AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

OTO Open
2020, 4(4) 1–7

DOI: 10.1177/2473974X20981021
http://oto-open.org
SAGE

Outcomes Associated With Fibrin Sealant Use in Lateral Neck Dissections

Luke Stanisce, MD[1], Michael Lai[2], Nadir Ahmad, MD[1,2], Thomas C. Spalla, MD[1,2], Lisa M. Reid, MD[1,3], John P. Gaughan, PhD, MS, MBA[4], and Yekaterina Koshkareva, MD[1,2]

Abstract

Objective. To determine whether the use of fibrin sealant tissue adhesives during lateral neck dissections is associated with a change in postoperative outcomes.

Study Design. Retrospective cohort.

Setting. Institutionally affiliated tertiary care center.

Methods. Various demographic, disease, and surgical data were collected for patients who underwent lateral neck dissections. Univariate regression analysis was performed with the following outcomes: total drain output and duration of drain placement, as well as incidence of postoperative infection, hematoma, seroma, chyle leak, and salivary leak.

Results. A total of 133 patients underwent lateral neck dissections. Fibrin sealant was used in 35% of cases (n = 46). Its use was not associated with differences in total drain output (P = .77) or the number of days that the drains were in place (P = .83). On secondary analysis, the use of fibrin sealant was not associated with a difference in postoperative incidence of hematoma (P = .65), seroma (P = .68), chyle leak (P = .42), or salivary leak (P = .73). These results were consistent when stratified by the presence of intraoperative complications. Its use accompanied an average cost of $674 per case.

Conclusions. Fibrin sealant use during lateral neck dissections was not associated with a reduction in drain output or days that the drains remained in situ. Although the current study was limited by sample size, fibrin sealant use was not associated with a decreased risk of postoperative adverse events. The evidence in this report suggests that the routine use of these products adds cost without clear benefit.

Keywords

fibrin sealant, lateral neck dissection, surgical drains, adverse outcomes

Received September 20, 2020; accepted November 11, 2020.

Cervical lymphadenectomy, or neck dissection, is a frequently performed procedure for the management of head and neck cancer. Although it is generally considered safe, the number of intra- and postoperative complications may contribute to patient morbidity, including hematoma, seroma, infection, or chylous fistula. The placement of closed drainage systems within the operative field is regularly performed to provide an egress of fluid out of the surgical bed and promote wound healing. However, drain placement can significantly contribute to patient discomfort, serve as a potential route or nidus for wound infection, and extend postoperative hospital stays.[1,2]

Fibrin sealants, a class of biocompatible and biodegradable surgical tissue adhesives, have been shown to help achieve hemostasis and reduce surgical site output in a variety of specialties ranging from orthopedics to vascular surgery.[2-5] To date, studies defining their role in head and neck surgery have been limited. In a recent meta-analysis, Bawja et al found that fibrin sealant use may reduce drain output in certain procedures, such as rhytidectomy; however, definite conclusions are restricted by the considerable heterogeneity of existing studies.[6] These limitations hold particularly true in the context of lateral neck dissections. The current use of these products during these procedures is largely based on personal experience, institutional practices, and extrapolated evidence.

[1]Division of Otolaryngology–Head and Neck Surgery, Cooper University Hospital, Camden, New Jersey, USA
[2]Cooper Medical School, Rowan University, Camden, New Jersey, USA
[3]Division of Surgical Oncology, Department of Surgery, Cooper University Hospital, Camden, New Jersey, USA
[4]Cooper Research Institute, Cooper University Hospital, Camden, New Jersey, USA

This article was presented at the 2020 COSM Virtual Poster Session via the Triological Society 123rd Annual Meeting; May 15–June 15, 2020.

Corresponding Author:
Luke Stanisce, MD, Division of Otolaryngology–Head and Neck Surgery, Cooper University Hospital, Three Cooper Plaza, Suite 411, Camden NJ 08103, USA.
Email: Stanisce-Luke@CooperHealth.edu

The aim of this analysis was to determine if the routine use of fibrin sealant during lateral neck dissections was associated with a difference in postoperative outcomes. Concurrently, the financial cost related to its use was estimated by appraising accompanying operative charges. The discussion herein provides clinicians with evidence-based data on the use of sealant in lateral neck dissections.

Methods

We retrospectively reviewed the electronic medical records of all adult patients at our tertiary care institution who underwent lateral neck dissections from January 2013 to October 2018. Approval from the Cooper Health System Institutional Review Board (18-159EX) was obtained prior to the study. The study cohort was identified through *CPT* codes (*Current Procedural Terminology*) for all variants of lateral neck dissections. Inclusion criteria comprised adult patients who underwent multilevel neck dissections with the placement of closed drainage systems in the lateral neck surgical beds. Patients were included who underwent concurrent extirpative procedures to address malignancies (mucosal [oral cavity, oropharyngeal, laryngeal], thyroid, parotid, and cutaneous), as well as patients whose extirpative procedures entailed communication with the neck. Operative notes, in-hospital progress notes, and outpatient clinic notes were reviewed. The following exclusion criteria were selected: age <18 years, single-level cervical lymph node dissection, dissections that involved level VII, lack of detailed information on drain output, and patients who were discharged on the same day of surgery without prompt outpatient follow-up information.

The following information was retrieved from the electronic medical records: patient age, sex, preprocedure diagnosis, history of neck surgery, history of radiation therapy to the neck, history of chemotherapy, date of surgery, procedures performed, surgeon performing the procedure, use of preoperative antibiotics, preoperative clinical cancer staging (including nodal involvement), postoperative pathologic cancer staging, pathologic nodal involvement, levels and laterality of neck dissection, use of fibrin sealant, use of additional hemostatic agents (Surgicel, Floseal), intraoperative complications, free flap reconstruction (dichotomous), number and type of drains placed, total drain output at the time of removal, duration of drain placement, incidence of postoperative complication (infection, hematoma, seroma, salivary leak, and chyle leak [dichotomous]), and complications unrelated to the procedure prolonging hospital stay. The Tisseel prefilled PRIMA syringe application system (Baxter International Inc) was the only fibrin sealant product used, and its application complied with manufacturer instructions.

The primary endpoints for analysis were the duration of drain placement (days; also referred to as *drain days*) and total drain output (milliliters) at the time of removal. Secondary endpoints were the incidence of postoperative infection, hematoma, seroma, salivary leak, and chyle leak. Descriptive statistics were calculated for the study cohort.

Table 1. Patient Demographic, Disease, and Treatment Characteristics.[a]

	Total (N = 133)	Nonsealant (n = 87)	Fibrin sealant (n = 46)
Mean age, y	54	55	52
Male sex	63 (47)	43 (49)	20 (43)
Primary diagnosis			
Mucosal	79 (60)	58 (67)	21 (46)
Thyroid	43 (32)	19 (22)	24 (52)
Parotid	7 (5)	6 (7)	1 (2)
Cutaneous	4 (3)	4 (4)	0 (0)
T stage			
T1	22 (17)	13 (15)	9 (20)
T2	29 (22)	18 (21)	11 (24)
T3	52 (39)	35 (40)	17 (36)
T4	30 (22)	21 (24)	9 (20)
N stage			
N0	37 (28)	25 (29)	12 (26)
N1	65 (49)	42 (48)	23 (50)
N2	26 (19)	17 (20)	9 (20)
N3	5 (4)	3 (3)	2 (4)
Salvage	42 (32)	30 (34)	12 (26)
Previous			
Radiation	24 (18)	15 (17)	9 (20)
Surgery	15 (11)	9 (10)	6 (13)
Reconstruction	34 (26)	26 (30)	8 (17)
Bilateral	41 (31)	33 (38)	8 (17)
Unilateral, left	48 (36)	34 (39)	14 (30)
Levels dissected			
I	48 (36)	33 (38)	15 (33)
II	126 (94)	85 (98)	41 (89)
III	124 (93)	84 (96)	40 (87)
IV	103 (77)	68 (78)	35 (76)
V	28 (21)	17 (19)	11 (24)
VI	25 (19)	12 (14)	13 (28)

[a]Values are presented as No. (%) unless noted otherwise.

The association between each factor and outcome of interest (length of drain placement, total drain output, infection, hematoma, seroma, chyle leak, salivary leak) was evaluated with univariate logistic regression analysis. The difference in means were calculated for continuous outcomes, and odds ratio (OR) estimates were calculated for dichotomous outcomes. In addition, 95% CIs were calculated with Wald chi-square testing, and $P < .05$ was considered statistically significant. Multivariate analysis was unable to be conducted due to the low incidence of outcomes. All statistical analyses were conducted with SPSS version 26 (IBM Corp).

Results

A total of 133 patients undergoing lateral neck dissections were included in the final study cohort. Patient demographics, surgery, and tumor characteristics are summarized in **Table 1**. Mucosal malignancies were the most common primary diagnosis (n = 79), followed by thyroid (n = 43),

parotid (n = 7), and cutaneous (n = 4) malignancies. Nearly 30% (n = 39) of cases were composed of cervical lymphadenectomy alone. Concurrent neck dissections were performed with ablative procedures in the oral cavity (n = 32), thyroid bed (n = 26), laryngeal complex (n = 16), oropharynx (n = 14), and parotid bed (n = 6). Ablative defects that resulted in direct communication between the primary cavity and the neck were noted in almost 20% (n = 26) of the operative reports.

Neck dissections were unilateral in 92 cases (69%; left, n = 48; right, n = 44) and bilateral in 41 cases (31%). All procedures entailed multiple-level dissections, and level II was most commonly included (n = 126). Per the American Head and Neck Society classification, 42 procedures (32%) were considered salvage neck dissections: 24 patients underwent primary chemoradiation; 15 had previous surgery; and 3 received chemotherapy.[7] Every patient received preoperative antibiotic prophylaxis. Free flap reconstructive efforts for closure of the primary defect were entailed in 34 cases (26%). Intraoperative complications were noted in 8 (6%) procedures: 1 episode of bleeding that required transfusion and vessel suture repair, 1 unplanned sacrifice of cranial nerve XII, and 6 chyle leaks. Fibrin sealant was used for all 6 intraoperative chyle leaks. No sealant or hemostatic agents were used in the case that experienced hemorrhage.

Fibrin sealant was used in 46 procedures (35%). The indications for fibrin sealant use were individual surgeon preference (n = 40) and the presence of intraoperative chyle leak (n = 6). All surgeons in the group used fibrin sealant. A mean 1.5 cervical drains were placed at the conclusion of the case (median, 1; range, 1-4). The mean total drain output at the time of removal was 278 mL (median, 154 mL; range, 0-4085 mL). Drains were in place for a mean 6.5 days (median, 5 days; range, 1-33 days).

Overall, postoperative complications were noted in 28 cases (21%): chyle leak (n = 8), salivary leak (n = 7), seroma (n = 4), endometabolic abnormalities (n = 4), nonfatal cardiac arrhythmias (n = 3), and hematoma (n = 2). Zero surgical site infections were noted in the study cohort. Among these complications, only 21 (16%) were direct sequelae of the neck dissection. Of the 6 patients who experienced intraoperative chyle leaks treated with Tisseel, 4 (66%) had persistent postoperative leaks. All 7 salivary leaks occurred in procedures that entailed communication between the primary defect cavity and the lateral cervical bed. Neither of the postoperative hematomas experienced intraoperative complications or bleeding.

On univariate regression analysis, the use of fibrin sealant was not associated with a difference in the number of days that the drains were in place, with a calculated mean reduction of 0.21 days (95% CI, –2.24 to 1.81; $P = .83$). Similarly, fibrin sealant use was not associated with a mean reduction in total drain output (mean difference [MD], –24.8 mL; 95% CI, –143.02 to 192.57; $P = .77$). Bilateral neck dissections were associated with increased drain output (MD, 257.1 mL; 95% CI, 89.82-424.4; $P = .003$) and length of drain placement (MD, 5.68 days; 95% CI, 3.82-7.53; $P < .001$). Although the type of primary malignancy was not associated with drain output or length of drain placement, intraoperative communication between the primary defect and lateral neck bed was associated with increased output (MD, 448.2 mL; 95% CI, 64.12-783.24; $P = .004$) and drain days (MD, 2.87; 95% CI, 1.18-6.71; $P = .002$). Free flap reconstruction after neck dissection, previous neck surgery, and stage N2c disease were all associated with longer drain days ($P < .001$, $P = .003$, and $P = .009$, respectively) but not significantly associated with increased total output. With each incremental increase in the number of levels involved in the procedure, the mean length of drain placement increased by nearly 1 half-day ($P = .01$). The incidence of postoperative complications was significantly associated with increased drain output ($P < .001$) and drain days ($P < .001$). The use of adjunct hemostatic agents (Floseal and/or Surgicel), whether alone, together, or in combination with Tisseel, was not significantly associated with decreased total output or time of drain placement. The aforementioned relationships were observed when stratified by the presence of intraoperative complications. The comprehensive univariate regression analyses for the primary outcomes are detailed in **Table 2**.

On secondary analysis, the use of fibrin sealant was not associated with a significantly decreased risk for any postoperative complications: chyle leak (OR, 0.63; $P = .43$), salivary leak (OR, 0.75; $P = .73$), seroma (OR, 0.62; $P = .69$), or hematoma (OR, 1.9; $P = .65$). There were no differences in complications among the surgeons performing the procedure. Tumor staging, nodal metastases, salvage surgery, prior radiation, the use of adjunct hemostatic materials, or the use of free tissue reconstruction was not associated with an increased risk of adverse outcomes. Again, similar nonsignificant relationships were observed when the analysis was stratified by the presence of intraoperative complications.

The risk of developing a postoperative salivary leak was significantly increased by procedures that entailed communication between the primary defect and lateral neck (OR, 4.36; $P = .04$). Similarly, an increased risk of salivary leak was seen in procedures for mucosal primary malignancies (OR, 1.67; $P = .01$). As compared with unilateral procedures, bilateral neck dissections were 1.85 times more likely to develop a salivary leak (OR, 1.85; $P = .03$).

The risk of developing a postoperative chyle leak was not significantly increased for left-sided dissections as compared with right-sided dissections (OR, 2.87; $P = .37$). When assessing levels of dissection as individual factors (nominal), level IV dissection was not a significant risk for the incidence of chyle leak (OR, 1.80; $P = .94$). However, with each incremental increase in the number of levels dissected, we noted that the risk of chyle leak nearly doubled (OR, 1.96; $P = .023$). This relationship was not observed for the other adverse events examined. A summary of the regression analyses for secondary outcomes is detailed in **Table 3**.

Table 2. Univariate Analysis of Factors Associated With Drain Output and Drain Days.[a]

	Drain output				Drain days			
	Estimate	95% CI		*P* value	Estimate	95% CI		*P* value
Male sex	−12.5	−24.1	5.8	.743	−3.4	−5.4	1.5	.124
Age	−1.39	−1.5	3.0	.534	0.07	−0.01	0.15	.054
Primary diagnosis								
Mucosal	91.9	−167.6	191.8	.838	3.24	−1.2	9.8	.676
Thyroid	−98.7	−304.6	107.5	.348	−1.21	−5.6	1.2	.341
Parotid	−30.5	−241.6	180.9	.777	−0.64	−4.3	0.9	.223
Cutaneous	−69.2	−379.5	240.9	.661	2.18	−1.6	4.3	.438
T stage								
T1	−30.1	−550.1	494.4	.907	−1.11	−7.1	4.8	.715
T2	70.7	−185.7	327.1	.908	0.67	−2.2	3.5	.653
T3	162.9	−84.0	409.7	.596	−1.08	−3.8	1.8	.475
T4	53.9	−80.7	541.8	.545	2.39	−4.7	9.5	.511
N stage								
N1a	−166.3	−569.4	236.9	.419	−0.47	−2.6	3.5	.765
N1b	86.8	−128.0	301.6	.428	−3.73	−6.4	1.1	.508
N2a	120.7	−490.7	733.2	.699	−1.23	−8.8	6.3	.749
N2b	31.7	−306.2	242.7	.821	0.98	−2.5	4.3	.593
N2c	233.6	−97.1	564.4	.166	**5.39**	**1.3**	**9.5**	**.009**
N3	66.6	−573.6	440.4	.796	0.90	−7.2	5.4	.777
Salvage	155.6	−390.2	80.1	.197	1.38	−4.2	2.7	.331
Previous								
Surgery	45.8	−230.5	138.9	.627	**3.21**	**1.1**	**5.4**	**.004**
Radiation therapy	57.0	−309.2	195.2	.658	0.50	−3.6	2.6	.748
Left	54.8	−77.8	187.4	.418	0.09	−0.5	2.4	.199
Bilateral	**257.1**	**89.8**	**424.4**	**.003**	**5.68**	**3.8**	**7.53**	**<.001**
Communication[b]	**448.2**	**64.1**	**783.2**	**.004**	**2.87**	**1.2**	**6.7**	**.002**
Sealant use	*24.8*	*−143.0*	*192.6*	*.772*	*−0.21*	*−2.2*	*1.8*	*.834*
Reconstruction	100.3	−81.9	282.5	.281	**5.95**	**3.9**	**7.9**	**<.001**
Level								
I	−10.2	−176.4	156.0	.903	−1.65	−3.6	0.2	.230
II	−58.7	−303.9	186.5	.639	−1.48	−4.5	1.5	.327
III	177.4	−99.6	454.4	.209	0.28	−3.1	3.7	.867
IV	168.9	−12.1	349.4	.674	1.60	−0.6	3.8	.155
V	157.6	−27.2	342.5	.946	−0.39	−2.6	1.9	.738
VI	101.7	−317.6	521.1	.634	0.09	−4.9	5.1	.972
N levels[c]	68.2	−9.81	146.3	.087	**0.48**	**0.3**	**2.2**	**.010**
Postoperative complications	**668.5**	**468.4**	**854.4**	**<.001**	**8.79**	**6.5**	**11.1**	**<.001**

[a]Bold indicates statistical significance ($P < .05$). Italics indicate the focus of the study.
[b]Communication represents procedures entailing an intraoperative connection between the primary defect and lateral neck bed.
[c]N level represents incremental increase in the number of levels dissected.

Overall, $31,050 in direct costs were spent on fibrin sealant in the study cohort, at an average cost of $674 per case.

Discussion

In this retrospective study, the use of fibrin sealant during lateral neck dissections was not associated with decreased drain output, duration of drain placement, or risk of postoperative complications. When controlling for intraoperative complications and stratifying the analysis accordingly, similar nonsignificant associations were observed. Before this review was conducted, fibrin sealant was anecdotally used at our institution as a prophylactic measure with aims to decrease surgical site output, lower the incidence of chyle leak, and treat intraoperative complications. The evidence herein suggests that the routine use of fibrin sealant has little to no effect on surgical site production and risk of adverse outcomes associated with lateral neck dissections.

To our knowledge, this is the largest report examining outcomes related to fibrin sealant usage in lateral neck dissections. In a prospective analysis, Huang et al demonstrated

Table 3. Univariate Analysis of Factors Associated With Chyle Leak and Salivary Leak.[a]

	Chyle leak			Salivary leak		
Factor	*P* value	OR	95% CI	*P* value	OR	95% CI
Male sex	.66	1.40	0.3-6.5	.93	—	—
Age	.29	0.97	0.9-1.0	.29	1.03	0.9-1.1
Primary diagnosis						
Mucosal	.74	1.52	0.5-12.6	**.01**	**1.67**	**1.4-3.4**
Thyroid	.32	—	—	.26	0.72	—
Parotid	.92	—	—	.65	2.31	0.4-4.7
Cutaneous	.96	—	—	.87	—	—
T stage, 1-4	.97-.92	—	—	.99-.88	—	—
N stage, 0-3	.98-.81	—	—	.95-.86	—	—
Salvage	.76	0.84	0.1-7.5	.93	2.16	0.4-12.2
Previous						
Surgery	.39	1.90	0.4-8.4	.95	—	—
Radiation therapy	.91	1.13	0.1-9.8	.16	3.48	0.6-19.8
Left	.37	2.87	0.3-28.6	.95	0.95	—
Bilateral	.24	2.37	0.6-10.2	**.03**	**1.85**	**1.2-33.7**
Communication[b]	.89	0.82	—	**.04**	**4.36**	**2.1-6.7**
Sealant use	*.43*	*0.63*	*0.1-2.8*	*.73*	*0.75*	*0.5-2.1*
Reconstruction	.39	0.39	—	.32	1.2	0.9-20.1
Level						
I	.51	0.52	0.1-2.9	.06	4.83	0.9-29.9
II	.26	0.34	—	.96	—	—
III	.96	—	—	.97	—	—
IV	.95	—	—	.95	—	—
V	.18	6.05	0.8-26.9	.96	—	—
VI	.33	—	—	.98	—	—
N levels[c]	**.02**	**1.96**	**1.1-3.6**	.17	1.57	0.8-2.9

Abbreviation: OR, odds ratio.

[a]Bold indicates statistical significance ($P < .05$). Italics indicate the focus of the study. Dashes (—) indicate that one of the estimated values is <0.01 or >99 (all nonsignificant).

[b]Communication represents procedures entailing an intraoperative connection between the primary defect and lateral neck bed.

[c]N level represents incremental increase in the number of levels dissected.

no significant differences in drainage amount and duration of drain placement with fibrin sealant use.[8] In contrast, Mushi et al and Earnshaw et al reported decreased drain output, length of drain placement, and length of hospitalization in retrospective cohort reviews of selective neck dissections.[9,10] Of note, the first 2 studies were significantly underpowered (8 and 15 patients in the intervention groups, respectively), and all 3 reports did not account for a variety of patient, disease, and surgical factors. Without controlling for such elements, the latter 2 reports inappropriately conclude that fibrin sealant spray and tissue adhesives dramatically reduce length of hospitalization. Our study was primarily interested in determining the effects that fibrin sealant has on the risk of developing clinically significant adverse outcomes. For example, a slight reduction in the amount of surgical site production may hold little clinical value and relevance. Moreover, drain output may be extraneously related to length of hospitalization, as patients may be discharged with drains in situ, as is practice at our institution. By using a univariate regression model with dichotomous primary endpoints—as compared with the case-control comparative approach in prior reports—risk related to sealant use could be calculated from our heterogeneous cohort.

The results of our study align with contemporary investigations assessing fibrin sealant usage in central neck dissections. In a randomized prospective study, Kim et al showed that fibrin sealant use was not associated with clinically significant reductions in postoperative drain output or complications after total thyroidectomy and central neck dissection.[11] In a meta-analysis specific for soft tissue surgery of the head and neck, Bawja et al found a definite benefit in rhytidectomy procedures. However, no difference in drain output or adverse events was seen with sealant use in lateral neck dissections.[6] It should be noted that each trial included in the meta-analysis excluded patients who underwent prior surgery. Furthermore, drain output is an extraneous measurement for certain procedures—such as rhytidectomy—in which drains are typically removed within 24 to 48 hours following

surgery. Although a great deal of heterogeneity exists amid the entire body of literature involving fibrin sealant use, our results agree with most well-designed prospective studies involving fibrolymphatic dissections in the breast, axillary, and inguinofemoral regions.[12-14]

A multitude of limitations with our study should be acknowledged, particularly those concerning the secondary analysis. Paralleling the majority of existing investigations, there was great heterogeneity among our study cohort. Variation in patient, disease, and surgical characteristics introduces confounding factors that may influence the analysis.

While endorsed to achieve hemostasis, the utility of fibrin sealant in preventing chyle leak or salivary fistulas has not been established, nor is it promoted by manufacturer guidelines. Many head and neck surgeons, including those in our practice, employ a variety of adjuncts to decrease the risk of chyle leak when performing level IV dissections. Extra suture ties, surgical clips, strap-muscle rotational flaps, and fibrin sealants are anecdotally utilized, particularly when an intraoperative leak is detected. Although our study is limited by sample size, 66% of our patients with noted intraoperative chyle leaks who received sealant still experienced postoperative leaks. To our knowledge, the use of fibrin sealants to reduce salivary leaks has not been investigated. There is current insufficient evidence to support these products to reinforce esophageal anastomoses following esophagectomy.[15,16] While definite conclusions cannot be drawn from our data, this report serves to critically analyze the cost-benefit ratio of these products and promote future investigation.

Our sample size was restricted by the retrospective nature of the review. Without an established intervention effect size, a high fidelity sample size estimation could not be calculated. In a post hoc exercise, a percentage relative effect of 31% risk reduction of adverse events (relative risk, 0.69) was extrapolated.[6] Based on a power of 80% with an alpha of 0.05 and an assumption that the incidence of chyle leak is 5% for lateral neck dissections, 2466 patients would need to be enrolled in a 2-sample study to achieve adequate power. Due to our cohort, a single incidence of postoperative complication, including salivary leak or chyle leak, holds significant statistical weight that may skew the analysis. The lack of statistical association between level IV dissections and the incidence of chyle leak in our cohort supports this notion. With few occurrences of the secondary outcomes and a likely underpowered cohort, these data should serve as foundation for larger, multi-institutional studies in the future.

The analysis on length of drain placement may be influenced by surgeon preference and purpose of drain placement. Typical institutional practice is removal of drains when the recorded output is <30 mL in 24 hours. However, surgical drains may be retained following certain operations until postoperative assessments are completed. For example, it is common practice to maintain a drain near the pharyngeal closure following a laryngectomy until a swallow study and oral feeding trials are initiated to monitor for salivary leak. The inclusion of these patients, who may have otherwise met output criteria for removal, would certainty affect the results observed on length of placement.

Although our univariate analysis included a comprehensive list of variables, additional factors may influence the incidence of adverse outcomes of interest. Examples include platelet counts, systemic anticoagulant medications, or preexisting diagnosis of diabetes. These effects are somewhat mitigated by clinical judgment in surgical decision making and institutional adherence to general guidelines on perioperative anticoagulation management.[17]

Previous reports outside the head and neck estimated that fibrin sealants cost approximately \$50 to \$100/mL, at an average cost of up to \$1000 per case.[18,19] In our study, \$31,050 in direct charges were spent on fibrin sealant, at a mean cost of \$674 per case. A more comprehensive analysis examining costs associated with complications—such as hospital stay, unplanned returns to the operating room, home care drain management, medication usage, and dietary modifications—is needed to determine the potential cost-saving benefits of these products. Nonetheless, without clear benefit observed with its routine application, these tangible costs must be judiciously scrutinized amid the stringent financial conditions in contemporary health care.

Conclusions

This retrospective single-center review demonstrated that the application of fibrin sealant during lateral neck dissections was not associated with decreased drain production and length of drain placement. Although the study was restricted by sample size, fibrin sealant was not associated with a reduced risk of postoperative infection, chyle leak, hematoma, seroma, or salivary leak. Until appropriately powered randomized trials demonstrate a clear benefit, surgeons must continue to balance clinical benefits and economic costs associated with the use of fibrin sealants.

Author Contributions

Luke Stanisce, conception and design, acquisition of data, statistical analysis, analysis and interpretation, drafting the article, critical revision of the article, final approval of the article, overall responsibility; **Michael Lai**, conception and design, acquisition of data, analysis and interpretation, drafting the article, critical revision of the article, final approval of the article; **Nadir Ahmad**, critical revision of the article, analysis and interpretation, final approval of the article; **Thomas C. Spalla**, critical revision of the article, final approval of the article; **Lisa M. Reid**, critical revision of the article, final approval of the article; **John P. Gaughan**, statistical analysis, analysis and interpretation, critical revision of the article, final approval of the article; **Yekaterina Koshkareva**, conception and design, analysis and interpretation, critical revision of the article, final approval of the article, overall responsibility.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

References

1. Amir I, Morar P, Belloso A. Postoperative drainage in head and neck surgery. *Ann R Coll Surg Engl*. 2010;92(8):651-654.
2. Samraj K, Gurusamy KS. Wound drains following thyroid surgery. *Cochrane Database Syst Rev*. 2007;17(4):CD006099.
3. Sabatini L, Trecci A, Imarisio D, et al. Fibrin tissue adhesive reduces postoperative blood loss in total knee arthroplasty. *J Orthop Traumatol*. 2012;13(3):145-151.
4. Nenezić D, Ayguasanosa J, Menyhei G, et al. A prospective, single-blind, randomized, phase III study to evaluate the safety and efficacy of Fibrin Sealant Grifols as an adjunct to hemostasis compared with manual compression in vascular surgery. *J Vasc Surg*. 2019;70(5):1642-1651.
5. Schwartz M, Madariaga J, Hirose R, et al. Comparison of a new fibrin sealant with standard topical hemostatic agents. *Arch Surg*. 2004;139(11):1148-1154.
6. 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(6):1141-1152.
7. Robbins KT, Clayman G, Levine PA, et al. Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology–Head and Neck Surgery. *Arch Otolaryngol Head Neck Surg*. 2002;128(7):751-758.
8. Huang CW, Wang CC, Jiang RS, et al. The impact of tissue glue in wound healing of head and neck patients undergoing neck dissection. *Eur Arch Otorhinolaryngol*. 2016;273:245-250.
9. Mushi E, Kinshuck A, Svecova N, et al. The use of Tisseel fibrin sealant in selective neck dissection—a retrospective study in a tertiary head and neck surgery centre. *Clin Otolaryngol*. 2015;40:93-97.
10. Earnshaw CH, Kinshuck AJ, Loh C, et al. An audit of fifty patients receiving Artiss fibrin sealant in lateral selective neck dissections. *Clin Otolaryngol*. 2020;45(2):264-267.
11. Kim TW, Choi SY, Jang MS, et al. Efficacy of fibrin sealant for drainage reduction in total thyroidectomy with bilateral central neck dissection. *Otolaryngol Head Neck Surg*. 2012;147(4):654-660.
12. Carless PA, Henry DA. Systematic review and meta-analysis of the use of fibrin sealant to prevent seroma formation after breast cancer surgery. *Br J Surg*. 2006;93:810-819.
13. Neuss H, Raue W, Koplin G. Intraoperative application of fibrin sealant does not reduce the duration of closed suction drainage following radical axillary lymph node dissection in melanoma patients: a prospective randomized trial in 58 patients. *World J Surg*. 2008;32:1450-1455.
14. Mortenson MM, Xing Y, Weaver S. Fibrin sealant does not decrease seroma output or time to drain removal following inguino-femoral lymph node dissection in melanoma patients: a randomized controlled trial (NCT00506311). *World J Surg Oncol*. 2008;6:63.
15. Sdralis E, Tzaferai A, Davakis S, et al. Reinforcement of intrathoracic oesophago-gastric anastomosis with fibrin sealant (Tisseel) in oesophagectomy for cancer: a prospective comparative study. *Am J Surg*. 2020;219(1):123-128.
16. Plat VD, Bootsma BT, van der Wielen N, et al. The role of tissue adhesives in esophageal surgery, a systematic review of literature. *Int J Surg*. 2017;40:163-168.
17. Jethwa AR, Khariwala SS. When should therapeutic anticoagulation be restarted following major head and neck surgery? *Laryngoscope*. 2018;128(5):1025-1026.
18. Azoury SC, Rodriguez-Unda N, Soares KC, et al. The effect of TISSEEL fibrin sealant on seroma formation following complex abdominal wall hernia repair: a single institutional review and derived cost analysis. *Hernia*. 2015;19(6):935-942.
19. Spotnitz WD. Hemostats, sealants, and adhesives: a practical guide for the surgeon. *Am Surg*. 2012;78(12):1305-1321.