

The role of abdominal ultrasonography in patients with isoattenuating pancreatic carcinoma

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Aims. The main objective of this study was to determine the sensitivity of abdominal ultrasonography (US) in patients with isoattenuating pancreatic carcinoma and to compare the frequency of secondary signs on abdominal US and endoscopic ultrasonography (EUS) in these tumours.

Methods. Twenty-four patients with histologically or cytologically verified isoattenuating pancreatic carcinoma who underwent abdominal US, contrast-enhanced CT and EUS of the pancreas as part of the diagnostic workup were included in this retrospective study. The sensitivity of abdominal US in detecting the isoattenuating pancreatic carcinoma was investigated and the frequency of secondary signs of isoattenuating pancreatic carcinoma on abdominal US and EUS was compared.

Results. In 5 of 24 patients (21%) with isoattenuating pancreatic carcinoma, a hypoechogenic pancreatic lesion was directly visualised on abdominal US. Secondary signs were present on US in 21 patients (88%). These included dilatation of the common bile duct and/or intrahepatic bile ducts in 19/24 (79%), dilatation of the pancreatic duct in 3/24 (13%), abnormal contour/inhomogeneity of the pancreas in 1/24 (4%), and atrophy of the distal parenchyma in 1/24 (4%). Pancreatic duct dilatation was observed more frequently on EUS than on abdominal US ($P=0.002$). For other secondary signs, there was no significant difference in their detection on abdominal US and EUS ($P=0.61-1.00$).

Conclusion. Abdominal US is capable of detecting secondary signs of isoattenuating pancreatic carcinoma with high sensitivity and has the potential to directly visualise these tumours.

Key words: pancreatic cancer, isoattenuating, ultrasound, ultrasonography, computed tomography, endoscopic ultrasonography

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INTRODUCTION

The incidence of pancreatic adenocarcinoma is increasing in the long term¹. While in 2000 there were 1608 newly diagnosed cases in the Czech Republic, in 2018 there were 2332 cases².

In the absence of effective screening methods, pancreatic carcinoma is usually diagnosed at an advanced stage^{3,4}. In the surveillance of individuals at high risk of pancreatic cancer, clinical stage I was found only by endoscopic ultrasonography (EUS), not by MRI (magnetic resonance imaging) or CT (computed tomography) (ref.⁵). Early stage pancreatic carcinoma is associated with a more favourable 5-year survival rate of 86% for clinical stage 0, and 69% for clinical stage IA (ref.³). The prognosis of a patient with pancreatic carcinoma depends on the size of the lesion at the time of diagnosis⁶.

A possible diagnostic problem is isoattenuating pancreatic carcinoma, which cannot be directly visualised on contrast-enhanced CT. In isoattenuating pancreatic carcinoma, the difference in attenuation between the area of the suspected tumour and surrounding parenchyma is usually less than 10–15 HU (Hounsfield Units) and only the secondary signs are present^{7–9}. The reported incidence of isoattenuating pancreatic carcinomas on CT is 5.4–14% (ref.¹⁰).

Isoattenuating pancreatic carcinomas have almost twice the chance of surgical treatment than hypoattenuating carcinomas⁹. It is therefore very important to diagnose these isoattenuating tumours correctly and early, at a stage when surgical treatment is still possible^{8,10}. Resection is considered to be the only potentially curative method of treatment for pancreatic carcinoma^{11,12}.

There are only a few studies on radiologically defined isoattenuating pancreatic carcinoma^{7–9,13–16}. To date, only

the sensitivity of MRI, PET (positron emission tomography) / CT (ref.⁸) and EUS with fine-needle aspiration (FNA) (ref.⁹) in isoattenuating pancreatic carcinoma has been examined. To our knowledge, the sensitivity of abdominal ultrasonography (US) in the diagnosis of isoattenuating pancreatic carcinoma has not yet been evaluated in detail.

The main objective of this study was to determine the sensitivity of abdominal US in patients with isoattenuating pancreatic carcinoma and to compare the frequency of secondary signs on abdominal US and EUS in these tumours.

MATERIALS AND METHODS

The study was performed in a single tertiary referral center after approval by the institutional review board (number EK/15/2021). A total of 24 consecutive patients with CT isoattenuating pancreatic carcinoma who underwent abdominal US and EUS-FNA of the pancreas as part of the diagnosis of pancreatic carcinoma were included in this retrospective study. In all patients, abdominal US was performed as the initial method, followed by CT of the pancreas and EUS-FNA as the last method.

Histology was the gold standard for the final diagnosis in operated patients⁹. In patients without surgical treatment, the diagnosis of pancreatic carcinoma was based on positive cytology from EUS-FNA or ERCP (endoscopic retrograde cholangiopancreatography)-guided brushings and concurrent clinical and radiographic disease progression during 1-year follow-up.

Technique of the ultrasound examination

Pancreatic US was performed by radiologists and/or gastroenterologists as part of routine abdominal US examination with a convex probe (1–7 MHz) in the supine position. The head and body of the pancreas were evaluated in longitudinal and transverse scans from the epigastric and right subcostal region. The left intercostal scan was used to assess the pancreatic tail³. The patient could be asked to hold his/her breath at any time during the examination. When gas in the colon transversum or the stomach limited the view, the gradual compression method of gas displacement was used. If limited visibility of the pancreas persisted in the supine position, the patient was positioned into the left lateral decubitus position.

Definition of isoattenuating pancreatic carcinoma and outcome measure

Isoattenuating pancreatic carcinoma was defined as the area of the suspected tumour on contrast-enhanced CT in the arterial and portal-venous phase with an attenuation difference of less than 15 HU compared to the adjacent parenchyma^{9,16}. If no mass was visible on CT, the presumed localisation of the isoattenuating pancreatic carcinoma was considered to be downstream from the interrupted main pancreatic duct, dilated common bile duct or at the level of abnormally contoured parts of the pancreas^{9,16}.

The sensitivity of abdominal US in the detection of isoattenuating pancreatic carcinoma was investigated. Frequency of secondary signs (dilatation of the common bile duct and/or intrahepatic bile ducts, dilatation of the pancreatic duct, inhomogeneity/abnormal contour of the pancreas and atrophy of the distal pancreatic parenchyma) of isoattenuating pancreatic carcinoma on abdominal US and EUS were compared. Further, the size and localisation of isoattenuating pancreatic carcinomas on abdominal US and EUS were examined. Information on the frequency of secondary signs, lesion size and patient characteristics were obtained from the hospital information system.

Pancreatic duct dilatation was determined as a maximum size of the main pancreatic duct > 3 mm (ref.¹⁵). Parenchymal atrophy was defined as atrophy distal to the tumour. Bulging or focal enlargement of the pancreas was considered as an abnormal contour. Inhomogeneity was defined as a focal difference in the echostructure of an otherwise homogeneous pancreas. Dilatation of the common bile duct was considered when the maximum diameter of the short axis of the common bile duct > 7 mm in patients younger than 60 years and > 9 mm above 60 years⁷.

Statistical methods

The data were processed using descriptive statistics for basic patient data. For categorical variables, absolute and relative frequencies and *P*-values from Fisher's exact test are reported. Statistical software NCSS 12 from Number Cruncher Statistical Systems (Kaysville, Utah, USA) was used for data analysis. The significance level was set as $P < 0.05$.

RESULTS

Basic characteristics of patients

There were 10 women and 14 men in the cohort. The mean age of patients was 66.9 ± 9.3 years (range 40–88 years). The mean size of the lesions on EUS was 18.5 ± 5.0 mm (median 19.5 mm). Of the 24 patients with isoattenuating pancreatic carcinoma, a total of 22 (92%) were located in the head/uncinate process and 2 (8%) in the body of the pancreas. No lesion was located in the tail of the pancreas. The basic characteristics of the patients are summarized in Table 1.

Significance of abdominal ultrasonography and comparison with EUS

Abdominal US was performed in all patients with isoattenuating carcinoma, of which 5 (21%) were directly visualised as hypoechoic lesions (3 of them were localized in the head and 2 in the body of the pancreas). The size of the lesions directly detected on US was 21.2 ± 5.7 mm at the largest dimension (median 22 mm), see Fig. 1.

Secondary signs were present on abdominal US in 21 patients (88%), and included dilatation of the common bile duct and/or intrahepatic bile ducts in 19/24 (79%), dilatation of the pancreatic duct in 3/24 (13%), abnor-

Table 1. Basic characteristics of patients (n=24).

	Number (frequency)
Women	10 (42%)
Localisation of the tumour:	
Head/uncinate process of the pancreas	22 (92%)
Body of the pancreas	2 (8%)
Tail of the pancreas	0
	Mean $\pm$ SD
Age (years)	66.9 $\pm$ 9.3
Size of the tumour on abdominal US (n=5)	21.2 $\pm$ 5.7 mm
Size of the tumour on EUS (n=24)	18.5 $\pm$ 5.0 mm

SD, standard deviation

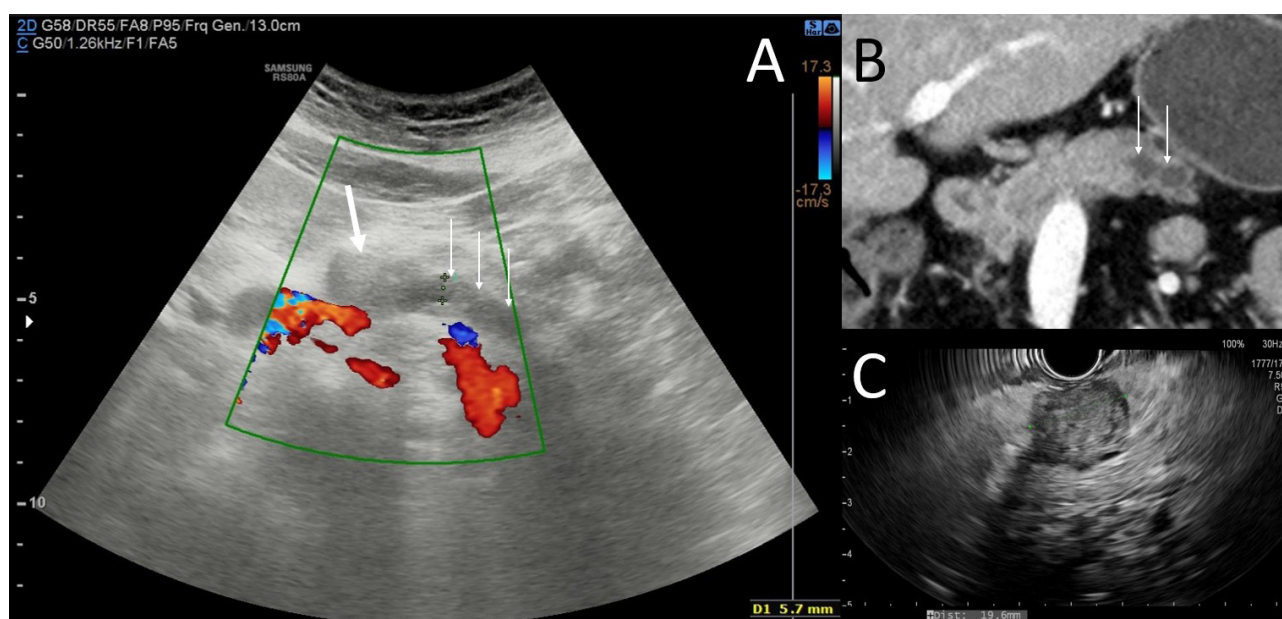


Fig. 1. A. Abdominal US using a convex probe shows a lesion of the pancreatic body (thick arrow) with a dilated pancreatic duct (thin arrows). B. CT scan in portal-venous phase in the coronal plane shows an interrupted and dilated pancreatic duct (slender arrows) caused by an isoattenuating lesion in the pancreatic body. C. EUS confirmed pancreatic body tumour, aspiration biopsy during EUS proved adenocarcinoma.

Table 2. Comparison of the frequency of secondary signs on abdominal US and EUS.

Secondary signs	Abdominal US	EUS	<i>P</i> value**
At least one sign	21/24 (88%)	23/24 (96%)	0.609
Dilatation of the common bile duct and/or intrahepatic bile ducts*	19/24 (79%)	20/24 (83%)	1.000
Pancreatic duct dilatation	3/24 (13%)	14/24 (58%)	0.002
Contour abnormality/ inhomogeneity of the pancreas	1/24 (4%)	2/24 (8%)	1.000
Distal parenchymal atrophy	1/24 (4%)	3/24 (13%)	0.609

*dilatation of the common bile duct and/or intrahepatic bile ducts in the left hepatic lobe on EUS

**Fisher's exact test

mal contour/inhomogeneity of the pancreas in 1/24 (4%) and atrophy of the distal pancreatic parenchyma in 1/24 (4%). Dilatation of the pancreatic duct was observed on EUS in 14 (58%) patients, significantly more often than on abdominal US ($P=0.002$). The frequencies of other secondary features on EUS and abdominal US differed

non-significantly ($P=0.61-1.00$). No secondary signs were present in 3 (13%) patients on abdominal US and in 1 (4%) patient on EUS. Comparison of the frequency of the secondary signs on abdominal US and EUS is shown in Table 2.

DISCUSSION

Abdominal US is usually the initial imaging method used to diagnose pathologies of the pancreas and hepatobiliary tract. Evaluation of the pancreas on US is often difficult due to the patient's habitus and possible flatulence^{17,18}. The disadvantages of US, apart from patient factors, are its low specificity and dependence on the experience of the examiner¹⁹. The reported sensitivity of abdominal US in detecting pancreatic tumours ranges from 50–90% (ref.¹⁷).

It is known and confirmed by many studies that US is a less sensitive method than CT in the diagnosis of pancreatic cancer²⁰. However, CT has its limitations in isoattenuating pancreatic carcinomas, which are indicated only by secondary signs^{7–9}.

According to our study, isoattenuating pancreatic carcinoma could be directly visualised on non-targeted abdominal US in 21% of cases, which is less than the above-mentioned sensitivity of US for detecting all pancreatic cancers¹⁷. This may be due to the generally smaller size of isoattenuating carcinomas compared to hypoattenuating pancreatic carcinomas^{7,9,10,14}. It is reported that the sensitivity of US in detecting lesions smaller than 2 cm decreases significantly²⁰. In comparison, direct visualisation of isoattenuating carcinoma on MRI and PET/CT was determined to be 79.2% and 73.7%, respectively⁸. Direct detection of pancreatic tumour on abdominal US could be increased by thorough preparation of the patient, e.g. filling the stomach with water (100–300 mL) before the examination and special positioning of the patient during the examination^{3,21}.

According to Choi et al., lesions located in the neck and body of the pancreas have a higher chance of detection on abdominal US than lesions in other parts of the pancreas²². Consistent with these findings, both pancreatic body tumours in our study were directly visualised on abdominal US.

An important result of this study is that in 5 of 24 patients with isoattenuating pancreatic tumours, the lesions were directly visualised only on abdominal US, not on CT. Therefore, the result of abdominal US should be respected especially in cases where only a secondary sign is present on CT without a clearly visible tumour. EUS is the appropriate method to confirm the findings on abdominal US and CT (ref.⁹). FNA or FNB (fine-needle biopsy) is required to confirm the diagnosis of isoattenuating pancreatic carcinoma on EUS (ref.^{18,19}).

Based on our study, abdominal US achieved a high sensitivity (88%) in detecting secondary signs in isoattenuating pancreatic carcinomas. The presence of secondary signs on US may guide us to further investigate the patient. The most frequently detected secondary sign on US was dilatation of extra or intrahepatic bile ducts similar to EUS (79% vs 83%; $P=1.00$). There was a significant difference ($P=0.002$) in the detection of a dilated pancreatic duct, with US detecting dilatation in only 13% of cases, whereas on EUS dilatation was evident in 58% of cases. Dilatation of the pancreatic duct is one of the most common secondary signs described in early forms of pancre-

atic cancer without detectable lesion on CT (ref.^{4,8,13,23}). However, the relatively low specificity of secondary signs is a limitation. The pancreatic duct physiologically dilates in old age, and is further dilated in patients with chronic pancreatitis or main-duct intraductal papillary mucinous neoplasms of the pancreas. Bile ducts also dilates after cholecystectomy, in benign stenosis of the papilla of Vateri, choledocholithiasis and other nosological entities^{18,20,24}. In addition, parenchymal abnormalities (streaks, hyperechogenic foci, cysts) are found in 28% of healthy individuals on EUS and the percentage increases with age²⁵. The finding of pancreatic duct stenosis without associated tumour mass is also significant. In these patients, early stages can be detected cytologically using the SPACE (serial pancreatic-juice aspiration cytologic examination) method²⁶.

The limitations of our study are the retrospective data collection and the relatively small patient population. Abdominal US was performed by different examiners, which may be a source of bias, but in our opinion reflects real clinical practice. Neither the extent of pancreatic visualization on abdominal US nor the body mass index of the patients was considered in the study. Analysis of these parameters in relation to direct and indirect detection of pancreatic tumours could be the focus of further studies to identify patients in whom isoattenuating pancreatic cancer could be directly visualized on abdominal US. It would also be valuable to perform abdominal US in patients with secondary signs on CT – i.e. with an already explicit suspicion of isoattenuating pancreatic carcinoma. As EUS is usually performed only after CT, the comparison with abdominal US, which is performed as an initial examination, was biased with a sampling error.

CONCLUSION

Abdominal ultrasonography is a method capable of detecting secondary signs of isoattenuating pancreatic tumours with high sensitivity and has the potential to directly visualise these tumours in 21%. In this study, endoscopic ultrasonography detected a dilated pancreatic duct in isoattenuating pancreatic carcinomas significantly more often than abdominal ultrasonography.

ABBREVIATIONS

CT, Computed tomography; ERCP, Endoscopic retrograde cholangiopancreatography; EUS, Endoscopic ultrasonography; FNA, Fine-needle aspiration; FNB, Fine-needle biopsy; HU, Hounsfield Unit; MRI, Magnetic resonance imaging; PET, Positron emission tomography; SPACE, Serial pancreatic-juice aspiration cytologic examination; US, Ultrasonography.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board Vitkovice Hospital, Ostrava, Czech Republic (EK/15/2021; 3 February 2021).

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