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Evaluating the Efficacy of Dual Antiplatelet Therapy in Reducing Recurrent Stroke in High-Risk Patients

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Abstract

Introduction: Still among the primary causes of illness and death worldwide is stroke. Comparatively to single antiplatelet therapy (SAPT), dual antiplatelet therapy (DAPT) has been suggested as a successful approach to lower the risk of recurrent strokes in high-risk patients. This study sought to assess whether DAPT would be effective in avoiding recurrent strokes among high-risk patients at Lady Reading Hospital (LRH) in Peshawar.

Methodology: Using 92 high-risk stroke patients, 92 were assigned to DAPT (n=46) or SAPT (n=46). Over a follow-up period concluding in August 2024, data on demographic, clinical, stroke recurrence rates, and safety outcomes was gathered. Outcomes were assessed using statistical analyses comprising Kaplan-Meier survival analysis and Cox proportional hazards modeling.

Results: With a stroke recurrence rate of 13% instead of 30% in the SAPT group (p=0.026), the DAPT group displayed with p=0.017 the Kaplan-Meier analysis revealed a stroke-free survival rate of 87% in the DAPT group against 70% in the SAPT group. The Cox model showed that DAPT reduced the incidence of recurrent stroke by 60% (HR=0.40). The incidence of major bleeding events was low, with 4.3% in the DAPT group and 2.1% in the SAPT group (p=0.53), indicating an acceptable safety profile.

Conclusion: This study supports the use of DAPT as a more successful tactic than SAPT for low-risk individuals' recurrent stroke prevention. The results highlight the significance of using DAPT in clinical practice and provide important data for the management of stroke in different populations.

Keywords: recurrent stroke, dual antiplatelet therapy, high-risk individuals, single antiplatelet therapy, stroke prevention, randomized controlled trial

Introduction

Leading cause of mortality and long-term impairment, stroke is among the most common and terrible medical disorders affecting people all over [1]. According to the World Health Organization (WHO), around 5 million of the approximately 15 million estimated annual stroke sufferers worldwide either die or live with permanent disability [2]. Stroke survivors especially run a great risk of recurrence, which increases their susceptibility to later ischemic episodes. Emphasizing the need of efficient secondary prevention methods to reduce this risk, recurrent strokes usually have more severe outcomes including higher rates of morbidity, disability, and mortality [3]. Usually combining aspirin with another antiplatelet medication, such clopidogrel, dual antiplatelet therapy (DAPT) has shown to be a possibly better therapeutic method in preventing recurrent strokes in high-risk individuals. These patients range in risk of stroke recurrence from non-cardioembolic ischemic strokes, atrial fibrillation, advanced atherosclerosis, and transient ischemic attacks (TIAs). Usually involving aspirin or clopidogrel alone, single antiplatelet treatment (SAPT) has long been the basis of secondary stroke prevention [4].

Since stroke accounts for a significant percentage of morbidity and death in Pakistan and South Asia, it is a serious public health concern. According to estimates, there are 250 stroke cases for every 100,000 individuals

in Pakistan [5]. The incidence of stroke is expected to rise as the prevalence of risk factors including smoking, diabetes, and hypertension rises. Because of a combination of genetic predisposition and insufficient treatment of modifiable risk factors, South Asia has one of the highest rates of stroke worldwide. This emphasizes the critical need for efficient secondary prevention techniques, such DAPT, to lower the risk of stroke recurrence in those who are already at high risk [6].

Research on the possible benefits of combining antiplatelet drugs to improve the suppression of platelet aggregation and thrombus development two important processes in the pathogenesis of ischemic stroke has, however, lately attracted more attention. Recent large-scale clinical trials, such as “CHANCE (Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events) and POINT (Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke)”, have yielded promising results regarding the efficacy of short-term DAPT in reducing the risk of recurrent strokes [7]. Particularly in the immediate phase following a first ischemic stroke or TIA, these trials showed that DAPT could considerably reduce the recurrence rate when compared to SAPT [8]. DAPT's long-term use is linked, thus, to a higher risk of hemorrhagic complications including gastrointestinal and cerebral bleeding that complicate clinical practice's decision-making process [9]. Therefore, knowledge of the ideal duration and patient selection for DAPT remains a vital topic of research since doctors have to balance the two objectives of lowering bleeding hazards and reducing recurrent ischemic events.

Furthermore, some groups such as those with underlying comorbidities including diabetes, hypertension, and hyperlipidemia have particular difficulties preventing strokes10. DAPT may provide different degrees of benefit to these patients; hence therapeutic options should take particular consideration of their distinct risk profiles [11]. The variation in antiplatelet therapy responses emphasizes the need of customized ways to treatment instead of depending just on a "one-size-fits-all" strategy.

In order to fill up these important gaps, this research carefully considered the risks of bleeding and other adverse events associated with DAPT while evaluating its efficacy in lowering the chances of recurrent stroke in high-risk people. The research looked at how several patient-specific characteristics, such age, gender, and the existence of comorbidities, affected the DAPT's clinical results. The research looked at these factors in an effort to provide insights that can aid medical professionals in optimizing stroke prevention plans specific to high-risk patients.

Materials and methods

Study Design and Setting: This prospective, randomized, controlled study was finished at Lady Reading Hospital (LRH) in Peshawar, Khyber Pakhtunkhwa (KPK), Pakistan. Comparing DAPT's efficacy in cutting down on ischemic stroke recurrence in those at high risk for SAPT was the primary objective. Over a 12-month period, starting in September 2023 and finishing in August 2024, the research was carried out. Once each participant provided written, informed permission, the institutional review board granted its ethical approval.

Study Population: At great risk for repeat strokes, the trial sample consisted of 92 patients who had recently suffered an ischemic stroke or TIA. Patients enrolled from LRH's outpatient cardiology and neurology departments both. Participants had to be at least one main risk factor for stroke recurrence hypertension, diabetes mellitus, dyslipidemia, or atrial fibrillation 18 years or above. Patients excluded were those who had a hemorrhagic stroke, had contraindications to antiplatelet medication, or were taking anticoagulants.

Sample Size Calculation: Based on other studies assessing the lower recurrent stroke risk with dual antiplatelet medication, the sample size of 92 was decided upon. With a power of 80%, a significance level of 0.05, and a 30% decrease in stroke recurrence assumed from DAPT against SAPT, the necessary sample size was computed to be 84. We raised the sample size to 92 to accommodate dropouts. Despite the small sample size, it was sufficient to detect meaningful differences in clinical outcomes

Randomization and Intervention: A computer-generated randomizing sequence assigned patients at random to two treatment groups. For ninety days the DAPT group took aspirin (81 mg) and clopidogrel (75 mg daily). Daily aspirin for the SAPT group was 81 mg. Both groups received standard treatment comprising management of risk factors and lifestyle modification advice. Diaries kept by patients and follow-up visits tracked medication adherence. The 90-day duration was based on previous studies showing DAPT's efficacy in reducing stroke recurrence while managing bleeding risks associated with prolonged use.

Data Collection: At recruitment, baseline data including demographic traits (age, gender), clinical information (stroke subtype, risk factors), and laboratory results blood pressure, blood sugar levels, lipid profiles was gathered. To evaluate clinical outcomes, follow-up visits were scheduled thirty, sixty, and ninety days following randomization. The primary outcome was the frequency of recurrent ischemic strokes within ninety days following therapy start. Major adverse cardiovascular events (MACE), including myocardial infarction, and safety outcomes mostly bleeding episodes were among the secondary outcomes.

Outcome Measures: Considered as a new neurological dysfunction lasting more than 24 hours, recurrent stroke was the main outcome measure and was verified by neuroimaging. Secondary outcomes were major cardiovascular events and blood problems. Hospital standards let one classify bleeding occurrences according to degree.

Statistical Analysis: Using SPSS version 26, data were examined. Along with “frequencies and percentages for categorical variables, descriptive statistics means and

standard deviations for continuous variables were presented". "Chi-square tests for categorical data and t-tests for continuous variables" allowed one to evaluate stroke recurrence rates in the DAPT and SAPT groups. For both groups, "Kaplan-Meier analysis" was used to project the time to stroke recurrence; log-rank test differences were then used to evaluate changes. The two groups' incidence of stroke recurrence and bleeding episodes was also compared using a chi-square test. To account for possible confounders and determine the hazard ratios for recurrent stroke, multivariate regression analysis was done with the Cox proportional hazards model. For all analyses, a p-value less than 0.05 was regarded as statistically significant.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Ethical approval

Ethical approval was from the IRB MTI Lady Reading Hospital, Peshawar.

Results

The experiment had 92 people in total, of which 46 were randomly assigned to the SAPT group and 46 to the DAPT group. Participants ranged in age from 38 to 89 years old, with a mean age of 64.7 years (SD = 9.5). The mean age of the DAPT group was 65.2 years (SD = 9.1), whereas the mean age of the SAPT group was 64.2 years (SD = 9.8). In both groups, the majority of patients had dyslipidemia (52% vs. 48%), hypertension (68% in DAPT vs. 65%), and diabetes mellitus (47% vs. 50%). The two groups' baseline characteristics did not differ statistically significantly, confirming balanced randomization ($p > 0.05$ for all) as shown in Table 1.

Table 1: Baseline Characteristics of the Study Population

Characteristics		DAPT Group (n=46)	Percentage (%)	SAPT Group (n=46)	Percentage (%)	p-value
Age (mean ± SD)		65.2 ± 9.1 years	-	64.2 ± 9.8 years	-	0.62
Hypertension		31	68%	30	65%	0.79
Diabetes Mellitus		22	47%	23	50%	0.82
Dyslipidemia		24	52%	22	48%	0.74
Gender	Male	25	55%	28	60%	0.69
	Female	21	45%	18	40%	

Twenty-three patients (25%) had a recurrent ischemic stroke over the ninety-day follow-up period. With six patients (13%) in the DAPT group reporting a recurrent stroke and fourteen patients (30%) in the SAPT group, the recurrence rate in the former group was notably much lower. With a chi-square value of 4.93 and a p-value of 0.026, the two groups' statistically significant variance in recurrence rates was The DAPT group specifically showed a 13% (6 out of 46) recurrence rate while the SAPT group showed a 30% (14 out of 46) recurrence rate as figure 1 illustrates.

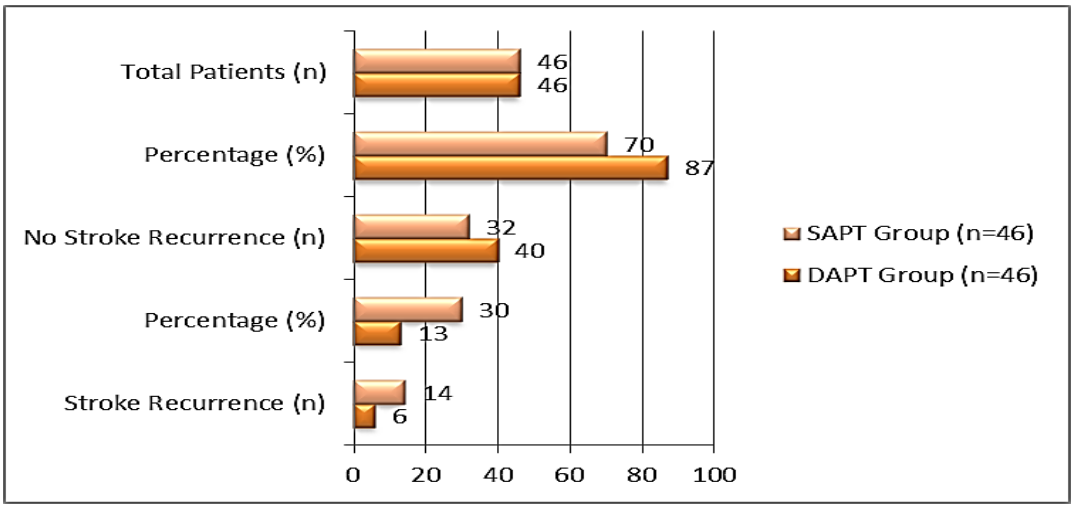

Figure 1: Stroke Recurrence in DAPT vs. SAPT Groups

The two groups' rates of stroke-free survival varied somewhat, according to the Kaplan-Meier survival analysis. During the 90-day follow-up period, the DAPT group had an overall stroke-free survival rate of 87%, while the SAPT group had a rate of 70%. "The log-rank test confirmed that there was a statistically significant variation in the two survival curves, with a chi-square value of 5.71 and a p-value of 0.017". Furthermore, the median time to a stroke recurrence was 42 days (interquartile range: 23–67 days) for the DAPT group and 34 days (interquartile range: 18–55 days) for the SAPT group as shown by table 2.

Table 2: Kaplan-Meier Survival Analysis (Stroke-Free Survival)

Group	Stroke-Free Survival (n)	Percentage (%)	Median Time to Stroke Recurrence (days)	Log-rank test (p-value)
DAPT Group (n=46)	40	87%	42 days (IQR: 23-67)	0.017
SAPT Group (n=46)	32	70%	34 days (IQR: 18-55)	

Age, hypertension, diabetes, and dyslipidemia were among the possible confounding factors adjusted for using a multivariate Cox regression analysis. With an adjusted hazard ratio (HR) of 0.40 and a 95% confidence interval (CI) of 0.18 to 0.88, the study found that the DAPT group had a 60% lower risk of recurrent stroke than the SAPT group. With a p-value of 0.021, Table 3 shows that DAPT stayed rather strongly linked with a reduced risk of recurrent stroke after considering possible variables.

Table 3: Cox Proportional Hazards Model for Stroke Recurrence

Variable	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
DAPT vs. SAPT	0.40	0.18 - 0.88	0.021
Age	1.02	0.98 - 1.06	0.40
Hypertension	1.15	0.65 - 2.04	0.62
Diabetes Mellitus	1.12	0.60 - 2.07	0.71
Dyslipidemia	0.98	0.54 - 1.79	0.95

With two patients (4.3%) in the DAPT group and one patient (2.1%), in the SAPT group, major bleeding episodes happened in three patients (3.2%) total across the study population. With a chi-square value of 0.39 and a p-value of 0.53 the chi-square test used to evaluate the bleeding events revealed no statistically significant variation between the two groups. The DAPT group's bleeding rate was specifically 4.3% (2 out of 46 patients), while the SAPT group's bleeding rate was 2.1% (1 out of 46 patients) as seen in figure 2.

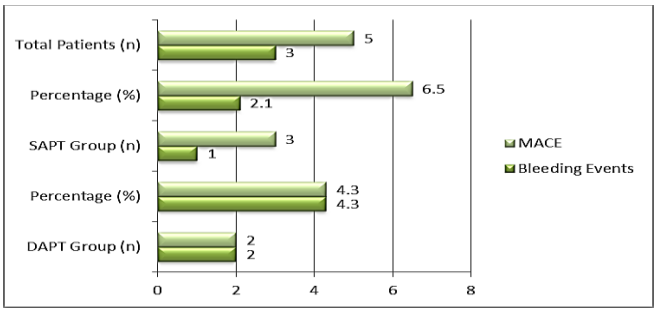

Figure 2: Bleeding Events and Major Adverse Cardiovascular Events (MACE)

Five patients (5.4%) in all had a significant adverse cardiovascular event (MACE), comprising cases of myocardial infarction, throughout the follow-up period. With 6.5%, the SAPT group had a somewhat higher MACE incidence than the DAPT group, at 4.3%. With a p-value of 0.67, this difference was not statistically significant though. MACE specifically affected three patients (6.5%) in the SAPT group and two patients (4.3%), in the DAPT group. Key findings of the study showed that, with a p = 0.026, the stroke recurrence rate in the DAPT group was 13% whereas in the SAPT group it was 30%. With an 87% "stroke-free survival rate in the DAPT group against 70% in the SAPT group (p = 0.017), the Kaplan-Meier survival analysis showed" For the "DAPT group, the Cox regression analysis produced a hazard ratio of 0.40 (95% CI: 0.18-0.88, p = 0.021)", therefore signally lowering the risk of recurrent stroke. Furthermore lacking statistically significant variation in bleeding episodes between the DAPT and SAPT groups (p = 0.53) These findings show that in lowering the recurrence of ischemic strokes without appreciable increase in severe bleeding events, dual antiplatelet medication was far more successful than single antiplatelet therapy.

Discussion

The results of this study on the efficacy of DAPT in lowering recurrent stroke among high-risk patients match past results in the literature, therefore confirming the possible advantages of DAPT in avoiding ischemic episodes. Consistent with past studies emphasizing the benefits of DAPT over SAPT, the observed stroke recurrence rate of 13% in the DAPT group and 30% in the SAPT group is particularly in patients with a history of ischemic events, many trials have shown a notable decrease in vascular events with clopidogrel plus aspirin as compared to aspirin alone [12]. This indicates that the integration of DAPT might efficiently lower the probability of recurrent ischemic strokes, especially in individuals with established risk factors, therefore supporting the hypothesis that dual therapy may have a protective benefit in high-risk groups [13]. Reflecting a notable difference (p = 0.017), the Kaplan-Meier survival analysis found a stroke-free survival rate of 87% in the DAPT group against 70% in the SAPT group [14].

This result is in line with results showing better stroke-free survival with DAPT than with single therapy in individuals with small strokes and high-risk transient ischemia events [15]. DAPT's capacity to maintain extended stroke-free intervals points to a key role in patient management at high risk for recurrence [16]. Consistent with prior studies showing DAPT greatly

reduces the risk of major cardiovascular events in individuals with atherosclerotic disease, the multivariate analysis revealed patients on DAPT had a 60% reduced risk of recurrent stroke (HR = 0.40) compared to those on SAPT [17]. This modified hazard ratio underlines the therapeutic benefit of DAPT and the necessity of rigorous patient treatment for those having high cardiovascular risk [18]. Fascinatingly, the bleeding occurrences in both groups 4.3% in DAPT and 2.1% in SAPT were modest and no statistically significant difference was found (p = 0.53) [19]. This is consistent with results of research implying that the higher bleeding risk connected with DAPT does not significantly exceed its advantages in terms of lower stroke risk [20].

Careful patient selection and monitoring help to explain the low incidence of bleeding episodes in this trial, therefore reflecting advice from guidelines supporting the sensible use of DAPT in populations at high risk of stroke. Although other research have shown the effectiveness of DAPT, our results add to the body of knowledge already in use by including particular data from a Pakistani population, generally underrepresented in clinical trials. The risk profiles and demographic features of our study subjects mirror the increasing frequency of stroke and related comorbidities in South Asia. This emphasizes the significance of localized data guiding therapy plans. Furthermore, the findings support an increasing agreement that DAPT is especially helpful for patients who have had transient ischemic episodes or recurrent strokes [21].

Our findings underline that patients in Pakistan may also benefit much from DAPT, compared to previous data from Western populations, so stressing the significance of include DAPT in clinical procedures designed for high-risk persons in such demographic environments. All things considered, our results confirm already published data supporting the use of DAPT in high-risk stroke patients by showing notable decrease in stroke recurrence while preserving a good safety profile. The study emphasizes the requirement of customized therapy techniques and the need of more research to maximize treatment tactics in different demographics, therefore guaranteeing that every patient gets the best possible treatment.

Limitations and Future Research

The research has many limitations, including a small sample size of 92, which may affect how broadly the conclusions can be applied, and a single-center design, which may introduce biases in selection. The follow-up duration may also be insufficient for assessing the long-term benefits and safety of dual antiplatelet medication. Future research should include larger, multi-center randomized controlled trials to confirm these findings and examine the optimal length of treatment, its effects across various demographic groups, and its cost-effectiveness. Additionally, examining the mechanisms through which DAPT reduces the risk of stroke recurrence may provide significant novel insights for patient management strategies.

Conclusion

Based on good rates of stroke-free survival and a tolerable safety profile, this research concludes that, when compared to SAPT, DAPT significantly reduces the risk of recurrent stroke in high-risk patients. These findings emphasize the need of using DAPT in clinical settings for individuals who have had recurrent strokes or transient ischemic events in the past. This research stresses the importance of individualized treatment approaches to enhance patient outcomes in stroke prevention and contributes to the growing body of evidence supporting the use of DAPT in various populations by providing localized evidence.

Conflict of interest

The authors state no conflict of interest.

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

References

1. Lee HL, Kim JT, Lee JS, Park MS, Choi KH, Cho KH, Kim BJ, Park JM, Kang K, Lee SJ, Kim JG. Comparative effectiveness of dual antiplatelet therapy with aspirin and clopidogrel versus aspirin monotherapy in mild-to-moderate acute ischemic stroke according to the risk of recurrent stroke: an analysis of 15 000 patients from a nationwide, multicenter registry. Circulation: Cardiovascular Quality and Outcomes. 2020 Nov;13(11):e006474.

2. Trifan G, Gorelick PB, Testai FD. Efficacy and safety of using dual versus monotherapy antiplatelet agents in secondary stroke prevention: systematic review and meta-analysis of randomized controlled clinical trials. Circulation. 2021 Jun 22;143(25):2441-53.

3. Ding L, Peng B. Efficacy and safety of dual antiplatelet therapy in the elderly for stroke prevention: a systematic review and meta-analysis. European Journal of Neurology. 2018 Oct;25(10):1276-84.

4. Toyoda K, Uchiyama S, Yamaguchi T, Easton JD, Kimura K, Hoshino H, Sakai N, Okada Y, Tanaka K, Origasa H, Naritomi H. Dual antiplatelet therapy using cilostazol for secondary prevention in patients with high-risk ischaemic stroke in Japan: a multicentre, open-label, randomised controlled trial. The Lancet Neurology. 2019 Jun 1;18(6):539-48.

5. Dawson J, Merwick Á, Webb A, Dennis M, Ferrari J, Fonseca AC, European Stroke Organisation. European Stroke Organisation expedited recommendation for the use of short-term dual antiplatelet therapy early after minor stroke and high-risk TIA. European stroke journal. 2021 Jun;6(2):CLXXXVII-XCI.

6. Brown DL, Levine DA, Albright K, Kapral MK, Leung LY, Reeves MJ, Sico J, Strong B, Whiteley WN, American Heart Association Stroke Council.

Benefits and risks of dual versus single antiplatelet therapy for secondary stroke prevention: a systematic review for the 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack. Stroke. 2021 Jul;52(7):e468-79.

7. Sumaya W, Geisler T, Kristensen SD, Storey RF. Dual antiplatelet or dual antithrombotic therapy for secondary prevention in high-risk patients with stable coronary artery disease?. Thrombosis and Haemostasis. 2019 Oct;119(10):1583-9.

8. Bhatia K, Jain V, Aggarwal D, Vaduganathan M, Arora S, Hussain Z, Uberoi G, Tafur A, Zhang C, Ricciardi M, Qamar A. Dual antiplatelet therapy versus aspirin in patients with stroke or transient ischemic attack: meta-analysis of randomized controlled trials.

9. Tsung-Lin Lee MD, Yu-Ming Chang MD, Pi-Shan Sung MD. Clinical updates on antiplatelet therapy for secondary prevention in acute ischemic stroke. Acta Neurologica Taiwanica. 2023 Sep;32(3):138-44.

10. Kim D, Park JM, Kang K, Cho YJ, Hong KS, Lee KB, Park TH, Lee SJ, Kim JG, Han MK, Kim BJ. Dual versus mono antiplatelet therapy in large atherosclerotic stroke: a retrospective analysis of the Nationwide multicenter stroke registry. Stroke. 2019 May;50(5):1184-92.

11. Li, Y., Jing, Q., Wang, B., Wang, X., Li, J., Qiao, S., Chen, S., Angiolillo, D.J. and Han, Y., 2020. Extended antiplatelet therapy with clopidogrel alone versus clopidogrel plus aspirin after completion of 9-to 12-month dual antiplatelet therapy for acute coronary syndrome patients with both high bleeding and ischemic risk. Rationale and design of the OPT-BIRISK double-blinded, placebo-controlled randomized trial. *American Heart Journal*, *228*, pp.1-7.

12. Chen PL, Chen YJ, Chung CP, Seak CJ, Jeng JS, Hsieh MJ, Lien LM, Chen JH, Chen YW, Chiu TF, Lee JT. Dual antiplatelet therapy in the management of acute minor ischemic stroke and high-risk transient ischemic attack: an expert consensus statement from taiwan stroke society and taiwan society of emergency medicine. Journal of Acute Medicine. 2022 Sep 9;12(3):85.

13. Ohnishi N, Fujieda Y, Hisada R, Nakamura H, Kato M, Oku K, Bohgaki T, Amengual O, Yasuda S, Atsumi T. Efficacy of dual antiplatelet therapy for preventing recurrence of arterial thrombosis in patients with antiphospholipid syndrome. Rheumatology. 2019 Jun 1;58(6):969-74.

14. Jing J, Meng X, Zhao X, Liu L, Wang A, Pan Y, Li H, Wang D, Johnston SC, Wang Y, Wang Y. Dual antiplatelet therapy in transient ischemic attack and minor stroke with different infarction patterns: subgroup analysis of the CHANCE randomized clinical trial. JAMA neurology. 2018 Jun 1;75(6):711-9.

15. Albay CE, Leyson FG, Cheng FC. RETRACTED ARTICLE: Dual versus mono antiplatelet therapy for acute non-cardio embolic ischemic stroke or transient ischemic attack, an efficacy and safety analysis-updated meta-analysis. BMC neurology. 2020 Dec;20:1-1.

16. Kim JT, Park MS, Choi KH, Cho KH, Kim BJ, Park JM, Kang K, Lee SJ, Kim JG, Cha JK, Kim DH. Comparative effectiveness of dual antiplatelet therapy with aspirin and clopidogrel versus aspirin monotherapy in acute, nonminor stroke: a nationwide, multicenter registry-based study. Stroke. 2019 Nov;50(11):3147-55.

17. Xie X, Wang X, Laskowitz DT, Zhao X, Miao Z, Liu L, Li H, Meng X, Wang Y, Wang Y, CHANCE investigators. Effect of dual versus mono antiplatelet therapy on recurrent stroke modulated by activated partial thromboplastin time. European Journal of Neurology. 2019 Sep;26(9):1168-e78.

18. Yang Y, Zhou M, Zhong X, Wang Y, Zhao X, Liu L, Wang Y. Dual versus mono antiplatelet therapy for acute non-cardioembolic ischaemic stroke or transient ischaemic attack: a systematic review and meta-analysis. Stroke and vascular neurology. 2018 Jun 1;3(2).

19. Deng T, He W, Yao X, Chen J, Liu X, Liu L, Zhang T, Lu H. Safety and efficacy of short-term dual antiplatelet therapy combined with intensive rosuvastatin in acute ischemic stroke. Clinics. 2023 Mar 17;78:100171.

20. Huang YC, Lee JD, Weng HH, Lin LC, Tsai YH, Yang JT. Statin and dual antiplatelet therapy for the prevention of early neurological deterioration and recurrent stroke in branch atheromatous disease: a protocol for a prospective single-arm study using a historical control for comparison. BMJ open. 2021 Nov 1;11(11):e054381.

21. Valgimigli M, Frigoli E, Heg D, Tijssen J, Jüni P, Vranckx P, Ozaki Y, Morice MC, Chevalier B, Onuma Y, Windecker S. Dual antiplatelet therapy after PCI in patients at high bleeding risk. New England Journal of Medicine. 2021 Oct 28;385(18):1643-55.