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Authors

David, Abel
Zebolsky, Aaron
Park, Andrea
et al.

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ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Effect of microporous polysaccharide hemospheres on anterolateral thigh free flap donor site complications

Abel P. David MD[1] | Aaron L. Zebolsky MS[1,2] | Andrea M. Park MD[1] | Chase M. Heaton MD[2] | P. Daniel Knott MD[1] | Rahul Seth MD[1]

[1]Division of Facial Plastic and Reconstructive Surgery, Department of Otolaryngology-Head & Neck Surgery, University of California, San Francisco, California, USA

[2]Division of Head and Neck Oncologic Surgery, Department of Otolaryngology-Head & Neck Surgery, University of California, San Francisco, California, USA

Correspondence
Rahul Seth, MD, Division of Facial Plastic and Reconstructive Surgery, Department of Otolaryngology-Head and Neck Surgery, 2233 Post Street, 3rd Floor, San Francisco, CA 94115, USA.
Email: rahul.seth@ucsf.edu

Abstract

Background: Postoperative seroma is the most common donor site complication following anterolateral thigh (ALT) free flap harvest for head and neck reconstruction. The utility of novel microporous polysaccharide hemospheres (MPH) has not been studied as a hemostatic agent in this setting.

Methods: Prospective, single-blind, randomized controlled trial of patients undergoing fasciocutaneous ALT harvest for head and neck reconstruction at a tertiary academic medical center between April 2018 and February 2020. The intervention (MPH) group received 3 g of topical MPH to the ALT donor site prior to closure whereas the control group did not receive application of MPH. Outcomes included total drain output (ml), drain output during postoperative days (POD) 1–3 alone, drain duration (days), and incidence of donor site hematoma, seroma, or infection.

Results: Twenty-nine patients were randomized to the MPH group and 26 to the control group. For MPH and control groups, mean total drain output was 284.7 ± 153.0 ml versus 317.9 ± 177.6 ml ($p = .527$), mean POD 1–3 drain output alone was 169.3 ± 88.8 ml versus 157.9 ± 78.7 ml ($p = .749$), and drain duration was 5.9 ± 1.5 days versus 6.5 ± 1.6 days ($p = .144$), respectively. There was no significant difference in seroma ($p = .733$), hematoma ($p = .492$), or infection ($p = 1.000$). Drain output was not significantly influenced by gender, age, body weight, or smoking habits.

Conclusion: MPH administration to ALT free flap donor sites did not significantly improve drain output, hematoma formation, or seroma formation.

Level of Evidence 2

KEYWORDS

anterolateral thigh free flap, hemostasis, microporous polysaccharide hemospheres, microvascular reconstruction, randomized controlled trial

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1 | INTRODUCTION

The anterolateral thigh (ALT) free flap has become a workhorse for head and neck reconstruction since it was described in 1984.[1] The availability of various tissue types at the donor site allows for fasciocutaneous, myocutaneous, myofascial, and/or adipofascial flap harvesting.[2,3] As a result, the ALT free tissue donor site is highly versatile and permits reconstruction of a wide variety of defects requiring skin coverage, soft tissue volume, internal nasal lining, bone, and cutaneous defects, or even vascularized facial nerve reconstruction.[4–9] Complications are uncommon, but may result in extended hospital stay, additional surgical interventions, and increased cost to the healthcare system.[10] Seroma is the most common donor site complication and may occur in ~5%–6% of cases.[11,12] Unfortunately, this risk persists despite the use of surgical drains and there is a paucity of literature describing reliable interventions to prevent seroma formation.[13]

A variety of hemostatic agents has been developed in attempt to limit hematoma and seroma development. Microporous polysaccharide hemosphere (MPH) technology is designed to absorb the fluid component of blood and concentrate clotting factors, which has resulted in accelerated hemostasis in animal studies[14,15] and reduced rates of seroma formation in a mouse mastectomy model.[16] The use of MPH in head and neck reconstruction or in ALT free flap harvest has not yet been explored.

Hematoma and seroma formation is linked to postoperative surgical drain output. Generally, an output of <50–100 ml over 24 h is accepted as an arbitrary threshold for safe surgical drain removal without increasing the risk of hematoma or seroma.[17] In this study, we performed a prospective randomized controlled trial to determine if the application of MPH during closure of the ALT donor site reduces postoperative drain output as well as seroma or hematoma formation.

2 | METHODS AND MATERIALS

2.1 | Study design

A prospective, single-blinded randomized controlled trial of patients undergoing ALT free flap harvest for the reconstruction of head and neck defects was conducted at a single tertiary academic medical center. The inclusion criteria were patient age ≥ 18 years undergoing ALT free flap reconstruction of a head and neck defect. Patients were excluded if (1) they chose not to participate, (2) the donor site was unable to be closed primarily, (3) they had an underlying clotting or bleeding disorder, or (4) they required additional anticoagulant medications beyond standard deep vein thrombosis prophylaxis. During analysis, patients were also excluded if any primary outcome data was missing. Patients who were enrolled in the study provided written informed consent obtained by a surgery resident, research study coordinator, or attending surgeon during preoperative clinic visits or in the preoperative area. Institutional review board approval was granted by the University of California, San Francisco, CA (IRB Number 15–17004) and the study was registered at clinicaltrials.gov (NCT02477774).

2.2 | Study enrollment, randomization, and outcomes

Between April 2018 and February 2020, 62 patients satisfied inclusion and exclusion criteria, provided informed consent, and were enrolled in the study. They were randomized into the MPH versus control (no-MPH) study arms using the iOS mobile application "Randomizer for Clinical Trial" (Medsharing).[18] Randomization occurred after the free flap was harvested from the thigh and after standard hemostasis was achieved. The surgeon was blinded until this point, then contacted the research study coordinator who informed them of the patient randomization assignment.

The primary outcome for this study was total ALT donor site drain output, drain output for postoperative days (POD) 1–3, and days until drain removal. Secondary outcomes included postoperative complications such as seroma-requiring drainage in the hospital or clinic, hematoma requiring operating room take back or bedside drainage, and donor site infections requiring prescription antibiotics. All patients were followed for a full 6 months to assess for outcomes.

2.3 | Surgical technique and drain management

All patients received peri-operative antibiotic prophylaxis prior to incision. The ALT flaps were raised by one of four fellowship-trained microvascular surgeons assisted by a microvascular surgery fellow. Hemostasis was achieved using electrocautery, ultrasonic shears, and/or suture/surgical clip ligation. The intervention group received a 3 g dose of MPH (Arista AH Absorbable Hemostat, Bard Davol, Warwick, RI) topically to the wound bed just prior to closure of the ALT donor site (Figure 1), which has an approximate institutional cost of $150–200. The MPH was applied in a light layer that covered most of the surfaces of the wound soft tissues, and care was taken to avoid depositing MPH directly onto the drain. For the control group, no MPH was applied.

All thighs underwent similar closure technique. The donor site was closed over a closed suction drain (a single 10 French flat drain) placed between the vastus lateralis and the rectus femoris and beneath the skin flaps. The drain exited the wound via a separate stab incision based inferior and lateral to the harvest site. The deep dermis was approximated with 3-0 Vicryl, and skin was closed with 5-0 fast absorbing gut sutures. The incision was dressed with a non-adherent gauze that was removed on the second postoperative day.

Drains were managed by bedside nurses. Every 4 h, the drains were stripped, measured, and recorded into the patient's medical record. Patients were allowed and encouraged to ambulate on the

first postoperative day. The donor site was examined at least twice daily by the inpatient service to monitor for signs or symptoms of postoperative donor site complications or drain malfunction. Drains were removed once 24-h output dropped below 60 ml. Additional care consisted of twice-daily application of petroleum-based ointment to the incision.

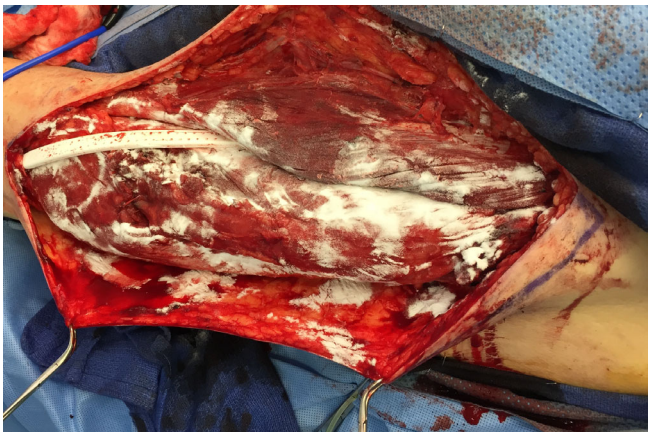

FIGURE 1 Topical application of 3 g of MPH to the ALT donor site wound bed. The knee is on the left side of the image and the hip is on the right side

2.4 | Statistical analysis

A sample size calculation was performed before initiating the study. To detect a 20% reduction in drain output with a significance level of 0.05 and power of 0.8, a sample size of 25 patients in each group was required, assuming mean output of 500 ml and standard deviation of 125 ml based on preliminary data.[19]

Descriptive statistics were used to report continuous and categorical variables. Student's *t*-test, Mann–Whitney U, chi-square, and Fisher exact tests were used for analysis as appropriate. Effect size calculations were performed to compare the impact of key variables on the total drain output. Some of these variables were dichotomized including age (≥65 years vs. <65 years), BMI (≥30 kg/m^2 vs. <30 kg/m^2), and smoking status (current or former vs. never smokers). Effect size was calculated using the Hedges' method (g) due to the difference in sample sizes. A negligible effect size was defined as <0.20; a

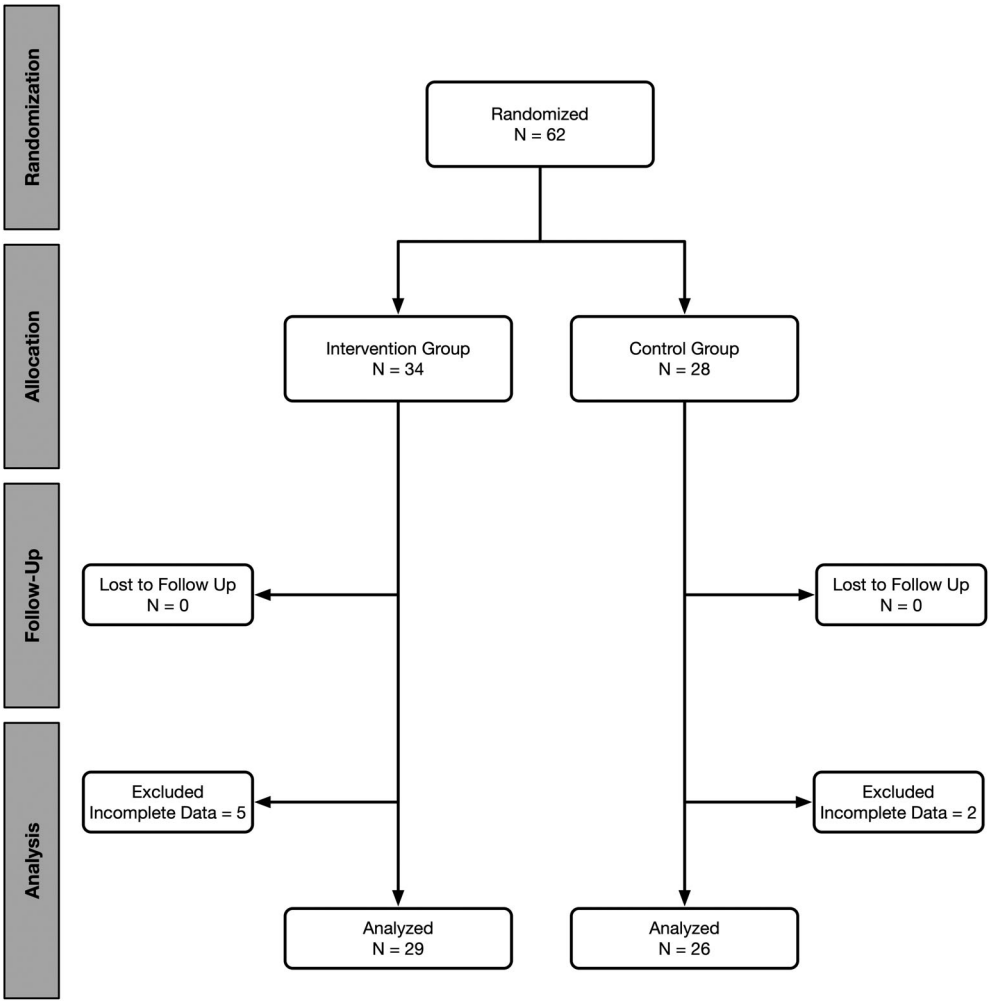

FIGURE 2 Study diagram of patients who were enrolled in the clinical trial

TABLE 1 Baseline characteristics of patients undergoing ALT free flap reconstruction stratified by treatment group

	Overall ($N = 55$)	MPH Group ($N = 29$)	Control Group ($N = 26$)	*p*-value
Male gender, *n* (%)	41 (74.5)	19 (65.5)	22 (84.6)	1.000
Age (years)				
Mean ± SD (range)	64.7 ± 12.7 (20–88)	65.0 ± 12.1 (32–83)	64.4 ± 13.6 (20–88)	.867
BMI (kg/m^2)				
Mean ± SD (range)	24.2 ± 3.9 (17.3–34.9)	24.3 ± 4.2 (17.3–34.9)	24.0 ± 3.6 (18.9–32.3)	.828
Weight (kg)				
Mean ± SD (range)	70.4 ± 13.4 (48.1–105)	70.8 ± 14.4 (50–105)	70.0 ± 13.4 (48.1–101.5)	.811
Length of stay (days)				
Mean ± SD (range)	7.7 ± 4.5 (4–33)	7 ± 2.6 (4–17)	8.5 ± 5.9 (4–33)	.305
Smoking history				
Current, *n* (%)	9 (16.4)	5 (17.2)	4 (15.4)	.812
Former, *n* (%)	25 (45.5)	12 (41.4)	13 (50.0)	
Never, *n* (%)	21 (38.2)	12 (41.4)	9 (34.6)	
Fascia lata harvested	23 (41.8)	15 (51.7)	8 (30.7)	.194
Indication for reconstruction				
Tumor	46 (83.6)	24 (82.7)	22 (84.6)	.530
Osteonecrosis	5 (9.1)	2 (6.9)	3 (11.5)	
Infection	1 (1.8)	1 (3.4)	0 (0.0)	
Microstomia	1 (1.8)	0 (0.0)	1 (3.8)	
Frontal sinus obliteration	1 (1.8)	1 (3.4)	0 (0.0)	
Fistula	1 (1.8)	1 (3.4)	0 (0.0)	
Recipient sites				
Oral cavity	12 (21.8)	5 (17.2)	7 (26.9)	.675
Parotid	12 (21.8)	7 (24.1)	5 (19.2)	
Scalp	9 (16.4)	5 (17.2)	4 (15.4)	
Larynx	8 (14.5)	4 (6.9)	4 (15.4)	
Maxilla	6 (10.9)	2 (6.9)	4 (15.4)	
Oropharynx	3 (5.5)	2 (6.9)	1 (3.8)	
Lateral temporal bone	2 (3.6)	2 (6.9)	0 (0)	
Frontal bone/skull base	2 (3.6)	2 (6.9)	0 (0)	
Neck	1 (1.8)	0 (0)	1 (3.8)	

small effect size was 0.20–0.49; a moderate effect size was 0.50–0.79; and large effect size at least 0.80. All analyses were performed using the R statistical programming language (version 3.6.2, Vienna, Austria).[20] Sample size and power calculations were performed using the "pwr" package[21] and effect sizes were calculated using the "effsize" package.[22]

3 | RESULTS

3.1 | Study population

Sixty-two patients were enrolled in the study and randomized: 34 patients to the intervention group and 28 to the control group. Seven patients were discharged with surgical drains still in place and drain output data were not recorded; therefore, these patients were excluded. All remaining patients were followed for at least 6 months, there were no patients lost to follow up. In total, 55 were analyzed: 29 in the intervention (MPH) group and 26 in the control (no-MPH) group (Figure 2).

After randomization, there were no statistically significant differences in baseline patient characteristics (Table 1). Overall, the study population consisted largely of men (74.5%) with a mean age of 64.7 ± 12.7. Most were former (45.5%) or current (16.4%) smokers with a mean BMI of 24.2 ± 3.9. The most common indication for reconstruction was ablation of a head and neck tumor (83.6%), but other indications included osteoradionecrosis (9.1%), infection (1.8%), microstomia (1.8%), fistula (1.8%), and a

TABLE 2 Outcomes of ALT free flap reconstruction stratified by treatment group

	Overall ($N = 55$)	MPH group ($N = 29$)	Control group ($N = 26$)	p-value
Total drain output (ml), Mean ± SD (range)	300.4 ± 164.4 (53–685)	284.7 ± 153.0 (65–585)	317.9 ± 177.6 (53–685)	.527
POD1-3 drain output (ml), Mean ± SD (range)	163.9 ± 83.6 (23–366)	169.3 ± 88.8 (50–366)	157.9 ± 78.7 (23–290)	.749
Drain duration (days), Mean ± SD (range)	6.2 ± 1.6 (4–10)	5.9 ± 1.5 (4–10)	6.5 ± 1.6 (4–10)	.144
Complications				
Seroma, *n* (%)	10 (18.2)	6 (20.6)	4 (15.4)	.733
Hematoma, *n* (%)	2 (3.6)	2 (6.9)	0 (0)	.492
Donor site infection, *n* (%)	4 (7.3)	2 (6.9)	2 (7.7)	1.000

TABLE 3 Effect size of various predictors including gender, age, body mass index, smoking status, and MPH use on total drain output after ALT free flap harvest

Variable	Patients, *n*	Total drain output, Mean ± SD (ml)	Difference in mean total drain output (Δ ml)	Effect size, hedges g (95% CI)
Gender				
Male	41	293.6 ± 164.7	26.6	0.158 (−0.454 to 0.771)
Female	14	320.2 ± 167.9		Negligible
Age				
<65 years	28	279.3 ± 146.0	42.9	0.257 (−0.278 to 0.793)
≥65 years	27	322.2 ± 181.7		Small
BMI				
<30 kg/m^2	50	302.2 ± 167.4	20.1	0.120 (−0.808 to 1.047)
≥30 kg/m^2	5	282.1 ± 145.0		Negligible
Smoking status				
Never	21	300.6 ± 173.9	0.4	−0.002 (−0.551 to 0.546)
Current or former	34	300.2 ± 160.9		Negligible
TFL not harvested	32	313.2 ± 184.2	30.7	0.183 (−0.358 to 0.725)
TFL harvested	23	282.5 ± 133.8		Negligible
MPH				
No MPH	26	317.9 ± 177.6	33.2	0.198 (−0.337 to 0.733)
MPH used	29	284.7 ± 153.0		Negligible

Note: A negligible effect size was defined as <0.20; a small effect size was 0.20–0.49; a moderate effect size was 0.50–0.79; and large effect size at least 0.80.

postfrontal sinus obliteration defect (1.8%). The top three recipient reconstructive sites include the oral cavity (26.9%), parotid (9.2%, and the scalp (15.4%%). In 23 (41.8%) participants in the study, fascia lata was harvested for reconstruction and there was no significant difference in the proportion of those with fascia lata harvest between the MPH and the control group ($p = .194$).

3.2 | Primary outcomes

The mean drain output was 284.7 ± 153.0 ml for the MPH group compared to 317.9 ± 177.6 ml for the control group ($p = .527$). During POD 1–3 alone, the mean drain output was 169.3 ± 88.8 for the MPH group compared to 157.9 ± 78.7 for the control group ($p = .749$). Surgical drains were removed after a mean of 5.9 ± 1.5 days in the MPH group compared to 6.5 ± 1.6 days in the control group ($p = .144$).

3.3 | Secondary outcomes

Within 6 months postoperatively, six patients (20.6%) in the MPH group developed a seroma compared to four (15.4%) in the control group ($p = .733$). These were initially diagnosed and drained an average of 24.8 ± 10.2 days after surgery (range 12–49 days). Hematomas developed in two patients (6.9%) in the MPH group and there were none in the control group, and this difference was not statistically significant ($p = .492$). There was also no statistically significant difference

in donor site infections between the MPH (7.3%) and control (7.7%) groups ($p = 1.000$). The primary and secondary outcomes are summarized in Table 2.

3.4 | Effect size comparison

Table 3 depicts effect sizes for clinically important baseline patient characteristics. Gender, BMI, smoking status, fascia lata harvest, and use of MPH all had negligible effect sizes in regard to drain output. Age had a small effect size ($g = 0.257$, 95% CI −0.278 to 0.793) with regard to drain output; there was an absolute difference of 42.9 ml higher mean drain output among older patients.

4 | DISCUSSION

This study represents the first randomized controlled trial evaluating topical MPH administered to ALT donor site wound beds after free flap harvest for head and neck reconstruction. Despite promising animal studies[14,15] and a recent retrospective study of MPH use in ALT donor sites where the use of MPH was associated with lower rates of seroma formation and were associated with earlier drain removal,[19] we did not detect a significant difference in postoperative drain output, seroma development, or hematoma development with the use of MPH. This is consistent with other randomized controlled trials that found no significant improvement in postoperative surgical site drainage with MPH after mastectomy or total thyroidectomy.[23,24] On the other hand, in an unpublished retrospective cohort of more than 100 patients performed at our institution prior to initiating this trial, we found that MPH use was associated with decreased rates of ALT donor site seroma formation and earlier surgical drain removal. MPH has shown some benefit in certain surgical procedures such as improved hemostasis following brain tumor resection in a case series of 33 patients.[25] It has also been demonstrated to reduce hemostasis time, rates of chest tube placement, and need for blood transfusion in a retrospective cohort study of patients undergoing cardiothoracic surgery.[26]

As previously mentioned, two randomized controlled trials have not found significant benefit in the use of MPH.[23,24] In fact, bandages with MPH applied to skin defects from Mohs surgery actually increased bleeding through the bandage and did not significantly affect bleeding after bandage removal.[27] MPH may similarly worsen bleeding after total knee arthroplasty[28] and in one animal study, it resulted in an increased risk of distal tip necrosis of local skin flaps.[29] In light of this, MPH should be used cautiously in areas undergoing locoregional reconstruction or within free flap recipients sites. Overall, MPH only appears useful for a select group of surgical procedures and in our study was not shown to have a significant or consistent benefit in ALT free flap donor site morbidity.

Several other materials have been developed to reduce the risk of postoperative hematoma and seroma formation. Fibrin sealant was the first product approved in the USA as an all-in-one hemostat, sealant, and adhesive.[30] A large systematic review and meta-analysis demonstrated that fibrin sealant significantly decreases drain output in head and neck surgery, specifically after thyroidectomy, rhytidectomy, and neck dissection.[31] Flowable thrombin-based hemostatic agents may also be useful in head and neck surgery.[32] Compared to MPH, flowable thrombin-gelatin matrix demonstrated significantly improved hemostasis in porcine models.[33] Future work is needed to understand if these results can be translated to human patients with clinically significant outcomes through the execution of well-designed randomized control trials.

Reliable interventions for preventing seroma and hematoma development after free flap harvest remain elusive. This makes the identification of risk factors critical for reconstructive surgeons. Increased body weight and smoking may be associated with the risk of seroma development among breast surgery patients.[24,34,35] Higher BMI and smoking correlate with impaired wound healing after ALT harvest.[36] Although seroma is a relatively common complication, there is a paucity of literature examining the impact of these risk factors on ALT donor site hematoma or seroma development. We did not find any associations between smoking and BMI with drain output in this study, but larger studies with greater power are warranted before dismissing these potential predisposing risks. There was a surprisingly high rate of seromas in this study population compared to rates of about 5%–6% in the literature.[11,12] As the seroma rate was similar between the groups, and found among surgeons who had previously reported lower seroma rates, we hypothesize that the particular attention that was focused in this population revealed seromas that otherwise might have otherwise escaped clinical detection.

The key limitation in this study is our sample size and power. Although only 25 patients per group were required based on our pre-study sample size calculation, patients in this study demonstrated unexpectedly high variability in postoperative drain outputs, resulting in larger standard deviations. Due to this variation, a post hoc power analysis using the mean total drain output and standard deviation in this study revealed that more than 400 patients would be required in each group to detect a 20% improvement in drain output with a significance level < 0.05 and power > 0.8. A prospective multi-institution randomized study design would likely be necessary to confirm the utility of MPH in reducing donor site complications after ALT free flap harvest. Additionally, size and volume of the harvested free flaps were not included in the analysis and this may influence drainage amount and potential seroma formation. Future studies should consider recording the flap dimensions, measuring volume of water displacement, or weighing the flap intraoperatively just after harvest.

5 | CONCLUSION

In this randomized controlled trial, we found no significant, clinically relevant benefit of topical MPH applied to ALT free flap donor sites. Volume of postoperative drain output was similar with or without MPH, as were rates of donor site hematoma and seroma. Drain output was not significantly influenced by gender, age, BMI, or smoking

habits. A smaller than expected MPH effect size and higher than expected drain output variability limited the statistical power of this study as designed; however, these results suggest no drastic improvements with MPH. Larger scale studies are warranted to detect more subtle differences in outcomes and identify other interventions for reducing ALT donor site complications and seroma formation.

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CONFLICT OF INTEREST

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

ORCID

Abel P. David https://orcid.org/0000-0003-1687-8240
Aaron L. Zebolsky https://orcid.org/0000-0003-3632-0498
P. Daniel Knott https://orcid.org/0000-0002-8986-5961
Rahul Seth https://orcid.org/0000-0003-2775-530X

REFERENCES

1. Song YG, Chen GZ, Song YL. The free thigh flap: a new free flap concept based on the septocutaneous artery. *Br J Plast Surg*. 1984;37:149-159.
2. de Virgilio A, Iocca O, Di Maio P, et al. Head and neck soft tissue reconstruction with anterolateral thigh flaps with various components: development of an algorithm for flap selection in different clinical scenarios. *Microsurgery*. 2019;39:590-597.
3. Park CW, Miles BA. The expanding role of the anterolateral thigh free flap in head and neck reconstruction. *Curr Opin Otolaryngol Head Neck Surg*. 2011;19:263-268.
4. Brody RM, Pandey NC, Bur AM, et al. Anterior lateral thigh osteomyocutaneous free flap reconstruction in the head and neck: the anterolateral thigh osteomyocutaneous femur bone flap. *Head Neck*. 2016;38:1788-1793.
5. Naunheim M, Seth R, Knott PD. Sternocleidomastoid contour restoration: an added benefit of the anterolateral thigh free flap during facial reconstruction. *Am J Otolaryngol*. 2016;37:139-143.
6. Seth R, Revenaugh PC, Scharpf J, Shipchandler TZ, Fritz MA. Free anterolateral thigh fascia lata flap for complex nasal lining defects. *JAMA Facial Plast Surg*. 2013;15:21-28.
7. Ciolek PJ, Prendes BL, Fritz MA. Comprehensive approach to reestablishing form and function after radical parotidectomy. *Am J Otolaryngol*. 2018;39:542-547.
8. Graboyes EM, Hornig JD. Evolution of the anterolateral thigh free flap. *Curr Opin Otolaryngol Head Neck Surg*. 2017;25:416-421.
9. Strohl MP, Junn JC, House AE, et al. Long-term stability of vascularized Adipofascial flaps in facial reconstruction. *Facial Plast Surg Aesthet Med*. 2020;22:262-267.
10. Han M, Ochoa E, Zhu B, et al. Risk factors for and cost implications of free flap take-backs: a single institution review. *Laryngoscope*. 2021;131:E1821-E1829.
11. Hanasono MM, Skoracki RJ, Yu P. A prospective study of donor-site morbidity after anterolateral thigh fasciocutaneous and myocutaneous free flap harvest in 220 patients. *Plast Reconstr Surg*. 2010;125:209-214.
12. Knott PD, Seth R, Waters HH, et al. Short-term donor site morbidity: a comparison of the anterolateral thigh and radial forearm fasciocutaneous free flaps. *Head Neck*. 2016;38(Suppl 1):E945-E948.
13. Srivastava V, Basu S, Shukla VK. Seroma formation after breast cancer surgery: what we have learned in the last two decades. *J Breast Cancer*. 2012;15:373-380.
14. Ersoy G, Kaynak MF, Yilmaz O, Rodoplu U, Maltepe F, Gokmen N. Hemostatic effects of microporous polysaccharide hemosphere in a rat model with severe femoral artery bleeding. *Adv Ther*. 2007;24:485-492.
15. Murat FJ, Le CQ, Ereth MH, Piedra MP, Dong Y, Gettman MT. Evaluation of microporous polysaccharide hemospheres for parenchymal hemostasis during laparoscopic partial nephrectomy in the porcine model. *JSLS*. 2006;10:302-306.
16. Egeli T, Sevinc AI, Bora S, et al. Microporous polysaccharide hemospheres and seroma formation after mastectomy and axillary dissection in rats. *Balkan Med J*. 2012;29:179-183.
17. Tamplen ML, Tamplen J, Shuman E, et al. Comparison of output volume thresholds for drain removal after selective lateral neck dissection: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2017;143:1195-1199.
18. Medsharing. Randomizer for Clinical Trial [iOS Mobile App]; 2020. https://itunes.apple.com.
19. Benjamin T, David AP, Zebolsky AL, et al. Utility of microporous polysaccharide hemosphere on anterolateral thigh free flap donor site complications. *Facial Plast Surg Aesthet Med*. 2021. doi: 10.1089/fpsam.2021.0141
20. R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing; 2019.
21. Champely S. pwr: Basic Functions for Power Analysis. 2020. https://github.com/heliosdrm/pwr.
22. Torchiano M. effsize: Efficient Effect Size Computation. 2020. https://CRAN.R-project.org/package=effsize.
23. Kunduz E, Aysan E, Idiz UO, et al. Evaluation of local hemostatic effect of microporous polysaccharide hemospheres products in thyroid surgery: a prospective randomized controlled study. *Turk J Surg*. 2019;35:49-53.
24. Suarez-Kelly LP, Pasley WH, Clayton EJ, Povoski SP, Carson WE, Rudolph R. Effect of topical microporous polysaccharide hemospheres on the duration and amount of fluid drainage following mastectomy: a prospective randomized clinical trial. *BMC Cancer*. 2019;19:99.
25. Tschan CA, Nie M, Schwandt E, Oertel J. Safety and efficacy of microporous polysaccharide hemospheres in neurosurgery. *Neurosurgery*. 2011;69:ons49-ons63.
26. Bruckner BA, Blau LN, Rodriguez L, et al. Microporous polysaccharide hemosphere absorbable hemostat use in cardiothoracic surgical procedures. *J Cardiothorac Surg*. 2014;9:134.
27. Tan SR, Tope WD. Effectiveness of microporous polysaccharide hemospheres for achieving hemostasis in mohs micrographic surgery. *Dermatol Surg*. 2004;30:908-914.
28. Gleason S, Mehl D, Payne W, Parry S, Stein AB. Microporous polysaccharide hemosphere efficacy and safety in primary total knee arthroplasty. *J Orthop*. 2019;16:19-24.
29. Offodile AC II, Chen B, Aherrera AS, Guo L. Microporous polysaccharide Hemospheres potentiate ischemia-induced skin flap necrosis in a murine model. *Plast Reconstr Surg*. 2017;139:59e-66e.
30. Spotnitz WD. Fibrin sealant: the only approved hemostat, sealant, and adhesive-a laboratory and clinical perspective. *ISRN Surg*. 2014;2014:203943.
31. Bajwa MS, Tudur-Smith C, Shaw RJ, Schache AG. Fibrin sealants in soft tissue surgery of the head and neck: a systematic review and

meta-analysis of randomised controlled trials. *Clin Otolaryngol*. 2017; 42:1141-1152.
32. Partsafas AW, Bascom DA, Jorgensen SA, Wax MK. Effects of Tisseel and FloSeal on primary ischemic time in a rat fasciocutaneous free flap model. *Laryngoscope*. 2004;114:301-304.
33. Lewis KM, Atlee H, Mannone A, Lin L, Goppelt A. Efficacy of hemostatic matrix and microporous polysaccharide hemospheres. *J Surg Res*. 2015;193:825-830.
34. Kuroi K, Shimozuma K, Taguchi T, et al. Evidence-based risk factors for seroma formation in breast surgery. *Jpn J Clin Oncol*. 2006;36: 197-206.
35. Sforza M, Husein R, Atkinson C, Zaccheddu R. Unraveling factors influencing early seroma formation in breast augmentation surgery. *Aesthet Surg J*. 2017;37:301-307.
36. Abe Y, Kashiwagi K, Ishida S, Mineda K, Yamashita Y, Hashimoto I. Risk factors for delayed healing at the free anterolateral thigh flap donor site. *Arch Plast Surg*. 2018;45:51-57.

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