

Prognostic Significance of Echocardiographic and ECG Changes in Patients with Acute Pancreatitis

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ABSTRACT

Background: Acute pancreatitis is a primarily noninfectious inflammatory disease of the pancreatic gland. The cardiovascular system involvement has been described before, in the form of electrocardiogram (ECG) changes and echocardiographic findings (diastolic, systolic or combined dysfunction, wall motion abnormalities and pericardial effusion). The current study aimed to detect echocardiographic and ECG changes in acute pancreatitis and investigate the significance of these changes on prognosis. **Patients and methods:** A prospective observational study was conducted on 54 patients with acute pancreatitis (according to Atlanta score) admitted to Internal Medicine Department, Assiut University, Egypt. All patients were subjected full clinical and laboratory evaluation in addition to assessment of ECG changes and echocardiographic findings. **Results:** The mean age of patients was 45.72 (SD 12.3) years and ranged from 19 to 70 years, with 51.9% of them were females. The probable cause in the majority of the study patients was gall stone (42.6%). The present study showed several possible ECG changes; T-wave Changes and Prolonged Q-R Interval had significant impact on the rate of complications. Also, left ventricular (LV) diastolic dysfunction and pericardial effusion at discharge had significant impact on the rate of complications. At discharge echo changes had no impact on the rate of complications. Poor R-wave progression (PRWP), ST segment elevation and T-wave changes had significant association with mortality. Female sex, comorbidity, Ranson Severity Score, white blood cells (WBCs), blood urea nitrogen (BUN) follow up, calcium Level, albumin, Basal deficit, ST segment elevation, regional wall motion abnormality (RWMA) baseline, left ventricular diastolic dysfunction (LVDD) on discharge and right ventricular systolic dysfunction (RVSD) on discharge could significantly predict mortality among cases.

Conclusion: Echocardiographic and ECG changes in patients with acute pancreatitis could predict the outcome of those patients. Future studies on larger sample sizes are warranted to confirm such findings.

Keywords: Acute pancreatitis, echocardiography, Ranson Severity Score, Atlanta score.

INTRODUCTION

Although gallstones and alcohol consumption are the most common causes of acute pancreatitis (AP), hypertriglyceridemia, endoscopic retrograde cholangiopancreatography (ERCP), trauma, obesity, diabetes are also well-known triggers of local and systemic inflammation (1,2).

The Atlanta classification of AP has been used to differentiate between severe and mild cases of acute pancreatitis, according to this classification, patients are diagnosed with severe acute pancreatitis (SAP) if they show evidence of organ failure, local complications (e.g., necrosis, abscess, pseudocyst), Ranson score of 3 or higher or acute physiology and chronic health evaluation II (APACHE II) score of 8 or higher (3).

SAP has a wide range of affection on nearly all body systems with various degrees of affection than affect both the clinical picture and the prognosis of the disease (4).

The cardiovascular system involvement has been described before, in the form of electrocardiogram (ECG) changes (sinus tachycardia, arrhythmias, conduction abnormalities) and echocardiographic findings (diastolic, systolic or combined dysfunction, wall motion abnormalities, pericardial effusion (5).

In the current study our aim was to detect echocardiographic and ECG changes in acute pancreatitis and investigate the significance of these changes on prognosis.

PATIENTS AND METHODS

Study design

A prospective observational study was conducted on 54 patients who were admitted to Al-Rajhi Intensive Care Unit (ICU) and at Internal Medicine Department, Assiut University Hospital, Assiut University, in the period from 2019 to 2022.

Study Setting

Gastroenterology & Hepatology Unit and ICU at Internal Medicine Department, Assiut University Hospital, Assiut University.

Inclusion criteria: All patients with acute pancreatitis aged more than 18 years admitted to Al-Rajhi ICU of all etiologies.

Exclusion criteria: Patients with known cardiac diseases.

All patients were subjected to:

1. **Full history taking** including age, gender, special habits of medical importance, comorbidities, previous operations.
2. **General examination:** Blood pressure, temperature, respiratory rate, pulse.
3. **Local examination:** Abdominal examination including inspection, palpation, percussion and auscultation.
4. **Laboratory investigations:** Complete Blood Count. Kidney function tests (creatinine, urea, blood urea

nitrogen (BUN). Liver function tests (alanine transaminase (ALT), aspartate transaminase (AST), bilirubin, and albumin). Serum sodium (Na), potassium (K), calcium (Ca), lactate dehydrogenase (LDH), and serum Amylase and lipase.

Diagnosis and classification of acute pancreatitis (6):

- Serum lipase > 3 folds of the upper limit of normal.
- Serum amylase > 3 folds of the upper limit of normal.

Severity of acute pancreatitis was assessed using Ranson Score for severity of acute pancreatitis

Imaging:

- **12-lead ECG:** V1 to V6 to be applied on the front of patient’s chest. Thereafter, limb leads are applied on both upper and lower limbs.
- **Transthoracic echocardiography within 24 h of admission and at discharge:** Transthoracic echocardiography imaging was obtained from parasternal long-axis window and 4 apical windows with 2.5-3.5 MHz transducer by using ACUSON X300 ultrasound machine. Echocardiographic measurements were performed according to the recommendations for quantitation of the left ventricle (LV) by two-dimensional echocardiography.

Ethical consideration:

An approval of the study was obtained from Assiut University Academic and Ethical Committee. The purpose of the study was explained to all participants, and written informed consent was obtained. The study was registered on clinicaltrials.gov with NCT04196504. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data was collected and analyzed by using SPSS (Statistical Package for the Social Sciences, version 20, IBM, and Armonk, New York). Quantitative data were expressed as mean and standard deviation (SD) and compared using Student’s t.test. Nominal data are given as number (n) and percentage (%). Chi² test was implemented on such data. Multivariate regression analysis was used to determine possible risk factors for complications and mortality among patients with AP. Level of confidence was kept at 95% and hence, P value was considered significant if <0.05.

RESULTS

Baseline characteristics of the studied sample (Table 1): Mean age of the studied sample was 45.72 (SD 12.3) years, and 51.9% of them were females and 48.1% were males. The probable cause of pancreatitis in the studied sample was most commonly gall stone (42.6%), followed by post-endoscopic retrograde cholangiopancreatography (ERCP) (25.9%).

Table (1): Baseline characteristics of the studied sample.

| Variable | Category | N = 54 |
|----------------|---------------------|--------------|
| Age in years | Mean ± SD | 45.72 ± 12.3 |
| | Median (Range) | 45 (19 – 70) |
| Sex | Male | 26 (48.1%) |
| | Female | 28 (51.9%) |
| Comorbidities | | 22 (40.7%) |
| Probable Cause | Gall Stone | 23 (42.6%) |
| | Post-ERCP | 14 (25.9%) |
| | Malignancy | 4 (7.4%) |
| | Drug Induced | 3 (5.6%) |
| | Cryptogenic | 3 (5.6%) |
| | Viral | 3 (5.6%) |
| | Hyper-triglyceremia | 2 (3.7%) |
| | Alcohol Consumption | 1 (1.9%) |
| | Hypercalcaemia | 1 (1.9%) |

Data expressed as mean (SD), median (range), frequency. ERCP: endoscopic retrograde cholangiopancreatography; SD: standard deviation.

Laboratory Findings and outcome of the studied sample (Table 2):

The mean Ranson Severity Score was 2.69 (SD 1.3). The length of hospital stays among this study patient was 8.39 (SD 1.6) days ranging from 2 days to 37days. No complications were detected in 53.7% of cases. 46.3% had complications.

Table (2): Laboratory findings of the studied sample

| Variable | Category | N = 54 |
|---|-----------|----------------|
| Haemoglobin (mg/dl) | Mean ± SD | 12.52 ± 2.1 |
| Leucocytes *10 ³ | Mean ± SD | 12.01 ± 2.0 |
| Platelet *10 ³ | Mean ± SD | 346.83 ± 21.9 |
| Kidney and Liver Function Parameters | | |
| Creatinine (µmol/L) | Mean ± SD | 122.87 ± 29.5 |
| Urea (mg/dL) | Mean ± SD | 7.92 ± 1.4 |
| Aspartate transaminase (U/L) | Mean ± SD | 160.21 ± 27.9 |
| Bilirubin (µmol/L) | Mean ± SD | 2.10 ± 0.41 |
| Albumin (g/L) | Mean ± SD | 3.68 ± 0.8 |
| Lactate dehydrogenase (U/L) | Mean ± SD | 352.74 ± 83.4 |
| S. Amylase (U/L) | Mean ± SD | 588.83 ± 127.3 |
| S. Lipase (U/L) | Mean ± SD | 360.23 ± 9.1 |
| Ranson Severity Score | Mean ± SD | 2.69 ± 0.51 |
| Length of Hospital Stay/days | Mean ± SD | 8.39 ± 1.6 |
| Complications | | 25 (46.3%) |
| Mortality | | 8 (14.8%) |

Data expressed as mean (SD), median (range). SD: standard deviation

Effect of ECG Changes on the Rate of Complications (Table 3):

It was found that the occurrence of T-wave changes was significantly different between patients with and without complications (48% of patients with complications had T-wave changes and 17.2% of patients without complications had T-wave changes, $P=0.015$). 44% of patients with complications had Prolonged Q-R Interval, while 13.8% of patients without complications had Prolonged Q-R Interval, the difference was statistically significant ($P=0.013$).

Table (3): Effect of ECG changes on the rate of complications.

| Variable | No Complication (N= 29) | Complication (N= 25) | P-value |
|-----------------------------------|-------------------------|----------------------|---------|
| Sinus Tachycardia | 18 (62.1%) | 14 (56%) | 0.651* |
| Atrial fibrillation | 0 (0%) | 1 (4%) | 0.463** |
| Premature ventricular contraction | 7 (24.1%) | 3 (12%) | 0.215* |
| Bradycardia | 0 (0%) | 2 (8%) | 0.344** |
| Poor R wave progression | 0 (0%) | 3 (12%) | 0.055** |
| RBBB | 0 (0%) | 1 (4%) | 0.463** |
| ST Segment Elevation | 0 (0%) | 3 (12%) | 0.055** |
| ST Segment Depression | 1 (3.4%) | 4 (16%) | 0.133** |
| T-wave Changes | 5 (17.2%) | 12 (48%) | 0.015* |
| Prolonged Q-R Interval | 4 (13.8%) | 11 (44%) | 0.013* |

Date expressed as frequency (percentage). *P* value was significant if <0.05 . RBBB: right bundle branch block.

*Chi-square test was used to compare differences in frequency between groups.

**Fisher's Exact test was used to compare differences in frequency between groups.

Effect of Echocardiographic Changes on the Rate of Complications (Table 4):

Left ventricular (LV) diastolic dysfunction at admission was detected in 64% of patients with complications, while it was detected in 34.5% of patients without complications. The difference was statistically significant ($P= 0.019$). Pericardial Effusion at admission was detected in 13.8% and 36% of patients without and with complications, respectively. The difference was statistically significant ($P= 0.044$).

All the Echo changes detected at discharge had a significant relation to the occurrence of complications, where detection of echocardiographic changes at discharge was significantly higher in patients with complications than patients without complications.

Table (4): Impact of echocardiographic changes on the rate of complications

| At Admission | | | |
|--------------------------|-------------------------|----------------------|-------------|
| Variable | No Complication (N= 29) | Complication (N= 25) | P-value |
| Increased Cardiac Index | 13 (44.8%) | 12 (48%) | 0.816* |
| Regional WMA | 0 (0%) | 2 (8%) | 0.344* * |
| LV Systolic Dysfunction | 0 (0%) | 3 (12%) | 0.055* * |
| LV Diastolic Dysfunction | 10 (34.5%) | 16 (64%) | 0.019* * |
| RV Systolic Dysfunction | 2 (6.9%) | 4 (16%) | 0.265* * |
| Pericardial Effusion | 4 (13.8%) | 3 (36%) | 0.044* * |
| At Discharge | | | |
| Variable | No Complication (n= 29) | Complication (n= 17) | P-value |
| Increased Cardiac Index | 9 (31%) | 4 (23.5%) | 0.424* |
| Regional WMA | 0 (0%) | 0 (0%) | ----- |
| LV Systolic Dysfunction | 0 (0%) | 1 (5.9%) | 0.370* * |
| LV Diastolic Dysfunction | 10 (34.5%) | 9 (52.9%) | 0.220* |
| RV Systolic Dysfunction | 1 (3.4%) | 1 (5.9%) | 0.608* * |
| Pericardial Effusion | 3 (10.3%) | 3 (17.6%) | 0.389* |

Date expressed as frequency (percentage). *P* value was significant if <0.05 . WMA: wall motion abnormalities; LV: left ventricular; RV: right ventricular

*Chi-square test was used to compare differences in frequency between groups.

**Fisher's Exact test was used to compare differences in frequency between groups.

Predictors of complications among cases: Multivariable logistic regression (Table 5):

Ranson Severity Score, diastolic blood pressure (DBP), respiratory rate (RR), leucocytes, blood urea nitrogen (BUN) at baseline, Calcium Level, T-wave Changes, Prolonged Q-R Interval, left ventricular diastolic dysfunction (LVDD) at admission and left ventricular systolic dysfunction (LVSD) at admission were significant predictors of occurrence of complications among cases.

Age and sex couldn't significantly predict occurrence of complications among cases.

Table (5): Predictors of complication among cases: Multivariable logistic regression.

| Predictor | OR (95% CI) | P-value |
|-----------------------------------|------------------------|---------------|
| Age/years | 1.007 (0.968 – 1.035) | 0.671 |
| Sex (Female) | 0.661 (0.159 – 2.755) | 0.570 |
| Ranson Severity Score | 1.349 (1.002 – 3.248) | 0.006* |
| Diastolic blood pressure (mmHg) | 0.950 (0.905 – 0.997) | 0.038* |
| Respiratory rate (Cycle/min) | 1.106 (1.015 – 1.205) | 0.021* |
| Leucocytes (*10 ³ /ul) | 1.320 (1.012 – 1.722) | 0.040* |
| Baseline BUN (mg/dl) | 4.325 (1.211 – 8.435) | 0.024* |
| Calcium Level (mg/dl) | 0.135 (0.021 – 0.897) | 0.036* |
| T-wave Changes | 8.035 (1.783 – 18.216) | 0.007* |
| Prolonged Q-R Interval | 8.748 (1.801 – 14.479) | 0.012* |
| LVDD on Admission | 2.052 (1.099 – 4.551) | 0.031* |
| LVSD on Admission | 2.410 (1.082 – 5.021) | 0.043* |

P value was significant if <0.05. BUN: blood urea nitrogen; LVDD: left ventricular diastolic dysfunction; LVSD: left ventricular systolic dysfunction; OR: odd's ratio; CI: confidence interval.

Predictors of mortality among cases: Multivariable logistic regression (Table 6):

Female sex, comorbidity, Ranson Severity Score, leucocytes count, follow up blood urea nitrogen level, serum calcium Level, albumin, Basal deficit, ST segment elevation, and regional wall motion abnormalities (RWMA) Baseline can significantly predict occurrence of mortality among cases.

Table (6): Predictors of mortality among cases: Multivariable logistic regression.

| Predictor | OR (95% CI) | P-value |
|---------------------------------------|-----------------------|---------------|
| Age/years | 1.007 (0.968 – 1.035) | 0.671 |
| Sex (Female) | 0.512 (0.098 – 0.721) | 0.009* |
| Comorbidity | 3.021 (1.048 – 5.811) | 0.039* |
| Ranson Severity Score | 2.198 (1.055 – 4.147) | 0.024* |
| Leucocytes (*10 ³ /ul) | 1.502 (1.011 – 3.099) | 0.039* |
| Follow up blood urea nitrogen (mg/dl) | 3.008 (1.041 – 5.927) | 0.041* |
| Calcium Level | 0.672 (0.081 – 0.901) | 0.032* |
| Albumin | 1.221 (1.029 – 3.266) | 0.040* |
| ST Segment Elevation | 4.994 (1.068 – 7.155) | 0.012* |
| RWMA Baseline | 2.124 (1.061 – 3.086) | 0.042* |

P value was significant if <0.05. OR: odd's ratio; CI: confidence interval; RWMA: regional wall motion abnormalities.

DISCUSSION

The current study aimed to detect echocardiographic and ECG changes in acute pancreatitis patients and to investigate the impact of these changes on prognosis. It was conducted as prospective observational study on 50 patients with acute pancreatitis.

In the current study, the mean age of patients was 45.72 (SD 12.3) years. In agreement with this study **Thandassery et al.** ⁽⁵⁾ reported that the median age, 41 years; range 19–81 years. Also, mean age of acute pancreatitis patients in **Pon Raj** ⁽⁷⁾ study was 39.9 (SD 7) years. Other studies were consistent with these findings ^(8,9).

Among the study participants, 51.9% of them were females. The probable cause in the majority of the study patients was gall stone (42.6%). 25.9% had post-ERCP acute pancreatitis. Other less frequently found causes were malignancy, drug-induced, cryptogenic, viral, hyper-triglyceremia, alcohol consumption and hypercalcaemia.

In agreement with this **Kaya et al.** ⁽¹⁰⁾ found that biliary pancreatitis was the most common form (53%) among AP patients. **Prasada et al.** ⁽⁸⁾ found that of 65 acute pancreatitis patients, the etiology: was alcohol 47.7%, followed by gallstone disease 43.1%, and others 3%.

No comorbidities were detected in 40.7% of the current study patients. Diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD) and liver cirrhosis was found in 18.6%, 7.4%, 5.6% and 5.6% of the study patients. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were 121.76 (SD 18.1) mmHg and 81.67 (SD 12.8) mmHg, respectively. The mean pulse was 105.04 (SD 26.8) beat/min.

Also, **Prasada et al.** ⁽⁸⁾ reported that among patients with acute pancreatitis SBP was 128.62 (SD 20.35) mmHg and DBP was 78.83 (SD 9.78) mmHg ⁽¹¹⁾. Among the current study patients the most commonly ECG changes among the study patients were sinus tachycardia in 59.3%, T-wave changes in 31.5%, Prolonged Q-R Interval in 27.8%. Other less detected ECG changes were premature ventricular contraction, ST Segment Depression, PRWP, ST Segment Elevation, Bradycardia, atrial fibrillation and right bundle branch block 18.5%, 9.3%, 5.6%, 5.6%, 3.7% 1.9% and 1.9%, respectively ⁽⁸⁾.

In agreement with current findings, **Thandassery et al.** ⁽⁵⁾ found that Sinus tachycardia was the most commonly detected ECG change and AF was the least commonly found change among acute pancreatitis patients. **Rubio-Tapia et al.** ⁽¹¹⁾ reported that acute pancreatitis evokes changes in ECG from baseline in 55% of confirmed cases, the most common changes being nonspecific repolarization, sinus tachycardia, and left anterior hemiblock.

On the other hand, **Prasada et al.** ⁽⁸⁾ found that ECG abnormalities were observed in 40% of acute pancreatitis patients. A majority of them had ST segment depression

with T wave inversion, seen in 85% patients whereas 1.5% had atrial fibrillation.

Among this study, patients at admission 46.3% had increased cardiac index. About 44.4% had LV Diastolic Dysfunction (GI, GII and GIII in 22.2%, 20.3% and 1.9%, respectively). Pericardial effusion and right ventricular systolic dysfunction was found in 24.1% and 11.1%. At discharge LV diastolic dysfunction was found in 41.3%. Increased cardiac index was found in 28.3% and pericardial effusion in 13%.

This is also supported by **Thandassery et al.**⁽⁵⁾ study result, it was found that 38.9% of acute pancreatitis patients had diastolic dysfunction, while only 11.1% had Systolic Dysfunction and Mild pericardial effusion was seen in 8.3%. **Prasada et al.**⁽⁸⁾ reported that left ventricular systolic dysfunction (left ventricular ejection fraction <55%) was seen in 13.8% of patients with AP.

Nadkarni et al.⁽¹²⁾ have evaluated 52 patients with AP and found that whereas no patient had systolic dysfunction, 59.6% had diastolic dysfunction. All those who died had diastolic dysfunction. In the current study, the mean Ranson Severity Score of our patients was 2.69 (SD 1.3). The mean length of hospital stay was 8.39 (SD 1.6) days. About 53.7% of the patients had no complications. The most commonly found complications were acute kidney injury (AKI), pneumonia, septic shock and disseminated intravascular coagulopathy in 11.1%, 11.1%, 5.6% and 3.7%. The mortality rate was 14.8%.

On the other hand, among patients with AP in the study of **Prasada et al.**⁽⁸⁾ 43% had organ failure. Respiratory failure was present in 32.3% patients, AKI in 16.9% patients. According to **Pon Raj**⁽⁷⁾ study, pseudocyst, acute renal failure, pancreatic necrosis and multi organ failure was found in 37.5%, 25.0%, 25.0% and 12.5% of patients with AP, respectively.

Of fifty-four SAP patients enrolled in **Huang et al.**⁽¹³⁾ study, 32 patients had respiratory failure, 12 patients had acute renal failure, and 12 patients had both respiratory and renal failure. The mortality rate was 11%.

The present study showed that ECG changes; T-wave Changes and Prolonged Q-R Interval had significant association to the rate of complications. LV diastolic dysfunction and pericardial effusion at discharge had significant impact on the rate of complications. Although At discharge echocardiographic changes had no impact on the rate of complications.

In current study, Ranson Severity Score, diastolic blood pressure, respiratory rate, leucocytes, baseline blood urea nitrogen, calcium level, T-wave changes, prolonged Q-R interval, LV diastolic dysfunction on admission and LV systolic dysfunction on admission can significantly predict occurrence of complication among cases. This was supported by **Inal et al.**⁽¹⁴⁾ study.

Also, **Hagiwara et al.**⁽¹⁵⁾ detected that Ranson Severity Score is predictor of serious local complications in patients with SAP. Poor R wave progression (PRWP), ST segment elevation and T-wave changes had significant impact on mortality. Regional wall motion

abnormalities (RWMA) and LV diastolic dysfunction at admission had significant impact on mortality. Similarly, **Thandassery et al.**⁽⁵⁾ study has shown that left ventricular end diastolic volume, stroke volume index, cardiac index, and diastolic dysfunction predicted mortality in AP.

Nadkarni et al.⁽¹²⁾ have reported that in patients with AP. All those who died had diastolic dysfunction. Prolonged corrected QT interval, pericardial effusion and diastolic dysfunction are associated with higher mortality. Female sex, comorbidity, Ranson Severity Score, leucocytes, blood urea nitrogen follow up, calcium level, albumin, Basal deficit, ST segment elevation, RWMA baseline can significantly predict mortality among cases.

This can be supported by **Xu et al.**⁽¹⁶⁾ study results. Serum total bilirubin and albumin were independent predictors for SAP and in-hospital mortality in AP patients. Also, **Kaya et al.**⁽¹⁰⁾ found that base excess in AP patients has prognostic value for predicting both mortality and morbidity.

Senol et al.⁽¹⁷⁾ were able to identify risk factors on admission that predict mortality in AP patients (age, leucocytes count, platelet count, calcium level, blood urea nitrogen level, red cell distribution width (RDW), and albumin level). In contrast **Sharma et al.**⁽¹⁸⁾ reported that among AP patients females had a significantly lower likelihood of mortality.

In conclusion, echocardiographic and ECG changes in patients with AP have prognostic significance on morbidity and mortality. Future studies should help us to identify parameters of cardiac function that indicate poor outcome and strategies to correct cardiac dysfunction to improve overall outcome. Serial echocardiographic evaluations are needed in the future studies.

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