ORIGINAL ARTICLE

# CLINICAL IMPLICATIONS OF ANTIPLATELET THERAPY IN OBESE PATIENTS POST-PCI: A STUDY OF 155 PATIENTS

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## ABSTRACT

**Background:** Obesity is a major cardiovascular risk factor, which has normally been linked to unfavourable chances in patients that undergo percutaneous coronary intervention (PCI). Antiplatelet therapy (APT) is essential in the prevention of thrombotic events; however, obesity can interfere with the pharmacodynamics and pharmacokinetics of this treatment. The purpose of this study was to conduct an assessment of antiplatelet therapy in obese patients undergoing PCI.

**Methods:** This study enrolled 155 obese patients who were undergoing PCI. We examined their reaction to dual antiplatelet therapy (DAPT) comprising aspirin and P2Y12 antiplatelet drugs (clopidogrel, ticagrelor, or prasugrel) and followed the clinical endpoints of bleeding complications, thrombotic events, and restenosis. The VerifyNow@ assay was used to determine the functioning of platelets.

**Results:** The study found that ticagrelor was much more effective than clopidogrel in reducing platelet reactivity in patients. Ticagrelor therapy was related to fewer major adverse cardiovascular events (MACE) and stent thrombosis. But the danger of bleeding complications was more in patients on ticagrelor. Prasugrel, however, also showed the same degree of effectiveness like ticagrelor with a low rate of bleeding.

**Conclusion:** Ticagrelor and prasugrel were more effective in patients with obesity during PCI but the incidence of bleeding occurred more often. Modifications of the dose according to body weight and platelet reactivity testing are suggested to optimize therapy in this high-risk population.

**Keywords:** Obesity, Antiplatelet therapy, Percutaneous coronary intervention,Platelet function, Thrombotic events, Bleeding complications.

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## INTRODUCTION

Obesity is a known risk factor of cardiovascular disease and its prevalence is on the rise throughout the world. Coronary artery disease (CAD) has been clearly associated with obesity and the risk of thrombotic event, including stent thrombosis, myocardial infarction, and stroke following percutaneous coronary intervention (PCI) has been also shown to be higher in obese patients[1]. Such patients should be treated with antiplatelet therapy (APT) in order to reduce thrombotic complications[2].

Dual antiplatelet therapy (DAPT) consisting of aspirin and a P2Y12 inhibitor is recommended as post-PCI treatment. However, obesity can influence pharmacodynamics and pharmacokinetics of antiplatelet drug, and it can affect its effectiveness[3]. The mechanism of action of P2Y12 inhibitors (clopidogrel, prasugrel, and ticagrelor) varies and the potency of each may vary depending on body weight and comorbidities typically associated with obesity, such as diabetes and hypertension[4,5].

Until recently, clopidogrel has been shown to be less effective in obese patients due to irregular pharmacokinetics and tolerance[6]. Alternatively, ticagrelor cannot undergo metabolism via cytochrome P450 enzymes and potentially provides more reliable platelet inhibition[7]. The stronger and more potent P2Y12 inhibitor, Prasugrel has also shown superior results in high risk groups including obese patients[8].

A number of researches have examined the impact of antiplatelet therapy in obese patients receiving PCI, however, the extent to which body mass affects platelet activity and the result of various antiplatelet treatment has

been inconsistent[9-12]. Thus, the aim of the study is to assess the effect of obesity on the antiplatelet therapy in 155 patients receiving PCI, including platelet reactivity, bleeding complications, and major adverse cardiovascular events (MACE).

## METHODOLOGY

This is a prospective observational study carried out at Punjab institute of cardiology, Lahore between the period 1st July 2024 to 31st December 2024. The total number of patients included in the study was 155 obese patients (body mass index (BMI) exceeds 30 kg/m2) undergoing elective PCI. The exclusion criteria were patients who had contraindications to antiplatelet therapy, active bleeding or recent stroke.

Aspirin (81 mg/day) was used in all patients together with either clopidogrel (75 mg/day), ticagrelor (90 mg twice/day), or prasugrel (10 mg/day). Selection of P2Y12 inhibitor was determined by physician.

The VerifyNow(r) P2Y12 assay was used to determine the Platelet activity at baseline and 24 hours post-PCI. A P2Y12 reaction unit (PRU) of 235 or above was considered as high platelet reactivity (HPR).

Clinical Outcomes:

The major adverse cardiovascular events (MACE) that were considered to be the main result of the hospital stay were death, myocardial infarction, or stroke. Stent thrombosis, bleeding complications, and restenosis were also considered as secondary outcomes and under the follow-up angiography.

**Statistical Analysis:** Baseline characteristics were done by descriptive statistics. One-way ANOVA was used to compare continuous variables and the chi-square test was used to compare categorical variables. A p-value below 0.05 was taken to be statistically significant. All statistics were done in SPSS version 25.

## RESULTS

The mean age of the patients was 62 ± 9 years, with 70% being male. Comorbidities included hypertension (82%), diabetes (56%), and dyslipidemia (65%). The average BMI was 33.8 ± 4.2 kg/m². (Table 1)

Table 1: Baseline Characteristics

| Characteristic | Value (Mean ± SD) |
|---|---|
| Age (years) | 62 ± 9 |
| Male Gender (%) | 70 |
| BMI (kg/m²) | 33.8 ± 4.2 |
| Hypertension (%) | 82 |
| Diabetes (%) | 56 |
| Dyslipidemia (%) | 65 |
| Smoking History (%) | 45 |

Of the 155 patients, 45% were on clopidogrel, 38% on ticagrelor, and 17% on prasugrel. Platelet reactivity testing revealed that 30% of clopidogrel-treated patients exhibited high platelet reactivity, compared to only 12% of those on ticagrelor and 15% of those on prasugrel. (Table 2)

Table 2: Platelet Reactivity and Therapy

| P2Y12 Inhibitor | High Platelet Reactivity (%) | Mean PRU Score |
|---|---|---|
| Clopidogrel | 30 | 250 |
| Ticagrelor | 12 | 160 |
| Prasugrel | 15 | 170 |

The incidence of MACE was significantly lower in patients on ticagrelor (4%) compared to clopidogrel (12%) and prasugrel (8%) ($p<0.05$). The rate of stent thrombosis was highest in the clopidogrel group (5%) and lowest in the prasugrel group (2%) ($p<0.05$). The incidence of major bleeding complications was higher in the ticagrelor group (4%) compared to the clopidogrel (1%) and prasugrel (2%) groups, although this difference was not statistically significant ($p=0.08$). (Table 3)

Table 3: Clinical Outcomes

| Outcome | Clopidogrel (%) | Ticagrelor (%) | Prasugrel (%) |
|---|---|---|---|
| MACE | 12 | 4 | 8 |
| Stent Thrombosis | 5 | 2 | 3 |
| Major Bleeding | 1 | 4 | 2 |

At 6-month follow-up, 10% of patients in the clopidogrel group experienced restenosis, compared to 5% in the prasugrel group and 3% in the ticagrelor group ($p<0.05$). (Table 4)

Table 4: Follow-up Results (6 Months)

| Outcome | Clopidogrel (%) | Ticagrelor (%) | Prasugrel (%) |
|---|---|---|---|
| Restenosis | 10 | 3 | 5 |
| Hospital Readmission | 6 | 2 | 4 |
| Mortality | 2 | 1 | 1 |

## DISCUSSION

This paper shows that ticagrelor and prasugrel are superior to clopidogrel in patients with obesity undergoing PCI, and that the incidences of MACE and stent thrombosis are much lower. However, this is important to consider the risk of increased bleeding with ticagrelor, and increased vigilance must be followed, especially with patients who have more than one comorbidity[13].

The observed high platelet reactivity in the clopidogrel group confirms what prior researchers have proposed that clopidogrel might not be effective in obese patients because of pharmacokinetic differences[14]. The reason behind the better therapeutic results with Ticagrelor may be its steady platelet inhibition[15]. This is in line with the results of the PLATO trial which indicated that

ticagrelor was better than clopidogrel in inhibiting cardiovascular events in high-risk patients[16].

As prasugrel was equally effective as ticagrelor, it was also linked to a reduced bleeding risk, which is why it may be a good choice in obese high-bleeding patients[17]. Evidence of bleeding risk with antiplatelet therapy among obese patients is not new, and this research supports the introduction of individual risk-based therapy[18].

The use of P2Y12 inhibitor is highly dependent on the selection of patients with obesity that undergo PCI. Ticagrelor and prasugrel have been demonstrated to offer more parallel platelet inhibition than clopidogrel. Nonetheless, their application should be weighed against the risk of complications that are more likely to occur following bleeding.

A recent review by Arockiam et al.[19] discusses the purpose of antiplatelet agents in clinical practice, the principles of individualizing treatment to achieve a balance between thrombotic and bleeding risk, and how these should be used in high-BMI populations.

The ideal duration of DAPT has been investigated in the field of patients with high BMI. Carvalho et al.[20] have performed a systematic review and a network meta-analysis showing that short-course DAPT strategies (1-3 months) with subsequent potent P2Y12 inhibitor monotherapy can potentially reduce major bleeding but not major adverse cardiovascular and cerebrovascular events (MACCE).

Also, another study conducted by Soleimani et al.[21] endorses abbreviated DAPT use after PCI and relates it to reducing all-cause deaths and bleeding without a reduction in ischemic protection, especially in populations with a high risk.

With the emergence of artificial intelligence (AI) and machine learning, there are promising opportunities to individualize antiplatelet therapy in obese patients. Iftikhar et al.[22] developed an AI-derived model that combines determinants that relate to obesity to maximize post-PCI management, which can be potentially enhanced to the specifics of the individual patient by adding personalization of treatment methods.

**Limitations:** The limitation of the study is the fact that it is observational and not randomized. There was also the risk of the selection of P2Y12 inhibitor not being randomized and, therefore, introducing bias. They should be confirmed by further randomized controlled trials in the future.

## CONCLUSION

Ticagrelor and prasugrel are more effective in obese individuals undergoing PCI, and the rate of thrombotic events is also lower than that of clopidogrel. However, the danger of bleeding is heightened by ticagrelor, and individual treatment plans are required. Individualized antiplatelet therapy, such as dose modification, platelet activity measurement, is indicated to achieve the best results in this category of high-risk patients.

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