Surgical Resection of Cutaneous Head and Neck Lesions

Does Aspirin Use Increase Hemorrhagic Risk?

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Objective: To determine whether the antiplatelet agent aspirin increases hemorrhagic risk in patients undergoing surgical resection of cutaneous head and neck lesions.

Design: Retrospective cohort study.

Setting: Regional referral center.

Patients: All cases of cutaneous head and neck lesions surgically resected during a 10-year period were included.

Main Outcome Measures: Outcome measures were incidence of significant postoperative hemorrhage, defined as postoperative hematoma or hemorrhage necessitating surgical reexploration; and total postoperative hemorrhage, defined as any hemorrhage lasting longer than 4 hours despite external pressure, requiring medical review, and resulting in prolongation of the patient’s hospital stay or readmission to the hospital.

Results: Seven hundred eleven patients (974 cases) were eligible for inclusion, of whom 320 were receiving aspirin therapy at the time of surgery. The incidence of significant postoperative hemorrhage in the aspirin and non-aspirin groups was 5 (1.6%) and 0, respectively ($P = .004$), and aspirin use was the only risk factor for significant postoperative hemorrhage. The incidence of total postoperative hemorrhage in the aspirin and nonaspirin groups was 7 (2.2%) and 1 (0.1%), respectively ($P = .002$). At multivariate analysis, aspirin use and local flap reconstruction were independent risk factors for total postoperative hemorrhage. Cases receiving aspirin therapy who also underwent local flap reconstruction were at exponential (124-fold) increased risk of total postoperative hemorrhage compared with cases with neither risk factor.

Conclusions: Aspirin intake at the time of surgery to resect cutaneous head and neck lesions confers a small but statistically increased risk of postoperative hemorrhage. This risk is particularly pronounced in patients undergoing local flap reconstruction.

aspirin therapy or any cova riable increased the risk of post- 
operative hemorrhage or impaired wound healing after 
surgery to resect cutaneous lesions of the head and neck.

METHODS

A 10-year retrospective case review of all surgical resections of 
cutaneous lesions of the head and neck performed at the Depart- 
ment of Otolaryngology–Head and Neck Surgery, Raigmore Hospi- 
tal, Inverness, Scotland, from January 1, 1996, to December 31, 
2005, was undertaken. The unit serves as the regional referral cen- 
ter for head and neck plastic surgery for the Highlands of Scot- 
land. Cases were identified from a universal electronic database 
using procedure-specific codes. A predefined data extraction sheet 
was used. The primary data source was the patient medical rec- 
ord in which physician and nurse entered all patient demog- 
raphic data, current medications, and management details in sepa- 
rate, unique, and structured forms in parallel fashion. The nurses’ 
form also included specific provisions for recording the time of 
ocurrence of postoperative events and the dryness and appear- 
ance of the wound. In addition, a comprehensive review of con- 
solidated discharge summaries, drug prescription and consump- 
tion charts, outpatient records, electronic databases of operative 
details, and primary care records was undertaken to correlate, con- 
firm, and collect any missing data.

The policy in our department is to not stop aspirin therapy preoperatively. Patients were considered to have taken aspirin if the drug had been consumed within 4 days before surgery. Patients not taking regular aspirin and who had not con- 
sumed the drug within 4 days before surgery were considered 
control subjects for comparison. This time frame was chosen 
because aspirin irreversibly inhibits platelet function for the life 
of the platelet (ie, approximately 7-10 days). Therefore, after 
5 days, half of all circulating platelets would be newly pro- 
duced and functional and would be ample for adequate hemo- 
stasis.

Patients were considered to have taken a nonsteroidal 
anti-inflammatory drug if it had been consumed within 3 days 
before surgery. For this study, the consultant was considered 
the surgeon if he or she performed or assisted in the proce- 
sure, and the trainee was considered the surgeon if he or she 
performed the procedure independent of the consultant.

Blood and coagulation data were not routinely checked pre- 
operatively. For surgery, local anesthesia was preferred, with a 
standard preincisional infiltration of 2% lignocaine and 1:80 000 
epinephrine tartrate. A surgical knife was used for incision and 
dissection. Bipolar diathermy was used for hemostasis, and, when 
possible, the wound was closed in layers. The method of repair 
was determined by the site and size of the defect and the choice 
of the individual surgeon. When primary closure was possible, a variety of local flaps (simple rotation, bilobed, rhombo- 
doid, nasolabial, forehead, melolabial, advancement [single, bi- 
lateral, and V-Y], Ian, Karapandzic, and Abbe-Estlander) or skin 
grafts were used for skin cover. Dressings were not applied. A 
corticosteroid (0.5-1 g 4 times daily) was prescribed for analgesia, and patients were 
observed for 2 to 4 hours in the recovery unit before discharge. 
Sutures were removed on postoperative days 5 to 7. Follow-up 
was at the clinic at 1 to 4 weeks postoperatively or until the wound 
had satisfactorily healed.

OUTCOME MEASURES

Primary Outcome Measures

Significant postoperative hemorrhage (SPH) was defined as post- 
operative hematoma or hemorrhage necessitating surgical re-

Secondary Outcome Measure

Wound healing, assessed at 1 to 4 weeks postoperatively, was 
determined by the incidence of partial or complete necrosis of 
flap or graft, or wound dehiscence greater than 5 mm as a re- 
sult of hematoma, seroma, infection, or indeterminate cause. 
Minor complications such as crusting, ecchymosis, and se-

STATISTICAL ANALYSIS

Univariate analysis was performed to identify possible risk fac- 
tors for SPH and TPH. Variables analyzed were age and sex; 
medical illness, overall and individually for hypertension, pe-

RESULTS

We identified 1006 cases from the electronic database. The medical records for 14 of these patients were 
unavailable. In another 18 patients, none of whom experi-
enced postoperative hemorrhage, details of medication 
intake at the time of surgery were unclear. Thus, 974 cases 
(711 patients) were eligible for inclusion. Table 1 lists 
the characteristics of the included cases. In patients given 
aspirin, the dose varied from 75 to 300 mg. Suction drains 
were not routinely used, but were used in 8 cases (0.8%), 
most of whom underwent resection of large scalp le-
sions with local flap reconstruction.

Five cases experienced significant postoperative hem- 
orrhage, all of whom were taking aspirin (P = .004). There 
was no other risk factor for SPH at univariate analysis; 
thus, multivariate analysis was not performed. Total post-
operative hemorrhage occurred in 8 cases, 7 of whom were
Taking aspirin (P = .002). Local flap or skin graft repair and age were other possible risk factors for TPH (Table 2). At multivariate analysis, aspirin use and repair with local flap remained as independent risk factors for TPH (Table 2). In subgroup analysis of cases with TPH, 5 cases with local flap repair experienced necrosis of the flap. One of these cases was taking aspirin (P = .67); hence, aspirin therapy did not protect against flap necrosis.

### Table 1. Characteristics of Cases

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases (N = 974)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (±SD), y</td>
<td>69.9 (14.9)</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>652/322</td>
</tr>
<tr>
<td>Medical illness</td>
<td>399 (42.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>354 (36.3)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>10 (1.0)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>39 (4.0)</td>
</tr>
<tr>
<td>Previous radiotherapy to head and neck</td>
<td>5 (0.5)</td>
</tr>
<tr>
<td>Medication at time of surgery</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>320 (32.8)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drug</td>
<td>94 (9.6)</td>
</tr>
<tr>
<td>Newer generation antiplatelet drug†</td>
<td>19 (1.9)</td>
</tr>
<tr>
<td>Peripheral vasodilator‡</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Prophylactic antibiotic</td>
<td>16 (1.6)</td>
</tr>
<tr>
<td>Resected skin diameter, mean (±SD), cm²</td>
<td>6.6 (2.5)</td>
</tr>
<tr>
<td>Site of lesion</td>
<td></td>
</tr>
<tr>
<td>Scalp</td>
<td>173 (17.8)</td>
</tr>
<tr>
<td>Nose</td>
<td>240 (24.7)</td>
</tr>
<tr>
<td>Eyelid§</td>
<td>17 (1.7)</td>
</tr>
<tr>
<td>Ear†</td>
<td>270 (27.8)</td>
</tr>
<tr>
<td>Cheek¶</td>
<td>233 (23.9)</td>
</tr>
<tr>
<td>Neck</td>
<td>40 (4.0)</td>
</tr>
<tr>
<td>Anesthesia, local/general</td>
<td>826/148</td>
</tr>
<tr>
<td>Suction drain</td>
<td>8 (0.8)</td>
</tr>
<tr>
<td>Method of repair</td>
<td></td>
</tr>
<tr>
<td>Simple closure</td>
<td>604 (62.0)</td>
</tr>
<tr>
<td>Local flap#</td>
<td>282 (29.0)</td>
</tr>
<tr>
<td>Skin graft**</td>
<td>88 (9.0)</td>
</tr>
<tr>
<td>Histologic findings</td>
<td></td>
</tr>
<tr>
<td>Benign and preinvasive lesions</td>
<td>373 (38.3)</td>
</tr>
<tr>
<td>Malignant lesions</td>
<td>601 (61.7)</td>
</tr>
<tr>
<td>Surgeon, consultant/trainee</td>
<td>720/254</td>
</tr>
</tbody>
</table>

### Table 2. Risk Factors for Total Postoperative Hemorrhage

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
<th>Adjusted Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.04</td>
<td>.29</td>
<td>1.04 (0.97-1.1)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>.002</td>
<td>.01</td>
<td>13.9 (1.6-117.3)</td>
</tr>
<tr>
<td>Local flap or skin graft</td>
<td>.03</td>
<td>.02</td>
<td>6.4 (1.3-32.6)</td>
</tr>
<tr>
<td>Local flap, excluding skin grafts</td>
<td>.01</td>
<td>.009</td>
<td>8.9 (1.7-45.8)</td>
</tr>
</tbody>
</table>

Findings from the present study show that surgical resection of head and neck cutaneous lesions in patients receiving aspirin therapy confers a higher risk of hemorrhagic complications. This is consistent with a recent meta-analysis that found that aspirin therapy increased postoperative hemorrhagic risk in several surgical procedures, in particular, intracranial surgery, prostatectomy, gastrointestinal endoscopy, tonsillectomy, and dental extraction. Aspirin-related postoperative hemorrhage occasionally led to adverse surgical outcomes, including death. However, the few studies that have analyzed cutaneous surgery failed to demonstrate such increased risk. There are several possible reasons for this. In most studies, the number of patients recruited was small, limiting the power to detect differences in hemorrhage rates. The largest study to date was performed by Otley et al, who retrospectively studied 803 procedures but did not differentiate between hemorrhagic and nonhemorrhagic complications. This study was further nonspecific in that patients taking aspirin or nonsteroidal anti-inflammatory drugs, 2 agents with distinct differences in pharmacodynamics and potency in platelet aggregation inhibition, were combined as a single study group. Further, none of these studies focused exclusively on the head and neck region but included all regions of the body. Head and neck plastic surgery differs from plastic surgery elsewhere owing to the greater emphasis on cosmetics and wider choice of local flaps and skin grafts. Because of proximity to cosmetically and functionally...
sensitive structures, facial wounds, unlike wounds elsewhere, are not routinely amenable for postoperative pressure dressings or insertion of drains. Anatomically, the head and neck region is distinguished by its rich vascular supply and the intricate relationship between its superficial fascia, areolar and dense fibrous tissue planes, and deep fascia. Thus, results derived from general cutaneous series cannot be reliably applied to the head and neck region.

Only 1.6% to 2.2% of cases taking aspirin in the current study experienced postoperative hemorrhage. This rate is lower than that cited for noncutaneous surgery. While variations in the definition of hemorrhage may be a factor, the lower rate is also attributable to the easier accessibility of cutaneous wounds, which facilitates external pressure tamponade in the recovery unit, thereby potentially mitigating the severity of hemorrhage, enhancing the likelihood of achieving hemostasis and preventing acute hematomas, thus reducing the need for surgical reexploration.

Aspirin causes irreversible loss of the cyclooxygenase activity of platelet prostaglandin (PG) G and PGH synthase 1. This results in decreased conversion of arachidonate to PGG2 and, ultimately, of PGH2 and thromboxane A2, which are important mediators in platelet aggregation and thrombi formation. Platelets are exquisitely sensitive to aspirin. A dosage of only 30 mg effectively eliminates the synthesis of thromboxane A2. The minimum documented dosage of aspirin in our patients (75 mg) is higher than this threshold. Experimental animal models have demonstrated that aspirin therapy attenuates the vasospasm after hemorrhage. Thus, we postulate that, even after apparently adequate hemostasis at the completion of surgery, the failure to form adequate and stable thrombi, in concert with an attenuated vasospastic response, predispose to postoperative hemorrhage from capillaries and small to medium vessels. The increased risk of TPH with local flap reconstruction is attributable to more extensive tissue mobilization and a potentially larger dead space created under the flap.

Some shortcomings of this study must be noted. First, all retrospective studies include incomplete data and have limited scope for standardization. However, in this study, multiple sources were used to collect, correlate, and confirm the data, thereby minimizing deficiencies and maximizing accuracy. Only the most morbid, clinically rel-

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### Table 3. Characteristics of Postoperative Hemorrhage

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Aspirin</th>
<th>Concurrent Nonaspirin Antiplatelet Agent*</th>
<th>Medical Illness</th>
<th>Performed by Consultant</th>
<th>Site</th>
<th>Area of Resected Skin, cm²</th>
<th>Method of Repair</th>
<th>Histologic Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/82</td>
<td>Yes</td>
<td>No</td>
<td>HT</td>
<td>No</td>
<td>Ear</td>
<td>3.8</td>
<td>Simple closure</td>
<td>SCC</td>
</tr>
<tr>
<td>2/F/70</td>
<td>Yes</td>
<td>No</td>
<td>HT</td>
<td>Yes</td>
<td>Eyelid</td>
<td>3</td>
<td>Rhomboid flap</td>
<td>BCC</td>
</tr>
<tr>
<td>3/M/81</td>
<td>No</td>
<td>. . .</td>
<td></td>
<td>No</td>
<td>Yes</td>
<td>3.6</td>
<td>Bilobed flap</td>
<td>BCC</td>
</tr>
</tbody>
</table>

*Nonsteroidal anti-inflammatory drug, dipyridamole, ticlopidine, or clopidogrel.
†Suction drain inserted because of resection of large lesion with flap reconstruction.

### Table 4. Management of Postoperative Hemorrhage

<table>
<thead>
<tr>
<th>Patient</th>
<th>Postoperative Hemorrhage and Management</th>
<th>Complications of Wound Healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemorrhage for 16 h, significant bruising; pressure bandage</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Hemorrhage for 12 h, significant periorbital bruising</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>Hemorrhage for 16 h, significant periorbital bruising</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>Hemorrhage for 48 h; suction drain removed 48 h postoperatively; at 1 wk, hematoma under flap, expressed after stitch removal; pressure dressing and antibiotic therapy</td>
<td>Necrosis of tip of flap</td>
</tr>
<tr>
<td>5</td>
<td>Acute hematoma 3 h postoperatively; return to operating room, wound reexplored, bipolar diathermy to bleeding point under flap; suction drain and antibiotic therapy</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>Hemorrhage for 24 h, hematoma twice (at 24 and 72 h); on both occasions, aspirated blood; pressure bandage and antibiotic therapy</td>
<td>Flap necrosis</td>
</tr>
<tr>
<td>7</td>
<td>Hemorrhage for 72 h; at 1 wk; hematoma under flap, expressed after stitch removal; pressure dressing and antibiotic therapy</td>
<td>Flap necrosis</td>
</tr>
<tr>
<td>8</td>
<td>Hemorrhage for 6 h; returned to operating room for reexploration; stitching at bleeding point</td>
<td>None</td>
</tr>
</tbody>
</table>
evant, and objectively valuable factors have been used to define hemorrhagic outcomes. A prospective study is ideal but would not be cost-effective, given the infrequent occurrence of postoperative hemorrhage. Second, smoking was not examined as a risk factor, although it has been implicated as compromising cutaneous wound healing and survival of facial cutaneous flaps. However, smoking exerts its deleterious effects through its thrombogenic, vasospastic, and deoxygenating potential and is not known to enhance bleeding after cutaneous surgery. Third, because surgeons were not blinded to patient medication intake, more care could have been exercised in achieving hemostasis in the aspirin group, thereby biasing the results toward underestimating the hemorrhagic potential of aspirin therapy.

The implications of the findings of the present study need to be examined in a larger clinical context. Overall, the risk of hemorrhage with aspirin therapy is small and the outcome is nonfatal. However, the safety of temporary discontinuation of aspirin therapy is unclear; some anecdotal evidence suggests that it may predispose to a small risk of thromboembolism. Nevertheless, postoperative hemorrhage is associated with significant morbidity and confers a high risk of wound necrosis. Therefore, in the outpatient clinic, we actively elicit a history of aspirin intake from all patients scheduled for surgery. Those taking the drug are fully informed of the associated hemorrhagic risk, and only if aspirin is being taken for its cardiovascular protective effect do we advocate its discontinuation. Surgery is preferably scheduled in the morning, meticulous hemostasis is secured before skin closure, and the wound is closely monitored in the recovery unit, with external pressure used, if necessary, to control minor oozing of blood. Once the wound is dry for at least 2 hours, the patient is discharged with careful instructions to remain vigilant for hemorrhage and hematoma.

Patients taking aspirin who undergo local flap reconstruction incur an exponential increase in hemorrhagic risk compared with those with neither risk factor. Therefore, in this subgroup, it may be prudent to withhold aspirin during the perioperative period. The absence of robust studies examining the safety of temporary discontinuation of aspirin precludes definitive recommendations, and urgent studies on this subject are warranted. Alternate options such as simplifying the repair or using skin grafts may be considered, but at the cost of an inferior cosmetic result.

Conservative treatment of postoperative hemorrhage is associated with a high incidence of wound necrosis (Table 4). Therefore, we now have a low threshold for returning patients with postoperative hemorrhage for surgical reexploration, and urgently return every patient with flap reconstruction and hematoma in an attempt to salvage the flap.

CONCLUSIONS

Aspirin intake at the time of surgery to resect cutaneous head and neck lesions confers a small but statistically increased risk of postoperative hemorrhage. This risk is particularly pronounced in patients undergoing local flap reconstruction. Limited data also suggest that, in patients with flap repair who develop postoperative hematomata, failure to surgically reexplore the wound results in flap necrosis, and that aspirin does not protect against flap necrosis and, therefore, its role in minimizing microvascular thrombosis and improving local flap survival is questionable.

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Author Contributions: Dr Dhiwakar had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Dhiwakar and McClymont. Acquisition of data: Dhiwakar and Khan. Analysis and interpretation of data: Dhiwakar. Drafting of the manuscript: Dhiwakar. Critical revision of the manuscript for important intellectual content: Khan and McClymont. Statistical analysis: Dhiwakar. Administrative, technical, and material support: Khan. Study supervision: Dhiwakar and McClymont.

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REFERENCES


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