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PERIOPERATIVE MANAGEMENT IN CRANIOTOMY PATIENTS ON ANTIPLATELET AND ANTICOAGULANT THERAPY: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN PAKISTAN

Amina sultan[1], Lubna Naz[1], Rahida[1], Mushafa[1], Shahid Mabood[1]

1. Department of Anaesthesia, Irfan General Hospital, Peshawar, Pakistan

Corresponding Email: pathaninaz@gmail.com

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ABSTRACT

BACKGROUND: The perioperative period, comprises the time before and after surgery, with a range from one week before surgery to four weeks following it. The five weeks are marked by occurrences during which most thrombotic and bleeding complications associated with perioperative antithrombotic management take place. Management of these risks presents a clinical challenge, particularly in neurosurgical procedures such as craniotomy due to high hemorrhagic potential of the procedure.

OBJECTIVE: To evaluate perioperative management strategies and associated complications in patients undergoing craniotomy while receiving antiplatelet and anticoagulant therapy.

METHODOLOGY: This is a cross-sectional study, conducted on 300 craniotomy patients over two years from 1st February 2022 till 1st January 2024 at the Irfan General Hospital, Peshawar. Patients aged 20 years and older receiving antiplatelet (aspirin, clopidogrel) or anticoagulant therapy (VKA, DOACs, and LMWH) were included. Data collection focused on patients' demographics, perioperative management strategies, and post-op complications. SPSS software was used to analyze the data.

RESULTS: Among 300 patients, 195 (65%) received AP therapy, while 105(35%) were on AC therapy. Aspirin (36.7%) and clopidogrel (28.3%) were commonly used AP drugs. Whereas, VKA (18.3%) was primarily an AC drug. Perioperative management strategies varied, with 35% of patients temporarily discontinuing anticoagulants, 25% receiving bridging therapy with heparin, and 10% switching to LMWH. In AP therapy, minimal bleeding was observed in most patients (96, 49.2%), while in AC therapy, moderate bleeding was noticed at a greater rate of 38, 35.2%) indicating a significant difference in bleeding severity ($p < 0.01$).

CONCLUSION; This study highlights the prevalence of antithrombotic therapy among craniotomy patients and enhances the importance of individualized perioperative management to minimize complications. Temporary discontinuation and bridging strategies are some of the perioperative techniques commonly used.

KEYWORDS: Antiplatelet, Anticoagulants, Craniotomy, Perioperative.

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INTRODUCTION

The term, the perioperative period, comprises the time before and after surgery, with a range from one week before surgery to four weeks following it. The five weeks are marked by occurrences during which most thrombotic and bleeding complications associated with perioperative antithrombotic management take place.1 The perioperative care of patients on anticoagulants has become a major medical difficulty for which elderly individuals find themselves more amenable to antiplatelets and/or anticoagulants and then are subjected to surgery or invasive procedures than the younger age cohorts.2,3 Peri-operative antithrombotic management attempts to achieve that balance between the risk of thrombosis against major bleeding.4 Common antithrombotic drugs that are used in the prevention and treatment of cerebrovascular and other hemorrhagic, traumatic brain injury which are of two major types: antiplatelet agents that inhibit platelet activation, and anticoagulants that regulate thrombin generation and stabilization of clot formation for halting coagulation Approximately 10-20% of surgical patients are on some form of antithrombotic therapy, with increased prevalence in neurosurgical patients.5,6

The complication of the surgical population increases when the use of antiplatelet and anticoagulant drugs is considered in the prevention of thrombotic hazards in some patients, whereas in neurosurgery, procedures themselves are highly hemorrhagic, so that this management becomes difficult.6 Thus, aspirin and P2Y12 inhibitors are the most common antiplatelet medications, either prescribed alone or constituting DAPT, while oral anticoagulants can be generally divided into two groups: vitamin K antagonists (VKAs) and direct-acting oral anticoagulants (DOACs).7 Meta-analysis showed that DOACS reduce intracranial hemorrhage risk by approximately 40-60% in comparison to VKAs. In patients undergoing neurosurgery, the use of DOACs was associated with a reduced incidence of spontaneous bleeding complications;8 however, the use of anticoagulants, in both acute TBI and elective surgery, poses a major challenge in this

delicate balancing act between thromboembolic prevention and hemorrhagic risk.9

The hurdles lie in balancing thromboembolic risk, which varies among individuals, against the potential for hemorrhagic problems depending on the procedure. Continuation of complete anticoagulation can unpredictably raise the risk of both bleeding and thromboembolism if therapy is either withheld or reversed. The optimal management strategy must, therefore, be guided by detailed patient risk determination than the assessment of thromboembolic risk against perioperative bleeding risk, which decides whether therapy may be temporarily stopped or bridging therapy is mandated through administration of short-acting anticoagulant such low-molecular-weight heparin (LMWH) or unfractionated heparin while warfarin is paused before surgery and resumed postoperatively until therapeutic range is achieved.1

Perioperative management of patients who undergo craniotomy while on antiplatelet and anticoagulant medication is not clearly documented by specific locations in Pakistan. While most existing guidelines might not reflect local behaviors or outcomes since they are aimed at western populations. There is limited research on balancing risks, bridging procedures, and optimal timing for cessation of drugs in neurosurgical contexts. Thus, this research study aims to evaluate the prevalence of antiplatelet or anticoagulant therapy in craniotomy patients and its implications on perioperative care, especially concerning thromboembolic risks and bleeding complications.

METHODOLOGY:

This cross-sectional study was conducted from the data of the past two years, from 1st February 2022 to 1st January 2024, and was collected from a Tertiary Care Hospital named Irfan General Hospital, Peshawar, to evaluate anticoagulation management strategies, bleeding complications, and thromboembolic outcomes. A total of 300 participants were recruited through a convenient sampling technique. All eligible cases that satisfied the inclusion criteria during the study period were used to determine the sample size, which was not determined statistically. Patients aged 20 years or older who underwent craniotomy while on antiplatelet agents (such as aspirin or clopidogrel) or anticoagulants (such as vitamin K antagonists or DOACs) were included. Eligibility required documented perioperative management strategies, including continuation, discontinuations, or bridging therapy the short-term use of short-acting anticoagulants during the perioperative interruption of long-term antithrombotic therapy), and preoperative, perioperative, and postoperative data on bleeding and thromboembolic events. Exclusion criteria encompassed patients with incomplete medical records regarding anticoagulation management, emergency craniotomies with unknown anticoagulation status, or concurrent hematological disorders affecting coagulation.

Data collection was carried out retrospectively for one year. A standardized form was used to collect relevant clinical information. Patients' data was extracted from past medical records. The data included patient demographics, type and duration of antithrombotic therapy, perioperative management strategies, surgical details, and postoperative outcomes over the past year. The primary outcome included the incidence of major bleeding (intracranial hemorrhage, excess surgical site bleeding), thromboembolic events (stroke, deep vein thrombosis), and mortality. Team members collected data from patients' records via direct observations.

Statistical analysis was performed using SPSS version 26. Descriptive statistics were used to summarize demographic and clinical variables. Categorical variables were presented as frequency and percentage, while continuous variables were summarized using mean and standard deviation. Associations between antithrombotic therapy and perioperative outcomes were assessed using the Chi-square test for categorical variables. A p-value < 0.05 was considered significant.

The institutional review board granted ethical approval with IRB number 'IRB-AINS-2024-012', and informed consent was obtained from each participant.

RESULTS

The study recruited 300 patients, underwent craniotomy while receiving antiplatelet and anticoagulation therapies. According to age distribution majority of the patients, 70(23.3%), ranged between 50-59 years, followed by those who were greater than 60 years of age, 65(21.7%), while 50(16.7%) were between 40-49 years. Our study population had a male predominance of 180 (60%). Regarding comorbidities, 124 (41.3 %) were suffering from hypertension,165(55%) from diabetes mellitus which was more prevalent, and 145(48.3%) were non-smokers.

The commonest diagnosis that led to craniotomy were brain tumors 105(35%), followed by traumatic brain injury 90(30.0%), by stroke 75(25.0%) and aneurysm 30(10%). Elective procedures were more common (56.7%) than emergency surgeries (43.3%) as shown in Table 1.

Table 1: Baseline Characteristics

Demographics	Category	Frequency	Percentage
Age (years)	20-29	55	18.3
	30-39	60	20.0
	40-49	50	16.7
	50-59	70	23.3
	>60	65	21.7
Gender	Male	180	60
	Female	120	40
Hypertension	Yes	124	41.3
	No	176	58.7
Diabetes Milletus	Yes	165	55
	No	135	45
Smoking status	Current smoker	84	28.0
	Former smoker	71	23.7
	Non-smoker	145	48.3
Diagnosis	TBI	90	30.0
	Hemorrhage	75	25.0
	Brain tumor	105	35.0
	Aneurysm	30	10.0
Surgical procedure type	Elective craniotomy	170	56.7
	Emergency craniotomy	130	43.3

N=300; TBI=Traumatic Brain Injury

The following table presents the distribution of antiplatelet (AP) and anticoagulation (AC) agents used by craniotomy patients. Out of a total of 300 participants, 195 patients received AP therapy, with Aspirin being the most common and frequently prescribed drug, which accounted for 110(36.7%) patients, whereas 105 patients received AC therapy, with vitamin K antagonists (VKA) widely prescribed to 55(18.3%) patients. Generally, antiplatelet therapy was more prevalent than anticoagulant therapy, accounting for 65% of patients who were using Aspirin and Clopidogrel, respectively (Table 2).

Table 2: Types Of Antithrombotic Agents Used.

Therapy Type	Category	Frequency	Percentage (%)
AP therapy	Aspirin (ASA)	110	36.7
	Clopidogrel	85	28.3
AC therapy	VKA	55	18.3
	DOACs	35	11.7
	LMWH	15	5.0

N=300, AP=Antiplatelet, AC=Anticoagulant, VKA=Vitamin K Antagonist, DOACs=Direct Oral Anticoagulants,

Analysis of preoperative interruption and postoperative resumption time is been shown in Table 3. It included Aspirin, Clopidogrel, Vitamin K Antagonists, Direct Oral Anticoagulants, and Low Molecular Weight Heparin.

For aspirin, the majority of patients (28, 25.5%) had their medication interrupted for 2-4 days preoperatively, while the highest resumption (25, 22.7%) also occurred within the same 2–4-day window. For clopidogrel, 20(23.5%) interrupted 4-6 preoperatively and 20(23.5%) resumed postoperatively within 2-4 days. VKA interruption and resumption were frequently observed in 2-4 and 4-6 days before surgery, 24(43.6%) and after surgery, 20(36.4%). Similarly, DOACs were mainly interrupted for 2-4 days (9, 25.7%), but 7(20%) restarted within 1-2 days. Moreover, LMWH had an even distribution mentioned in the Table 3

Table 3: Frequency Distribution of Interruption and Resumption Time of AP and AC

Drug type	Interruption time preoperatively days	Frequency (%)	Resumption postoperatively (days)	Frequency (%)
Aspirin	None	10 (9.1)	None	10 (9.1)
	1-2	11 (10)	1-2	12 (11.0)
	2-4	28 (25.5)	2-4	25 (22.7)
	4-6	20 (18.2)	4-6	20 (18.2)
	6-8	16 (14.5)	6-8	10 (9.1)
	8-10	10(9.1)	8-10	12 (11.0)
	10-12	6(5.5)	10-12	7(6.4)
	12-14	6(5.5)	12-14	5(4.5)
	>14	3(2.7)	>14	9 (8.0)
Clopidogrel	None	6 (7.1)	None	3 (3.5)
	1-2	8 (9.4)	1-2	10 (12.0)
	2-4	18 (21.0)	2-4	20 (23.5)
	4-6	20 (23.5)	4-6	15 (17.6)
	6-8	10 (12.0)	6-8	12 (14.0)
	8-10	7 (8.2)	8-10	8 (9.4)
	10-12	12 (14.0)	10-12	5 (5.9)
	12-14	2 (2.4)	12-14	5 (5.9)
	>14	6 (7.1)	>14	7 (8.2)
VKA	None	5 (9.09)	None	5(9.09)
	1-2	4(7.27)	1-2	5(9.09)
	2-4	12(21.81)	2-4	10(18.18)
	4-6	12(21.81)	4-6	10(18.18)
	6-8	10(18.18)	6-8	8(14.45)
	8-10	5(9.09)	8-10	6(10.90)
	10-12	3(5.45)	10-12	4(7.27)
	12-14	2(3.63)	12-14	3(5.45)
	>14	2(3.63)	>14	4(7.27)
DOACs	None	2(5.7)	None	2 (5.7)
	1-2	6(17.1)	1-2	7 (20)
	2-4	9(25.7)	2-4	5 (14.3)
	4-6	4 (11.4)	4-6	2 (5.7)
	6-8	5 (14.3)	6-8	3 (8.6)
	8-10	2 (5.7)	8-10	4 (11.4)
	10-12	3 (8.6)	10-12	1 (2.9)
	12-14	3 (8.6)	12-14	6 (17.1)
	>14	1 (2.9)	>14	5 (14.3)
LMWH	None	1 (6.7)	None	1 (6.7)
	1-2	2 (13.3)	1-2	2 (13.3)
	2-4	3 (20)	2-4	3 (20)
	4-6	3(20)	4-6	2 (13.3)
	6-8	2(13.3)	6-8	2 (13.3)
	8-10	1 (6.7)	8-10	1 (6.7)
	10-12	1 (6.7)	10-12	1 (6.7)
	12-14	1 (6.7)	12-14	1 (6.7)
	>14	1 (6.7)	>14	2(13.3)

AP: antiplatelet, AC: anticoagulant, VKA: Vitamin K Antagonist, DOACs: Direct Oral Anticoagulants, LMWH: Low Molecular Weight Heparin

The following table outlines different perioperative anticoagulation management strategies for patients who underwent craniotomy. Temporarily stopping anticoagulation was the most common approach, implemented in 105(35%) patients. After that, bridging therapy with heparin was the second most prevalent strategy, applied in 75 patients (25.0%), while on the other hand, 30(10.0%) patients were switched to LMWH (Table 4).

Table 4: Perioperative Management Strategies

Management strategy	Frequency	Percentage (%)
Continued full Anticoagulation	50	16.7
Temporarily stopped Anticoagulation	105	35.0
Bridging therapy with Heparin	75	25.0
No change in Anticoagulation	40	13.3
Switching to LMWH	30	10.0

N=300, LMWH: Low Molecular Weight Heparin

Perioperative complications in craniotomy patients receiving AP and AC therapy are highlighted in Table 5. In AP therapy, minimal bleeding was observed in most patients (96, 49.2%), while in AC therapy, moderate bleeding was noticed at a greater rate 38, 35.2%) indicating a significant difference in bleeding severity ($p < 0.01$). Deep venous thrombosis was the most dominant thromboembolic complication in both groups [AP: 103 (52.8%), AC: 44 (41.9%) but no statistically significant association was found between the two groups (p 0.08). Moreover, regarding post-operative complications, hydrocephalus was prevalent in the AP therapy group (p 0.04), 54(28.0%), while seizures were frequently observed in the AC therapy group, 40(38.1%), respectively (p 0.03).

Table 5: Complications:

Complications		AP (n=195) n (%)	AC (n=105) n (%)	P Value
	Minimal bleeding	96 (49.2)	21(20.0)	< 0.01
	Moderate bleeding	41(21.0)	38(36.2)	< 0.01
Bleeding risk	Severe bleeding	12(6.2)	16(15.2)	0.02
	Transfusion required	32(16.4)	15(14.3)	0.41
	Post-op hematoma	14(7.2)	15(14.3)	0.04
	DVT	103(52.8)	44(41.9)	0.08
TEC	PE	24(12.3)	40(38.1)	< 0.01
	MI	28(14.4)	10(9.5)	
	Reoperation due to thrombus	40(20.5)	11(10.5)	0.56
	Hydrocephalus	54(28.0)	15(14.3)	0.04
	Seizures	50(25.6)	40(38.1)	0.03
PO complications	Cerebral edema	24(12.0)	18(17.1)	0.54
	Wound infection	28(14.4)	13(12.4)	0.92
	Mortality	39(20.0)	19(18.1)	0.57

TEC=Thromboembolic Complications, DVT= Deep Venous Thrombosis, PE= Pulmonary Embolism, MI=Myocardial Infarction, PO=Post Operative

DISCUSSION

The current study analyzed 300 craniotomy patients and provided detailed insights into medication interruption, resumption, and associated complications during perioperative management. The majority of patients (23.3%) were aged 50-59 years, with male predominance (60%), and brain tumors were the leading cause of craniotomy. In our study, aspirin was the most frequently used AP drug (36,7%) while vitamin K antagonists (VKA) were common in AC agents (18.3%). But preoperative interruptions and postoperative resumptions varied in such a way that aspirin was commonly interrupted for 2-4 days (25.5 %) and resumed within same period (22.7%), whereas clopidogrel was interrupted for 4-6 days (23.5%) and resumed within 2-4 days (23.5%). For VKA, the interruption and resumption timing were from 2-4 and 4-6 days (43.6%,36.4%). On comparison, Greuter et al. (2019) surveyed 130 neurosurgeons worldwide, focusing on their perioperative management strategies rather than patient-specific data. It found significant heterogeneity in practice, with 40.4% of neurosurgeons interrupted aspirin for 4-6 days, while the present study observed the highest interruption at 2-4 days. Clopidogrel had been interrupted for 6-8 days in the previous study, whereas my study reported 4-6 days as being the most prevalent. Additionally, while Greuter et al. (2024) reported that 35% of participants discontinued AC temporarily, 25% used bridging therapy with heparin, and 10% switched to LMW. Our study did not focus on bridging strategies but rather on specific resumption times. Overall, previous studies explored surgical decision-making worldwide; my study offered more patient-centered analysis, reinforcing the need for standardized perioperative management guidelines.[10]

Greuter et al. (2019) examined 143 patients with traumatic brain injury (TBI) who underwent craniotomy and craniectomy, with 47(32.9%) receiving AP/AC treatment. Unlike previous study, which aimed to examine the impact of AP/AC therapy on post-operative bleeding in TBI patients, current research assessed preoperative interruption and post operative resumptions strategies as well as wider range of diagnoses, including brain tumors (35%), TBI (30%), hemorrhage (25%) and 10% aneurysm. Additionally, our study provided comprehensive insights into medication usage. A key difference between the two studies lay in their findings on post-operative bleeding in such a way that present research findings revealed that minimal bleeding was more common among AP therapy patients (49.2%), whereas moderate bleeding was observed at a greater rate in AC therapy patients (35.2%). Further current study observed thromboembolic complications, highlighted deep venous thrombosis as the most frequent complication in both AP/AC groups (52.8/41.9%), but a previous Greuter et al. (2019 did not assess these complications.[11]

Ebel et al. (2021) focused on 215 craniectomy patients specifically for neurovascular pathologies, with 23.3% receiving PI/AC therapy. It found no statistically significant differences in bleeding rates between short (<5 days) and long (> 5 days) discontinuation groups (preoperative: 11.1% vs 10%, p=0.659; postoperative: 0% vs 13.2%, p=0.556) on contrast current study did not find any significant differences among both groups. Furthermore, another key difference was the evaluation of perioperative complications, thromboembolic events being primarily assessed by Ebel et al.,2021, and that study did not report detailed post-operative complications beyond mortality and time to bleed as explained by the current study.[12]

Rychen et al. (2023) discussed the effect of perioperative aspirin (ASA) management in elective craniotomies on hemorrhagic and thromboembolic hazards. The systematic review of seven studies involving 646 patients exhibited no substantial difference in hemorrhagic complications between ASA continuation (3%) and discontinuation (3%), with thromboembolic events being lower in the continuation group (3%) than in the discontinuation group (6%). In the same way, our study detected no significant increase in hemorrhagic complications using perioperative continuation of AT, recommending the safety of this strategy. However, our study offers a more wide-ranging view by incorporating several antiplatelet (AP) and anticoagulant (AC) treatments other than ASA, with a higher sample size (300 patients). Moreover, our research identifies certain complications like low bleeding in AP users (49.2%), medium bleeding in AC users (35.2%), and increased rates of deep vein thrombosis among AP users (52.8%). Whereas both studies confirm ASA continuation without a higher risk of bleeding, our findings generalize the debate to include other AT agents and postoperative adverse effects like hydrocephalus (28%) among AP users and seizures (38.1%) among AC users, providing a better assessment of perioperative AT management in craniotomy patient.[13]

The MARK study included 9700 patients who underwent a wide range of surgical procedures in Japan, while our study included 300 craniotomy patients. In the MARK study, antithrombotic agent discontinuation was linked with increased risk of thromboembolic events (1.7% vs. 0.6%) and major bleeding (7.6% vs. 0.4%), while heparin bridging augmented both thromboembolic and bleeding risks in high-bleeding-risk procedures. Conversely, our study noted a higher incidence of AP therapy (65%) compared to AC therapy (35%), with aspirin being the most frequently used medication (36.7%). Preoperative discontinuation differed by drug, with aspirin and DOACs predominantly discontinued for 2–4 days, whereas VKA had longer discontinuations (2–6 days). Our results concurred with the MARK study in emphasizing the fine balance between thrombosis and bleeding hazards of perioperative antithrombotic therapy. But our study only targets patients who have undergone craniotomy, where stringent interruption and continuation techniques are needed owing to the high risk involved in neurosurgery.[14]

Zhang et al. in their study of 2021 carried out a retrospective analysis. Out of a population of 621 patients, only a minority of 139 patients (22.4%) had received antithrombotic treatment. Of these, 110 patients were treated with antiplatelets and 35 with

anticoagulants. The time of resumption of antithrombotic therapy correlated with both recurrence and thromboembolic events. The mean time for resumption was 71 days (IQR 29-201), producing a recurrence rate of 10.8%. There were thrombotic complications in 12 cases, 8.6%, with five occurring before resumption; whereas, the present study analyzed 300 craniotomy patients under antithrombotic treatment: out of these, 195 patients were on AP agents, and 105 with AC therapy. For perioperative management, aspirin was discontinued preoperatively and resumed postoperatively (28, 25.5% for 2-4 days; 25, 22.7% for 2-4 days), clopidogrel (20, 23.5% for 4-6 days; 20, 23.5% for 2-4 days), and VKA (24, 43.6% for 2-4 and 4-6 days; 20, 36.4% after 4-6 days). Our study differs from the Singapore study, which finds no significant association between timing of resumption and recurrence and accounts for the frequency of certain perioperative management approaches and their possible outcomes in craniotomy patients. [15]

Earlier work had been done to study the potential risks and outcomes of anticoagulation being too early after craniotomy, focusing on the potential risks of catastrophic intracranial hemorrhage. The study found that risks associated with initiating anticoagulation within seven days after surgery were 5.6%, with emergent intervention required for intracranial bleeding; however, no extra parenchymal bleedings were observed, and the 90-day survival was at 100%. The present work instead examines the whole range of antithrombotic therapy in craniotomy patients, including describing the use of antiplatelet (AP) and anticoagulant (AC) therapy, interruption and resumption times, perioperative management strategies, and complications related to those therapies. Antiplatelet therapy, especially aspirin therapy, was used more often than anticoagulant therapies, being vitamin K antagonists being used most often among the different classes of anticoagulants. Notably, the analysis of perioperative management strategies revealed that the most commonly used was temporary interruption of anticoagulants (35%), while bridging with heparin was used in 25% of cases. Minor bleeding occurred more in the AP group (49.2%), and moderate bleeding occurred more in the AC group (36.2%). Other thromboembolic complications, namely deep venous thrombosis (DVT), dominated both groups: slightly more in the AP group (52.8%) as compared to the AC group (41.9%). In the AP group, post-operative complications like hydrocephalus were more frequent, whereas seizures were overwhelmingly more prevalent in the AC group. While the previous work mainly concerned the risks of ultra-early anticoagulation, specifically assessing the safety of these practices, the present study investigates a wider perioperative assessment of antithrombotic management .[16]

Overall, this research study provided a comprehensive evaluation of perioperative management, targeting key trends in medication interruption, resumption, and associated complications.

There are some limitations to this study; most importantly, it was a single-center retrospective study, which can limit it generalizability. It also lacked long-term follow-ups which restricted the assessments of late thromboembolic or hemorrhagic outcomes. Moreover, it did not evaluate the effects of specific bridging or dose management. Also, it did not show the stratification of risk factors which may have affected the bleeding or thrombotic risks.

Compared to prior research, the study needs more standardized protocols for the resumption of antithrombotic therapy in craniotomy patients. Future researches should emphasize the long-term outcomes of these strategies to balance thromboembolic and bleeding risks in neurosurgery patients.

CONCLUSION

The study highlights the prevalence of antithrombotic therapy among craniotomy patients and underscores the importance of individualized perioperative management to minimize complications. Temporarily discontinuation and bridging strategies were commonly implemented. These findings emphasize the need for further longitudinal studies to develop standardized protocols to optimize perioperative outcomes in neurosurgical patients from a larger sample size.

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Key Contributions of the Authors	
Author Names	**Author Contributions**
Amina sultan	A, B, C, D
Lubna Naz	A, B, C, D
Haseena Sabir	A, B, D
Rahida	B, C, D
Mushafa	B, C, D
Shahid Mabood	B, C,D

Key for Author Contributions:

A.Conception or Design
B.Acquisition, Analysis, or Interpretation of Data
C.Manuscript writing
D.Critical Review and approval

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved