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## RESEARCH ARTICLE

### A COMPARATIVE STUDY ON EFFICACY OF CLOPIDOGREL + ASPIRIN AND TICAGRELOR + ASPIRIN IN THE TREATMENT OF CORONARY ARTERY DISEASE

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#### ABSTRACT

**Aim and Objectives:** The aim of this study was to compare the efficacy of ticagrelor + aspirin and clopidogrel + aspirin in the treatment of coronary artery disease and to study the effectiveness of antiplatelet agents by evaluating the laboratory investigation like ECG, X-ray, 2D-ECHO, cardiac enzymes, blood test, cardiac catheterization. **Materials and Methods:** A prospective randomized observational study was conducted in coronary artery disease patients (from 30 years to 70 years of age) to compare the efficacy of two antiplatelets in the department of cardiology Durgabai Deshmukh Hospital. The study conducted for a period of six months from September 2019 to March 2020. **Results:** Among the total number of patients 80, ticagrelor + aspirin was prescribed to 40 patients whereas remaining 40 administered ticagrelor + aspirin irrespective of their age, sex. The efficacy of drugs is assessed based on evaluating the laboratory investigation like ECG, X-ray, 2D-ECHO, cardiac enzymes, blood test, cardiac catheterization. By comparing all the results, ticagrelor + aspirin showed more efficacy compared to clopidogrel + aspirin in all the factors. The efficacy in decreasing frequency is calculated by one-way Anova method whereas hospital stay duration calculated by using T-test. **Conclusion:** In this study, we compared the efficacy of ticagrelor + aspirin versus clopidogrel + aspirin in the treatment of coronary artery disease and we compared between both drugs that which drug is given more to the CAD patients and the result is that more efficacy is seen in patients receiving ticagrelor + aspirin drug and most of the CAD patients are treated with ticagrelor + aspirin drug then compared with clopidogrel + aspirin drug.

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## INTRODUCTION

Coronary artery disease or acute coronary syndrome is a condition that occurs when they become too small in the coronary arteries [Tortora, 2012]. The heart has coronary arteries that carry blood and oxygen into the heart.

CAD is generally explained with three types of diseases. Their titles are:

- Angina
- Myocardial infarction
- atherosclerosis

## RISK FACTORS

Risk factors are isolated into 2 kinds :

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## NON-MODIFIABLE

**Age and gender** - coronary course maladies are more common in men than ladies the purpose for this may be the assurance of sex hormones. individuals old enough 60-70 years are increasingly inclined to have CAD.

**Race and family history** - CAD death rates vary among the significant ethnic populaces. the distinction reflects connections of hereditary qualities, natural, and social exercises the blacks show higher mortality than white. many people with a solid family ancestry of coronary illness have one or other hazard factors to happen.

## MODIFIABLE

**Cholesterol and other lipids** - the risk of CAD increases with an increase in blood cholesterol levels lowering serum cholesterol levels reduces CAD risk from 20-50 % I age group of 40-70 years.

**Hypertension**—Hypertension is one of the most generally perceived cardiovascular dangers. In moderately aged populaces the connection between circulatory strain level and cardiovascular illness is profoundly straight reviewed and etiologically noteworthy. Hypertension likewise raises the danger of CKD and coronary cardiovascular breakdown and stroke assault.

**Diabetes** – both sort 1 and type 2 are significant hazard factors for CAD mortality and morbidity. Elevated glucose levels build the hazard for heart infections and stroke. Diabetes directly affects atherosclerosis, expanding diabetes makes atherosclerosis extreme [Peter Brubaker, 1961]

## SYMPTOMS

Majorly CAD is caused due to angina. The main symptom is chest pain. Other includes: shortness of breath, heaviness in the chest, the tightness of the chest, burning sensation near the heart, pain in the chest, improper digestion of food, generalized weakness [Rang and Dales, 2007]

## DIAGNOSIS

There are numerous analysis like a physical assessment or taking the clinical history or performing barely any test like:

- **Electrocardiogram:** it records the electrical movement and beat of the heart. On the off chance that an individual with stable creep shows QRS changes (pathologically q wave, divided QRS, reduced r wave adequacy), firmly recommend past myocardial infarction.
- **Echocardiogram:** This is an ultrasound sweep of the heart that screens the siphoning and working of the heart. Echocardiography is an important instrument for the appraisal of the heart structure and capacity in patients with coronary supply route ailment. Provincial divider movement variations from the norm correspond well with the critical stenosis of the coronary corridors; this turns out to be progressively obvious during stress.
- **Blood tests:** by and large blood cholesterol levels, any biomarkers are estimated. Increased levels of serum creatinine and urea levels depict the risk for coronary artery disease as well as kidney-related problems [Dipiro, 2008; Roger, 2008]

## TREATMENT

There is no finished remedy for CAD. There are approaches to deal with the state of the person. The better treatment includes making more beneficial way of life changes, stopping unfortunate propensities, having a fortifying diet, doing standard exercise [Richard, 2007]

A few prescriptions are utilized to diminish the symptoms of CAD.

### Medication

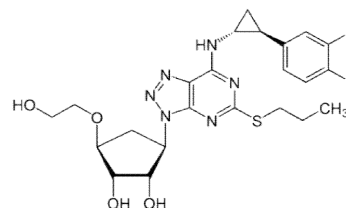
**Medications that individuals can take to lessen the effect of CAD include:**

- **Beta-blockers:** they are utilized to lessen pulse and pulse, particularly in patients having a cardiovascular failure.

- **Antiplatelet drugs:** they are the drugs that help in reducing the blood clot formed in the artery. For example: clopidogrel, aspirin, ticagrelor.
- **Calcium channel blockers:** These are utilized to broaden the coronary supply routes, improving the bloodstream to the heart, and decreasing hypertension.
- **Statins:** These are the medications that may positively affect results in CAD. They act by reducing the testimony of fats on the mass of supply routes. [6,13]

### Drugs in the study

#### TICAGRELOR



**Dose:** 90mg, 60mg

It is a platelet accumulation inhibitor delivered by Astra Zeneca. Ticagrelor is a rival of the P2Y<sub>12</sub> receptor.

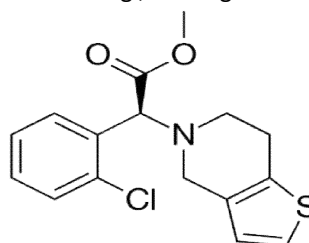
#### Pharmacology

**Mechanism of Action:** Ticagrelor and its significant metabolite reversibly cooperate with the platelet P2Y<sub>12</sub> ADP-receptor to forestall signal transduction and platelet activation. Restraint of platelet collection (IPA) It squares adenosine diphosphate (ADP) receptors of subtype P2Y<sub>12</sub> as opposed to the next antiplatelet drugs, Ticagrelor has a coupling site unique concerning ADP, making it an allosteric rival, and the blockage is reversible. Moreover, the medication needn't bother with hepatic enactment, which may work better for patients with hereditary variations in regards to the compound CYP2C19.<sup>[13]</sup>

**Pharmacokinetics:** The Bioavailability observed is 37%. The Peak Plasma Time for ticagrelor is 1.5 hr; 2.5 hr for dynamic metabolite. The ticagrelor which is metabolized by CYP3A4 is the significant catalyst answerable for the development of its significant dynamic metabolite (AR-C124910XX) and utilized less significantly by CYP3A5. The Half-life of ticagrelor is 7.5 hr and the half-life of the active metabolite is 9 hr. The drug ticagrelor is excreted 59% through excrement and 27% through pee.<sup>[7,12]</sup>

#### CLOPIDOGREL

**Dose :** 75mg, 150 mg



Signs Reduction of atherosclerotic occasions (eg, MI, stroke, vascular passing) in patients with atherosclerosis recorded by late stroke, late MI, or built up fringe blood vessel sickness. Treatment of intense coronary disorder (flimsy angina/non-Q-wave MI) including patients oversaw medicinally and those

made do with percutaneous coronary mediation (with or without stent) or coronary vein sidestep join.

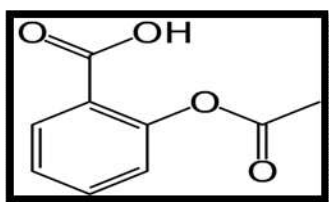
**Pharmacology**

**mechanism of Action :** Inhibitor of adenosine diphosphate (ADP)- the initiated pathway for platelet collection authoritative to platelet receptors and resulting ADP-intervened enactment of glycoprotein GPIIb/IIIa complex, in this way hindering platelet aggregation<sup>[12]</sup>

**Pharmacokinetics:** the Bioavailability observed is less than 50% .the Onset of action of the drug is 2.5 hr .the clopidogrel which is Metabolized in the liver by hepatic CYP450 catalysts to produce dynamic metabolite and by esterase to create an inert metabolite..the Half-life of clopidogrel is 6.5 hr and the half-life for the active metabolite is 45 min. the drug clopidogrel is excreted half through urine and 45% through feces [11,15<sup>1</sup>

**ASPIRIN:**

**dose:** 75-325mg every day



Signs Treatment of gentle to-direct torment; fever; different incendiary conditions; a decrease of the danger of death or MI in patients with past dead tissue or unsteady angina pectoris or repetitive transient ischemia assaults or stroke in men who have had transient mind ischemia brought about by platelet emboli.

**PHARMACOLOGY**

**Mechanism of action:**headache medicine is a progressively powerful inhibitor of both prostaglandin amalgamation and platelet accumulation which irreversibly inactivates COX using acetylation this forestalls the transformation of arachidonic corrosive to thromboxane A2 [Tripathi]

**Pharmacokinetics:** The Bioavailability of aspirin is 80-100%. the Onset of action is 5-25 min.the Peak plasma time of aspirin is 0.25-3 hr .the aspirin which is Metabolized by the liver through a microsomal protein framework. the Half-life of aspirin is 2-3 hr for low portion and 15-30 hr for high portion.the drug aspirin is excreted through 80-70% through urine and rest through sweat salivation [Tripathi; aspirin-medscape.com;343279]

**MATERIALS AND METHODS**

This prospective observational study was conducted for 6 months in department of cardiology, Durgabai Deshmukh Hospital, a 300 bedded multi-specialty hospital to assess patients (male and female) with coronary artery disease. Baseline demographic data will be collected from the patient case report.

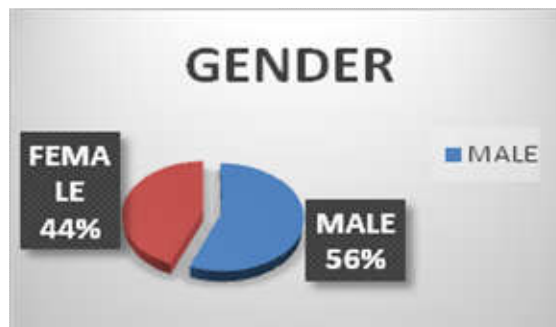
The sample size is 80 in which patients with age group of 30years to 70 years were included and Patients with the age group of <30 ,Patients undergoing surgery and Pregnancy and lactating women were excluded.All the relevant and necessary data will be collected from inpatient records, laboratory records, by interviewing patient and patient representative and prescription.

**Statistical analysis:** All the data was analysed using GraphPad Prism software version 5. Comparison among two groups was performed using ONE way ANOVA and p-value < 0.05 was considered statistically significant.

**RESULTS AND DISCUSSION**

A total of 80 patients of either sex who fulfilled inclusion criteria were taken for the study at cardiology department, Durgabai Deshmukh Hospital.

GENDER	NO.OF PATIENTS	PERCENTAGE
SAMPLE SIZE	80	100%
Male	45	56.25%
FEMALE	35	43.75%



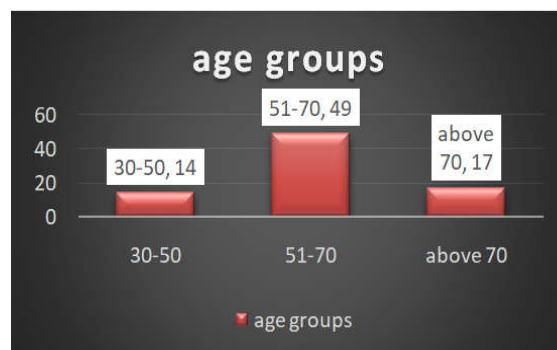
**GENDER DISTRIBUTION**

**Result:** The above graph describes that out of 80 patients with coronary artery disease, male patients were 45(56%)and female patients 35 (44%). it concludes that males are more prone to cardiovascular disease than females).

**AGE DISTRIBUTION**

**Table 5.2. Number of patient according to age**

AGE	No.of patients	PERCENTAGE
SAMPLE SIZE	80	100%
30-50	14	17.5%
51-70	49	61.25%
ABOVE 70	17	21.25%

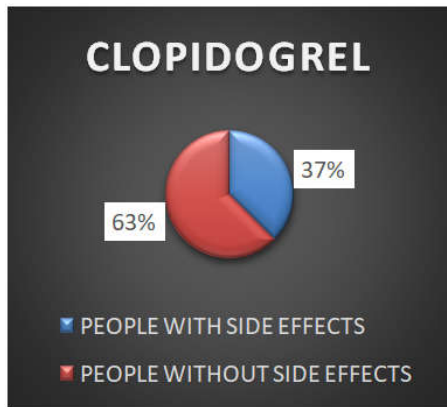


**Figure 5.2 Number of the patient according to age**

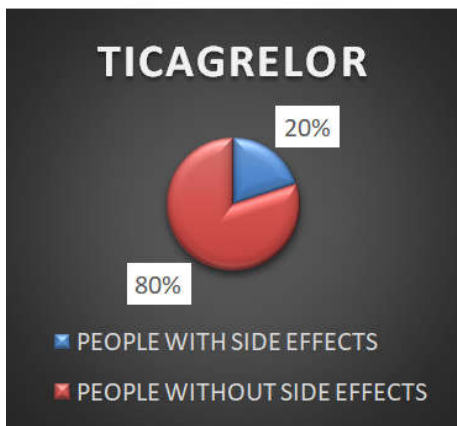
**Result:** The above chart describes that the age group 51-70 (61.25%) is more prone to have coronary artery disease than the age group 30-50 (17.5%) and above 70 (21.25%).

**Table 5.9. Side effects observed**

	Clopidogrel + aspirin	%	Ticagrelor + aspirin	%
Sample size	40	100%	40	100%
No. of people observed side effects	15	37%	8	20%
No. of people with no side effects	25	63%	32	80%



**Figure 5.9** side effects observed in the clopidogrel group



**Figure 5.10** side effects observed in the ticagrelor group

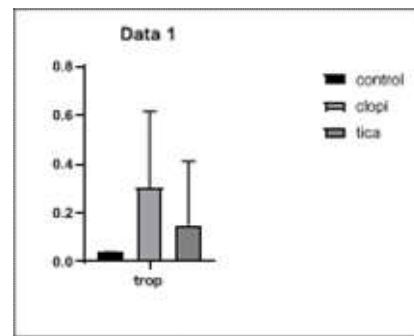
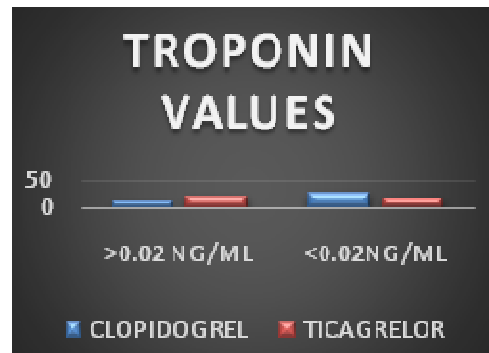
**Result:** The above graph describes that patients treated with group clopidogrel + aspirin are showing more side effects(37%) than patients treated with ticagrelor+aspirin (20%).

Table 5.10 abnormal troponin changes

**ABNORMAL TROPNIN VALUES DISTRIBUTION**

**Table 5.10. Abnormal troponin changes**

Troponin values	Clopidogrel + aspirin	Ticagrelor + aspirin
Sample size	40	40
>0.02ng/ml	12	23
<0.02ng/ml	28	17



The observed p value of the test is <0.0001

**Figure 5.11. Abnormal troponin changes**

Group	Adjusted p value	Statistical significance
Controlvs clopi	<0.0001	Yes
Control vs tica	0.0819	No
Clopi vs tica	0.0125	Yes

**Result:** the statistical analysis observed for the parameter is one-way ANOVA.

In the test we have taken 3 groups :  
 Group A- clopidogrel+aspirin  
 Group B- ticagrelor+aspirin  
 Group C- control group with normal values.

The results of the statistical test are :

From the above statistical values, after the patients are treated with clopidogrel + aspirin the troponin values are significant that is there is a large difference between the normal values and observed values, whereas in the patients treated with ticagrelor + aspirin the troponin values are not significant that means that there is no difference between the normal values and observed values. we can conclude that the patients treated with ticagrelor + aspirin show practically normal troponin values than patients treated with clopidogrel+aspirin.

**Reason:** increased troponin values signify that there is more damage done to the heart because troponin is a protein that is released if there is an injury to the heart.so patients with coronary artery disease initially have high troponin values .we can say that using of ticagrelor + aspirin can reduce the risk for the heart damage.

**CREATININE CHANGES DISTRIBUTION**

Creatinine	Clopidogrel	Ticagrelor
Sample size	40	40
>1.4mg/dl	15	29
<1.4mg/dl	25	11

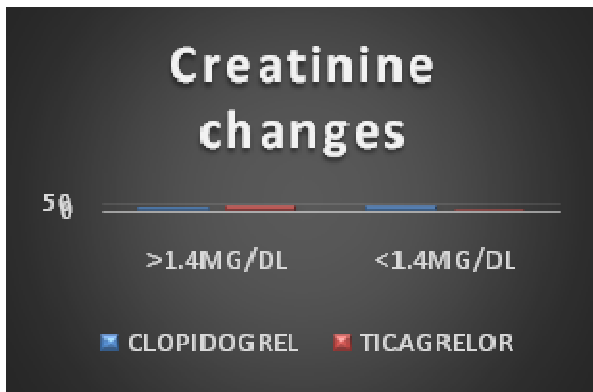
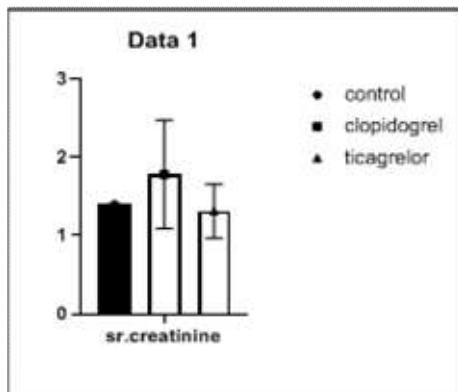


Figure 5.12. Abnormal creatinine changes



The observed p value of the test is <0.0001

**Result:** the statistical analysis observed for the parameter is one-way ANOVA.

In the test we have taken 3 groups :

Group A- clopidogrel+aspirin

Group B- ticagrelor+aspirin

Group C- control group with normal values.

From the above statistical values after the patients are treated with clopidogrel +aspirin the creatinine values are significant that is there is a large difference between the normal values and observed values, whereas in the patients treated with ticagrelor +aspirin the creatinine values are not significant that means that there is no difference between the normal values and observed values. we can conclude that the patients treated with ticagrelor +aspirin show practically normal creatinine values than patients treated with clopidogrel+aspirin.

**Reason:** increased creatine levels signify that there is increased damage to the kidney. since the patients with coronary artery disease have reduced blood flow due to the atheroma formed in the artery, amount of blood reaching to the kidney is also reduced .this may lead to kidney disease . we can conclude that using ticagrelor+aspirin the patients are at reduced risk for heart failure than clopidogrel+aspirin.

**BLOOD UREA CHANGES DISTRIBUTION**

Table 5.12. Abnormal blood urea changes

Urea	Clopidogrel +aspirin	Ticagrelor +aspirin
Sample size	40	40
>20mg/dl	11	18
<20mg/dl	29	21

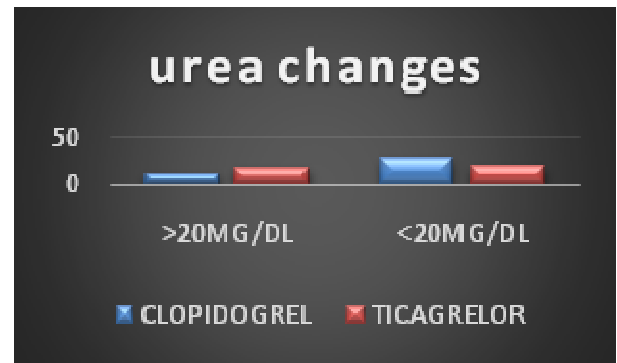
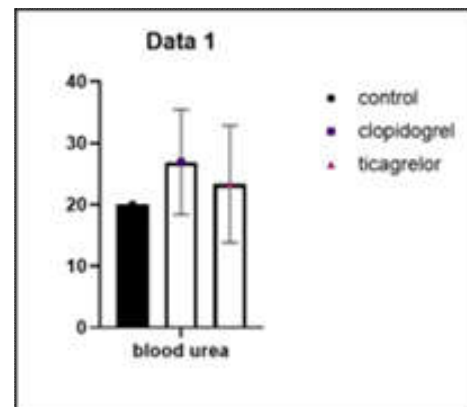


Figure 5.13. Abnormal blood urea changes



The observed p value of the test is 0.0003

**Result:** The statistical analysis observed for the parameter is one-way ANOVA.

In the test we have taken 3 groups:

Group A- clopidogrel+aspirin

Group B- ticagrelor+aspirin

Group C- control group with normal values.

From the above statistical values after the patients are treated with clopidogrel +aspirin the blood urea values are significant that is there is a large difference between the normal values and observed values, whereas in the patients treated with ticagrelor +aspirin the blood urea values are not significant that means that there is no difference between the normal values and observed values. we can conclude that the patients treated with ticagrelor +aspirin show practically normal creatinine values than patients treated with clopidogrel+aspirin.

**Reason:** Blood urea levels in the blood are increased due to decreased renal perfusion .the renal perfusion is decreased due to decreased cardiac output .the cardiac output is decreased due to reducing blood flow. the reduced blood flow is due to the atheroma formed in the artery hence the blood flow can be increased by reducing the atheroma using antiplatelet drugs such as clopidogrel and ticagrelor we can conclude that ticagrelor +aspirin can reduce the risk for heart failure than clopidogrel+aspirin.

**CONCLUSION**

In this study, we compared the efficacy of ticagrelor+aspirin versus clopidogrel+ aspirin in the treatment of coronary artery disease and we compared between both drugs that which drug is given more to the CAD patients.and the result is that more

efficacy is seen in patients receiving ticagrelor + aspirin drug and most of the CAD patients are treated with ticagrelor+aspirin drug then compared with clopidogrel+ aspirin drug.

#### ETHICS AND CONSENT

The entire study was conducted according to the ethical committee guidelines of durgabai deshmukh hospital. All the relevant and necessary data was collected from in patient records, laboratory reports, prescriptions and by interviewing the patients.

**CONFLICTS OF INTEREST:** None.

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