Research Article

Short-Term Mortality Rates Rise among Patients with Elevated Cardiac Troponin I Levels Who were Discharged from Emergency Department

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Abstract

Objectives: In this study, we aimed to determine the mortality, readmission and cardiac intervention rates of the patients with elevated cardiac troponin I (cTnI) levels, who had no Acute Coronary Syndrome (ACS), and who were discharged from Emergency Department (ED).

Methods: The 28-day mortality rate of the patients with elevated cTnI levels, who were admitted to a university hospital ED within a 30-month period, and who were discharged from ED, was retrospectively investigated. The Control Group was consisted of the patients with normal/low cTnI levels and who were discharged from ED. Both groups were compared in terms of mortality, readmission and cardiac intervention rates within a 28-day period.

Results: 3,288 (1.5% of all ED admissions) of patients had elevated cTnI levels. 336 (10.2%) patients with elevated cTnI and without ACS were discharged from the ED. The mortality rate (7.1% *vs.* 0.5%, p=0.00), the readmission rate (34.2% *vs.* 6.2% p=0.00) and the mortality rate for short-term readmission (20.8% *vs.* 8.3% p=0.00) were found to be significantly higher in patients with elevated cTnI levels compared with the control group. However, there was no significant difference between the two groups in terms of cardiac intervention rate for readmissions (12.2% *vs.* 12.5%).

Conclusion: The results of our study show that the readmission rates and the mortality rates (especially due to heart failure) at readmission significantly increased in the patients with elevated cTnI levels compared to normal/low cTnI levels.

Keywords: Emergency Department; cTnI, Discharge

Introduction

Cardiac markers are used for diagnosis and risk assessment in patients with suspected Acute Coronary Syndrome. According to the European Society of Cardiology (ESC) and American College of Cardiology (ACC) guidelines, especially cardiac troponins (cTn) are accepted as standard markers in the diagnosis and treatment of Acute Coronary Syndrome (ACS) [1]. Elevation of these cardiac troponins is indicative of myocardial damage, but does not show the etiology of this injury [2,3]. There are a few clinical trials on the elevation of cardiac troponin I (cTnI) levels in blood under conditions except for ACS. In this study, we aimed to determine the 28-day mortality rate of the patients with elevated cTnI levels, who had no acute coronary syndrome, and who were discharged from the ED.

Methods

This is a cross-sectional case-control study in which the 28-day mortality rates, the re-admission rates and the cardiac intervention rates were compared in adult (>18 years) patients with high cTnI levels (the Case group) and with low cTnI levels (the Control group) who were admitted to a tertiary Emergency Medicine (ED) and then were discharged.

The Case group consisted of 354 patients with elevated cTnI levels (>0.3ng/ml) who had no ACS admitted to the ED within a 30-month period and who were discharged. For excluding ACS, past medical history, chest pain risk assessment, cardiac monitorization, serial ECG recordings (0, 30, 60, 90 and 120 min) and serial cTnI measurements (0 and 6 hour) were planned in the patients who were followed up with the suspicion of ACS in the ED. The Control group consisted of 354 randomly selected patients with normal/low cTnI levels (≤0.3ng/ml) who had similar demographic characteristics and were discharged from the ED. The cTnI assays of the patients were measured as high-sensitivity cardiac troponin (hs-cTn) in the central laboratory of the hospital. Eighteen (5%) patients who refused to participate in the study or whose 28-day follow-up data were not available were excluded from the study.

After the patients were discharged, their demographic and clinical information and cTnI values were obtained retrospectively from the hospital data system. Information about readmission within 28 days was obtained from the electronic records at the regional center of the Social Security Institution (SSI) which keeps records of all patients nationwide. Even patients die out of hospital, the death records of the patients are also kept regularly by the SSI. Patients were called
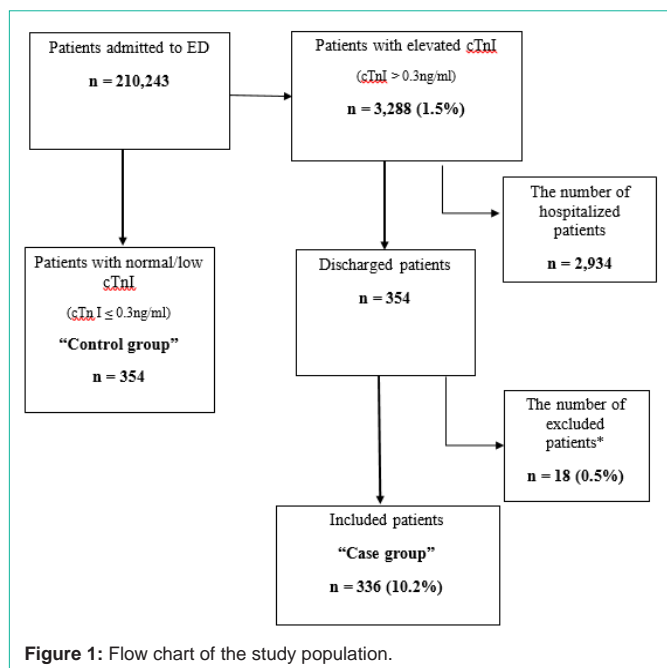
Figure 1: Flow chart of the study population.

Table 1: The demographic data of the patients.

Demographics	Case Group	Control Group	
Gender (Female)	181 (53.9%)	208 (58.8%)	P= 0.219
Mean Age (years)	73.2	62.7	
Minimum Age (years)	19	23	P= 0.001
Maximum Age (years)	105	93	
Standard Deviation	14.34	13.59	

Table 2: The complaints and findings on first admission and readmission.

Symptoms	First admission		Readmission	
	Case group	Control group	Case group	Control group
	n (%)†	n (%)	n (%)	n (%)
Chest pain	105 (31.3%)	112 (31.6%)	10 (8.7%)	0
Shortness of breath	75 (22.3%)	53 (15%)	13 (11.3%)	1 (4.1%)
CHF	28 (8.3%)	3 (0.9%)	34 (29.5%)	1 (4.1%)
Palpitation	27 (8%)	43 (12.1%)	6 (5.2%)	2 (8.3%)
Syncope	25 (7.4%)	43 (12.1%)	3 (2.6%)	3 (12.5%)
Epigastric pain	20 (6%)	60 (17%)	2 (1.7%)	5 (20.8%)
Others*	56 (16.7%)	40 (11.3%)	47 (40.8%)	12 (50.0%)
Total	336	354	115 (34.2%)‡	24 (6.7%)‡
	(p=0.089)		(p=0.001)	

CHF = Congestive Heart Failure
* Complaints related to other non-cardiac causes (Pneumonia, Cerebrovascular event etc.)
† Column percentage, ‡ Row percentage

twice by telephone to determine whether they readmitted to another institution. Patients whose data were not available were excluded from the study.

Statistical analysis of the data was performed using the IBM SPSS Statistics Version 15 Software Package (IBM SPSS, Inc., the USA). The Student's t-test was used to calculate the parametric variables and Mann-Whitney U test an Chi-square tests were used to calculate the non-parametric variables. Ethical approval was obtained from the Local Ethics Committee for Non-Interventional Studies.

Results

A total of 210,243 patients were admitted to the ED during the 30-month study period. Of all ED admissions, 3,288 (1.5%) of patients had elevated cTnI levels and 354 (10.7%) of them without a diagnosis of ACS were discharged from the ED. A total of 336 (10.2%) patients were included in the study (Case group) (Figure 1).

There was no significant difference between the Case and Control groups in terms of gender. However, the patients in the Case group were significantly older (Table 1).

The readmission rates were significantly higher in Case group than Control group (34.2% *vs.* 6.7%, p=0.001), respectively (Table 2). At the first admission to the ED in the Case group, the most common complaints of the patients were chest pain, shortness of breath and heart failure symptoms (31.2%, 22.3% and 8.3%, respectively) where in the Control group they were chest pain, abdominal pain and shortness of breath (31.6%, 17% and 15%, respectively). However, there was no significant relationship between the initial complaints in both groups (p=0.089).

In the Case group, 40.8% of readmitted patients were found to have non-cardiac complaints and the most common cardiac complaint was heart failure (29.6%). However, non-cardiac causes were frequently observed (50%), and the most common non-

cardiac complaint was epigastric pain (20.8%) in the Control group. According to the findings at readmission, cardiac symptoms were significantly common in the Case group (p=0.001) (Table 2).

The mortality rates were significantly higher in Case group than Control group (20.8% *vs.* 8.3%, p=0.001). In the Case group; two (0.5%) patients died on the first day and 22 (19.1%) died between 2-28 days among the readmitted patients; one had Chronic Obstructive Pulmonary Disease (COPD) and one had Congestive Heart Failure (CHF) died on the first day, and the rest of patients with CHF (n=12), chest pain (n=3), shortness of breath (n=2), cancer (n=2), syncope (n=2) and dizziness (n=1)) died on other days. CHF was not only the most common (29%) diagnosis but also the most common (38.2%) mortality reason among readmitted patients. In the Control group; no patients died on the first day, and only 2 (8.3%) died between 2-28 days among the readmitted patients; among these, one had malignancy and the other had sepsis. There was no death among the patients in both groups who had readmitted to another ED in 28-day period (Table 3).

When analyzed in terms of mortality and age, the median age was 80.5 years in the patients who died within a 28-day period and was 67 years in the patients who did not die within a 28-day period. This value was found to be high at a statistically significant level (p=0.001).

Fourteen (12.2%) of the 115 readmitted patients underwent PCI and only one (0.9%) received intravenous (IV) thrombolytic treatment in the Case group and three (12.5%) patients underwent PCI in the Control group. The one and only patient who received

Table 3: The mortality rates for readmissions.

Mortality	Readmission	
	Case Group n=115	Control Group n=24
	n (%)*	n (%)*
Mortality on the day 1	2 (1.7%)	0
Mortality between 2nd and 28th days	22 (19.1%)	2 (8.3%)
Total	24 (20.8%)‡	2 (8.3%)‡
	(p=0.001)	

* Column percentage, ‡ Row percentage

Table 4: Cardiac interventions performed at readmissions.

Cardiac interventions	Case group	Control group
	n (%)*	n (%)*
Percutaneous Coronary Intervention	14 (12.2%)	3 (12.5%)
IV thrombolytic treatment	1 (0.9%)	0
No intervention	100 (86.9%)	21 (87.5%)
Total	115	24
	(p=1.00)	

*= Column percentage

IV thrombolytic treatment in the Case group had acute pulmonary embolism (Table 4). However, there was no significant difference in terms of cardiac interventions at readmissions between the two groups (12.2% *vs.* 12.5%, p=1.00).

Discussion

In this study, we found that the mortality and the readmission rates were significantly higher in Case group than Control group (20.8% *vs.* 8.3%, p=0.001) and (34.2% *vs.* 6.7%, p=0.001), respectively,

According to the international guidelines, cardiac troponins are accepted as standard markers for the diagnosis and follow-up of patients with ACS [4]. Although cardiac troponins are sensitive and specific markers for the presence of myocardial cell necrosis, they are not specific about the etiology of the necrosis. There may be many reasons for cardiac troponins to rise without acute plaque rupture and to be associated with mortality. cTn elevation is an independent risk factor in many different patient populations such as heart failure [5], arrhythmia [6], pulmonary embolism [7], chronic obstructive pulmonary disease [8], renal failure [9], sepsis [10], and intracranial hemorrhage [11]. Moreover, cTn elevation was shown to be an indicator of high-risk mortality even in a healthy population outside the hospital [12].

However, there are not many studies on the follow-up and prognosis of patients with elevated cTnI levels who had been discharged from ED. In an Italian study, patients who were discharged from ED with high cTnI levels and controls with low cTnI levels were compared in terms of the mortality, readmission and hospitalization rates. Accordingly, the 30-day mortality rate was significantly higher in the patients with high cTnI levels compared to the patients with low cTnI levels (37.2% *vs.* 19.1%, p<0.01) [13]. In another study carried out in Canada, 172 patients with high cardiac troponins (either cTnI or cTnT) levels who were discharged from ED and 172 controls with low cardiac troponins levels were compared. Similarly, there was a significant increase in the mortality (17% *vs.* 8%, p=0.01)

and hospitalization rates (51% *vs.* 25%, p<0.01), but no significant increase in the 1-month readmission rate [14].

Also, Bardaji et al reported in Spain that the 1-year readmission rates for heart failure (8% *vs.* 1.8%, p<0.01) and 1-year mortality rates (30.2% *vs.* 4.7%, p<0.01) were significantly higher in 212 patients with elevated cTnI levels who had no ACS compared to 681 patients with normal cTnI levels [15].

We conducted this study with the highest number in cohort groups compared to groups with previously conducted studies in Italy, Canada and Spain. The median age of the 336 patients with high cTnI levels who were discharged from the ED was 70. They were demographically similar to the patient groups in previous studies and were older than the patients with normal cTnI levels. The rate of women was higher in our study according to previous studies (53.9%, *vs.* 38% and 49.5%) [14,15].

The most common initial complaint among patients with high cTnI levels who were discharged from ED was chest pain (31.3%). In the study of Bardaji et al, chest pain was seen at 6.6% and non-cardiac complaints were seen at 44% in the patients with elevated troponin levels who had no ACS and were discharged from ED. Brunner et al found that without specifying the admission complaints, the most frequent diagnoses at discharge were nonspecific chest pain (18%) and heart failure (8%), respectively. Discharge diagnoses were not examined individually in our study. However, when the initial complaints of the patients were compared with the complaints of the patients during short-term readmissions, it was found that the rate of non-cardiac complaints increased from 16% to 50.4%, and the rate of chest pain decreased from 31.3% to 8.7%. A similar relationship was observed in the Control group; the rate of cardiac complaints decreased from 88.7% to 41.6% and chest pain from 31.7% to zero, from first admission to readmission in 28 days. There was no significant difference between the both groups in terms of PCI rate for readmissions (12.2% vs. 12.5%).

These findings reveal that patients in both groups are more likely to readmit due to other reasons than ACS. When examining what these causes might be; we have observed that the most common diagnosis for the deaths at readmission was heart failure (54%), which was responsible for 13 out of 24 deaths in the Case group. However, the two patients in the Control group who one had malignancy and the other had sepsis, died at readmission.

There are studies in the literature showing that heart failure and cardiac troponin elevation are associated with mortality. In a study of Braga et al., among the patients with elevated cTn levels who had no ACS and were discharged from ED, there were a 9.7-fold increase in 30-day mortality rates, a 5.14-fold increase in cardiovascular readmissions and a 13.08-fold increase in hospitalizations due to ischemic heart disease [16]. The researchers have indicated that high cTn levels in patients with acute heart failure are associated with death and hospitalization due to cardiac reasons.

Diagnostic protocols that include different follow-up times are used for excluding ACS diagnosis in patients admitted to ED. It is stated that these patients can be safely discharged at the end of 2 or 3-hour follow-up using high-sensitivity cardiac troponin (hs-cTn) assays thanks to the Accelerated Diagnostic Protocols (ADP). In a

recent study on excluding AMI, it was reported that the 12-month mortality of the patients discharged according to the 1-hour protocol was comparable to that of the patients discharged according to the 3-hour protocol [17]. However, in a similar study conducted by the same author on making AMI diagnosis, it was also reported that hs-cTn elevation alone did not make a significant difference for the 1- and 3-hour protocols, but a significant value was reached with the addition of ECG findings. In another study using the Acute Cardiac Care Rule-In Algorithm (ESC-rule-in) of the European Society of Cardiology (ESC) Working Group, it was shown that hs-cTn had a good PPV value with the 3-hour protocol but may be insufficient for excluding the diagnosis. All these studies demonstrate that cTn elevation could not reach a 100% PPV for making the diagnosis or a 100% NPV for excluding the diagnosis in either standard assays or hs-cTn assays in ED. The curiosity about the short-term mortality of the patients who are admitted with chest pain and who are discharged from ED continues. In a recently published study comparing high-sensitivity cardiac troponin (hs-cTn) and soluble suppression of tumorigenicity 2 (sST2), it was reported that sST2 had a higher prognostic value [18].

As a result, our study show that the readmission rates and the mortality rates (especially heart failure) in the 28-day period after ED discharge increased in the patients with elevated cTnI levels compared to the patients with normal/low cTnI levels

Limitations

The first limitation of this cross-sectional case-control study was that the diagnostic coding in the discharged patients was usually based on symptoms instead of specific ICD-10 diagnostic codes. This limitation was also appeared at the institutions to which they had readmitted. For example, of the three patients who died at readmission, two were coded as syncope and one was coded as dizziness. These patients could have died due to arrhythmia. We have not been able to specifically identify the final diagnoses of these patients because of inadequate recordings.

The second limitation was that we did not know whether these patients had elevated cTnI levels due to really ACS or another cause because the specific diagnoses of the patients who had elevated cTnI were not followed further in the hospital admissions.

Another limitation was that, we could not gather detailed retrospective data on the severity of heart failure at hospital admission and/or before discharge. According to the results of this study, this prevented us from establishing a strong and definite connection between short-term mortality due to a new heart failure attack or acute decompensation and cTnI elevation.

Finally, although cTnI measurement every 6 hours was foreseen for excluding ACS in patients admitted to the ED, retrospective screening revealed that some patients were assessed with serum cTnI levels taken at shorter or longer intervals. These patients were not excluded from the study. Therefore, our data should not be interpreted and evaluated with the Accelerated Diagnostic Protocols (ADP).

In conclusion, the results of our study show that the readmission rates and the mortality rates at readmission (especially due to heart

failure) significantly increased in the patients with elevated cTnI levels compared to the patients with normal cTnI levels.

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