

Effect of Antiplatelet and Anticoagulant Therapy on Postoperative Hemostasis and Tissue Healing

USAMA MAZHAR¹, FIDA HUSSAIN², SAIMA BUKHARI³, RANA SHOAIB ASLAM⁴, ABRAR UL HASSAN PIRZADA⁵, ASADULLAH AWAN⁶

¹Senior Registrar Anesthesia, Doctor's Hospital & Medical Centre, Lahore

²Senior Consultant Surgeon, Allam Iqbal Teaching Hospital, D.G. Khan.

³Professor, Department of Pharmacology, Ayub Medical College, Abbottabad

⁴Assistant Professor Surgery, Rashid Latif Medical College, Lahore

⁵Associate Professor Surgical and Allied, Azra Naheed Medical College, Lahore

⁶Assistant Professor, Department of Plastic Surgery, Dow International Medical College & Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan
Correspondence to: Fida Hussain, Email: drfida0093@gmail.com

ABSTRACT

Background: Antiplatelet and anticoagulant drugs are extensively used as prevention against cardiovascular and thromboembolic diseases. There is a clinical dilemma in their perioperative management because it is associated with high risks of bleeding and possible wound healing impairments.

Objective: To evaluate the effect of antiplatelet and anticoagulant therapy on postoperative hemostasis and tissue healing in patients undergoing surgical procedures.

Methodology: This was a prospective observational study that involved 67 patients that underwent antithrombotic treatment and post-operative surgery between January and June 2023 at Allam Iqbal Teaching Hospital, D.G. Khan. Patients have been subdivided into three groups: the antiplatelet therapy, anticoagulant therapy and the combination therapy. Coagulation profile before the operation, blood loss during operation, blood loss after operation, wound healing condition, and postoperative complication were documented. ANOVA and Chi-square were used to conduct the statistical analysis, with $p < 0.05$ taken as significant.

Results: Patients receiving combined therapy showed significantly higher PT, APTT, and INR values ($p < 0.001$). Postoperative bleeding was more frequent in the combined therapy group (55%) compared to anticoagulant (36.4%) and antiplatelet groups (20%) ($p = 0.01$). Delayed wound healing and longer hospital stay were also significantly associated with combined therapy ($p = 0.04$ and $p = 0.01$ respectively). Major bleeding requiring re-operation or transfusion remained uncommon.

Conclusion: Antithrombotic therapy, particularly combined antiplatelet and anticoagulant use, increases postoperative bleeding risk and delays wound healing but rarely leads to severe complications. Careful perioperative management allows safe continuation of therapy in most patients.

Keywords: Antiplatelet, Anticoagulant, Postoperative bleeding, Hemostasis, Wound healing, Surgery.

INTRODUCTION

Anticoagulant and antiplatelet medications are important in the prevention of cardiovascular and thromboembolism like myocardial infarction, stroke, and deep vein thrombosis. As the rates of cardiovascular disease and aging population increase, there has been an increase in the number of patients who are taking long-term antithrombotic therapy following surgical procedures. This has posed a typical clinical dilemma to the surgeons and physicians on how to manage these medications perioperatively¹⁻³.

Anticlotting action of antiplatelet drugs is by inhibiting platelet aggregation which disrupts primary hemostasis, and anticoagulants disregard coagulation cascade and disrupt secondary hemostasis. Although these effects are positive in the prevention of thrombosis, it can also pose a danger to perioperative bleeding. Historically, it used to be advised that all these drugs need to be stopped before surgery to prevent excessive bleeding but on the other hand, termination of treatment can expose the patient to thromboembolic complications that can be fatal⁴⁻⁷.

The other significant issue, though not sufficiently studied is the effects of these medications on the healing of tissues. The initial process of wound repair is the formation of a stable clot that is necessary to achieve a good inflammatory response, angiogenesis, and tissue regeneration. Changes in platelet activity and coagulation factor can thus influence the outcome of epithelialization, the formation of granulation tissue and wound healing in general⁸⁻¹⁰.

Despite existing guidelines, evidence regarding the balance between bleeding risk and healing outcomes in patients continuing antithrombotic therapy remains limited, particularly in routine clinical settings. Therefore, this study was conducted to evaluate the effect of antiplatelet and anticoagulant therapy on postoperative hemostasis and tissue healing in patients undergoing surgical procedures.

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METHODOLOGY

This is a prospective observational study that was carried out at Allam Iqbal Teaching Hospital, D.G. Khan during six months January 2023 to June 2023 to examine the impact of antiplatelet and anticoagulant therapy on the postoperative hemostasis and tissue healing. The study involved 67 patients who were undergoing elective surgeries and were put under perioperative antithrombotic care. Participation of patients was in a continuous manner after they had signed the informed written consent.

The patients who used antiplatelet agents, anticoagulants, and both were 18 years of age and above and had established cardiovascular and thromboembolic reasons that made them undergo surgery. The patients who had known inherited bleeding disorders, severe liver, thrombocytopenia (platelet count less than 50,000/ μ L), active malignancy with chemotherapy-induced cytopenia, or denying consent were not to participate in the study.

The participants were divided into three groups with regard to their medication regimen; antiplatelet therapy group, anticoagulant therapy group, and combined therapy group. The investigators did not change decisions made by the treating physician on continuation or temporary discontinuation or bridging therapy based on conventional clinical guidelines. Laboratory tests such as platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR) were done within 24 hours before surgery.

Hemostatic results during intra-operative and post-operative were measured. The amount of blood that was lost during surgery was estimated by suction volume and surgical gauze. Primary hemorrhage (within 24 hours), reactionary hemorrhage (24-48 hours) and secondary hemorrhage (>48 hours) were monitored in patients. Local hemostatic measures, surgical re-intervention, blood transfusion and reoperation were recorded to be required.

The clinical assessment of tissue healing was done on the postoperative days 3, 7 and 14 based on standard wound assessment criteria such as edema, erythema, granulation tissue, epithelialization, infection, hematoma, or wound dehiscence. The

level of pain was assessed with the use of Visual Analogue Scale (VAS). The length of stay and the complications that were experienced after the operation were also noted.

Data were analyzed using SPSS version 26. Quantitative variables were expressed as mean \pm standard deviation and qualitative variables as frequency and percentage. Comparison among the three groups was performed using one-way ANOVA for continuous variables and Chi-square or Fisher's exact test for categorical variables. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The sample consisted of 67 patients who were administered perioperative antithrombotic treatment. The age, sex distribution, comorbidities, and duration of surgery were similar across the three groups, suggesting that baseline confounding was limited. There were no statistically significant differences between the groups in terms of demographic variables and clinical ones ($p > 0.05$), which indicates that they can be compared appropriately.

Table 1. Baseline characteristics of participants ($n = 67$)

| Variable | Antiplatelet (n=25) | Anticoagulant (n=22) | Combined (n=20) | p-value |
|---|------------------------|-------------------------|--------------------|---------|
| Age (years), mean \pm SD | 54.8 \pm 10.6 | 56.2 \pm 11.1 | 58.9 \pm 9.8 | 0.31 |
| Female, n (%) | 12 (48.0) | 9 (40.9) | 8 (40.0) | 0.79 |
| BMI (kg/m^2), mean \pm SD | 27.1 \pm 3.6 | 27.8 \pm 4.1 | 28.2 \pm 3.9 | 0.58 |
| Diabetes mellitus, n (%) | 8 (32.0) | 7 (31.8) | 9 (45.0) | 0.55 |
| Hypertension, n (%) | 13 (52.0) | 12 (54.5) | 12 (60.0) | 0.87 |
| Chronic kidney disease, n (%) | 3 (12.0) | 4 (18.2) | 5 (25.0) | 0.52 |
| Major surgery, n (%) | 10 (40.0) | 9 (40.9) | 9 (45.0) | 0.93 |
| Duration of surgery (min), mean \pm SD | 78 \pm 25 | 81 \pm 28 | 86 \pm 30 | 0.63 |

Table 2. Perioperative hemostasis profile and anticoagulation parameters

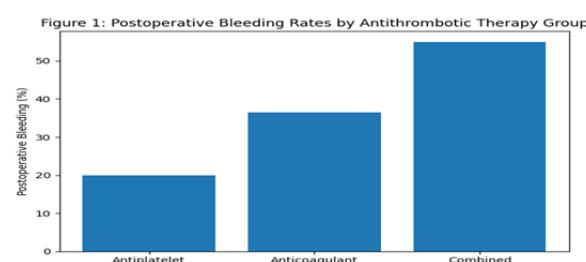
| Variable | Antiplatelet (n=25) | Anticoagulant (n=22) | Combined (n=20) | p-value |
|--|------------------------|-------------------------|--------------------|---------|
| Platelet count ($\times 10^9/\text{L}$), mean \pm SD | 246 \pm 58 | 238 \pm 61 | 231 \pm 55 | 0.68 |
| PT (seconds), mean \pm SD | 13.1 \pm 1.2 | 15.4 \pm 2.8 | 16.1 \pm 3.1 | 0.001 |
| APTT (seconds), mean \pm SD | 31.6 \pm 4.2 | 38.9 \pm 7.6 | 41.5 \pm 8.4 | <0.001 |
| INR, mean \pm SD | 1.07 \pm 0.12 | 1.62 \pm 0.52 | 1.79 \pm 0.60 | <0.001 |
| Bridging therapy used, n (%) | 2 (8.0) | 6 (27.3) | 8 (40.0) | 0.01 |

Table 3. Postoperative bleeding outcomes (Primary outcome: hemostasis)

| Outcome | Antiplatelet (n=25) | Anticoagulant (n=22) | Combined (n=20) | p-value |
|--|------------------------|-------------------------|--------------------|---------|
| Estimated blood loss (mL), mean \pm SD | 210 \pm 90 | 290 \pm 120 | 370 \pm 160 | <0.001 |
| Any postoperative bleeding, n (%) | 5 (20.0) | 8 (36.4) | 11 (55.0) | 0.01 |
| Bleeding requiring local measures | 4 (16.0) | 6 (27.3) | 9 (45.0) | 0.04 |
| Surgical intervention required | 1 (4.0) | 2 (9.1) | 3 (15.0) | 0.39 |
| Blood transfusion required | 0 (0.0) | 1 (4.5) | 2 (10.0) | 0.21 |
| Re-operation for bleeding | 0 (0.0) | 1 (4.5) | 1 (5.0) | 0.56 |

Table 4. Tissue healing outcomes and postoperative complications

| Outcome | Antiplatelet (n=25) | Anticoagulant (n=22) | Combined (n=20) | p-value |
|-------------------------|------------------------|-------------------------|--------------------|---------|
| Delayed wound healing | 4 (16.0) | 6 (27.3) | 9 (45.0) | 0.04 |
| Wound dehiscence | 1 (4.0) | 2 (9.1) | 3 (15.0) | 0.39 |
| Surgical site infection | 2 (8.0) | 3 (13.6) | 4 (20.0) | 0.46 |
| Hematoma/seroma | 2 (8.0) | 4 (18.2) | 6 (30.0) | 0.10 |
| Pain score Day 3 (VAS) | 4.3 \pm 1.5 | 4.8 \pm 1.6 | 5.4 \pm 1.7 | 0.06 |
| Hospital stay (days) | 2.1 \pm 1.2 | 2.7 \pm 1.4 | 3.4 \pm 1.8 | 0.01 |



The groups showed significant differences in parameters of the coagulation. Patients on anticoagulants and combined therapy showed increased PT, APTT and INR than those in the antiplatelet group ($p < 0.001$). More thromboembolic risk is also reflected by the fact that bridging therapy was more common in the combined therapy group.

The results of postoperative bleeding were significant in the groups. The combination therapy patients registered the greatest blood loss and rate of postoperative bleeding ($p < 0.05$). Nevertheless, the need to perform re-operation or transfusion due to severe bleeding was rare in all groups.

The rate of delay in the healing of wounds was markedly higher in the combined therapy group ($p = 0.04$). The anticoagulant therapy was associated with an increased stay in the hospital of patients who were receiving antiplatelet therapy ($p = 0.01$). Other complications like infection and hematoma demonstrated the tendency to increase in frequency but were not statistically significant.

DISCUSSION

The aim of the current research was to compare the effects of antiplatelet and anticoagulant treatment on the postoperative hemostasis and healing of tissues in patients subjected to surgery. The baseline features of the subjects were similar across the three intervention groups, and therefore, the variation in the bleeding and healing rates could have been a result of the pharmacological properties of the medicines and not demographic or clinical confounding factors. This enhances internal validity of the results¹¹⁻¹³.

There was a significant prolongation of PT, APTT, and INR in the patients under anticoagulant therapy and combined therapy, which is anticipated to manifest the pharmacodynamic effect of the medications on the coagulation cascade. The clinical manifestations of these changes were more intraoperative blood loss and higher incidence of postoperative bleeding especially in the combined therapy group. Nevertheless, in cases of severe bleeding with need of re-operation or transfusion was not very common, which means that the risk of bleeding is rather high, but it can be controlled in most cases with proper perioperative care^{14,15}.

It was also shown in the study that dual therapy had the strongest effect on postoperative hemostasis. The group of patients who were on both antiplatelet and anticoagulant medications had high levels of bleeding episodes as well as frequent need of local hemostatic control. This observation is in line with synergistic inhibition of both platelet aggregation and coagulation cascades, which undermine both the primary and secondary hemostasis¹⁸⁻²⁰.

The same pattern was observed in the tissue healing outcomes. Delayed healing and increased hospital stay were considerably higher in the combined therapy group. Clot dysfunction may break and interfere with the initial phases of inflammatory and proliferative response of wound healing, resulting in a delay in epithelialization and granulation tissue development. Infection and wound dehiscence were also more common in anticoagulant users but these differences were not statistically significant, which might be explained by the small sample size.

Notably, even though there was more minor bleeding and slower healing, life-threatening complications were uncommon in all the groups. This implies that the decision of antithrombotic therapy only because of minor surgical bleeding is not always reasonable because the thromboembolic risk of therapeutic discontinuation can be much greater than the bleeding risk which is manageable. Perioperative planning and local hemostatic measures play a significant role in these patients.

CONCLUSION

Antiplatelet and anticoagulant therapies significantly influence postoperative hemostasis, with the greatest bleeding risk observed

in patients receiving combined therapy. These medications are also associated with delayed wound healing and longer hospital stay, although major complications are uncommon. With appropriate perioperative management, most bleeding events can be effectively controlled without discontinuation of therapy. Therefore, individualized risk assessment rather than routine drug withdrawal is recommended to balance bleeding and thromboembolic risks in surgical patients.

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