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# CT in severe acute pancreatitis

## *Is there any relationship between the accumulated radiation dose and clinical parameters or radiological signs?*

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# 1. Abstract

**Purpose**

To evaluate the overall dose exposure due to follow-up computed tomography (CT) examinations in patients with acute pancreatitis (AP) in comparison with clinical, radiological parameters and patients' outcome.

**Method and Materials**

We retrospectively included 27 patients (22 men, mean age 65y) with AP requiring intensive care unit (ICU) for more than 24h and being followed-up by CT. Reviewing the CT images in consensus, two readers registered the CT severity index (CTSI) in each patient and collected patients' dose exposure parameters, i.e. dose-length product (DLP), effective dose (E) resulting from follow-up CT. Clinical and laboratory parameters indicating disease's severity, length of hospital and ICU stay, acute complications, need for intervention and/or surgery were registered and correlated with the accumulated radiation dose.

**Results**

In all patients 258 CT examinations were performed (mean 9.56, range 1-25) during their hospital stay. Six patients (22%) died from acute complications. Mean accumulated DLP and E per patient were 8741mGy.cm (range 682-29194) and 131mSv (range 10-438), respectively.

The individual CTSI significantly correlated with patients' laboratory parameters (amylasis, CRP), length of hospital stay, number of CT examinations, DLP, E, and number of radiological and surgical interventions.

The accumulated DLP and E per patient significantly correlated with CRP, septic shock, length of ICU and hospital stay, need for surgery, number of CT examinations, complications and radiological interventions.

**Conclusion**

The overall dose exposure resulting from follow-up CT examinations in patients with AP depends on disease's severity including complications. It is considerable and should not be neglected. We hope that in the future, the use of further developed iterative reconstruction with optimized protocols tailored to the individual patient's type will help reduce this dose burden

# 2. Introduction

Acute pancreatitis (AP) is an acute inflammatory condition of the pancreas resulting from the inappropriate intracellular activation of proteolytic pancreatic enzymes which leads to autodigestive injury of the pancreatic gland (1). The incidence of AP is increasing. AP is today the most common gastro-intestinal disease responsible for patients' admission in emergency (2). Although AP often runs a mild clinical course, up to 15% of the patients develop severe disease (1). In this context, patients are subject to a long lasting hospital stay and are at high risk of complications such as organ failure or infected necrosis with mortality rates of 35% and 20%, respectively (1).

There are multiple etiologies of AP. The two most common causes are alcohol abuse and gallstones. The general increase of abdominal obesity, which is a risk factor for gallstones, and the aging of the population possibly occurring together with excessive alcohol consumption contribute to the rise in incidence of AP (3). The diagnosis of AP is namely based on clinical criteria and the patient must fulfill at least two out of them: sudden onset of epigastric pain radiating to the back, serum amylase and/or lipase levels three times superior than the upper limit of the normal values, and/or characteristic findings of AP on imaging, usually on contrast-enhanced computed tomography (CT) (4). Therefore, normal CT findings, especially occurring at the initial stage of the disease do not exclude the diagnosis of AP.

Two distinct phases of AP were introduced by the revised Atlanta classification: the early phase that occurs within the first week after onset of the disease; and the late phase that starts in the second week often also lasting the subsequent weeks (5). After the first phase, pancreatic or peripancreatic edema may completely resolve, or fluid collections may develop, sometimes evolving towards definitive necrosis and/or liquefaction (6). Organ failure is the main severity criteria during the early phase. In fact, systemic inflammatory response syndrome and subsequent multiorgan failure are responsible for approximately 50% of all deaths. On the other hand, morphologic characteristics and inflammatory extent within and around the pancreas are not related to severity during this phase and may underestimate the severity of the disease (7).

The late phase mainly occurs in case of severe AP and it is characterized by increasing necrosis, infection, persisting systemic inflammatory response syndrome and multiorgan failure. This phase may last weeks or months. Pancreatic necrotic tissue is inclined to infection in 40 to 70% of cases (7). Infection directly influences the disease's course and outcome. Need for treatment and type of management are based on morphological changes detected by cross sectional imaging, namely CT. On CT examination pancreatic necrosis is defined as a sharply demarcated part of the parenchyma which does not enhance after intravenous administration of contrast agent (8). Superimposed infection occurs whenever a thin rim of contrast-enhancement surrounds an area of tissue necrosis or peripancreatic fluid collection. The latter is also called abscess. Both, morphologic and clinical criteria determine the severity of AP during the late phase (6). The terms severe and necrotizing pancreatitis are often used interchangeably (5).

Clinically, the severity of AP is defined by the presence or absence of organ failure, local complications, or both. Several clinical and laboratory scoring systems like Ranson criteria (Table 1) have been designed to accurately correlate the complications like organ failure and mortality in AP (9). In the past three decades, radiologic scoring systems have also been developed to accurately diagnose and correlate complications in AP with patients' outcome. In particular, the CT severity

index (CTSI) (Table 2), developed by Balthazar et al. in 1990 (10) has today become the most widely adopted scoring system for clinical and research settings. Balthazar CT severity index allows the staging of the severity of the inflammatory process, the evaluation of the pancreatic necrosis and the definition of the local complications, by differentiating mild (interstitial/edematous) AP from severe (necrotizing) AP and, thus, enabling the correct treatment. It also correlates well with morbidity, mortality and length of hospital stay (6,7). Compared to the clinical prognostic scoring system Ranson, CTSI more accurately diagnoses clinically severe disease and better correlates with the need for intervention and with pancreatic infection (11).

**Table 1**

Ranson criteria (7)

| | | |
|---|---|---|
| *At admission* | Age | > 55 years |
| | WBC count | > 16000 cells/$mm^3$ |
| | Blood glucose | > 200mg/dl |
| | Serum AST | >250 IU/L |
| | Serum LDH | >350 IU/L |
| *After 48 hours* | Corrected serum calcium | < 2 mmol/l |
| | Hematocrit fall | > 10% |
| | PaO2 | < 60mmHg |
| | BUN increase | > 1.8 mmol/l |
| | Sequestration of fluids | > 6l |
| | Base deficit | > 4 mEq/L |

*WBC : white blood cell, AST : aspartate transaminase, LDH : D-lactate dehydrogenase , PaO2 : partial pressure of arterial oxygen, BUN : blood urea nitrogen*

**Table 2**

Computed tomography severity index (CTSI) (10)

| Characteristics | Score |
|---|---|
| I Grading of pancreatitis | |
| Grade A: normal pancreas | 0 |
| Grade B: focal or diffuse enlargement of pancreas | 1 |
| Grade C: peripancreatic inflammation | 2 |
| Grade D: single acute fluid collection | 3 |
| Grade E: two or more acute fluid collections | 4 |
| II Pancreatic parenchymal necrosis | |
| None | 0 |
| Less than 30% | 2 |
| Between 30% and 50% | 4 |
| More than 50% | 6 |

Imaging plays an important role in the diagnosis and staging of AP. Imaging also helps for excluding other causes of acute abdomen. CT is the gold standard imaging technique for confirming clinically suspected AP and staging the disease's severity (10). However, the initial CT examination should be performed only at 72 hours after onset of symptoms, especially whenever clinical findings suggest severe AP (Ranson score≥3) (7, 10). CT performed shortly after onset of symptoms should be avoided since the peripancreatic inflammation and parenchymal necrosis may not have been reached their complete extension and, thus, imaging is not yet able to correctly show disease's severity (12).

However, CT imaging is invariably associated with radiation exposure and, due to the frequent complications, inherent in severe types of AP some patients may undergo multiple, since repeated,

CT examinations during their stay to accurately follow-up the disease's evolution. Therefore, these patients are exposed to considerable doses of ionizing radiations (8).

In Switzerland, the annual effective dose per inhabitant in 2013 was 5.6 mSv. The population's main source of man-made irradiation is medical exposure to X-rays. Medical imaging represents only 20 % of the annual effective dose but it accounts for >94 % of the man-made exposure. Moreover, CT is the most irradiating radiological modality and it delivers 70% of the overall dose resulting from medical imaging. On the other hand, the number of CT examinations only correspond to 9.6% of all radiological examinations (13).

The primary goal of this study is thus to evaluate the number of follow-up CT examinations and the consecutive overall radiation dose received by patients admitted to the intensive care unit (ICU) of the centre hospitalier universitaire vaudois (CHUV) for severe AP. Then, we will compare them to the radiological and clinical stage including severity parameters and the further clinical evolution of their pancreatitis.

# 3. Methods and Materials

## *3.1. Patients*

This retrospective study was approved by the ethics committee of "Canton de Vaud" with a waiver for written informed consent. According to our institutional medical database, a total of 51 consecutive patients with clinically diagnosed AP were admitted to the ICU of our institution between January 2012 and December 2014. Those patients were initially selected for further analysis. According to the guidelines, AP was defined as two or more of the following characteristics: abdominal pain, and serum amylase or lipase levels three or more times the upper limit of normal (> 210 U/L and > 180 U/L, respectively)(4).

Further criteria for inclusion in this study were the following: 1) Patients with clinically diagnosed severe AP. AP was defined as severe if patients were admitted to the ICU at least once during their hospital stay and spent there 24 hours or more. 2) Patients undergoing at least one CT examination during their hospital stay. The patients with missing clinical or radiological data were excluded. On the basis of these primary inclusion criteria, a total of 24 patients had to be excluded because they did not undergo any abdominal CT examination (n = 23), or the initial abdominal CT-examinations had been performed without intravenous injection of iodinated contrast medium, thus it was impossible to calculate the CTSI (n=1) (Figure 1).

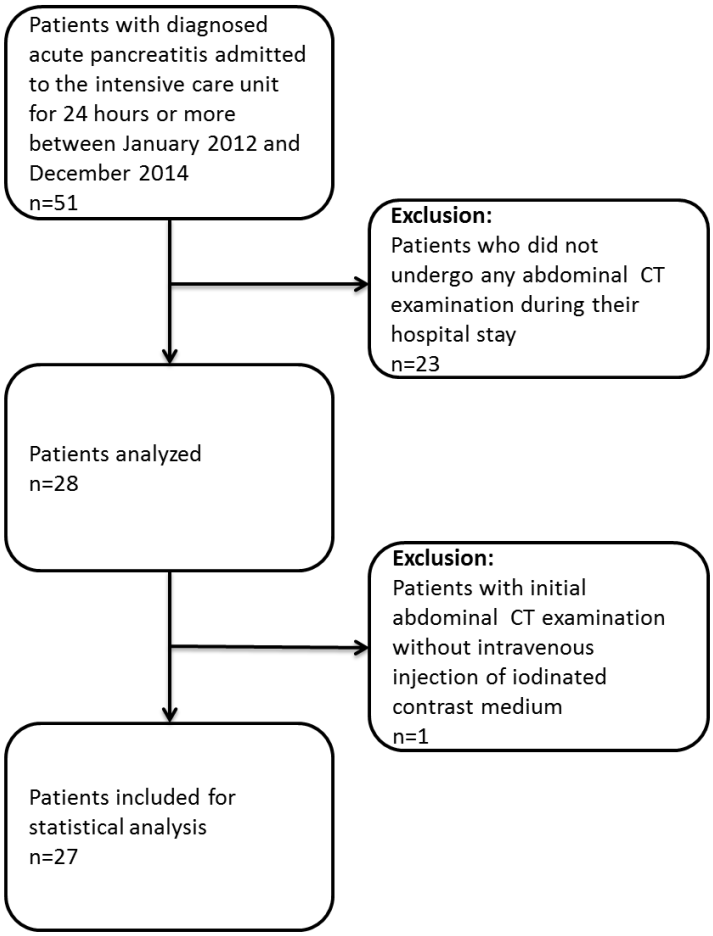


**Figure 1: Flow chart showing the process of patients' inclusion**

## 3.2. Data collection

First, the severity parameters have been collected and summarized in Table 3 for all the 27 patients. For each laboratory parameter, the highest value of the hospital stay was selected. In addition, the Ranson score was assessed for each patient at admission (age>55 y, white blood cell > 16000 cells/mm$^3$, glucose>200mg/dl, AST>250 IU/L, LDH>350IU/L) and after 48 hours (corrected serum calcium<2mmol/l, hematocrit fall>10%, PaO2<60mmHg, BUN increase>1.8mmol/l, sequestration of fluids >6l, base deficit > 4 mEq/L) (Table 1).

Second, the student and the tutor in consensus reviewed each CT examination performed during the hospital stay in our patients. Moreover, CT examinations performed at different hospitals before or after the patient had been transferred to the CHUV, that were indicated for the follow-up of the AP were included, whenever they had been entered into our imaging data base. By analyzing the images, the severity of pancreatitis per patient was rated using the original CTSI by Balthazar (Table 2). The extent of pancreatic necrosis was assessed on CT images acquired about 72 hours after onset of AP. Radiological complications including gastrointestinal (GI)-perforations, GI-bleeding and pseudo-aneurysms were also noted.

**Table 3**

**Severity parameters**

| Clinical parameters | Laboratory parameters | Radiological parameters |
|---|---|---|
| Age | Ranson score | Number of CT examinations |
| Intensive care unit length of stay | White blood cell | Number of phases |
| Hospital length of stay | Aspartate aminotransferase | Computed tomography severe index |
| Lung failure | Lactate dehydrogenase | Dose length product |
| Kidney failure | Glucose | Effective dose |
| Septic shock | Calcium | Size-specific dose estimates |
| Surgical interventions[1] | Lipase | Radiological complications[2] |
| Death | Amylase | Radiological interventions[3] |
| | Alanine aminotransferase | |
| | Total bilirubin | |
| | Alkaline phosphatase | |
| | Gamma-glutamyl transferase | |
| | C-reactive protein | |
| | Creatinine | |

*CT: computed tomography*

*[1]Surgical interventions: necrosectomy, intestinal resection*

*[2]Radiological complications are complications detected on CT images: gastrointestinal-perforation, gastrointestinal-bleeding, pseudo-aneurysm*

*[3]Radiologically-guided or minimally-invase Interventions: percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement*

## 3.3. CT examinations and radiation dose measurements

The CT examinations were performed on a 64-detector row CT machine (Light Speed VCT 64 Pro; GE Healthcare, Milwaukee, Wisconsin, USA). After the intravenous injection of iodinated contrast medium Accupaque®, (iohexol, 300 mgI/ml; volume in milliliters = body weight + 30ml, GE Healthcare) at a flow rate of 3ml/s (120 kV, 300 mA, table speed 55mm per rotation (0.8s), pitch 1.375), we acquired 2.5mm (reconstruction increment of 2mm) and/or 1.25mm (reconstruction increment of 1mm) reconstructed abdominal axial slices thickness during porto-venous phase (70s), and, if deemed necessary, preceded by a non-enhanced and/or an arterial phase (35s). In some

patients, according to the clinical indications, a chest acquisition was also performed. We used automatic tube current modulation in all three axes (SmartmA) as well as the iterative reconstruction algorithm ASIR.

The two readers reviewed all the images by means of the PACS (picture archiving and communication system) of the department of radiology of the CHUV. They registered the following parameters for each CT examination: type of examination (abdominal, thoracic or both), number of acquisition phases (non-enhanced, arterial, portal venous), the resulting CT dose index ($CTDI_{vol}$ in mGy), dose length product (DLP in mGy.cm) and size specific dose estimate (SSDE in mGy). The latter is used for a better patient dose estimation and image quality assessment. It is calculated by measuring the anteroposterior and lateral dimensions of each patient at the level of the navel on axial CT images using digital calipers. These two values are then summed to obtain a single metric to represent the patient size. The AAPM Report 204 provides tables based on patient size (anteroposterior + lateral dimensions) values that are used to find "f", the correction factor that, when multiplied by CTDI, yields SSDE (14). We calculated the SSDE for each patient using these tables based on a 32-cm phantom (Equation 1). The SSDE is a good estimation of the averaged dose delivered in the abdominal organs.

$$SSDE = f_{size}^{32X} \times CTDI_{vol}^{32}$$ **Equation 1**

Usually, risks related to radiation dose exposure in the low dose range (< 500 mGy) are estimated using the "effective dose" quantity (E). This quantity is reported in the standard SI units Sievert (Sv). According to Christner et al. (15) we determined the estimate for E as the product of DLP and the body region–appropriate DLP to E conversion coefficient, k (Equation 2). The values used for k were 0.015 mSv/mGy.cm for abdominal and thoracic examinations (15). The same k was used by Wichmann et al. for abdominal examinations (8).

$$E = k \times DLP$$ **Equation 2**

## *3.4. Statistical analysis*

All statistical analyses were performed by a statistician using the commercially available software R (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.r-project.org/.). Data are presented as numbers and relative percentages. Categorical variables were compared with the Chi-square test. The t-test was used to compare continuous variables of two independent samples. Since the CTSI score (1-10) was classified into 3 categories (0-3: mild AP; 4-6: moderate AP; 7-10: severe AP) the analysis of variance (ANOVA) was applied to determine whether there were any statistically significant differences between these three categories for continuous variables, followed by a post hoc unpaired t-test whenever ANOVA had shown a significant difference. The Pearson correlation coefficient was used to measure the linear relationship between two continuous variables. Statistical difference was considered significant for a p-value <0.05 and a trend was considered for a p-value <0.1.

# 4. Results

## *4.1. Baseline characteristics*

Our final study population consisted of 27 patients. (22 men, 5 women; age range, 32–82 years; mean age 65 years). The etiology of AP was as follows: alcohol (n=9, 33%), biliary stones (n=8, 30%) post-ERCP (n=1, 4%), hypertriglyceridemia (n=1, 4%), ischemia (n=1, 4%), iatrogenic (n=2, 7%) and unknown (n=5, 18%) (Figure 2).

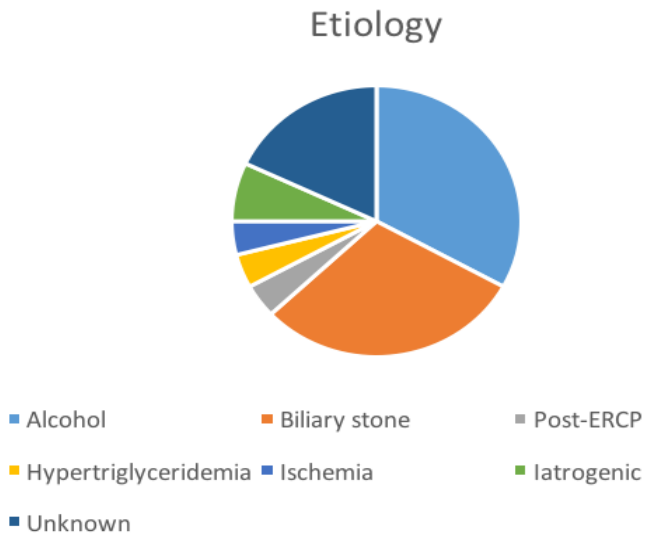


**Figure 2: Distribution of the different etiologies of acute pancreatitis in our study population**

The baseline characteristics of our patients are shown in Table 4. The cohort is characterized by a mean length of ICU stay and hospital stay of 20 days (range: 1-103) and 57 (range: 1-147), respectively. A total of 258 CT examinations were performed including 209 abdominal and 49 chest CT examinations. A mean of 9.56 (range: 1-25) CT examinations per patient were completed during their stay. The mean number of abdominal and thoracic CT examinations were 7.74 (range: 1-20) and 1.81 (range: 0-6), respectively. A total of 482 abdominal phases (non-enhanced, arterial, portal venous and delayed phase) were performed. A mean of 17.85 (range: 2-48) phases per patient were completed during their stay. The average DLP and E among the study cohorts was 8741 mGy.cm (range: 682-29194) and 131 mSv (range: 10-438), respectively. The mean CTDIvol was 12.06 mGy (range: 4.9-36). The mean number of complications detected by CT was 0.59 (range: 0-2). The latter included GI-perforation (n=11, 41%), GI-bleeding (n=5, 19%), while no pseudo-aneurysm was found. After their hospital stay 10 (37%) patients went back home, 11 (41%) patients were transferred to another institution and 6 (22%) patients died.

**Table 4**

General characteristics of the study population

| | **Patients N=27** |
|---|---|
| Male (%) | 22 (81) |
| Female (%) | 5 (19) |
| Mean age (median, range) | 65 (68, 32-82) |
| Number of patients transferred from another hospital to the CHUV(%) | 3 (11) |
| Number of patient transferred to another hospital after the CHUV (%) | 11 (41) |
| Mean intensive care unit (days) (median, range) | 20 (7, 1-103) |
| Mean hospital (days) (median, range) | 57 (38, 1-147) |
| Deaths (%) | 6 (22) |
| **Etiology (%)** | |
| Alcohol | 9 (33) |
| Biliary stone | 8 (30) |
| Post-ERCP | 1 (4) |
| Hypertriglyceridemia | 1 (4) |
| Ischemia | 1 (4) |
| Iatrogenic | 2 (7) |
| Unknown | 5 (18) |
| **Radiological parameters** | |
| Mean number of CT examinations (median, range) | 9.56 (6,1-25) |
| Abdominal CT examinations | 7.74 (5, 1-20) |
| Thoracic CT examinations | 1.81 (1, 0-6) |
| Mean number of abdominal phases | 17.85 (2-48) |
| CTSI score mean (median, range) | 5.85 (6, 2-10) |
| Grading of pancreatitis | |
| C: Inflammatory changes in pancreas and peripancreatic fat | 4 (15) |
| E: Two or more peripancreatic fluid collections | 23 (85) |
| Parenchymal necrosis (%) | 16 (60) |
| <30% | 9 (33) |
| 30–50% | 1 (4) |
| >50% | 6 (22) |
| Mean DLP (mGy.cm) (median, range) | 8741 (6531, 682-29194) |
| Mean E (mSv) (median, range) | 131 (98, 10-438) |
| Mean $CTDI_{vol}$ (mGy) (median, range) | 12.06 (12.7, 4.9-36) |
| Mean SSDE (mGy) (median, range) | 14.01 (13.86, 9.03-21.89) |
| Mean number of radiological complications[1] (median, range) | 0.59 (0, 0-2) |
| No complications (%) | 15 (56) |
| One complication (%) | 8 (30) |
| Two complications (%) | 4 (14) |
| Mean number of radiological interventions[2] (median, range) | 1.59 (1, 0-8) |
| No interventions (%) | 13 (48) |
| One intervention (%) | 4 (15) |
| Two interventions (%) | 3 (11) |
| Three or more interventions (%) | 7 (26) |
| Mean number of surgeries[3] (median, range) | 0.56 (0, 0-5) |
| No surgery (%) | 18 (67) |
| One surgery (%) | 6 (22) |
| Two or more surgeries (%) | 3 (11) |

*Post-ERCP: Post-endoscopic retrograde cholangiopancreatography, CT: Computed tomography, CTSI: CT severity index DLP: Dose Length Product, ED: effective dose, CTDIvol: CT dose index volume, SSDE: size specific dose estimate*

*[1]Radiological complications: gastrointestinal-perforation, gastrointestinal-bleeding*

*[2]Radiological interventions: percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement*

*[3]Surgery: necrosectomy, intestinal resection*

## *4.2. Relationship between disease's severity (CTSI score) and clinical, laboratory and radiological parameters*

In all 27 patients the CTSI score could be calculated and was divided into three categories, that is 1=mild (CTSI 0-3), 2=moderate (CTSI 4-6), and 3=severe (CTSI 7-10). According to this categorization 4 (15%) patients had a mild, 16 (59%) had a moderate and 7 (26%) had a severe CTSI score. When stratified by disease severity statistically significant differences in laboratory parameters (AST, lipasis, amylasis and CRP) ($p$=0.04, 0.04, 0.03, 0.04, respectively) length of hospital stay ($p$<0.01), number of CT examination ($p$=0.01), number of radiological interventions ($p$= 0.02), number of surgeries ($p$=0.02), DLP ($p$=0.02) and E ($p$=0.02) were noted, as shown in Table 5.

The post hoc unpaired t-test revealed a statistically significant difference or trend between the severe CTSI (3) and the other two categories, mild (1) and moderate (2) CTSI score, for amylasis ($p_{(CTSI3vsCTSI2)}$=0.02, $p_{(CTSI3vsCTSI1)}$=0.07), CRP ($p_{(CTSI3vsCTSI2)}$=0.07, $p_{(CTSI3vsCTSI1)}$=0.02), length of hospital stay ($p_{(CTSI3vsCTSI2)}$=0.01, $p_{(CTSI3vsCTSI1)}$<0.01), number of CT examinations ($p_{(CTSI3vsCTSI2)}$=0.04, $p_{(CTSI3vsCTSI1)}$=0.01), number of radiological interventions ($p_{(CTSI3vsCTSI2)}$=0.03, $p_{(CTSI3vsCTSI1)}$=0.01), DLP ($p_{(CTSI3vsCTSI2)}$=0.06, $p_{(CTSI3vsCTSI1)}$=0.03) and E ($p_{(CTSI3vsCTSI2)}$=0.06, $p_{(CTSI3vsCTSI1)}$=0.03) (Table 5).

Figure 4 illustrates the mean hospital stay in days stratified by disease's severity. For patients with a mild CTSI, the mean number of hospital days was 10, unlike 49 days for patients with moderate CTSI and 103 days for those with severe CTSI. The number of days spent at the hospital increases with rising CTSI score (Figure 3, Figure 4). The comparison between amylasis (Figure 5), CRP (Figure 6), number of CT examinations (Figure 7), number of radiological interventions (Figure 8), number of surgeries (Figure 9) DLP and E values (Figure 10) with the disease's severity revealed similar results.

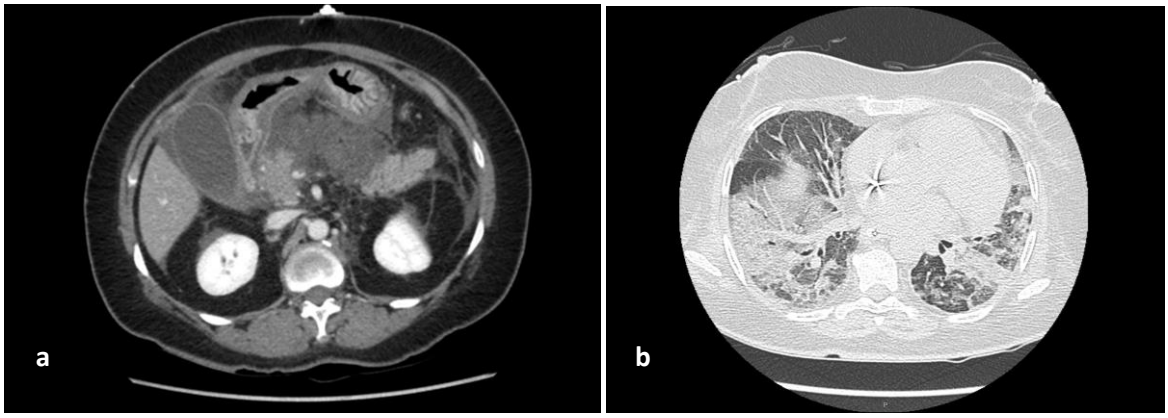


**Figure 3: Acute severe pancreatitis (CTSI 8) due to biliary gallstones in a 57-year-old woman. Contrast enhanced abdominal CT image (a), performed at onset, shows full width necrosis of the pancreatic body and proximal tail and reveals peripancreatic and pararenal space fluid collections. Parenchyma of the distal tail is seen to enhance normally. Follow-up thoracic CT examination (b) performed 38 days after the onset of the acute attack shows diffuse pulmonary consolidations, and ground-glass opacification corresponding to an acute respiratory distress syndrome. This patient spent 90 days at the hospital and DLP/E resulting from repeated follow-up CT examinations was 8283 mGy.cm and 124 mSv, respectively.**

**Table 5**

Severity parameters stratified by disease's severity expressed as CTSI score

| | CTSI | | | | Post hoc unpaired t-test | | |
|---|---|---|---|---|---|---|---|
| | 1: Mild (0-3, n=4) | 2: Moderate (4-6, n=16) | 3: Severe (7-10, n=7) | *p* | *P* (CTSI 3 vs CTSI 2) | *P* (CTSI 3 vs CTSI 1) | *P* (CTSI 2 CTSI vs 1) |
| Age (y) | 63 | 65 | 68 | 0.78 | - | - | - |
| WBC (G/l) | 13.05 | 14.50 | 15.00 | 0.84 | - | - | - |
| AST (U/l) | 1022 | 92 | 140 | 0.04* | 0.25 | 0.17 | 0.04* |
| LDH (U/l) | 1859 | 344 | 594 | 0.97** | - | - | - |
| Glucose (mmol/l) | 10.45 | 10.11 | 12.06 | 0.44 | - | - | - |
| Corrected serum calcium (mmol/l) | 2.15 | 1.94 | 1.99 | 0.46 | - | - | - |
| Ranson score | 3.25 | 3.21 | 4.86 | 0.12 | - | - | - |
| Lipasis (U/l) | 4104 | 1665 | 6585 | 0.04* | 0.01* | 0.54 | 0.15 |
| Amylasis (U/l) | 526 | 720 | 1708 | 0.03* | 0.02* | 0.07** | 0.63 |
| ALT (U/l) | 354 | 330 | 1116 | 0.33 | - | - | - |
| Total bilirubin (umol/l) | 47.25 | 52.50 | 58.43 | 0.94 | - | - | - |
| AP (U/l) | 237 | 339 | 420 | 0.37 | - | - | - |
| gGT (U/l) | 583 | 385 | 548 | 0.40 | - | - | - |
| CRP (mg/l) | 228 | 317 | 407 | 0.04* | 0.07** | 0.02* | 0.17 |
| Creatinine (umol/l) | 191 | 211 | 195 | 0.92 | - | - | - |
| Number of patients with lung failure | 0 | 1 | 1 | 0.66 | - | - | - |
| Number of patients with kidney failure | 2 | 11 | 6 | 0.45 | - | - | - |
| Number of patients with septic choc | 0 | 9 | 5 | 0.06** | - | - | - |
| ICU stay (d) | 3 | 20 | 31 | 0.29 | - | - | - |
| Hospital stay (d) | 10 | 49 | 103 | <0.01* | 0.01* | <0.01* | 0.07** |
| Number of deaths | 0 | 4 | 2 | 0.50 | - | - | - |
| Number of CT examinations | 2 | 9 | 16 | 0.01* | 0.04* | 0.01* | 0.08** |
| Number of patients with radiological complications[1] | 0 | 9 | 2 | 0.18 | - | - | - |
| Number of radiological interventions[2] | 0 | 1 | 3 | 0.02* | 0.03* | 0.01* | 0.27 |
| Number of patients with need for surgery[3] | 0 | 3 | 5 | 0.02* | | | |
| DLP (mGy.cm) | 1168 | 7961 | 14850 | 0.02* | 0.06** | 0.03* | 0.06** |
| E (mSv) | 18 | 119 | 223 | 0.02* | 0.06** | 0.03* | 0.06** |

*WBC: white blood cell, AST: aspartate transaminase, LDH: lactate dehydrogenase, ALT: alanine aminotransferase, AP: alkaline phosphatase, gGT : gamma-glutamyl transferase, CRP : C-reactive protein, ICU : intensive care unit, CT: computed tomography, DLP : dose length product, E:* effective dose

** Statistically significant*

*** Trend*

*[1] Radiological complications: gastrointestinal-perforation, gastrointestinal-bleeding*

*[2] Radiologically-guided, minimally-invasive interventions: percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement*

*[3] Surgery: necrosectomy, intestinal resection*

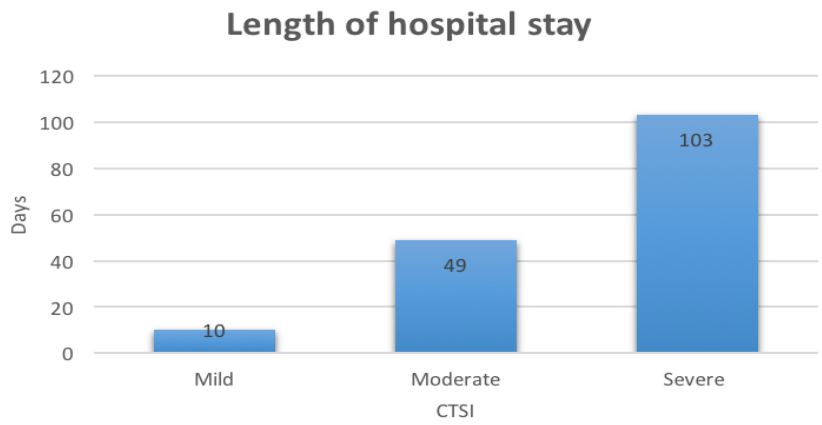


**Figure 4: The mean length of hospital stay (days) stratified by disease's severity (expressed as CTSI score)**

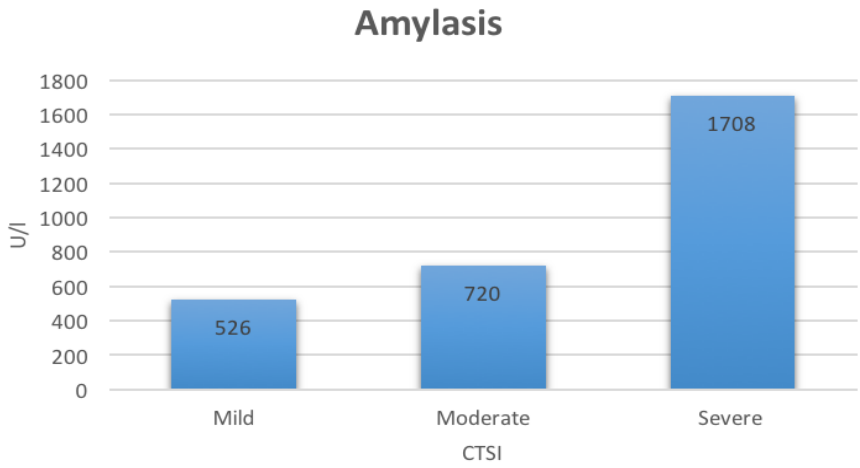


**Figure 5: The mean value of amylasis (U/l) stratified by disease's severity (expressed as CTSI score)**

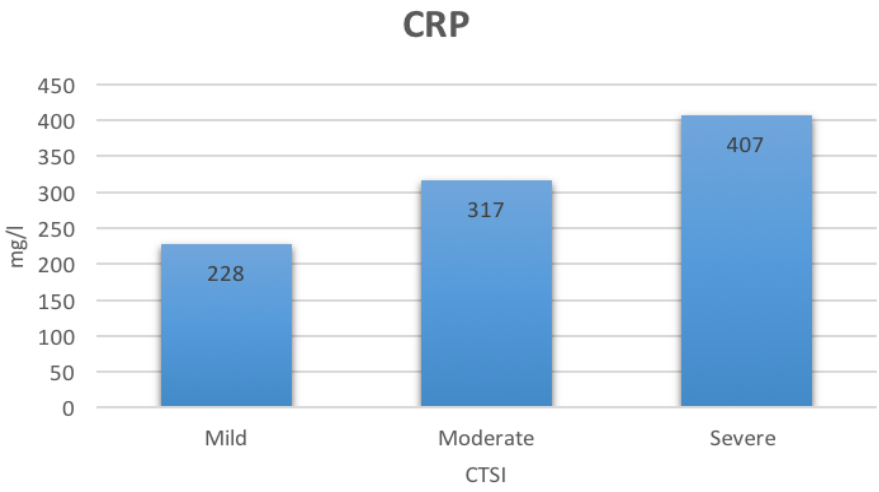


**Figure 6: The mean value of C-reactive protein (CRP, mg/l) stratified by disease's severity (expressed as CTSI score)**

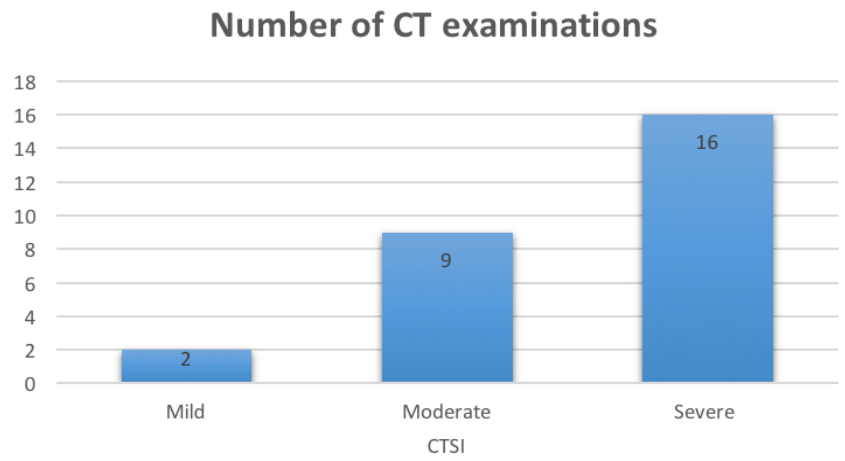


**Figure 7: The mean number of computed tomography (CT) examinations stratified by disease's severity (expressed as CTSI score)**

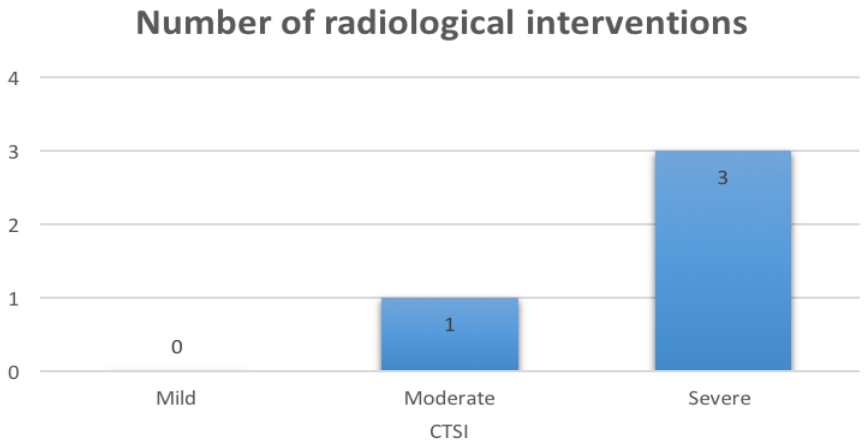


**Figure 8: The mean number of radiological interventions (percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement) stratified by disease's severity (expressed as CTSI score)**

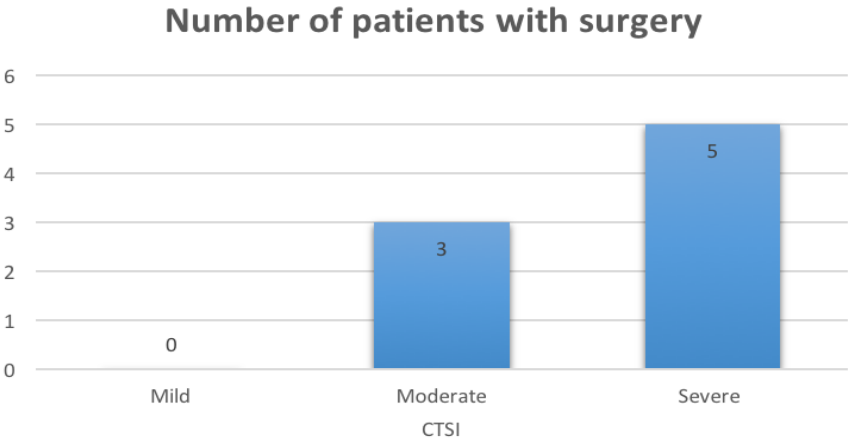


**Figure 9: The number of patients with need for surgery (necrosectomy, intestinal resection) stratified by disease's severity (expressed as CTSI score)**

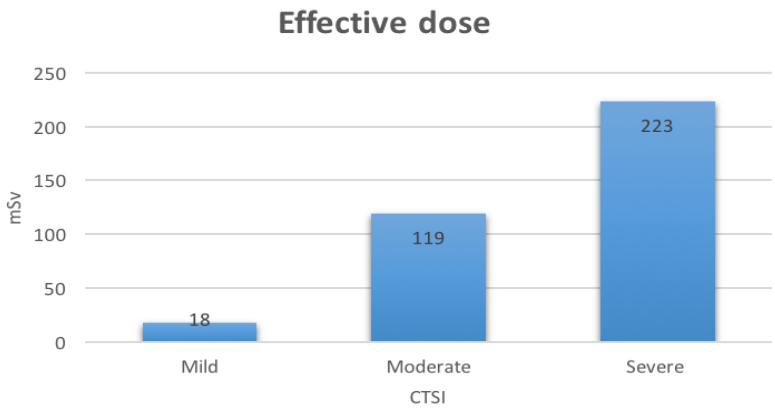


**Figure 10: The mean effective dose (E, mSv) stratified by disease's severity (expressed as CTSI score)**

## *4.3. Relationship between the DLP, the E and the clinical/radiological parameters*

There was a statistically significant relationship between the DLP, the E and CRP, length of ICU stay, length of hospital stay, number of CT examinations and number of radiological interventions. Corresponding Pearson correlation coefficients (r) and P values are shown in Table 6. Linear relationships between E and these parameters are illustrated in Figure 11 to Figure 15.

**Table 6**

Relationship between the DLP, the E and the clinical/radiological parameters

| | Correlation with the DLP and the E | |
|---|---|---|
| | *r* | *P* |
| Age (y) | 0.15 | 0.46 |
| Ranson score | 0.24 | 0.26 |
| CRP (mg/l) | 0.47 | 0.01* |
| Length of stay at the ICU (d) | 0.75 | <0.01* |
| Length of hospital stay (d) | 0.81 | <0.01* |
| Number of CT examinations | 0.95 | <0.01* |
| Number of radiological interventions[1] | 0.77 | 0.01* |

*DLP: dose length product, E:* effective dose*, CRP: C-reactive protein, ICU: intensive care unit, CT: computed tomography*

**Statistically significant*

*[1]Radiologically-guided, minimally-invasive interventions: percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement*

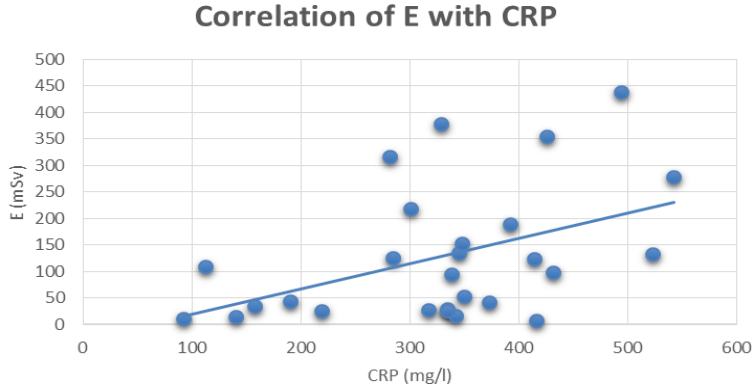


**Figure 11: Correlation of effective dose (E, mSv) with C-reactive protein (CRP, mg/l)**

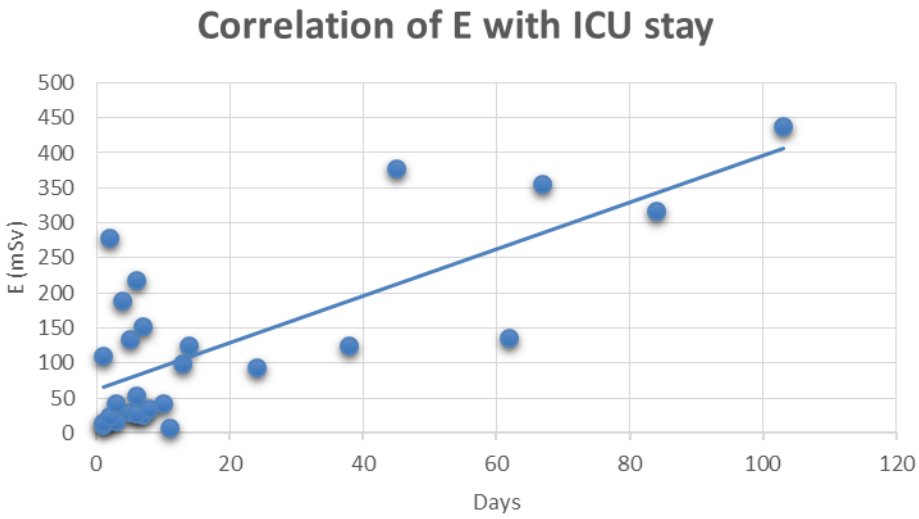


**Figure 12: Correlation of effective dose (E, mSv) with length of intensive care unit stay (ICU, days)**

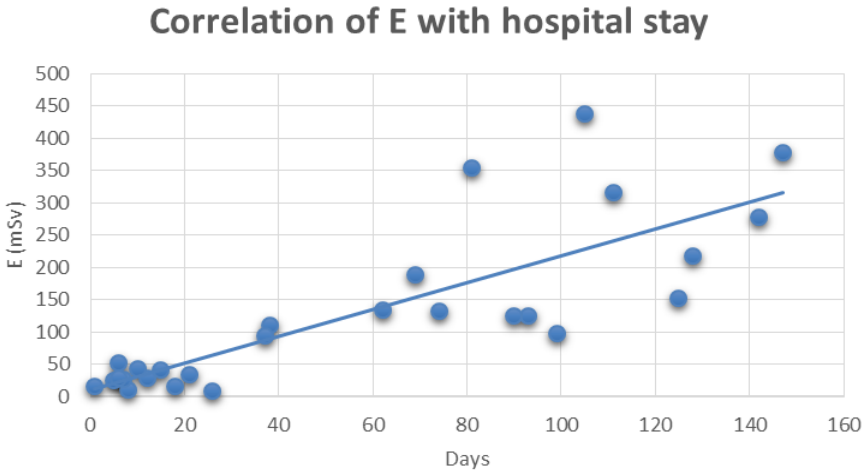


**Figure 13: Correlation of effective dose (E, mSv) with length of hospital stay (days)**

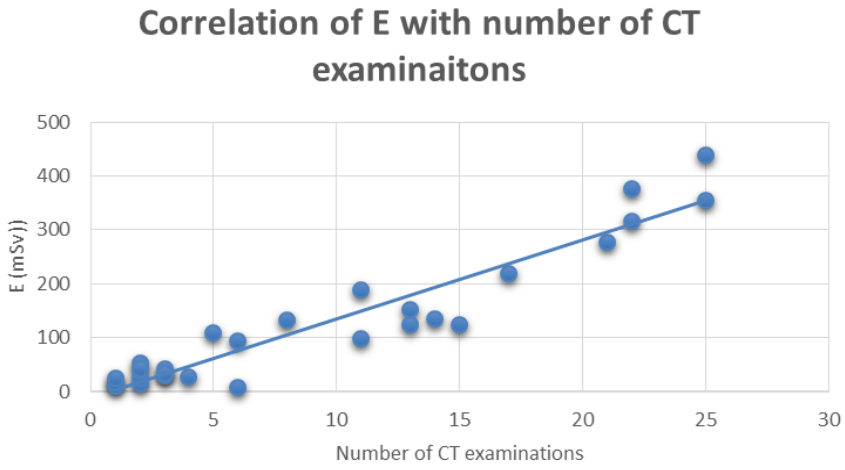


**Figure 14: Correlation of effective dose (E, mSv) with number of computed tomography (CT) examinations**

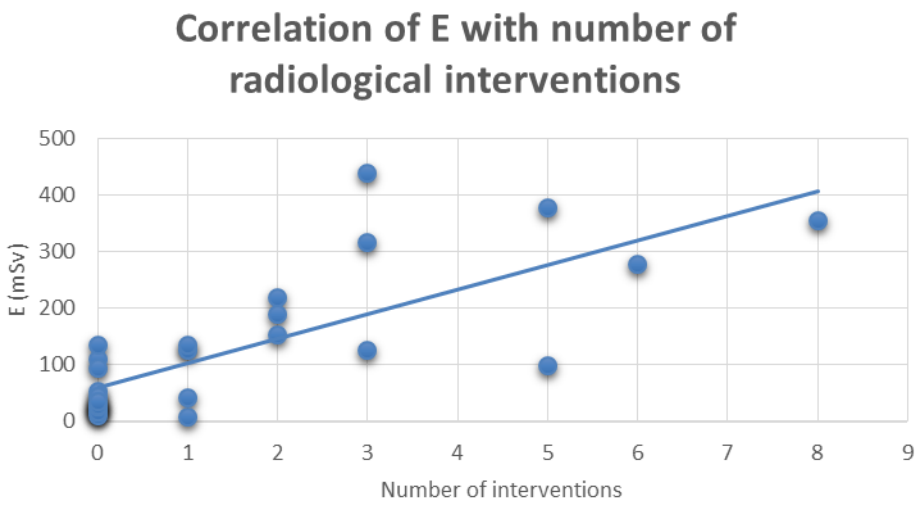


**Figure 15: Correlation of the effective dose (E, mSv) with the number of radiologically-guided, minimally-invasive interventions (percutaneous abdominal punctures, percutaneous abdominal and endoscopic drainages, endoscopy, embolization, venous/biliary stent placement)**

The evaluation of the relationship of the mean E with the type of clinical and the number of radiological complications related to AP resulted in significant differences for the presence/absence of septic choc, need for surgery and the number of complications detected on imaging (Table 7, Figure 16 to Figure 18).

**Table 7**

Comparison of the mean E with clinical and radiological complications related to AP

| | E (mSv) | *p* |
|---|---|---|
| Absence of lung failure (n=25) | 133 | 0.80 |
| Presence of lung failure (n=2) | 109 | |
| Absence of kidney failure (n=8) | 85 | 0.21 |
| Presence of kidney failure (n=19) | 151 | |
| Absence of septic choc (n=13) | 65 | <0.01* |
| Presence of septic choc (n=14) | 192 | |
| No radiological complication[1] (n=15) | 88 | <0.01* |
| One radiological complication[1] (n=8) | 115 | |
| Two radiological complications[1] (n=4) | 325 | |
| No surgery[2] | 69 | <0.01* |
| One or more surgeries[2] | 279 | |
| Alive (n=21) | 121 | 0.45 |
| Death (n=6) | 165 | |

*E:* effective dose

** Statistically significant*

*** Trend*

*[1] Radiological complications: gastrointestinal-perforation, gastrointestinal-bleeding*

*[2] Surgery: necrosectomy, intestinal resection*

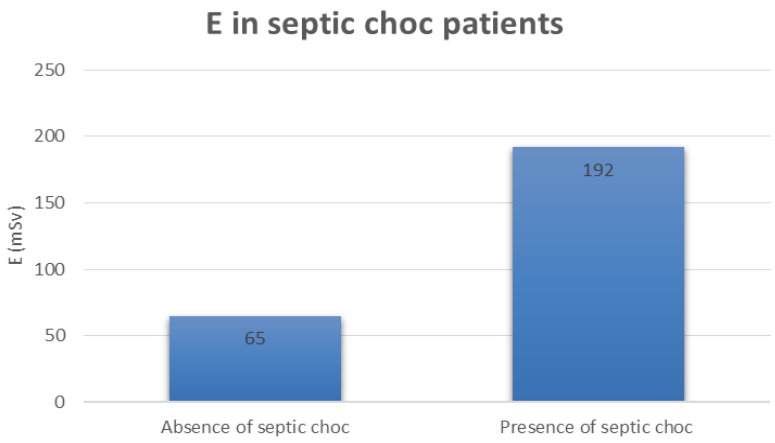


**Figure 16: Comparison of the mean effective dose (E, mSv) in patient with and without septic choc**

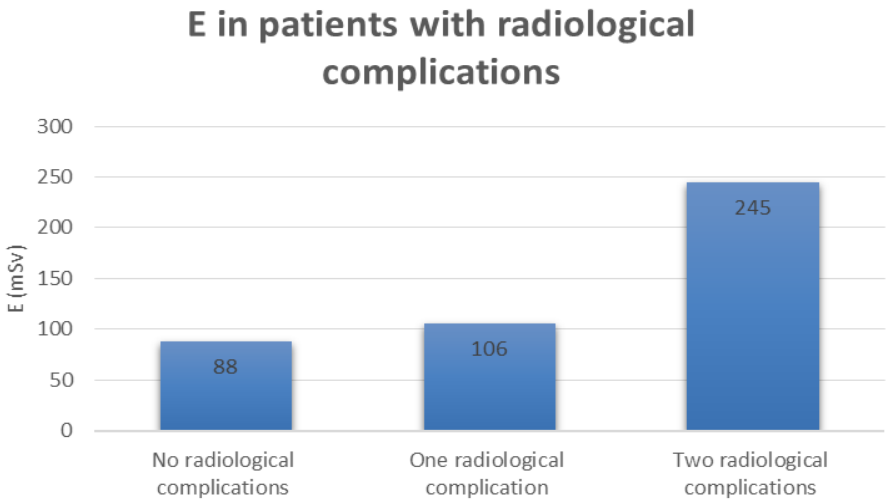


**Figure 17: The mean effective dose (E, mSv) stratified by the number of radiological complications (gastrointestinal perforation, gastrointestinal bleeding)**

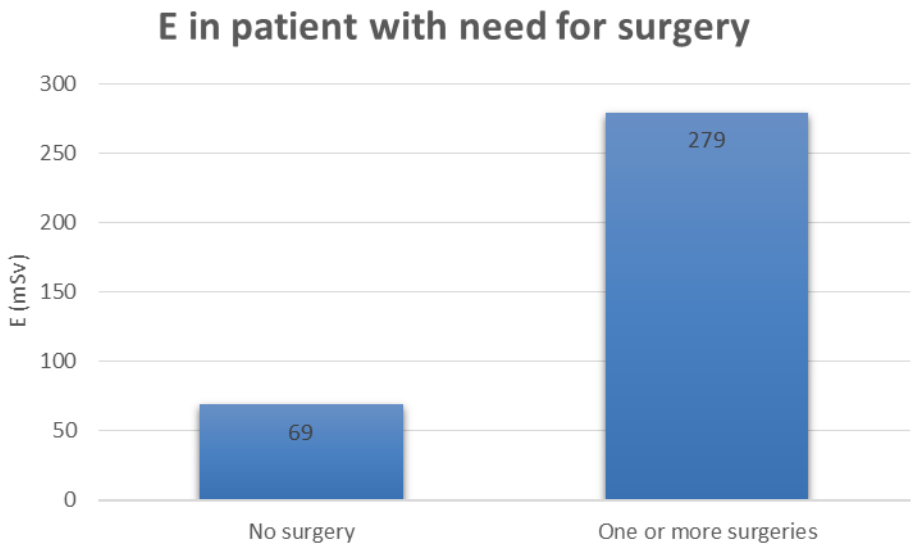


**Figure 18: Comparison of the mean effective dose (E, mSv) in patient with and without need for surgery (necrosectomy, intestinal resection)**

## *4.4. Relationship between the SSDE and the clinical and radiological parameters*

There was no statistically significant relationship between the SSDE and clinical (age, Ranson score, surgeries, length of ICU stay, length of hospital stay, death) or radiological (CT number, complications, interventions, CTSI) parameters.

## *4.5. Relationship between the number of acquisition phases per CT examination and clinical and radiological parameters*

The correlation between the mean number of phases acquired per CT examination for a patient with clinical (Ranson score, surgeries, presence/absence of lung failure, presence/absence of kidney failure, presence/absence of septic shock, length of ICU stay, length of hospital stay) or radiological (complications, interventions) parameters didn't show any statistically significant result.

# 5. Discussion

Our study consisted in evaluating the number of CT examinations and the consecutive overall radiation dose received by patients admitted to the ICU of the CHUV for severe AP. We retrospectively analyzed 27 patients with AP requiring ICU care for ≥24h and being followed-up by CT. Assessment of the initial severity and follow-up of complications is one of the most important issues in the management of AP.

Our results showed that the more severe the AP is the higher the laboratory parameters (amylasis and CRP) are, and also the longer the hospital stay, the higher the number of CT examinations, the number of radiological interventions, the number of surgeries, and the higher the DLP and thus E. Also, patients with severe AP based on CTSI showed a statistically significant difference with those who had a mild or moderate AP for the length of stay, the number of the CT examinations, the level of DLP and number of intervention. Only the number of acquisition phases per CT examination and the SSDE did not correlate with the clinical severity of the disease.

If we compare the number of abdominal CT examinations and estimated radiation dose of our AP population with the AP population studied by Morgan et al. (16), our patients had more abdominal CT examinations (mean 9.56, range 1-25) and were exposed to a higher radiation dose (mean 131mSv, range 10-438). Morgan et al.'s study population (16) consisted of 869 patients included in an interval of 5 years. Their mean age was 50.8 years and the mean number of abdominal CT examinations per patient per hospital stay was 1.9 (range 1-12), resulting in a mean estimated radiation dose of 31.03 ± 26.4 mSv (range, 14.7–176.9 mSv) per patient. We can explain these differences between these two populations by the fact that in our study we deliberately only included patients with severe AP admitted to the ICU unlike Morgan et al. who enrolled any patient with AP admitted to their hospital (16). Indeed, our purpose was to include in our evaluation the impact of imaging performed for the systemic complications of AP that particularly occur in these patients with AP that are admitted to the ICU.

In agreement with Morgan et al. (16) our comparison of the overall radiation dose exposure with several radiological and clinical parameters and the further clinical evolution yielded a significant correlation between disease's severity and the overall dose exposure due to CT. This means that patients with severe disease undergo more follow-up CT examinations than patients with less severe disease, since the former are followed-up at shorter intervals than the latter. We could argue that these frequent follow-up CT examinations are necessary to reassure the responsible physician because severely ill patients are often very difficult to evaluate clinically because of intubation and sedation. Thus, they may not have any clinical symptoms when complications occur, and regular follow-up CT seems mandatory to avoid missing any life-threatening complications. At the same time, CT images may reveal an indication for surgery or radiological intervention. Therefore, the received radiation dose seems to be justified medically and clinically, since we could show that patients with more severe pancreatitis are exposed to more radiation dose than patients with a mild disease's evolution.

CT remains the accepted standard of reference examination in AP for confirming clinically suspected AP and staging the disease's severity (7). Its widespread utility can be explained by the recommendation of the Acute Pancreatitis Working Group that proposes that typical findings on CT define the presence of the disease (16). Furthermore, the speed, availability, complete non-

invasiveness and reproducibility of CT, as well as the ability to accurately and objectively demonstrate morphologic changes in AP, make it an ideal first step imaging of patients with AP especially in patient with severe disease, systemic manifestations or poor general condition (17).

Although recent improvements in CT technology, namely the iterative reconstruction of CT images, have enabled to considerably lower the dose exposure in body CT (18) the average dose exposure due to CT examinations in our patients' population was high (mean 131 mSv (range: 10-438)). Given the cancer risk associated with low-dose radiation exposure (19), we need to ask ourselves if some of our follow-up CT examinations could not have been replaced by other, non-ionizing modalities (20), such as US or MRI. An analysis in view of a dose reduction strategy should be performed. Firstly, the required level of image quality for the detection of complications in AP and then the exact length of the data acquisition need to be defined. Another aspect is an analysis on the way the automatic exposure should be used. We should verify if the use of lower kVs could reduce the patient burden. Finally, the use of automatic dose collection software (such as Dose Watch) with a tracking of the patient history (indicating the number of examinations already performed on a given patient) might help the radiologist and the radiographer to better optimize the procedure. This is, in fact, what is meant by the third level of justification now required by law.

Ultrasound (US) is the first-line imaging modality performed on admission although the accuracy for the diagnosis of AP and its complications is quite low (6). It is the modality of choice for calculous cholecystitis, and reliably demonstrates gallstones and biliary dilatation. The latter may indicate possible impacted calculus in the bile duct, however seldom directly seen. US can also be helpful in monitoring the evolution of fluid collections, which occur as a result of AP, and in guiding therapeutic interventions (5). However, US can be limited by overlying bowel gas obscuring the retroperitoneal pancreatic parenchyma, and the performance may be hampered by overweight, bandages and operator inexperience. The main advantages of US are the possibility to perform a bed-side examination, the easy availability and cheap costs, but, above all, the absence of radiation exposure.

Recent technological developments, especially the increasing speed of image acquisition, have facilitated the use of magnetic resonance imaging (MRI) in patients with AP. MRI should generally be preferred to CT in radiosensitive populations (children, young patients, pregnant women) and must replace intravenously contrast-enhanced CT in patients with iodinated contrast agent allergy or renal failure. In fact, it should be emphasized that MRI is a non-ionizing cross sectional imaging method and has a safer intravenous contrast profile in comparison to CT (7). MRI is at least as effective as CT in determining the presence and the extension of pancreatic necrosis and in showing the presence, localization and the extension of fluid collections (21). According to several studies MRI is even superior in the characterization of fluid collections (22). However, a routine MRI examination of the pancreas still requires 15-20 minutes for data acquisition and generally includes breath hold sequences which represent a limiting factor in patients with a poor general condition which is frequent at the ICU (6). Artifacts can also affect the accuracy and reproducibility of the MR images. Moreover, MRI still remains less available than CT and the costs are higher. Finally, analyzing MR images still requires more routine working experience than CT images; therefore, the on-call radiologist may not immediately be familiar with MR examinations performed for complications of AP.

Despite all the advances in non ionizing technologies CT is still the gold standard in the evaluation of the patients with AP (7). Therefore, strategies to reduce radiation exposure remain crucial. These include ensuring the use of automatic exposure-control software, replacing outdated scanners, and reduction in the overall number of CT examinations by carefully assessing the likelihood of altering a patient's clinical management based on the results of a given CT examination (23). This may also be achieved, in part, by limiting short-term follow-up to single-phase studies, as reported by Wichman et al (8). Unfortunately, we could not observe this effort in our patients' population. Moreover, we did not observe either any correlation between the mean number of phases for a patient and clinical or radiological parameters. We explain this by the various clinical experiences of our on-call radiologists that control these emergency CT examinations. Thus, they mostly indicated the maximum of abdominal phases to perform by fear of missing any detail on the images and also possibly ignoring the exact clinical indication since it may have poorly been communicated.

Furthermore, Wichmann et al showed that single-phase examination can be performed with a reduced tube voltage of 100 kVp for additional radiation savings, as low-tube-voltage acquisition did not reveal significant differences compared to the standard 120-kVp acquisition. Indeed, this may be a good possibility for lowering the dose exposure, but the resulting image quality very much depends on the underlying body habitus, thus it should be indicated according to the patients' body mass index (BMI).

The SSDE has recently been created to better estimate the average dose delivered to a slice and thus to have a better control on image quality between different patient habitus. Our results yielded no relationship between the SSDE and clinical or radiological parameters, including the disease's severity. Again, this may at least partly be explained by a lack of experience of our on-call radiologists. They often use the same CT imaging protocol regardless of the exact clinical indication and the severity of the disease. Here is definitely room for improvement. The radiologists and also the radiographers need to be taught which individual image quality will be necessary for answering the clinical question raised when requesting a follow-up CT examination. Thus, a reduction of the dose exposure may be obtained in the near future.

This study had some limitations. Since we performed a retrospective study the data sampling was difficult, and sometimes incomplete. Additionally, the present study was limited by its moderate sample size. However, our purpose was to focus on patients with severe pancreatitis that necessitated ICU stay, and not to include any kind of pancreatitis. Thus, we deliberately limited our patients' selection on very ill cases that needed a high number of follow-up examinations.

# 6. Conclusion

The overall dose exposure resulting from follow-up CT examinations in patients with AP depends on the disease's severity (CTSI score). The high overall radiation should be kept in mind given the cancer risk associated with low-dose radiation exposure. Efforts, such as reducing the number of abdominal acquisitions per examination or the lowering of the kV (from 120 to 100kV) should be undertaken to reduce the number of these CT-examinations or to replace them by other, non-ionizing modalities. We hope that in the future, the use of further developed iterative reconstruction with optimized protocols tailored to the individual patient's type will help reduce this dose burden

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