Original Article

Cardiac Troponin Variation Trends in Patients With Acute Pulmonary Embolism

Mohammad Mehdi Peighambari[1], MD; Mohammad Javad Alemzadeh-Ansani[1*], MD; Golnoush Yaghoubzadeh[2], MD; Sepideh Masteri Farahani[2], MD

ABSTRACT

Background: Pulmonary embolism (PE) is among the deadliest diseases in that it can cause sudden death. The present study aimed to determine cardiac troponin I (CTnI) variation trends in patients with acute PE referred to Rajaie Cardiovascular Medical and Research Center.

Methods: This cross-sectional descriptive-analytical study consecutively enrolled 54 patients with acute PE. Variation trends of CTnI were measured in the study population at 5 different time points: upon admission and subsequently 8, 24, 48, and 72 hours post-admission. The relationships between CTnI variation trends and computed tomography angiography, echocardiography, and electrocardiography findings were investigated. CTnI variation trends were compared between a group undergoing catheter-directed thrombolysis (CDT) and a group receiving the conventional anticoagulant treatment. The data were analyzed using the SPSS software, version 20.

Results: A reduction was observed in the CTnI variation trends of all the samples. Both groups exhibited a decline in CTnI levels, but the slope of this reduction was steeper in the CDT group (P=0.04). Additionally, a significant relationship was also detected between CTnI reduction and right ventricular function improvement (P=0.04). No significant association was observed between systolic pulmonary artery pressure changes and CTnI variation trends.

Conclusions: The results indicated a significant relationship between reduced CTnI levels and improved right ventricular function. Additionally, the CDT group showed a significant fall in the CTnI level compared with the anticoagulant-only group. ***(Iranian Heart Journal 2022; 23(1): 198-204)***

KEYWORDS: Pulmonary thromboembolism, Anticoagulant, Cardiac troponin I

[1] Cardiovascular Intervention Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

*** Corresponding Author:** Mohammad Javad Alemzadeh-Ansani, MD; Cardiovascular Intervention Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
Email: mj.aansari@gmail.com **Tel:** +982123922071

Received: November 24, 2020 **Accepted:** March 28, 2021

Acute pulmonary embolism (PE), myocardial infarction, and stroke constitute the 3 major cardiovascular mortality factors that can sometimes result in syncope due to right ventricular (RV) dysfunction. [1] In addition, delays in the presentation can increase RV dysfunction and in-hospital mortality. [2] It is, therefore, essential to determine the degree of RV dysfunction in patients suffering from acute PE. Such dysfunction can be determined through clinical examinations indicating an increased pressure on the right side such as distended jugular veins, right-sided S3 gallops, and enhanced P2 sounds. Moreover, electrocardiography (ECG) can illustrate the tension in the RV leading to the emergence of various ECG symptoms such as T-wave inversions in leads V_1–V_4, S1Q3T3 patterns, and right bundle branch blocks. [3] Cardiac troponin I (CTnI) is a sensitive marker for the risk stratification and management of patients with PE similar to other types of myocardial injuries. Various studies have shown the usefulness of CTnI measurement for risk determination in unstable angina and myocardial infarction; there are, however, some controversies regarding the efficacy of such measurements in patients with PE. [4-6]

The results of a previous investigation indicated no relationship between PE severity and high CTnI levels. [7] Elsewhere, PE, pericarditis, and myocarditis were determined as the most important factors associated with increased non-coronary CTnI in the emergency department. [7-9] Further research showed that enhanced levels of CTnI could be the first and most reliable marker of RV dysfunction, and no significant difference was observed in the echocardiography results of patients with PE and increased or normal CTnI levels. [10]

In this regard, the current study aimed to determine CTnI variation trends in patients with acute PE in Rajaie Cardiovascular Medical and Research Center (RHC) in the Iranian capital, Tehran. Additionally, CTnI level changes were compared between a group undergoing catheter-directed thrombolysis (CDT) and a group receiving the conventional anticoagulant treatment.

METHODS

This cross-sectional descriptive-analytical study recruited 60 consecutive patients with acute PE symptoms whose PE diagnosis was established by pulmonary computed tomography (CT) angiography in RHC.

The inclusion criteria were age older than 18 years and the clinical suspicion of acute PE confirmed by pulmonary CT angiography. The exclusion criteria were surgery for clot removal and systemic thrombolytic medication. Patients were sequentially enrolled in this study. After the implementation of the inclusion and exclusion criteria, the study population underwent echocardiography and CT angiography for PE and risk stratification, and the findings were interpreted by an expert radiologist. The patients were divided into a CDT group and an anticoagulant group. Aside from demographic characteristics, the subjects' symptoms, vital signs, and ECG results were recorded daily. CTnI variation trends were recorded at 5 different time points: upon admission, 8 hours later, and then every 24 hours for both groups. Finally, the relationships between CTnI variation trends and echocardiography, CT angiography, and ECG findings were assessed according to information sheets. CTnI variation trends were also compared between the CDT group and the anticoagulant-only group.

The study protocol was approved by the Ethics Committee of RHC (No: IR.IUMS.REC1395.9311171040).

Statistical Analysis

The data were analyzed using the SPSS software, version 20, via the χ^2 test, the

Fisher exact test of independence, and logistic regression tests. A *P* value of 0.05 was considered statistically significant. The quantitative findings were reported as the mean and the standard deviation, and the qualitative findings were reported as frequencies.

RESULTS

In this case series study, 60 patients with suspected PE referred to our center were evaluated. The diagnosis of PE was established via CT angiography. Six patients were excluded: 4 underwent surgery for clot removal and 2 received systemic thrombolytic medication. The remaining 54 patients were composed of 30 (55.5%) men and 24 (44.5%) women. Thirty-five patients received thrombolytic treatment, whereas 19 patients received only anticoagulants. The baseline data of the study population are presented in Table 1.

CTnI variation trends for both groups were recorded at 5 different time points: upon admission, 8 hours post-admission, and thereafter every 24 hours (Table 2). CTnI variation trends among the CDT group showed a statistically significant descending trend (*P*=0.009). Both groups exhibited a decline in CTnI levels, but the reduction slope was steeper in the CDT group (*P*=0.04) (Fig. 1).

Among the 54 studied patients, 9 were diagnosed with massive PE. Although the initial level of CTnI was high in the patients with massive PE by comparison with the other patients, their CTnI variation trends demonstrated a steeper slope following treatment. Nonetheless, no significant relationship was observed between the variation trend of CTnI and massive PE (*P*= 0.1).

According to Figure 2, the CTnI level of the patients with the S1Q3T3 pattern in ECG was higher than that in those without this ECG symptom. After treatment, CTnI variation trends in this group exhibited a higher slope. Thus, the relationship between the appearance of the S1Q3T3 pattern and CTnI variation trends was statistically meaningful (*P*=0.04).

As is demonstrated in Table 3, a significant relationship existed between CTnI variation trends and RV function (odds ratio [OR], 1.38; 95% confidence interval [CI], 1.01 to 1.04; *P*=0.04). Based on this table, no significant relationship was observed vis-à-vis CTnI variation trends and RV function changes between the CDT group and the anticoagulant-only group (OR, 1.1; 95% CI, 0.6 to 2.2; *P*=0.5). In addition, CTnI variation trends and the changes in systolic pulmonary artery pressure (SPAP) were not significantly associated with each other (OR, 0.13; 95% CI, −2.8 to 3.1; *P*=0.9). As SPAP changes are time-consuming and do not tend to exhibit a significant difference within 72 hours, this result was somehow predictable.

Table 1. Frequency of pulmonary embolism risk factors

Variables		Anticoagulant (n=19 pts)	CDT (n=35 pts)	*P* value	Total (N=54 pts)
Mean age		54.3 ± 5.74	62.3 ± 7.21	0.071	59.5 ± 6.06
Sex	Male	9 (16.5%)	21 (39%)	0.391	30 (55.5%)
	Female	10 (18.5%)	14 (26%)	0.391	24 (44.5%)
Prior PE		0	1 (1.8%)	0.179	1 (1.8%)
Immobilization		6 (11%)	9 (16.5%)	0.025	15 (27.5%)
Major surgery		3 (5.6%)	1 (1.8%)	0.627	4 (7.4%)
Recent hospitalization		2 (3.7%)	4 (7.3%)	0.096	6 (11%)
OCP		3 (5.6%)	1 (1.8%)	0.627	4 (7.4%)

Cancer		1 (1.8%)	1 (1.8%)	0.179	2 (3.6%)
Trauma to limbs		1 (1.8%)	4 (7.3%)	0.031	5 (9.1%)
Cigarette smoker		2 (3.7%)	5 (9.3%)	0.650	7 (13%)
HTN (systemic arterial)		7 (13%)	3 (5.5%)	0.647	10 (18.5%)
DM		7 (13%)	2 (3.5%)	0.248	9 (16.5%)
DLP		8 (14.8%)	3 (5.5%)	0.642	11 (20.3%)
Mean creatinine		1.47 ± 0.35	1.02 ± 0.38	0.056	1.18 ± 0.37
Mean Hb (mg/dL)		13.5 ± 2.6	14.4 ± 2.9	0.046	14.09 ± 2.8
RV dysfunction	Mild	4 (7%)	7 (13%)	0.482	11 (20%)
	Mild to moderate	7 (13%)	5 (9%)	0.482	12 (22%)
	Moderate	5 (9%)	6 (11%)	0.482	11 (20%)
	Moderate to severe	2 (5%)	4 (7%)	0.482	6 (12%)
	Severe	3 (6%)	11 (20%)	0.482	14 (26%)
Mean SPAP (mm Hg)		50.4 ± 14.21	44.5 ± 13.61	1.245	46.6 ± 13.76

CDT, Catheter-directed thrombolysis; PE, Pulmonary embolism; OCP, Oral contraceptive pill; Hb, Hemoglobin; HTN, Hypertension; DM, Diabetes mellitus; DLP, Dyslipidemia; RV, Right ventricular; SPAP, Systolic pulmonary artery pressure

Table 2. CTnI variation trends (mean value) in the CDT and anticoagulant-only groups

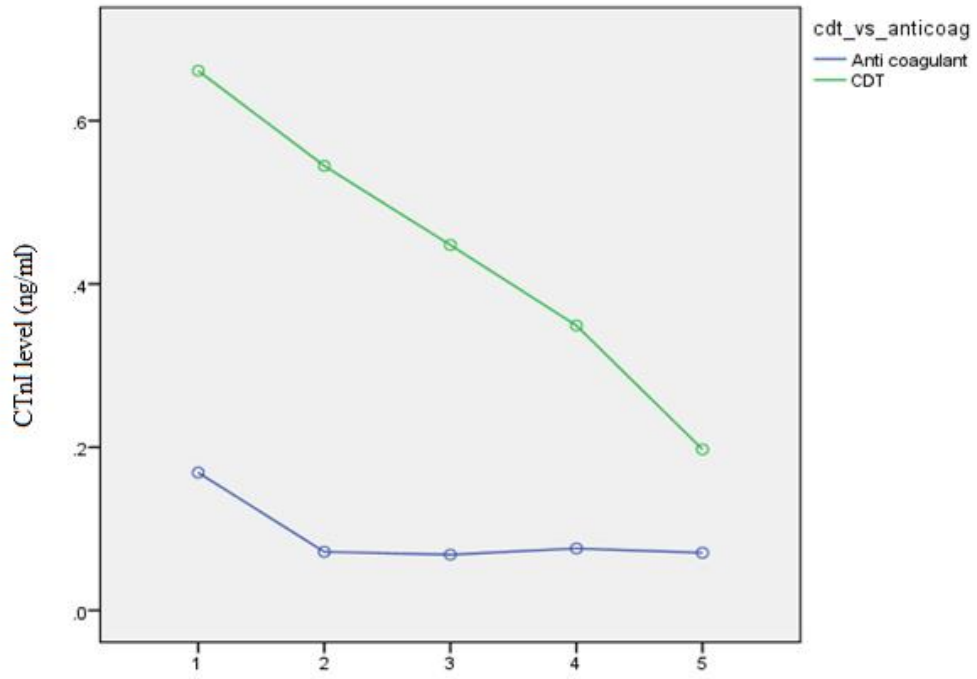
CTnI (ng/mL)	Anticoagulant (n=19 pts)	CDT (n=35 pts)	*P* value	Total (N=54 pts)
Time of admission	0.61 ± 0.20	0.45 ± 0.19	0.04	0.56 ± 0.19
8 h later	0.47 ± 0.17	0.40 ± 0.13	0.02	0.44 ± 0.16
24 h later	0.36 ± 0.13	0.32 ± 0.11	0.02	0.35 ± 0.12
48 h later	0.27 ± 0.09	0.24 ± 0.09	0.01	0.26 ± 0.09
72 h later	0.16 ± 0.06	0.15 ± 0.06	0.00	0.16 ± 0.06

CTnI, Cardiac troponin I; CDT; Catheter-directed thrombolysis

Table 3. Relationships between CTnI variation trends and SPAP changes and RV function

	OR	*P* value	95% CI	
RV function DIFF CTnI	1.38	0.04	1.01	2.04
RV function DIFF CTnI CDT vs Anticoagulant	1.1	0.5	0.6	2.2
SPAP DIFF CTnI	0.13	0.9	-2.8	3.1

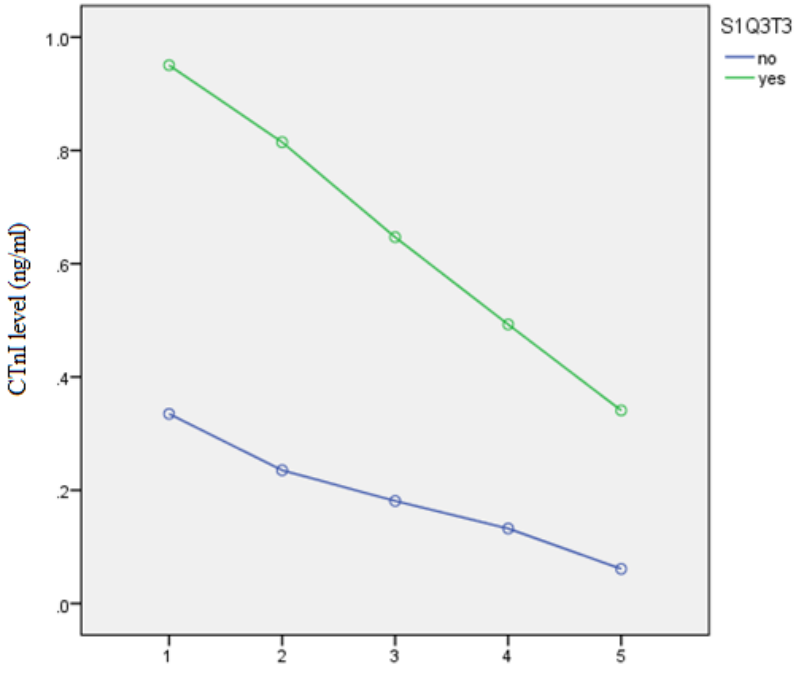
RV, Right ventricle; CTnI, Cardiac troponin I; CDT, Catheter-directed thrombolysis; SPAP, Systolic pulmonary artery pressure



Time points (1: at the time of admission; 2: 8 hours later; 3: 24 hours later; 4: 48 hours later; and 5: 72 hours later)

Figure 1. Variation trends of CTnI in the patients treated with CDT and those receiving anticoagulants are illustrated herein. Both groups exhibited a decline in the CTnI level, but the CDT group showed a more pronounced decrease as the slope of the CTnI reduction was higher in these patients (*P*=0.04).

CTnI, Cardiac troponin I; CDT, Catheter-directed thrombolysis



Time points (1: at the time of admission; 2: 8 hours later; 3: 24 hours later; 4: 48 hours later; and 5: 72 hours later)

Figure 2. Variation trends of CTnI in the patients with the ECG appearance of the S1Q3T3 sign compared with the trends in those with a normal ECG are illustrated herein. The CTnI level of the patients with the S1Q3T3 pattern was higher than that of the patients not exhibiting this ECG symptom. After treatment, the variation trend of this group exhibited a higher slope. Moreover, a significant relationship was detected between CTnI variation trends and the appearance of the S1Q3T3 pattern (*P*=0.04).

ECG, Electrocardiography; CTnI, Cardiac troponin I

DISCUSSION

The present case series study was conducted on 54 patients with acute PE referred to RHC. CTnI variation trends exhibited a descending pattern in the entire study population; this decline, however, had a steeper slope in the CDT group than in the anticoagulant-only group. CTnI variation trends in the 2 groups were assessed via echocardiography concerning SPAP and RV function and ECG regarding symptoms such as the S1Q3T3 pattern. The results indicated a significant relationship between declined CTnI variation trends and RV function improvement (*P*=0.04), although this relationship was not significant when the CDT and anticoagulant-only groups were compared.

SPAP changes and CTnI variation trends showed no significant relationship, which can be attributed to the time-consuming nature of SPAP variations. (SPAP does not show a significant difference within 72 hours.) The decline in CTnI levels occurred at a high rate among the patients with the S1Q3T3 pattern by comparison with the patients without this ECG symptom. This finding reflects the higher efficacy of the treatment in these patients.

Meyer et al [11] reported that more than one-third of their patients with a clinical diagnosis of PE exhibited enhanced CTnI levels, with the levels being higher among those with more segmental defects in the lung scan.

In another investigation in 2006 by Amorim et al [12] on 54 patients with PE, CTnI levels were elevated in 42 cases. Among patients with RV dysfunction, an 85% increase was observed in CTnI levels, while only a 35% increase was detected among those without RV dysfunction. Additionally, troponin-positive patients showed faster symptom emergence (24 h vs 144 h; *P*=0.02). The authors concluded that proximal artery embolism was more probable among troponin-positive patients.

In a study published in 2009 in Iran, the echocardiographic signs of RV dysfunction were observed in 1 out of 2 and 15 out of 40 troponin-positive and troponin-negative patients, respectively. No association was found between RV dysfunction and CTnI levels, which can be attributed to blood sampling immediately after embolism diagnosis and only a single measurement. [13]

A study in 2009 declared that increased CTnI levels were associated with a higher risk of in-hospital mortality and complications. [14]

In 2012, Gonca et al [15] evaluated 106 patients with suspected PE and established the disease in 63 cases. High CTnI levels were detected in 50% of the patients with PE and 11.6% of those without PE. The sensitivity and selectivity of CTnI in PE diagnosis were 50.7% and 88.3%, respectively. The ECG findings of the patients with PE with high or normal CTnI levels were similar, and about 75% of the patients with PE who had high CTnI levels had normal ECG findings. The most common pathologic variation was the S1Q3T3 pattern (≈31%). Moreover, Gonca and colleagues found no statistically significant difference apropos of transthoracic echocardiography findings among the patients with normal and increased CTnI levels.

A study in 2013 revealed that CTnI, in combination with the pulmonary embolism severity index (PESI), could provide better information for the prediction of early death in patients suffering from PE. [16]

Further studies are required to investigate whether the variation trend of CTnI, alone or in combination with other test factors, can be a proper guide to enhance treatment designs and prognoses in patients with PE. The inadequate recruitment of patients due to financial constraints and the assessment of CTnI levels only at 5 time points (the last one, 82 hours after diagnosis) were among the limitations of the current study.

REFERENCES

1. Jenab, Y., Lotfi-Tokaldany, M., Alemzadeh-Ansari, M.-J.Email Author, Seyyedi, S.R., Shirani, S., Soudaee, M., Ghaffari-Marandi, N., Correlates of Syncope in Patients with Acute Pulmonary Thromboembolism, Clinical and Applied Thrombosis/Hemostasis, Volume 21, Issue 8, 1 November 2015, Pages 772-776

2. Jenab Y, Alemzadeh-Ansari MJ, Fehri SA, Ghaffari-Marandi N, Jalali A. Effect of delay in hospital presentation on clinical and imaging findings in acute pulmonary thromboembolism. The Journal of emergency medicine. 2014 Apr 1; 46(4):465-71.

3. Giannitsis E, Muller-Bardorff M, Kurowski V, et al. Independent prognostic value of cardiac troponin T in patients with confirmed pulmonary embolism. Circulation 2000; 102:211-17.

4. Jenkins PO, Sultanzadeh J, Bhagwat M, et al. Should thrombolysis have a greater role in the management of pulmonary embolism? Clin Med 2009; 9:431-5.

5. Lankeit M, Konstantinides S. Thrombolysis for pulmonary embolism: past, present and future. Thromb Haemost 2010; 103:877-83.

6. Orde MM, Puranik R, Morrow PL, et al. Myocardial pathology in pulmonary thromboembolism. Heart 2011; 97:1695-9.

7. Demir N, Ekim N, Oguzulgen IK, Bukan N (2012) the Value of Cardiac Troponins in Diagnosis and Differential Diagnosis of Pulmonary Embolism. J Pulmon Resp Med 2:134.

8. Lauer B, Niederau C, Kühl U, et al. Cardiac troponin T in patients with clinically suspected myocarditis. J Am Coll Cardiol. 1997; 30:1354–1359.

9. Smith SC, Ladenson JH, Mason JW, et al. Elevations of cardiac troponin I associated with myocarditis: experimental and clinical correlates. Circulation. 1997; 95:163–168.

10. Emile Ferrari, Pamela Moceri, Christophe Crouzet, Denis Doyen, Pierre Cerboni. Timing of troponin I measurement in pulmonary embolism; Heart 2012 98: 732-735.

11. Meyer T, Binder L, Hruska N, Luthe H, Buchwald AB. Cardiac troponin I elevation in acute pulmonary embolism is associated with right ventricular dysfunction; J Am Coll Cardiol. 2000 Nov 1; 36(5):1632-6.

12. Amorim S, Dias P, Rodrigues RA, et al. Troponin I as a marker of right ventricular dysfunction and severity of pulmonary embolism; Rev Port Cardiol. 2006 Feb; 25(2):181-6.

13. Tavana S, Panahi Y, et al., coronary troponin I levels in the patients with acute pulmonary embolism and its relationship with right ventricular dysfunction; Journal of Mazanradan University of medical sciences; June 2009, (19), 70, 72-75

14. Margato R, Carvalho S, et al. Cardiac troponin I levels in acute pulmonary embolism; Rev Port Cardiol. 2009 Nov; 28(11):1213-22.

15. Gonca Kilinc, Omer Tamer Dogan, et al. Significance of serum cardiac troponin I levels in pulmonary embolism; J Thorac Dis. 2012 Dec; 4(6): 588–593.

16. Ozsu S, Abul Y, Orem A, Oztuna F, Bulbul Y, Yaman H, Ozlu T. Predictive value of troponins and simplified pulmonary embolism severity index in patients with normotensive pulmonary embolism. Multidisciplinary respiratory medicine. 2013 Dec 1;8(1):34.