variables between two groups, and the Kruskal Wallis test was used to match the variables between more than two groups. Post Hoc Bonferroni method was used to analyze the source of variation between groups (<-2SD -1, -2SD -1.0SD >0SD). Spearman correlation test was used to define the relationship between elastase, pancreas body elastography and disease duration. A P value less than 0.05 was considered significant in all analyses.

RESULTS

In our study, 42 patients were excluded. Of the 106 patients included in the study, 72 females and 34 males. The duration of CD was 4.1±2.5 years. Detailed data are shown in Table-1.

When patients were classified according to their kilogram SD (-2SD, -1, -2SD, -1.0SD,>0SD), there was a significant difference in their initial BMI and height SDs, with values increasing as the SD score increased. Again, as the SD score increased, an increase in pancreatic head and body thickness was observed. There was no difference in the elastography values of the pancreatic head between the groups Table 2 contains a detailed evaluation.

When the correlation between the duration of the disease and elastase and elastography values was evaluated, a positive correlation was found between the duration of the disease and elastography values. And a negative correlation between duration of the disease and elastase values. But all these correlations were not statistically significant (Table 3).

Table 1. Demographic data, height, weight, BMI, and pancreas measurements of the patients

Variable	Frequency (n)	Percent (%)
Gender		
Male	34	32.1
Female	72	67.9
Diet compliance		
No	31	29.2
Yes	75	70.8
	Mean±SD	**Median (Min-Max)**
Age of diagnosis (month)	100.4±97.5	89 (12-211)
Duration of disease (year)	4.1±2.5	3.9 (0.2-11.7)
Initial BMI	16.19±3.3	15.46 (11.85-34.52)
Final BMI	17.92±4.22	17.15 (12.12-31.47)
Weight SD	-0.92±1.25	-0.85 (-4.47-(+2.39))
Height SD	-1.02±1.17	-0.97 (-4.57-(+ 1.44))
Elastase(µg/g)	388.1±245.8	293 (32.4-720)
Pancreas head (mm)	13.8±2.6	13.3 (9-23)
Pancreas body (mm)	9.8±1.7	10 (6.5-15.1)
Pancreas tail (mm)	7.9±1.35	8 (5-11)
Pancreas body elastography (m/sn)	0.64±0.16	0.62 (0.34-1.15)

BMI, body mass index; SD, standard deviation

Table 2. Pancreatic thicknesses, elastography values, and other detailed comparisons

Variable	<-2SD	-1,-2SD	-1,0SD	>0SD	
	n(%)	**n(%)**	**n(%)**	**n(%)**	**p**
Gender					
Male	9 (37.5)	10 (41.7)	7 (20.6)	8 (33.3)	0.332
Female	15 (62.5)	14 (58.3)	27 (79.4)	16 (66.7)	
Diet compliance					
No	11 (45.8)	8 (33.3)	6 (17.6)	6 (25)	0.122
Yes	13 (54.2)	16 (66.7)	28 (82.4)	18 (75)	
	Mean±SD Median (Min-Max)	**Mean±SD Median (Min-Max)**	**Mean±SD Median (Min-Max)**	**Mean±SD Median (Min-Max)**	
Age of diagnosis (month)	86.7±35.9	85.4±34.9	114.2±162.2	109.4±48.7	0.308
	83 (24-150)	79 (23-153)	87 (12-211)	107.5 (36-187)	
Duration of disease (year)	4.8±2.9	4.2±2.3	3.8±2.5	4.15±2.5	0.596
	4.3 (0.9-11.8)	3.9 (0.65-10.4)	3.6 (0.26-11.2)	3.7 (1.05-10.9)	
Initial BMI	14.4±1.4	14.9±1.5	16.1±2.4	19.4±4.6	**<0.001**
	14.1(11.9-17.3)	14.8 (12.8-18.3)	15.7 (12.9-25.6)	18.3 (14.1-34.5)	
Final BMI	19.6±3.3	17.3±4.3	17.7±3.8	17.6±5.4	0.344
	20.4(14.1-23.6)	16.1(12.9-27.0)	17.8(12.8-25.4)	16.9(12.1-31.5)	
Lenght SD	-2.1±0.87	-1.4±0.9	-0.67±0.9	-0.04±0.96	**<0.001**
	-2.1 (-4.6- -0.6)	-1.49 (-2.53- 0.46)	-0.67(-2.26- 1.38)	0.02 (-1.83- 1.44)	
Elastase(µg/g)	431.9±253.9	377.6±258.5	391.4±259.8	333.7±221.6	0.909
	432.6 (127-720)	286 (37-720)	285 (115-720)	283.9 (324-861)	
Pancreas head (mm)	13.4±2.1	12.7±2.0	14.3±2.7	14.6±3.0	0.061
	13.2 (10.1-18)	12.8 (9-18.4)	13.8 (9.5-23)	14.1 (10.4-22.1)	
Pancreas body (mm)	9.75±1.4	8.9±1.5	10.2±1.8	10.7±1.9	**0.007**
	9.7 (6.7-12.1)	9 (6.5-12.1)	10.2 (6.5-14.2)	10.9 (7.4-15.1)	
Pancreas tail(mm)	7.75±0.9	7.2±1.4	8.14±1.4	8.4±1.4	**0.024**
	8 (6-10.1)	7.05 (5-10.1)	8.1 (5.1-11)	8.1 (6.2-11)	
Pancreas body elastography(m/sec)	0.57±0.1	0.61±0.17	0.67±0.13	0.67±0.19	0.054
	0.56 (0.37-0.87)	0.57 (0.34-1.15)	0.67 (0.43-0.93)	0.66 (0.4-1.14)	

BMI, body mass index; SD, standard deviation; Details are shown according to kilogram SD groups.

Table 3. Evaluation of the correlation between duration of the diseases and elastase and elastography values.

Variable	Duration of disease (year)	
	R*	p
Elastase(µg/g)	-0.072	0.631
Pancreas body elastography(m/sec)	0.040	0.684

* Spearman correlation test

DISCUSSION

In the current study, when pancreatic size and elastography were evaluated, it was observed that size of the pancreatic body and tail in addition to the pancreatic head increased as the weight SD values approached positive values between those with growth and developmental retardation and those without. One of the objectives was to evaluate the effect of changes in pancreatic parenchymal elastography on growth and development. The effects of changes in pancreatic parenchyma elasticity on SD distribution in CD were not statistically significant. Furthermore, there was no difference between fecal elastase values. Another important finding was that there was no significant correlation between duration of the disease and pancreatic elastography and fecal elastase values.

Although pancreatic dimensions are not a direct indicator of functional morphology, changes in dimension can indirectly provide information about function. In our study, an increase in pancreatic size was observed as the kilogram SD score increased. Fecal elastase directly demonstrates pancreatic exocrine function[10,11]. In our study there wasn't a difference in fecal elastase values between CD patient groups. We believe that other factors may have a role in this result[12]. These factors may include diet compliance or pancreatic exocrine functions not being affected in these patients.

In the literature, there is no previous study evaluating transabdominal pancreatic elastography results of CD patients. The goal of our study was to assess the elasticity of the pancreatic parenchyma in CD patients with growth retardation. When we look at the literature, it is seen that studies on pancreatic elastography are mostly related to the diagnosis of cystic fibrosis patients and pancreatic involvement of cystic fibrosis [13,14]. In a study conducted in children with Type 1 Diabetes Mellitus showed that the elastography screening is safe, non invasive, practical method for long term screening and follow up of endocrin function impairment of the pancreas tissue[15].

There are lots of studies about the uses of elastography on documentation of elastic features of particular soft tissues, pancreatic solid tumours diagnoses [16, 17].

Since there is not enough data in the literature related to our study, we did not have the chance to compare our values with other studies. We hope for researchers that this multicenter will be the horizon for new studies with a large sample size. Based on the results, it was found that pancreatic parenchymal elasticity did not differ in CD patients. Although CD is not a disease that directly affects the pancreas, pancreatic exocrine insufficiency develops in some of the patients. The incidence of pancreatic exocrine insufficiency evaluated by various non-invasive techniques ranges from 11.4% to 56.2%, and the incidence reported is higher in CD patients who have diarrhoea despite a gluten-free diet[14,18]. Prevalence of EPI is higher than recorded so it is important to detect it at an early stage by non-invasive methods like fecal elastase [19]. This raises the question of whether we, as clinicians, are failing to detect EPI. This kind of disease can not remain detected, especially in the early stages if symptoms are either mild or asymptomatic. We know that the extraintestinal manifestation of CD is increasing [20]. There is no universally accepted theory to explain the pathophysiology of EPI in CD. Disrupted excretion of pancreatic stimulating hormones from the atrophic proximal small bowel is thought to be a probable cause for EPI. This theory is supported by immunohistochemical studies that show important changes in enteric endocrine cells with an important reduction in secretin cells [21]. In our study, none of the patients had EPI, but we thought that the pancreas might be affected secondary to CD in these patients. This effect would likely not manifest as pancreatitis but rather as the pancreas being affected to a greater or lesser extent. Another noteworthy result of our study was that the pancreas size increased as the SD score increased. Morphologically, the pancreas structure is preserved and its elasticity does not change measurably, but the micro changes in the pancreatic structure cannot be demonstrated by measurements. Further studies are needed to clarify this situation.

Our study has a few limitations. Our study was conducted in a single center, with a little sample size

and measurements performed by a single radiologist. Another limitation was that measurements were taken exclusively from the pancreatic head. This region was chosen because it is the thickest part of the pancreas and is therefore easily visualized and quantified.

In conclusion, no difference was observed in pancreatic elastography values between CD patients according to patients kilogram SD score. However, pancreatic size increased as the kilogram SD score increased in CD patients. In CD, especially in patients with low kilogram SD score, evaluation of pancreatic size should be evaluated in detail to exclude other possible conditions that may be related to pancreatic insufficiency. Although the elastography values were not significant in our study, there is a need for multicenter studies with the participation of more patients.

Yazar Katkıları: Çalışma konsepti/Tasarımı: DGT, OD; Veri toplama: DGT, OD; Veri analizi ve yorumlama: DGT, OD; Yazı taslağı: DGT; İçeriğin eleştirel incelenmesi: DGT, OD; Son onay ve sorumluluk: DGT, OD; Teknik ve malzeme desteği: DGT, OD; Süpervizyon: DGT, OD; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Adana Şehir Eğitm ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan 27.01.2021 tarih ve 75/1292 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : DGT, OD; Data acquisition: DGT, OD; Data analysis and interpretation: DGT, OD; Drafting manuscript: DGT; Critical revision of manuscript: DGT, OD; Final approval and accountability: DGT, OD; Technical or material support: DGT, OD; Supervision: DGT, OD; Securing funding (if available): n/a.
Ethical Approval: For this study, ethical approval was obtained from the Clinical Research Ethics Committee of Adana Şehir Eğitim ve Araştırma Hospital with the decision dated 27.01.2021 and numbered 75/1292.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Sabatino AD, Corazza GR. Coeliac disease. Lancet. 2009;373:1480-93.
2. Kang JY, Kang AHY, Green A, Gwee KA, Ho KY. Systematic review: worldwide variation in the frequency of coeliac disease and changes over time. Aliment Pharmacol Ther. 2013;38:226-45.
3. Branski D, Ashkenazi A, Freier S, Lerner A, Dinari G, Faber J et al. Extraintestinal manifestations and associated disorders of celiac disease, in gluten-sensitive enteropathy. Front Gastrointest Res. 1992;19:164-75.
4. Freeman HJ. Pancreatic endocrine and exocrine changes in celiac disease. World J Gastroenterol. 2007;13:6344-6.
5. Vujasinovic M, Tepes B, Volfand J, Rudolf S. Exocrine pancreatic insufficiency, MRI of the pancreas and serum nutritional markers in patients with coeliac disease. Postgrad Med J. 2015;91:497-500.
6. Rana SS, Vilmann P. Endoscopic ultrasound features of chronic pancreatitis: a pictorial review. Endosc Ultrasound. 2015;4:10-4.
7. Yamashita Y, Ashida R, Kitano M. Imaging of fibrosis in chronic pancreatitis. Front Physiol. 2022;12:800516.
8. Öztürk M, Citil S, Menzilcioglu MS. Assessment of the pancreas with strain elastography in healthy children: correlates and clinical implications. Pol J Radiol, 2017;82:688-92.
9. Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: part 1: basic principles and terminology. Ultrasound Med Biol. 2015;41:1126-47.
10. Rana SS, Dambalkar A, Chhabra P, Sharma R, Nada R, Sharma V et al. Is pancreatic exocrine insufficiency in celiac disease related to structural alterations in pancreatic parenchyma? Ann Gastroenterol. 2016;29:363-6.
11. Leeds JS, Hopper AD, Hurlstone DP, Edwards SJ, McAlindon ME, Lobo AJ et al. Is exocrine pancreatic insufficiency in adult coeliac disease a cause of persisting symptoms? Aliment Pharmacol Ther. 2007;25:265-71.
12. Therrien A, Kelly CP, Silvester JA. Celiac disease: extraintestinal manifestations and associated conditions. J Clin Gastroenterol. 2020;54:8–21.
13. Yılmaz K, Hattapoğlu, S, Şen V, Karabel M, Kan A, Yılmaz EDS et al. Evaluation of children and adolescent with cystic fibrosis by pancreatic elastography. Pediatr Int. 2022;64:e14951.
14. Piskin FC,Yavuz S, Kose S, Cagli C, Dogruel D, Tumgor G et al. A comparative study of the pancreas in pediatric patients with cystic fibrosis and healthy children using two-dimensional shear wave elastography. J Ultrasound. 2020;*23*:535-42.
15. Öztürk M, Yildirim R. Evaluation of pancreas with strain elastography in children with type 1 diabetes mellitus. Pol J Radiol. 2017;82:767-72.
16. Gungor G, Yurttutan N, Bilal N, Menzilcioglu MS, Duymus M, Avcu S et al. Evaluation of parotid glands with real-time ultrasound elastography in children. J Ultrasound Med. 2016;35: 611–15.
17. Dyrla P, Gil J, Florek M, Saracyn M, Grala B, Jędrzejewski E et al. Elastography in pancreatic solid tumours diagnoses. Prz Gastroenterol. 2015;10:41–46.
18. Pezzilli R. Exocrine pancreas involvement in celiac disease: a review. Recent Pat Inflamm Allergy Drug Discov. 2014;8:167-72.
19. Leeds JS, Oppong K, Sanders DS. The role of fecal elastase-1 in detecting exocrine pancreatic disease. Nat Rev Gastroenterol Hepatol. 2011;8:405-15.

20. Laurikka P, Nurminen S, Kivelä L, Kurppa K. Extraintestinal manifestations of celiac disease: early detection for better long-term outcomes. Nutrients. 2018;10:1015.

21. Buchan AM, Grant S, Brown JC, Freeman HJ. A quantitative study of enteric endocrine cells in celiac sprue. J Pediatr Gastroenterol Nutr. 1984;3:665-71.