CT modern potential in acute pancreatitis visualization (part 1)

A. A. Filatau, A. A. Litvin

Gomel Regional Clinical Hospital,

Gomel State Medical University, Gomel, Belarus

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The incidence of acute pancreatitis (AP) has been steadily increasing in most countries. Patients with AP encounter 5-10% of surgical patients. In 15-20% of cases AP has necrotizing character [7]. The highest incidence of severe AP is found among people of working age, which gives this particular problem the socio-economic significance [29].

In 1992 a conference on AP in Atlanta (USA) adopted the international classification, which has been successfully used by the surgeons for 20 years. However, this classification system required some revision over time. To this end, international working group was gathered in 2008 (Acute Pancreatitis Classification Working Group), which spent four years in rework and improvement of the developed classification at the level of national pancreatic societies and international congresses, and in 2012 at a conference on AP in Miami (USA) all corrections were gathered together and a new classification of AP was formulated [16, 27]. One of the main features of the updated classification was its focus on the imaging. It implies an importance and necessity of an objective assessment of morphological changes in pancreas taking place and parapancreatic tissue (PPT) during AP, using a variety of present-day variables imaging techniques [13, 25, 27].

The aim of this article (Part 1) is to review literature on moderate opportunities of the computed tomography (CT) in the diagnostics and treatment of AP with emphasis on recommendations made in 2012. Part 2 will present CT data on modern AP classification definitions and other aspects of this quite multifaceted problem.

In the provisions of the revised classification (May 2012), contrast-enhanced CT is selected as a basic method of visualization to determine the acute inflammatory

changes in the tissues of the pancreas. This is due to a relatively small time of a scanning, accessibility and simple interpretability of the images received by surgeons and radiologists as compared to other methods of diagnosis [10, 13]. CT identifies characteristic changes that allow to diagnose AP and determine the severity of disease with a highest precision [9, 21].

The latest recommendations of the International and American Associations of Pancreatology IAP/APA define indications for performing CT in the AP as follows: 1) specification of the diagnosis; 2) presence of clinical signs of severe AP; 3) absence of the effect of conservative treatment of severe AP (level of evidence 1C). [19]

CT without intravenous contrast-enhancement study is not usually applied due to its low informative value for detecting expansion of pancreatic necrosis, as normal and abnormal tissues almost do not differ from each other in the X-ray density, measured in units of Hounsfield (Hu). Native CT-study only allows to differentiate acute edematous pancreatitis from other diseases of the abdominal cavity (Fig. 1), to identify other distinct changes in the X-ray pictures [9, 17].

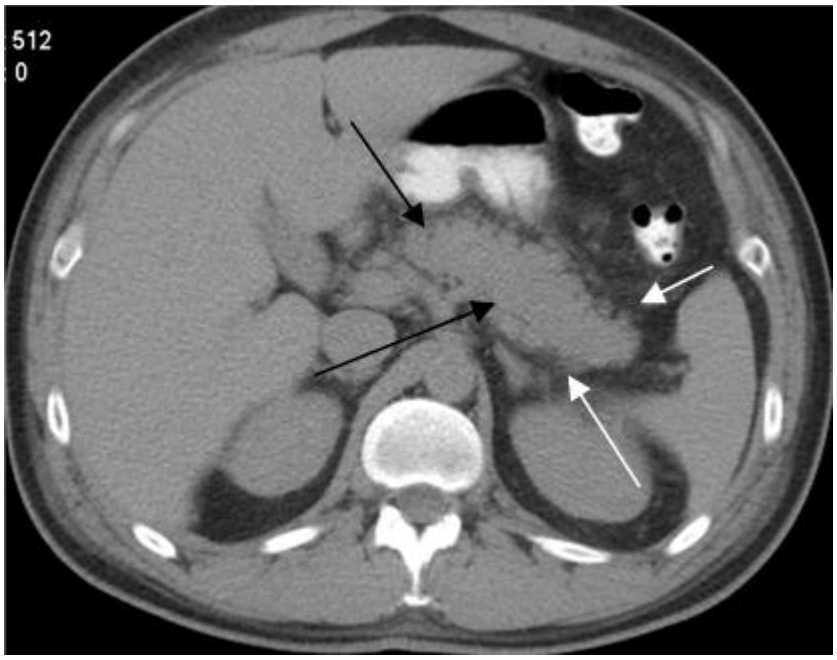

Fig. 1. CT without intravenous contrast enhancement. Patient K., 35 years, 5 days from onset. Edematous pancreatitis: marked increase in the size and swelling of the parenchyma of the pancreas (black arrows), small "banding" of PPT (white arrows).

The method of per os contrast for CT studies, which is performed in a specific way — 40 ml of 76% solution of urografin dissolved in 1.5 liters of boiled water; 500 ml of the resulting solution patient drinks the day before CT from 8 to 10 p.m., another 500 ml are drunk the next morning, and the remaining 500 ml — 30-20 minutes before the test — is not always applicable in patients with AP. This is due to the inability of contrast oral intake in connection with a stored paresis of the intestine, the lack of time for lengthy preparation for the examination [1, 9, 22].

Intravenous contrast enhancement can be done in two ways: "manual" and bolus intravenous contrast opacification. With the first method, the contrast is entered manually by radiographers, time and rate of administration are not regulated, the examination starts after the intake of contrast agents. This method is most often used on the "slow" devices of the first generation. In bolus contrast enhancement drug is administered intravenously by syringe injector with defined speed and time of material intake [23]. The purpose of the bolus of contrast enhancement is a delineation of contrast phases. On average, at a rate of injection of 4-5 ml/sec, the scanning starts in about 20-30 seconds after the start of the contrast by injector, wherein content arteries is visualized (arterial phase of contrast enhancement). In 40-60 seconds, the machine re-scans the same zone to highlight the portal-venous phase, which visualizes contrasting veins. Delayed release (parenchymal) phase (100-160 seconds after the start of the administration) is pointed out, in which there is a certain delay of the contrast agent in the pancreas and the removal through the urinary system [9, 20, 22].

By using the above techniques with bolus intravenous contrast enhancement viable parenchyma is more clearly differentiated, which is uniformly stored due to the contrasted vascular architectonics [20]. In edematous AP, enlarged pancreas with a uniform decrease in the signal from the tissue is defined. In the presence of acute necrotizing pancreatitis a heterogeneous pattern is formed with hypovascular and avascular areas [2] (Fig. 2).

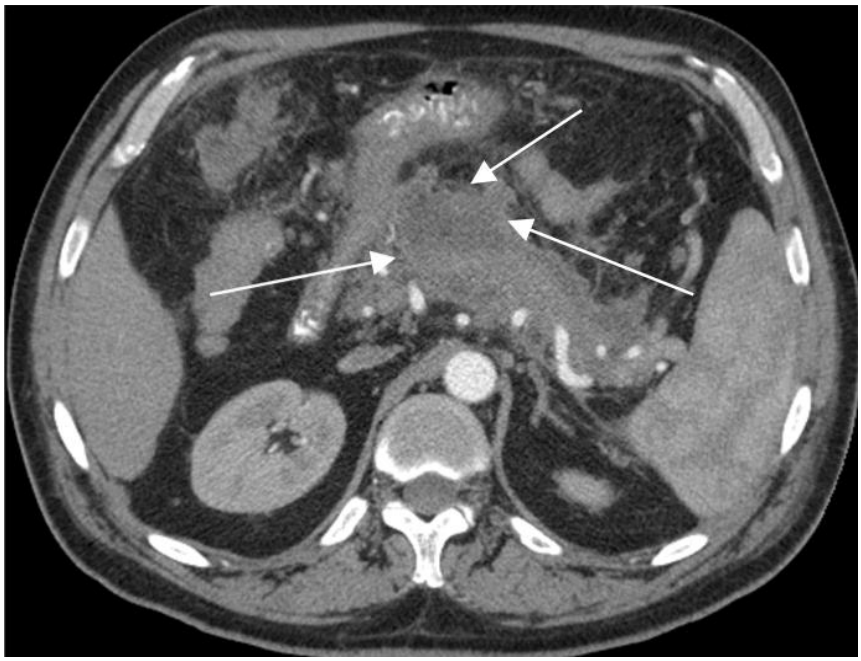

Fig. 2. Patient Ch., 50 years, 3 days from the beginning of abdominal pain. AP of alcoholic etiology. The arrows indicate areas of reduced contrast in the parenchyma of the pancreas. With this picture interstitial edematous pancreatitis and necrotizing pancreatitis can't be unambiguously differentiated, which will become possible in subsequent CT studies.

The question of the form of the disease (necrotizing pancreatitis or edema) is a key in the initial stage of AP diagnostics as the former one rarely requires surgery, while the latter one is an indication for intensive care of the disease, minimally invasive drainage operations [22]. According to the IAP/APA recommendations, the terms not earlier than 72-96 hours after the onset of the disease (1C) are optimal for an initial CT assessment [19]. This is explained by the fact that in the early stages of inflammation in the pancreas in the edematous AP form there is a violation of the microcirculation on the background of tissue edema, which can be defined as a diffuse decrease of echogenicity with some heterogeneity in the CT images. In its turn, the development of pancreatic necrosis in the early stages is characterized by similar radiological visual effects — the alternation of iso- and hypoechoic areas without the formation of clear zones of degradation (Fig. 2), and the most typical and significant changes are determined by CT in 3 days from the onset of the disease, when the informative value of this method reaches 85-90% [2, 12, 22] (Fig. 3). Overall, in the first three days of onset use of CT in the early stages is justified only

for the purpose of differential diagnosis of AP from other severe acute diseases of the abdominal cavity.

Fig. 3. CT scan of patient M., 49 years, 13 hours from the onset. There is a total pancreatic necrosis and PPT necrosis.

Indications for CT rescan, according to the revised AP classification 2012, should be considered: 1) change in the clinical status of patient, or the lack of clinical improvement during the treatment (for example, saving tachycardia, leukocytosis, fever, persistent multiple organ failure) — for the purpose of differential diagnosis of sterile and infected pancreatic necrosis (Fig. 4 and 5); 2) need to monitor morphological changes in the pancreaticoduodenal area in 7-10 day from the time of admission (or later), when the total score of CT severity index at admission ranged from 3 to 10; 3) for visual control of the results of treatment after surgical treatment (Fig. 6); 4) upon discharge of the patient with severe AP (Table 1) [28].

Table 1

Indications for CT with contrast enhancement in patients with AP [28]

Type of study	Indications
	1. Ambiguity of AP diagnosis 2. Presence of clinically severe AP, swelling and pain in the abdomen, hyperthermia and leukocytosis ≥39^{o}C (in order to detect complications) 3. Severity of the patient's condition >3 according to Ranson scale or >8 according to APACHE II scale 4. Absence of positive dynamics in 72 hours from the start of conservative therapy 5. Sudden changes in clinical status — renewal of fever, pain and shock — after initially

	successful drug therapy
	1. Changes in the clinical status of the patient (inability to eliminate the complications, primarily purulent ones) 2. 7-10 days from the date of admission (or later), if the CT severity index at admission ranged from 3 to 10 points 3. In order to determine and document the results of treatment after surgical or interventional procedures 4. Discharge of patient with severe AP

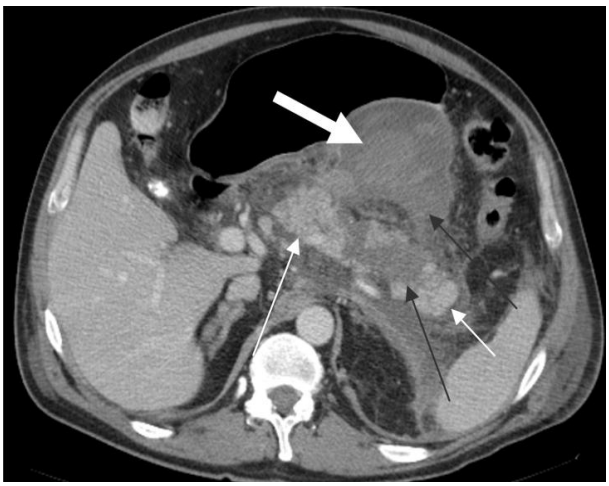

Fig. 4. Patient L., 56 years, in 3 days of the occurrence of pain. Determined large necrotic acute clusters in the PPT and the body of the pancreas (black arrows) with heterogeneous content (thick white arrow) and the preservation of the head and tail of the pancreas (white arrow).

Fig. 5. Patient L., 56 years, in 28 days from the onset of symptoms of the disease. Determined delimited necrosis (black arrow) with indirect signs of infection — gas bubbles (white arrows). CT is conducted in terms of changes of clinical and laboratory picture of the disease (leukocytosis, increased abdominal pain).

Fig. 6. Patient B., 49 years, the 15th day of the onset of the disease. Visualized expanded pancreatic and peripancreatic necrosis (black arrow) with heterogeneous content (thick white arrow) and catheter type «pigtail» in the lumen (white arrow) — drainage was ineffective, necessitating repeated surgical procedures.

In general, the control CT allows to improve topical diagnostics of pancreatic necrosis with more accurate identification of the prevalence, limitation, dominance of tissue or fluid components in the foci of purulent melting and destruction of the PPT, which is necessary for determining the tactics of treatment of patients and the choice of operative access [15]. In addition, CT is recommended for patients older 40 years with an attack of acute idiopathic pancreatitis in order to prevent swelling of the head of the pancreas with compression of the pancreatic duct and development of pancreatic hypertension [24].

The above-mentioned IAP/APA recommendations stipulate the following study protocol: 1) multislice CT with slice thickness of 5 mm; 2) 100-150 ml of nonionic contrast agent are administered intravenously at a rate of 3 ml/sec, the optimal score is 50-70 sec (pancreatic and portal phase) (1C).

According to the revised AP classification–2012 (Atlanta, 1992), with the aim of stratification of severe AP, in addition to clinical scales (Marshall, Ranson, APACHE II), CT scales are still being recommended: Balthazar scale, CT severity index according to Balthazar, modified CT severity index according to Mortele

(Table 2, 3) [14, 18]. A comparison of the effectiveness of these systems in predicting the AP severity did not reveal any significant statistical difference [14].

Table 2

Balthazar scale and CT severity index according to Balthazar

Stage	Signs	Points
A	Norm	0
B	Enlargement of the size of the pancreas	1
C	Inflammatory changes in the parenchyma and peripancreatic fatty tissue	2
D	Single fluid cluster, expressed extrapancreatic changes	3
E	Two or more clusters of liquid and gas in the retroperitoneal space	4
Volume of necrosis	- absent - takes 1/3 of the volume of the pancreas - takes 1/2 of the volume of the pancreas - takes more than 1/2 of the volume of the pancreas	0 2 4 6
In 0–3 points mortality is equal to 3%, rate of the complications — 8%; in 4–6 points 6 and 35% respectively; in 7–10 points — 17 и 92%		

Table 3

Modified CT severity index of AP

Prognostic index	Characteristics	М-КТИТ, points
Pancreatic inflammation	Normal pancreas	0
	Pancreatic and/or extrapancreatic inflammatory changes	2
	One or more fluid cluster or peripancreatic necrosis	4
Pancreatic necrosis	No necrosis	0
	Up to 30% of necrosis	2
	Up to 30% of necrosis	4
Extrapancreatic complications (pleuritis, ascites, vascular, gastrointestinal complications and others)		2
Sum of points ≥5 is associated with high morbidity and mortality		

A certain improvement in the quality of AP diagnostics can be achieved by the use of CT with the definition of tissue perfusion [30]. As it is known, the earliest and most important changes occur in AP at the level of the microvasculature. They are characterized by slowing blood flow velocity, aggregation and stasis of blood cells, tissue edema in the area of inflammation by increasing vascular permeability. Moreover, expression of these changes depends on the type of pancreatitis and the severity of destructive changes [26]. In applying this type of survey, all

manipulations are carried out using standard equipment, scanning starts simultaneously with intravenous contrast agent (the rate of 5 ml/sec) to produce the dynamic images. The second scan starts conventionally in 60 seconds after injection of contrast additional volume at 3.5 ml/sec. Subsequently, blood flow is estimated (Blood Flow, BF, ml/100 g tissue/min), as well as the volume of blood (Blood Volume, BV, ml/100 g tissue), time of reaching the peak concentration (Time-to-Peak, TTP, sec) and peak contrast enhancement (Peak Contrast Enhancement, PCE, Hu units). In inflammatory changes in the pancreas, indicators BV and BF are significantly reduced. Thus, in normal tissues BF is 77±13 ml/100 g tissue/min, and BV is 16±2 ml/100 g tissue, while AP data are: BF — 49±15 ml/100 g tissue/min and BV — 9±4 ml/100 g tissue (Fig. 7) [30].

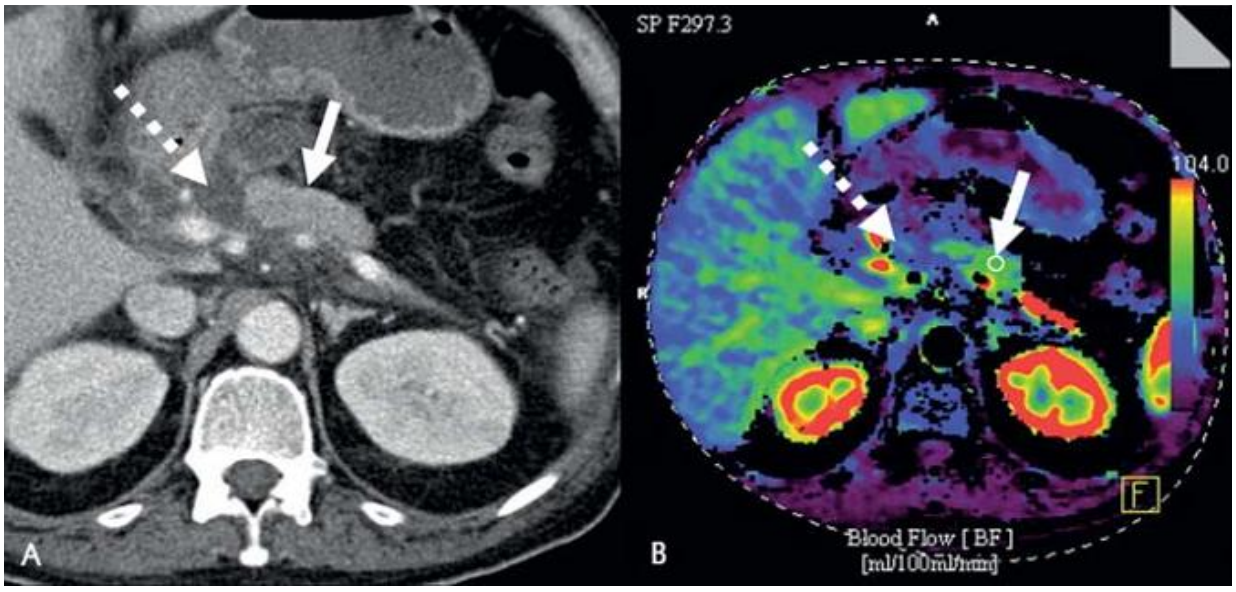

Fig. 7. Acute necrotizing pancreatitis of alcoholic etiology. The zone in the pancreatic head (dotted white arrow) has blood flow up to 15 ml/100 g/min, and blood volume up to 5 ml/100 g, indicating practically absent perfusion and corresponding to the area of necrosis. Inflamed tissue with characteristic edema (solid white arrow) show a corresponding reduction of BF and BV (BF — 56 ml/100 g/min, BV — 9 ml/100 g) in comparison with healthy tissues.

The advantage of this technique is the dynamic evaluation of contrast over time and accurate determination of the peak values, which is impossible upon a simple visual analysis. With the use of CT perfusion imaging it is much easier to identify areas of necrosis of the parenchyma of the pancreas, and thus eliminate the edematous form of AP, as the perfusion indices in the case of pancreatic necrosis are

close to zero [32]. When comparing the same CT protocol with angiography for the diagnostics of necrotizing pancreatitis, the advantage of the first method is noted [26].

With the introduction of multislice CT in the diagnostic practice, there is a possibility of using three-dimensional images obtained on the basis of mathematical algorithms of CT data processing [4]. The urgency of three-dimensional reconstruction in necrotizing pancreatitis is important due to the fact that the disease requires individual selection of treatment, choice of access and operation method [5, 6, 8]. The problem is best solved by a spatial reconstruction of CT images of the abdomen and retroperitoneal space. On the basis of CT data 3D-model of pathological changes of the pancreas and PPT is based. Three-dimensional reconstruction can be carried out on the workstation of scanner with special software, which better organizes opportunities of automatic segmentation of orhans and building more versatile 3D-models, there is a possibility of automatic volumetry [4] (Fig. 8, 9).

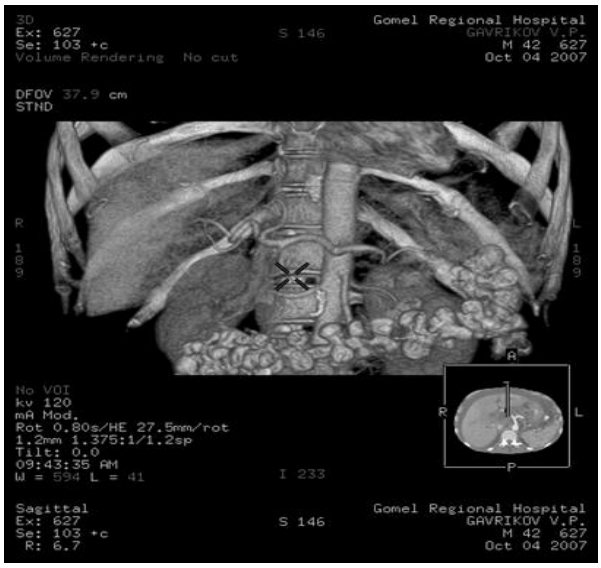

Fig. 8. Three-dimensional reconstruction with the help of scanner workstation.

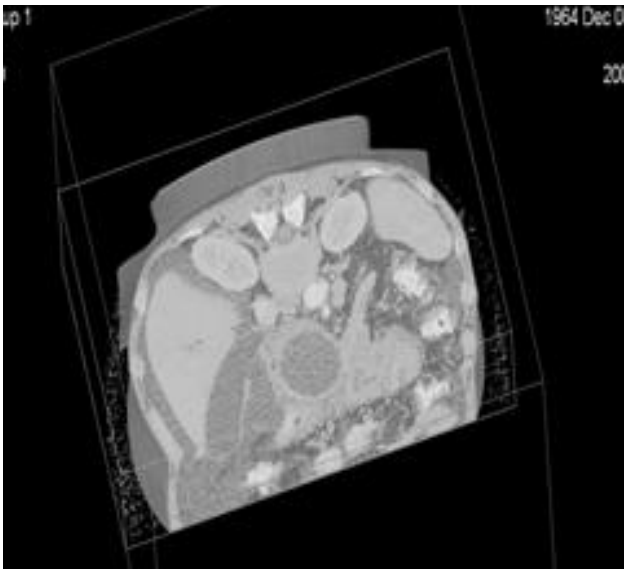

Fig. 9. Three-dimensional reconstruction with the help of program «E-Film Workstation».

According to the results of conducted spatial computer analysis, the most optimal surgical access to the pathological focus is chosen, as well as a method of surgical treatment (puncture-draining procedures, minilaparotomy and/or lumbotomy,

laparotomy with the retrolaparostoma formation and staged necrosectomy), depending on the prevalence and the limited necrotic process in the abdominal cavity and retroperitoneal space [4, 31]. In this method of study, high percentage of intraoperative data overlapping with the three-dimensional modeling is indicated in most cases [31].

Among modern capabilities of CT images processing that can improve the quality of AP diagnostics (in particular infected forms), analysis techniques of anisotropy of the pancreatic tissue and PPT should be noted. This method is based on calculating the brightness gradient values in the neighborhood of each pixel of CT image in the area of interest with the construction of circular orientation histograms, which determines the following indicators: extreme anisotropy coefficient (F1), integral anisotropy coefficient (F2), coefficient of the spatial inhomogeneity of the anisotropy (F3) and granularity of texture (G) [3]. Analysis of the CT images is performed via standard protocol: the size of the image and its characteristics (brightness, contrast, gamma, etc.) are not changed; CT data are analyzed on three transverse sections with 10 mm pitch; in each image all the parameters are evaluated in four areas — head, body, tail of the pancreas and PPT (12 study areas of CT of the pancreas) (Fig. 10) [11].

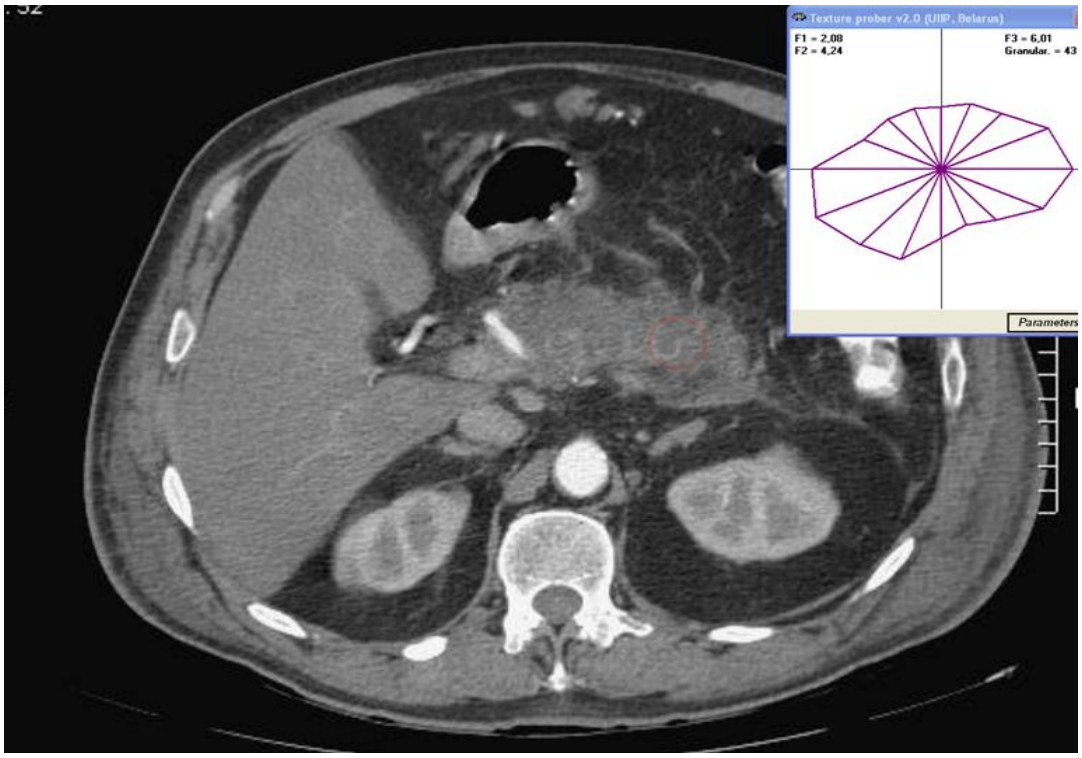

Fig. 10. The method of analysis of CT images with the assessment of pancreatic tissue anisotropy; the cursor (circle) is induced in the region of interest, window in the upper right corner shows the anisotropy parameters.

At the final stage the calculated values of the described four parameters are compared with thresholds indices (F1 — 3.3 units, F2 — 4.7 units, F3 — 8.5 units, G — 40 units), and decision is made on one or another variant of necrotizing pancreatitis. In the case of any of the values F1, F2, F3, G above the threshold infected pancreatic necrosis is diagnosed, and the determination of all the parameters F1, F2, F3, G below the thresholds shall be entitled to the diagnosis of "sterile pancreatic necrosis". If the results of anisotropy indicate the sterile necrotizing pancreatitis at the time of CT performance, re-CT study may be conducted with an additional assessment of the anisotropy upon the negative dynamics of the disease [11]. This method of analysis of CT images provides an additional opportunity to quantify the changes occurring in the pancreas, allows to carry out the non-invasive diagnosis of septic complications of severe AP.

In addition to the proven benefits of the use of CT for the diagnosis of AP, there are also negative aspects of this method, primarily related to the risk of contrast-induced nephropathy after intravenous contrast enhancement, especially in patients

with basic renal disease (chronic or acute on the background of AP). According to the IAP/APA recommendations, early CT study may increase the length of hospital stay due to the increased likelihood of allergic reactions to the contrast agent administered, its potential nephrotoxicity [23]. Carrying out the intravenous contrast as soon as possible from the beginning of the disease may not be desirable in view of possible worsening of microcirculation in the pancreas as a result of iodine-containing drug [2]. In turn, for the prevention of contrast-induced nephropathy in patients with pancreatic necrosis the following methods can be used: the abolition of nephrotoxic drugs (NSAIDs, some antibiotics, ACE inhibitors, loop diuretics), active intravenous hydration, and the use of hypoosmolar and isoosmolar contrast agents, "economical" use and dilution of the administered contrast [23].

Among the shortcomings of CT, we should note the presence of ionizing X-ray radiation, which is especially important for patients requiring repeated control tomography. The disadvantages also include the low diagnostic accuracy of detection of stones in the gall bladder and bile ducts; inadequate diagnostic efficiency (compared to MRI) for evaluating content of foci of pancreatic and peripancreatic necrosis [28].

Thus, currently the primary role in the diagnostics, stratification of AP and differentiation of its various forms is given to CT imaging and characterization of the morphological changes in the tissues of the pancreas and PPT by CT with intravenous bolus contrast agent. At the same time, despite some advantages of MRI and ultrasound, CT with contrast enhancement is the leading method of objectification of pancreatic pathology. This is due to the relatively high diagnostic accuracy, availability of the method (the location near the reception and intensive care units), performance in ventilated patients, faster scan time, and a relatively simple interpretation of the images by the clinicians and radiologists.

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CT modern potential in acute pancreatitis visualization (part 1)

A. A. Filatau, A. A. Litvin

Gomel Regional Clinical Hospital,

Gomel State Medical University, Gomel, Belarus

Key words: pancreas, acute pancreatitis, diagnostics, visualization, computed tomography

The article describes current trends in pancreatology with an emphasis on the visualization of morphological changes in pancreatoduodenal zone as the main criterion of diagnostics and determination of treatment strategy in acute pancreatitis, which corresponds to the recommendations of the revised Atlanta classification–2012 (Miami, 2012). The present article presents a review of the diagnostic capabilities of computed tomography in its different variants, indications and various procedures, as well as new techniques of medical visualization support. The primary attention is paid to the computed tomography with a contrast enhancement as the leading method to determine and objectify the pancreatic pathology in case of acute pancreatitis, in spite of all the MRI advantages and the USD prevalence.