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CORRELATION BETWEEN MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGY IN DIFFERENTIATION OF PANCREATIC DISEASES

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SUMMARY – In the last four decades, the incidence of pancreatic cancer has tripled in Western countries. More than 90% of all pancreatic cancers are detected in the advanced stage of the disease when surgical treatment is no longer possible and survival after initial diagnosis is usually very short. The aim of this study was to correlate magnetic resonance imaging (MRI) established diagnosis of chronic pancreatitis, benign lesion and malignant neoplasm with final histopathology. The study included 29 patients in whom the nature of pancreatic pathology could not be determined clinically and by other imaging modalities including abdominal ultrasonography, endoscopic retrograde cholangiopancreatography and multislice computed tomography. MRI examination was performed and radiological report was compared with histopathology assessment of the pancreatic lesion detected. The data obtained indicated systematic conformity between radiological and histopathology findings, confirmed high diagnostic accuracy of MRI for selected pancreatic pathology, and demonstrated the role of MRI as a problem solving diagnostic imaging modality in undetermined pancreatic changes.

Key words: *Magnetic resonance imaging; Tomography, spiral computed; Ultrasonography; Cholangiopancreatography, endoscopic retrograde; Pancreatitis, chronic; Carcinoma, pancreatic ductal*

Introduction

In the time of rapid development of diagnostic methods, pancreatic diseases and especially pancreatic cancer remain a major diagnostic challenge. Differentiation of pancreatic changes by diagnostic imaging methods (multislice computed tomography, MSCT; magnetic resonance imaging, MRI with magnetic resonance cholangiopancreatography, MRCP; ultrasonography, US; endoscopic retrograde cholangiopancreatography, ERCP; and endoscopic US) is a demanding procedure and the answer is often not unambiguous. The most important objective in the assessment of pancreatic disease is to determine whether the observed pathology represents a neoplasm, inflammatory change or occurrence of a neoplasm in chronic pancreatitis. Differential diagnosis of pancreatic masses is very broad and includes pancreatitis, adenocarcinoma, solid pseudopapillary tumor, neuroendocrine tumors, mucinous cystic tumors, serous cystadenoma and others[1]. If the lesion is diagnostically characterized as a neoplasm, it is necessary to distinguish whether it is benign or malignant. Malignant lesions are further classified according to the TNM staging system with special attention focused on the local spread to determine whether surgical treatment

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is possible. Among the neoplasms of gastrointestinal tract, pancreatic cancer is the most common cause of death[2] and mortality of patients is extremely high. The term "pancreatic cancer" in clinical practice implies adenocarcinoma, which usually makes up to 95% of all primary malignant lesions of the pancreas[3]. One of the most common diagnoses in pancreatic pathology besides pancreatic cancer is chronic pancreatitis. It is characterized by progressive and irreversible impairment of the pancreatic parenchyma, which results in permanent loss of exocrine and endocrine pancreatic function. Compared with general population, patients with chronic pancreatitis have a 2.3-18.5 times greater relative risk of pancreatic cancer[4]. More than 90% of all pancreatic carcinomas are detected in the advanced stage of the disease when surgical treatment is no longer possible and survival after initial diagnosis is usually very short. Therefore, the aim of diagnostic imaging is early detection of pancreatic cancer in order to expand therapeutic options from palliative to curable. MRI with MRCP is only comparable to endoscopic US in the quality of depiction of pancreatic ducts, biliary tree, pancreatic parenchyma and peripancreatic structures[5]. MRI and MRCP have a unique capability to provide assessment of all these structures in only one noninvasive examination[5], thereby allowing evaluation of the nature and extent of pancreatic disease. In the past few years, there have been many discussions regarding sensitivity and specificity of diagnostic procedures[6-8] used in diagnosing pancreatic pathology, particularly regarding diagnosing and spread assessment of pancreatic cancer. The aim of this study was to correlate MRI established diagnosis of chronic pancreatitis, benign lesion or malignant neoplasm with final histopathology in patients with clinically and radiologically undetermined pancreatic changes.

Patients and Methods

At the University Department of Diagnostic and Interventional Radiology, Sestre milosrdnice University Hospital Center, we conducted a retrospective study in the period of 6 years. In 80 patients (47 men and 33 women) referred for radiological diagnostic evaluation of suspected pancreatic pathology, we applied the following diagnostic algorithm: abdominal US, ERCP and MSCT examination. The study excluded 51 patients in whom previously proposed diagnostic algorithm revealed the nature of the disease and those without the histopathology assessment of the observed pancreatic change. The study included 29 patients (14 women and 15 men, 15 to 72 years of age), who participated in the suggested diagnostic algorithm and after inability to radiologically determine the nature of the pancreatic change, MRI examination was performed on a 1T scanner (MR Harmony Siemens, Erlangen, Germany). MRI sequences with breath hold included axial T1WI in phase (TR 132 ms; TE 3,65 ms), axial T1WI out of phase (TR 132 ms; TE 7,97 ms), axial T1WI with fat suppression (T1WI with FAT SAT; TR 176 ms; TE 3,75 ms), axial T2 true Fast Imaging with Steady Precession (trueFISP; TR 4,56 ms; TE 1,85 ms), axial T2 Half Fourier Acquisition Single Shot Turbo Spin Echo (HASTE; TR 1100 ms; TE 120 ms), axial dynamic contrast-enhanced T1WI in phase and out of phase after 30, 60, 90, 120 s and 180-200 s (the equilibrium phase) and delayed T1WI with FAT SAT after application of contrast medium. MRCP examination included coronal T2 HASTE volume (slice thickness 4 cm; TR 4500 ms; TE 755 ms) and coronal T2 HASTE (slice thickness 4 mm; TR 1430 ms; TE 87 ms). The intravenous contrast medium used was gadolinium DTPA (Bayer Schering Pharma AG, Berlin, Germany), 0.2 mL/kg. Pathologic MRI findings were suspected when the signal of the pancreatic parenchyma was lower compared to the signal of the liver parenchyma. Focal pancreatic lesion was suspected when the signal of the lesion was lower than the signal of the surrounding parenchyma on T1WI. Other sequences enabled characterization of the pathologic changes detected. A statistically significant correspondence between the diagnoses set by the radiologist and the pathologist was examined for the following pancreatic disorders: chronic pancreatitis, benign pancreatic lesion and malignant pancreatic neoplasm. The data obtained were analyzed with the following statistical tests: proportion of overall agreement, proportions of specific agreement, Fisher's exact test, kappa coefficient, tetrachoric correlation and McNemar's test. P value of <0.05 was taken as the level of statistical significance. Postoperative histopathologic analysis of samples was conducted according to the standard procedures for the preparation and analysis of formalin-fixed and paraffin embedded specimens.

Table 1. Frequency tables for the diagnosis of chronic pancreatitis, benign lesion and malignant neoplasm

Chronic pancreatitis				
		Histopathology		Total
		0	1	
MRI	0	14	3	17
	1	1	11	12
Total		15	14	29
Benign lesion				
		Histopathology		Total
		0	1	
MRI	0	21	0	21
	1	3	5	8
Total		24	5	29
Malignant neoplasm				
		Histopathology		Total
		0	1	
MRI	0	21	0	21
	1	3	5	8
Total		24	5	29

MRI = magnetic resonance imaging; 0 = absence of disease; 1 = presence of disease

Results

The radiologist classified 12 patients as chronic pancreatitis and the histopathology assessment revealed the presence of the disease in 14 cases. The proportion of overall agreement between the pathologist and the radiologist was 86.2%. A benign lesion was reported in 8 patients by the radiologist and histopathology confirmed the diagnosis in 5 patients. For a malignant neoplasm, the radiologist identified the lesion in 8 patients and histopathology proved the presence of the disease in 5 cases. The proportion of overall agreement for the diagnosis of benign lesion and malignant neoplasm between examiners was 89.7%. All proportions were statistically significant (Tables 1 and 2). The proportions of specific agree ment for positive agreement (presence of the disease) and negative agreement (absence of the disease) was equally high for chronic pancreatitis (84.6%; 87.5%). For the

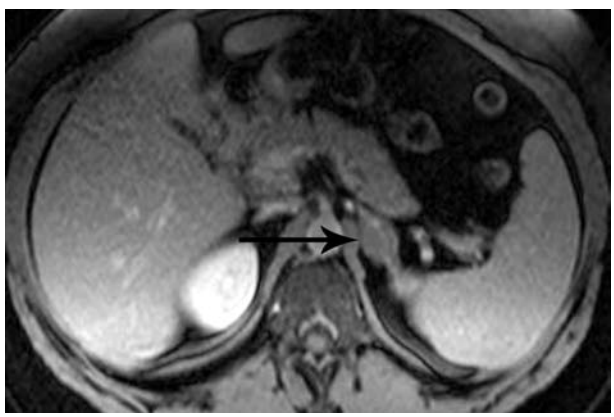

Fig. 1. Axial T1W1 with FAT SAT. Depiction of pancreatic morphology and surrounding fat planes. Left adrenal adenoma (arrow).

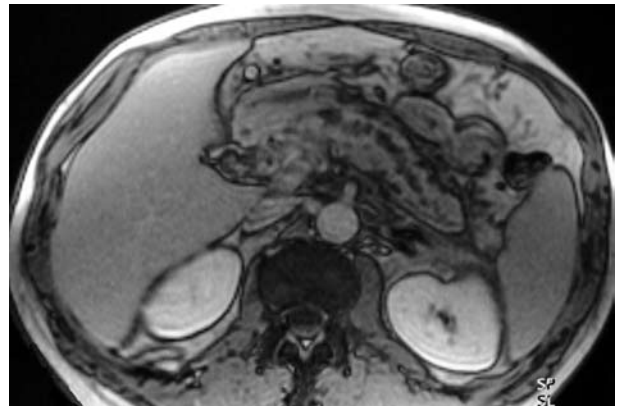

Fig. 2. Axial T1WI out of phase. Chronic pancreatitis. Parenchymal atrophy with dilatation and beading of the pancreatic duct.

Table 2. Proportion of overall agreement and proportions of specific agreement for the diagnoses of chronic pancreatitis, benign lesion and malignant neoplasm

Proportion of overall agreement			
	P_o	SE P_o	Fisher's exact test, *P*
Chronic pancreatitis	0.862	0.064	<0.001
Benign lesion	0.897	0.057	<0.001
Malignant neoplasm	0.897	0.057	<0.001

Proportions of specific agreement				
	P_{s+}	SE P_{s+}	P_{s-}	SE P_{s-}
Chronic pancreatitis	0.846	0.067	0.875	0.061
Benign lesion	0.769	0.078	0.933	0.046
Malignant neoplasm	0.769	0.078	0.933	0.046

P_o = proportion of overall agreement
P_{s+} = proportion of specific agreement for positive answers
P_{s-} = proportion of specific agreement for negative answers
SE = standard error

Table 3. Exact test based on cumulative binomial distribution for positive findings of chronic pancreatitis, benign lesion and malignant neoplasm

	P
Chronic pancreatitis	0.625
Benign lesion	0.250
Malignant neoplasm	0.250

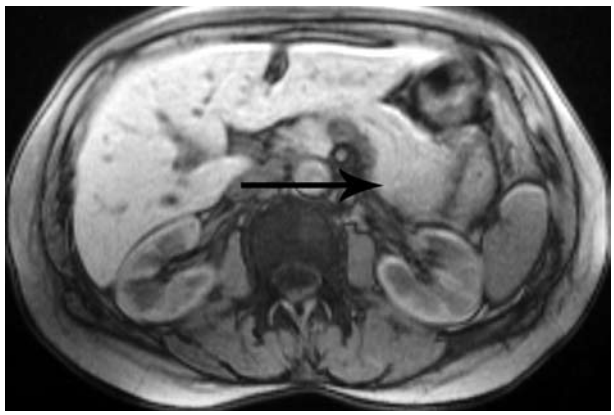

Fig. 3. Axial T1WI out of phase. Enlargement of the pancreatic tail (arrow) with slightly lower signal intensity compared to the surrounding pancreatic parenchyma.

diagnoses of benign lesion and malignant neoplasm, the proportions of specific agreement between the pathologist and the radiologist was very high for negative agreement (93.3%), but positive agreement was much lower (76.9%) (Table 2). Whether this difference was statistically significant we examined using the exact test based on the cumulative binomial distribution. There were no statistically significant differences in marginal frequencies for both appraisers (Table 3). Kappa coefficients were statistically significant and the values were as follows: chronic pancreatitis 0.722, benign lesion 0.707 and malignant neoplasm 0.707 (Table 4). Tetrachoric correlation showed very high level of agreement between evaluators for all three pathologic entities. All coefficients were statistically significant and close to 1, which represents maximal agreement (Table 5). The most important

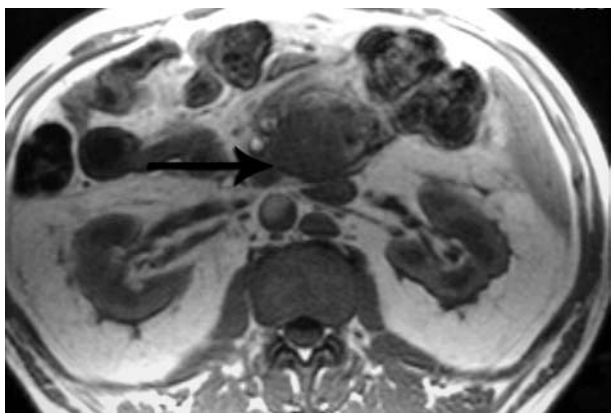

Fig. 4. Axial T1WI. Expansive lesion in the head of the pancreas (arrow) with displacement of the superior mesenteric artery and vein.

Table 4. Kappa coefficients for the diagnoses of chronic pancreatitis, benign lesion and malignant neoplasm

	Kappa	Standard error Kappa	*P*
Chronic pancreatitis	0.722	0.128	<0.001
Benign lesion	0.707	0.153	<0.001
Malignant neoplasm	0.707	0.153	<0.001

Table 5. Tetrachoric correlation for the diagnoses of chronic pancreatitis, benign lesion and malignant neoplasm

	rho	Standard error rho	*P*
Chronic pancreatitis	0.921	0.077	<0.001
Benign lesion	0.897	0.113	<0.001
Malignant neoplasm	0.897	0.113	<0.001

rho = tetrachoric correlation

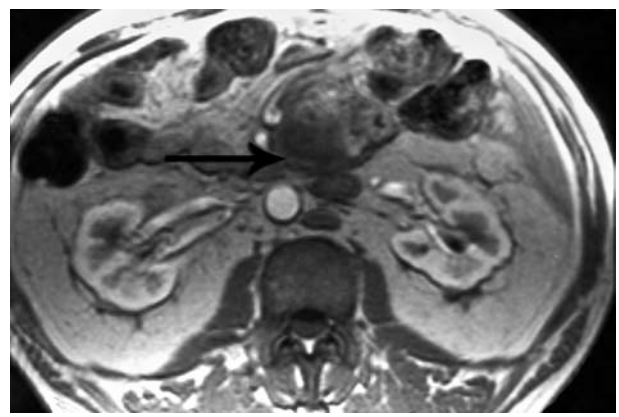

Fig. 5. Axial T1WI after IV contrast medium administration. Expansive lesion in the head of the pancreas (arrow). Lower signal intensity of the lesion compared to the surrounding pancreatic parenchyma. Displacement of the superior mesenteric artery and vein.

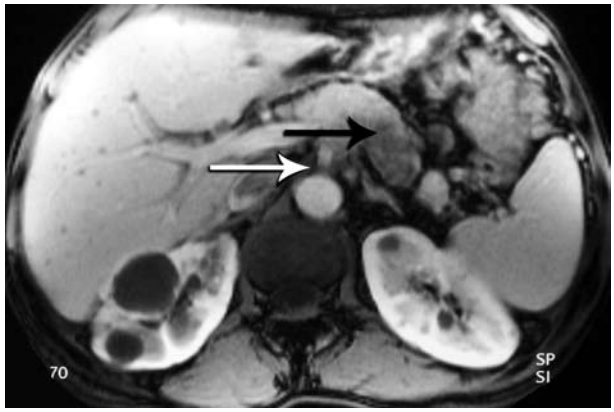

Fig. 6. Axial T1WI with FAT SAT after IV contrast medium administration. Thrombus in the superior mesenteric artery (white arrow). Expansive lesion in the body and tail of the pancreas (black arrow).

MRI imaging features of the pancreas and selected pancreatic pathology are represented in the following figures. Pancreatic parenchyma and clear depiction of surrounding fat planes is shown on T1WI with FAT SAT (Fig. 1). Imaging features of chronic pancreatitis are presented in Figure 2. Detection and characterization of a pancreatic lesion is based on the change in size and shape of the pancreas, as well as observation of post-contrast enhancement (Figs. 3, 4 and 5). Involvement of vascular structures in case of a malignant lesion is shown in Figure 6. The importance of T2WI in delineation of fluid containing lesion and pancreatic duct is presented in Figures 7 and 8. MRCP is shown in Figure 9.

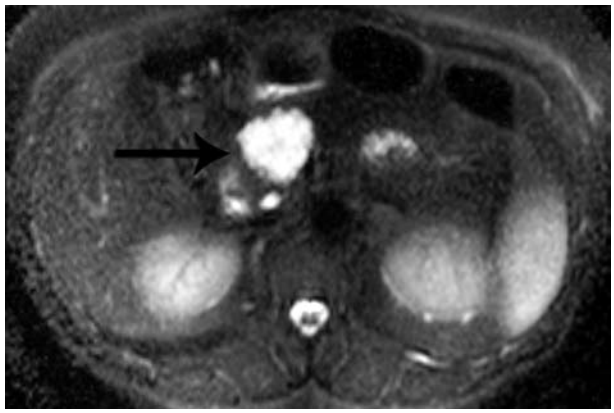

Fig. 7. Axial T2 HASTE. Cystic lesion in the head of the pancreas (arrow).

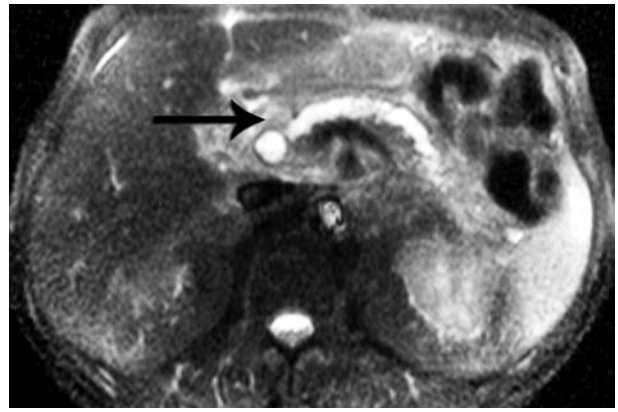

Fig. 8. Axial T2 HASTE. Dilatation and beading of the pancreatic duct (arrow).

Discussion

In the last four decades, the incidence of pancreatic cancer has tripled in Western countries and accounts for approximately 3% of cancers in both sexes. The incidence rate for pancreatic cancer in Croatia in 2008 was 15.5 *per* 100,000 men and women *per* year[9]. In Croatia, 374 new pancreatic carcinomas in men and 316 new pancreatic carcinomas in women were diagnosed in 2008. The 75-79 age group was most commonly affected[10]. Risk factors for pancreatic cancer are still not clearly defined[11].

Data obtained from this study indicate systematic conformity between evaluations made by the radiologist using MRI and the histopathology report in characterization and differentiation of chronic pancreatitis, benign lesion and malignant neoplasm.

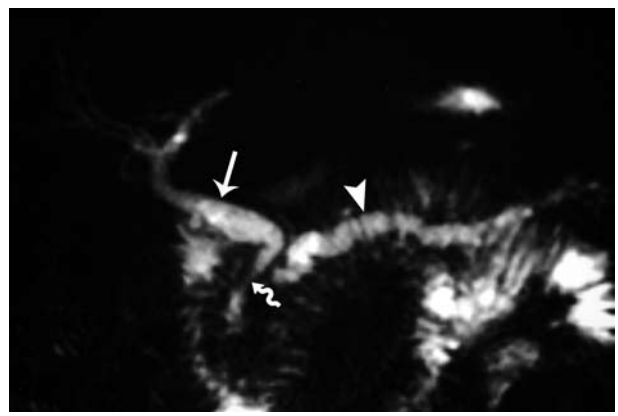

Fig. 9. MRCP. Dilatation of the common bile duct (arrow) with stenosis at the level of the ampulla of Vater (curved arrow). Dilatation of the pancreatic duct (arrowhead).

The proportion of overall agreement between the radiologist and the pathologist was 86.2% for chronic pancreatitis, 89.7% for benign lesion and 89.7% for malignant neoplasm. As the proportion of overall agreement does not distinguish agreement on positive (presence of the disease) and negative (absence of the disease) answers, we applied the proportions of specific agreement. Positive agreement and negative agreement was equally high for chronic pancreatitis (84.6%; 87.5%), indicating a satisfactory level of agreement for positive and negative findings. For the diagnosis of benign lesion and malignant neoplasm, the situation was different. Considering that benign and malignant lesions are a less common pancreatic pathology, negative agreement between the radiologist and the pathologist was very high (93.3%), but positive agreement was lower (76.9%), suggesting that the radiologist in the interpretation of MRI tends to overlook these lesions, probably because of their lower occurrence in general population. Whether this difference was statistically significant we examined using McNemar's test. The assumption for the use of McNemar's test is that the sum of frequencies in cases where appraisers do not agree should be greater than or equal to 10. Since this assumption was not met in our case, we used the exact test based on a cumulative binomial distribution. There were no statistically significant differences in marginal frequencies for both appraisers, indicating that there is no greater or lesser tendency of the radiologist to give a positive or negative answer in relation to the findings of the pathologist. We concluded that the formerly mentioned difference observed with the evaluation of benign lesions and malignant neoplasms could be declared random. An additional measure that describes the congruence between assessments was obtained using kappa statistics. The agreement of the evaluators was slightly higher for the diagnosis of chronic pancreatitis than for the diagnoses of benign lesion and malignant neoplasm. Since all kappa coefficients were statistically significant, the agreement between the radiologist and the pathologist was greater than it would be expected randomly. As a better measure of the agreement between evaluators for categorical data than kappa coefficients, we used tetrachoric correlation. It was shown that the agreement between the observers was very high and statistically significant for all three pathologic entities (all coefficients were close to 1, which represents maximal agreement). Based on the statistical analysis of the data provided, we concluded that MRI has a high degree of diagnostic accuracy for selected pancreatic pathology. Abdominal US is often used as the first imaging modality in patients with suspected pancreatic pathology. Disadvantages of abdominal US include dependence on the experience of the observer and frequent inability to perform appropriate examination due to air in gastrointestinal tract[5]. MSCT is widely available, highly diagnostically accurate[12] and hence is commonly the initial imaging method used in patients with suspected pancreatic cancer. However, small solid masses as well as development of carcinoma in chronic pancreatitis remain a major diagnostic problem[13]. Drawbacks of MSCT also include the application of ionizing radiation and the possibility of complications due to intravenous administration of iodine contrast medium. ERCP is very sensitive in detecting bile and pancreatic duct disorders but it is not always highly specific and it is associated with a 5%-10 % risk of significant complications[14]. MRI differentiation of a malignant lesion in chronic pancreatitis can also be very difficult. Gross morphology of the pancreas and clear depiction of fat planes surrounding the pancreas is best shown on T1WI with FAT SAT, which also provides good contrast between pancreatic parenchyma and focal pancreatic masses. The imaging features of chronic pancreatitis include low-signal-intensity pancreas on T1WI with FAT SAT, decreased and delayed enhancement after IV contrast administration, parenchymal atrophy or enlargement, formation of pseudocysts, dilatation and beading of the pancreatic duct often with intraductal calcifications[15]. A smoothly dilated pancreatic duct with an abrupt interruption, dilatation of both biliary and pancreatic duct ("double-duct sign") and obliteration of the perivascular fat planes favor the diagnosis of cancer. Detection and characterization of a pancreatic neoplasm and assessment of the spread of a malignant lesion is based on the change in size and shape of the pancreas as well as on the observation of post-contrast enhancement. To reveal the nature of the solid pancreatic lesion noticed, we performed a dynamic contrast-enhanced study. Early arterial phase is of exceptional importance for the depiction of hypervascular lesions (such as insulinomas). Malignant pancreatic

lesions can be detected during arterial (20-40 s after contrast medium administration) and venous (60-80 s after contrast medium administration) phase as areas of lower signal intensity on T1WI compared to the surrounding pancreatic parenchyma. On postcontrast images we can also assess the local and distant spread of the malignant disease, as well as the possible involvement of vascular structures. On T2WI, fluid has a high signal intensity, therefore fluid containing lesions inside and outside of the pancreas, neoplasms with liquid content, cystic lesions, pancreatic and biliary ducts can be depicted. MRCP is based on a heavily T2WI with a possibility to utilize cross-section thickness from 20 to 100 mm. All signals except from structures filled with static or slowly moving liquid are diminished and a selective display of pancreatic, extrahepatic and intrahepatic ducts with great accuracy and minimal artifacts is obtained. ERCP could be diagnostically replaced with MRCP but MRCP does not provide the opportunity to perform interventional procedures[16,17]. Drawbacks of MRI also include the inability to acquire samples for cytology analysis, decreased sensitivity for the detection of focal lesions in chronic pancreatitis and therefore reduced ability to detect malignant lesions.

This retrospective study demonstrated the role of MRI as a problem solving diagnostic imaging method in radiologically and clinically unclear pancreatic changes detected by other imaging modalities. Our results suggest that the improved tissue contrast of MRI and the ability to evaluate primary lesion and its effect on the adjacent structures make MRI advantageous over other imaging methods in characterization of undetermined pancreatic changes.

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Sažetak

KORELACIJA IZMEĐU SLIKOVNOG PRIKAZA MAGNETSKOM REZONANCIJOM I HISTOPATOLOGIJE U DIFERENCIJACIJI BOLESTI GUŠTERAČE

A. Šverko, A. Tripalo-Batoš, M. Marotti, M. Mustapić, M. Bekavac Bešlin i *B. Krušlin*

U posljednja četiri desetljeća incidencija karcinoma gušterače se u zapadnim zemljama utrostručila. Više od 90% svih karcinoma gušterače otkriva se u uznapredovalom stadiju kada kirurško liječenje više nije moguće, a preživljavanje bolesnika nakon postavljene dijagnoze je najčešće vrlo kratko. Cilj istraživanja bio je usporediti nalaz magnetske rezonancije s histopatološkim nalazom promjena u gušterači u bolesnika oboljelih od kroničnog pankreatitisa te dobroćudnih i zloćudnih novotvorina gušterače. U istraživanje je uključeno 29 bolesnika kod kojih se narav patološke promjene gušterače nije mogla utvrditi klinički niti drugim radiološkim metodama koje su uključivale ultrazvučni pregled, endoskopsku retrogradnu kolangiopankreatografiju te višeslojnu kompjutoriziranu tomografiju. Podaci istraživanja upućuju na podudaranje u radiološkoj i histopatološkoj prosudbi opaženih promjena, potvrđuju visoku točnost magnetske rezonancije u dijagnostici patoloških promjena gušterače i ilustriraju njenu važnost u procjeni naravi nejasnih promjena gušterače.

Ključne riječi: *Magnetska rezonancija, slikovni prikaz; Tomografija, spiralna kompjutorizirana; Ultrazvuk; Kolangiopankreatografija, endoskopska retrogradna; Pankreatitis, kronični; Karcinom gušterače, duktalni*