

## TIMI frame count as a predictor of major adverse cardiovascular events during the first month after primary PCI

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### Abstract

**Background:** This study evaluated the correlation between corrected Thrombolysis in Myocardial Infarction (TIMI) frame count (CTFC) and major adverse cardiovascular events (MACE) within the first month following primary percutaneous coronary intervention (PPCI).

**Methods:** Eighty patients who underwent PPCI at Ayatollah Rouhani teaching Hospital in Babol Eighty patients who underwent PPCI at Ayatollah Rouhani teaching Hospital in Babol were included. CTFC, a measure of coronary blood flow, was assessed. Demographic and clinical data, were collected. ST segment resolution, a criterion for successful PPCI, was evaluated. MACE, including cardiac deaths, need for repeat revascularization of culprit vessels, and recurrent non-fatal myocardial infarction, and CVA (cerebrovascular accident) were recorded. Statistical analyses were performed to assess the association between CTFC and demographic/clinical variables, as well as ST resolution and MACE.

**Results:** The majority of patients were (78.8%) men and (81.2%) nonsmokers. No significant association was found between CTFC and demographic/clinical variables. The left anterior descending (LAD) artery was the most commonly involved vessel (48.8%). ST segment resolution of more than 50% was observed in 51.2% of patients. During the one-month follow-up, 13.7% of patients experienced MACE, including 7 cardiac deaths. However, there was no significant association between CTFC and MACE. (P=0.30)

**Conclusion:** This study concludes that CTFC is not a reliable predictor of MACE within the first month after PPCI. Furthermore, ST segment resolution of more than 50% was associated with a lower prevalence of cardiovascular events.

**Keywords:** Thrombolysis, Coronary intervention, Myocardial infarction

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Acute myocardial infarction (AMI) continues to be a leading cause of morbidity and mortality worldwide. Reperfusion therapy plays a crucial role in the management of AMI, with the primary goal of achieving Thrombolysis in Myocardial Infarction (TIMI) 3 flow in the infarct-related artery (IRA). Percutaneous transluminal coronary angioplasty (PTCA) has emerged as the preferred reperfusion strategy due to its higher recanalization rates and reduced residual stenosis compared to thrombolytic therapy.(1-6) Despite the successful restoration of TIMI 3 flow in the IRA without residual stenosis, impaired myocardial tissue perfusion can persist, resulting in the "no-reflow" or "low-reflow" phenomenon. This phenomenon occurs during reperfusion and is attributed to microcirculatory damage caused by ischemia (7-9). It is increasingly recognized that evaluating not only the achievement of TIMI 3 flow but also the adequacy of myocardial tissue perfusion is crucial for predicting patient outcomes and optimizing treatment strategies (10, 11).

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The corrected TIMI frame count (CTFC) has shown promise as a clinical tool for assessing quantitative indexes of coronary blood flow. This method involves counting the number of cineangiographic frames from the initial contrast opacification of the proximal coronary artery to the opacification of distal arterial landmarks while considering the length of the left anterior descending coronary artery (LAD) (10, 11). CTFC provides a more accurate assessment of coronary blood flow and has been shown to be valuable in predicting the outcome of thrombolytic therapy after AMI (12).

However, limited research has been conducted to investigate the relationship between CTFC immediately after successful PTCA (TIMI 3) and clinical outcomes in patients with AMI. Also, we have frequently encountered the reality that despite achieving TIMI 3 flow with PPCI, more than 50% ST resolution was not achieved all the time. Therefore, there is a need to evaluate the role of CTFC as a predictor of flow recovery and its association with major adverse cardiovascular events (MACE) in this patient population. Understanding the potential of CTFC to predict the success of reperfusion therapy and its prognostic value can improve patient risk stratification and guide treatment decisions (13). To address this gap in knowledge, our study aimed to investigate the predictive value of CTFC and its association with MACE during the first month after PPCI.

## Methods

**Study design and setting:** This prospective cohort study was conducted at Ayatollah Rouhani university hospital in Babol. The research sample comprised all patients who were candidates for primary percutaneous coronary intervention (PPCI) within a one-year period from September 2019 to September 2020. The study protocol was approved by the hospital's ethics committee, under the ethical code of IR.MUBABOL.HRI.REC.1398.369.

**Patient selection:** Patients were included in the study if they underwent PPCI and achieved TIMI 3 flow after the procedure. Exclusion criteria included delayed PPCI (more than 24 hours after symptom onset) or TIMI flow less than 3. All patients received PPCI as soon as possible (a maximum up to one hour) after the diagnosis of ST-segment elevation myocardial infarction (STEMI) and within 24 hours of symptom onset. STEMI diagnosis was based on typical chest pain and confirmation of electrocardiographic criteria (14)

**Data collection:** A comprehensive checklist was prepared to collect data on demographic information, cardiovascular risk factors, physical examination findings at admission,

blood pressure at onset, duration of symptoms until treatment, location of myocardial infarction, TIMI flow grade, CTFC, resolution of ST segment, ejection fraction (EF) at discharge and one month later, TIMI risk score, and MACE. MACE components included cardiac death, recurrent non-fatal reinfarction, cerebrovascular accident (CVA), and the need for repeat revascularization of target arteries. Data were collected at the time of hospitalization and one month later.

**Procedures:** All patients received chewable aspirin (300 mg), clopidogrel (600 mg), and atorvastatin (80 mg). In the setting of acute STEMI, PPCI was performed exclusively in the culprit artery associated with the infarction. Glycoprotein IIb/IIIa inhibitors and thrombus suction were used as needed, and all patients received drug-eluting stents. Angiography files of patients were reviewed, and the TIMI frame count was measured. The CTFC was calculated as the number of cineframes required for contrast to reach a standardized distal coronary landmark in the culprit vessel. The frame count was adjusted for the left anterior descending coronary artery (LAD) using a correction factor of 1.7 for the longer distance to the TIMI landmark. Patients were categorized into two groups based on CTFC values:  $CTFC \leq 20$  and  $CTFC > 20$  (15)

**Data analysis:** Collected data were entered into SPSS software for analysis. Descriptive statistics such as mean, median, mode, variance, standard deviation, range, coefficient of variation, frequency, percentage, and prevalence were used to describe the data. Inferential statistical tests including parametric tests (t-student, chi-square) and non-parametric tests (Mann-Whitney) were employed to test study hypotheses. The normality of the data was assessed before applying the appropriate statistical tests. Statistical analysis was performed using SPSS software Version 25, and a significance level of  $p < 0.05$  was considered statistically significant.

## Results

A total of 80 patients were included in the study. The mean age of the enrolled patients was found to be  $60.20 \pm 11.86$  years. The CTFC had a mean value of  $17.79 \pm 7.45$ . Tables 1 and 2 provide a detailed overview of the baseline characteristics of the studied patients. Among the participants, the majority were males, accounting for 78.8% of the patients. The majority of patients (81.2%) were nonsmokers. Furthermore, a significant proportion of patients had no history of addiction (91.3%), no family history of heart disease (68.8%), and no history of diabetes (48.8%).

**Table 1. Demographic characteristics**

Variables	Percentage	Number
Gender		
Men	78.8	63
Women	21.2	17
smoking		
Yes	18.8	15
No	81.2	65
History of addiction		
Yes	8.8	7
No	91.3	73
Familial history Of premature CAD		
Yes	31.2	25
No	68.8	55
History of diabetes		
Yes	51.2	41
No	48.8	39

**Table 2. Baseline measurements**

Variables	Maximum	Minimum	Middle	Standard deviation	Average
Age (year)	87	31	60/20	11/86	60/20
Systolic blood pressure ( mmHg )	200	50	130	25/14	128/90
Diastolic blood pressure ( mmHg )	130	35	80	17/10	79/79
Time from onset of symptoms to treatment (minutes)	1200	30	240	237/88	324/77
Admission time to treatment (minutes)	300	10	80	11/07	146

The admission time to treatment is different from the diagnosis time to treatment. The latter was always less than one hour. The evaluation of the involved vessels revealed that among the studied patients, 39 (48.7%) individuals had involvement of the left anterior descending artery (LAD), 31 (38.8%) patients had involvement of the right coronary artery (RCA), and 10 (12.5%) patients had involvement of the left circumflex artery (LCX) (figure 1).

The data regarding the ejection fraction (EF) at baseline and follow-up, as well as the occurrence of MACE, are summarized in table 3. During the follow-up period, a total

of 11 patients experienced MACE, which included 7 cases of cardiac death, 3 cases of revascularization of the culprit vessel, and 1 case of recurrence of non-fatal myocardial infarction.

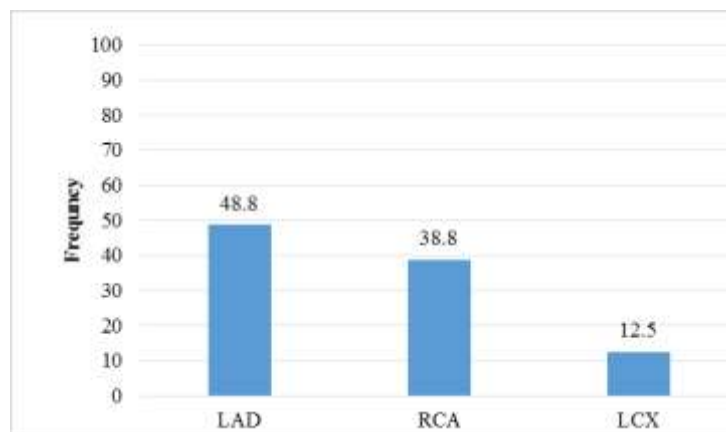
The data on EF at baseline and follow-up are available in table 3, shedding light on the changes in cardiac performance over time. The association between CTFC and demographic/clinical data was assessed by establishing a cutoff value of 20 for CTFC. The results of this analysis are presented in 3 separate tables (tables 4, 5, 6) to examine the relationship between CTFC scores and various factors.

**Table 3. Clinical and medicine-related characteristics**

Variables	Frequency	Percent of Frequency
<b>ECG after PPCI?</b>		
NO	8	10/0
Yes	72	90/0
<b>ST-resolution (%)</b>		
50≥	39	48/8
50<	41	51/2
<b>LV systolic dysfunction</b>		
Mild	39	48/8
Moderate	24	30/0
Severe	17	21/3

Variables	Frequency	Percent of Frequency
<b>LV systolic dysfunction at One month</b>		
Mild	55	68/8
Moderate	25	31/3
<b>Cardiovascular events</b>		
No	69	86/3
Cardiac death	7	8/8
Recurrence of non-fatal myocardial infarction	1	1/3
Revascularization culprit vessel	3	3/8

ECG= electrocardiogram, PPCI= primary percutaneous coronary intervention, LV= left ventricle



**Figure 1. Distribution of vessel involvement. LAD= left anterior descending artery, RCA= right coronary artery, LCX= left circumflex artery.**

Upon evaluating the association between CTFC and demographic variables, presented in table 4, it was found that none of the calculated p-values reached statistical significance. This implies that CTFC scores, whether below or above 20, were not significantly associated with the demographic characteristics of the patients. These findings suggest that demographic factors such as age, gender, smoking status, history of addiction, family history of premature CAD and history of diabetes may not serve as reliable predictors of CTFC scores.

Similarly, when analyzing the association between CTFC and clinical variables, as shown in table 5, no statistically significant p-values were observed. This indicates that CTFC scores did not exhibit a significant

association with clinical factors such as the involved vessels, ST-resolution, EF at baseline and follow-up, and the occurrence of cardiovascular events. These results suggest that CTFC may not be a reliable predictor for the occurrence of MACE during the one-month period following PPCI. Furthermore, table 6 presents the comparison of blood pressure, time of onset of symptoms and admission to treatment, and TIMI score with CTFC. The p-values obtained from this analysis were not statistically significant, indicating that CTFC scores below or above 20 were not significantly associated with these clinical variables. Therefore, based on these findings, CTFC may not serve as a strong predictor for the evaluated clinical parameters in this study.

**Table 4. Comparison of demographic variables based on CTFC above and below 20**

Variables	CTFC≤20	CTFC>20	P value*
<b>Age (year)</b>			
60≥	30 (50/0)	10 (50/0)	0/99
60<	30 (50/0)	10(50/0)	
<b>Gender</b>			
Male	47 (78/3)	16 (80/0)	0/87
Female	13 (21/7)	4 (20/0)	

Variables	CTFC≤20	CTFC>20	P value*
<b>Smoke</b>			
No	50 (83/3)	15 (75/0)	0/40
Yes	10 (16/7)	5 (25/0)	
<b>Addiction</b>			
No	56 (93/3)	17 (85/0)	0/25
Yes	4 (6/7)	3 (15/0)	
<b>History of premature CAD</b>			
No	40 (66/7)	15 (75/0)	0/48
Yes	20 (33/3)	5 (25/0)	
<b>Diabetes</b>			
No	29 (48/3)	10 (50/0)	0/89
Yes	31 (51/7)	10 (50/0)	

CTFC= corrected TIMI frame count, CAD= coronary artery disease

**Table 5. Comparison of clinical variables based on CTFC above and below 20**

Variables	CTFC≤20	CTFC>20	P value*
<b>Involved vessel</b>			
LAD	30 (50/0)	9 (45/0)	0/31
LCX	9 (15/0)	1 (5/0)	
RCA	21 (35/0)	10 (50/0)	
<b>ST-resolution (%)</b>			
50≥	30 (50/0)	9 (45/0)	0/78
50<	30 (50/0)	11 (55/0)	
<b>LV systolic dysfunction</b>			
Mild	33 (55/0)	6 (30/0)	0/15
Moderate	16 (26/7)	8 (40/0)	
Severe	11 (18/3)	6 (30/0)	
<b>LV systolic dysfunction at One month</b>			
Mild	43 (71/7)	12 (60/0)	0/33
Moderate	17 (28/3)	8 (40/0)	
<b>Cardiovascular events</b>			
No	53 (88/3)	16 (80/0)	0/30
Cardiac death	5 (8/3)	2 (10/0)	
Recurrence of non-fatal myocardial infarction	-	1 (5/0)	
Revascularization	2 (3/3)	1 (5/0)	

CTFC= corrected TIMI frame count, LV= left ventricle

**Table 6. Comparison of post-PPCI characteristics based on CTFC above and below 20**

Variables	CTFC≤20 Mean(SD)	CTFC>20 Mean(SD)	P value*
<b>Systolic blood pressure (mmHg)</b>	129/85(26/37)	126/10(21/42)	0/56
<b>Diastolic blood pressure (mmHg)</b>	79/67(18/43)	80/15(12/72)	0/91
<b>The onset of symptoms to treatment (minutes)</b>	317/87(262/17)	345/50(312/8)	0/69
<b>Admission time to treatment (minutes)</b>	130/54(11/09)	142/23 (11/13)	0/41
<b>Score TIMI</b>	2/88(1/78)	2/55(1/60)	0/46

CTFC= corrected TIMI frame count, PPCI= primary percutaneous coronary intervention, TIMI= thrombolysis in myocardial infarction

The comparison of patients' left ventricular ejection fraction (LVEF) levels at hospital and one month after the intervention showed a significant improvement in LV systolic function. Among the patients with severe LV dysfunction at discharge, 15 out of 17 demonstrated an increase in LVEF, leading to a reclassification as having mild dysfunction one month after the intervention. Similarly, patients with moderate dysfunction at discharge showed an improvement to mild dysfunction. These findings indicate a statistically significant increase in LV systolic function following the intervention ( $p < 0.001$ ), highlighting the positive impact of the intervention on cardiac function (table 7).

The assessment of recovery based on LVEF at discharge and one month after the intervention revealed positive outcomes. Among the patients, 24 individuals (30%)

showed improvements in LVEF, while 56 (70%) patients demonstrated no change in LVEF. None of the patients experienced a reduction in LVEF during the follow-up period.

Furthermore, the analysis of ST-resolution rate in relation to the recovery rate based on LVEF showed that there was no statistically significant difference between patients with more than 50% ST resolution and those with less than 50% ST resolution ( $P=0.88$ ). Notably, 90.2% of patients with more than 50% ST resolution experienced no cardiovascular complications during their hospital stay, indicating a significant association between ST resolution and a lower incidence of cardiovascular complications ( $P=0.02$ ). These findings highlight the potential benefits of ST resolution in predicting positive clinical outcomes following the intervention (table 8).

**Table 7. Comparison of patients' improvement based on EF at the time of discharge and one month after the intervention**

		LV systolic dysfunction at One month		P value*
		Mild	Moderate	
LV systolic dysfunction at hospital	Mild	33 (60/0)	6 (24/0)	<0.001
	Moderate	7 (12/7)	17 (68/0)	
	Severe	15 (27/3)	2 (8/0)	

LV= left ventricle

**Table 8. Comparison of recovery rate and cardiovascular events based on ST-resolution**

ST-resolution	50 $\geq$	50<	P value*
<b>Recovery EF</b>			
No	27 (69/2)	29 (70/7)	0/88
Yes	12 (30/8)	12 (29/3)	
<b>Cardiovascular events</b>			
No	32 (82/1)	37 (90/2)	
Cardiac Death	6 (15/4)	1 (2/4)	0/02
Recurrence of non-fatal myocardial infarction	1 (2/6)	-	
Revascularization	-	3 (7/3)	

EF= ejection fraction

## Discussion

The present study aimed to investigate the relationship between CTFC and the prevalence of adverse cardiovascular events during the first month after primary percutaneous coronary intervention (PPCI). To the best of our knowledge, no previous study has examined this relationship in our region. However, the results of some studies have shown that counting angiographic frames using CTFC is a suitable method for predicting cardiac events (16, 17). In our study, no significant association was observed between CTFC and major adverse cardiovascular events,

indicating that CTFC may not be a reliable indicator for predicting such events at one month. This finding is in line with previous studies that have reported varying results regarding the predictive value of CTFC (18). It is important to note that CTFC is influenced by several factors, including the complexity of the coronary lesion and individual variations in coronary anatomy, which may contribute to the lack of a significant association. Another criterion of successful PPCI is the resolution of ST-segment elevation. In our study, we evaluated the association between ST-segment resolution and cardiovascular events. Our findings



revealed that an increase in the rate of ST-segment resolution to more than 50% was associated with a reduction in cardiovascular events. This suggests that ST-segment resolution can serve as a practical criterion for predicting major adverse cardiovascular events, aligning with previous studies highlighting its importance (19-21). Although we did not find a correlation between the rate of ST-segment resolution and patients' recovery based on LVEF, we observed a significant improvement in LVEF one month after the intervention compared to the time of discharge. Approximately 30% of patients showed an increase in LVEF, indicating that the intervention led to improved left ventricular systolic function. These results underscore the positive impact of PPCI on cardiac function and support its effectiveness as a treatment strategy for patients with STEMI (15, 22). Mortality is a critical outcome measure in patients undergoing PPCI. The findings of our study revealed that cardiac death was the most reported complication, accounting for 63.6% of major cardiovascular events. This finding highlights the need for comprehensive strategies to improve patient outcomes and reduce cardiac mortality following PPCI.

Examining the demographic characteristics based on CTFC in patients undergoing PPCI, we found no significant differences in CTFC based on age, gender, smoking status, addiction history, or family history of heart disease. This suggests that CTFC may not be influenced by these demographic factors and further supports the notion that CTFC alone may not be a strong predictor of major adverse cardiovascular events. Vakili et al. showed that in 69.2% of cases  $CTFC \leq 20$  and in 30.8% of cases  $CTFC > 20$  was observed. In the group with  $CTFC \leq 20$  the rate of EF at discharge was 42.1% and in the group with  $CTFC > 20$ , this rate was 43.5%. No significant difference was found between CTFC and EF at discharge (15, 19) which was similar to the present study. Pavlović et al. showed that patients undergoing PPCI with faster TIMI 3 flow ( $CTFC \leq 27$ ), had greater rate of ST resolution within 90 minutes after PPCI in comparison with the group with slower TIMI 3 flow ( $CTFC 28-40$ ). However, in our study; the rate of ST-resolution in two groups of patients with CTFC greater and less than 20, had no significant differences (15).

Regarding the involvement of coronary vessels, our study showed that the LAD was the most commonly affected vessel, followed by the RCA and LCX. These findings are consistent with previous studies conducted in our region (16). In our study, the resolution of ST-segment elevation was observed in more than 50% of patients, indicating a favorable response to PPCI. This finding is

consistent with previous studies that have reported high rates of ST-segment resolution following successful PPCI (23-25). The resolution of ST-segment elevation is an important marker of myocardial reperfusion, and our study adds to the growing body of evidence supporting its prognostic value in predicting major adverse cardiovascular events.

Despite the valuable findings presented in this study, there are certain limitations that should be acknowledged. Firstly, the small sample size of this study, with only 80 patients meeting the inclusion criteria, may limit the generalizability of the results to a broader population. A larger sample size would have provided more robust statistical power and enhanced the representativeness of the findings. Secondly, the single-center design of the study introduces the possibility of selection bias and limits the external validity of the results. Future studies with multi-center collaborations could overcome this limitation and provide a more comprehensive understanding of the relationship between CTFC and adverse cardiovascular events. Furthermore, the follow-up period of only one month might not capture the long-term outcomes and potential delayed cardiovascular events.

A longer follow-up period would be beneficial to assess the sustainability of the observed associations. Lastly, the study did not evaluate certain confounding factors such as comorbidities and medication use, which might influence the occurrence of adverse cardiovascular events. Future studies should consider incorporating these factors to obtain a more comprehensive understanding of the relationship between CTFC and cardiovascular outcomes. In conclusion, our study did not find a significant association between CTFC and major adverse cardiovascular events at one month, suggesting that CTFC may not be a reliable predictor in this regard. However, the rate of ST-segment resolution was strongly correlated with a reduced prevalence of cardiovascular events, emphasizing its utility as a practical criterion for predicting outcomes. Additionally, PPCI was found to significantly improve left ventricular systolic function, highlighting its beneficial effects on cardiac recovery. Further research is needed to explore additional factors and markers that may enhance the predictive accuracy of adverse cardiovascular events following PPCI.

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**Authors' contribution:** Design: KA, NN. Data collection: KA, NN, IJ, SFJ, NZ. Analysis: KA, NN. Writing: KA, NN

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