ORIGINAL ARTICLE

ENDOS KOPİ COPY GASTROINTESTINAL 2020; 28(2): 60-66

Evaluation of the relationship between recurrent pancreatitis and endoscopic ultrasonography in pediatric patients

Pediatrik hastalarda rekürren pankreatit ve endoskopik ultrasonografi arasındaki ilişkinin değerlendirilmesi

Fatma DEMİRBAŞ[1], Mustafa KAYMAZLI[2], Gönül ÇALTEPE[1], Esra EREN[1], Ayhan Gazi KALAYCI[1], Ahmet BEKTAŞ[2]

Departments of [1]Pediatric Gastroenterology, Hepatology and Nutrition, and [2]Gastroenterology, Ondokuz Mayıs University School of Medicine, Samsun

Background and Aims: *Data regarding the role of endoscopic ultrasonography in pediatric chronic/recurrent pancreatitis is limited. The aim of this study is to evaluate the role of endoscopic ultrasonography in the diagnosis and clinical observation of recurrent pancreatitis in childhood.* ***Materials and Methods:*** *Between September 2016 and September 2017 endoscopic ultrasonography findings of 17 patients with recurrent pancreatitis and 20 patients in a control group were evaluated retrospectively, and the findings were compared. The control group consisted of patients who underwent endoscopic ultrasonography for cholecystolithiasis but had no pancreatitis.* ***Results:*** *The most common endoscopic ultrasonography finding was ≥ 3 mm hyperechoic strands in 15 (88.2%) of the patients. According to the conventional criteria, 11 patients (64.7%) had ≥ 3 pathological findings. No patient in this study fulfilled the Rosemont criteria for the definitive diagnosis of chronic pancreatitis. While pancreas parenchymal and ductal pathologies were not detected in the control group, 55% patients had < 2 mm hyperechoic strands.* ***Conclusion:*** *In this study, hyperechoic line is the most common endoscopic ultrasonography finding of recurrent pancreatitis in childhood. The threshold number of endoscopic ultrasonography criteria for the diagnosis of chronic pancreatitis in pediatric patients is unclear. However, in our opinion, the conventional criteria are more suitable than the Rosemont criteria for the diagnosis of chronic pancreatitis in childhood. Further studies are needed in this field.*

Key words: *Child, endoscopic ultrasonography, recurrent/chronic pancreatitis*

Giriş ve Amaç: *Pediatrik kronik/tekrarlayan pankreatitte endoskopik ultrasonografini rolüne ilişkin veriler sınırlıdır. Bu çalışmanın amacı, çocukluk çağında rekürren pankreatitin tanı ve klinik gözleminde endoskopik ultrasonografinin rolünü değerlendirmektir.* ***Gereç ve Yöntem:*** *Eylül 2016 - Eylül 2017 tarihleri arasında rekürren pankreatitli 17 hastanın ve kontrol grubundaki 20 hastanın endoskopik ultrasonografi bulguları retrospektif olarak değerlendirildi ve bulgular karşılaştırıldı. Kontrol grubu kolesistolitiyazis nedeniyle endoskopik ultrasonografi uygulanan ancak pankreatiti olmayan hastalardan oluşmaktaydı.* ***Bulgular:*** *Hastaların en sık endoskopik ultrasonografi bulgusu ≥ 3 mm hiperekoik banttı (15 hasta %88.2). Konvansiyonel kriterlere göre 11 hastada (%64.7) ≥ 3 patolojik bulgu bulundu. Hiçbir hasta, kronik pankreatitnin kesin tanısı için Rosemont kriterlerini karşılamadı. Kontrol grubunda parankimal ve duktal patolojiler saptanmaz iken, %55 hastada < 2 mm hiperekoik bant vardı.* ***Sonuç:*** *Bu çalışmada hiperekoik bantın çocukluk çağında rekürren pankreatitin en sık endoskopik ultrasonografi bulgusu olduğu görülmüştür. Pediyatrik hastalarda kronik pankreatit tanısı için endoskopik ultrasonografi kriterlerinin eşik sayısı belirsizdir. Bununla birlikte, bizim görüşümüze göre, konvansiyonel kriterler, çocuklukta kronik pankreatit tanısı için Rosemont kriterlerinden daha uygundur. Bu alanda daha fazla çalışmaya ihtiyaç vardır.*

Anahtar kelimeler: *Çocuk, endoskopik ultrasonografi, rekürren/kronik pankreatit*

INTRODUCTION

Chronic pancreatitis (CP) is an inflammatory disease of the pancreas characterized by the loss of exocrine and/or endocrine functions, which may lead to irreversible damage in the pancreas (1).

The 1 of 3 criteria of typical clinical symptoms; abnormal imaging and abnormal pancreas function test results is sufficient to establish the diagnosis of CP (1). However, the role of abdominal pain is controversial in pediatric CP patients. Therefore, as it is more difficult to make a diagnosis based on clinical symptoms in children, there is a greater importance of laboratory and imaging methods as objective criteria. Magnetic resonance cholangiopancreatography (MRCP) imaging is widely used in the diagnosis of CP due to its unmatched soft tissue contrast resolution, radiation-free nature and non-invasiveness (2,3). Diagnosis of CP is made by the presence of MRCP findings such as main pancreatic duct irregularity, parenchymal changes and cysts of varying sizes, but in cases with no evident changes, the diagnosis is delayed due to the lack of optimal evaluation of pancreatic parenchyma (4). However, delay in diagnosis of RP patients may lead to skipped CP diagnosis and delayed treatment. Endoscopic ultrasonography findings (EUS), which were first used in the diagnosis of CP in 1986, evaluate the parenchymal and duct changes of the pancreas in detail (4-11). Recent studies show that its sensitivity is higher than MRCP in the diagnosis of CP (12).

The use of EUS is not as widespread in pediatric CP cases as it is in adult patients (13-15). The aim of this study is to

Demirbaş F, Kaymazlı M, Çaltepe G, et al. Evaluation of the relationship between recurrent pancreatitis and endoscopic ultrasonography in pediatric patients. Endoscopy Gastrointestinal 2020;28:60-66.

DOI: 10.17940/endoskopi.670315

Correspondence: Fatma DEMİRBAŞ
Ondokuz Mayıs University Faculty of Medicine,
Department of Pediatric Gastroenterology, Hepatology and Nutrition
Kurupelit, Samsun 55520 Turkey • E-mail: fatmademirbas81@hotmail.com
Manuscript received: 04.01.2020 Accepted: 29.07.2020

This study was presented as poster presentation at the ESPGHAN 51st Annual Meeting 2018 on May 09-08, 2018 in Geneva.

retrospectively evaluate the role of EUS in the diagnosis and clinical follow-up of children with RP. The secondary aim was to evaluate the EUS findings of the patients that were characterized with RP attacks compared to EUS findings of the control group.

MATERIALS and METHODS

Patients

Seventeen pediatric patients with recurrent episodes of pancreatitis who were screened with EUS at least once in their clinical follow-ups between September 2016 and September 2017 were evaluated retrospectively. The patients undergone EUS because of the initial diagnosis of RP. Our patient group was determined according to acute recurrent pancreatitis (ARP) (4 patients) diagnostic criteria [at least two discrete episodes of acute pancreatitis (AP) as defined by the INSPPIRE (the International Study Group of Pediatric Pancreatitis In Search for a Cure) criteria in the absence of evidence of irreversible, structural changes in the pancreas] since all of our patients who underwent EUS did not meet the CP (13 patients) diagnostic criteria (Pediatric CP is defined by INSPPIRE as as the presence of at least one of the following; irreversible structural changes in the pancreas such as diffuse or focal destruction, sclerosis, pancreatic duct abnormalities/obstruction with some periods of consistent abdominal pain or lipase or amylase ≥ 3 times upper limit of normal (ULN), irreversible, structural changes in the pancreas such as diffuse or focal destruction, sclerosis, pancreatic duct abnormalities/obstruction with exocrine or endocrine pancreatic insufficiency) (1). The control group consisted of 20 age-matched children who have never had an attack of proven pancreatitis and received EUS for cholecystolithiasis.

Detailed information about clinical parameters such as age at the onset of symptoms, duration and number of acute attacks, follow-up duration, history with respect to etiology (presence of chronic disease, infection, trauma and medication use), percentile and Z scores of weight, height and body mass index (BMI) (according to WHO criteria) were recorded. Liver and kidney function tests during attack periods, fasting lipid levels, genetic analysis of cystic fibrosis, immunoglobulin G4 (IgG4) levels, abdominal ultrasonography (USG) and MRCP findings (reported by an experienced pediatric radiologist) were recorded from the patient follow-up system.

EUS procedure

All the EUS procedures were performed by an experienced gastroenterologist using a radial echo endoscope (Fujinon EG-530 UR2). After a 6-hour fasting period, while administering midazolam, propofol or ketamine to patients, O2 saturation with pulse oximetry and heart rate were monitored by the anesthesia team throughout the procedure. The results of the EUS were scored by an experienced gastroenterologist. Parenchymal and/or ductal changes on EUS as per Conventional criteria (16), hyperechoic foci, hyperechoic strands, lobular contour, cysts, main duct dilatation, duct irregularity, hyperechoic margins, visible side branches and stones were noted. A total presence of 0-2 criteria was recorded as normal. A total presence of 0-2 criteria was recorded as normal or low probability, 3-4 criteria was recorded as indeterminate or intermediate probability and 5-9 criteria was recorded as high probability. Patients with 3 or more of these criteria were determined to be pathological.

The Rosemont classification was recorded as Major A, B and Minor based on the parenchymal and duct criteria in endoscopic ultrasound. Major criteria A included hyperechoic foci (> 2 mm in length/width with shadowing) and major duct calculi (echogenic structure(s) within the major pancreatic duct (MPD) with acoustic shadowing); Major criteria B included lobularity (≥ 13 contiguous lobules = 'honeycombing'), while Minor criteria included cyst (anechoic, round/elliptical with or without septations), dilated duct (≥ 3.5 mm in body or > 1.5 mm in tail), irregular duct contour (uneven or irregular outline and ectatic course), dilated side branch (> 3 tubular anechoic structures each measuring ≥ 1 mm in width, budding from the MPD, hyperechoic duct wall (echogenic, distinct structure > 50% of entire MPD in the body and tail), hyperechoic strands (≥ 3 mm in at least 2 different directions with respect to the imaged plane), hyperechoic foci (> 2 mm in length/width with non-shadowing) and lobularity (> 5 mm, non-contiguous lobules).

According to the Rosemont criteria, the patients were classified as Normal: < 3 minor features with no major features, Indeterminate: Major B feature alone or with < 3 minor features, or 3 to 4 minor features, Suggestive of: Major A feature plus < 3 minor features, or Major B feature plus ≥ 3 minor features, or ≥ 5 minor features with no major features, and Consistent with CP: 2 major A features, or 1 major A feature plus 1 major B feature, or 1 major A feature plus ≥ 3 minor features (17).

Ethics

The study was approved by the Ethics Committee of University Hospital (decision no: 2017/361). Written informed consent forms were obtained from the parents and/or relatives of all the patients in the study.

Statistical Methods

All statistical analyses were performed using SPSS v.21 (Statistical Package for the Social Sciences, Inc.). Conformity of the data to normal distribution was evaluated with the Kolmogorov-Smirnov test. Data showing normal distribution were stated as mean ± standard deviation values, and tho-

se not showing normal distribution were stated as median (min-max) values. Independent paired groups of data with normal distribution were compared using the t-test, and in paired comparisons, the Tukey test was used. Paired groups of data that did not show normal distribution were compared with the Mann Whitney U test. Percentages of qualitative data were compared using the Pearson Chi-squared test and the z-test. A value of $p < 0.05$ was considered statistically significant. Performance of different models was assessed by the area under the receiver operating characteristic (ROC) curve.

RESULTS

Endoscopic ultrasound was performed on 17 patients with RP attacks between September 2016 and September 2017 at our department. Out of 17 patients, 10 (59%) were female, and 7 (40%) were male. The median age of the patients at the time of EUS application was 13.4±1.3 years (range: 3.7-17.6 years), and these patients had a median follow-up period of 39.8 months (range: 9-89 months). At the time of the EUS procedure, 2 patients were determined to have BMI in the < 3^{rd} percentile, and 4 patients had BMI in the > 97^{th} percentile. The number of attacks were recorded as 3 in 13 (76%) patients, 4 in 2 (23.5%), 5 in 1 (5.8%) and 15 in 1 (5.8%). All recurrent pancreatitis patients had MRCP before EUS. Thirteen patients were diagnosed with CP and 4 patients were ARP according to INSPPIRE criteria. Among EUS-applied patients, 5 of them were monitored for RP episodes with MRCP findings of chronic changes and exocrine insufficiency (looking at fecal elastase), 8 patient for RP episodes with MRCP findings of parenchymal and ductal changes, 4 patient for RP episodes only. The mean time between the last attack and EUS was 8 months (range: 1-18 months) (Table 1).

The etiological reasons of the 5 patients in our study were as follows; progressive familial intrahepatic cholestasis (PFIC) type 1, cystic fibrosis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) syndrome, glutaric acidemia type 2 and familial hyperlipidemia. No etiology was found in the other 12 patients. Exocrine pancreatic insufficiency was present in five patients (29.4%), and no endocrine pancreatic insufficiency was present in any of the patients.

EUS was applied to the patients whose transabdominal ultrasound and MRCP were performed in their first evaluation. There was a maximum period of 3 months (mean: 1.2 months) between MRCP and EUS.

The most common EUS finding of the followed-up patients with RP attacks was hyperechoic strands by ≥ 3mm in the pancreatic parenchyma in 15 (88.2%) patients. Other frequently seen findings were hyperechoic focus without shadow (n = 12, 70.5%), lobularity (n = 6, 35.2%), hyperechogenic duct wall (n = 5, 29.4%) and dilatation in the main duct (n = 4, 23.5%) (Figure 1). According to the Conventional criteria,

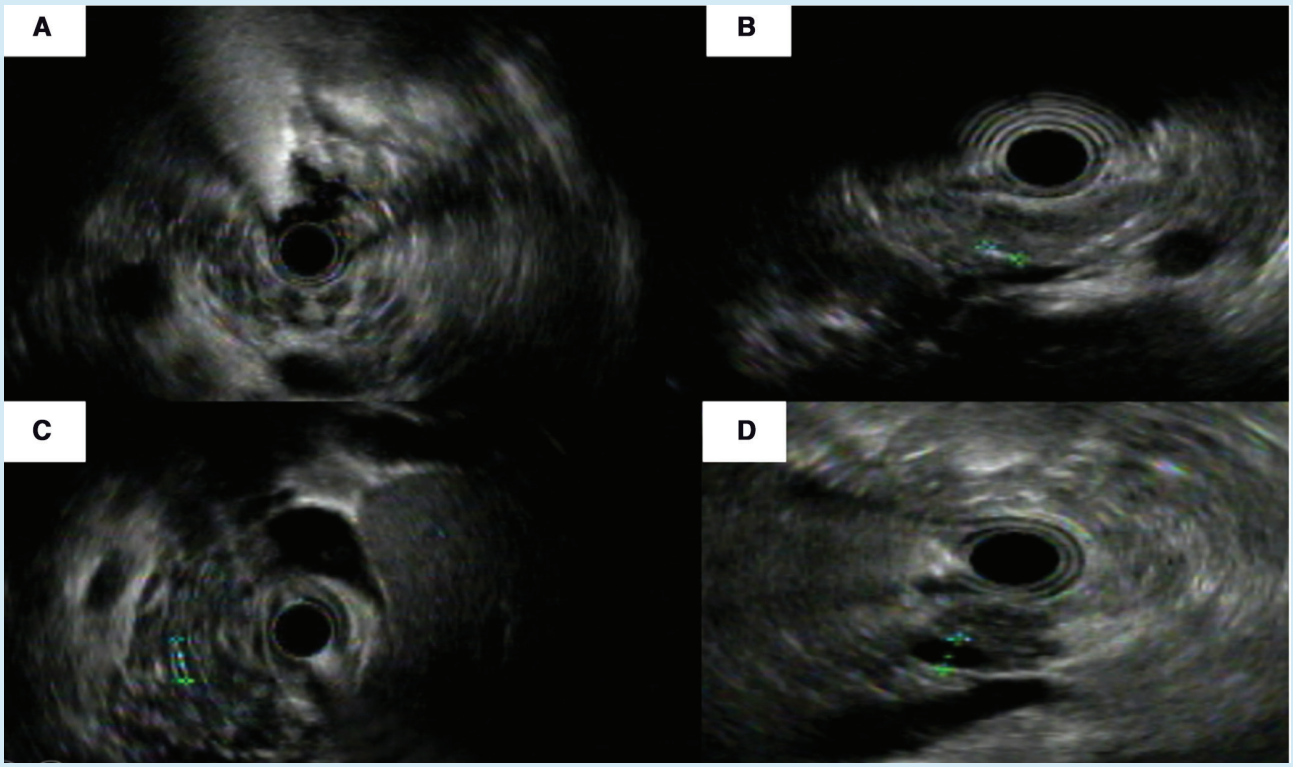

Figure 1. Endoscopic ultrasonography findings of the patients. Hyperechoic strands **(A)**, lobularity **(B)**, hyperechoic duct wall **(C)** and dilatatation of the main pancreatic duct **(D).**

≥ 3 pathological findings were determined in 11 (64.7%) patients (3 criteria in 10 patients, 4 criteria in 1 patient), and 2 pathological findings were determined in 4 (23.5%) patients. Cysts, stones or any visible side branch findings were not observed in any patients. None of the patients met the exact criteria for CP based on the Rosemont criteria. There were 1 major B + 2 minor findings in 6 patients, 3 minor findings in 5 and 2 minor findings in 4 (Table 2). Pathological findings were not determined with EUS in 2 patients. In one, EUS and USG results were normal, and in the other, there was pancreas divisum on MRCP. While the MRCP findings were normal in 3 patients, the EUS findings in 2 patients were hyperechoic foci, hyperechoic strands and lobularity (he was cystic fibrosis, 12 years old male and duration of follow-up 9 months, other patient 17 years old female and duration of follow-up 21 months) and hyperechoic focus, hyperechoic strands and hyperechogenous duct wall in the other patient (17 years old male and duration of follow-up 57 months).

Table 1. Pathological findings of patients with recurrent pancreatitis.

Case No	Age	Gender	Attacks	EUS	MRCP	USG	CP	EI	Duration of Follow-ups (month)
1	7 y 6 m	F	5	1. Hyperechoic strands 2. Hyperechoic foci 3. Hyperechoic duct margin	1. Ductal irregularity	Heterogenous parenchyma	+	-	24
2	17 y 6 m	F	3	1. Normal	1. Pancreas divisum	Normal	-	-	89
3	8 y 3 m	M	3	1. Hyperechoic strands 2. Hyperechoic foci	1. Parenchymal atrophy	Heterogenous parenchyma	+	-	54
4	12 y 3 m	M	3	1. Hyperechoic strands 2. Hyperechoic foci 3. Lobularity	1. Normal	Heterogenous parenchyma	+	+	9
5	10 y 3 m	F	4	1. Lobularity 2. Hyperechoic foci 3. Hyperechoic strands	1. Dilated main duct	Heterogenous parenchyma	+	-	34
6	17 y 6 m	F	3	1. Hyperechoic strands 2. Hyperechoic foci 3. Lobularity	1. Normal	Normal	-	-	21
7	16 y 4 m	M	3	1. Hyperechoic strands 2. Lobularity 3. Hyperechoic duct margin	1. Parenchymal atrophy	Heterogenous parenchyma	+	+	73
8	17 y 6 m	M	3	1. Hyperechoic strands 2. Dilated main duct 3. Hyperechoic duct margin	1. Parenchymal atrophy 2. Ductal irregularity	Heterogenous parenchyma	+	-	10
9	12 y 6 m	F	15	1. Hyperechoic strands 2. Dilated main duct 3. Hyperechoic duct margin	1. Dilated main duct 2. Parenchymal atrophy	Heterogenous parenchyma Dilated main duct	+	+	36
10	10 y 8 m	F	4	1. Hyperechoic strands 2. Hyperechoic foci 3. Lobularity	1. Heterogenous parenchyma	Normal	+	+	30
11	11 y 6 m	F	3	1. Hyperechoic strands 2. Hyperechoic foci	1. Parenchymal atrophy	Heterogenous parenchyma	+	-	18
12	17 y 9 m	F	3	1. Hyperechoic strands 2. Hyperechoic foci	1. Parenchymal atrophy	Heterogenous parenchyma	+	-	57
13	17 y 9 m	F	3	1. Hyperechoic strands 2. Hyperechoic foci 3. Dilated main duct	1. Normal	Heterogenous parenchyma	-	-	40
14	17 y	M	3	1. Hyperechoic strands 2. Hyperechoic foci	1. Parenchymal atrophy	Normal	+	-	44
15	10 y 8 m	M	3	1. Normal	1. Normal	Normal	-	-	49
16	14 y	M	3	1. Hyperechoic strands 2. Hyperechoic foci 3. Dilated main duct 4. Lobularity	1. Heterogenous parenchyma	Normal	+	+	71
17	3 y 7 m	M	3	1. Hyperechoic strands 2. Hyperechoic foci 3. Dilated main duct	1. Ductal irregularity 2. Dilated main duct	Heterogenous parenchyma	+	-	19

y: years; m: month; F: female; M: male; USG: Ultrasonography; EUS: Endoscopic ultrasonography; MRCP: Magnetic resonance cholangiopancreatography EI: Exocrine insufficiency.

Table 2. Comparison of endoscopic ultrasonography findings of patients with Conventional criteria and Rosemont criteria

Conventional Criteria[16] (N = 17)	Rosemont Criteria[17] (N = 17)
Normal (or low probability) consistent with 6 (%35.2)	Normal 9 (%52.9)
Indeterminate or intermediate probability 11 (%64.7)	Indeterminate 6 (%35.2)
	Suggestive of -
High probability -	Consistent with -

Comparison to the Control Group

The pancreas findings of the control group were reviewed from the reports of EUS-applied 20 pediatric patients (14 females, 6 males; mean age: 11.4±4.09 years) because of cholecystolithiasis. In 11 (55%) patients, hyperechoic bands by < 2 mm were determined in the pancreatic parenchyma. No other pathological findings were determined in the pancreas.

When all patients' EUS findings (according to Conventional criteria) were evaluated by ROC analysis the area under the curve was found to be 0.90 (95% CL: 0.802-0.995) and at cut-off ≥ 2 criteria the CP diagnostic sensitivity and specificity were 92% and 91%, respectively ($p < 0.001$).

DISCUSSION

Chronic pancreatitis, although rarely seen in childhood leads to an irreversible damage in the pancreas (1,13). Transabdominal USG and magnetic resonance imaging (MRI) are the first-line imaging methods in the diagnosis and follow-up of CP in children since they are radiation-free and non-invasive (18). Additionally, these imaging modalities may only reveal advanced morphological changes, and therefore, the diagnostic capacity of these modalities is limited in the diagnosis of early stages of pancreatitis (19). In this study, EUS was performed in pediatric patients with RP, and it was found that 64% of the patients had pathological changes in the pancreas.

EUS is accepted as the most sensitive imaging method for the diagnosis of pancreatic diseases because of the feasibility to place the transducer close to the pancreas (19,20). In comparison to the use of EUS in adult CP patients, experience of EUS in pediatric patients has been rarely reported (21,22). In the most recent report on the management of pediatric pancreatitis published by the European Pancreas Association, it was stated that EUS could be useful in the evaluation of CP and gallbladder stones in children, as well as in the treatment of complications (18).

The diagnostic value of EUS in CP patients has been shown to be better than MRCP and endoscopic retrograde cholangiopancreatography (ERCP) since it has the advantages of visualizing main duct dilatation, side branches, hyperechogenicity in the duct wall, and ability to show other parenchymal abnormalities at the same time (23). Even if no abnormality is seen in traditional imaging or functional tests, studies have reported that EUS has shown fine differences in the pancreatic parenchymal and ductal structures (24-29). A recently published meta-analysis of studies which evaluated MRCP and EUS showed that EUS had advantages in diagnosing CP at the rate of 10% in comparison to the 1% for MRCP (18). In determination of early changes in CP, EUS is a more sensitive method than ERCP (9). In a study conducted on adult patients, EUS was reported to have 100% sensitivity in the determination of early stage changes in CP (8). In this study, parenchymal and ductal pathologies were shown on EUS in 17.6% of the patients who had normal results in the conventional evaluation as well as on MRCP, which suggests that EUS can show the parenchyma in more detail in CP. One of the patient had cystic fibrosis and the other two were older children and these patients had a longer period of follow-up. The EUS findings of chronic pancreatitis may occur in children of older age and with long-term follow-up as the results are interpreted. In one patient, EUS was normal, but MRCP showed pancreas divisum. Several studies have recommended MRCP for visualization of biliopancreatic duct anomalies like pancreatic divisum (26,27). Mariani et al. confirmed the superiority of MRCP taken after secretin stimulation compared to EUS and ERCP in the diagnosis of pancreatic divisum (28). Although our patient had RP attacks, she did not meet the diagnosis of CP. Although INSPPIRE consensus stated that pancreatic divisum may play a role in the development of ARP or CP, this finding may not be causative in itself and further investigation is warranted (1).

According to the Conventional criteria, 11 (64.7%) patients in this study had ≥ 3 criteria (10 patients with 3 criteria, 1 patient with 4 criteria). The most frequently seen EUS finding in this study was hyperechoic strands of ≥ 3 mm in the pancreas parenchyma in 15 (88.2%) patients. In this study, the hyperechoic strand in EUS findings that interpreted histopathologically as bridging fibrosis is known as one of the important indications of early CP diagnosis (24). More than three EUS criteria for CP were associated with histological diagnosis of CP (29). In the study by Wiersema et al. (9) the parameters of ≥ 3 criteria were shown to have 80% sensitivity, 86% specificity and 84% accuracy. No patient in this study had cysts, side branches or stones in EUS imaging. According to the Rosemont criteria, 1 major B + 2 minor criteria were determined in 6 patients, 3 minor criteria were found in 5, and 2 minor criteria were observed in 4. The diagnosis of CP was supported by conventional criteria in 11 of patients with CP and no patient in this study fulfilled the Rosemont criteria for the diagnosis of definitive CP. This could be explained by

the fact that our patients were at an early stage of CP or cysts, stones and visible side branches may be seen less frequently in childhood. Although our patient group does not constitute patients with definite diagnosis of CP, it may be more appropriate to use conventional criteria rather than Rosemont criteria in pediatric RP patients to avoid delayed diagnosis and treatment of early stage CP. No advantage of the Rosemont criteria over conventional method was shown in the evaluations of adult groups for the accurate and consistent diagnosis of early and non-calcific CP (30-32). Moreover, there is a need for more data on the evaluation of the Rosemont criteria for diagnosis of CP in the pediatric age group.

In the study by Singh et al. (21), CP was determined in 31% of 32 children with RP (≥ 4 conventional criteria were used for the definitive diagnosis of CP), and Mahajan et al. (33) determined in 58.7% of 71 (≥ 5 criteria was used for diagnosis of CP). In this study, ≥ 3 criteria were used as a pathological finding and this was determined in 64% of the patients. All patients with ≥ 2 criteria of EUS findings had a sensitivity of 92%, and a specificity of 91% to diagnose CP ($p < 0.001$). In this study, the mean time from the last attack of the patient to the EUS application was 8 months (range: 1-18 months). EUS may be applied at least 4 weeks after an acute attack. Therefore, the changes seen in this study may be considered as a reflection of a chronic state rather than acute disease. In the study by Yusoff et al. (34), EUS was applied at a minimum of 4 weeks after an acute attack to ensure that acute pancreatic parenchymal changes were eliminated. Thevenot et al. (35) recommended application of MRCP/EUS after a longer period of time as inflammation and/or necrosis may prevent visualization of pancreatic lesions in the acute period.

Rajan et al. (23) evaluated the pancreatic parenchyma in 120 adult patients with no pancreatic disease who were examined with EUS for non-pancreatobiliary reasons, and at least one parenchymal or ductal change was determined in 28% of the patients. In our study, hyperechoic strands of < 2 mm were determined in 11 (55%) of the control group cases. To our knowledge, there is no CP study with a control group in childhood in the literature. In our opinion, as small hyperechoic bands were observed in the control group, as in adults, hyperechoic strands greater than or equal to 3 mm should be considered as pathological in respect to chronic changes. In 29.4% of the patients (four of them had three and one patient had four pathological EUS findings), exocrine pancreas insufficiency was determined, and pancreas enzyme replacement therapy was started for these patients. In all the patients with exocrine insufficiency, there were EUS findings of lobularity and hyperechoic band, and in 2 patients, there was duct dilatation. Stevens et al. found similar correlations between EUS and pancreatic exocrine insufficiency in the presence of both minimal and severe structural changes (35). Advanced inflammatory damage of pancreatic tissue, presence of calcifications and ductal dilatation are interpreted as the increased risk for exocrine and/or endocrine insufficiency in CP. Singh et al. (21), reported exocrine insufficiency as 20%, and in the INSPPIRE cohort (36), 34% of children with CP were determined to have exocrine insufficiency at the time of diagnosis. It is recommended that pediatric patients with RP are evaluated at least once a year in respect to exocrine and/or endocrine insufficiency (1).

The limitations of this study are the small number of patients and inability to study genetic results on the RP patients. EUS elastography that determines tissue stiffness to increase diagnostic efficiency and contrast enhanced EUS which significantly improves the ability to visualize vascularity are not used in this study.

In this study, the EUS findings of pediatric patients with RP attacks were evaluated, and EUS was found to be an effective and reliable tool in diagnosis and clinical follow-up. The threshold number of EUS criteria for the diagnosis of CP in pediatric patients is unclear. To achieve standardization in the interpretation of results, it is needed to develop childhood EUS diagnostic criteria. Thus, there is need for further studies in this area.

Compliance with Ethical Statements

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding No financial or nonfinancial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors. The study was approved by the Ethics Committee of Ondokuz Mayis University (OMU KAEK decision number 2017/361).

Informed consent: Written informed consent was obtained from all individual participants included in the study and their parents (or legal guardians). All procedures performed involving human participants were in accordance with the ethical standards of the local ethics committee and with the 1964 Helsinki declaration and its later amendments.

REFERENCES

1. Cheryl E Gariepy, Melvin B. Heyman, Mark E. Lowe et al. The causal evaluation of acute recurrent and chronic pancreatitis in children: Consensus from the INSPPIRE Group. J Pediatr Gastroenterol Nutr 2017;64:95-103.
2. Adzick NS. The pancreas. In: Coran AG, Adzick NS, T.M K, et al., (Eds.) Pediatric Surgery 2012;1371-84.
3. Darge K, Anupindi S. Pancreatitis and the role of US, MRCP and ERCP. Pediatr Radiol 2009;39:153-7.
4. Sivak MV, Kaufman A. Endoscopic ultrasonography in the differential diagnosis of pancreatic disease. A preliminary report. Scand J Gastroenterol Suppl 1986;123:130-4.
5. Stevens T. Update on the role of endoscopic ultrasound in chronic pancreatitis. Curr Gastroenterol Rep 2011;13:117-22.
6. Seicean A. Endoscopic ultrasound in chronic pancreatitis: where are we now? World J Gastroenterol 2010;16:4253-63.
7. Wiersema MJ, Hawes RH, Lehman GA, et al. Prospective evaluation of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in patients with chronic abdominal pain of suspected pancreatic origin. Endoscopy 1993;25:555-64.
8. Buscail L, Escourrou J, Moreau J, et al. Endoscopic ultrasonography in chronic pancreatitis: a comparative prospective study with conventional ultrasonography, computed tomography, and ERCP. Pancreas 1995;10:251-7.
9. Sahai AV, Zimmerman M, Aabakken L, et al. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancreatography. Gastrointest Endosc 1998;48:18-25.
10. Catalano MF, Lahotu S, Geenen JE Hogan WJ. Prospective evaluation of endoscopic ultrasonography, endoscopic retrograde pancreatography, and secretin test in the diagnosis of chronic pancreatitis. Gastrointest Endosc 1998;48:11-7.
11. Kahl S, Glasbrenner B, Leodolter A, et al. EUS in the diagnosis of early chronic pancreatitis: a prospective follow-up study. Gastrointest Endosc 2002;55:507-11.
12. Rickes S, Uhle C, Kahl S, et al. Echo enhanced ultrasound: a new valid initial imaging approach for severe acute pancreatitis. Gut 2006;55:74-8.
13. Varadarajulu S, Wilcox CM, Eloubeidi MA. Impact of eus in the evaluation of pancreaticobiliary disorders in children. Gastrointest Endosc 2005;62:239-44.
14. Gordon K, Conway J, Evans J, et al. EUS and EUS-guided interventions alter clinical management in children with digestive diseases. J Pediatr Gastroenterol Nutr 2016;63:242-6.
15. Morinville VD, Husain SZ, Bai H, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. J Pediatr Gastroenterol Nutr 2012;55:261-5.
16. Kalmin B, Hoffman B, Hawes R, Romagnuolo J. Conventional versus Rosemont endoscopic ultrasound criteria for chronic pancreatitis: comparing interobserver reliability and intertest agreement. Can J Gastroenterol 2011;25:261-4.
17. Catalano MF, Sahai A, Levy M, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. Gastrointest Endosc 2009;69:1251-61.
18. Parniczky A, Maisam Abu-El-Haija, Husain S, Lowe M. EPC/HPSG evidence-based guidelines for the management of pediatric pancreatitis. Pancreatology 2018;18:146-60.
19. Gardner TB, Levy MJ. EUS diagnosis of chronic pancreatitis. Gastrointest Endosc 2010;71:1280-9.
20. Morris-Stiff G, Webster P, Frost B, et al. Endoscopic ultrasound reliably identifies chronic pancreatitis when other imaging modalities have been non -diagnostic. JOP 2009;10:280-3.
21. Singh SK, Srivastava A, Rai P, Yachha SK, Poddar U. Yield of endoscopic ultrasound in children and adolescent with acute recurrent pancreatitis. J Pediatr Gastroenterol Nutr 2018;66:461-5.
22. Scheers I, Ergun M, Aouattah T, et al. Diagnostic and therapeutic roles of endoscopic ultrasound in pediatric pancreaticobiliary disorders. J Pediatr Gastroenterol Nutr 2015; 61:238-47.
23. Rajan E, Clain JE, Levy MJ, et al. Age-related changes in the pancreas identified by EUS: a prospective evaluation. Gastrointest Endosc 2005;61:401-6.
24. Raimondo M, Wallace MB. Diagnosis of early chronic pancreatitis by endoscopic ultrasound. Are we there yet? JOP 2004;5:1-7.
25. Gleeson FC, Topazian M. Endoscopic retrograde cholangiopancreatography and endoscopic ultrasound for diagnosis of chronic pancreatitis. Curr Gastroenterol Rep 2007;9:123-9.
26. Manfredi R, Costamagna G, Brizi MG, et al. Severe chronic pancreatitis versus suspected pancreatic disease: dynamic MR cholangiopancreatography after secretin stimulation. Radiology 2000;214:849-55.
27. Ortega AR, Gomez-Rodriguez R, Romero M, et al. Prospective comparison of endoscopic ultrasonography and magnetic resonance cholangiopancreatography in the etiological diagnosis of “idiopathic” acute pancreatitis. Pancreas 2011;40:289-94.
28. Mariani A, Arcidiacono PG, Curioni S, Giussani A, Testoni PA. Diagnostic yield of ERCP and secretin-enhanced MRCP and EUS in patients with acute recurrent pancreatitis of unknown aetiology. Dig Liver Dis 2009;41:753-8.
29. Bhutani MS, Arantes VN, Verma D, et al. Histopathologic correlation of endoscopic ultrasound findings of chronic pancreatitis in human autopsies. Pancreas 2009;38:820-4.
30. Del Pozo D, Poves E, Tabernero S, et al. Conventional versus Rosemont endoscopic ultrasound criteria for chronic pancreatitis: interobserver agreement in same day back-to-backprocedures. Pancreatology 2012;12:284-7.
31. Stevens T, Lopez R, Adler DG, et al. Multicenter comparison of the interobserver agreement of standard EUS scoring and Rosemont classification scoring for diagnosis of chronic pancreatitis. Gastrointest Endosc 2010;71:519-26.
32. Mahajan R, Simon EG, Chacko A, et al. Endoscopic ultrasonography in pediatric patients--Experience from a tertiary care center in India. Indian J Gastroenterol 2016;35:14-9.
33. Yusoff IF, Raymond G, Sahai AV. A prospective comparison of the yield of EUS in primary vs. recurrent idiopathic acute pancreatitis. Gastrointest Endosc 2004;60:673-8.
34. Thevenot A, Bournet B, Otal P, et al. Endoscopic ultrasound and magnetic resonance cholangiopancreatography in patients with idiopathic acute pancreatitis. Dig Dis Sci 2013;58:2361-8.
35. Stevens T, Conwell DL, Zuccaro G Jr, et al. Comparison of endoscopic ultrasound and endoscopic retrograde pancreatography fort the prediction of pancreatic exocrine insufficiency. Dig Dis Sci 2008;53:1146-51.
36. Braganza JM, Lee SH, McCloy RF, McMahon MJ. Chronic pancreatitis. Lancet 2011; 377:1184-97.