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Reconstructive

Full versus Baby Dose Aspirin for Antithrombotic Prophylaxis in Free Tissue Transfer: Does Size Matter?

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Background: The postoperative prophylactic use of aspirin is a common practice among plastic surgeons after free tissue transfer. The use of baby aspirin (81 mg) has become more popular due to previously published literature in other fields. We hypothesized that a full dose daily aspirin is nonsuperior to a baby dose daily aspirin in preventing arterial thrombosis in free tissue transfer.

Methods: All patients undergoing free tissue transfer of the extremities from 2008 to 2020 were retrospectively reviewed. They were divided into two groups based on the postoperative dose of aspirin administered (full versus baby dose). The decision to administer full or baby dose was based on the surgeon's preference. Primary outcome was revision of the arterial anastomosis. Secondary outcomes included flap complications.

Results: A total of 183 patients were identified. Out of those, 78 patients received full dose aspirin postoperatively, whereas 105 received a baby dose of aspirin. Patients who received baby aspirin did not have a higher incidence of returning to the operating room for revision of their arterial anastomosis [7.6% versus 7.7%; adjusted odds ratio, 0.93 (95% confidence interval, 0.28-3.11); adjusted *P*, 0.906]. No differences were found between the two groups in complete and partial flap loss, wound dehiscence, or infection. None of the patients experienced any aspirin-related gastrointestinal complications.

Conclusions: In patients undergoing free tissue transfer, thrombosis of the arterial anastomosis is rare. Administration of a full dose of aspirin postoperatively was not superior to a baby dose of aspirin in preventing arterial-related complications.

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INTRODUCTION

The use of prophylactic aspirin (ASA) following free tissue transfer is well established in the previously published literature.[1–8] Nevertheless, the question with regard to the optimal dosing of aspirin for free tissue transfer remains unanswered.[1,9] Plastic and reconstructive surgeons universally administer prophylactic aspirin to prevent anastomotic thrombosis after free tissue transfer. However, there is a paucity of data regarding the optimal dose required to prevent postoperative thrombosis and subsequent flap failure.

Previously published literature in other medical and surgical disciplines such as cardiology and vascular surgery[10–12] have shown that a full dose is nonsuperior to the use of baby dose aspirin, with some studies suggesting a weight-based dosing as the optimal way to administer it. Furthermore, literature supports that in some cases, the utilization of baby aspirin may result in lower rates of medication-related complications compared with the full dose. We hypothesized that a full dose daily aspirin is nonsuperior to an attenuated baby dose daily aspirin in preventing arterial thrombosis in free tissue transfer.

METHODS

After institutional review board approval, all patients undergoing free tissue transfer to reconstruct the extremities at a level I academic trauma center from 2005 to 2019 were retrospectively identified. Patients with missing records were excluded from further analysis. The patients' demographics were extracted from the medical records. Comorbidities known to be associated with impaired wound healing (diabetes and smoking) were identified. The presence of cardiovascular disease or peripheral vascular disease was also identified for each of the patients. The intraoperative details were reviewed.

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Table 1. Protocol of Postoperative Management of Free Tissue Transfer

Every patient receives rectal aspirin upon arrival to the ICU (300 mg)
Patient is kept NPO for 24 h
Extremity is elevated and wrapped in a bear hugger to maintain normothermia
IVF is kept to <7 mL/kg/h, boluses are avoided unless necessary to prevent hypotension
Flap checks are performed q 1 h for the first 24 h
Flap checks include evaluation of implantable cook Doppler (artery and vein) and physical examination
Plastic surgery fellow is available 24/7 to assess the flap if there are any concerns
Patient is kept in strict bed rest for the first 24 h
ASA is switched to oral 24 h after surgery

All patients receive standardized postoperative care (Table 1) in our institution. Following the completion of the surgery, every patient receives 300 mg of rectal ASA before transfer to the intensive care unit where they remain for 3–5 days for postoperative flap monitoring. The patient remains NPO (nil per os—nothing by mouth) for the first 24 hours in case of emergency return to the operating room (OR) for anastomotic revision is warranted. After the first 24 postoperative hours, the patient is started on a diet that is advanced as tolerated. The patient's antithrombotic prophylaxis is switched from rectal to PO (per os—oral) aspirin. The decision to administer a full dose (325 mg per day) or a baby dose of aspirin (81 mg per day) is dependent on the physician's and treating team's preference. The antithrombotic prophylaxis is continued for a total of 30 days. The rest of the postoperative monitoring and progressive mobility is similar and standardized for every patient (Table 1). The study population was divided into two cohorts based on the aspirin dose administered.

The present study aimed to assess whether a higher dose of aspirin administered was superior to a smaller dose in preventing arterial anastomotic thrombosis and emergent return to the OR for revision. The primary outcome was the need for revision of the arterial microanastomosis. Secondary outcomes were flap-related wound complication and aspirin-related gastrointestinal (GI) complications.

Takeaways

Question: Is there a difference in outcomes in free flaps if a patient receives 81 mg of aspirin versus 325 mg of aspirin postoperatively?

Findings: There is no significant difference in outcome between the two groups.

Meaning: Using 81 mg postoperatively does not increase postoperative complications in free flap outcomes, and may decrease the incidence of bleeding versus 325 mg.

STATISTICAL ANALYSIS

The two groups were compared for differences using a bivariate analysis. Dichotomous variables were compared using the Fisher exact test or chi-square as appropriate. The continuous variables were examined for normality of distribution using the Shapiro–Wilkis test. Normally distributed variables were compared using the Student *t* test, while non-normally distributed variables were compared via the Mann–Whitney U test. To account for cofounding factors, a logistic regression was then performed using the return to the OR for arterial anastomosis revision as the dependent variable. Any of the previously tested variables from the univariate analyses that differed at a *P* value less than 0.05 were included in the regression. Adjusted odds ratios (95% confidence interval) were derived from the regression. The process was replicated for the rest of the secondary outcomes.

RESULTS

During the study period, a total of 183 patients were identified. Out of these, 78 received a full dose of ASA (325 mg daily) and 105 received a baby dose of ASA (81 mg daily). The demographics are shown in Table 2. The majority of the patients were men (68%) with a mean age of 31 years. Sixty percent of the flaps were muscle flaps, while 40% were perforator flaps. A total of 79 patients were active smokers, while 50 had diabetes (Table 2). Most patients had two veins anastomosed to assist with flap drainage (105). The mean flap dimension was 24 cm, and the mean operative time was 570

Table 2. Demographics and Clinical Characteristics

Characteristic	Full Dose ASA (n = 78)	Baby Dose ASA (n = 105)	Overall (n = 183)	*P*
Age				
>50	19.2 (15)	31.4 (33)	26.2 (48)	0.089
Female sex	46.2 (36)	21.0 (22)	31.7 (58)	< 0.001
Type of flap				
Muscle	61.5 (48)	57.1 (60)	59.0 (108)	
Perforator	38.5 (30)	42.9 (45)	41.0 (75)	0.649
Extremity reconstructed				
Upper	26.9 (21)	17.1 (18)	21.3 (39)	
Lower	73.1 (57)	82.9 (87)	78.7 (144)	0.144
Comorbidities				
Diabetes mellitus	23.1 (18)	30.5 (32)	27.3 (50)	0.315
Smoking	37.2 (29)	47.6 (50)	43.2 (79)	0.176
PVD	9.0 (7)	13.3 (14)	11.5 (21)	0.092
History of cardiac disease	9.0 (7)	5.7 (6)	7.1 (13)	0.131
Type of wound				
Acute	60.3 (47)	57.1 (60)	58.5 (107)	
Chronic	39.7 (31)	42.9 (45)	41.5 (76)	0.762

PVD, peripheral vascular disease.

Table 3. Perioperative Characteristics

Characteristic	Full Dose ASA (n = 78)	Baby Dose ASA (n = 105)	Overall (n = 183)	*P*
No. veins anastomosed				
1	53.8 (42)	60.0 (63)	57.4 (105)	
2	46.2 (36)	40.0 (42)	42.6 (78)	0.451
Superficial venous system used	14.1 (11)	27.6 (29)	21.9 (40)	0.031
Largest flap dimension (cm)	22±8	25±11	23.6±9.9	0.065
Operative time (min)	537±188	591±183	568±187	0.051
Type of anastomosis				
End to end	93.6 (73)	94.3 (99)	94.0 (172)	
End to side	6.4 (5)	5.7 (6)	6.0 (11)	0.792
Type of flap				
Muscular	50 (64.1)	61 (58.1)	111(60.7)	
Fasciocutaneous	28 (35.9)	44 (41.9)	72 (39.3)	0.502
Fluid administration (ml/kg/h)	7.5±4.0	8.7±3.7	8.2±3.8	0.032

Table 4. Outcomes

Outcome	Full Dose ASA (n = 78)	Baby Dose ASA (n = 105)	Overall (n = 183)	*P*
Revision of arterial anastomosis	7.7 (6)	7.6 (8)	7.7 (14)	1
For patients with vascular disease	28.6 (2/7)	28.6 (4/14)	28.6 (6/21)	1
GI-related complications	5.1 (4)	4.8 (5)	4.9 (9)	0.983
Complete flap loss	16.7 (13)	11.4 (12)	13.7 (25)	0.385
Partial flap loss	2.6 (2)	1.9 (2)	2.2 (4)	1
Dehiscence	6.4 (5)	4.8 (5)	5.5 (10)	0.746
Infection	9.0 (7)	22.9 (24)	16.9 (31)	0.016

minutes. In our institution, the main muscular flap used is a latissimus dorsi, while the most common fasciocutaneous flap is the anterolateral thigh flap. Patients who received a baby dose of aspirin were more likely to have the superficial venous system used as the recipient vein for drainage, and more likely to receive more fluids intraoperatively (Table 3).

Table 4 depicts the unadjusted outcomes for the study population. Patients who received a baby dose of aspirin had the same incidence of arterial thrombosis of the anastomosis requiring a revision in the operating room when compared with patients who received a full dose (7.6% versus 7.7%; $P = 1$). Similarly, for patients who had a history of vascular disease, the dose of aspirin did not have an impact on the incidence of arterial thrombosis (33.3% versus 36.4%; $P = 0.872$). The dose of perioperative aspirin similarly had no impact on complete flap loss (11.4% versus 16.7%; $P = 0.385$), partial flap loss (1.9% versus 2.6%; $P = 1$), and dehiscence of the flap (4.8% versus 6.4%; $P = 0.746$; Table 4). Two patients experienced intraoperative thrombosis of the anastomosis mandating a reexploration while in the operating room and were excluded from further analyses. After adjusting for differences between the baseline characteristics, including sex of the patient, comorbidities, and smoking status, the dose of aspirin did not have an impact on the odds of developing any of the complications (Table 5).

Table 5. Adjusted Outcomes

	AOR (95% CI)	Adjusted, *P*
Revision of arterial anastomosis	0.93 (0.28–3.11)	0.906
For patients with vascular disease	0.99 (0.73–2.19)	0.982
GI-related complications	1.02 (0.65–1.72)	0.991
Complete flap loss	0.52 (0.20–1.36)	0.185
Partial flap loss	1.28 (0.07–25.26)	0.873
Dehiscence	0.73 (0.18–3.07)	0.671
Infection	2.52 (0.97–6.54)	0.081

AOR, adjusted odds ratio.

DISCUSSION

The present study is, to our knowledge, the first study to suggest that a full dose of aspirin administered postoperatively as prophylaxis in free tissue transfer is nonsuperior to a baby dose of aspirin. This study uses only patients undergoing extremity free flap reconstruction for several reasons. The use of Caprini score has been shown to be a reliable tool in identifying patients with higher risk of thromboembolic complications in the postoperative period.[13,14] Patients with Caprini scores more than 7 have a higher probability of developing thrombotic events and as such further prophylaxis is recommended. Trauma or malignancy-related free flap reconstruction usually meets these criteria. The study population of the present article underwent free flap reconstruction due to either traumatic events or following resections of malignant tumors. In addition, peripheral vascular disease is more prominent in the extremities. Plaques may result in destabilization of a microsurgical anastomosis and usually require antiplatelet therapy to prevent occlusion during the time period when the pseudointima forms. Extremity free flap reconstruction has the highest incidence of failure due to arterial anastomotic complications, and as a result, the use of antithrombotic prophylaxis becomes more relevant.[15]

Since Craven's early observations with regard to aspirin's antiplatelet properties,[16] aspirin has become widely utilized in medicine, from being used for the primary prevention of cardiovascular disease[17] to the application of its antiplatelet properties in protecting newly formed microanastomoses.[1] Although the practice of using aspirin in free tissue transfer has been well described,[1–8] the literature remains lacking of a strong evidence to support or refute its use.[18,19] Moreover, little literature in the plastic and reconstructive field compares the effects of administering a full dose (325 mg) versus the attenuated baby dose (81 mg).[1,9]

The noninferiority of an attenuated aspirin dose in providing antiplatelet effects has been described in other disciplines such as cardiology and vascular surgery.[10–12]

It needs to be noted that in the present study, both groups received an immediate dose of 300 mg of rectal aspirin postoperatively. The two arms were separated into baby and full dose aspirin essentially on postoperative day 1. For the first 24 hours, both groups received the same dose. Previous literature suggests that most anastomotic complications in free tissue transfer occur within the first 24 hours after the index operation.[20] Our article is in accordance with the published literature. The vast majority of arterial anastomotic complications did occur within the first 24 hours (11 of 14, 79%). This might suggest that the most important dose is the initial dose of 300 mg of rectal aspirin. Subsequent administration of baby or full dose aspirin did not show an impact on the incidence of anastomotic complications in this study population.

Peripheral vascular disease is a significant risk factor in arterial anastomoses.[21,22] The presence of significant plaque makes microanastomoses more challenging as it can destabilize the plaque, which, in turn, can propagate a cascade of events leading to thrombosis of the anastomosis or distal embolization of microthrombi. The latter can result not only in distal flap ischemia, but also in foot embolization and loss of tissue, if an end-to-side anastomosis is required. Our group avoids end-to-side anastomoses in such patients, unless there is evidence that sacrificing a main artery to perform an end-to-end anastomosis might result in distal limb ischemia. The present study had only two patients with such conditions (one vessel run off and significant plaque that mandated an end-to-side anastomosis). As a result, thromboembolic prophylaxis in these instances is even more critical. The high incidence of arterial complications mandates a higher clinical suspicion of flap ischemia and early return to the OR for revision. Technical pearls include tacking the plaque down with sutures by suturing from the lumen to the adventitia in an attempt to stabilize the plaque. It needs to be noted, however, that even in these cases, different doses of aspirin had no impact on the incidence of arterial anastomotic complications.

All patients in our institution receive the same protocolized and standardized postoperative care. In addition, with the exception of gender, all preoperative demographics were similar between the two groups. Several intraoperative factors are known to be associated with higher flap-related complications. Stranix et al[23] analyzed 361 flaps used for lower extremity reconstruction and concluded that the utilization of two veins instead of one resulted in a fourfold decrease in complications. Ahmadi et al[24] performed a meta-analysis and concluded that the type of arterial anastomosis (end to end versus end to side) was not associated with an increased probability of arterial thrombosis. Finally, the type of flap utilized has been extensively studied, and there is controversy regarding the optimal type of flap that is associated with a lower incidence of complications.[25–27] It is important though to point out that in the present study, patients who received a baby dose of aspirin underwent harvesting of larger flaps and had a longer operative time compared with their counterparts. However, the type of flap (muscle versus fasciocutaneous), the type of anastomosis, and the number of veins anastomosed did not differ between the groups.

There are several limitations to this study. The lack of a control group (a group that did not receive aspirin at all) makes it difficult to assess the clinical importance of the use of such antithrombotic prophylaxis in general. However, this was not the goal of the present study. In addition, the retrospective nature of the study did not allow for randomization of the patients. As a result, only a relationship and not a causation between the use of aspirin and the studied outcome can be assumed.

CONCLUSIONS

Although thrombosis of arterial anastomosis in free tissue transfer remains a rare event, it carries dire consequences. After the administration of 300 mg of rectal aspirin, subsequent administration of full dose or baby dose aspirin did not result in significant differences in the incidence of arterial thrombosis of free tissue transfer of the extremity.

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