

Reducing the rate of fistula: does a fibrin sealant act as an adjunct in pharyngeal closure? A two-centre experience

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Main Article

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Abstract

Background. Pharyngocutaneous fistula is a troublesome complication. Recently, synthetic materials such as fibrin sealant have been used as a secondary measure to treat fistula. This work assessed whether the primary use of fibrin sealant can reduce the rate of fistula.

Method. A retrospective review of 50 cases from 2 centres was completed. Tisseel was an adjunct to primary closure in all cases.

Results. In the first centre, 3 out of 34 cases developed pharyngocutaneous fistula (fistula rate of 9 per cent). All three were salvage cases. In the second centre, 0 out of 16 cases developed a fistula.

Conclusion. The incidence of pharyngocutaneous fistula post-radiation and post-chemoradiotherapy in laryngectomy cases has been quoted as 23 per cent and 34 per cent respectively. This study represents the first patient series on the use of fibrin sealant as an adjunct in primary closure following laryngectomy. The results are promising, encouraging the use of Tisseel as an adjunct to meticulous closure.

Introduction

The first laryngectomy is recorded as being performed by Bilroth, in Vienna in 1873, who reported his work in 1874;¹ as Stell comments in his 1975 paper,¹ that patient had a ‘large pharyngocutaneous fistula’. It is not unreasonable to suggest that, since that time, pharyngocutaneous fistula remains a troublesome post-operative complication that is of concern to the head and neck surgeon, despite medical advances and progress. If anything, current medical and therapeutic practice is perhaps at least maintaining, if not increasing the incidence of pharyngocutaneous fistula. It is often discussed why (in the era of organ preservation protocols, following the 1991 publication from the Department of Veteran Affairs Laryngeal Cancer Study Group²) the risk of pharyngocutaneous fistula is higher in salvage laryngectomy.

It is important, but sometimes challenging, to achieve balance between functional swallowing and the best possible communication, or the post-laryngectomy ‘voice’. In their attempts to accomplish such an important aim, head and neck surgeons try an armoury of different techniques and materials, both natural and synthetic, to achieve the best possible healing in the reconstructed (neo)pharynx that has been compromised by a pharyngocutaneous fistula. Flaps such as the pectoralis major flap, pharyngeal interposition flap and vascularised onlay grafts have been used to reduce the incidence of pharyngocutaneous fistula. In addition, synthetic materials such as fibrin sealants have recently been used as a secondary measure to complement mucosal closure.³

This study examined the use of a commercially available fibrin sealant, Tisseel[®], as an adjunct in closure. In this context, the fibrin sealant is considered a ‘prophylactic’ measure, which is being used to prevent fistula formation. This is different to published work where such agents are used as part of the repair after a fistula has formed.³ The proposed benefit of such an adjunct is its ability to act as an additional barrier, reducing minor salivary leaks from the suture line, thereby improving tissue healing and reducing the rate of pharyngocutaneous fistulas.

Fibrin sealants

These products are also described or known as tissue adhesives or tissue glues.⁴ They are often human plasm-derived, fibrinogen- and thrombin-based sealants. Their use and benefits include promoting the adherence of autologous skin grafts to burn wounds, the haemostasis of surgical bleeding, and the prophylactic prevention of colonic anastomoses leakage.^{5–7} Viamonte *et al.* indicated an improved rate in anastomotic leak in 425 cases,⁷ whilst a systematic review by Vakalopoulos *et al.* showed promising results for ileal anastomoses and positive results for colorectal anastomoses.⁶

Table 1. Pharyngocutaneous fistula rates at both treatment centres

Treatment centre (dates)	Total cases (n)	Salvage cases (n)	Identified fistulas (n (%))	Fistulas in primary surgery (n)	Fistulas in salvage surgery (n (%))
First centre (January 2015 to March 2016)	34	10	3 (9)	0	3 (30)
Second centre (June 2017 to July 2018)	16	7	0 (0)	0	0 (0)
Both centres (January 2015 to July 2018)	50	17	3 (6)	0	3 (18)

Table 2. Pharyngocutaneous fistula incidence rates in previously published studies

Study (year)	Pharyngocutaneous fistula incidence
Sayles & Grant (2014) ⁸	References literature rates of 14–61% in salvage surgery cases. Paper's own results: fistula incidence rates of 14.3% in primary surgery cases, 22.8% in post-RT salvage surgery cases, 34.1% in post-CRT salvage surgery cases & 10.3% in salvage surgery cases with an 'onlay' flap
Busoni <i>et al.</i> (2015) ⁹	Overall rate of 24.4%; 28.6% in post-RT salvage surgery cases & 30.3% in post-CRT salvage surgery cases
Mattioli <i>et al.</i> (2015) ¹⁰	References literature rates of 8–22% in laryngectomy cases. Paper's own results: 34.8% of cases
Eryilmaz <i>et al.</i> (2016) ¹¹	References literature rates of 5–65% in primary surgery cases & 14–61% in salvage surgery cases
Dedivitis <i>et al.</i> (2007) ¹²	References literature rates of 3–65%. Paper's own results: 12.7% of cases overall

RT = radiotherapy; CRT = chemoradiotherapy

These agents are for topical use only. The fibrin sealant system initiates the last phase of physiological blood coagulation. Thrombin activates the conversion of fibrinogen into fibrin, which occurs by splitting fibrinogen into fibrinogen monomers and fibrinopeptides. The fibrinogen monomers polymerise and form a fibrin clot. Factor XIIIa, which is activated from factor XIII by thrombin, crosslinks the fibrin. Haemostasis or sealing of tissues is therefore achieved when the formed fibrin clot adheres to the wound surface.

Tisseel additionally contains aprotinin, which has been shown to increase the resistance of the fibrin sealant clot to degradation in a fibrinolytic environment.

Aim

This study investigated the use of the fibrin sealant Tisseel as an adjunct to primary closure, to improve healing and help reduce the incidence of pharyngocutaneous fistula. We postulated that there may be a reduction in the incidence of pharyngocutaneous fistula associated with the use of Tisseel when compared to rates published in the literature.

Materials and methods

This work involved a sequential, retrospective review of cases. The treatment of all cases was led by a senior surgeon, standardised as per their technique. Tisseel was used as an adjunct to primary closure in 34 patients in the first period, and in 16 patients in the second. Thirty-four cases were completed from January 2015 to March 2016 in one centre, and 16 cases were completed between June 2017 and July 2018 in the second centre. Data were captured from operating theatre logbooks, multidisciplinary team meeting records and patient notes.

All the cases were treated using the following standardised technique. Primary closure of the neopharynx was performed using Vicryl® size 3–0 extramucosal sutures; this was followed by the application of a layer of Tisseel. All closures were either tension-free horizontal closures or 'Y'-shaped closures. Subsequent muscle closure was achieved with Vicryl 3–0 sutures, followed by the application of a second layer of Tisseel over the suture line.

Post-operatively, all the patients were treated based on the standard post-laryngectomy protocol; this entailed antibiotics for 5 days, videofluoroscopy or contrast study 1 week later, neck suture removal after 1 week, and stomal suture removal at 10 days. All the patients who passed the swallow test were allowed to drink sterile water first, and then gradually build up feeds under the guidance of dietitians and speech therapists.

When reviewing the patient information, no leak or fistula was defined as: (1) successful contrast swallow test results, with the absence of a leak; (2) patient discharged home on oral intake; and (3) no intervention needed for a leak, and no alternative feeding regime needed for a fistula or leak.

Results

The fistula rates were calculated in total, and separately according to non-irradiated and irradiated surgical fields. In the first set of 34 laryngectomies (Table 1), 24 were primary and 10 were salvage. In the non-irradiated larynx group, none of the patients developed a fistula. Three patients developed a fistula in the radiated group. The overall fistula rate was 9 per cent (3 out of 34), with 0 per cent in the non-irradiated group and 30 per cent (3 out of 10) in the radiotherapy group. In the second set of 16 laryngectomies (Table 1), 9 were primary and 7 were salvage. None of the patients developed a fistula. The overall fistula rate was 0 per cent. When the data from the two periods are combined (Table 1), the aggregated data give a pharyngocutaneous fistula rate of 6 per cent overall and 18 per cent in salvage cases.

Discussion

The data for this small cohort indicate that the use of Tisseel in the primary laryngectomy group was effective.

Discussion continues regarding the incidence of pharyngocutaneous fistula and the risk factors, particularly in salvage or 'secondary' surgery. The incidence of pharyngocutaneous fistula ranges from 14 per cent in primary laryngectomies, increasing significantly to 23 per cent in the post-irradiation larynx, and to 34 per cent in patients who have undergone chemotherapy and radiotherapy.⁸ When compared to such published rates, the results of this study suggest that the use of Tisseel results in a reduction in the incidence of pharyngocutaneous fistula.

This is important in the context of head and neck cancer care overall. A reduction in the incidence of

pharyngocutaneous fistula facilitates a shorter in-patient stay, and any improvement in the care pathway for the patient will also improve patient outcomes.

Nevertheless, further studies are required, not only with larger numbers, but also to specifically investigate the irradiated groups. There may also be a role for a trial with a control cohort.

The importance of our results is only fully appreciated when compared to published rates (Table 2),^{8–12} as this is a correlating marker to assess for any reduction in the incidence of pharyngocutaneous fistula. In our case series, the overall fistula rate was only 6 per cent. This is less than the lowest rate identified in our literature search (10.3 per cent in cases with an onlay flap⁸). Whilst 6 per cent is better than the reported rates, this must be acknowledged in context of flap use in salvage laryngectomy.

The authors also recognise that, as a preliminary study, this work has no control cohort to demonstrate statistical significance. However, the improvement in outcomes is evident. At the very least, the use of a fibrin sealant such as Tisseel, used alongside optimised pharyngeal closure, can be acknowledged as having been beneficial in this surgeon's hands.

The literature search indicates that our study comprises the largest patient group in which a fibrin sealant has been used as an adjunct in primary closure. This human study is consistent with the laboratory findings of a rat model study by Eryilmaz *et al.*,¹¹ who demonstrated positive changes created by the fibrin tissue adhesive, at the histopathological level, with no detected fistula.

- Pharyngocutaneous fistula prevention after laryngectomy and/or pharyngectomy is an important consideration in head and neck surgery
- Current practice recognises the use of tissue flaps, particularly in salvage cases undergoing surgery after chemoradiotherapy or radiotherapy
- Medical literature recognises the role of fibrin sealants in the repair of pharyngocutaneous fistula
- This work identifies the potential of fibrin sealants in preventing pharyngocutaneous fistula, in primary and salvage surgery cases

Conclusion

The authors present these data as evidence that the addition of fibrin sealants at the time of initial surgical closure of the

neopharynx is not only safe, but very likely to be beneficial to patients. There is certainly room for further research, not only for larger numbers of cases, but to focus on the benefit that can be afforded to the difficult patient group of head and neck cancer patients requiring salvage surgery. However, in the interim, this author group will continue to make use of the adjunct benefit of fibrin sealant in the treatment of their patient population.

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