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The Effectiveness of Warfarin Versus Novel Oral Anticoagulants in Preventing Stroke Recurrence

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Abstract: ***AIM:To study the effectiveness of warfarin VS novel oral anticoagulants in preventing stroke recurrance with atrial fibrillation ,CSVT and cardio embolic stroke***
MATERIALS AND METHODS: All the relevant and necessary data will be collected from patients record, lab reports, prescriptions and communicating with health care professionals
RESULT:Out of 70 subjects screened according to inclusion and exclusion criteria, 47 were male and 53 were female; these subjects had a history of stroke due to CSVT, cardioembolics, or atrial fibrillation and had responded well to therapy. The research included 48 people who were using NOACs and 24 people who were taking warfarin.
CONCLUSION:By summarizing the statistical data of our study we have observed that the total number of patients who were both on warfarin and NOAC's have same effectiveness in preventing stroke recurrence . The tolerability of all the drugs is almost same among the study population. The risk of having a recurrent stroke is more in patients with CSVT than that of patients with Atrial fibrillation and cardioembolism.
Based on reviewing literatures and reference articles , the studies that have been carried out on NOAC's have shown that NOAC's are equally effective as warfarin and has an advantage of reduced complications like cerebral bleeding and has a fixed dosage regimen due to these advantages NOAC's can be used in place of warfarin. As there are limited number of samples the results may not be yet generalised.
Further studies can be carried out on large scale population for more accurate evaluation.
Keywords: Warfarin, Novel oral anticoagulants-NAOC'S, Stroke, Atrial fibrillation, Cerebral sinus venous thrombosis-CSVT, cardioembolic stroke, Ischemic stroke, Hemorrhagic stroke, Transient ischemic attack-TIA, Recurrent Stroke, Hemorrhagic conversion, Effectiveness, Safety, Tolerability

I. INTRODUCTION

In India, stroke was found to be the second most common cause of death. According to neurology specialists at the All India Institute of Medical Sciences (AIIMS), there are approximately 1,85,000 stroke cases recorded annually in India, with one stroke fatality occurring every four minutes and a stroke occurring roughly every forty seconds. As per the Global Burden of Diseases (GBD), India was responsible for a majority of the stroke burden, accounting for 68.6% of stroke incidence, 70.9 percent of stroke fatalities, and 77.7% of Disability Adjusted Life Years (DALYs) lost
With so many people in the nation living in resource-poor environments, these numbers are concerning. A concerning and significant discovery from the GBD 2010 stroke study is that 5.2 million (or 31%) of the strokes seen were in youngsters under the age of 20. India has a higher stroke incidence rate, particularly among younger and middle-aged individuals. [1]

II. STROKE AND STROKE RECURRENCE

The current WHO definition of stroke is: "suddenly appearing clinical symptoms suggesting localized or systemic disruption of brain function, with symptoms continuing for at least 24 hours or progressing to mortality, with no obvious reason other than a vascular etiology".
Recurrent stroke was defined as a new neurological deficit presenting after a period of clinical stability,lasting for more than 24 hours with attributable new ischemic or hemorrhagic lesions.stroke deprives the brain of oxygenTrusted Source and can cause significant damage that affects a person's long-term neurological functioning. Recurrent strokes may cause additional damage, increasing the risk of disability and death. Death rates are higher after a recurrent stroke, according to a 2022 study[2]

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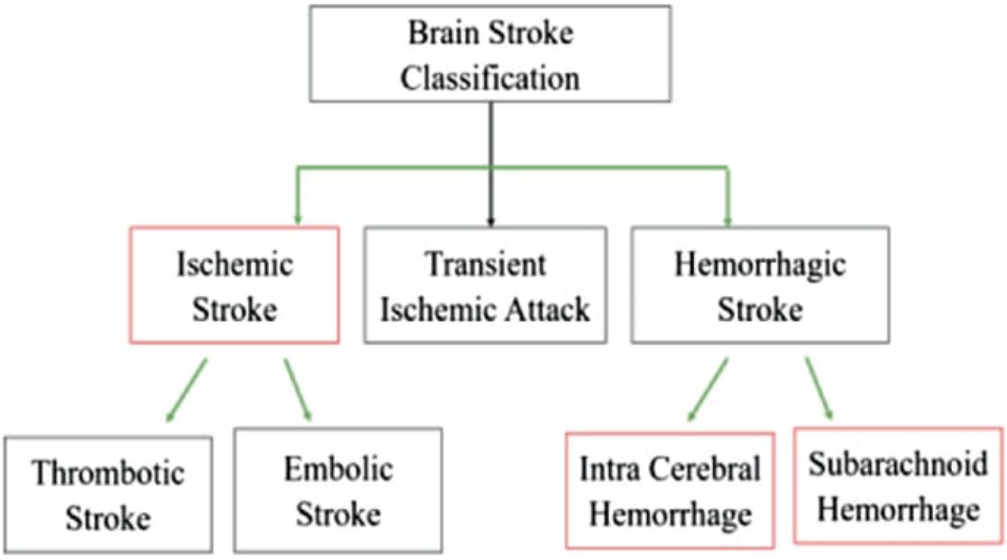
III. BRAIN ANATOMY AND ITS FUNCTION

All of our bodily functions—including thinking, remembering, feeling, touching, moving, seeing, breathing, temperature regulation, hunger—are controlled by the intricate brain. Central nervous system (CNS) refers to the network of nerves and muscles that extends from the brain and spinal cord. [3]

IV. CLASSIFICATION

Stroke can be classified into two major categories: ISCHEMIC AND HEMORRHAGIC



A. Haemorrhagic Stroke

Hemorrhagic stroke is brought on by the rupture of a blood vessel or an abnormal vascular structure, whereas ischemic stroke is caused by disruption of the blood supply to the brain. Hemorrhagic strokes account for the remaining 27% of stroke cases. Inside regions of ischemia, bleeding can occur; this is referred to as "hemorrhagic transformation.[21]

B. Ischaemic Stroke

According to the American Heart Association, a transient ischaemic attack (TIA) is "a brief episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia without acute infarction," while an ischemic stroke is characterized by symptoms that last longer than 24 hours and is caused by a focal infarction of the brain, spinal cord, or retina.Because the symptoms of TIAs are short-lived (lasting less than 24 hours but more than a few minutes), the condition is sometimes called a mini-stroke. For the Trial of Organ 10172 in Acute Stroke Treatment (TOAST), categories of ischemic stroke were created primarily based on the cause and the process that led to the blockage of blood vessels. [21]

The most popular one is the TOAST categorization, which encompasses:

- Large-vessel atherothrombosis;
- Cardioembolism;
- Small-vessel disease
- Undetermined causes.

C. Transient Ischemic Attack (TIA)

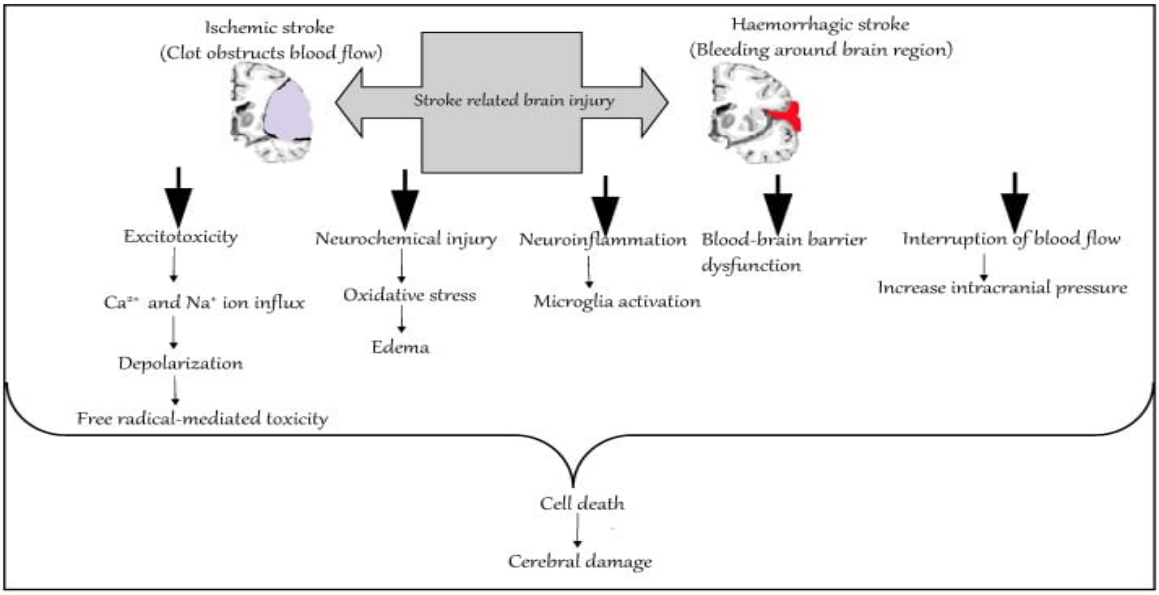
A transient ischemic attack (TIA) is a neurologic episode that can be reversed and is brought on by a brief, focal hypoperfusion of the central nervous system.A brief period of focal brain, spinal cord, or retinal ischemia-related neurologic impairment without acute infarction or tissue damage is what is meant by this definition.[22] A TIA is now defined by tissue rather than by time. More frequently than not, a TIA lasts minutes rather than an hour. The risk of an oncoming ischemic stroke is highest in the 48 hoursafter a transient ischemic attack (TIA), which might be regarded as a major warning sign.[23]

V. SIGNS AND SYMPTOMS

Stroke symptoms usually begin abruptly, lasting a few seconds to several minutes, and they rarely get worse.
The afflicted brain region determines the symptoms.[34]The likelihood of losing more functions increases with the extent of the damaged brain region.
There are some types of stroke that can produce extra symptoms.

- Sudden-onset face weakness, arm drift and abnormal speech
- Numbness or weakness that comes on suddenly, especially if it only affects one side of the body
- drooping face, especially on just one side
- Sudden confusion
- Trouble speaking or making decisions
- A sudden, severe headache that may differ from a person's usual headache pattern
- Dizziness, lack of balance, low coordination, or trouble walking
- Difficulty seeing[34] [35]

VI. RISK FACTOS



Risk factors for stroke are classified as modifiable or non-modifiable
Once a person reaches the age of 55, their risk of stroke doubles due to age-related increases. Hypertension, coronary artery disease, and hyperlipidemia are some of the preexisting medical problems that increase a person's risk. Nearly 60% of all strokes occur in patients who have had a history of TIAs. It is possible to alter some of the risk factors for stroke, but not all of them.

VII.PATHOPHYSIOLOGY

The embolism in an embolic stroke results from reduced blood supply to the affected area of the brain, which in turn causes severe stress and the early death of cells (necrosis). Neuronal function is lost during necrosis, which disrupts the plasma membrane and causes organelles to expand and release cellular contents into extracellular space. [48]
The cerebral circulation becomes involved when emboli that began in other parts of the circulatory system—often the heart as a consequence of atrial fibrillation or the carotid arteries—break off, enter, lodge in, and block blood vessels in the brain, leading to embolic infarction. When cerebral blood vessels get clogged, the brain's energy levels plummet, and the injured region returns to anaerobic metabolism. [49]
Other important events that lead to stroke pathology include inflammation, energy failure, loss of homeostasis, acidosis, increased intracellular calcium levels, excitotoxicity, cytokine mediated cytotoxicity, complement activation, blood brain barrier disruption, glial cell activation, oxidative stress, and leukocyte infiltration.

Hemorrhagic strokes are categorized based on the pathophysiology that causes them. Some of the many potential causes of hemorrhagic stroke include hypertensive hemorrhage, drug-induced bleeding, burst AV fistula, transformation of prior ischemic infarction, and ruptured aneurysms. By compressing tissue from an increasing hematoma or hematomas, they cause tissue damage. Furthermore, the blood discharged by a brain hemorrhage appears to have direct harmful effects on brain tissue and vasculature, and the pressure may cause a loss of blood flow to the damaged area, which could result in an infarction. After a hemorrhage, inflammation plays a role in the subsequent brain injury.[50]

Roughly 10-15% of all strokes are hemorrhagic strokes, which have a high death rate.

Blood vessels burst in this illness as a result of internal injuries and stress on the brain tissue.

It causes the vascular system to become toxic, which leads to infarction. [51]There are two types of hemorrhages: subarachnoid and intracerebral. In ICH, blood clots in the blood arteries cause an abnormal build-up of blood in the brain. Hypertension, abnormal vasculature, overuse of anticoagulants, and thrombolytic medications are the primary causes of ICH.When there is a head injury or cerebral aneurysm,blood builds up in the brain's subarachnoid space, resulting in subarachnoid hemorrhage.[51] [52]

VIII. MATERIALS AND METHODS

All the relevant and necessary data will be collected from patients record, lab reports, prescriptions and communicating with health care professionals Casesheets, lab reports, communication with health care professionals

IX. STATISTICAL ANALYSIS

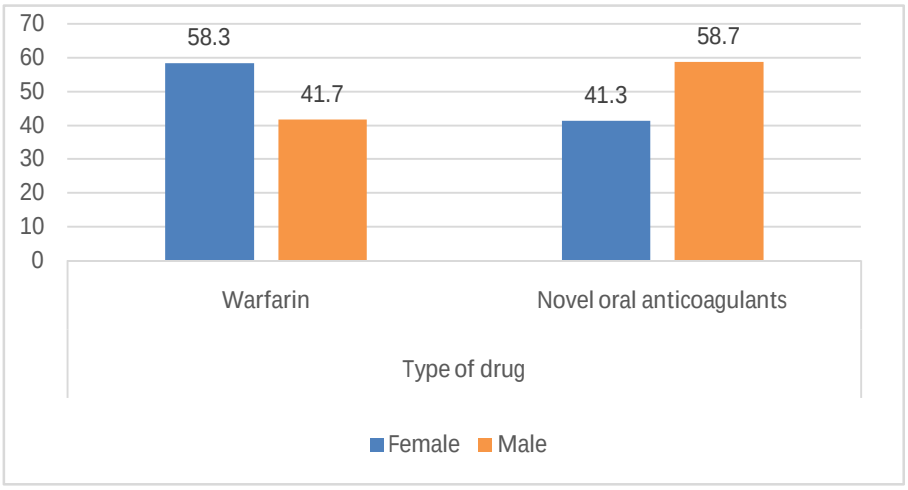
1) All categorical variables were presented as frequency and percentages. Continuous variables were presented as mean ± SD. Student t-test or Mann-Whitney's U test was used to test significant differences between two continuous variables as appropriate. Chi-square test/Fisher exact test was used to test the difference between proportions as appropriate. p-value <0.05 was considered here the as statistically significant.
2) The demographics and other baseline characteristics of the patients (ex: age ,genderetc) are summarised in the tables.
3) The above methods were used to find out the Effectiveness and significance of the drugs that are in study with disease conditions like atrial fibrillation, CSVT, cardioembolic strokes and leading to stroke recurrence.
4) Adverse events experienced by the patients during the course of oral anticoagulant drug therapy were approximately summarised and tabulised
5) Patients with multiple commodities (DM,HTN,CAD)were considered for the risk of stroke recurrence.
6) Past medication history of stroke of patients prior the study weresummarised
7) The patients while on anticoagulant therapy and subjected to stroke recurrence are tabulised.

X. RESULT

Out of 70 subjects screened according to inclusion and exclusion criteria, 47 were male and 53 were female; these subjects had a history of stroke due to CSVT, cardioembolics, or atrial fibrillation and had responded well to therapy. The research included 48 people who were using NOACs and 24 people who were taking warfarin.

TABLE 1:Gender wise distribution of warfarin versus NOAC's

Gender	Frequency	Type of drug		Total No. (%)	Mc Nemer test (P value) (α=<0.05)
		Warfarin No. (%)	Novel oral anticoagulantsNo. (%)		
Female	33	14 (58.3)	19 (41.3)	33 (47.1)	0.175
Male	37	10 (41.7)	27 (58.7)	37 (52.9)	
Total	70	24	46	70	



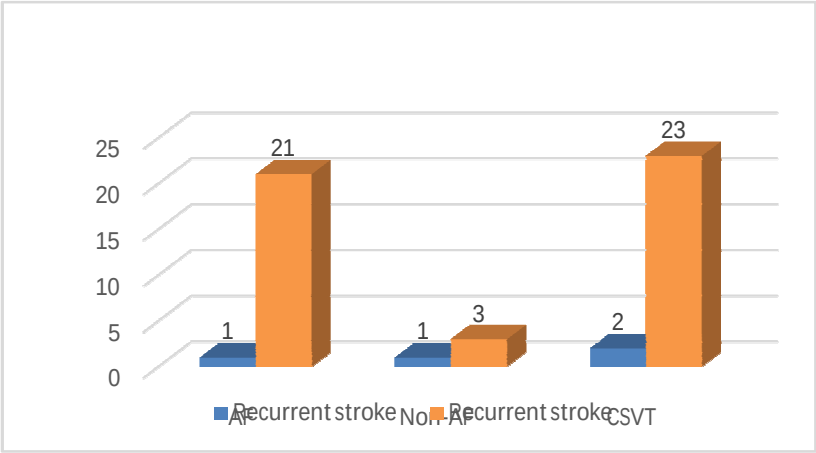
GRAPH 1 :Gender wise distribution of warfarin versus NOAC's

Out of the 70 patients, warfarin was recieved by 24 patients in which females were 14(58%) and males were 10 (42%). NOAC's were recieved by 45 patients in which females were 19 (41%) and males were 27(59%).

As the calculated P value is 0.175 which shows that there is no significant difference between warfarin and NOAC's based on gender.

TABLE 2:Diagnosis wise distribution of recurrent stroke

Diagnosis	Frequency	Recurrent stroke		Total	P value (α= <0.05)
		Yes	No		
AF	22	1 (25%)	21 (44.6%)	22 (43.2%)	0.375
Non-AF	4	1 (25%)	3 (6.5%)	4 (7.8%)	
CSVT	25	2 (50%)	23 (48.9%)	25 (49%)	
Total	51	4	47	51	



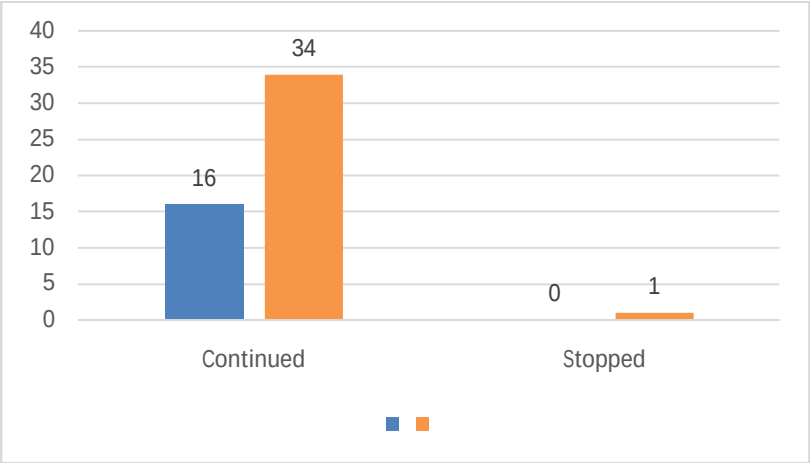
GRAPH 2: Diagnosis wise distribution of recurrent stroke

Out of 51 patients who were followed up on, 22 had atrial fibrillation, 1 of whom had a recurrent stroke; 4 had non-atrial fibrillation, 1 of whom had a recurrent stroke; and 25 had CSVT, 2 of whom had a repeat stroke.

As the calculated P value is 0.375 which shows that there is no significant difference between recurrent stroke patients and non recurrent stroke patients.

TABLE 3:No. of patients continuing the same drug therapy after stroke recurrence

Drugs after recurrence	Frequency	Type of drug		Total	P value (α= <0.05)
		Warfarin	Novel oral anticoagulants		
Continued	50	16 (100%)	34 (97.2%)	50 (98%)	0.450
Stopped	1	0 (0%)	1 (28%)	1 (2%)	
Total	51	16	35	51	



GRAPH 3 :Number of patients continuing the same drug therapy after stroke recurrence

Out of 51 follow-up patients, 50 patients continued same drug after recurrence in which 16 were on warfarin and 13 were on NOAC's; 1 patient discontinued NOAC's after stroke recurrence.

As the calculated P value is 0.450 which shows that there is no significant difference in choosing the same drug after stroke recurrence.

XI. CONCLUSION

By summarizing the statistical data of our study we have observed that the total number of patients who were both on warfarin and NOAC's have same effectiveness in preventing stroke recurrence . The tolerability of all the drugs is almost same among the study population. The risk of having a recurrent stroke is more in patients with CSVT than that of patients with Atrial fibrillation and cardioembolism.

Based on reviewing literatures and reference articles , the studies that have been carried out on NOAC's have shown that NOAC's are equally effective as warfarin and has an advantage of reduced complications like cerebral bleeding and has a fixed dosage regimen due to these advantages NOAC's can be used in place of warfarin. As there are limited number of samples the results may not be yet generalised.

Further studies can be carried out on large scale population for more accurate evaluation.

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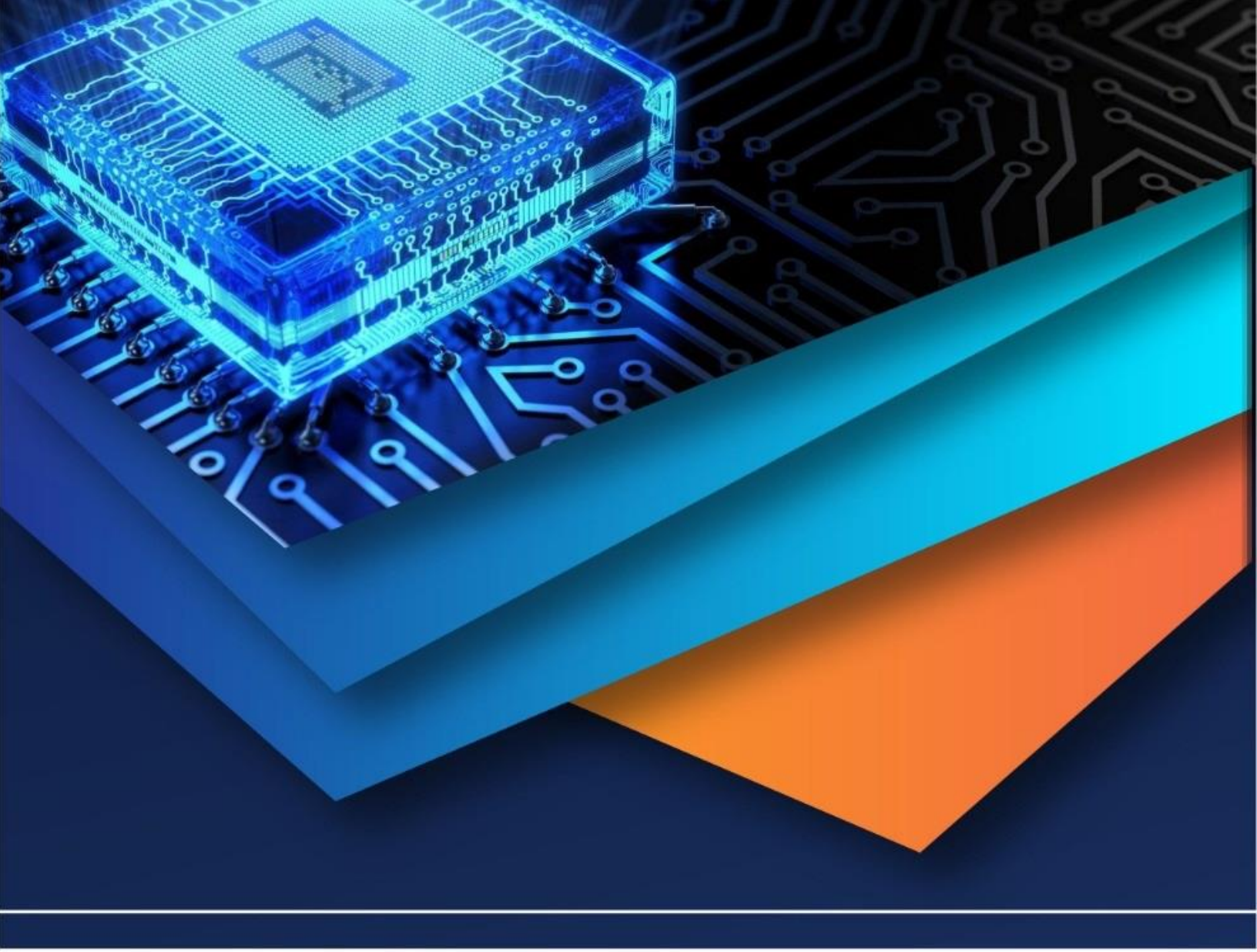

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