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## Steatometry and elastometry as methods of noninvasive diagnostics of pancreatic steatosis and fibrosis in children

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**Abstract. Background.** Obesity is associated with accumulation of fat in parenchymal organs, including pancreas, with formation of its steatosis. Pancreatic steatosis can lead to chronic inflammation and fibrosis of the pancreas. Limitation in invasive studies in children causes need of development and implementation of advanced non-invasive methods for pancreatic observation. The **purpose** of our study was to investigate the possibility of ultrasound diagnosis of steatosis and fibrosis of the pancreas in children using steatometry (estimation of ultrasound attenuation) and elastometry. **Materials and methods.** We examined 60 children hospitalized in the Department of Pediatric Gastroenterology of SI "Institute of Gastroenterology of NAMS of Ukraine". The patients were grouped on the basis of obesity and overweight presence: group 1 consisted of 44 patients with obesity and overweight, group 2 consisted of 16 children with normal weight. Sonological research, elastometry, steatometry of the pancreas were made using apparatus Ultima PA Expert ("Radmir", Ukraine). The presence and degree of pancreatic steatosis using pair-wise comparison of pancreatic echogenicity with renal and retroperitoneal fat echogenicity. **Results.** 25 patients of group 1 (56.8 %) were found to have sonological signs of pancreatic steatosis; third of patients had sonographic signs of non-specific inflammatory changes in the pancreas. We found that the average coefficient of ultrasound attenuation was significantly higher in children of group 1 compared to group 2 ( $p < 0.05$ ) and amounted to  $(2.45 \pm 0.39)$  dB/cm in group 1 and  $(1.8 \pm 0.23)$  dB/cm in group 2. The average pancreas stiffness in children with normal weight group was higher compared to patients with obesity and overweight, but the significance of differences was not sufficient and amounted  $(3.69 \pm 0.78)$  kPa in group 1 and  $(3.78 \pm 0.27)$  kPa in group 2. **Conclusions.** We established that the average coefficient of ultrasound attenuation during pancreatic sonological study in children with obesity and overweight was significantly higher compared to the patients with normal weight that can be explained by the presence of pancreatic steatosis in children with obesity/overweight. The study demonstrates the possibility of steatometry and elastometry usage for diagnosis of pancreatic steatosis and fibrosis in children.

**Keywords:** pancreatic steatosis; steatometry; elastometry; children

### Introduction

In recent years, it has been observed the global trend for increase in rates of pancreatic diseases [1]. Pancreatic disorders in children with obesity deserve special attention due to the high possibility of development of nonalcoholic fatty pancreas disease (NAFPD). It is known that morphological basis of NAFPD is presented by deposition of fat in the pancreas (steatosis) that can be followed by inflammation and fibrosis of the pancreatic parenchyma [2].

Inaccessibility of the pancreas and its secretions, the limitation of complex invasive studies in children promotes the development and implementation of new non-invasive methods in public health practice [3]. Ultrasound (US)

examination is the most affordable method for diagnosing fibrosis and steatosis, but the sensitivity of this method ranges from 37 to 94 % and specificity — from 48 to 100 % [4]. Exploring sensitive non-invasive methods for diagnosis of the pancreatic disorders contributed to development of shear-wave elastography of the pancreas, which allows to perform quantitative determination of parenchyma stiffness for fibrosis diagnosis; diagnosis of active inflammation, differentiation of bulk structures. The ability to measure the coefficient of attenuation of the ultrasonic waves (steatometry) significantly enhances the method capabilities by qualitatively and quantitatively determination of pancreatic steatosis. Shear-wave elastography can be realized by using the SWEI tool

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(Real-Time Shear Wave Elastography) and ARFI (Acoustic Radiation Force Impulse). SWEI is realized by the so-called pushing ultrasonic waves, that gives a quantitative stiffness estimation in the form of Young's modulus quantified in kPa or meters per second (m/s) (kPa or m/s). For ARFI method is commonly used short ultrasonic pulses that mechanically deform tissue, generating their local bias, the results usually expressed in m/s [5, 6].

There are a limited number of studies devoted to stiffness of pancreatic parenchyma in children. The study of E.V. Feoktistova et al., devoted to the possibility of using elastography (ARFI elastography) in children, showed that pancreatic parenchyma stiffness in healthy children of different age groups was not significantly different [7].

Research of Mireen Friedrich-Rust et al. was devoted to the study of pancreatic parenchyma stiffness in patients with cystic fibrosis aged 12 to 60 years using ARFI elastography. ARFI-measurement in the pancreas was significantly lower in patients with pancreatic insufficiency as compared to patients without. The authors concluded that patients with pancreatic atrophy and fatty infiltration might account for the softer tissue in patients with cystic fibrosis [8].

The study A. Mateen et al. (2012) was dedicated to the usage of ARFI elastography for the diagnosis of inflammatory diseases of the pancreas, it were examined 166 patients aged 6 to 80 years (although patients with overweight and obesity were excluded from the study). Authors found that in patients with abdominal pain, an average ARFI value was higher than 2.2 m/s that with high possibility showed the existing acute inflammation of the pancreas. It is believed that higher values of ARFI in acute pancreatitis (as in acute hepatitis) can be explained due to high content of fluid in the inflamed organs [9]. Chronic inflammation contributes to activation of the pancreatic stellate cells with the development of fibrosis, manifesting in increased stiffness of the pancreas [5, 6].

Thus, the presence of fatty pancreas can lead to decreased pancreatic parenchyma stiffness, but the presence of active and chronic inflammation associated with growth of this parameter.

Ultrasound examination is a useful method for detection of steatosis; sonological classification of fatty pancreas based on the visual assessment of pancreas echogenicity, compared to the echogenicity of the kidneys, liver and retroperitoneal fat. The sensitivity of ultrasound increases with the growth of steatosis degree: in the case of liver fat content from 10 to 19 %, sensitivity of ultrasound is up to 55 %, which rises to 80 % when fat infiltration reaches to 30 % [10, 11]. Morbid obesity reduces the sensitivity and specificity of the method to the 49 and 75 %, respectively, due to technical difficulties of examination in this group of patients [10, 12].

Subjectivity of ultrasound research and inability to precise quantitative assessment of fat content for determination of the early stages of steatosis — potentially limiting the use of B-ultrasound method in clinical practice [10]. The introduction of new, more sensitive methods for the quantitative determination of lipid content in the pancreas parenchyma, including determining of ultrasound attenuation coefficient is still actual [13].

Research devoted to the determination of ultrasound attenuation during sonological study of the pancreas in children has not yet presented. However, there are enough studies on the evaluation of ultrasound attenuation (CAP — controlled attenuation parameter) during transient liver elastography (Fibroscan 502 Touch), especially in children. Established that this technique can detect early stage liver fibrosis by measuring the stiffness (liver stiffness measurement — LSM) and its steatosis that is implemented by CAP function. Transient elastography with CAP determination helps to diagnose the early stages of steatosis — if fat is more than 10 % of hepatocytes, while standard ultrasound shows signs of steatosis in case of involvement of at least 20 % of hepatocytes [13, 14]. Therefore, we believe that the study of ultrasound attenuation coefficient during pancreatic sonography in children can be a perspective method.

**The purpose of the study** was to explore the possibility of ultrasound diagnosis of pancreatic steatosis and fibrosis in children with the use of steatometry (estimation of ultrasound attenuation coefficient) and elastometry.

## Materials and methods

We examined 60 children aged 6–17 years that were observed in the department of pediatric gastroenterology of SI “Institute of Gastroenterology of the NAMS of Ukraine” in 2016.

The study concluded anthropometric measures to determine body mass index (BMI). Trophic status assessment was conducted by WHO recommendations according to BMI values considering to age and gender [15]. Elastometry and steatometry (estimation of ultrasound attenuation coefficient) was performed using apparatus Ultima PA Expert® (“Radmir”, Ukraine). At the first, the study was performed in B-mode, to determine the size, structure, echogenicity of the pancreas, the character of its contours, the state of Wirsung's duct and surrounding tissue. The presence of pancreatic steatosis was determined by the method that has been proposed by J.S. Lee et al. (2009), based on pairwise comparison of pancreatic echogenicity with echogenicity of the kidneys and retroperitoneal fat [16]. Pancreatic steatosis was diagnosed when there was an increase in echogenicity of the pancreas compared with the kidney. Then in the supine position, with calm breathing, without sensor compression, elastometry and steatometry were conducted. During elastometry and steatometry study we performed 5 measurements in every part of the pancreas to obtain recurring quantities of stiffness and ultrasound attenuation coefficient.

The average age of patients was  $(11.27 \pm 2.76)$  years. The groups were homogeneous for age and gender distribution. Depending on the presence of obesity and overweight, patients were divided into 2 groups: group 1 (main) amounted 44 children with obesity or overweight, 2 group (control) — 16 patients with normal weight (patients who had chronic gastritis or gastroduodenitis in the period of remission).

Statistical analysis of the data was done using Statistica version 7.0 Characteristics of the study subjects were presented descriptively. All normally distributed continuous variables were expressed as means  $\pm$  SD. Most parameters were not normally distributed, therefore nonparametric

tests were applied: Mann-Whitney U test (group differences). Normally distributed data were analyzed based on parametric tests: the Student's t-test (group differences). The chi-square test was used to analyze for evaluation of the relationship between categorical variables. A p value of less than 0.05 was considered significant.

### Results

Analyzing the data of ultrasound research we found that increased echogenicity and graininess of the pancreas occurred significantly more often in main group compared to control group ( $p < 0.05$ ) (tabl. 1). It was found that among the patients of the 1 group 25 children (56.8 %) had sonological signs of pancreatic steatosis, presented by enhancing of its echogenicity compared with the kidney. We also found that among patients of the 1 group 9 children (20.5 %) had 1st grade of steatosis, 13 children (29.5 %) — 2<sup>nd</sup> grade, 3 children (6.8 %) — 3<sup>rd</sup> of grade of steatosis. Changes in ultrasound parameters in steatosis manifested not only by changes of echogenicity, but in 13 (29.5 %) patients of the 1 group by fuzzy contours of the pancreas and in 19 (43.8 %) patients by changes of it graininess. The thickness of the head and tail of the pancreas was significantly higher in patients of the 1 group compared to the 2 group. Thus, more

than half (56.8 %) patients at the 1 group had an ultrasound signs of steatosis and third of patients had sonographic signs of nonspecific inflammatory changes in pancreatic parenchyma. Among children with normal weight in 2 (12.5 %) patients we observed changes in echogenicity of the pancreas that may be explained by reactive changes on the background of gastroduodenal disorders comorbidity.

Analysis of data of steatometry, we found that the average coefficient of ultrasound attenuation in the 1 group was significantly higher than the corresponding data of the 2 group ( $p < 0.05$ ) and amounted ( $2.45 \pm 0.39$ ) dB/cm in patients of the 1 group and ( $1.80 \pm 0.23$ ) dB/cm in patients of the 2 group. Median of average coefficient of ultrasound attenuation in children of the 1 group amounted 2.43 dB/cm, with minimum value — 1.70 dB/cm and a maximum — 3.81 dB/cm (fig. 1).

The mean average coefficient of ultrasound attenuation of the 2 group was ( $1.80 \pm 0.23$ ) dB/cm, median — 1.86 dB/cm, the minimum value — 1.35 dB/cm, maximum 2.19 dB/cm.

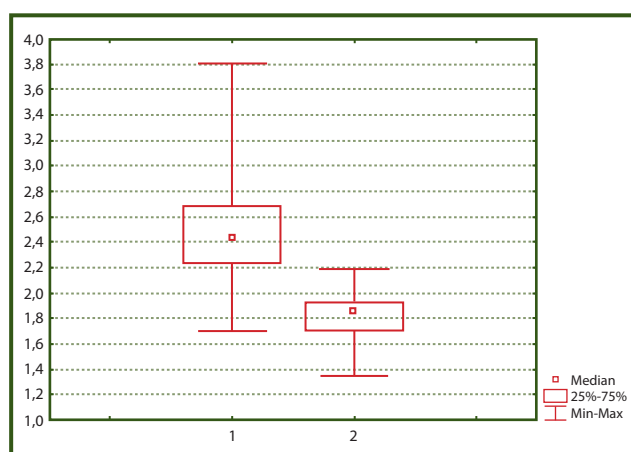
These data suggest that steatometry is a promising method for diagnosing pancreatic steatosis in children. Given the fact that steatometry allows obtaining a quantitative description of the average ultrasound attenuation coefficient during the ultrasound study of pancreas; it is possible to determine not only the presence but also the degree of pancreatic steatosis. However, it is necessary to conduct further research on the morphological confirmation of the results.

The average index of stiffness of pancreatic parenchyma in children with normal weight was higher than that of patients with obesity and overweight, but the significance of differences was not sufficient.

The mean of pancreatic stiffness in 2 group was ( $3.69 \pm 0.78$ ) kPa, median — 3.56 kPa, the minimum value — 2.27 kPa, maximum — 5.40 kPa. We found that 2 children (members of 1 group) had pancreatic stiffness that corresponds to the 1 grade of fibrosis.

Children of 2 group were presented by mean of pancreatic amounted to ( $3.78 \pm 0.27$ ) kPa, median — 3.61 kPa, minimum — 2.9 kPa, maximum — 4.65 kPa.

We assumed that the relative decrease of pancreatic stiffness during elastography in children with obesity and overweight can be explained by echo attenuation due to



**Figure 1 — Distribution of average coefficient of pancreatic ultrasound attenuation in patients of the 1 and 2 groups**

**Table 1 — Characteristics of the pancreatic sonological study and the group comparison**

Parameter	1	2
	N = 44	N = 16
The thickness of the head of the pancreas, mm	19.52 ± 3.20*	17.13 ± 2.3
The thickness of the body of the pancreas, mm	10.98 ± 2.03	10.08 ± 1.27
The thickness of the tail of the pancreas, mm	17.49 ± 2.80*	14.50 ± 1.89
Changes in pancreatic contours, abs. number (%)	13 (29.5)	2 (12.5)
Increased echogenicity of the pancreas abs. number (%)	25 (56.8)*	2 (12.5)
Increased graininess of the pancreas abs. number (%)	19 (43.8)*	2 (12.5)
Ultrasound attenuation coefficient, dB/cm	2.46 ± 0.39*	1.8 ± 0.23
Pancreatic stiffness, kPa	3.64 ± 0.78	3.78 ± 0.51

**Note.** \* — Significance of differences between groups compared with 2 group,  $p < 0.05$ .

pancreatic steatosis. While the long course of steatosis associated with inflammation and fibrosis development, that characterized by changes in the elastic properties with decreasing of pancreas elasticity.

Search of sensitive non-invasive methods for diagnosis of steatosis in children is extremely important. Implementation of steatometry and elastometry in pediatric practice will improve the diagnosis of steatosis and fibrosis of the pancreas in children.

## Conclusions

1. The apparatus Ultima PA Expert® (“Radmir”, Ukraine) allows to conduct SWEI elastography (elastometry) and estimation of the ultrasound attenuation (steatometry) for determination of the stiffness and the presence/degree of steatosis of the pancreatic parenchyma.

2. It was established that the average coefficient of ultrasound attenuation during pancreatic sonography in children with obesity and overweight is significantly higher compared to patients with normal weight, which explained by the presence of pancreatic steatosis in children with obesity/overweight.

3. The study demonstrates the possibility of steatometry and elastometry usage for diagnosis of steatosis and fibrosis of the pancreas in children.

**Conflicts of interests.** Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

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## Стеатометрія й еластометрія як методи неінвазивної діагностики стеатозу та фіброзу підшлункової залози у дітей

**Резюме. Актуальність.** Ожиріння асоційовано з ектопічним накопиченням жиру з відкладенням жиру у паренхіматозних органах, у тому числі у підшлунковій залозі (ПЗ) з формуванням її стеатозу. Тривалий перебіг стеатозу підшлункової залози здатний призводити до хронічного запалення та фіброзу органа. Обмеженість проведення інвазивних досліджень у дітей обумовлює потребу у розробці та впровадженні

в практику охорони здоров'я новітніх неінвазивних методів обстеження підшлункової залози. **Мета:** вивчити можливість ультразвукової діагностики стеатозу та фіброзу підшлункової залози у дітей з використанням методу стеатометрії (оцінка швидкості згасання ультразвуку) та еластометрії. **Матеріали та методи.** Було обстежено 60 дітей, які знаходились на стаціонарному лікуванні у відділенні дитячої гастроентерології

ДУ «Інститут гастроентерології НАМН України». Розподіл за групами відбувся на основі наявності ожиріння й надмірної маси тіла: 1-шу групу становили 44 пацієнти з ожирінням і надмірною масою тіла, 2-гу групу — 16 дітей з нормальною масою тіла. Сонологічне дослідження, еластометрія та стеатометрія проводились на апараті Ultima PA Expert («Радмір», Україна). Наявність та ступінь стеатозу підшлункової залози визначались при попарному порівнянні ехогенності ПЗ з ехогенністю нирок та заочеревинного жиру. **Результати.** Було виявлено, що серед пацієнтів 1-ї групи 25 дітей (56,8 %) мали сонологічні ознаки стеатозу підшлункової залози, третина хворих мала ехографічні ознаки неспецифічних запальних змін паренхіми залози. Аналіз даних стеатометрії ПЗ виявив, що середня величина коефіцієнту затухання ультразвуку у представників 1-ї групи була вірогідно вище за відповідний показник 2-ї групи ( $p < 0,05$ ) і становила ( $2,45 \pm 0,39$ ) дБ/см у представників 1-ї групи та ( $1,80 \pm 0,23$ ) дБ/см у пред-

ставників 2-ї групи. Середній показник жорсткості паренхіми ПЗ у дітей із нормальною масою тіла був вище за аналогічний показник пацієнтів з ожирінням і надмірною масою тіла, але вірогідність відмінностей не була достатньою. У представників 1-ї групи середнє значення жорсткості паренхіми ПЗ становило ( $3,69 \pm 0,78$ ) кПа та ( $3,78 \pm 0,27$ ) кПа — у 2-ї групі. **Висновки.** Встановлено, що середній показник коефіцієнту затухання ультразвуку під час сонографії підшлункової залози у дітей з ожирінням і надмірною масою тіла є вірогідно вищим порівняно з пацієнтами, які мають нормальну масу тіла, що свідчить на користь наявності стеатозу підшлункової залози у дітей з ожирінням/надмірною масою тіла. Проведене дослідження свідчить про можливість використання стеатометрії та еластометрії як методів діагностики стеатозу й фіброзу підшлункової залози у дітей.

**Ключові слова:** стеатоз підшлункової залози; стеатометрія; еластометрія; діти

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### Стеатометрия и эластометрия как методы неинвазивной диагностики стеатоза и фиброза поджелудочной железы у детей

**Резюме. Актуальность.** Ожирение ассоциировано с эктопическим накоплением жира с отложением жира в паренхиматозных органах, в том числе в поджелудочной железе (ПЖ) с формированием ее стеатоза. Длительное течение стеатоза поджелудочной железы способно приводит к хроническому воспалению и фиброзу органа. Ограниченность проведения инвазивных исследований у детей обуславливает потребность в разработке и внедрении в практику здравоохранения новых неинвазивных методов обследования поджелудочной железы. **Цель:** изучить возможность ультразвуковой диагностики стеатоза и фиброза поджелудочной железы у детей с использованием метода стеатометрии (оценка скорости затухания ультразвука) и эластометрии. **Материалы и методы.** Было обследовано 60 детей, находящихся на стационарном лечении в отделении детской гастроэнтерологии ГУ «Інститут гастроентерології НАМН України». Распределение по группам состоялось на основании наличия ожирения и избыточного веса: 1-ю группу составили 44 пациента с ожирением и избыточной массой тела, 2-ю группу — 16 детей с нормальной массой тела. Сонологическое исследование, эластометрия и стеатометрия проводились на аппарате Ultima PA Expert («Радмір», Україна). Наличие и степень стеатоза поджелудочной железы определялись при попарном сравнении эхогенности ПЖ с эхогенностью почек и забрюшинного жира. **Результаты.** Было обнаружено, что среди пациентов 1-й группы у 25 детей (56,8 %) имели место сонологические

признаки стеатоза поджелудочной железы; треть больных имела эхографические признаки неспецифических воспалительных изменений паренхимы железы. Анализ данных стеатометрии ПЖ обнаружил, что средняя величина коэффициента затухания ультразвука у представителей 1-й группы была достоверно выше соответствующего показателя 2-й группы ( $p < 0,05$ ) и составила ( $2,45 \pm 0,39$ ) дБ/см у представителей 1-й группы и ( $1,80 \pm 0,23$ ) дБ/см у представителей 2-й группы. Средний показатель жесткости паренхимы ПЖ у детей с нормальной массой тела был выше аналогичного показателя пациентов с ожирением и избыточной массой тела, но достоверность различий не была достаточной. У представителей 1-й группы среднее значение жесткости паренхимы ПЖ составило ( $3,69 \pm 0,78$ ) кПа и ( $3,78 \pm 0,27$ ) кПа — во 2-й группе. **Выводы.** Установлено, что средний показатель коэффициента затухания ультразвука при проведении сонографии поджелудочной железы у детей с ожирением и избыточной массой тела достоверно выше по сравнению с пациентами с нормальной массой тела, что свидетельствует о наличии стеатоза поджелудочной железы у детей с ожирением/избыточной массой тела. Проведенное исследование свидетельствует о возможности использования стеатометрии и эластометрии в качестве методов диагностики стеатоза и фиброза поджелудочной железы у детей.

**Ключевые слова:** стеатоз поджелудочной железы; стеатометрия; эластометрия; дети