Using post-operative trend in C-reactive protein to predict fistula in neopharyngeal repairs following laryngectomy and pharyngectomy surgery in fifty-five patients

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INTRODUCTION

- The most desirable outcome following laryngectomy and pharyngectomy surgery is complete healing of the neopharyngeal mucosal repair along with the superficial cutaneous wound.
- Pharyngocutaneous fistula is a major post-operative complication; one recent meta-analysis reported the incidence at 21%.[1]
- Being able to predict the likelihood of fistula formation would aid the clinician in deciding the optimum time to start oral intake.
- *Aim:* To determine if post-operative trend in CRP after laryngectomy and pharyngectomy can predict pharyngocutaneous fistula.
- Our current practice is to take daily CRP measurements for five days following surgery. The percentage change from the maximum CRP recorded within the five-day period to the value recorded at day five was calculated. The hypothesis was that a drop in CRP could be used to indicate favourable post-operative outcome with no fistula.

METHODS

- Retrospective analysis of a prospectively recorded database of all patients undergoing major head and neck resections at our unit between January 2015 and June 2020.
- All patients included: primary or salvage surgery to the neck for cancer resection, with or without neck dissection, with any method of neopharyngeal repair or reconstruction (primary closure, pedicled flap, free flap), with or without Montgomery Salivary Bypass Tube post-operatively.
- CRP recorded daily for the first five days after surgery. The percentage change from maximum recorded CRP to the CRP recorded at day five was calculated.
- Primary outcome was absence of a pharyngocutaneous fistula confirmed by water-soluble contrast swallow, normally performed at day 10. For patients with a Montgomery Salivary Bypass Tube, the swallow was performed after tube removal (two weeks for primary or three weeks for salvage cases).

RESULTS

Table 1: Patient demographics.

Characteristic	Patients (n (%))
Sex	
– Male	47 (85)
– Female	8 (15)
Site of pathology	
– Larynx	30 (55)
– Tongue	13 (24)
– Hypopharynx	10 (18)
– Neopharynx	2 (4)
Primary or salvage surgery	
– Primary	34 (62)
– Salvage	21 (38)
Operation performed	
– Total laryngectomy	33 (60)
– Laryngo-glossectomy	11 (20)
– Laryngo-pharyngectomy	8 (15)
– Pharyngectomy	2 (4)
– Laryngo-glossectomy and mandibulectomy	1 (2)
Montgomery Salivary Bypass Tube inserted intraoperatively?	
– No	36 (65)
– Yes	19 (35) *

* All but one of the patients who had a Montgomery Salivary Bypass Tube inserted intraoperatively had it for flap-assisted surgery.

Table 2: Patient outcomes (healed or fistula formation) for primary and salvage surgery, with separate subgroup analysis for patients undergoing total laryngectomy.

	Primary surgery (n (%))	Salvage surgery (n (%))	Total (n (%))
All operations			
Healed	31 (91)	16 (76)	47 (85)
Fistula	3 (9) *	5 (24) *	8 (15)
Total	34 (100)	21 (100)	55 (100)
Subgroup analysis for total laryngectomy only			
Healed	24 (96)	5 (63)	29 (88)
Fistula	1 (4) ⁺	3 (38) ⁺	4 (12)
Total	25 (100)	8 (100)	33 (100)

* The proportion of patients who developed a fistula was higher in the salvage surgery group although this difference was not statistically different, $p = 0.236$ (two-sided Fisher's exact test).

⁺ In the total laryngectomy subgroup, the proportion of patients who developed a fistula was significantly higher in the salvage surgery group, $p = 0.036$ (two-sided Fisher's exact test).

- Fifty-five patients were identified for inclusion. Patient demographics are displayed in Table 1.
- Eight (15%) patients developed a fistula (Table 2). Three of these were managed conservatively, five required further surgery.
- Two (4%) patients had missing CRP data and were excluded from further analysis; neither of these patients developed a fistula.
- A ROC curve illustrates the relationship between percentage drop in CRP and successful healing without fistula (Figure 1). The area under the curve was 0.881. This curve demonstrates the optimal value for a screening test to identify those patients who healed as a 35% reduction from maximum CRP to the CRP recorded at post-operative day five.
- This test predicted favourable post-operative outcome with no fistula with a sensitivity 84%, specificity 88%, positive predictive value (PPV) 97% and negative predictive value (NPV) 50% (Table 3). The predictive value of this test was significant, $\chi 2$ (1, N = 53) = 18.088, $p < 0.000$.

Figure 1: ROC curve to illustrate the relationship between percentage drop in CRP and whether the patient successfully healed following surgery.

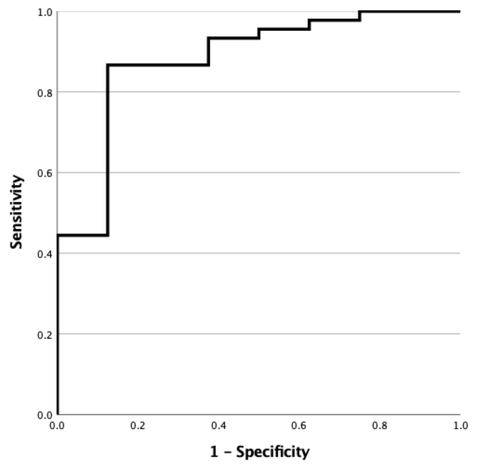

Table 3: Results from the CRP screening test compared to the actual outcome for each patient. A 35% reduction from maximum CRP to the CRP recorded at post-operative day five was used to predict healing without pharyngocutaneous fistula. Numbers represent numbers of patients within each group.

		Actual outcome: Healed	Actual outcome: Fistula	Total	
All operations					
CRP screening test result	Predicted healed	38	1	39	PPV = 97 (38/39)
	Predicted fistula	7	7	14	NPV = 50 (7/14)
	Total	45	8	53	
		Sensitivity = 84 (38/45)	Specificity = 88 (7/8)		
Subgroup analysis for total laryngectomy only					
		Healed	Fistula	Total	
CRP screening test result	Predicted healed	22	1	23	PPV = 96 (22/23)
	Predicted fistula	5	3	8	NPV = 38 (3/8)
	Total	27	4	31	
		Sensitivity = 81 (22/27)	Specificity = 75 (3/4)		

PPV: positive predictive value, NPV: negative predictive value

CONCLUSION

- A 35% reduction in maximum CRP to the CRP at post-operative day five is a strong predictor of neopharyngeal healing without fistula formation.
- High PPV may allow early oral intake in these patients, resulting in faster recovery times and reduced hospital stays.
- We believe that this is the first study to use post-operative trend in CRP and also the first to use CRP as a screening test to predict healing in patients undergoing head and neck cancer surgery.

(1) Wang M *et al.* Risk factors of pharyngocutaneous fistula after total laryngectomy: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol 2020;277:585-599.