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Original Article

The advantage of using CEUS time-intensity curves vs. conventional ultrasound in the differential diagnosis of mass pancreatitis and pancreatic cancer

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Abstract: Objective: This study was designed to explore the advantages of using CEUS time-intensity curves (TIC) vs. conventional ultrasound in the differential diagnosis of mass pancreatitis and pancreatic cancer. Methods: From January 2017 to December 2019, 51 patients with mass pancreatitis and 57 patients with pancreatic cancer were recruited as the study cohorts and examined using CEUS and conventional ultrasound. TIC were used to analyze and calculate the arrival times of the contract medium in the lesion (AT), the times to peak (TTP), the peak intensities (Imax), and the transition times (TT). The advantages of using the TIC indices vs. conventional ultrasound in the diagnosis of pancreatic cancer were compared. Results: (1) The AT was significantly shorter and the Imax was significantly higher in the patients with mass pancreatitis ($P<0.05$), but no significant differences in the TTP or TT were observed ($P>0.05$). (2) The accuracy and positive/negative predictive value were significantly higher than the accuracy and positive/negative predictive value of conventional ultrasound when pancreatic cancer was diagnosed according to the criteria of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%. The sensitivity was significantly higher than the sensitivity obtained using conventional ultrasound when the criteria of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14% were followed in the diagnosis. The specificity yielded when the diagnostic criteria of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14% were referenced in the diagnosis of pancreatic cancer was significantly higher than it was when using conventional ultrasound, especially the highest accuracy and sensitivity when AT ≥ 9.45 s or Imax ≤ 72.14% was used. Conclusion: Compared with conventional ultrasound, TIC was better at differentiating mass pancreatitis from pancreatic cancer; in particular, its higher accuracy when AT ≥ 9.45 s or Imax ≤ 72.14% was adopted as the diagnostic criterion.

Keywords: CEUS, TIC, conventional ultrasound, mass pancreatitis, pancreatic cancer

Introduction

Because it is chronic and a risk factor for pancreatic cancer [1, 2], mass pancreatitis is related to the pathological changes of chronic inflammatory cell infiltration and progressive fibrous hyperplasia. Pancreatic cancer is a common and severe malignant tumor of the digestive tract with a poor prognosis that is often lethal [3, 4], as shown by its 5-year survival rate of only 6%. Both mass pancreatitis and pancreatic cancer are focal lesions in the pancreas, which lies at a shallow place behind the peritoneum, resulting in unconspicuous clinical symptoms and signs when it experiences pathological changes, making early diagnosis difficult [5], as the organ is often attacked insidiously. Clinical therapies for mass pancreatitis and pancreatic cancer are entirely different. If pancreatic cancer is mistaken as mass pancreatitis, the patients may suffer from treatment delays that threaten their lives. Therefore, the early and correct differential diagnoses of mass pancreatitis and pancreatic cancer are particularly important.

In the clinic, CT, MRI, and ultrasound are generally used to differentially diagnose mass pancreatitis and pancreatic cancer. However, the first two options are expensive and not suitable for patients with a renal inadequacy, so their clinical applications are limited [6]. Ultrasound

is invasive, affordable, reproducible, and radiation free, and it is often used in the clinical differentiation of mass pancreatitis and pancreatic cancer [7]. The ultrasonic images of mass pancreatitis and pancreatic cancer may be similar, as both diseases are local lesions in the pancreas, and they may be subject to interference from factors such as the subject's body shape and gas in the abdomen. Therefore, conventional ultrasound is limited to differentiating mass pancreatitis and pancreatic cancer.

The highly safe CEUS supports the dynamic and continuous observation of the microcirculation perfusion at the lesion and plays an important role in the differential diagnosis of mass pancreatitis and pancreatic cancer [8]. When CEUS TIC is used in the quantitative analysis of CEUS images, the microperfusion in the tissues can be observed more accurately and objectively. Therefore, in this study, conventional ultrasound and CEUS examinations were performed on patients with mass pancreatitis and pancreatic cancer. The TIC indices were compared, and the diagnostic advantages of the TIC indices and conventional ultrasound in pancreatic cancer were analyzed in order to provide a supplementary reference for the early differential diagnosis of mass pancreatitis and pancreatic cancer.

Materials and methods

General materials

51 patients with mass pancreatitis and 57 patients with pancreatic cancer admitted to our hospital from January 2017 to December 2019 were included as the study cohorts according to the following criteria: (1) patients pathologically diagnosed with mass pancreatitis or pancreatic cancer after surgery, (2) patients who received conventional ultrasound and CEUS examinations. Patients with tumors at multiple sites or who suffered from mental diseases preventing them from normal communication and pregnant or lactating women were excluded. The mass pancreatitis patients consisted of 28 males and 23 females ranging in age from 42 to 66, with a mean age of (54.31± 8.13) years. Their weights varied from 39 to 77 kg, and their average weight was (57.28± 12.64) kg. The pancreatic cancer patients included 32 males and 25 females. Their ages ranged from 42 to 69, with a mean value of (54.69±8.54) years, and their weights ranged from 41 to 75 kg, with an average of (56.82± 12.46) kg. No significant differences in gender, age, or weight were observed (P>0.05). This study was approved by the Medical Ethics Committee of the hospital, and all the patients provided an informed consent.

Methods

All the patients received CEUS and conventional ultrasound examinations after fasting for at least 8 hours. The instrument was a LOGIQ E9 high-grade color ultrasound diagnostic apparatus from GE, USA. The probe frequency was set to 2~4 MHz, and the mechanical index was set to 0.08~0.10. During the examination, the patients lied on their backs. The pancreas was scanned using conventional ultrasound to observe the features such as lesion location, boundary, size and echo, and then by CEUS with SonoVue as the contract medium. Before use, the SonoVue was thawed and mixed with 5 ml of normal saline to prepare a suspension. The pancreas area around the lesion was taken as the control. The lesion was continuously perfused with the suspension at a volume of 2 ml each time and observed on a real-time basis for at least 90 seconds. During CEUS, the patients were required to breathe normally, and the tangent plane selected for imaging was kept unchanged. At the end of CEUS, the dynamic imaging pictures were saved and imported into the SonoLiver. As the lesion and the pancreas area around the lesion (the control) were selected, an ROI sampling box was placed at the selected area with maximal efforts to avoid dilated pancreatic ducts and great vessels. TIC began to calculate the AT, the TTP, the Imax, and the TT, of which, Imax is a relative value expressed as a percentage, expressed as the ratio of echo intensity at the lesion to that of the pancreas area around the lesion. TTP is defined as the time elapsed from the beginning of the echo enhancement at the lesion to Imax, and TT is defined as the time elapsed from the beginning of the echo enhancement to the Imax dropping by 50%. As TTP and TT are related to Imax, the TIC indices are diagnosed with AT and Imax, with AT defined as ≥ 9.45 s and Imax as ≤ 72.14%. The ultrasonic contrast images of mass pancreatitis and pancreatic cancer are shown in **Figures 1** and **2**.

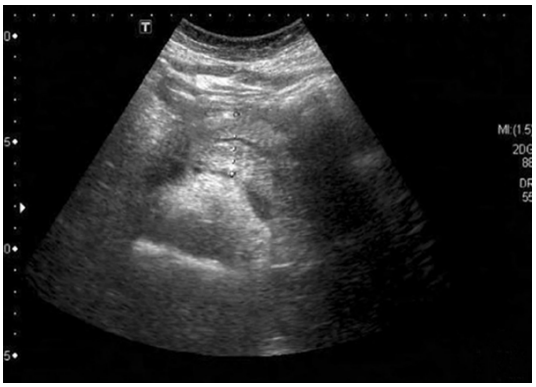

Figure 1. Ultrasonic image of mass pancreatitis.

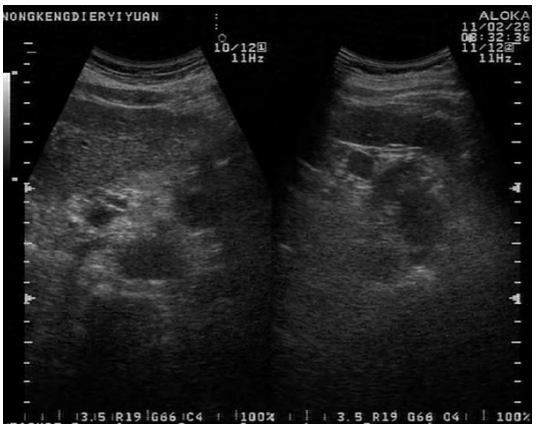

Figure 2. Ultrasonic image of pancreatic cancer.

Observation indices

The AT, TTP, Imax, and TT were compared between the patients with mass pancreatitis and those with pancreatic cancer. The accuracy, sensitivity, specificity, and positive/negative predictive values of the TIC indices (AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%) and of conventional ultrasound in the diagnosis of pancreatic cancer were analyzed.

Statistical analysis

The statistical analysis was performed using SPSS 22.0. The patients' genders, and their true positive/negative (TP/TN) and false positive/negative (FP/FN) data were expressed as n, and independent-samples X^2 tests were carried out. The AT, TTP, Imax, and TT were expressed as the means ± standard deviation, and independent-samples t tests were carried out. For all the statistical comparisons, significance was defined as P<0.05.

Results

TIC indices

The AT, Imax, TTP, and TT were (8.44±2.66) s, (86.66±22.41)%, (8.34±2.55) s, and (27.43±9.03) s in the patients with mass pancreatitis and (11.12±3.62) s, (44.37±12.58)%, (8.69±2.47) s, and (27.87±8.81) s in the patients with pancreatic cancer (P<0.05 for AT and Imax, P>0.05 for TTP and TT) (**Table 1**; **Figures 3** and **4**).

The advantages of TIC indices and of conventional ultrasound in the diagnosis of pancreatic cancer

The number of TP, FP, FN, and TN cases were 43, 14, 14 and 37 according to AT ≥ 9.45 s, 41, 17, 16, and 34 according to Imax ≤ 72.14%, 53, 20, 4, and 31 according to AT ≥ 9.45 s or Imax ≤ 72.14%, 31, 10, 26, and 11 according to AT ≥ 9.45 s and Imax ≤ 72.14%, and 25, 28, 32, and 23 when done using conventional ultrasound (**Table 2**).

The sensitivity and specificity of the TIC indices and of conventional ultrasound in diagnosing pancreatic cancer

In diagnosing pancreatic cancer: (1) The accuracies of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 74.07%, 69.44%, 77.78%, 66.67% and 44.44% (P<0.05); and (2) The sensitivities of Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, and conventional ultrasound were 75.44%, 71.93%, 92.98% and 43.86% (P<0.05). In the case of AT ≥ 9.45 s and Imax ≤ 72.14%, the sensitivity was only 54.39% (P>0.05); (3) The specificities of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 72.55%, 66.67%, 80.39% and 45.10% (P<0.05). In case of AT ≥ 9.45 s or Imax ≤ 72.14%, the specificity dropped to 60.78% (P>0.05); (4) The positive/negative predictive values of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 75.44%/72.55%, 70.69%/68.00%, 72.60%/88.57%, 75.61%/61.19%, and 47.47%/41.82% (P<0.05) (**Table 3**).

Table 1. A comparison of the TIC indices between mass pancreatitis and pancreatic cancer ($\bar{x} \pm s$)

Group	n	AT (s)	TTP (s)	Imax (%)	TT (s)
Mass pancreatitis	51	8.44±2.66	8.34±2.55	86.66±22.41	27.43±9.03
Pancreatic cancer	57	11.12±3.62	8.69±2.47	44.37±12.58	27.87±8.81
t		4.341	0.723	12.256	0.256
P		<0.001	0.471	<0.001	0.798

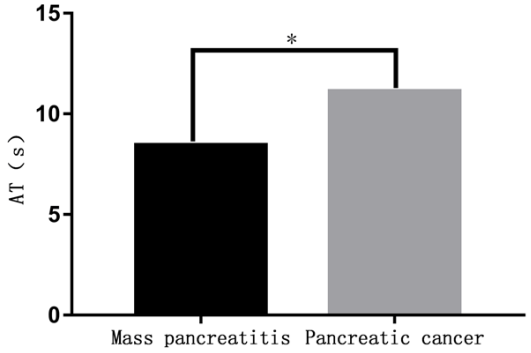

Figure 3. Comparison of the AT between mass pancreatitis and pancreatic cancer. The AT in patients with mass pancreatitis is significantly lower than it is in patients with pancreatic cancer (P<0.05). *P<0.05 for intergroup comparison.

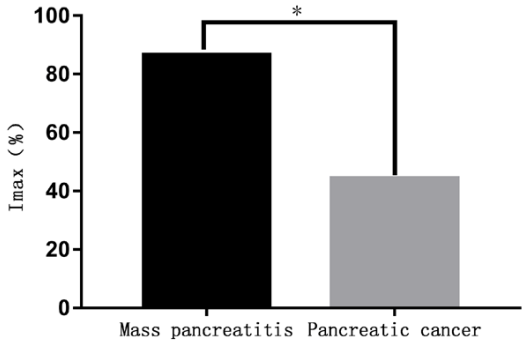

Figure 4. Comparison of the Imax between mass pancreatitis and pancreatic cancer. The Imax in patients with mass pancreatitis is significantly higher than it is in patients with pancreatic cancer (P<0.05). *P<0.05 for intergroup comparison.

Discussion

The concealment of pancreatic cancer in the early onset stage results in most patients missing the best treatment window and already being at the middle-to-advanced stage when they are first referred to a specialist. Even after surgical treatment, the 5-year survival is not optimistic [9, 10]. Mass pancreatitis has a long duration and local masses due to long-term tissue fibrosis and inflammatory cell infiltration, and it is a known hazard of pancreatic cancer [11, 12]. Pancreatic cancer is similar to mass pancreatitis in its ultrasonic manifestation, clinical symptoms, and signs. They are difficult to differentiate, and they are treated using entirely different therapies. Therefore, an early differential diagnosis and symptomatic treatment would play a significant role in improving the prognosis.

Conventional ultrasound is usually used for the preliminary screening of pancreatic lesions. However, most pancreatic lesions are manifested as mixed or low echoes. The similarity exerts an influence on the accuracy of this tool in the differential diagnosis of mass pancreatitis and pancreatic cancer [13, 14], while the subject's body shape and gas in the abdomen also affect its sensitivity. In contrast, CEUS supports pure blood pool imaging by conducting the CEUS medium into the tissue gaps, in order to accurately reflect the low-volume and low-flowrate blood signals in the lesion and to continuously observe the tissues concerned on a real-time basis. In this way, CEUS plays a key role in the differential diagnosis of local pancreatic lesions [15, 16]. However, some studies have pointed out that the visual observation of normal pancreatic tissues and pancreatic lesions for enhancement degrees and reinforcement times may be subjective [17, 18]. Therefore, TIC was adopted in this study to quantitatively analyze mass pancreatitis and pancreatic cancer based their TIC indices, and a comparison was performed between the TIC indices and conventional ultrasound to determine their advantages in the differential diagnosis of the two diseases.

For patients with mass pancreatitis, the AT was significantly shorter than the AT of the patients with pancreatic cancer. The reason is that the vascular density in patients with mass pancreatitis or pancreatic cancer was decreasing, but the tissue reconstruction, necrosis, thrombus, and bleeding produced in the course of chronic inflammation can lead to cicatrix fracture and

Table 2. The diagnosis of pancreatic cancer using TIC indices and conventional ultrasound

Criterion	Results	Pathological results	
		Pancreatic cancer	Mass pancreatitis
AT ≥ 9.45 s	Pancreatic cancer	43	14
	Mass pancreatitis	14	37
Imax ≤ 72.14%	Pancreatic cancer	41	17
	Mass pancreatitis	16	34
AT ≥ 9.45 s or Imax ≤ 72.14%	Pancreatic cancer	53	20
	Mass pancreatitis	4	31
AT ≥ 9.45 s and Imax ≤ 72.14%	Pancreatic cancer	31	10
	Mass pancreatitis	26	41
Conventional ultrasound	Pancreatic cancer	25	28
	Mass pancreatitis	32	23

Table 3. The sensitivity and specificity of TIC indices and conventional ultrasound in diagnosing pancreatic cancer

Criterion	Accuracy	Sensitivity	Specificity	Positive predictive value	Negative predictive value
AT ≥ 9.45 s	74.07 (80/108)	75.44 (43/57)	72.55 (37/51)	75.44 (43/57)	72.55 (37/51)
Imax ≤ 72.14%	69.44 (75/108)	71.93 (41/57)	66.67 (34/51)	70.69 (41/58)	68.00 (34/50)
AT ≥ 9.45 s or Imax ≤ 72.14%	77.78 (84/108)	92.98 (53/57)	60.78 (31/51)	72.60 (53/73)	88.57 (31/35)
AT ≥ 9.45 s and Imax ≤ 72.14%	66.67 (72/108)	54.39 (31/57)	80.39 (41/51)	75.61 (31/41)	61.19 (41/67)
Conventional ultrasound	44.44 (48/108)	43.86 (25/57)	45.10 (23/51)	47.17 (25/53)	41.82 (23/55)

contraction of the entire gland, so that the contrast medium can rapidly enter the lesions [19, 20]. However, in patients with pancreatic cancer, the tumor tissue was densely enveloped by microvessels, which slowed down the speed of the contrast medium approaching the tumor center [21, 22]. In this study, it was also found that the Imax in patients with mass pancreatitis was significantly higher than it was in patients with pancreatic cancer. The reason lies in the enhanced vasa vasorum in a shape of a strip found in or around the tumor during the arterial phase imaging, and the contrast medium flowed from the periphery to the center [23, 24]. Furthermore, there are fewer microvessels in a cancerized pancreas than there are in a normal one, and the vasa vasorum are generally deployed around the tumor lesion where fibrous tissues proliferate and the vascular density is relatively low. So, the enhancement and the Imax in patients with pancreatic cancer are at a low level [25, 26]. Moreover, no significant differences in TTP (the time elapsed from the beginning of echo enhancement at the lesion to Imax) or in TT (the time elapsed from the beginning of echo enhancement to Imax dropping by 50%) were observed in this study, which may have a possible relevance with their definitions.

Studies have shown that CEUS is of great significance in the diagnosis of thymic tumors and peripheral pulmonary lesions in the elderly, and its diagnostic value is higher than that of conventional ultrasound [27]. In this study, CEUS was applied to the diagnosis of pancreatic cancer through a quantitative analysis, which is different from most previous studies. The results showed that the value of the different indicators of ultrasound TIC in the diagnosis of pancreatic cancer was higher than that of conventional ultrasound TIC. Therefore, AT ≥ 9.45 s or Imax ≤ 72.14% had the highest accuracy and sensitivity in the diagnosis of pancreatic cancer (77.78% and 92.98% respectively), which is consistent with the findings of Fan et al. [28]. Those results proved that TIC quantitative analysis, especially AT ≥ 9.45 s or Imax ≤ 72.14%, was more advantageous in the differential diagnosis compared with conventional ultrasound.

To sum up, when compared with patients with pancreatic tumors, patients with mass pancre-

atitis had lower AT and higher Imax values but significant differences in TTP and TT were not observed, indicating that AT and Imax can be used as an important basis for the differential diagnosis of mass pancreatitis and pancreatic cancer. When compared with conventional ultrasound, TIC is better at differentiating mass pancreatitis and pancreatic cancer and has a particularly high accuracy when AT ≥ 9.45 s or Imax ≤ 72.14% is used. Therefore, TIC indices can be used in the objective and accurate differential diagnosis of mass pancreatitis and pancreatic cancer. Nevertheless, there are also limitations to this study: ultrasound examinations will be affected by gastrointestinal gas and a patient's body shape. The TIC quantitative analysis is subject to factors such as breathing, psychology, and normal pancreatic depth, but this study was relatively limited in terms of the size of the cohorts, so an in-depth study with a large sample size is still needed in the future.

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Disclosure of conflict of interest

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References

[1] Aljiffry M, Habib R, Kotbi E, Ageel A, Hassanain M and Dahlan Y. Acute pancreatitis: a complication of intragastric balloon. Surg Laparosc Endosc Percutan Tech 2017; 27: 456-459.

[2] Vege SS, DiMagno MJ, Forsmark CE, Martel M and Barkun AN. Initial medical treatment of acute pancreatitis: American Gastroenterological Association Institute technical review. Gastroenterology 2018; 154: 1103-1139.

[3] Lwin TM, Murakami T, Miyake K, Yazaki PJ, Shivley JE, Hoffman RM and Bouvet M. Tumor-specific labeling of pancreatic cancer using a humanized Anti-CEA antibody conjugated to a near-infrared fluorophore. Ann Surg Oncol 2018; 25: 1079-1085.

[4] Klein AP, Wolpin BM, Risch HA, Stolzenberg-Solomon RZ, Mocci E, Zhang M, Canzian F, Childs EJ, Hoskins JW, Jermusyk A, Zhong J, Chen F, Albanes D, Andreotti G, Arslan AA, Babic A, Bamlet WR, Beane-Freeman L, Berndt SI, Blackford A, Borges M, Borgida A, Bracci PM, Brais L, Brennan P, Brenner H, Bueno-de-Mesquita B, Buring J, Campa D, Capurso G, Cavestro GM, Chaffee KG, Chung CC, Cleary S, Cotterchio M, Dijk F, Duell EJ, Foretova L, Fuchs C, Funel N, Gallinger S, M Gaziano JM, Gazouli M, Giles GG, Giovannucci E, Goggins M, Goodman GE, Goodman PJ, Hackert T, Haiman C, Hartge P, Hasan M, Hegyi P, Helzlsouer KJ, Herman J, Holcatova I, Holly EA, Hoover R, Hung RJ, Jacobs EJ, Jamroziak K, Janout V, Kaaks R, Khaw KT, Klein EA, Kogevinas M, Kooperberg C, Kulke MH, Kupcinskas J, Kurtz RJ, Laheru D, Landi S, Lawlor RT, Lee IM, LeMarchand L, Lu L, Malats N, Mambrini A, Mannisto S, Milne RL, Mohelníková-Duchoňová B, Neale RE, Neoptolemos JP, Oberg AL, Olson SH, Orlow I, Pasquali C, Patel AV, Peters U, Pezzilli R, Porta M, Real FX, Rothman N, Scelo G, Sesso HD, Severi G, Shu XO, Silverman D, Smith JP, Soucek P, Sund M, Talar-Wojnarowska R, Tavano F, Thornquist MD, Tobias GS, Van Den Eeden SK, Vashist Y, Visvanathan K, Vodicka P, Wactawski-Wende J, Wang Z, Wentzensen N, White E, Yu H, Yu K, Zeleniuch-Jacquotte A, Zheng W, Kraft P, Li D, Chanock S, Obazee O, Petersen GM and Amundadottir LT. Genome-wide meta-analysis identifies five new susceptibility loci for pancreatic cancer. Nat Commun 2018; 9: 556.

[5] Kaneko R, Mitomi H, Nakazaki N, Yano Y, Ogawa M and Sato Y. Primary hepatic lymphoma complicated by a hepatic inflammatory pseudotumor and tumor-forming pancreatitis. J Gastrointestin Liver Dis 2017; 26: 299-304.

[6] Ofori E, Ramai D, Etienne D, Reddy M and Shahzad G. Large dermoid cyst presenting as recurrent pancreatitis. Gastroenterology Res 2017; 10: 322-324.

[7] Meyer MA, Baer JM, Knolhoff BL, Nywening TM, Panni RZ, Su X, Weilbaecher KN, Hawkins WG, Ma C, Fields RC, Linehan DC, Challen GA, Faccio R, Aft RL and DeNardo DG. Breast and pancreatic cancer interrupt IRF8-dependent dendritic cell development to overcome immune surveillance. Nat Commun 2018; 9: 1250.

[8] Gaur K, Mandal S, Mahajan N, Saluja S and Godhi S. Xanthogranulomatous pancreatitis -a rare case defying clinical, radiological and tumor marker diagnostics with a review of literature. Turk Patoloji Derg 2019; 35: 144-150.

[9] Wills SE, Beaufrère HH, Brisson BA, Fraser RS and Smith DA. Pancreatitis and systemic coronavirus infection in a ferret (Mustela putorius furo). Comp Med 2018; 68: 208-211.

[10] Shah AS, Gupta AK and Ded KS. Assessment of PANC3 score in predicting severity of acute pancreatitis. Niger J Surg 2017; 23: 53-57.
[11] Muraki T, Kim GE, Reid MD, Mittal P, Bedolla G, Memis B, Pehlivanoglu B, Freedman A, Erbarut Seven I, Choi H, Kooby D, Maithel SK, Sarmiento JM, Krasinskas A and Adsay V. Paraduodenal pancreatitis: imaging and pathologic correlation of 47 cases elucidates distinct subtypes and the factors involved in its etiopathogenesis. Am J Surg Pathol 2017; 41: 1347-1363.
[12] Baltatzis M, Jegatheeswaran S and Siriwardena AK. Geographical variance in reporting of elective surgery for chronic pancreatitis. Eur J Gastroenterol Hepatol 2019; 31: 303-311.
[13] Massey TH. Efficiency in the diagnosis of acute pancreatitis increased by improved electrophoresis of amylase isoenzyme P3 on cellulose acetate. Clin Chem 1985; 31: 70-75.
[14] Werner M, Steinberg WM and Pauley C. Strategic use of individual and combined enzyme indicators for acute pancreatitis analyzed by receiver-operator characteristics. Clin Chem 1989; 35: 967-971.
[15] Avanthi US, Bale G, Aslam M, Talukdar R, Duvvur NR and Vishnubhotla RV. PRSS1 (R122H) mutation in an Indian family with low penetrance is associated with pancreatitis phenotype. Indian J Gastroenterol 2018; 37: 67-69.
[16] Leclerc P and Forest JC. Variations in amylase isoenzymes and lipase during acute pancreatitis, and in other disorders causing hyperamylasemia. Clin Chem 1983; 29: 1020-1023.
[17] Neoptolemos JP, Kleeff J, Michl P, Costello E, Greenhalf W and Palmer DH. Therapeutic developments in pancreatic cancer: current and future perspectives. Nat Rev Gastroenterol Hepatol 2018; 15: 333-348.
[18] Balmaña M, Duran A, Gomes C, Llop E, López-Martos R, Ortiz MR, Barrabés S, Reis CA and Peracaula R. Analysis of sialyl-Lewis x on MUC5AC and MUC1 mucins in pancreatic cancer tissues. Int J Biol Macromol 2018; 112: 33-45.
[19] Ozaka M, Ishii H, Sato T, Ueno M, Ikeda M, Uesugi K, Sata N, Miyashita K, Mizuno N, Tsuji K, Okusaka T and Furuse J. A phase II study of modified FOLFIRINOX for chemotherapy-naïve patients with metastatic pancreatic cancer. Cancer Chemother Pharmacol 2018; 81: 1017-1023.
[20] Hagiwara Y, Ohashi Y, Uesaka K, Boku N, Fukutomi A, Okamura Y, Konishi M, Matsumoto I, Kaneoka Y, Shimizu Y, Nakamori S, Sakamoto H, Morinaga S, Kainuma O, Imai K, Sata N, Hishinuma S, Ojima H, Yamaguchi R, Hirano S and Sudo T; JASPAC 01 Study Group. Health-related quality of life of adjuvant chemotherapy with S-1 versus gemcitabine for resected pancreatic cancer: results from a randomised phase III trial (JASPAC 01). Eur J Cancer 2018; 93: 79-88.
[21] Carotenuto P, Zito D, Previdi MC, Raj M and Braconi C. Abstract 4977: MIR1307 mediates pancreatic cancer resistance to FOLFIRINOX chemotherapy by affecting response to DNA damage. Cancer Res 2018; 78: 4977.
[22] Torgeson A, Garrido-Laguna I, Tao R, Cannon GM, Scaife CL and Lloyd S. Value of surgical resection and timing of therapy in patients with pancreatic cancer at high risk for positive margins. ESMO Open 2018; 3: e000282.
[23] Harris PA, Marinis JM, Lich JD, Berger SB, Chirala A, Cox JA, Eidam PM, Finger JN, Gough PJ, Jeong JU, Kang J, Kasparcova V, Leister LK, Mahajan MK, Miller G, Nagilla R, Ouellette MT, Reilly MA, Rendina AR, Rivera EJ, Sun HH, Thorpe JH, Totoritis RD, Wang W, Wu D, Zhang D, Bertin J and Marquis RW. Identification of a RIP1 kinase inhibitor clinical candidate (GSK3145095) for the treatment of pancreatic cancer. ACS Med Chem Lett 2019; 10: 857-862.
[24] Almawash SA, Mondal G and Mahato RI. Coadministration of polymeric conjugates of docetaxel and cyclopamine synergistically inhibits orthotopic pancreatic cancer growth and metastasis. Pharm Res 2018; 35: 17.
[25] Mueller S, Engleitner T, Maresch R, Zukowska M, Lange S, Kaltenbacher T, Konukiewitz B, Öllinger R, Zwiebel M, Strong A, Yen HY, Banerjee R, Louzada S, Fu B, Seidler B, Götzfried J, Schuck K, Hassan Z, Arbeiter A, Schönhuber N, Klein S, Veltkamp C, Friedrich M, Rad L, Barenboim M, Ziegenhain C, Hess J, Dovey OM, Eser S, Parekh S, Constantino-Casas F, de la Rosa J, Sierra MI, Fraga M, Mayerle J, Klöppel G, Cadiñanos J, Liu P, Vassiliou G, Weichert W, Steiger K, Enard W, Schmid RM, Yang F, Unger K, Schneider G, Varela I, Bradley A, Saur D and Rad R. Evolutionary routes and KRAS dosage define pancreatic cancer phenotypes. Nature 2018; 554: 62-68.
[26] Orozco CA, Martinez-Bosch N, Guerrero PE, Vinaixa J, Dalotto-Moreno T, Iglesias M, Moreno M, Djurec M, Poirier F, Gabius HJ, Fernandez-Zapico ME, Hwang RF, Guerra C, Rabinovich GA and Navarro P. Targeting galectin-1 inhibits pancreatic cancer progression by modulating tumor-stroma crosstalk. Proc Natl Acad Sci U S A 2018; 115: E3769-E3778.
[27] Hu MX, Liu K and Lei X. The value of ultrasound contrast imaging time-intensity curve in the detection of thymic tumors in the elderly. Chinese Journal of Gerontology 2017; 37: 109-111.
[28] Fan ZH, Yan K, Wu W, Yin SS, Dai Y, Yang W and Chen MH. Quantitative analysis with CEUS in differential diagnosis of pancreatic carcinoma and mass forming pancreatitis. Chin J Med Imaging Technol 2012; 28: 1354-1358.