***Article Type:*** *Full Length Article*

# Evaluation of the Role of Pentraxin 3, B-type Natriuretic Peptide and Troponin I in Acute Carbon Monoxide Cardiotoxicity

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## Abstract

**Background**: Acute carbon monoxide induced cardiotoxicity is one of the main causes of mortality. It is considered as a poor prognostic factor in patients with carbon monoxide intoxication.Although early diagnosis of cardiac injury is often difficult and might be misdiagnosed.

This study aimed to assess the role of Pentraxin 3 and B-type natriuretic peptide in comparison with cardiac Troponin I as early predictors of cardiotoxicity in patients presented with acute CO poisoning.

**Methods**: Thirty patients with acute CO poisoning were recruited from PoisonControl Center, Ain Shams University Hospitals. Serum levels of Cardiac biomarkers (Pentraxin3, BNP and Troponin I) were measured on admission and after 10 hours after exposure.

**Conclusion:** Our results revealed that, B-type natriuretic peptide and Troponin I were more reliable cardiac biomarkers in early prediction of cardiotoxicity in acute CO poisoning patients.While Pentraxin3 had low sensitivity and specificity to predict the cardiotoxicity in acute CO poisoning in comparing with BNP and Troponin I.

***Key words****: Cardiotoxicity, acute carbon monoxide poisoning, BNP, Pentraxin 3, Troponin I.*

## Introduction

Carbon monoxide (CO) is a toxic gas known as "silent killer". It is produced as a resultof incomplete combustion of substances and fuels containing carbon atom. Exposure to factory and exhaust gases, breathing of fire smoke and exist in places where firewood and coal were burned with poor ventilation are the main causes of carbon monoxide poisoning [(2)].

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Despite the recent measures in prevention and treatment of CO poisoning, it is still one of the most common causes of mortality and morbidity, regardless of intentional or accidental exposure. Most of the cases are mainly intoxicated in winter season[(10)].

Carbon monoxide poisoning can lead to permanent tissue damage mainly to organs that require more oxygen and sensitive to hypoxia such as the brain, heart, kidneyand muscles through tissue hypoxia or direct cell damage [(3)].

Carbon monoxide competes with oxygen for hemoglobin binding site with affinity 250 times higher or more than oxygen, leading to shift of the oxyhemoglobin dissociation curve to the left with reduction of oxygen delivery to tissues [(4)].

Carbon monoxide causes cardiotoxicity through electrical, functional and morphological changes in the heart. Impaired cardiac function is usually related to acute myocardial ischemia or direct toxic effect on the myocardium with normal coronary arteries. Myocardial injury usually occurs in patients with moderate and severe CO poisoning. The presence of myocardial damage is a significant predictor of mortality[1].

Electrocardiography (ECG) and biochemical markers (such as: Troponin I (TnI), Creatine kinase-MB, ischemia-modified albumin, human fatty acid binding protein and B-type natriuretic peptide) are the proper keys to diagnose cardiac injury in patients with CO poisoning[12].

B-type natriuretic peptide (BNP) is a neurohormone that is released from the cardiac cells. Its elevation is a predictive marker for myocardial injury and heart failure[13]. ***Ismail et al.***[9] reported that, B-natriuretic peptide was a sensitive marker to identify cardiac dysfunction and was significantly increased in CO poisoning.

Pentraxin 3 (PTX3) is also a sensitive and specific biomarker for diagnosis of acute coronary syndromeand had an additional diagnostic value when measured in combination with cardiac enzymes.PTX3 is a member of CRP-like inflammatory protein group which is abundantly expressed in atherosclerotic plaques and cardiac myocytes.PTX3 level is significantly elevated in the acute stages of acute myocardial infarction and unstable angina even before the appearance of ECG changes[14].

Few studies were done to assess the role of Pentraxin 3 and BNP as cardiac biomarkers to predict the cardiotoxicity in patients with acute carbon monoxide poisoning. So this study aimed to assess the role of Pentraxin 3 and B-type natriuretic peptide in comparison with cardiac Troponin I as early predictorsof cardiotoxicity in patients presented with acute CO poisoning.

## Materials and Methods

**Study design and setting**:

This is a prospective cross sectional study which was conducted on 30 patients admitted to PCC-ASUH with moderate or severe acute CO poisoning during the period from the beginning of October 2018 to the end of March 2020.

**Patients:**

Thirty patients with acute CO poisoning were included in this study and 28 healthy persons were also included to measure serum level of cardiac biomarkersas a control group.

Diagnosis of acute CO poisoning was established according to the history of exposure, clinical characteristics of acute CO poisoning and confirmed by elevated blood carboxyhemoglobin (COHB) levels more than 5%.Moderate and severe carbon monoxide poisoning was diagnosed according to**Goldfrank**[6] classification.

**Mild**: headache, nausea, vomiting, dizziness, blurred vision.

**Moderate:**confusion, syncope, weakness, chest pain, dyspnea, tachycardia and tachypnea.

**Severe:**seizures, Coma, arrhythmias, Hypotension, myocardial ischemia, Cardiac arrest, Respiratory arrest, non-cardiogenic pulmonary edema and rhabdomyolysis.

The outcome in the current studyamong 30 acutely CO poisoned patientswas divided into survived and non-survived.

**Exclusion criteria:**

§ Patients with history of: cardiac diseases,renal impairment, respiratory diseases, malignant diseases and diabetes mellitus.

§ Patients admitted to the emergence department after receiving preconsulation treatment.

§ Mild cases of carbon monoxide poisoning, smokers, anemic or pregnant patients

§ Patients with history of chronic exposure to carbon monoxide as garage workers, fire fighter … etc.

**Methods:**

Venous blood about 5 cc were collected from 30

patients and 28 healthy persons(as a control group)under aseptic precautions.

Venous blood samples were drawn to measure serum levels of cardiac biomarkers(Pentraxin3, BNP and Troponin I) that were measured on admission (the first sample) and after 10 hours after exposure (the second sample).

## Results and Discussion

In the current study, comparison between the first and the second serum levels of cardiac biomarkers were done showing significate relation between the first and the second serum samples of Troponin I and BNP .While no relation was found between the first and the second serum samples of Pentraxin 3, as shown in figure (1) and (2) .

This result was nearly similar to a study done by ***Baydin et al.*** [2] which reported that, Pentraxin 3 had low prognostic role as cardiac biomarker to predict cardiotoxicity in acute CO poisoning in comparison with cardiac Troponin I.

On the other hand , other studies reported that Pentraxin 3 was more sensitive and specific biomarker during the first 3-6 hours after the onset of symptoms in comparison with cardiac Troponin I in acute CO toxicity[11], [14].

***Inoue et al.*** [8] reported that, Pentraxin 3 after 24 hours had a significant prognostic value than on admission to assess myocardial damage after acute CO poisoning.

In the current study, significate relation was found between the first and the second serum samples of cardiac biomarkers in acutely CO poisoning cases in comparison with the control group, as shown in table (1).

This result was similar to a study done by***Ismail et al.***[9] who reported that, cardiac Troponin I was significantly higher in acute CO poisoned patients compared to the control group.

Also ***Ezzat et al.*** [5] found that the mean serum levels of Pentraxin 3 was significantelevated in CO poisoned patients compared with the control group.

In the current study Receiver Operating Characteristic (ROC) curve was done to analyze the sensitivity and the specificity of the first and the second serum samples of cardiac biomarkers in predicting cardiotoxicity in acutely CO poisoned patients. Concerning the first serum samples of the cardiac biomarkers, it was found that the best cut off point of serum levels of Troponin I, Pentraxin 3and BNP were more than 0.8 ng/ml, 3 ng/ml and 160 ng/l respectively.

The cut off level of > 0.8 ng/ml of the first serum samples of Troponin I achieved 96.67% sensitivity and 85.71 % specificity. While, The cut off level of >3 ng/ ml of the first serum samples of Pentraxin 3 achieved 83.3 % sensitivity and 89.29 % specificity to discriminate between CO poisoning cases with cardiotoxicity and the control group , as shown in table (2).

As regards the first serum samples of BNP, it was found that cut off level >160 ng/ l achieved 96.6 % sensitivity and 100 % specificity. This cut off point had the best positive predictive value and negative predictive value to discriminate between CO poisoning cases with cardiotoxicity and the control group, in comparing with the first serum levels of Troponin I and Pentraxin 3, as shown in table (2) and figure (3) .

Concerning the second serum samples of cardiac biomarkers, it was found that the best cut off point of Troponin I, Pentraxin 3and BNP were >0.8 ng/ml, >3 ng/ml and >120 ng/l respectively.

The cut off level of > 0.8ng/ml of the 2nd serum samples of Troponin I achieved 50 % sensitivity and 100 % specificity to discriminate between CO poisoning cases with cardiotoxicity and control group, as shown in table (3).

The cut off level of >3 ng/ ml of the serum level of the second serum sample of Pentraxin 3 achieved 66.6 % sensitivity and 89.92 % specificity to discriminate between CO poisoning cases with cardiotoxicity and control group. As regard the second serum samples of BNP it was found that cut off level >120 ng/ l achieved 93.33% sensitivity and 82.14% specificity to discriminate between CO poisoning cases with cardiotoxicity and control group, as shown in figure (4).

The cut off level > 0.8 of the second serum samples of Troponin I had the best specificity to discriminate between CO poisoning cases with cardiotoxicity and control cases. Also,cut off level >120 ng/ l of the second serum samples of BNP had the best sensitivity to discriminate between CO poisoning cases with cardiotoxicity and control group, as shown in table (3).

On the contrary, other study compared the sensitivity and the specificity of Pentraxin3 with Troponin I to diagnosis acute myocardial injury using ROC curves. They found that Pentraxin3 had sensitivity and specificity (94 % and 86% respectively) for the diagnosis of acute myocardial injury than Troponin I (94% and 70% respectively). Also they reported that the area under the curve values for Pentraxin3 and Troponin I were 0.962 and 0.916 respectively[14].

***Lee et al.*** [12] the author reported that BNP is a good cardiac biomarker that can be correlated with the severity of symptoms and prognosis of cardiac injury in patients with CO toxicity. Also they concluded that BNP level >100 pg/mL had a sensitivity of 80% and a specificity of 68% in the detection of left ventricular systolic dysfunction (LVSD) in patients with acute CO toxicity.

As regard the outcome of acutely CO poisoned patients in the current study, no significant correlation was found between the cardiac biomarkers and the outcome of acutely CO poisoned patients.

***Inoue et al.*** [8] concluded that, the actual values of PTX3 and BNP on hospital admission were not significant correlated with short term mortality in acute CO poisoned patients, but had only moderate prognostic value for one year mortality.

**Limitations:**

This study also has some limitations. Small patient's size may affectthe results of our study. In addition, we could not performfollow-up for the patients after discharge.

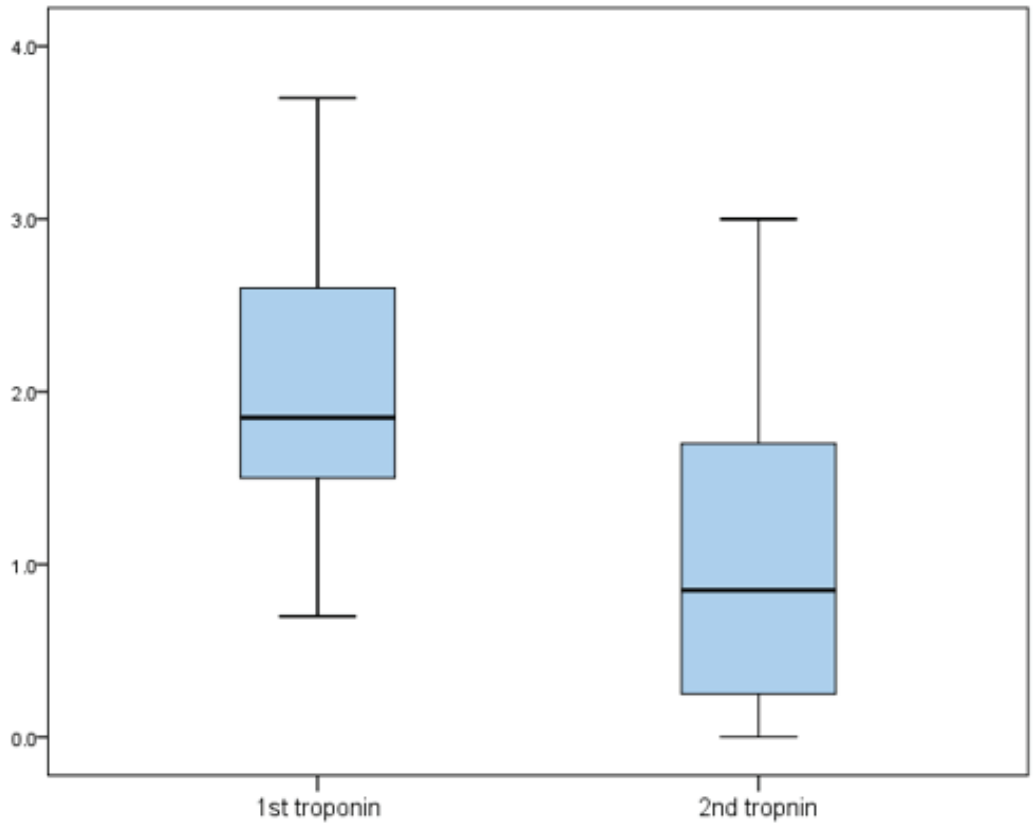


**Figure (1): Box and whisker plot of the relation between the first and the second serum samples of Troponin I of acute CO poisoning patients.**

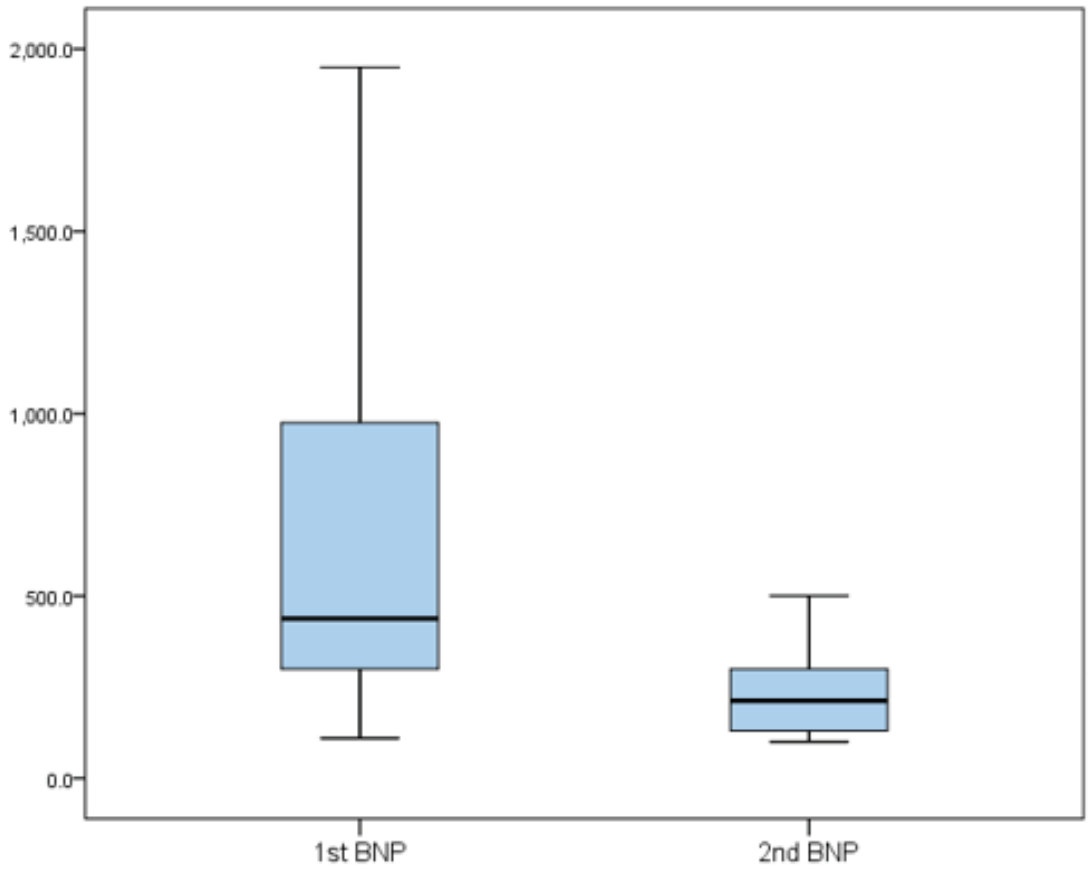


**Figure (2): Box and whisker plot of the relation between the first and the second serum samples of BNP of acute CO poisoning patients in the current**

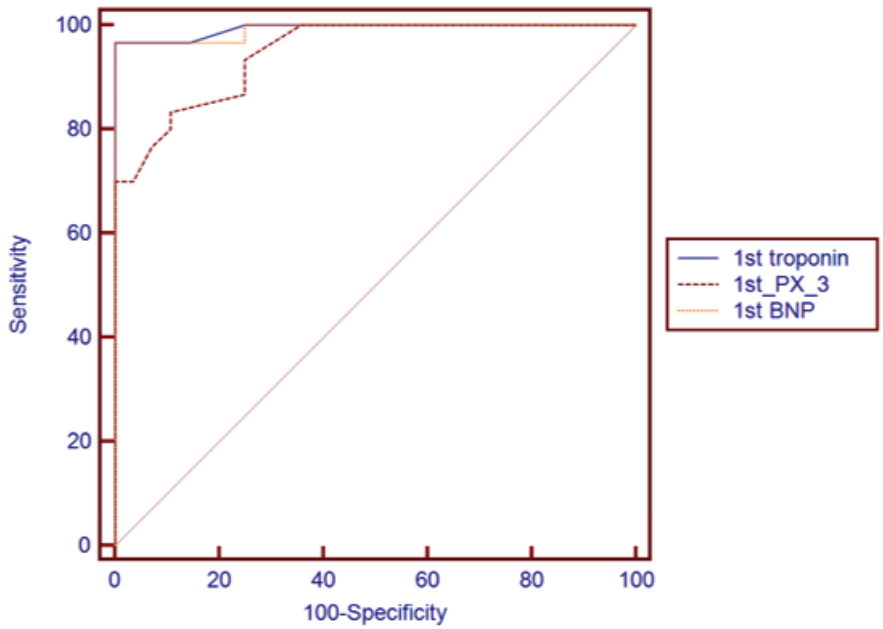


**Figure (3): ROC Curve displaying the diagnostic accuracy of the first serum sample of cardiac biomarkers in the current study.**

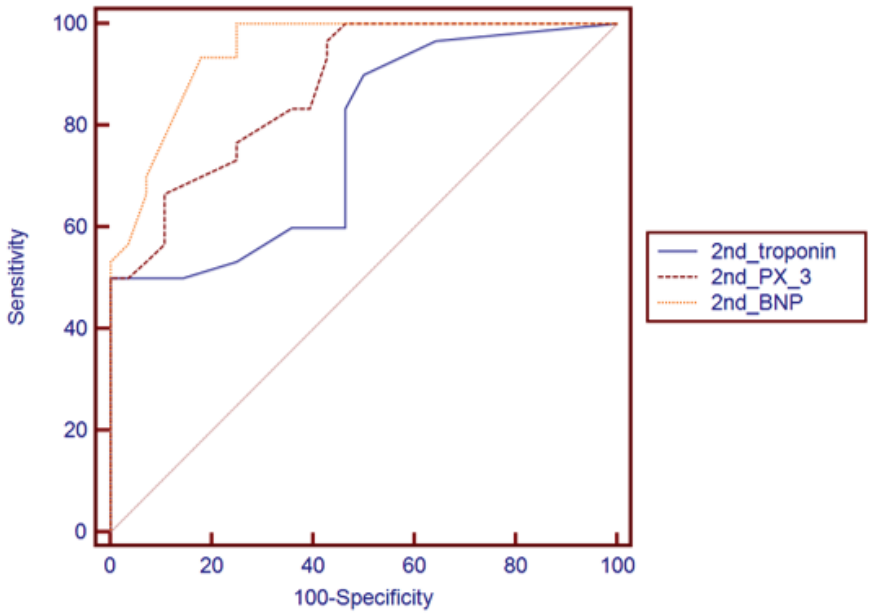


**Figure (4): ROC Curve displaying the diagnostic accuracy of the first serum sample of cardiac biomarkers in the current study.**

**Table (1): Mann Whitney test statistical analysis of the relation between the first and the second serum samples of the cardiac biomarkers among 30 acutely CO poisoned cases and control grouppresented to the PCC-ASUH during the period from the beginning of October 2018 till the end of March 2020.**

| | | Group A (Patients ) | Group B (Control group) | Test value ≠ | P-value |
|---|---|---|---|---|---|
| | | No.= 30 | No.= 28 | | |
| **The first serum sample (on admission)** | | | | | |
| Troponin I (ng/ml) | Median (IQR) | 1.85 (1.5 – 2.6) | 0.15 (0.15 – 0) | -6.472 | 0.000* |
| | Range | 0.7 – 5.5 | 0 – 0.8 | | |
| PTX3 (ng/ml) | Median (IQR) | 5.4 (4 – 8) | 1.05 (1.05 – 0.2) | -5.853 | 0.000* |
| | Range | 2.5 – 32 | 0.1 – 4.2 | | |
| BNP (ng/l) | Median (IQR) | 437.5 (300 – 975) | 20 (20 – 10) | -6.443 | 0.000* |
| | Range | 110 – 2250 | 5 – 160 | | |
| **The second serum sample (after 10 hours from exposure)** | | | | | |
| Troponin I (ng/ml) | Median (IQR) | 0.85 (0.25 – 1.7) | 0.15 (0.15 – 0) | -3.511 | 0.000* |
| | Range | 0 – 7 | 0 – 0.8 | | |
| PTX3 (ng/ml) | Median (IQR) | 4.25 (2.8 – 7) | 1.05 (1.05 – 0.2) | -4.896 | 0.000* |
| | Range | 1.2 – 24 | 0.1 – 4.2 | | |
| BNP (ng/l) | Median (IQR) | 212.5 (130 – 300) | 20 (20 – 10) | -5.857 | 0.000* |
| | Range | 100 – 500 | 5 – 160 | | |

P-value >0.05: Non significant (NS); P-value <0.05: Significant* (S) ,PTX-3: Pentraxin 3, BNP: B type natriuretic peptide .

**Table (2): Best cut off point of the serum levels of the first serum samples of cardiac biomarkers among 30 acutely CO poisoned patients presented to the PCC-ASUH during the period from the beginning of October 2018 till the end of March 2020.**

| Parameter | AUC | Cut off Point | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| First Troponin I (ng/ml) | 0.993 | >0.8 | 96.67 | 85.71 | 87.9 | 96.0 |
| First PTX3 (ng/ml) | 0.947 | >3 | 83.33 | 89.29 | 89.3 | 83.3 |
| First BNP (ng/l) | 0.992 | >160 | 96.67 | 100.0 | 100.0 | 96.6 |

PTX-3: Pentraxin 3, BNP: B type natriuretic peptide, AUC: area under curve. PPV: positive predictive value, NPV: negative predictive value

**Table (3): Best cut off point of the serum levels of the second serum samples of cardiac biomarkers among 30 acutely CO poisoned patients presented to the PCC-ASUH during the period from the beginning of October 2018 till the end of March 2020.**

| Parameter | AUC | Cut off Point | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| second Troponin I (ng/ml) | 0.767 | >0.8 | 50.0 | 100.0 | 100.0 | 65.1 |
| second PTX3 (ng/ml) | 0.874 | >3 | 66.67 | 89.92 | 87.0 | 71.4 |
| second BNP (ng/l) | 0.946 | >120 | 93.33 | 82.14 | 84.8 | 92.0 |

PTX-3: Pentraxin 3, BNP: B type natriuretic peptide, AUC: area under curve. PPV: positive predictive value, NPV:negative predictive value

## Conclusion

This study concluded that, the cut off level >160 ng/ l of the first serum samples of BNP had the best positive predictive value and negative predictive value to discriminate between CO poisoning cases with cardiotoxicity and the control group, in comparison with the first serum levels of Troponin I and Pentraxin 3.

The cut off level > 0.8 of the second serum samples of Troponin I had the best specificity to discriminate between CO poisoning cases with cardiotoxicity and the control group. Also cut off level >120 ng/ l of the second serum samples of BNP had the best sensitivity to discriminate between CO poisoning cases with cardiotoxicity and the control group.

No significant correlation was found between the outcome and the cardiac biomarkers of acutely CO poisoned patients.

The present study revealed that, BNP and Troponin I were more reliable cardiac biomarkers in early prediction of cardiotoxicity in acute CO poisoning patients .While

Pentraxin 3 had low sensitivity and specificity to predict the cardiotoxicity in acute CO poisoning in comparing with BNP and Troponin I.

**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Source of Funding:** Self

**Ethical Consideration:** Ethical approval was taken from the Research Ethical Committee of Faculty of Medicine, Ain Shams University, Egypt; Federal Wide Assurance No. FWA000017585. Written informed consent from every patient was obtained from the patients or their legal guardians.

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