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Evaluation of the effect of pancreatic volume on mortality in patients with acute pancreatitis

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ABSTRACT

Background: Pancreatic volume is enlarged in acute pancreatitis.
Objective: This study aimed to evaluate whether there was a difference in pancreatic volume between survivors and non-survivors with acute pancreatitis using computer-generated 3D imaging.
Method: This single-center retrospective observational cohort study was conducted between January 2015 and December 2020. The hospital automation system was used to get the patients diagnosed with acute pancreatitis by using International Classification of Diseases (ICD) (ninth edition, code 577.0 or 10th version, code K 85.0) codes. The patients' pancreatic volumes, computed tomography severity index (CTSI), and modified computed tomography severity index (mCTSI) scores were calculated using the data obtained from the hospital automation system. The pancreatic volumes of the patients were measured using the computer-generated 3D imaging method. Pancreatic volume, CTSI, and mCTSI were then statistically compared in terms of mortality prediction by using the receiver operating characteristic (ROC) analysis.
Results: Of the 143 patients, 57.34% were female and 42.66% were male. The cut-off value of pancreatic volume in determining mortality was>81.5 cm^3 OR:17.43 (%95 CI: 2.2–138.1) Cohen's d:1.126, at which it had 92.3% sensitivity, 60.0% specificity, 18.8% positive predictive value, and 98.7% negative predictive value. As a result of the ROC analysis of pancreatic volume in mortality prediction, the area under curve (AUC) value was determined as 0.787 [95% confidence interval (CI): 0.711–0.851]. The ROC analysis of the CTSI and mCTSI scores in mortality prediction revealed AUC values of 0.822 (95%CI: 0.750–0.881) and 0.955 (95%CI: 0.907–0.983) respectively.
Conclusion: Although CTSI scores pancreatic enlargement and mCTSI scores pancreatic necrosis and inflammation, the pancreatic volume value is not clearly scored in both. In this study population, pancreatic volume above 81.5 cm was associated with increased mortality. Both CTSI and mCTSI scores outperformed pancreatic volume in predicting mortality.

1. Introduction

The annual incidence of acute pancreatitis has been reported 34 per 100,000 globally [1]. However, in 20% of patients, acute pancreatitis can progress into a more serious condition leading to organ failure [2]. When accompanied by organ failure, acute pancreatitis has mortality rates varying between 15% and 30% [3]. The presence of persistent organ failure exceeding 48 h constitutes the most serious manifestation since it increases the mortality rate to 43% [4].

The most often utilized imaging modality in the diagnosis of acute pancreatitis is abdominal tomography [5]. Also the current Computed Tomography(CT) technology allows for the isolation of every organ, tissue, mass, and nodule, and performing geometrical measurements using 3D software [6]. In addition, changes in pancreatic size (diameter, area, and length) have been investigated in many diseases [7]. The precise identification of these alterations has the potential to reduce mortality and morbidity while introducing novel approaches to the diagnosis and treatment of acute pancreatitis.

In acute pancreatitis, there are two frequently used scoring systems calculated using CT; CT severity index (CTSI) and modified CTSI (mCTSI). While only the CT findings of patients are included in CTSI, extra pancreatic complications of patients have been added to mCTSI [8].

The primary aim of this study was to determine whether there was a difference in pancreatic volume between the survivors and non-survivors of acute pancreatitis. Our secondary aim was to

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determine the cut-off value of pancreatic volume in the prediction of mortality due to acute pancreatitis and compare this value with the currently used mCTSI and CTSI scores.

2. Methods

2.1. Study design and setting

Patients diagnosed with acute pancreatitis in the emergency department at xxxx Hospital between January 2015 and December 2020 were included in this retrospective, single-center observational study. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University H. (Ethical committee approval no: 2021/514/208/12).

2.2. Participants

Patients diagnosed with acute pancreatitis with the International Classification of Diseases (ICD) (ninth version, code 577.0 or 10th version, code K 85.0) codes, their epicrisis, medical history, blood test results and CT images were retrospectively obtained from the hospital automation system.

Inclusion criteria:

1. Meeting the definition of acute pancreatitis by the American College of Gastroenterology (presence of two of three following criteria: (i) abdominal pain consistent with the disease, (ii) serum amylase and/or lipase greater than three times the upper limit of normal, and/or (iii) charasteristic findings from abdominal imaging) [9].
2. Being over 18 years old.
3. Presenting to the hospital and having a CT scan at least 72 h after symptom onset (to differentiate between the necrotizing and interstitial edema forms of acute pancreatitis) [9,10].
4. Having undergone an abdominal CT in the portal venous phase at the emergency department.

Exclusion criteria:

1. Pregnancy.
2. Incomplete data.
3. History of pancreatic surgery.
4. Mortality of causes other than pancreatitis.
5. History of chronic pancreatitis and/or clinical and morphological findings of chronic pancreatitis.

2.3. Variables

The patients' demographic data, vital signs at admission, symptom onset, blood test results, presence of pancreatic edema, necrosis, and rectovesical collection on contrast-enhanced CT, type of pancreatitis, length of hospital stay, and mortality status were transferred to a data form prepared for the current study. Using these data, the patients were evaluated in accordance with the American College of Gastroenterology's current guidelines to confirm the diagnosis of acute pancreatitis [9]. All patient CT scans were assessed independently by two radiologists with at least 15 years of experience who were blinded to the study.

2.4. Data sources and pancreatic volume measurement

Patients were scanned in the hospital automation system using International Classification of Diseases (ICD) (ninth edition, code 577.0 or 10th version, code K 85.0) codes between January 2015 and December 2020, which encompasses the study period. Then, patients on the obtained patient list who had blood tests and imaging were added to the data form. One medical secretary did a random audit of the trial after entering the pertinent patient variables onto the data forms. In this way, the data was validated. In this study, the complete case analysis method was utilized.

In our hospital, a standard protocol is applied to all patients undergoing CT with the preliminary diagnosis of acute pancreatitis. Accordingly, 80 ml of iohexol80 ml (Omnipol 300 m g/ml, Polifarma Pharmaceuticals, Tekirdag, Turkey) was given to each patient as a contrast agent during the CT scan. Subsequently, 20 ml of saline was administered intravenously. The contrast material was administered to the patients with an automatic injector (Opti Vantage dual-CT contrast delivery system, Guerbet, Paris, France). Approximately 85 s after this application, the CT scans of the patients were taken. With this technique, preferred in light of the literature recommendations, edema and necrosis in the pancreas of the patients could be detected [11].

All the CT scans were performed using the Philips Medical Systems (Cleveland), Ingenuity 256-detector row scanner. The intravenous contrast-enhanced abdominal CT scans of the patients at the time of first admission to the emergency department were re-evaluated for pancreatic volume measurement and pancreatitis findings (edema, necrosis, and rectovesical collection). The pancreas of the patients was then measured using three-dimensional upstream software, INFINITT Xelis 3D, which can automatically measure the volume of any tissue, mass, or organ in the body very precisely [6] (Fig. 1).

2.5. Sample size

Sample size was calculated using MedCalc (MedCalc Software for Statistics in Medicine, Mariakerke, Belgium). Taking the margin of error for type 1 for the ROC analysis as 5%, power as 95%, and minimum AUC as 0.750, the optimal sample size was calculated as a total of 108, including 12 non-survivors and 96 survivors.

2.6. Statistical analysis

Statistical analyses were performed using SPSS 22.0 for Windows and MedCalc. Descriptive criteria were presented as mean and standard deviation values and percentage distribution. The Kolmogorov-Smirnov test was used to examine the conformance of the data to the normal distribution. The ROC analysis was performed to establish the cutoff values of risk scores for predicting mortality. The DeLong method was used to compare the ROC curves of the risk scores and pancreatic volume. The significance threshold was determined to be $p < 0.05$.

3. Results

During the five-year study period, a total of 197 patients were identified to have undergone CT within 72 h of the onset of their complaints and received a diagnosis of acute pancreatitis. One hundred eighty-seven patients met the criteria for inclusion. Of these patients, 16 due to a history of chronic pancreatitis, 13 due to a history of pancreatic surgery, nine due to incomplete data, six due to mortality of non-pancreatitis causes were excluded. As a result, the total number of patients included in the analysis was 143.

The patients' demographic data, vital signs, blood test results, mean CTSI and mCTSI scores, and mean pancreatic volume values are presented in Table 1.

Of the patients, 57.34% were female and 42.66% were male. The statistical analysis showed that the median age of the non-survivors (72.8 years) was statistically significantly higher than that of the survivors (60.8 years) ($p = 0.01$). Biliary pancreatitis (43.35%) was the most common etiological cause in our cohort. The most common CT finding was pancreatic edema ($n = 9$). When the length of hospital stay was examined, the mean value was determined as 6.8 ± 5 days for the survivor group and 19.9 ± 18.9 days for the non-survivor group, indicating no statistically significant difference ($p = 0.057$). Among the vital findings, the mean respiratory rate per minute was found to be 14.8 ± 3.2 breaths/min in the survivor group and 17.9 ± 5.8

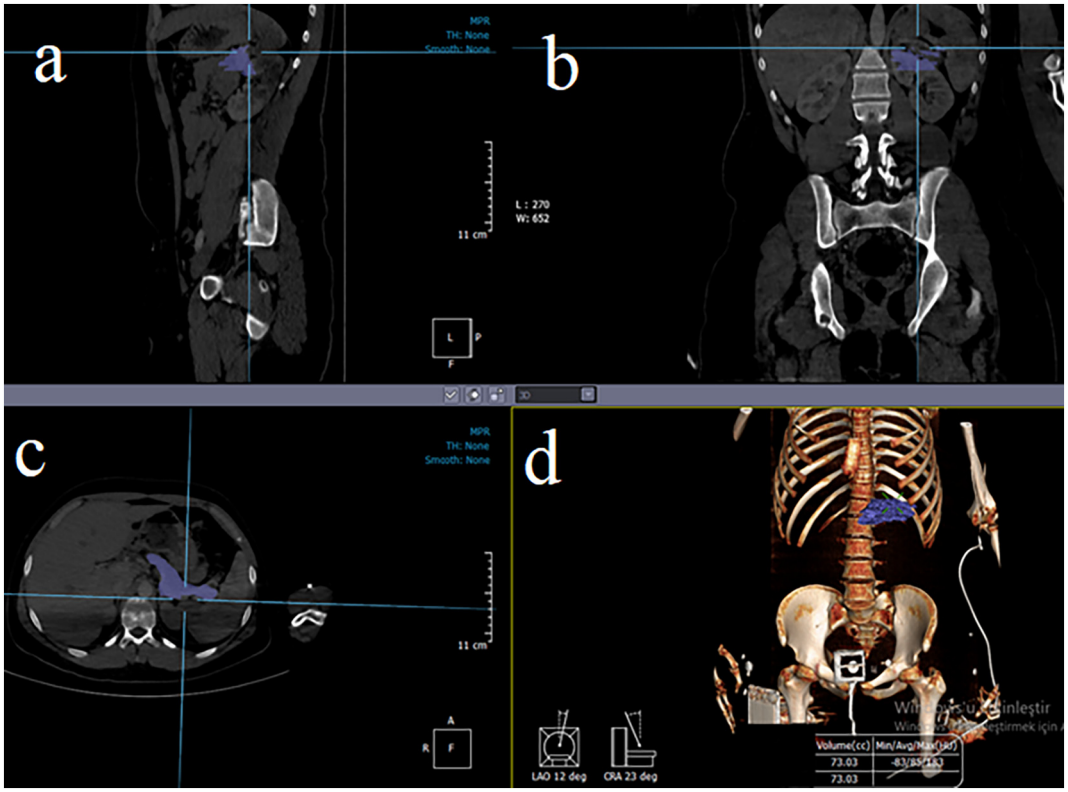

Fig. 1. Measurement technique of pancreatic volume. A three-dimensional image of the pancreas was obtained by marking it on the sagittal(a), coronal(b) and axial(c) axes. Then the program automatically generated a three-dimensional image measuring the pancreas volume (d).

breaths/min in the non-survivor group, and the difference was statistically significant ($p = 0.027$).

As a result of the statistical analysis, the mean values of albumin, aspartate aminotransferase, urea, lactate dehydrogenase, calcium, creatinine, sulfur dioxide, lactate, count of the non-survivors were statistically significantly higher compared to those of the survivors. All values were summarized in Table 1.

According to the ROC analysis of the CTSI, mCTSI scores and pancreatic volume in mortality prediction, we found the AUC values 0.822 [95% confidence interval (CI): 0.750–0.881], 0.955 (95%CI: 0.907–0.983), 0.787 (95%CI: 0.711–0.851) respectively. Table 2 provides a summary of the statistical information for CTSI, mCTSI, and pancreatic volume.

4. Discussion

To the best of our knowledge, this is the first study in the current literature in which pancreatic volume was measured in acute pancreatitis using computer-generated 3D imaging and its relationship with mortality was examined. In this study, the sample consisted of 143 patients, and female gender was found to be dominant (57.3%), which is consistent with the literature [12].

In a study evaluating 3098 patients, the mean pancreatic volume in adults was found to be 76.9 cm^3 (95% CI: 71.2–82.7) [13]. In the same study, there was an increase in pancreatic volume, especially in obese patients [13]. In another study, the mean pancreatic volume was also reported 67.71 ± 16.03 cm^3 [14]. In a study using CT, the mean pancreatic volume was measured to be 79.2 ± 24.1 cm^3 in both genders [15]. However, since these measurements are operator-dependent and time-consuming, their reliability is controversial. In contrast, the technique we used in our study, computer-generated 3D imaging, objectively selects the pancreas according to tissue density, and then measures the volume through manual marking.

Acute pancreatitis is an inhomogeneous disease full of unknowns. The clinician may encounter different manifestations ranging from mild to severe life-threatening conditions [16]. The early evaluation of the patient using developing technological innovations in terms of mortality prediction can positively affect clinical outcomes. Today, contrast-enhanced CT is a standard method used to diagnose acute pancreatitis and determine its severity [17,18]. Given that acute pancreatitis causes an increase in pancreatic volume [19], the use of it as a variable and measuring this parameter using computer-generated 3D imaging can increase the mortality prediction capabilities of clinicians. This is also supported by our findings revealing that pancreatic volume was 77.7 ± 23.7 cm3 in the survivor group, which is close to the normal pancreatic volume reported in the literature [13,15]. In contrast, the pancreatic volume of the non-survivor group was increased, with the mean value being determined as 119.7 ± 48.9 cm^3.

The CTSI and mCTSI scoring systems, which are used to predict mortality in acute pancreatitis, were found to be very effective in our patient population (AUC > 0.75). However, there are studies in the literature comparing these two scoring systems but reporting different results. Some authors suggest that mCTSI is more effective than CTSI in both predicting complications and predicting mortality(AUC: 0.883 vs 0.796, $p = 0.005$) [20]. The differences of AUC with our study may be due to the distribution frequency of etiological causes, methodological differences between the studies and the higher mean age of our patients. When we took pancreatic volume as a stand-alone predictor of mortality and compared it with the other two scores, we found that the most effective predictor was the mCTSI score. However, a pancreatic volume over 81.5 cm^3 being so strongly associated with mortality [AUC: 0.787 (95% CI:

Table 1
Comparison of various characteristics and risk scores in patients with acute pancreatitis between the survivor and non-survivor groups.

	Survivor $n = 130$		Non-survivor $n = 13$		p value
	Mean Median Number	SD IQR %	Mean Median Number	SD IQR %	
Age	60.8	16.2	72.8	13.8	**0.01**
	59.0	22	80.0	26	
Gender					0.134
Female	72	55.4	10	76.9	
Male	58	44.6	3	23.1	
Biliary pancreatitis	57	52.3	5	41.7	0.485
Hyperlipidemia	8	9.9	3	25.0	0.130
Alcohol-induced pancreatitis	7	8.5	0	0	0.293
Drug-inducedpancreatitis	2	2.5	0	0	0.577
Tumor-induced pancreatitis	2	2.5	1	7.7	0.320
Idiopathic	50	54.9	7	58.3	0.824
Pancreatic edema on computed tomography	7	8.9	2	16.7	0.399
Pancreaticnecrosis	1	1.3	0	0	0.695
Rectovesical collection on computed tomography	4	5.1	1	8.3	0.643
Hospital stays	6.8	5.0	19.9	18.9	0.057
(days)	5.0	4	11.0	30	
Systolic pressure	142.8	98.1	128.3	25.1	0.453
mmHg	130.0	15	130.0	34	
Diastolic pressure (mmHg)	78.4	9.8	75.1	9.4	0.370
	76.0	15.0	75.0	15	
Pulse (beat/min)	77.3	11.4	83.2	14.4	0.190
	75.5	15.0	80.0	26	
Body temperature	36.3	0.7	36.7	1.0	0.218
(Celsius)	36.2	0.5	36.4	1.0	
SaO_2 (%)	96.8	2.1	95.0	4.2	0.232
	97.0	3.0	96.0	7.0	
Respiratory rate	14.8	3.2	17.9	5.8	**0.027**
Minute/respiration	14.0	3.0	15.0	7.0	
Albumin (g/L)	19.4	15.3	13.3	14.6	**0.016**
	27.0	29.5	3.2	24.3	
ALT (U/L)	69.6	77.3	377.6	752.7	0.822
	49.5	75	38.0	350	
AST (U/L)	42.9	40.8	1156.5	2765.5	**0.015**
	28.0	27.0	46.0	331.0	
CRP (mg/dl)	117.1	84.5	153.1	89.8	0.129
	93.0	114.9	111.0	165.4	
Glucose (mg/dl)	107.1	49.3	134.5	65.4	0.065
	94.0	39	132.0	97.0	
Urea (mg/dl)	30.5	24.2	66.9	51.7	**0.003**
	24.0	17.0	48.0	79.0	
Sodium (mmol/L)	137.8	3.3	141.4	6.4	0.095
	138.0	4	140.0	10.0	
Potassium (mmol/L)	3.9	0.5	4.0	0.9	0.836
	3.8	0.7	3.7	1.8	
LDH (U/L)	300.0	303.1	551.7	243.8	**0.001**
	247.0	159.0	476.0	396.0	
Calcium (mg/dl)	8.5	0.5	7.9	0.8	**0.014**
	8.5	0.8	7.8	1.5	
Chloride (mmol/L)	101.5	3.9	100.2	6.9	0.494
	102.0	5.0	101.0	12.0	
Creatinine (mg/dl)	0.87	0.97	1.35	1.08	**0.044**
	0.66	0.36	0.91	1.48	
Lactate (mmol/L)	1.96	0.73	3.97	3.06	**0.006**
	1.80	0.80	2.80	3.90	
HCO_3 (mmol/L)	25.3	2.4	28.9	9.4	0.091
	25.3	3.0	27.4	14.1	
PaO_2(mmHg)	37.5	13.3	71.1	51.4	0.18
	36.9	18.4	41.5	88.4	
PCO_2 (mmHg)	43.7	8.1	45.3	5.9	0.784
	44.4	8.5	44.3	7.9	
pH	7.39	0.05	7.42	0.15	0.206
	7.39	0.06	7.42	0.16	
PLT (10^3/uL)	215.7	82.9	264.0	166.0	0.539
	212.0	86.8	220.0	147.0	
HGB (g/dl)	11.85	1.83	11.02	1.56	0.159
	11.60	2.13	11.10	2.60	
HCT (%)	36.5	9.2	33.3	6.2	0.354
	34.9	7.4	34.5	7.8	
WBC (10^3/uL)	9.3	4.2	10.6	2.8	0.070

(continued on next page)

Table 1 (*continued*)

	Survivor $n = 130$		Non-survivor $n = 13$		p value
	Mean Median Number	SD IQR %	Mean Median Number	SD IQR %	
	8.3	4.9	10.9	3.7	
CTSI	2.0	0.9	4.8	2.9	**0.001**
	2.0	0.0	4.0	5.0	
mCTSI	3.6	1.3	7.2	1.9	**0.001**
	4.0	0.0	6.0	3.0	
Pancreatic volume (cm^3)	77.7	23.7	119.7	48.9	**0.001**
	78.4	36.8	102.5	77.9	

Mann-Whitney U and chi-square analysis.
SD: Standard deviation, SaO_2: Oxygen saturation, ALT: Alanin aminotranspherase, AST: Aspartate aminotransferase, CRP: C-reactive protein, LDH: lactate dehydrogenase, HCO_3: Bicarbonate PaO_2: Partial Pressure of Oxygen PCO_2: Partial Pressure of Carbon dioxide, PLT: Platelets, HGB: Hemoglobin, HCT: Hematocrit, WBC: White Blood Cell, CTSI: Computed Tomography Severity Index, mCTSI: modified Computed Tomography Severity Index.

Table 2
Predictive ability of CTSI andmCTSI scores and pancreatic volume for mortality in patients with acute pancreatitis

	AUC	Cut-off	Sensitivity	Specificity	+LR	-LR	PPV	NPV	Youden index
CTSI	0.822 (0.750–0.881)	>3	69.2	92.3	9.0	0.3	47.4	96.8	0.615
mTCSI	0.955 (0.907–0.983)	>4	92.3	96.2	24.0	0.08	70.6	99.2	0.884
Pancreaticvolume	0.787 (0.711–0.851)	>81.5	92.3	60.0	2.3	0.1	18.8	98.7	0.523

CTSI: computed tomography severity index, mCTSI: modified computed tomography severity index, +LR:Positive Likelihood ratio, −LR: Negative Likelihood ratio, PPV: positive predictive value NPV: negative predictive value.

0.711–0.851] suggests that it may be beneficial to use it alone or add this variable to scoring systems to be developed in future.

4.1. Limitations

There are some limitations to our study. First, the retrospective nature of the study, its single-center design, and being conducted in a certain region hinder the generalizability of the results. Second, while using pancreatitis severity scoring, it would be beneficial to include variables, such as intensive care requirement and ward admission. In future studies involving non-hospitalized patients, also daily ultrasonography measurements may help detect the rate and amount of pancreatic growth.

5. Conclusion

According to the results of our study in patients with acute pancreatitis, a pancreatic volume above 81.5 cm^3 is strongly associated with mortality. Measuring the pancreatic volume of patients and using it as a parameter can assist clinicians in identifying critically ill cases. Both CTSI and mCTSI scores outperformed pancreatic volume in predicting mortality.

Compliance with ethical standards

University of Health Sciences, Kartal Dr. Lutfi Kirdar City Hospital Ethics Committee approved for the study (Ethics Committee protocol number: 2021/514/208/12).

This article has not been previously presented at any event (congress, symposium etc.)

Human rights

The principles set out in the Helsinki Declaration were followed. The need for informed consent was waived due to the retrospective nature of the study.

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CRediT authorship contribution statement

Ummahan Dalkılınç Hökenek: Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Ömer Aydıner:** Validation, Resources, Investigation. **Julide Sayın Kart:** Writing – review & editing, Software, Resources, Methodology, Conceptualization. **Gülten Arslan:** Writing – review & editing, Resources, Investigation. **Kemal Tolga Saracoglu:** Writing – review & editing, Validation, Methodology, Conceptualization.

Declaration of Competing Interest

None.

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None.

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