



Ketorolac for Prevention of Microvascular Thrombosis in Head and Neck Free Flaps

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Abstract

Intro: Prevention of microvascular thrombosis in free tissue transfer for head and neck reconstruction is paramount to maintaining a viable reconstruction. Various anti-thrombotic agents have been used in the past for this purpose. The aim of this study is to show the non-inferiority of Ketorolac for prevention of flap failure.

Methods: This is a retrospective review of all head and neck free tissue transfers performed at a quaternary care center by the two senior authors who routinely use ketorolac for prevention of microvascular thrombosis. Patients who were ineligible to receive ketorolac were included in the study for descriptive purposes.

Results: From 2010 – 2020, there were 322 patients who underwent free tissue transfer of the head and neck. Within the cohort, 278 patients were administered Ketorolac and 44 were not, most commonly due to kidney dysfunction or cardiac comorbidities requiring aspirin. Within the Ketorolac group, the flap failure rate was 2.5% with a venous and arterial thrombosis incidence of 2.2% and 1.4% respectively. Hematoma incidence was 9.4% in Ketorolac group and 6.8% in non-Ketorolac group. Rate of acute kidney injury were 3.6% in Ketorolac group and 11.4% in non-Ketorolac group.

Conclusion: This is the largest study of Ketorolac usage in head and neck free tissue transfer patients. The flap failure rate of 2.5% is comparable to the literature rate of 5% (p-value=0.054). Ketorolac was not associated with increased rate of acute kidney injury when used in patients without kidney dysfunction. The incidence of hematoma is slightly higher than previous studies; however, 23% of hematoma patients received Ketorolac and full dose anticoagulation such as a heparin drip. Ketorolac in combination with other full dose anticoagulants may lead to increased risk of hematoma. This study demonstrates the safety and efficacy of Ketorolac for prevention of microvascular thrombosis and free flap failure in head and neck reconstruction patients.

Tables/Figures

Table 1: Demographics

	Non-Ketorolac (N=44)	Ketorolac (N=278)	Total (N=322)	p value
Sex				0.167
Female	10 (22.7%)	94 (33.8%)	104 (32.3%)	
Male	34 (77.3%)	184 (66.2%)	218 (67.7%)	
Ethnicity				0.486
Hispanic or Latino	1 (2.3%)	17 (6.6%)	18 (6.0%)	
Not Hispanic or Latino	42 (97.7%)	240 (93.4%)	282 (94.0%)	
Race				0.883
American Indian / Alaskan Native	1 (2.3%)	9 (3.3%)	10 (3.1%)	
Asian	1 (2.3%)	9 (3.3%)	10 (3.1%)	
Black or African American	1 (2.3%)	3 (1.1%)	4 (1.3%)	
White	40 (93.0%)	250 (90.6%)	290 (90.9%)	
Patient age at surgery				0.001
Mean	69.3	62.3	63.2	
American Society of Anesthesiologists physical status classification				0.040
ASA I-Normal healthy patient	0 (0.0%)	6 (2.2%)	6 (1.9%)	
ASA II-Mild systemic disease	5 (11.4%)	81 (29.1%)	86 (26.7%)	
ASA III-Severe systemic disease	38 (86.4%)	186 (66.9%)	224 (69.6%)	
ASA IV-Severe systemic disease that is a constant threat to life	1 (2.3%)	5 (1.8%)	6 (1.9%)	
Category of flap performed				0.005
Fasciocutaneous	24 (54.5%)	100 (36.0%)	124 (38.5%)	
Muscular/musculocutaneous	6 (13.6%)	22 (7.9%)	28 (8.7%)	
Osseous	11 (25.0%)	148 (53.2%)	159 (49.4%)	
Other	3 (6.8%)	8 (2.9%)	11 (3.4%)	
Specific flap performed				0.004
Anterolateral thigh	15 (34.1%)	63 (22.7%)	78 (24.2%)	
Radial forearm	11 (25.0%)	52 (18.7%)	63 (19.6%)	
Fibula	9 (20.5%)	134 (48.2%)	143 (44.4%)	
Scapula	3 (6.8%)	18 (6.5%)	21 (6.5%)	
Lattissimus	4 (9.1%)	7 (2.5%)	11 (3.4%)	
Other	2 (4.5%)	4 (1.4%)	6 (1.9%)	
Use of heparin for DVT prophylaxis				0.814
Yes	39 (88.6%)	240 (86.3%)	279 (86.6%)	
No	5 (11.4%)	38 (13.7%)	43 (13.4%)	
Use of anticoagulant other than prophylactic heparin dosing				< 0.001
Yes	36 (81.8%)	34 (12.2%)	70 (21.7%)	
No	8 (18.2%)	244 (87.8%)	252 (78.3%)	
Name of other anticoagulant used				
Aspirin	30 (83.3%)	12 (35.3%)	42 (60.0%)	
Coumadin	2 (5.6%)	4 (11.8%)	6 (8.6%)	
Heparin or lovenox therapeutic dosing	2 (4.5%)	14 (5.0%)	16 (5.0%)	
Other	2 (4.5%)	4 (1.4%)	6 (1.0%)	
Diabetes diagnosis				0.178
Yes	10 (22.7%)	40 (14.4%)	50 (15.5%)	
No	34 (77.3%)	238 (85.6%)	272 (84.5%)	
History of radiation				1.000
Yes	23 (53.5%)	146 (52.5%)	169 (52.6%)	
No	20 (46.5%)	132 (47.5%)	152 (47.4%)	

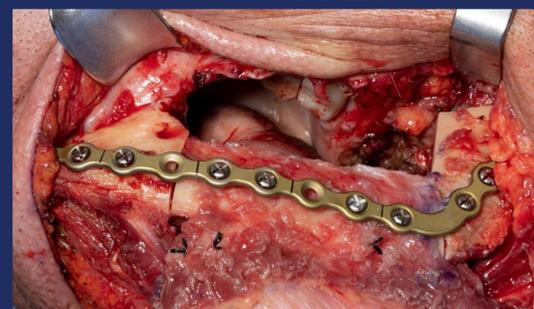


Figure 1: Ketorolac fibula patient

Discussion

- Ketorolac has potent analgesic properties with similar efficacy to opioids that make it an ideal anti-platelet drug to enhance patient recovery. ¹
- Patients in the Ketorolac group were given 30mg or 15mg of Ketorolac every 6 hours for 5 days based on age (age >65 given 15mg, age <65 given 30mg).
- Patients in the non-Ketorolac group were older (mean age 69 vs 62) and had higher ASA classification, otherwise no significant differences in demographics.
- The rate of flap failure within Ketorolac group was 2.5%, comparable to literature rate of 5%.
- There was no association between sex, ethnicity, race, patient age, ASA, category of flap performed, specific flap performed, diabetes and the three outcomes (full flap failure, arterial thrombosis and venous thrombosis) in the Ketorolac group.
- Hematoma was defined as need for return to the operating room for bleeding, with a rate of 9.4% in Ketorolac group and 6.8% in non-Ketorolac group.
- The hematoma incidence in Ketorolac group is higher than previously seen in literature (0-7%)²; however, 23% of Ketorolac hematoma patients were given additional anticoagulation other than DVT prophylaxis. Use of Ketorolac with additional anticoagulation may lead to increased bleeding.
- Ketorolac did not lead to increased rates of acute kidney injury (3.6%) compared to non-Ketorolac group (11.4%).
- This is the largest study to date of Ketorolac usage in head and neck free flaps demonstrating it's efficacy for prevention of microvascular thrombosis.

References

1. Moodie JE, Brown CR, Bisley EJ, Weber HU, Bynum L. The safety and analgesic efficacy of intranasal ketorolac in patients with postoperative pain. *Anesth Analg*. 2008;107(6):2025-2031.
2. Barton BM, Riley CA, Fitzpatrick JC, Hasney CP, Moore BA, McCool ED. Postoperative anticoagulation after free flap reconstruction for head and neck cancer: A systematic review. *The Laryngoscope*. 2018;128(2):412-421.

Tables/Figures



Figure 2: Ulnar flap in Ketorolac patient

Table 2: Complications

	Non-Ketorolac (N=44)	Ketorolac (N=278)	p value
Venous Thrombosis			1.000
Yes	0 (0.0%)	6 (2.2%)	
Venous thrombosis post op day			
Mean (SD)	NA	3.0 (1.8)	
Range	NA	1.0 - 6.0	
Arterial thrombosis			1.000
Yes	0 (0.0%)	4 (1.4%)	
Arterial thrombosis post op day			
Mean (SD)	NA	4.8 (3.0)	
Range	NA	1.0 - 8.0	
Hematoma			0.780
Yes	3 (6.8%)	26 (9.4%)	
Return to OR			0.252
Yes	7 (15.9%)	69 (24.8%)	
Reason for return to the OR			
Fistula	0 (0.0%)	10 (14.5%)	
Hematoma	3 (42.9%)	23 (33.3%)	
Infection	0 (0.0%)	4 (5.8%)	
Arterial thrombosis	0 (0.0%)	2 (2.9%)	
Venous thrombosis	0 (0.0%)	5 (7.2%)	
Multiple reasons	0 (0.0%)	4 (5.8%)	
Other	4 (57.1%)	21 (30.4%)	
Partial flap failure			0.632
Yes	2 (4.5%)	8 (2.9%)	
Full flap failure			0.599
Yes	0 (0.0%)	7 (2.5%)	
Acute kidney injury			0.040
Yes	5 (11.4%)	10 (3.6%)	
Length of hospital stay			0.682
Median	11.5	12.0	

Table 3: Hematoma group anticoagulants

	Non-Ketorolac (N=3)	Ketorolac (N=26)	Total (N=29)
Use of heparin for DVT prophylaxis			
Yes	3 (100.0%)	21 (80.8%)	24 (82.8%)
No	0 (0.0%)	5 (19.2%)	5 (17.2%)
Other anticoagulant used			
Yes	2 (66.7%)	6 (23.1%)	8 (27.6%)
No	1 (33.3%)	20 (76.9%)	21 (72.4%)
Name of other anticoagulant used			
Aspirin	2 (100.0%)	0 (0.0%)	2 (25.0%)
Therapeutic dosing heparin or lovenox	0 (0.0%)	6 (23.1%)	1 (12.5%)