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Prospective Study

Study to Evaluate the Safety, Efficacy, and Duration of Dual Antiplatelet Therapy in Coronary Artery Disease Patients

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Abstract

Coronary artery disease (CAD) is a leading cause of mortality globally, characterized by the formation of atherosclerotic plaques that impede blood flow to the myocardium. Dual antiplatelet therapy (DAPT), combining aspirin with a P2Y12 inhibitor, is essential for reducing ischemic events post-coronary stenting. This paper aimed to evaluate the safety, efficacy, and optimal duration of DAPT with ECOSPRIN+TICAGRELOR versus ECOSPRIN+CLOPIDOGREL in CAD patients.

Methodology: This single-arm prospective observational study included 106 CAD patients from Yashoda Hospital, Secunderabad, over six months. Patients were divided into two groups (53 each) receiving ECOSPRIN+TICAGRELOR or ECOSPRIN+CLOPIDOGREL. Follow-ups were conducted at intervals of up to three months, assessing ischemic risk, major adverse cardiovascular and cerebrovascular events (MACCE), bleeding risk, and symptom relief. Statistical analysis was performed using SPSS with significance set at $p < 0.,05$.

Results: The study comprised 87 male (82%) and 19 female (18%) patients, predominantly aged 56-74. The Ticagrelor group showed better symptom relief 103% compared to Clopidogrel 98% ($p < 0.001$) and was related to a lower risk of stent thrombosis and MACCE but a high bleeding risk (2.58 ± 1.58 *vs.* 1.88 ± 1.33, $p = 0.0144$) Common side effects for Clopidogrel included GI upset (24.49%), dizziness (20.75%), numbness (16.98%) and tingling sensation (11.32%), while Ticagrelor caused mild dyspnoea (18.86%), bradycardia (16.98%), bruising (11.32%) and bleeding (7.54%).

Conclusion: Despite a higher bleeding risk, Ticagrelor shows superior protection against ischemic events and better symptom relief than Clopidogrel. This study highlights the importance of individualising DAPT duration and choice based on patient risk profiles to optimise therapeutic outcomes.

More Information

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Introduction

Coronary artery disease, a common heart disease, is caused by atherosclerotic plaque in blood channel lumens. Coronary artery disease deprives the myocardium of blood and oxygen. Blockages in the coronary arteries produce an oxygen shortage [1]. It usually involves blood-blocking plaques in the coronary artery lumen. It's the leading murderer worldwide. At the turn of the 20th century, it killed rarely. CAD is the foremost cause of death worldwide, despite a decline since the mid-1960s [2].

CAD, often known as coronary heart disease, is common. Plaque in the coronary arteries cuts off heart blood flow [3]. This contracts and hardens them. Plaque contains cholesterol and other compounds. Due to decreased blood flow, the heart receives fewer oxygen and nutrients. Heart failure and arrhythmias increase with heart muscle attenuation. Plaque in the arteries is called atherosclerosis. Obstructions can cause arterial plaque to break, cutting off blood flow and raising heart attack risk [4].

Dual Antiplatelet Therapy (DAPT)

In order to lessen the likelihood of ischemic events such as stent thrombosis, myocardial infarction, and ischemic stroke, patients experiencing coronary stenting must take DAPT, which consists of aspirin plus a P2Y12 inhibitor such as clopidogrel, prasugrel, or ticagrelor [5]. Platelets play a crucial role in forming blood clots, and antiplatelet agents prevent

their clumping, thus mitigating the risk of sudden coronary stent blockage. Aspirin irreversibly inhibits the COX-1 enzyme, preventing thromboxane A2 synthesis, but it poses risks such as bleeding and gastrointestinal complications. P2Y12 inhibitors block ADP receptors on platelets, preventing their activation and aggregation. Clopidogrel, a commonly used prodrug, requires enzymatic activation and genetic polymorphisms can affect its efficacy [6]. Ticagrelor, a reversible P2Y12 inhibitor, offers potent and rapid action but comes with side effects like dyspnea and increased bleeding risk. Balancing the benefits and risks of DAPT, especially concerning bleeding, is critical for patient management, with contraindications including hypersensitivity, active pathological bleeding, and hepatic impairment.

Duration

Current guidelines recommend using DAPT for 12 months in all patients with acute coronary syndrome (ACS), with ticagrelor 60 mg suggested for up to 3 years in high-risk patients. The duration of DAPT after drug-eluting stent (DES) establishment varies: ≥12 months for ACS and six months for stable CAD [7]. The European Society of Cardiology (ESC) suggests 6-12 months, while the American Heart Association (AHA) recommends at least 12 months for stable patients, extending beyond 12 months for low bleeding risk and six months for high bleeding risk. These guidelines are based on trials like CURE, PLATO, and TRITON-TIMI 38, which support 12-month DAPT for ACS. Short-term DAPT (≤6 months) may be considered for high bleeding risk patients. For chronic coronary syndrome, the AHA recommends six months of DAPT post-PCI with DES, extendable if bleeding risk remains low [8]. The duration of DAPT represents a trade-off between the advantages of fewer ischemia episodes and the dangers of bleeding; among patients at high risk of bleeding, both short-term and 12-month DAPT had comparable effects.

Materials and methodology

Study design

This study is a single–arm prospective observational multi-center study in the department of cardiology in Yashoda Hospitals, Secunderabad. It is mainly designed to evaluate the safety, efficacy, and duration of ecosprin + ticagrelor in comparison with ecosprin + clopidogrel in the management of coronary artery disease patients.

The certainty of the study population was said to be 120 patients based on the flow of cases in that particular hospital, especially in the cardiology department it has been reduced to 106 patients among which 53 of them belonged to the Ecosprin+Ticagrelor group, and the remaining 53 to the Ecosprin+Clopidogrel treatment group, we have maintained the required equality in both of the study arms.

Study period and population

It took a whole six months, from June 2023 to December 2023, to collect and analyse all of the data and 106 patients were involved in the study.

Study patients

Patients who were hospitalised for acute coronary syndrome, with or without ST-segment elevation, and whose symptoms began during the previous 24 hours were eligible to register. At least two of the three requirements listed below had to be fulfilled by patients with the acute coronary syndrome who did not have ST-segment elevation: A positive biomarker test showing myocardial necrosis; ST-segment changes on ECG indicating ischaemia; or one of several risk factors (age ≥60 years; prior myocardial infarction or Coronary Artery Bypass Grafting (CABG); coronary artery disease with stenosis of ≥50% in at least two vessels; prior ischaemic stroke, transient ischaemic attack, carotid stenosis of at least 50%, or cerebral revascularisation); diabetes mellitus; peripheral arterial disease; or chronic renal dysfunction, as indicated by a creatinine clearance <60 millilitres per minute per 1.73 square meters of body surface area. The intention to do primary PCI and persistent ST-segment elevation of at least 0.1 mV in at least two contiguous leads or a fresh left bundle-branch block were the two inclusion criteria for patients with acute coronary syndrome with ST-segment elevation. Any contraindication to DAPT use, fibrinolytic medication within 24 hours prior to randomisation, the requirement for oral anticoagulation therapy, an elevated risk of bradycardia, and concurrent therapy with a potent cytochrome P-450 3A inhibitor or inducer, pregnancy, and breastfeeding, history of intracranial hemorrhage, active/recent major bleeding were major exclusion factors.

Data collection

The data was collected based on the inclusion and exclusion criteria of the patients who were selected from Yashoda Hospital Secunderabad.

This prospective observational study evaluated 106 Coronary Artery Disease (CAD) patients, split into two treatment arms: 53 on ecosprin+ticagrelor (75 mg + 90 mg) and 53 on ecosprin+clopidogrel (75 mg + 75 mg). Follow-ups were conducted at intervals of up to three months, and beyond that, via phone or review checkups. The study assessed the safety and efficacy of these regimens by analyzing ischemic risk, MACCE, bleeding risk, symptom relief, and patient recovery status, using chest pain scores before and after treatment. Consent was obtained from patients, and the hospital authorities approved the study protocol. Data were collected from both in-patient and out-patient records, covering patient demographics, comorbidities, drug types, dosages, and relevant cardiac events. Analysis of the collected data, from June 2023 to December 2023, included personal details, comorbidities, drug names and doses, allergies, safety endpoints, side effects, symptom alleviation, and treatment duration.

Data evaluation

The data collected from all the subjects were evaluated by using SPSS. Version 24. The confidence interval is 95% hence

the *p* - value is considered significant. The tests performed are independent t-test, dependent t-test, and chi-square test. The significance of the data was summarised in the Results section.

Results

Socio-demographic characteristics

The study was carried out with a sample size of 106 patients of either sex, which includes patients who are on dual antiplatelet medication ecosprin+ticagrelor (53) and ecosprin+clopidogrel (53) who are diagnosed with coronary artery disease from the department of cardiology.

A. Distribution of subjects based on gender and age: Table 1 represents the demographics of the study participants, where *n* = 106 individuals in total, with male patients making up the majority with 87, or 82%, and female patients (Figure 1) following with 19, or 18%, age group 56 - 74 (48%) patients are highest in number, followed by 37 - 55 (39%), >75 (8%) and 18 - 36 (5%),(Figure 2) respectively.

B. Distribution of subjects based on comorbidities: As seen in Table 2, considering the comorbidities of coronary artery disease patients, out of 106 patients: 38 (36%) are suffering from both hypertension and diabetes mellitus followed by diabetes mellitus alone 16 (15%), hypertension alone 8 (8%), hypertension+diabetes milletus+hypothyroidism together (5%), hypothyroidism 2 (2%), denovo hypertension and diabetes 1(1%), other comorbidities AKD, CLD, HTN+DM+AKI, HTN+DM+DYSLIPDEMIA, DM+DYSLIPIDEMIA 7 (6%), and patients with no comorbidities sum up to 29 (27%) (Figure 3) respectively.

C. Distribution of subjects by dapt score based on age intervals: By using the DAPT Score Calculator the DAPT score of every individual has been calculated depending upon the patient comorbidities, indications, and condition (Table 3 and Figure 4). As per the DAPT Score based on age intervals, the age group of 56 – 74 patients shows the DAPT Score 0, 1, 2, 3, and 4, with 02, 13, 17, 17, and 03, respectively. Age range 37 – 55 records the DAPT Score 1, 2, 3, and 4, with a number of patients 06, 21, 12, and 02, respectively. Age group >75: records 02, and 07 patients with DAPT Score 0, and 1, respectively. For the age range of 18 to 36, the DAPT Score 2, and 3 is marked with 2 patients each.

D. Distribution of subjects based on coronary stent placement: By analyzing the collected data, the coronary

Table 1: Demographics of participants.

Gender	No of Patients	Percentage (%)	*p* - value
Male	87	82%	<.001
Female	19	18%	
Age Group (In Years)	**No. of patients**	**Percentage (%)**	
18-36	05	05%	
37-55	41	39%	
56-74	51	48%	
>75	09	08%	

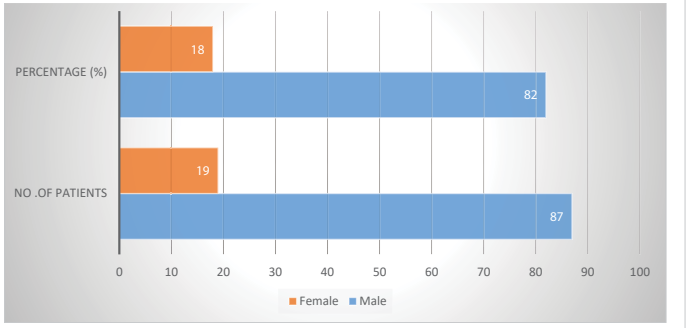

Figure 1: Gender Distribution of the subjects.

Table 2: Comorbidities of the subjects enrolled in the study (*n* = 106).

Comorbidities	No. of Patients	(%)	*p* - value
Hypertension	08	8%	<0.001
Diabetes mellitus	16	15%	
Hypothyroidism	02	2%	
HTN+DM (Type-2)	38	36%	
H HTN+DMT2+Hypothyroidism	05	5%	
Denovo HTN and DM (T-2)	01	01%	
Others	07	06%	
Nil	29	27%	

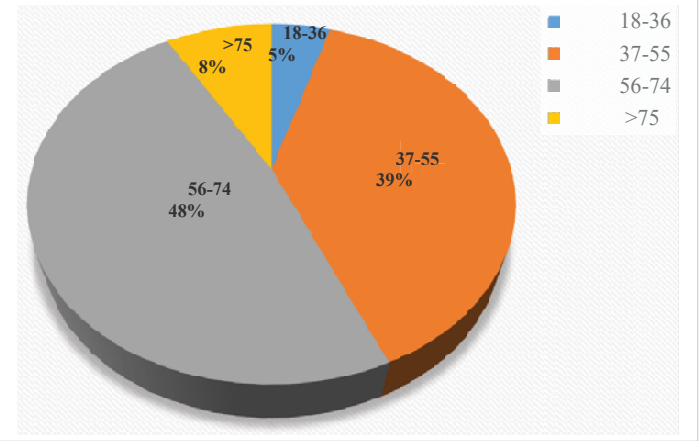

Figure 2: Age Distribution of the subjects.

Table 3: DAPT Score Based on Age Interval.

Age Interval (years)	DAPT Score					*p* - value
	0	1	2	3	4	
18-36	0	0	2	2	0	0.0010*
37-55	0	6	21	12	2	
56-74	2	13	17	17	3	
>75	2	7	0	0	0	

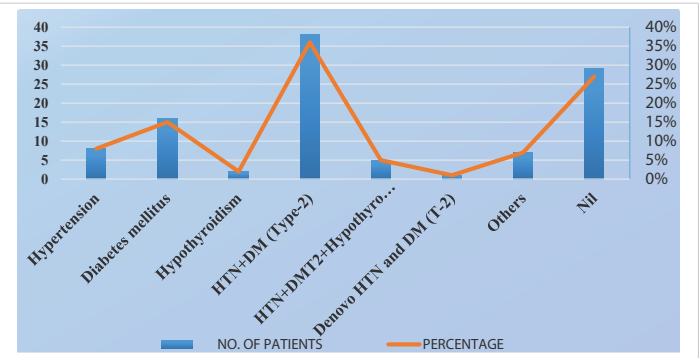

Figure 3: Percentage of comorbidities among coronary artery disease patients.

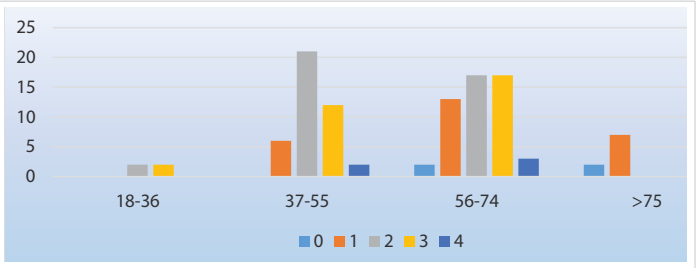

Figure 4: DAPT SCORE based on age intervals.

stent placement location has been determined for better study purposes. For better study purposes, the location of the coronary stent implantation has been established, with the majority of stent placement frequency to LAD - 80(75%), followed by RCA-40 (38%), LCX-26-(25%), LMCA-14(13%), and RAMUS-07-(07%) (Table 4 and Figure 5).

Safety characteristics of the drug ticagrelor and clopidogrel

1. Side effects: In a comparison of ECOSPRIN+TICAGRELOR with ECOSPRIN+CLOPIDOGREL, coronary artery disease patients who have been administered dual antiplatelet therapy comprising of ECOSPRIN+TICAGRELOR, are found to be less prone to side effects (Table 5 and Figure 6).

2. Comparing the safety measures ticagrelor and clopidogrel: When comparing the Stent Thrombosis, MACCE, and Bleeding Risk hazard in two treatment groups, that is, Group I: Ecosprin+Ticagrel, and Group II: Ecosprin+Clopidogrel, it is observed that group 2, which is receiving ECOSPRIN+CLOPIDOGREL has a greater risk of incidence, and for Bleeding Risk both the DAPT regimen demonstrate near values but slightly higher for group 1 (Table 6 and Figure 7).

3. Comparing the risk of therapy caused by ticagrelor and clopidogrel when discontinued: Group 2 receiving ecosprin+clopidogrel had a significantly increased incidence of stent thrombosis and MACCE when the therapy

Table 4: Stent placement location.

Stent Location	Frequency	Percentage (%)
LMCA	14	13
LAD	80	75
LCX	26	25
RAMUS	07	07
RCA	40	38

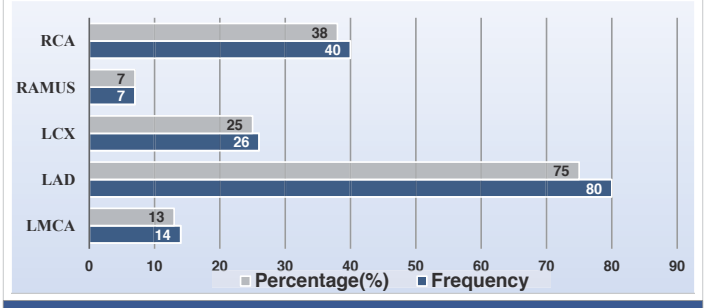

Figure 5: Location of stent placement in CAD subjects.

Table 5: Common side effects observed in patients with coronary artery disease on administration of DAPT therapy with ecosprin+ticagrelor and ecosprin+clopidogrel.

Common side effects	No. of patients	(%)	p - value
Dyspnea(mild)	10	18.86%	<.011
Bleeding	4	7.54%	
Bruising	6	11.32%	
Bradycardia	9	16.98%	
Allergic Reactions	4	7.54%	
Patient with no side effect	20	7.73%	
ECOSPRIN+CLOPIDOGREL			
Anemia	04	08%	<.001
Numbness	09	16.98%	
Tingling sensation (hands and legs)	06	11.32%	
Dizziness	11	20.75%	
GI upset	13	24.49%	
Patient with no side effects	10	18.86%	

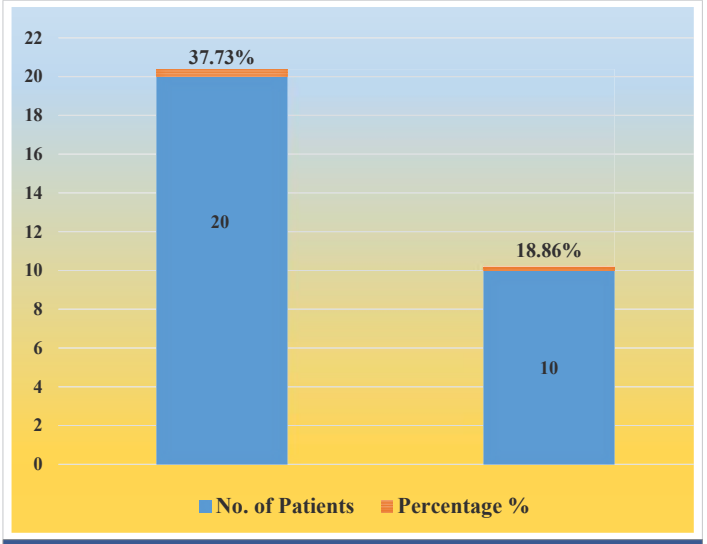

Figure 6: Comparision Of Ecosprin+Ticagrelor With Ecosprin+Clopidogrel

Table 6: Comparison of Stent Thrombosis, MACCE, and Bleeding Risk hazard in two treatment groups. Group I: Ecosprin+Ticagrel and Group II: Ecosprin+Clopidogrel.

RISK	GROUP I	GROUP II	*p* - value
Stent thrombosis	2.69±0.94	3.37±2.50	0.0215*
MACCE	4.44±0.58	4.67±0.47	0.0312*
Bleeding risk	2.58±1.58	1.88±1.33	0.0144*

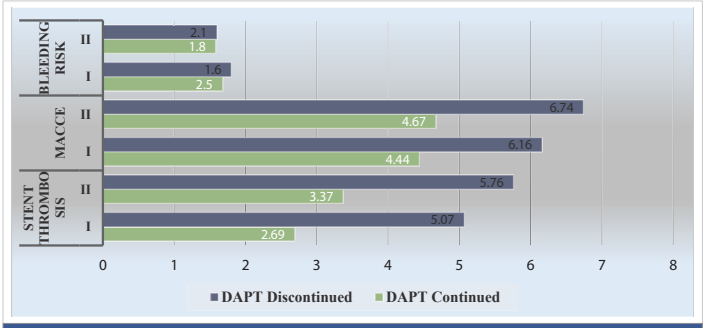

Figure 7: Comparing the risk of therapy when continued and discontinued in both groups.

was discontinued, in comparison to group 1 receiving ecosprin+ticagrelor. There is a significant decrease in bleeding risk in the ecosprin+clopidogrel receiving treatment group compared to the ecosprin+ticagrelor receiving treatment group as seen in Table 7 and Figure 7.

Comparing the risk difference between dapt continued and discontinued

The risk difference between the two treatment groups when DAPT is continued and in the case where it is discontinued is shown in Table 8 and Figures 7 and 8.

Efficacy characteristics of the drug ticagrelor and clopidogrel

The effectiveness of the drugs is determined based on the symptom relief of patients when comparing being treated by ecosprin+ticagrelor with ecosprin+clopidogrel. Comparing before and after therapy with the Dual antiplatelet drugs in two groups respectively, the treatment group receiving the ECOSPRIN+TICAGRELOR 103% therapy demonstrated a better response in symptom relief when compared to the other treatment group receiving ECOSPRIN+CLOPIDOGREL 98% (Table 9 and Figure 9).

Duration characteristics of the drug ticagrelor and clopidogrel

Correlation between DAPT duration and age in Group I with ECOSPRIN+TICAGRLOR treatment was not found to be significant as seen in Figure 10. Similar results were also found for that in Group II with ECOSPRIN+CLOPIDOGREL treatment (Figure 11).

Table 7: Comparing the risk of Stent Thrombosis, MACCE, and Bleeding Risk in two treatment groups if the therapy is discontinued.

Risk	Group I	Group II	*p* - value
Stent thrombosis	5.07 ± 1.88	5.76 ± 2.34	**0.0943**
MACCE	6.16 ± 1.86	6.74 ± 1.60	**0.0894**
Bleeding risk	1.60 ± 1.26	2.15 ± 1.06	**0.0178***

Table 8: Summary of the risk difference between the two treatment groups, Group I: Ecosprin+Ticagrelor and Group II: Ecosprin+Clopidogrel.

Risk	Group	DAPT		*p* - value
		Continued	Discontinued	
Stent thrombosis	I	2.69 ± 0.94	5.07 ± 1.88	<0.0001*
	II	3.37 ± 2.50	5.76 ± 2.34	<0.0001*
MACCE	I	4.44 ± 0.58	6.16 ± 1.86	<0.0001*
	II	4.67 ± 0.47	6.74 ± 1.60	<0.0001*
Bleeding risk	I	2.58 ± 1.58	1.60 ± 1.26	<0.0001*
	II	1.88 ± 1.33	2.15 ± 1.06	<0.0001*

Group I: Ecosprin+Ticagrelor; Group II: Ecosprin+Clopidogrel

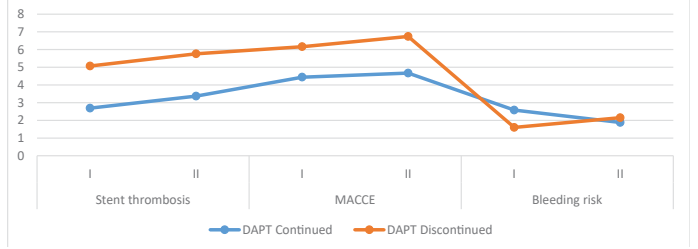

Figure 8: The risk difference between DAPT continued and discontinued in Groups I and II

Table 9: Before and After Treatment with E+T and E+C.

Treatment	Mean value E+T	(%)	*p* - value
Before treatment	99.6	94%	<.001
After treatment	110.4	103%	
Mean value e+c			
Before treatment	99.5	93.80%	<.001
After treatment	104.9	98.11%	

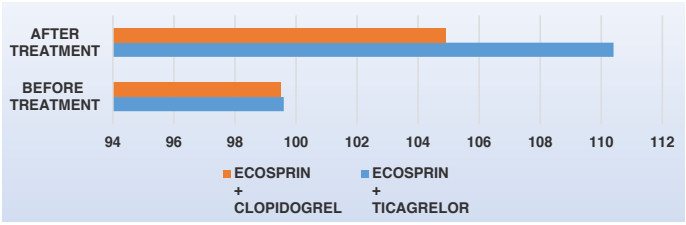

Figure 9: Comparison of effectiveness of drugs after and before treatment.

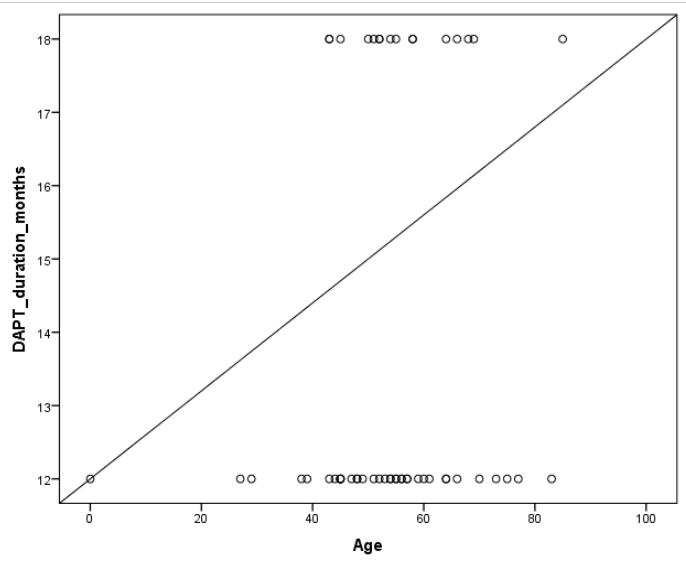

Figure 10: Correlation between DAPT duration and age in Group I (ECOSPRIN+TICAGRLOR). $r = 0.148$ and $p = 0.289$

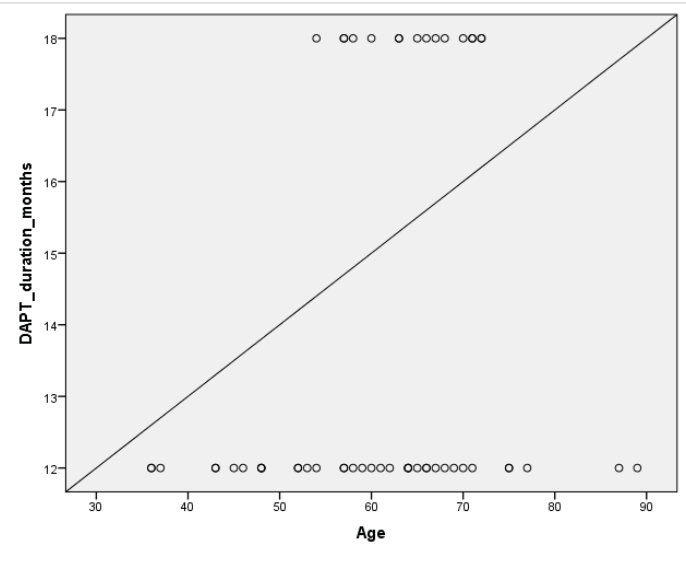

Figure 11: Correlation between DAPT duration and age in Group II (ECOSPRIN+CLOPIDOGREL). $r = 0.214$ and $p = 0.124$

Discussion

Coronary Artery Disease (CAD) involves narrowed or blocked coronary arteries due to plaque buildup, leading to chest pain or heart attacks. This prospective observational study included 53 patients in each treatment arm, examining the socio-demographic characteristics, safety, and efficacy of Ticagrelor and Clopidogrel. The study found that men (82%) were more affected than women (18%), with the majority aged 56 - 74. Comorbidities included hypertension (8%), diabetes (15%), and both (36%). The DAPT scores varied by age, with older patients generally having higher scores. Side effects for Clopidogrel included GI upset (24.49%), dizziness (20.49%), and numbness (16.98%), while Ticagrelor caused mild dyspnea (18.86%), bradycardia (16.98%), and bruising (12.5%). Ticagrelor showed a lower risk of stent thrombosis and major adverse cardiovascular and cerebrovascular events (MACCE) but a higher bleeding risk compared to Clopidogrel. When DAPT was discontinued, Clopidogrel had higher risks of stent thrombosis and MACCE, whereas Ticagrelor had a higher bleeding risk. Ticagrelor demonstrated greater efficacy (103%) in alleviating symptoms compared to Clopidogrel (98%). The study suggests that Ticagrelor offers better ischemic event protection and platelet inhibition, although with higher associated bleeding risk in comparison to clopidogrel.

The major limitation of this study is the population size, which is relatively minimal, comprising only 106 subjects. The study does not intervene in the patient medication adherence rate, which may impact the patient therapeutic outcomes; another drawback of the study is the exclusion of high-risk populations; moreover, this study lacks randomisation and is observational in nature.

Conclusion

This study delivers a complete comparison of the safety, efficacy, and optimal duration of dual antiplatelet therapy with ECOSPRIN+TICAGRELOR versus ECOSPRIN+CLOPIDOGREL in managing coronary artery disease. The results indicate that Ticagrelor offers superior ischemic event protection and more effective symptom relief compared to Clopidogrel. However, the increased bleeding risk associated with Ticagrelor necessitates careful patient selection and monitoring. Key findings include those patients on Ticagrelor demonstrated better symptom alleviation and a lower incidence of stent thrombosis and MACCE compared to those on Clopidogrel. While Ticagrelor showed a higher bleeding risk, its overall safety profile was acceptable with manageable side effects such as mild dyspnea and bradycardia. The study emphasizes the need for individualized treatment plans, balancing the benefits of reduced ischemic events with the risks of bleeding, to optimize therapeutic outcomes in CAD patients.

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