Original Article

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Comparison of Outcomes in Patients Presenting to the Emergency Department with Myocardial Infarction: Initial Administration of Oral Antithrombotic (P2Y12 Antagonist) Loading Therapy in the Emergency Setting

Nuşin Yalımol[1], Mustafa Yalımol[2], Ali Sarıdaş[1], Ertuğrul Okuyan[3]

1 Prof. Dr. Cemil Tascioglu City Hospital, Department of Emergency Medicine, Istanbul, Türkiye
2 Department of Council of Forensic Medicine, Council of Forensic Medicine, Istanbul, Turkiye
3 Department of Cardiology, Bagcilar Training and Research Hospital, Istanbul, Türkiye

Abstract

Objective: We investigated the effect of the initial P2Y12 loading therapy in emergency department to clinical and angiographic results in patients admitted to the emergency department with myocardial infarction.

Material and Methods: The initial P2Y12 loading therapy in emergency department with clinical and angiographic results in the patients admitted to the emergency department with myocardial infarction and had undergone to coronary angiography in year 2015 were investigated retrospectively. The age, gender, co-morbid diseases, the loading P2Y12 therapy in emergency department, the TIMI flow rate and myocardial Blush grade before and after the angiography was recorded. The effect of the initial P2Y12 loading therapy in emergency department to clinical and angiographic results in patients admitted to the emergency department with myocardial infarction were investigated.

Results: The mean age of the males was 54.4±12.2 years and females was 65.2±13.9 years. The mean age of the females are greater than males significantly. Stent thrombosis is detected in 5.7% of the patients. The stent thrombosis was more frequently seen in patents with previous coronary artery disease. In-hospital mortality was 3.7%; the mortality rate after angioplasty was 1.98%. There was not any loading therapy in 65.3% of the patients; clopidogrel was loaded in 25%, ticagrelor was 2.2% and prasugrel was 7.4%. The TIMI score and blush grade was similar before angioplasty in all groups; also the TIMI score and blush grade was similar after angioplasty.

Discussion: In conclusion, the results the loading therapy with clopidogrel, ticagrelor and prasugrel in emergency department were similar. Both of the three agents effectivity are similar.

Key words: P2Y12, Myocardial Infarction, Coronary Angiography, TIMI Flow Rate, Myocardial Blush Grade

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for approximately 17.9 million annual deaths (1). A significant proportion of these deaths result from acute coronary syndromes (ACS), including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UA). ACS is a critical condition characterized by myocardial ischemia and necrosis, arising from a sudden reduction in coronary flow due to atherosclerotic plaque rupture or erosion (2). Despite advances in diagnosis and treatment, ACS continues to pose a major public health burden in terms of morbidity and mortality, underscoring the need for research to optimize early intervention strategies and improve clinical outcomes.

The pathophysiology of ACS hinges on the dynamic interplay between vulnerable atherosclerotic plaques, platelet activation, and thrombosis. Plaque rupture or erosion triggers platelet adhesion, aggregation, and the formation of occlusive or subocclusive thrombi, leading to myocardial ischemia (3). STEMI involves transmural myocardial necrosis due to complete coronary occlusion, necessitating urgent reperfusion therapy (4). In contrast, NSTEMI and UA are typically associated with partial or

Corresponding author: Nusin Yalimol
e-mail: nusnbel@gmail.com
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ORCID:
Nusin Yalimol: orcid.org/ 0000-0002-4558-0868
Mustafa Yalimol: orcid.org/ 0000-0003-4333-592X
Ali Saridas: orcid.org/ 0000-0002-2725-6001
Ertugrul Okuyan: orcid.org/ 0000-0002-0626-2939

transient occlusion and are managed with anti-ischemic and antithrombotic therapies (5).

ACS diagnosis relies on clinical evaluation, electrocardiography (ECG), and cardiac biomarkers. ECG serves as the cornerstone tool, guiding therapeutic decisions through findings such as ST-segment elevation or depression (6). Cardiac troponins, sensitive and specific indicators of myocardial injury, have revolutionized risk stratification and diagnostic accuracy (7). However, challenges in distinguishing NSTEMI from biomarker-negative UA highlight the need for rapid and precise diagnostic algorithms (8).

ACS management has evolved significantly, emphasizing early reperfusion, antiplatelet therapy, and secondary prevention. Central to this approach are P2Y12 receptor antagonists, which inhibit adenosine diphosphate (ADP)-mediated platelet activation. Clopidogrel, a first-generation thienopyridine, has long formed the backbone of dual antiplatelet therapy (DAPT) alongside aspirin (9). However, its variable pharmacokinetic response and delayed onset of action have spurred the development of newer agents, such as prasugrel and ticagrelor, which provide faster and more consistent platelet inhibition (10).

Current guidelines recommend early administration of P2Y12 inhibitors, particularly in ACS patients undergoing percutaneous coronary intervention (PCI) (11). However, the timing of loading doses—whether administered in the emergency department (ED) or delayed until coronary anatomy is clarified—remains contentious. Proponents of early (ED or prehospital) loading argue that rapid platelet inhibition may reduce thrombotic complications and enhance reperfusion success (12). Conversely, concerns over bleeding risks, particularly in patients requiring urgent coronary artery bypass grafting (CABG), warrant cautious adoption of this strategy (13).

Epidemiological data indicate a rising burden of ACS in developing countries, including Turkey. The TEKHARF study reported 420,000 annual coronary events in Turkey, with ACS-related mortality rates exceeding European averages (14). The high prevalence of risk factors such as hypertension, diabetes, smoking, and dyslipidemia underscores the need for personalized preventive and therapeutic interventions (15). Despite increased access to invasive strategies like coronary angiography and PCI, delays in presentation, guideline non-adherence, and socioeconomic disparities contribute to inequitable outcomes (16).

The role of oral P2Y12 antagonists in the ED requires further investigation. While trials such as TRITON-TIMI 38 and PLATO demonstrated the superiority of prasugrel and ticagrelor over clopidogrel in reducing ischemic events (17), the optimal timing of loading doses remains uncertain. Early administration may enhance platelet inhibition during PCI but paradoxically increase bleeding risk (18). Furthermore, the impact of ED loading on angiographic outcomes—such as TIMI flow grade or myocardial perfusion—has not been comprehensively evaluated (19).

This study aims to compare clinical and angiographic outcomes between early (ED) and delayed (post-angiography) oral P2Y12 antagonist loading in patients presenting to the ED with myocardial infarction. By analyzing parameters such as infarct size, stent thrombosis, bleeding events, and mortality, the benefit-risk balance of early antithrombotic therapy will be clarified (20). The findings may guide clinical practice, particularly in resource-limited settings with constrained access to timely PCI (21).

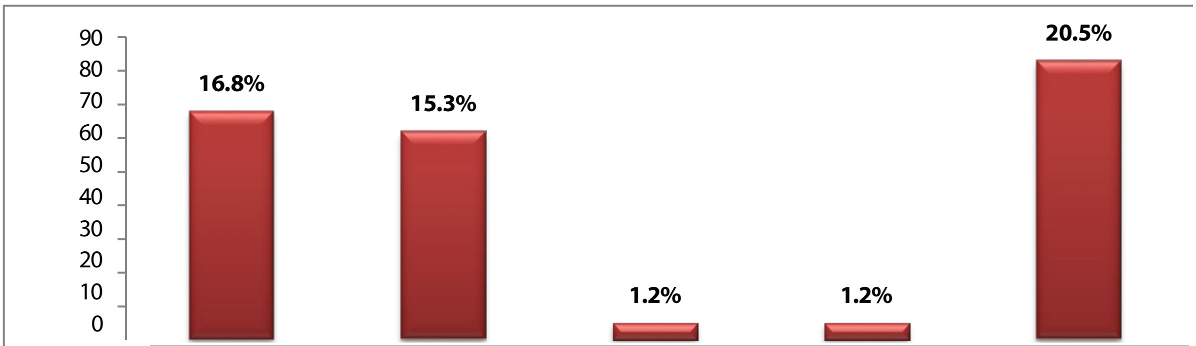
In conclusion, ACS remains a critical challenge in modern cardiology, requiring a balance between rapid reperfusion, effective antithrombotic therapy, and minimized bleeding risk (22). This study contributes to the growing evidence on optimizing P2Y12 inhibitor use in the ED, with the ultimate goal of improving survival and quality of life in ACS patients (23).

Method

This retrospective study was designed to analyze data from patients presenting to the emergency department (ED) with acute myocardial infarction (STEMI/NSTEMI) who underwent emergency coronary angiography at Bağcılar Training and Research Hospital, following approval by the Institutional Ethics Committee. The study period spanned from January 1, 2015, to December 31, 2015. The study population included individuals with complete diagnostic, therapeutic, and angiographic data in the hospital registry system. Patients with missing data, unavailable medical records, or those referred to other centers were excluded.

Demographic (age, gender) and clinical data (hypertension, diabetes, dyslipidemia, smoking history) were collected from electronic health records and patient files. Antithrombotic therapies administered in the ED (clopidogrel, prasugrel, ticagrelor) were recorded, and patients were grouped according to the type of P2Y12 antagonist used. Coronary angiography findings were evaluated, including the culprit artery, thrombus burden (TIMI thrombus classification), pre- and post-procedure TIMI flow grade (0–3), myocardial blush grade (MBG; 0–3), and stent thrombosis. In-hospital mortality and recurrent ischemic events were verified through clinical records.

Statistical analyses were performed using SPSS 17.0 software. Descriptive statistics for continuous variables are presented as mean ± standard deviation, while categorical variables are reported as frequencies and percentages (%). For non-normally distributed continuous data, the Mann-Whitney U test was used for intergroup comparisons, and the Chi-square or Fisher's exact test was applied for categorical variables. A p-value <0.05 was considered sta-



	DM	HT	HL	KKY	KAH
Percentage	16.8%	15.3%	1.2%	1.2%	20.5%
Number	68	62	5	5	83

* DM: Diabetes Mellitus, HT: Hypertension, HL: Hyperlipidemia, KKY: Congestive Heart Failure (CHF), KAH: Coronary, Artery Disease (CAD)

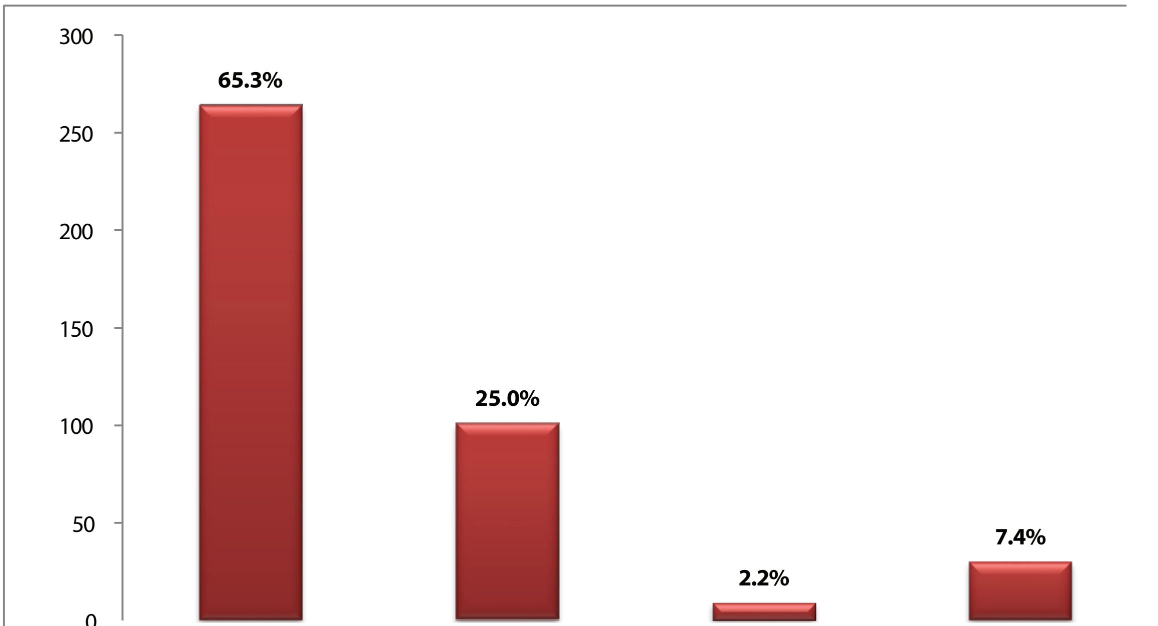
Figure 1. Prevalence of comorbidities in the study population.

tistically significant, and all analyses were conducted with a 95% confidence interval. The retrospective design, potential for missing data, and single-center nature of the study were reported as limitations that may affect generalizability.

Results

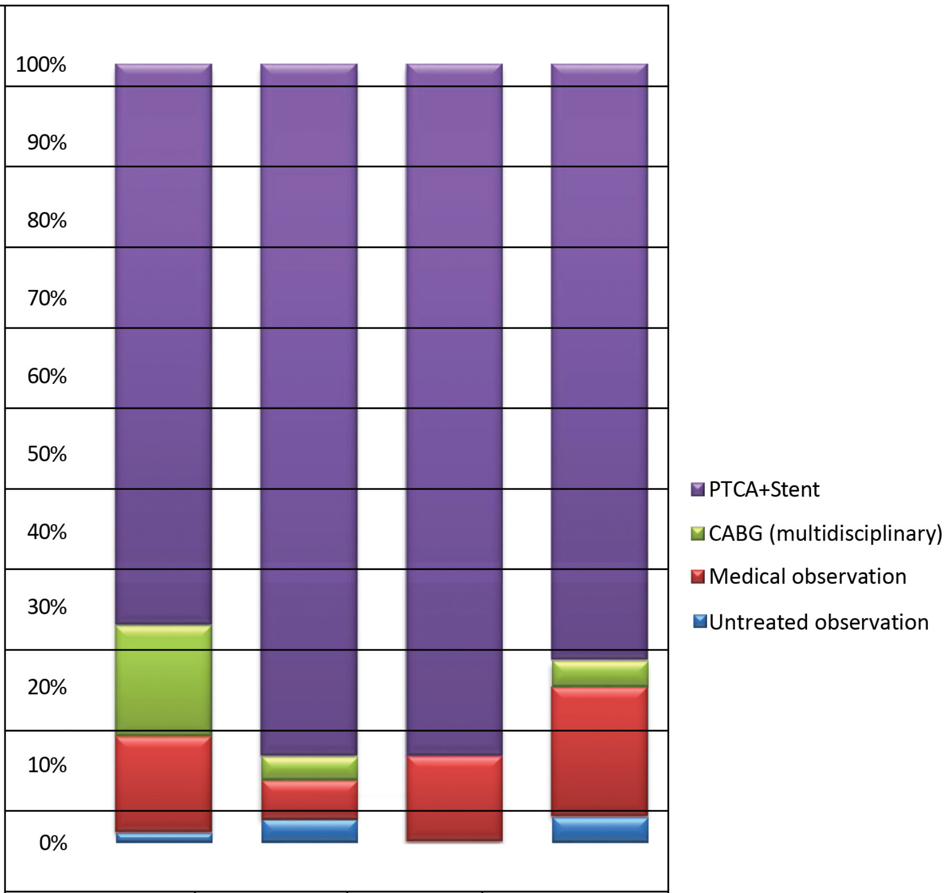
This retrospective study included 404 patients diagnosed with acute myocardial infarction (STEMI/NSTEMI) who presented to the emergency department (ED) of Bağcılar Training and Research Hospital and underwent emergency coronary angiography between January 1, 2015, and December 31, 2015. The mean age of the cohort was 56.6 ± 13.3 years, with 75.7% (n=306) being male. The mean age of female patients (65.2 ± 13.9 years) was significantly higher than that of males (54.4 ± 12.2 years; $p<0.001$). The most prevalent comorbidities were coronary artery disease (CAD; 20.5%), diabetes mellitus (DM; 16.8%), and hypertension (HT; 15.3%), while hyperlipidemia (1.2%) and congestive heart failure (CHF; 1.2%) were rare (Figure 1).

Analysis of antithrombotic loading in the ED revealed that 65.3% (n=264) received no loading, 25% (n=101) received 600 mg clopidogrel, 7.4% (n=30) received 180 mg ticagrelor, and 2.2% (n=9) received 60 mg prasugrel (Figure 2). The rate of coronary artery bypass grafting



	No loading dose provided	Klopidogrel	Prasugrel	Ticagrelor
Percentage	65.3%	25.0%	2.2%	7.4%
Number	264	101	9	30

Figure 2. Emergency department loading therapy administration status.



	No loading dose provided	Klopidogrel	Prasugrel	Ticagrelor
PTCA+Stent	72.1%	89.0%	88.9%	76.7%
CABG (multidisciplinary)	14.3%	3.0%	0.0%	3.3%
Medical Observation	12.4%	5.0%	11.1%	16.7%
Untreated observation	1.2%	3.0%	0.0%	3.3%

Figure 3. Treatment outcomes stratified by ED loading therapy administration.

(CABG) by council decision was notably higher in the non-loading group (14.3%) compared to other groups (Figure 3). Percutaneous transluminal coronary angioplasty (PTCA) with stent implantation was performed in 75.7% (n=306) of the population, while medical observation (10.6%) and no intervention (1.7%) were less common (Figure 4).

Stent thrombosis occurred in 5.7% (n=17) of patients. It was significantly higher in those with a history of CAD (12.1%) compared to those without (4.2%; p=0.029). No statistical association was found between stent thrombosis and comorbidities such as DM (4.5%), HT (10.3%), or hyperlipidemia (25%; p>0.05). In-hospital mortality was 3.7% (n=15). Mortality rates were 4.2% (n=11) in the non-loading group and 2.9% (n=4) in the loading group, with no significant difference (p=0.508). No mortality was observed in the prasugrel group, while rates were 3.3% (n=1) in the ticagrelor group and 3.0% (n=3) in the clopidogrel group (Table 1).

Table 1. Mortality distribution according to loading therapy administration status in the emergency department

	In-ED Mortality		
	No	Yes	p
Untreated observation	253 (%95.8)	11 (%4.2)	
Klopidogrel	98 (%97.0)	3 (%3.0)	0.881
Prasugrel	9 (%100)	-	
Ticagrelor	29 (%96.7)	1 (%3.3)	

Angiographic findings identified Grade II thrombus (45.9%) as the most common culprit lesion (Figure 5). No significant association was observed between ED antithrombotic loading and thrombus grade (p=0.815; Figure 6). Pre-procedural TIMI flow grade was "0" (complete occlusion) in 71.4% of cases, decreasing to 2% post-procedure. Post-procedural TIMI 3 flow (normal flow) increased to 82.2% (Figure 7). Similarly, myocardial blush

Table 2. TIMI flow grades before and after procedure according to loading therapy status in the emergency department

ED loading therapy status	TIMI flow grade before intervention	TIMI flow grade after reperfusion therapy	P
Untreated observation	0.68±1.17	2.75±0.64	**<0.001**
Klopidogrel	0.78±1.21	2.77±0.52	**<0.001**
Prasugrel	1.29±1.38	2.86±0.38	**0.041**
Ticagrelor	0.30±0.88	2.83±0.39	**<0.001**
p	0.135	0.979	

Table 3. Post-intervention TIMI flow grades stratified by ED loading therapy

	TIMI flow grade after reperfusion therapy			
Emergency department loading therapy	**0**	**1**	**2**	**3**
Untreated observation	5 (%2.7)	5 (%2.7)	22 (%11.8)	154 (%82.8)
Klopidogrel	1 (%1.1)	1 (%1.1)	15 (%17.0)	71 (%80.7)
Prasugrel	-	-	1 (%14.3)	6 (%85.7)
Ticagrelor	-	-	4 (%17.4)	19 (%82.6)

grade (MBG) improved from 77.6% “0” (no perfusion) pre-procedure to 52.1% “3” (normal perfusion) post-procedure (Figure 8). Post-procedural TIMI and MBG scores were significantly higher across all antithrombotic groups compared to pre-procedural values (p<0.001). For example, in the non-loading group, TIMI flow improved from 0.68 ± 1.17 to 2.75 ± 0.64, while the prasugrel group improved from 1.29 ± 1.38 to 2.86 ± 0.38 (Table 2).

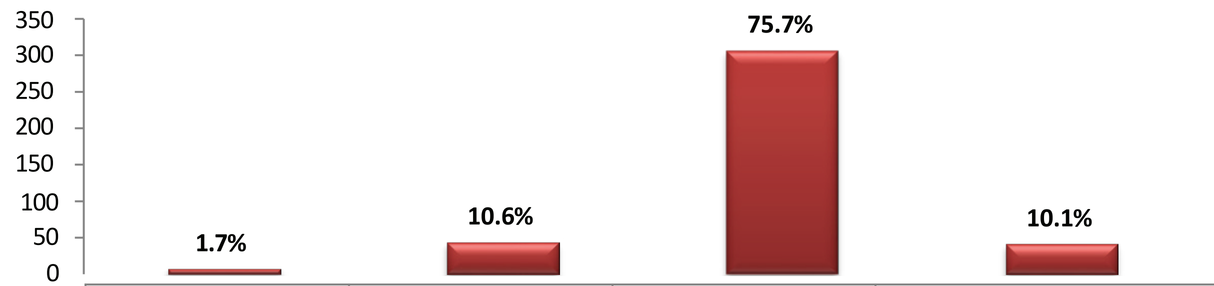
In conclusion, this study found no significant impact of ED antithrombotic loading on stent thrombosis or mortality. However, marked improvements in post-angiography TIMI flow and myocardial perfusion parameters were observed in all groups. Specifically, TIMI 3 flow rates post-procedure were 85.7% in the prasugrel group and 82.6% in the ticagrelor group (Table 3). These findings suggest that early antithrombotic therapy supports coronary reperfusion success but does not confer a clear short-term clinical advantage.

The comorbid conditions of the patients are presented in Figure 1. The most frequently observed comorbidity was coronary artery disease (CAD), followed by diabetes mellitus (DM) and hypertension (HT). Figure 1 illustrates the distribution of comorbid diseases among the study population.

Analysis of loading dose administration at ED admission showed that 65.3% of patients were not given loading therapy during initial evaluation (Figure 2).

Figure 3 shows the distribution of procedures or outcome decisions based on loading therapy administration in the emergency department. Across all medication groups and in patients who did not receive loading therapy, PTCA + Stent was the most frequently performed procedure. Additionally, the highest rate of CABG by council decision (14.3%) was observed in the group that did not receive loading therapy in the ED. In patients administered prasugrel, either PTCA + Stent or medical observation was decided.

Percutaneous transluminal coronary angioplasty (PTCA) with stent implantation was performed in 75.7% of patients, while 1.7% were managed with watchful waiting (Figure 4). Seven patients died without undergoing any intervention, and eight patients died during follow-up after PTCA with stent implantation.



	Untreated observation	Medical Observation	PTCA + Stent	Surgery by multidisciplinary team decision
Percentage	1.7%	10.6%	75.7%	10.1%
Number	7	43	306	41

Figure 4. Frequency of clinical outcomes in patients.

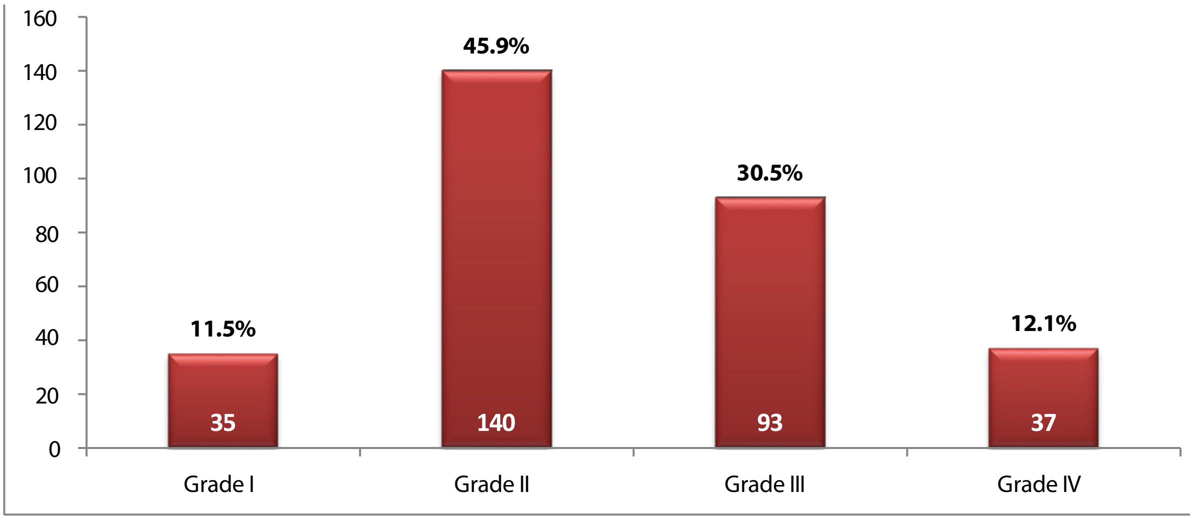


Figure 5. Frequency distribution of thrombus grades detected during angiography in patients.

Figure 5 shows the distribution of thrombus grades detected in the culprit artery during angiography of study patients. Grade II thrombus was most frequently observed, while Grade I thrombus was least common.

Figure 6 displays the distribution of thrombus grade percentages according to loading therapy administration status in the emergency department. No statistically significant association was found between thrombus grade and ED loading therapy (p=0.815).

Figure 7 shows the frequency distribution of TIMI flow grades before and after the procedure. While 71.4% of patients had TIMI flow grade '0' pre-procedure, this rate decreased to 2% post-procedure. Conversely, the proportion of patients with TIMI flow grade '3' increased from 17.1% pre-procedure to 82.2% post-procedure.

Figure 8 shows the frequency distribution of Myocardial Blush Grades (MBG) before and after the procedure. While 77.6% of patients had MBG '0' (no perfusion) pre-procedure, this rate decreased to 6.9% post-procedure. Conversely, the proportion of patients with MBG '3' (normal perfusion) increased from 6.6% pre-procedure to 52.1% post-procedure.

Table 2 presents the mean TIMI flow scores before and after the procedure according to loading therapy administration in the emergency department. Pre-procedural TIMI flow grades were similar across all groups; likewise, post-procedural TIMI scores were comparable in all groups (p-values: 0.135 and 0.979, respectively). Moreover, post-procedural TIMI flow grades were significantly higher than pre-procedural values across all loading therapy subgroups (Table 2). Additionally, Table 14 shows the distribution of post-procedural TIMI flow scores stratified by ED loading therapy status.

Table 4 presents the mean myocardial blush grades (MBG) before and after the procedure according to loading therapy administration in the emergency department. Pre-procedural MBG was similar across all groups, as was post-procedural MBG (p-values: 0.188 and 0.873,

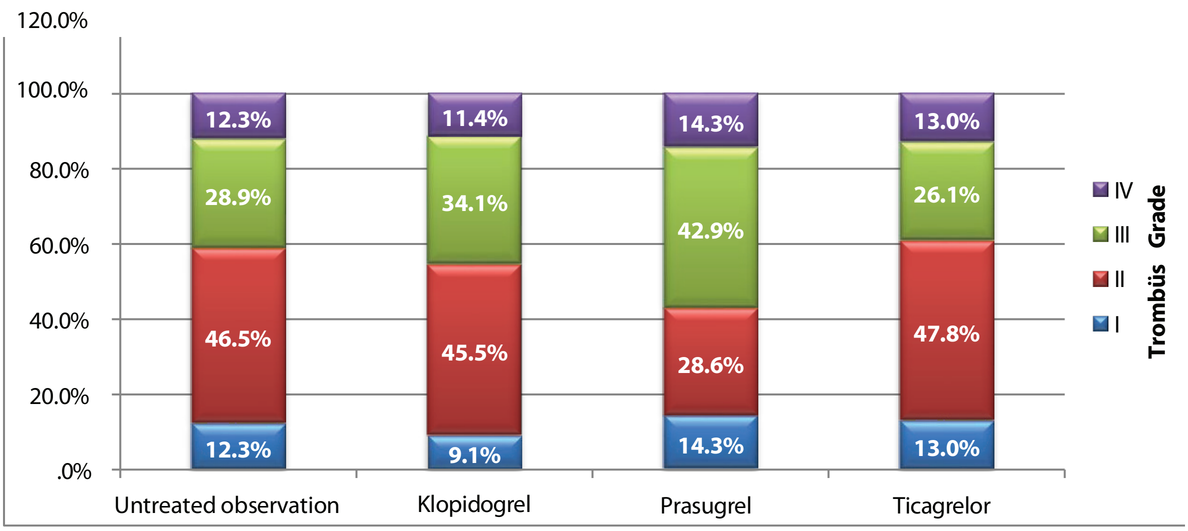
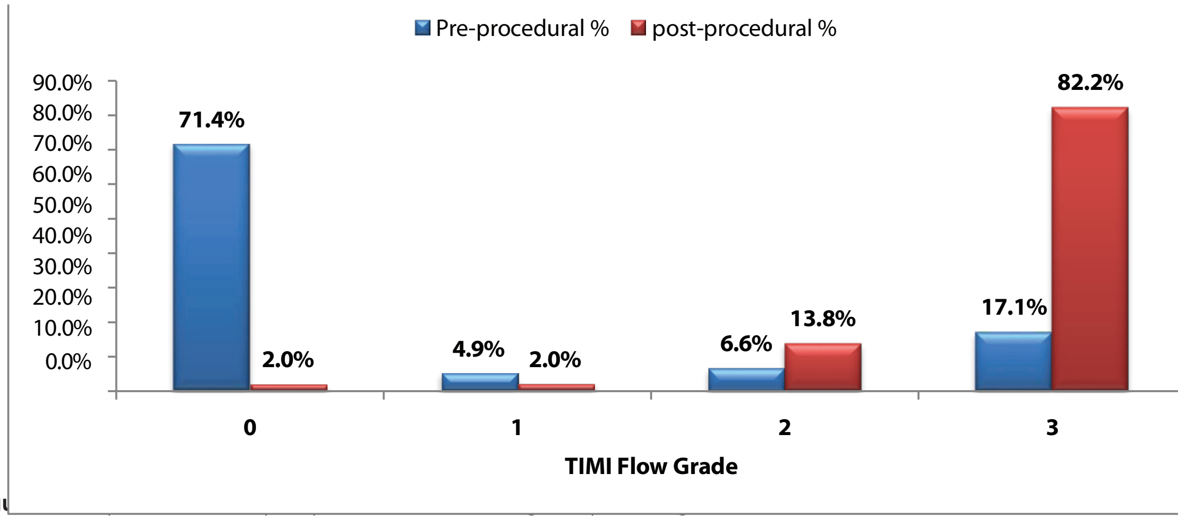


Figure 6. Thrombus grade percentages in patients receiving loading therapy in the emergency department.



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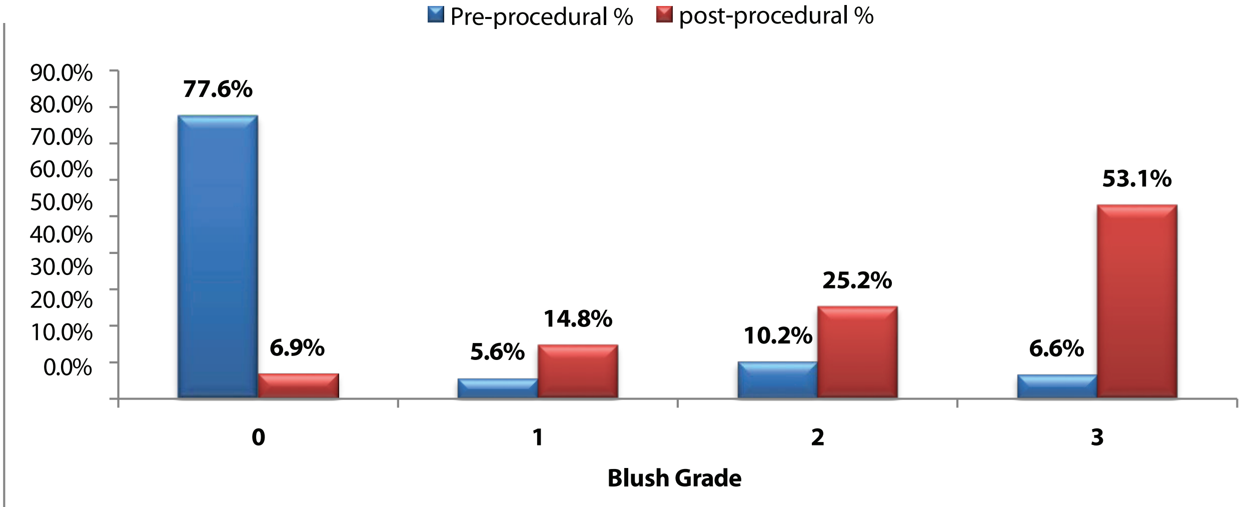

Figure 8. Myocardial Blush Grade (MBG) percentages before and after procedure.

respectively). Furthermore, post-procedural MBG was significantly higher than pre-procedural values in all loading therapy subgroups (Table 15). Additionally, Table 16 shows the distribution of post-procedural MBG stratified by ED loading therapy status.

Discussion

The increased incidence of myocardial infarction (MI) with advancing age has been consistently reported in numerous studies. In Fuster et al.'s 1992 study, the prevalence of angina was shown to rise with age in both sexes: in women, prevalence increased from 5–7% in the 45–64 age group to 10–12% in the 65–84 age group, while in men, the rates were 4–7% and 12–14%, respectively, in the same age groups (2). These findings support the progressive nature of coronary artery disease (CAD) with aging.

Rittersma et al. (2005) and Stone (2004) reported a higher frequency of angina in middle-aged women com-

Table 4. Pre-procedural and post-procedural myocardial blush grade (MBG) according to loading therapy status in the emergency department

Emergency department loading therapy	Pre-procedural myocardial blush grade (MBG)	Post-procedural myocardial blush grade (MBG)	P
Untreated observation	0.45±0.92	2.27±0.96	**<0.001**
Klopidogrel	0.50±0.92	2.19±0.93	**<0.001**
Prasugrel	1.00±1.41	2.29±0.95	**0.038**
Ticagrelor	0.22±0.74	2.26±0.96	**<0.001**
p	0.188	0.873	

pared to men, attributing this to the higher prevalence of functional CAD forms (e.g., microvascular angina) in women and the increased prevalence of atherosclerotic disease in older age (24). However, in our study, the mean age of women (65.2 ± 13.9 years) was significantly higher than that of men (54.4 ± 12.2 years). Contrary to previous studies, this finding suggests that angina frequency may be more pronounced in elderly women. Similarly, Matsis et al. (2016) reported that MI occurs at younger ages in men but at later ages in women (25). These results indicate that age and sex distributions may change over time, possibly due to evolving sociodemographic and risk factor profiles. Nevertheless, MI incidence remains higher in men overall.

In our study, 75.7% (n=306) of patients were male, consistent with the 72.4% male prevalence reported by Matsis et al. (25). Aygül et al. (2009) also demonstrated a significantly higher MI frequency in men compared to women in Turkey, though incidence increased with age in women (16). These findings highlight the role of sex-specific risk factors (e.g., loss of hormonal protection, postmenopausal metabolic changes) and diagnostic delays.

Comorbidities and Stent Thrombosis

The most common comorbidities observed in our patients were CAD (20.5%), diabetes mellitus (DM, 16.8%), and hypertension (HT, 15.3%). Stent thrombosis was detected in 5.7% (n=17) of patients. No significant differences were found between patients with and without stent thrombosis regarding age, sex, DM, HT, hyperlipidemia (HL), chronic heart failure (CHF), or mortality. However, stent thrombosis incidence was 4.5% in those with DM, 10.3% in HT, 25% in HL, and 12.1% in patients with a history of CAD. These data suggest that comorbidities heterogeneously influence stent thrombosis risk.

Van Werkum et al. (2009) reported a thrombosis rate of 22.3% in drug-eluting stents (DES) among DM patients versus 13.6% in other stents, indicating that DM may increase thrombosis susceptibility in DES (26). Similarly, HL and CAD history were associated with higher thrombosis risk in DES (26). In Turkey, Aygül et al. (2009) reported DM prevalence at 21% and HT at 35% (16). These variations may stem from ethnic, geographic, and treatment protocol differences.

Antithrombotic Loading Strategies in the Emergency Department

Prasugrel was used exclusively in CAD-diagnosed patients. In other comorbidities, the rate of withholding antithrombotic loading exceeded 50%, particularly in hypertensive patients (>50%). This approach may reflect preemptive bleeding risk assessment and deferred treatment decisions pending coronary imaging. However, it may delay antithrombotic therapy initiation, potentially increasing ischemia risk.

In-Hospital and Post-Procedural Mortality

In-hospital mortality was 3.7%, with post-procedural mortality at 1.98%. Mortality was 4.2% in the no-loading group versus 2.9% in the loading group, though this difference was not statistically significant (p>0.05). This suggests that antithrombotic loading alone does not dictate mortality, emphasizing the importance of multidisciplinary approaches (e.g., early revascularization, hemodynamic support).

The TEKHARF study reported an annual mortality rate of 1.14% over 25 years (27), though direct comparisons are limited due to its broader cardiovascular focus. Notably, in-hospital MI mortality declined from 17.6% in a 1991 multicenter study (28) to 2.9% in a 2016 cohort of 322,523 patients with obstructive CAD (29), likely due to standardized primary percutaneous coronary intervention (PPCI) protocols, stent advancements, and optimized anticoagulation.

P2Y12 Inhibitor Selection

Antithrombotic loading was withheld in 65.3% of emergency department patients. Among those loaded, clopidogrel (25%) was most frequently used, followed by prasugrel (7.4%) and ticagrelor (2.2%). This distribution may reflect clopidogrel's broad indications, lower bleeding risk, and cost-effectiveness. However, prasugrel and ticagrelor's faster onset and stronger platelet inhibition could reduce mortality in select patients.

Angiographic Findings

Grade II thrombus (43.1%) was most common in infarct-related arteries, while Grade I thrombus was rare (8.2%). No significant association was found between thrombus grade and antithrombotic loading or mortality. However, all untreated patients had Grade II thrombus, suggesting thrombus burden may influence clinical decision-making.

TIMI Flow and Blush Grade Outcomes

Post-procedural TIMI 0 flow decreased from 71.4% to 2%, while TIMI 3 flow increased from 17.1% to 82.2%. Similarly, Blush Grade 0 cases declined from 77.6% to 6.9%, and Blush Grade 3 rose from 6.6% to 52.1%. Mont'Alverne-Filho JR et al. (2016) reported higher TIMI 3 rates with prasugrel/ticagrelor versus clopidogrel (18), but our study found no inter-agent differences. Perl et al. (2015) noted a 73.3% Blush Grade 3 rate with prasugrel (30), versus 57.1% in our cohort, possibly due to population and revascularization timing differences.

Conclusion

Our study found no significant impact of emergency department antithrombotic loading on TIMI flow or Blush Grade. However, factors underlying mortality reduction (e.g., early revascularization, ICU protocols) warrant further investigation in larger cohorts. Evolving age- and sex-based risk distributions are critical for personalized preventive strategies.

Limitations

This study was designed as a focused, single-center analysis with the advantage of retrospective data collection, allowing for in-depth clinical evaluation. The findings demonstrate a pioneering approach that underscores the critical importance of rapid decision-making processes in acute coronary syndrome management. However, the interpretations should be considered in light of certain limitations. A significant limitation is the lack of systematic data on aspirin use, which is a cornerstone of ACS management; this gap may affect the interpretation of the overall medical intervention strategies and their outcomes. Additionally, while the carefully selected patient population provides a unique clinical perspective, the generalizability to other centers is limited, underscoring the need for validation through prospective multicenter studies.

Conclusion

The lack of aspirin usage data in this study may be regarded as a seminal starting point that creates novel research opportunities. This gap paves the way for groundbreaking studies that could enable more comprehensive evaluation of antithrombotic treatment interactions. Furthermore, the rigorously restricted use of prasugrel has made an innovative contribution to clinical practice by highlighting the need to develop prospective personalized treatment protocols for high-bleeding-risk patients

The high proportion of non-loaded patients in this study reflects the rapid intervention culture in emergency departments that prioritizes coronary anatomy assessment. This finding serves as an illuminating reference for optimizing decision-making strategies in time-sensitive clinical scenarios. Ultimately, this study has established an inspirational foundation for academic research, demonstrating potential to evolve into a gold-standard model particularly through multicenter prospective designs.

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