



Computerized Tomography Score for the Assessment of Multiple Organ Failure and Determining Severity of Pancreatitis: Key Principles for the Assessment of Affected Organs

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Abstract

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BACKGROUND: Pancreatitis severity is an important death rate indicator that plays a crucial role in deciding on proper handling of patients at their initial admission, when making a decision on patient's transfer to the intensive care unit. Many studies point out a direct relation between death rate and the number of affected organs. In view of that, looking for new criteria for assessment of multiple organ failure is still useful in clinical practice. Assessment of multiple organ failure with patients undergoing treatment in the intensive care unit is carried out with the use of various integrated indicators based both on clinical laboratory assessment of patient's condition, and on data obtained with the help of advanced imaging methods. However, many researchers point out that the facilities of diagnostic radiology, including in particular computerized tomography (CT), are not used to the full extent.

AIM: We proposed expanding functionality of abdominal CT examination by means of pancreatitis severity assessment that takes into account changes in the pancreas and in addition enables assessing multiple organ failure with examined patients. We identified the organs and systems whose changes need to be monitored through CT imaging to be able to assess multiple organ failure in the patients with pancreatitis.

METHODS: Out of 314 patients, 100 patients were selected diagnosed with pancreatitis confirmed by changes demonstrated by the laboratory test results. Of those, 24 patients (24.0%) revealed presence of multiple organ failure (maximum of 5 organ systems), 46 patients revealed a single organ failure.

RESULTS: Development of early organ failure accompanied 82% of cases of severe pancreatitis and considerably aggravated predicted outcome and course of severe AP. Among them, 30 patients had pancreatitis without changes of the vital organs and 70 patients had dysfunctions of the vital organs, suffered from organ or multiple organ failure, and received treatment in the surgery unit and the intensive care unit of the Department of Surgical Conditions of Karaganda Medical University. In view of CT results, we assessed a relation between multiple organ failure and specific failure of a single organ and necrosis and death rate. We analyzed a relation between organ failure and degree of the pancreas necrosis.

CONCLUSION: Identified changes enabled us to create a CT score for the assessment of pancreatitis severity that can be used not only for identification but also for the prediction of organ failure at an early stage of pancreatitis with high accuracy as compared against conventional CT systems for the assessment of patients' condition. It can also be used to differentiate extent organ dysfunction and the number of affected organs.

Introduction

Timely and correct assessment of acute pancreatitis (AP) severity increases the likelihood of appropriate treatment and improves predicted outcome [1], [2], [3], [4], [5]. According to the guidelines for the treatment of pancreatitis, one of the criteria of pancreatitis severity is organ failure that remains within 24 h after admission [3]. All clinical recommendations over the past 6 years specify the requirement to assess patient's condition severity immediately after diagnosing and to carry out reassessment over time, especially within 48 h [6], [7], [8].

All clinical recommendations for the assessment of expected response to the treatment of AP in clinical

practice employ two approaches that include using various integrated score and examination of individual laboratory findings [9], [10], [11], [12].

There is a great number of surgical assessment scores such as Ranson APACHE-II, MODS 2, and Glasgow that enable accurate determining severity of patient's condition, likelihood of fatal outcome, and intensity of biochemical changes [12], [13], [14], [15], [16], [17].

The range of diagnostic radiology methods used for imaging of pathological changes of the pancreas is quite wide and choice of a method depends on examination purpose, clinical symptoms, time of symptom onset, and on laboratory testing data. However to this day, the majority of researchers prefer computerized tomography (CT) in various clinical situations [17], [18], [19], [20], [21]. According to data

of the American College of Gastroenterology from 2013 and Japanese recommendations on treatment of AP from 2015, CT is generally agreed to be the golden standard in diagnosing pancreatitis as it enables assessment of condition of the pancreas and the surrounding areas. For this reason, alongside the integrated surgical scores based on clinical and laboratory assessment, the scores based on data obtained through CT examinations received global acceptance [17], [18], [19], [20], [21].

At present, the most frequent use is made of such radiologic scores as CT severity index (CTSI), modified CTSI, pancreas size index, extrapancreatic point (EP), assessment of extrapancreatic inflammation on CT (EPIC – is assessed by presence of ascites, pleuritis, and retroperitoneal and mesenteric edema), assessment of mesenteric edema and peritoneal fluid (MOP – assessment of presence or absence of peritoneal edema and/or mesenteric fluid), and the Balthazar score [22], [23], [24]. Altogether it was pointed out that regardless of a selected method, CT demonstrates a very high accuracy among assessment scores for severity level prediction. There have not been any statistically significant differences between predictive accuracy of CT and the clinical assessment scores [25], [26], [27], [28], [29], [30].

However, we have noted that estimation scores based on data obtained through CT examinations used in case of pancreatitis do not account entirely for condition of the surrounding organs due to the limitation of the area of interest by the pancreas only and the surrounding tissues within a short distance from the pancreas [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35]. It is acknowledged by many researchers that the capacities of computerized diagnosing are not used to the full extent [17], [24].

As many other researchers, we have come to the conclusion that the existing surgical systems of assessment scores are quite effective in prediction of organ failure under the conditions of AP. However, they are cumbersome in use and, therefore, have limitations in clinical application. We believe that there is still a need in the development of new approaches, which is acknowledged by scientists from different countries [18], [24].

Since it is CT that is a golden standard in diagnosing conditions of the pancreas and it covers a sufficient examination area enabling to assess condition of almost all large organs and systems, we have proposed a way informative value of this method by means of more detailed examination of these organs and systems in the course of analysis of a standard CT investigation. The investigation's goal was to identify CT signs of organ changes in patients whose test results indicate organ failure. It was proposed to divide changes identified during CT examination in accordance with pancreatitis classification having three severity levels and to determine the extent to which CT presentation corresponds to clinical assessment of patient's condition. Hence, performance

of a standard abdominal CT scanning in addition to the assessment of any changes in the pancreas can also identify presence of any single and multiple organ changes caused by AP, which will enable timely correction of severity level and treatment of this disease.

Materials and Methods

A randomized study was carried out at the premises of two regional clinics and one private clinic of the city of Karaganda during 2017–2019 years. We examined 314 patients with suspected or clinically confirmed pancreatitis who were sent for CT scanning of abdominal organs. The inclusion criteria were as follows: Patients of both genders at least 18 years old who were admitted to an inpatient hospital through emergency room diagnosed with AP during the 1st stage of the disease. The criteria for exclusion from the study were as follows: Medical history with diabetes mellitus and other endocrine, autoimmune, contagious, oncological diseases, existing severe concomitant cardiovascular morbidity, cardiac insufficiency, and medical history with allergic reactions. Clinical and laboratory data were taken from patient medical records and confirmed existence of a single or several organ failure. Respiratory failure was identified as PaO₂ under 60 mmHg or as a need in ventilatory care. Renal failure was identified by creatinine in serum if it exceeded 300 µmol/l or by drop of urine output below 500 ml/24 h or below 180 ml/8 h as well as the need in hemodialysis or peritoneal dialysis. Hepatic failure was identified by serum bilirubin level exceeding 100 µmol/l or by alkaline phosphatase level exceeding 3 times the upper limit of normal range.

All studies were performed using CT machines (Somatom Definition AS, Siemens) applying the standard CT conclusion for abdominal imaging. Then, images were processed and reconstructed in axial plane with 5 mm slice thickness. All CT data obtained in our institute were reviewed independent of one another at two work stations with the aid of Syngo Imaging software, version VB36A, Siemens Medical Solutions.

Two radiation therapists (the first author and the second author), having over 3 years of experience in abdominal radiology, carried out an independent check of all CT images without knowing any patient specifics and their clinical outcome. A result was considered to be final when both radiation therapists, independent of each other, reached the same conclusion with regard to the presence of alterations and process severity. When CT results were controversial, the final result was achieved based on consensus. All patients had the Balthazar score points calculated and recorded based on review of CT images.

Statistical processing of the material was carried out using the software tools STATISTICA v. 6.0. After preparing the data file, which consisted of finding

and fixing errors, an array in the form of a *.xls file was imported into the STATISTICA package with conversion to an STA file and then processed in accordance with the task. The normality of the distribution was checked using the Shapiro-Wilks test. The hypothesis of statistical homogeneity of the two samples was tested using the Student's and Pearson χ^2 criteria. Univariate analysis of variance was used to identify predictors of multiple organ failure. All patients with pancreatitis revealed a statistically significant relationship between the underlying disease and the affected organ system. In particular, in patients with a mild disease severity, damage to the gallbladder and perinephric fiber was noted ($\chi^2 = 5.1$; $p < 0.05$ and $\chi^2 = 5.5$; $p < 0.05$, respectively), and in patients with a severe degree, pancreatitis was the leading in the structure of multiple organ failure syndrome of portal hypertension ($\chi^2 = 3.4$; $p < 0.05$). Based on the results of the study, we identified signs characteristic of pancreatitis of varying severity, determined by CT scan of the abdominal cavity with contrast. Of these signs, by means of statistical selection, we determined those that meet the Pearson's reliability criterion χ^2 .

Discussion and Results

Out of 314 patients, 100 patients were selected diagnosed with pancreatitis confirmed by changes demonstrated by the laboratory test results. Of those, 24 patients (24.0%) revealed presence of multiple organ failure (maximum of 5 organ systems), 46 patients revealed a single organ failure. Development of early organ failure accompanied 82% of cases of severe pancreatitis and considerably aggravated predicted outcome and course of severe AP. Complications in two body systems were identified in 60% of observations; complications in more than 2 systems were in 40% of observations. Early organ failure during the 1st stage of the disease was the cause of two fatal outcomes, which amounted to 4.65% of the total number of persons with severe AP. In this study, we have established that frequency of organ failure rises with greater extent of necrosis (Table 1).

Table 1: Organ failure and multiple organ failure. Patient distribution per severity level and failure of organs and systems

Without organ failure	30		
Organ failure	46		
Multiple organ failure	24		
Affected organ	Total	Moderate level	Severe level
Lungs	41	21	20
Liver	33	11	22
GIT	21	9	12
Kidneys	9	5	4
Vessels	7	4	3

From among the specified types of multiple organ failure, we factored in five system changes in which can be visualized by employing contrast-enhanced abdominal CT. One of the most frequent complications is acute respiratory failure [36]. Pulmonary dysfunction is considered the most commonly encountered and according to various

researchers accounts for 30% of patients [37]. Its development is caused by progressing intoxication that involves the respiratory center into the process. The greater activity of pancreatic enzymes cause pleural-pulmonary complications as wet pleuritis, atelectasis, pneumonia, pulmonary edema [38]. In our study, among the patients suffering a single organ failure, 21 patients revealed pulmonary failure signs of which can be identified by means of CT image review in lung window. When dealing with a mild case of pancreatitis, minor changes were identified manifested as increased pulmonary vascularity. As a more severe condition developed, CT identified signs of pneumatization disorder (in 16 cases) (Figure 1).

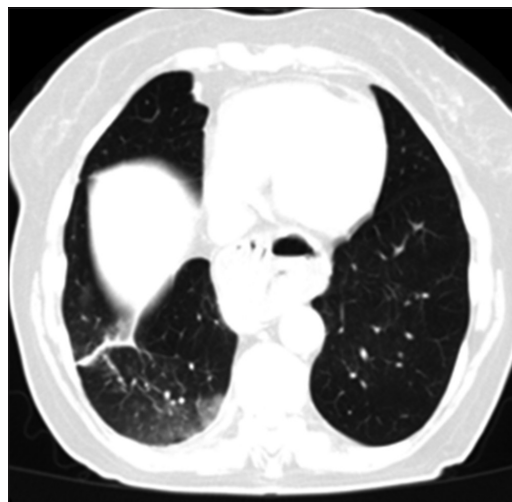


Figure 1: Patient K with medium severity acute pancreatitis. Disorder of pneumatization of lung tissue in the form of ground-glass opacity

According to the data of the clinical study 2, patients with pancreonecrosis manifested pleural fluid, saturation disorder, and their condition was assessed as severe. This was confirmed during CT examination where in addition to wet pleuritis, signs of bronchopneumonic infiltration were identified as well (Figure 2).



Figure 2: Patient S with pancreonecrosis. One can identify wet pleuritis on the right, bronchopneumonic infiltration, signs of congestion in both lungs

According to the study data, liver insufficiency develops in 20–75% of cases of acute destructive pancreatitis, which significantly aggravates morbidity [39], [40]. The leading cause of functional

changes in liver in case of AP is the developing deep microcirculatory abnormalities, degenerative-dystrophic changes of hepatocytes, and decompensation of detoxification mechanisms. In 72.7% of observations, pancreatitis is accompanied by the development of total extrahepatic portal hypertension which is confirmed by presence of both portoportal and portosystemic shunts (Figure 3).



Figure 3: Patient S with acute pancreatitis. There are signs of portal hypertension – phlebectasia of portal and splenic vein

According to our studies, if patients already having liver diseases are excluded from the area of interest, then they will be identified only in 33 cases most frequently manifested as signs of portal hypertension in patients with pancreatitis of medium severity level.

Damage or dysfunction of intestines and gastrointestinal tract is one of the routes of multiple organ failure development, formidable, and understudied complication of AP. These are observed, as different authors have different data, in 5–10% of patients on average [41], [42], [43]. Blood loss during AP aggravates hypovolemia and organ hypoxia and contributes to the development of further destructive changes in the pancreas.

The most frequent location of bleeding acute ulcers and erosions is stomach. Other locations of the pathological process are usually combined with stomach; rarely, isolated extragastric damage of the gastrointestinal tract is encountered [41].

The main in pathogenesis of acute erosions and ulcers, progression of early ulcerous-necrotic changes in the mucous lining, and hence emergence of acute bleeding is disruption of microcirculation in the digestive tract walls. In such a case, an important role is played by disruption of portal blood flow, which leads

to hypoxia of the digestive tract's mucous lining (more frequently stomach' lining), impairment of its resistance, and development of dystrophic processes in it [42].

The next cause of ulcerous damage is increased aggressive factors in the stomach. As known, AP is accompanied by enhanced release of kinins, permanent impairment of gastric secretion with hypergastrinemia manifested in hypersecretion, and continuous acidogenesis. An important cause is flatulent distention, pylorus dysfunction, and duodenogastric reflux. Alongside this, there is a decrement of the mucous lining protective factors (reduced emission of gastric mucin, secretion of the pancreas bicarbonates, and consequences of using hormonal preparations) [43].

Enteral insufficiency syndrome may be included with other GIT damages. Before everything else, the motor function of the stomach is disrupted with the development of flatulent distention (Figure 4).

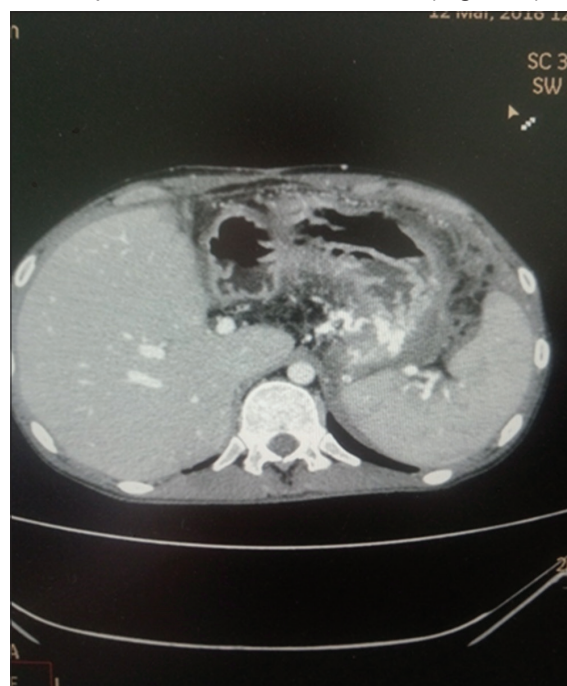


Figure 4: Patient Zh with medium severity acute pancreatitis. Contrast-enhanced abdominal computerized tomography. Inhomogeneity and thickening of the stomach walls, dysperistalsis

It is not always possible to clearly differentiate severity levels of gastrointestinal loss because presence of violent peristalsis and dyspeptic processes persists at severe levels of pancreatitis and often prevents assessment of occurring changes.

We were able in our study to differentiate changes in GIT as moderate thickening of intestinal walls, lumen dilation in case of mild damage, inhomogeneity of intestine wall structure, dysperistalsis as manifestations of medium severity level, and indications of intestinal obstruction, infiltration of circumintestinal fat tissue in severe situations.

Among identified organ lesions, the fourth place was given to renal failure that we diagnosed with nine patients. Close relation of kidney failure pathogenesis

with pancreatitis is explained by common blood supply and nearly the same anatomic substrate. It is not infrequent for acute renal failure to occur during AP and less often during chronic pancreatitis, which is due to a sudden reduction in effective renal blood flow [44]. This happens due to a combination of several factors: Spastic stricture of renal microvasculature (endothelium dysfunction), microthrombosis, as well as fluid loss and redistribution (sequestration). All of these phenomena stem from systemic effects of pancreatitis and attest to the respective stage of the adaptive process [45].

Results of laboratory testing: Elevated urea nitrogen and creatinine levels in serum reflect reduced removal of nitrogenous waste. The multicenter study that was carried out by Ke *et al.* [10] revealed that acute renal failure occurs in almost 70% of cases of severe AP with patients who were admitted to ICU.

We adopted the early indicators of changes to be decrease in density of parenchyma and thickening of Gerota's fascia that could be identified in three patients with mild AP.

Further changes on CT were identified as changes in size and hydronephrosis in a time of marked severity of the patient's condition. Use of contrast agent was contraindicative, but even by means of examinations performed without contrasting, we could identify marked changes of parenchyma (Figure 5).



Figure 5: Patient O. Medium severity acute pancreatitis with signs of hydronephrosis.

Of no small importance in assessment of multiple organ failure is cardiac involvement, but during our study, analysis of cardiac norm and pathology showed excessive data spread, which made data unreliable to be used for assessment. However, it seems possible to assess on CT images changes of large vessels that enable indirect assessment of the patient's condition severity.

According to literary sources, AP can lead to various vascular events in 5% of cases including venous and arterial conditions [44], [45], [46]. Among venous complications frequently encountered are porto-spleno-mesenteric venous thrombosis that often

includes thrombosis in the portal vein trunk, in the splenic vein, or even the superior mesenteric vein. This can lead to gastric or esophageal variceal bleeding, to ascites, portal hypertension, and hepatic failure [45].

Another consequence of local inflammation is damage of vessels in the pancreas that manifests itself by endothelial activation and endothelium damage, by higher vascular permeability, coagulation activation, and increased leukocyte rolling, adhesion, and transmigration into the pancreas tissue [46].

In our study, we identified vascular abnormalities in seven patients. Predominantly, those were in the form of dilation, thrombosis, and emergence of pathological anastomoses (Figure 6).

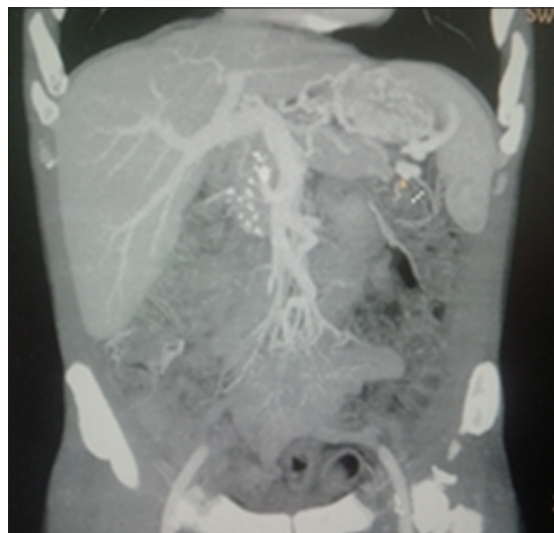


Figure 6: Patient V with moderate severity acute pancreatitis. Splenorenal anastomoses

Based on review of CT images, all patients had the Balthazar score points calculated and recorded. Ranson and Apache condition severity assessment scores were also calculated for each patient.

Based on the obtained data, we developed and proposed for use our condition severity assessment score.

The score also includes information about changes in condition of the pancreas itself according to the standard signs that correspond to the pancreas damage severity the best. On top of that, we took note of the fact that in determining severity level, it is not of small importance to consider the number of affected organs, which we could also reflect in the Table 2.

Further use of this score in review of CT examinations confirmed its applicability in clinical practice. We must admit that our study has a series of limitations. First, the study covered not very many people as it included only 100 patients. Second, we did our analysis only for the subgroup of patients with AP within consecutive group of patients who had CT scanning within 24 h after emergence of symptoms in the first 3 days after admission. Some patients with severe AP received treatment without CT scanning,

Table 2: Score for computerized tomography-based assessment of pancreatitis severity

Group No.	Organ system	Points			
		0	1	2	3
1	Pancreas	No changes	Inflammatory changes of pancreas	Inflammatory changes of pancreas and surrounding tissues	Areas of necrosis in pancreas
2	GIT	No changes	Moderate thickening of intestinal walls, lumen dilation	Inhomogeneity in structure of intestinal wall, dysperistalsis	Indications of intestinal obstruction and infiltration of circumintestinal fat tissue
3	Liver and spleen	No changes	Dilation of common bile duct and distal segments of hepatic ducts	Changes in density (transient difference in liver density), hepatomegaly, splenomegaly	Ascites
4	Lungs	No changes	Prominence of perihilar markings	Disorder of pneumatization (ground glass), pleural effusion	Bronchopneumonic infiltration
5	Kidneys	No changes	Decreased density of parenchyma	Change of kidneys size	Thinning of kidney parenchyma and hydronephrosis
6	Vessels	No changes	Changes of one large vessel (dilation, thrombosis)	Dilation of portal and splenic veins, mesenteric vein	Emergence of portosystemic bypasses, unstable anastomosis, thrombosis
7	Number of affected systems	Other organs not affected	One organ affected	Two organs affected	Three organs affected

which possibly contributed to a lower death rate in our group. These limitations could introduce inaccuracy into results of our study.

Conclusions

Nonetheless, in concluding, we would like to point out that following the results of this study, we conclude a quite high potential of CT in assessment of organ abnormalities, and the developed score for CT-based assessment of pancreatitis severity can be used not only for identification but also for prediction of failure of various organs at the early stage of pancreatitis to a high accuracy as compared with the conventional CT-based systems for the assessment of condition of patients with pancreatitis. It can also be used to differentiate severity of organ failure and the number of affected organs.

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