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CLINICAL OUTCOMES OF COMBINED GLYCOPROTEIN IIB/IIIA INHIBITORS AND P2Y12 RECEPTOR ANTAGONIST IN ELECTIVE PCI FOR PATIENTS OVER 65

65 YAŞ ÜSTÜ HASTALARDA ELEKTİF PKG'DE GLİKOPROTEİN IIB/IIIA İNHİBİTÖRLERİ İLE P2Y12 RESEPTÖR ANTAGONİSTİ KOMBİNASYONUNUN KLİNİK SONUÇLARI

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ABSTRACT

Introduction: Glycoprotein IIb/IIIa inhibitors (GPIs) are potent antiplatelet agents used during percutaneous coronary intervention (PCI) to reduce thrombotic complications. While their efficacy in acute coronary syndromes is established, their role in elective PCI, particularly among elderly patients, remains uncertain.

Methods: This retrospective, single-center study included 85 patients aged ≥65 years who underwent elective PCI between 2021–2023 and received GPIs due to high thrombus burden or no-reflow. All patients received aspirin and a P2Y12 inhibitor (clopidogrel , prasugrel, or ticagrelor); abciximab or tirofiban was used as the GPI. Clinical, laboratory, and procedural data were analyzed, focusing on major bleeding, haemoglobin drop, transfusion requirement, and hospital stay.

Results: The mean age was 70 years and 83% were male. Tirofiban was administered in 83% and abciximab in 17% of cases. Major bleeding occurred in 26%, most frequently in the abciximab plus potent P2Y12 group, though differences were not statistically significant. Hospital stay was longer in patients receiving abciximab. Haemoglobin drop was significantly greater across groups, but no difference was observed in haemoglobin levels at one-month and one-year follow-up. Creatinine values were comparable. No stent thrombosis or mortality was reported.

Conclusions: In elderly patients undergoing elective PCI, GPIs appear to be the main determinant of bleeding risk, with no additional impact from the choice of P2Y12 inhibitor. These findings emphasize the need for a selective approach to GPI use in this setting.

Keywords: Glycoprotein IIb/IIIa inhibitors; P2Y12 inhibitors; elective PCI; bleeding; elderly patients

ÖZET

Giriş: Glikoprotein IIb/IIIa inhibitörleri (GPI'ler), perkütan koroner girişim (PKG) sırasında trombotik komplikasyonları azaltmak için kullanılan güçlü antiplatelet ajanlardır. Akut koroner sendromlarda etkinlikleri gösterilmiş olsa da, elektif PKG'de özellikle yaşlı hastalarda klinik yararları ve güvenlik profilleri tartışmalıdır.

Yöntemler: Bu retrospektif, tek merkezli çalışmaya, 2021–2023 yılları arasında elektif PKG sırasında yüksek trombüs yükü veya no-reflow nedeniyle GPI tedavisi verilen, 65 yaş ve üzeri toplam 85 hasta dahil edildi. Tüm hastalara asetilsalisilik asit ve bir P2Y12 inhibitörü (klopidogrel, prasugrel veya tikagrelor) uygulandı; GPI olarak abciximab veya tirofiban kullanıldı. Klinik, laboratuvar ve işlem verileri incelendi; majör kanama, hemoglobin düşüşü, transfüzyon ihtiyacı ve hastanede kalış süresi değerlendirildi.

Bulgular: Hastaların ortalama yaşı 70 yıl olup %83'ü erkekti. Tirofiban %83, abciximab %17 oranında kullanıldı. Majör kanama oranı %26 idi ve en yüksek oran abciximab + potent P2Y12 grubunda gözlendi. Ancak gruplar arasında istatistiksel fark yoktu. Hastanede kalış süresi abciximab alanlarda daha uzundu. Hemoglobin düşüşü gruplar arasında anlamlı farklılık gösterirken, 1. ay ve 1. yılda Hb değerleri benzerdi. Kreatinin düzeyleri arasında fark yoktu, mortalite veya stent trombozu görülmedi.

Sonuç: Yaşlı elektif PKG hastalarında GPI tedavisi kanama riskini artıran temel faktördür. P2Y12 inhibitörünün klopidogrel veya potent ajan olmasının kanama üzerine ek etkisi görülmemiştir. Bulgular, GPI kullanımında seçici yaklaşımın önemini vurgulamaktadır.

Anahtar Kelimeler: Glikoprotein IIb/IIIa inhibitörleri; P2Y12 inhibitörleri; elektif PKG; kanama; yaşlı hasta

INTRODUCTION

Glycoprotein IIb/IIIa inhibitors (GPIs) are potent antiplatelet agents that have been shown to improve clinical outcomes when administered during percutaneous coronary intervention (PCI) in the setting of acute coronary syndromes (ACS). However, in non-ACS settings such as stable angina, the clinical benefit of their use during elective PCI remains uncertain. Glycoprotein IIb/IIIa inhibitors (GPIs) are currently indicated mainly for patients at high thrombotic risk, where they can provide clinical benefit; however, their use is also associated with an increased risk of bleeding (1-3).

Intravenous glycoprotein IIb/IIIa inhibitors(GPIs) exert their antithrombotic effect by blocking the binding of fibrinogen to GP IIb/IIIa receptors on the platelet surface. This inhibition disrupts platelet aggregation and plays a key role in thrombus formation (4-5).

Current guidelines recommend potent P2Y12 inhibitors such as prasugrel and ticagrelor, which demonstrate a faster onset of action, greater potency, and superior clinical outcomes compared to clopidogrel (6).

The use of next-generation P2Y12 inhibitors has raised questions about the, the benefit—and more importantly, the

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safety—of glycoprotein IIb/IIIa inhibitors (GPIs) has become controversial. Furthermore, recommendations for GPI use during PCI in patients with no-reflow or thrombotic complications (Class IIa, Level of Evidence C), and in patients who were not pre-treated with P2Y12 inhibitors (Class IIb, Level of Evidence C), are not supported by any randomized controlled trials. Findings regarding GPI use with prasugrel and ticagrelor are limited and mostly derived from subgroup analyses of existing studies.

There are currently three FDA-approved glycoprotein IIb/IIIa inhibitors: abciximab, tirofiban, and eptifibatide.

Current guidelines recommend the use of glycoprotein IIb/IIIa inhibitors as “bailout therapy” in patients with a high thrombus burden or thrombotic complications such as no-reflow. These agents are typically given as a bolus dose during PCI, followed by a 12–24 hour infusion at the operator’s discretion in patients at high ischemic risk (6).

Our study aimed to evaluate the clinical outcomes associated with combined glycoprotein IIb/IIIa inhibitors and P2Y12 receptor antagonist therapy in elective PCI patients over aged 65 years.

METHODS

This single-center, retrospective study included 85 patients aged ≥65 years who underwent elective PCI and received GP IIb/IIIa inhibitors due to high thrombotic burden or slow coronary flow at Başkent University Hospital between 2021-2023.

The study included patients who received abciximab or tirofiban, aspirin (ASA), and a P2Y12 receptor inhibitor (clopidogrel, prasugrel, or ticagrelor). Exclusion criteria were thrombolytic therapy, thrombocytopenia (<100,000 cells/μL, advanced liver or kidney disease, known active malignancy and age under 65 years.

Management of the patients was in accordance with the current Chronic Coronary Disease ESC guidelines.

Patients received a loading dose of clopidogrel (600mg followed by 75 mg/day), ticagrelor (180 mg followed by 90 mg twice daily), and prasugrel (60 mg followed by 10mg/day), in combination with unfractionated heparin (50-70IU/kg IV bolus, adjusted to maintain an activated clotting time (ACT) of 200-250 seconds). Additionally, GPI treatment could be considered at the discretion of the operator for bail-out (no reflow or thrombotic complications) or in case of high thrombus burden after angiography was performed. Intracoronary abciximab (0,25mg/kg bolus followed by, 0.125 μg/kg/min infusion for 12–36 hours) or tirofiban (25 μg/kg over 3 minutes, followed by 0.15 μg/kg/min infusion for 18–24 hours). GPI infusion was continued in the coronary care unit, with dosage modifications guided by renal function when necessary.

Patient records were reviewed to obtain medical history. Prior to PCI, physical examination was performed and blood samples were collected to assess haemoglobin, platelet count, creatinine, and estimated glomerular filtration rate (eGFR). The estimated glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault Formula (7).

Bleeding events was any intra-hospital bleeding complication such as superficial subcutaneous bleeding, hematoma at the access site, gastrointestinal bleeding, and retroperitoneal bleeding. A significant decrease in haemoglobin was defined as a reduction of ≥ 3 g/dL.

Statistical analysis

Statistical analyses were performed using SPSS Statistics Version 22.0 for Windows.

The distribution of continuous variables was assessed by the Kolmogorov-Smirnov test. Variables with a normal distribution are presented as mean ± standard deviation, while non-normally distributed variables are expressed as median (interquartile range). Categorical variables are reported as counts and percentages (%). Comparisons between categorical variables were performed using the Chi-square test, whereas continuous variables were compared using either the Student’s t-test or the Mann-Whitney U test, as appropriate. A two-tailed p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 85 patients were included in the study. The mean age was 70 ± 4.4 years, and 83.5 % patients were male.

Of the entire cohort, 48.2 patients received ticagrelor or prasugrel and 51.8 were treated with clopidogrel. The choice of P2Y12 inhibitor type and loading dose was made in the catheterization laboratory at the operator’s discretion, based on thrombus burden assessed after diagnostic angiography and prior to PCI (bail out strategy). Arterial access site was only trans femoral. There was no significant difference in the distribution of female and male patients across the treatment groups (p>0.05).

There was no age-related difference in the preference for clopidogrel versus other potent P2Y12 inhibitors.

Abciximab was preferred as GP IIb/IIIa inhibitor therapy for 16.5% patients and tirofiban for 83.5% patients.

Baseline characteristics data are shown in Table 1.

Major bleeding occurred in about one quarter of the patients (26%). The highest incidence was seen in those treated with abciximab combined with a potent P2Y12 inhibitor (45.5%), followed by the tirofiban plus potent P2Y12 inhibitor group (36.4%). In contrast, the tirofiban plus clopidogrel group had the lowest rate (4.5%). Despite these numerical differences, the comparisons were not statistically significant (p>0.05).

The most common site of bleeding was an access-site hematoma (inguinal), which developed in 23 patients, followed by superficial subcutaneous bleeding. The frequency of inguinal hematoma was again highest in the abciximab plus potent P2Y12 inhibitor group (52.2%), but without statistical significance across the groups. Similarly, transfusion requirements did not differ meaningfully between groups (p>0.05).

Although some tirofiban-based groups showed lower glomerular filtration rate (GFR) values, these differences were not significant. By contrast, hospital stay did vary significantly between treatment groups (p<0.05). The longest stays were observed in the abciximab plus clopidogrel group (mean 55.8 h) and the abciximab plus potent P2Y12 inhibitor group (mean 55.2 h).

While the overall rates of major bleeding did not differ significantly, the extent of haemoglobin drop during hospitalization was significantly different among groups (p<0.05). However, no differences were found in haemoglobin levels at either the one-month or one-year follow-ups (p>0.05). Creatinine levels also remained comparable across groups (p>0.05). Finally, the type of coronary artery undergoing PCI showed significant variation

Table 1. Baseline Characteristics

Variables	Clopidogrel + Abciximab (n=5)	Clopidogrel + Tirofiban (n=39)	Potent P2Y12 inh + Abciximab (n=9)	Potent P2Y12 inh + Tirofiban (n=32)	p-value
Age	71 ± 2.3	70 ± 4.8	71 ± 5.6	70 ± 4.0	0.563
Male sex	5 (100.0%)	31 (79.5%)	7 (77.8%)	28 (87.5%)	0.419
HT	3 (60.0%)	31 (79.5%)	7 (77.8%)	20 (62.5%)	0.393
DM	1 (20.0%)	11 (28.2%)	3 (33.3%)	5 (15.6%)	0.542
Hb drop 0–1 g/dL	2 (40.0%)	14 (35.9%)	6 (66.7%)	13 (40.6%)	
Hb drop 1–2 g/dL	1 (20.0%)	13 (33.3%)	0 (0.0%)	10 (31.3%)	
Hb drop 2–3 g/dL	0 (0.0%)	4 (10.3%)	2 (22.2%)	8 (25.0%)	
Hb drop 3–4 g/dL	0 (0.0%)	2 (5.1%)	1 (11.1%)	1 (3.1%)	0.019*
Hb drop >4 g/dL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
No Hb drop	2 (40.0%)	6 (15.4%)	0 (0.0%)	0 (0.0%)	
Bleeding – Inguinal	1 (20.0%)	10 (25.6%)	0 (0.0%)	12 (37.5%)	
Bleeding – Retroperitoneal	0 (0.0%)	1 (2.6%)	2 (22.2%)	2 (6.3%)	
Bleeding – Subcutaneous	1 (20.0%)	8 (20.5%)	2 (22.2%)	4 (12.5%)	
Bleeding – GI	0 (0.0%)	6 (15.4%)	1 (11.1%)	4 (12.5%)	0.341
No bleeding	3 (60.0%)	14 (35.9%)	4 (44.4%)	10 (31.3%)	
PCI vessel – LAD	1 (20.0%)	12 (30.8%)	3 (33.3%)	7 (21.9%)	
PCI vessel – CX	0 (0.0%)	3 (7.7%)	0 (0.0%)	9 (28.1%)	
PCI vessel – RCA	1 (20.0%)	7 (17.9%)	1 (11.1%)	10 (31.3%)	
PCI vessel – Saphenous graft	3 (60.0%)	5 (12.8%)	5 (55.6%)	2 (6.3%)	0.005*
PCI vessel – Other/combination	0 (0.0%)	12 (30.8%)	0 (0.0%)	4 (12.5%)	
Hospital stay (h)	55.2 ± 23.4	47.6 ± 25.8	70 ± 19	66 ± 19.8	0.003*
Baseline Hb	14.8 ± 1.4	14 ± 1.6	14.8 ± 1	14.9 ± 1.6	0.443
1-month Hb	15 ± 0.6	13.4 ± 1.6	13.8 ± 1.7	13.7 ± 1.6	0.181
1-year Hb	14.8 ± 0.8	14 ± 1.2	15 ± 1.1	14.5 ± 1.7	0.228
Creatinine (mg/dL)	1.0 ± 0.2	1.0 ± 0.4	1.0 ± 0.2	0.9 ± 0.2	0.064
GFR (mL/min/m²)	78 ± 11.4	80 ± 19	79 ± 22	87 ± 16	0.205
Platelet count	240 ± 23.6	271 ± 71.3	244 ± 42.2	260 ± 63	0.521

Data are presented as mean ± SD for continuous variables and as n (%) for categorical variables. Potent P2Y12 inhibitors = prasugrel or ticagrelor. $p < 0.05$ was considered statistically significant.

Abb. h:hours; Hb: Haemoglobin; GFR:Glomerular filtration rate; PLT: Platelet count; GI : Gastrointestinal; HT: Hypertension; DM :Diabetes mellitus; PCI: Percutaneous coronary intervention.

among treatment groups ($p<0.05$).Stent thrombosis and mortality were not observed in any treatment group.

Our findings are consistent with the 2023 ESC ACS Guidelines, which advise against using GP IIb/IIIa inhibitors routinely. Instead, these drugs should be reserved for special situations such as large thrombus burden or no-reflow, because their extra benefit in reducing ischemic events is small while their bleeding risk is well known (6).

DISCUSSION

In our study, bleeding and ischemic complications were evaluated in elective PCI patients who received tirofiban or abciximab infusion in addition to DAPT due to high thrombotic burden or no-reflow. Patients who received GPIs on top of potent oral P2Y12 inhibitors (ticagrelor or prasugrel) had similar rates of bleeding complications—including significant haemoglobin drop, gastrointestinal bleeding, and access-site hematoma—compared with those who received GPIs on top of clopidogrel.

No significant difference was observed in the incidence of in-hospital or one-year bleeding events between clopidogrel and the more potent P2Y12 receptor inhibitors. This lack of difference may be partly explained by the preferential use of clopidogrel in patients at higher bleeding risk. Notably, patients treated with clopidogrel were older and included a higher proportion of females, suggesting that clopidogrel was often selected for individuals with an increased bleeding risk. Another possible explanation is the relatively small sample size, which may have limited the statistical power to detect differences. Indeed, although the absolute number of bleeding events was higher in the abciximab plus potent P2Y12 inhibitor group, this did not reach statistical significance.

Our findings echo what was observed in the subgroup analyses of the TRITON-TIMI 38 and PLATO trials. In both studies, prasugrel and ticagrelor continued to show better protection against ischemic events compared with clopidogrel, regardless of whether a GP IIb/IIIa inhibitor was added. What changed with the addition of GP IIb/IIIa inhibitors was not efficacy, but safety: bleeding risk clearly increased, irrespective of the P2Y12 inhibitor used (8,9).

This is very similar to our own results. In our study, patients who received GP IIb/IIIa inhibitors experienced more bleeding overall, but the choice between clopidogrel and a more potent P2Y12 inhibitor did not make a major difference. Since our patients were older and the sample size was small, our results suggest that the main driver of bleeding risk is the GP IIb/IIIa inhibitor itself, rather than which P2Y12 inhibitor is used.

To date, no dedicated randomized trial has specifically evaluated the benefit or risk of GP IIb/IIIa inhibitors in combination with prasugrel or ticagrelor. However, subgroup analyses of TRITON-TIMI 38 and PLATO, along with a meta-analysis, consistently demonstrated that the benefit of

prasugrel and ticagrelor versus clopidogrel was independent of GPI use (8-10).

Furthermore, a meta-analysis including 16 randomized trials demonstrated that the use of GP IIb/IIIa inhibitors during elective PCI in patients with stable coronary artery disease was associated with a reduction in short- and mid-term major adverse cardiovascular events (MACE). However, this benefit came at the cost of an increased risk of minor bleeding. These findings support a selective approach to GPI use in elective PCI, particularly favouring their administration in patients with a low baseline risk of bleeding (11).

CONCLUSION

Although there are concerns that combining GP IIb/IIIa inhibitors with oral P2Y12 inhibitors may increase the risk of major bleeding, evidence suggests that this strategy can be safely implemented, particularly in carefully selected elective PCI patients at high ischemic risk.

Concurrent use of abciximab or tirofiban with potent P2Y12 receptor inhibitors has not been shown to increase bleeding rates. However, careful monitoring for bleeding risk is recommended, especially in patients with elevated creatinine levels.

In patients with stable coronary artery disease, further studies are needed to better understand the benefits the combination of glycoprotein IIb/IIIa inhibitors with potent P2Y12 inhibitors and to determine which patient groups may benefit the most.

Limitations

The major limitations of our study were the small sample size, retrospective design, and its single-centre nature. Physicians may have chosen different antiplatelet agents according to the patients' overall clinical condition and comorbidities during PCI, potentially resulting in heterogeneity among the groups. While potent P2Y12 receptor inhibitors are typically preferred for acute coronary syndrome, their use in this specific subgroup was limited to elective PCI patients presenting with a high thrombus burden.

In addition, although we intended to perform matching for baseline characteristics such as age, sex, hypertension (HT), diabetes mellitus (DM), heart failure (HF), and coronary artery disease (CAD), propensity score matching could not be conducted due to the limited sample size.

Ethics Committee Approval: Approval for the study was obtained from Başkent University Clinical Research Ethics Committee (decision number: 25/320, date: 03.09.2025).

Informed Consent: Informed consent was not obtained from the patients owing to the retrospective design of the study.

Authorship Contributions: Concept – E.K; S.H.H.; Design – A.N.A; S.H.H.; Supervision – E.K.; Data collection &/or processing – S.H.H ; A.N.A.; Analysis &/or interpretation – S.H.H; A.N.A Literature search – A.N.A Writing – A.N.A; S.H.H; Critical review – E.K; A.N.A.

Conflict of Interest: None declared.

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