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Risk factors involved in stomal recurrence following laryngectomy

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Abstract
Stomal recurrence after surgery for laryngeal tumours is an extremely serious complication, with a dismal prognosis despite aggressive surgical therapy or high-dose irradiation. Data from 209 patients who underwent total laryngectomy for cancers of the larynx and hypopharynx were retrieved from the registry of the Department of Otorhinolaryngology at the Hospital 'Virgen de las Nieves' of Granada. Stomal recurrence developed in 8.1 per cent of them (17 cases). We analysed several parameters from each case: first, those parameters significantly associated with stomal recurrence were detected, and secondly, a logistic regression analysis was done. Three factors were found independently related to stomal recurrence: T-staging, site of the primary tumour and prior tracheostomy. Together with a review of the literature, we discuss our findings and a proposal for management of the high risk patient.

Key words: Laryngeal neoplasms; Laryngectomy

Introduction

Stomal recurrence after surgery for laryngeal tumours is an extremely serious complication, with an overall incidence of 6 per cent (Table I). The factors most strongly implicated in peristomal recurrence have been pre-operative tracheotomy and subglottic involvement by a tumour that is either primary in the subglottis or extends inferiorly from a glottic or transglottic primary. Other factors reported are tumour size, antecedent hemilaryngectomy and metastatic lymphadenopathy. There is no unanimity amongst authors on predisposing clinico-pathological mechanisms such as (1) submucosal extension or undetected neoplasm at the margin of resection; (2) development of an additional primary; (3) neoplastic cell implantation at the time of surgery; and (4) recurrence spawned by metastases to paratracheal and pretracheal lymph nodes. The main problem to be resolved is the exact impact of every mechanism in the genesis of stomal recurrence, and the purpose of this paper is to try to find out the precise role of prior tracheostomy.

Material and methods

Two hundred-and-nine patients with squamous cell carcinoma of the larynx were included in the study. None of them received radiotherapy or chemotherapy before surgery. There were 206 males and 3 females and the ages ranged from 37 to 77 years (average 60.7). Tumours were classified as originiating from the supraglottic region (39.1 per cent), glottis (34.2 per cent), subglottis (4.5 per cent) or pyriform fossae (5 per cent). Thirty-five cases were considered transglottic (17.2 per cent) (Kirchner *et al.*, 1974). Tumours were graded as either well (64 cases), moderately (104 cases) or poorly differentiated (35 cases). Five were verrucous carcinomas and one was diagnosed as spindle-cell carcinoma.

TABLE I

Authors	Patients	Stomal Recurrence	%
Bauer *et al.* (1962)	86	6	7
Bonneau and Lehman (1975)	92	11	12
Burnam and Hudson (1968)	109	13	12
Castro *et al.* (1991)	350	20	6.5
Condon (1969)	110	6	6
De Jong (1969)	114	2	1.7
Present authors (1993)	209	17	8.1
Lahoz *et al.* (1989)	349	10	2.86
Latella *et al.* (1952)	240	8	3
Loewy and Laker (1968)	138	4	3
Keim *et al.* (1965)	116	17	14.7
Keuhn and Tennant (1971)	124	9	7
Mantravadi *et al.* (1981)	507	26	5
McCombe and Stell (1991)	189	7	3.7
Modlin and Ogura (1969)	243	12	5
Myers and Ogura (1979)	452	33	7.3
Norris (1959)	181	7	4
Sneider *et al.* (1975)	246	31	12.6
Stell and Van der Broek (1971)	196	8	4.1
Weismann *et al.* (1979)	251	14	6
Total	4281	261	6.09

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Surgical techniques consisted in total laryngectomy, either alone or associated to neck dissection. Ipsilateral functional neck dissection was performed in 47 cases and bilateral in 39. Radical ipsilateral neck dissection was done in 30 patients, and a bilateral procedure in 8. Neck dissection was carried out at clinical stage IV disease and at stage III disease as indicated by the presence of or a high risk of cervical metastases and by the specific site of the primary tumour. Post-operative radiation therapy was determined on an individual case basis by a multispeciality joint tumour board (otolaryngologist, oncologist, pathologist). Each case was carefully staged to conform to the 1987 criteria of the American Joint Committee for Cancer Staging and End Results Reporting (Kleinsasser, 1987). T-staging (pathological) yielded one T1, 20 T2, 126 T3 and 59 T4 cases. In three cases accurate staging was not possible. Overall, 26.4 per cent of the patients were found to bear metastatic lymph nodes at the time of surgery. Follow-up ranged from 5 to 12 years.

Statistical analyses were performed without any knowledge of the clinical stage, treatment, or further course of the disease. From each case we recorded several parameters (Table II) that were codified and introduced into a Data-General MV-15000 computer. The relative risk (RR), a measure of association, and its 95 per cent confidence interval were estimated (Kleinbaum *et al.*, 1982). RR in this study is the ratio of the rate of stomal recurrence in exposed *versus* unexposed (reference group). Statistical analyses were performed by the BMDP package (1988 version), especially the programs 7D, 4F and LR. Fisher's exact test, one-way analysis of variance and chi-square tests were applied when appropriate. The stepwise logistic regression was used to select the best predictors for 'stomal recurrence'.

TABLE II
PARAMETERS INCLUDED IN THE STUDY

Age
Smoking habits
Alcohol intake
Previous laryngeal history
First symptom
Main symptom
Length of symptoms
Mirror laryngoscopy/flexible fiberscopy image
Direct laryngoscopy findings
Vocal fold mobility
X-R, tomographs, CT-scan imaging
Prior tracheostomy
Length of prior tracheostomy
Functional neck dissection
Radical neck dissection
Symptom onset to diagnosis interval
Diagnosis-surgery interval
Length of post-op
Staging (AJC)
Complications post-op
Blood group of the patient (ABO/Rh)
Radiotherapy after surgery
Degree of differentiation
Tumour site
Cartilage involvement
Tumor burden (maximum diameter)
Number of neck metastases
T-staging (Pathol.)
N-staging (Pathol.)
T-staging (Clin.)
N-staging (Clin.)

TABLE III
VARIABLES INVOLVED IN STOMAL RECURRENCE

Variable	Cases	% Recurrence	RR	95% CI
Previous tracheostomy				
Yes:	36	25	5.38	2.22–12.99
No:	173	4.6	1 (reference)	
Tumour site				
Transglottic	47	12.77	4.72	0.99–22.43
Glottic	62	8.06	2.98	0.60–14.85
Subglottic	9	44.4	16.44	3.49–77.48
Supraglottic	74	2.7	1 (reference)	
Pyriform	10	0		
N-staging (Clin.)				
N0	167	8.3	1 (reference)	
N1–3	42	8.1	0.97	0.29–3.20
T-staging (Clin.)				
T1–2	49	4.08	1 (reference)	
T3	136	9.55	2.34	0.55–10.1
T4	21	9.5	2.33	0.35–10.01
N-staging (Pathol.)				
N0	153	8.5	1 (reference)	
N1–3	55	7.27	0.86	0.29–2.51
T-staging (Pathol.)				
T1–3	147	2.72	1 (reference)	
T4	59	22.03	8.10	2.75–23.8
AJC staging				
E1–3	118	2.5	1 (reference)	
E4	88	15.9	6.26	1.86–21.11

RR = relative risk; CI = confidence interval.

Results

Of the 209 patients, 36 underwent a tracheostomy at least 24 hours before surgery; the remaining 173 had their tracheostomies created at the time of the operation. Overall, the stomal recurrence rate was 8.1 per cent. Nine of the 36 patients with pre-operative emergency tracheostomy developed stomal recurrences (25 per cent) while this occurred in only 8 of the 164 whose tracheostomy was intraoperative (4.6 per cent) (Table III). That is, stomal recurrence was five times more frequent in patients who underwent previous tracheostomy, this difference being significant (the 95 per cent confidence interval does not include unity). The relationship between stomal recurrence and site of the primary tumour is also displayed in Table III. There is a striking difference between subglottic and transglottic tumours, on the one hand, and glottic, supraglottic and pyriform fossae tumours, on the other. The site of the primary in the subglottis (with a highly significant increase of 16.4 times the rate of stomal recurrence) and transglottic tumours (with an almost significant increase of 4.7) were strongly associated with stomal recurrence (Table III). The site of the lesion and thus subglottic involvement in our series is a major factor in the genesis of the recurrence. It is worthy of note that none of the hypopharyngeal tumours developed a stomal recurrence.

Five variables related to tumour extent were assessed. Clinical variables, namely T and N-staging, did not show a significant relationship with stomal recurrence, although T3 and T4 tumours increased by about twice the risk of recurrence. Similarly, N-staging assessed by the pathologist was not associated. However, the pathological T-staging increased the rate of recurrence in the stoma more than eight-fold (22.03 per cent for the T4 *versus* 2.72 per cent for < T4). The AJC staging of the tumour also yielded significant differences: stage IV tumours showed

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TABLE IV
RESULTS OF THE LOGISTIC REGRESSION ANALYSIS

Term	Coefficient β	SE (β)	OR	*p*-Value
Site				
Supraglottic (reference)				
Glottic	0.915	0.91	2.5	0.258
Transglottic	1.82	0.93	6.18	0.05
Subglottic	3.00	1.15	20.16	0.009
Pyriform	−13.05	885	2×10^{-5}	0.993
T-stage (Path.)	2.11	0.69	8.26	<0.001
Prior tracheostomy	1.309	0.66	3.7	0.047
Constant	−11.22	2.66	—	<0.001

Goodness of fit Chi-square: 21.425, df 44. $p = 0.998$. SE: standard error. OR: Odds ratio; df: degrees of freedom.

a recurrence figure of 15.9 per cent against 2.5 per cent for less advanced stages.

In a second step, the above mentioned variables were included in a stepwise logistic regression analysis. Only three variables were related independently to stomal recurrence, and they were: site of the primary tumour, T-staging (pathological) and prior tracheostomy (Table IV).

Discussion

The incidence of peristomal recurrence after total laryngectomy has been reported to be 1.7 to 14.7 per cent (Table I), prior tracheostomy being the most commonly found risk factor (Keim *et al.*, 1965; Loewy and Laker, 1968; Condon, 1969; Modlin and Ogura, 1969; Stell and Van der Broek, 1971; Bonneau and Lehman, 1975; Schneider *et al.*, 1975; Batsakis *et al.*, 1976; Myers and Ogura, 1979; Weissman *et al.*, 1979; Davis and Shapshay, 1980; Alvarez-Vicent *et al.*, 1982; Lahoz *et al.*, 1989; Castro *et al.*, 1991). Stomal recurrence has at least five different pathological causes: tumour implanted at the track of a tracheostomy, incompletely excised tumour, a second tumour arising in the tracheal epithelium, paratracheal lymph nodes overlooked at the time of laryngectomy, and a tumour tracking down within the sheath of the sternomastoid muscle (McCombe and Stell, 1991). Only the first of these five can be related to prior tracheostomy and therefore affected by a policy of emergency laryngectomy, a procedure advocated by several groups (Hoover and King, 1954; Keim *et al.*, 1965; Molinari and Bucco, 1967; Baluyot *et al.*, 1971; Stell and Van der Broek, 1971; Bonneau and Lehman, 1975; Capella and Morello, 1978; Myers and Ogura, 1979; Alvarez-Vicent *et al.*, 1982; Wickham *et al.*, 1990; McCombe and Stell, 1991) as other techniques, such as pre-operative radiotherapy, have failed to improve results (Breneman *et al.*, 1988).

While there is general agreement on the role of subglottic extension in the genesis of peristomal recurrence (Norris, 1959; Keim *et al.*, 1965; Burnam and Hudson, 1967; Modlin and Ogura, 1969; Bonneau and Lehman, 1975, Mantravadi *et al.*, 1981; Griebie and Adams, 1987), which can be established in between 30 per cent (Keim *et al.*, 1965) and 71 per cent of the patients (Weismann *et al.*, 1979), inoculation of tumour cells in the tracheal wound has both proponents and detractors. This can explain stomal recurrences after surgery for tumours of the oral cavity (Myers and Ogura, 1979), or supraglottic tumours (2 in our series), or for stomal recurrences developed after partial laryngectomy for small tumours. Implantation of exfoliated cells in the granulation tissue of the tracheotomy wound was reported previously (Baluyot *et al.*, 1971; Myers and Ogura, 1979; Alvarez-Vicent *et al.*, 1982; Armstrong and Price, 1992), as an intact mucosa does not favour tumour implants (De Jong, 1969). However, there is evidence of a more important role for other mechanisms, such as the spread of tumour through the paratracheal tissue and thyroid gland (Harrison, 1971) or the presence of metastatic delphian or paratracheal lymph nodes (Norris, 1959; Harrison, 1975). Others, such as the possibility of a second tumour arising from the trachea, could be considered anecdotal due to their low incidence (Li *et al.*, 1990).

Most of the tumours reported in the different series are bulky, often with subglottic extension, and the patients present with severe respiratory distress and undergo emergency tracheostomy. Exfoliated cells can be obtained from the tumours, but more often there is a direct extension to the thyroid and paratracheal tissues (Norris, 1959; Keim *et at.*, 1965; Modlin and Ogura, 1969; Harrison, 1971; Stell and Van der Broek, 1971; Kirchner *et el.*, 1974; Bonneau and Lehman, 1975; Myers and Ogura, 1979; Davis and Shapshay, 1980; Harrison, 1986). As subglottic tumours and many hypopharyngeal carcinomas metastasize in the paratracheal lymph nodes, some stomal recurrences can be originated by hidden metastases at the time of surgery which simulated posteriorly the clinical picture of a peristomal recurrence (Modlin and Ogura, 1969; Harrison, 1971; Kirchner *et al.*, 1974; Harrison, 1990). From our results, there is an obvious relationship between prior tracheostomy and stomal recurrence ($p = 0.002$, Table III). The logistic regression analysis demonstrates three main factors: subglottic extension (tumour site: subglottis, transglottic with subglottic extension), T-staging (extra-laryngeal spread, and tumour burden) and prior tracheostomy. Although tumour burden and subglottic involvement very often promote the use of emergency tracheostomy, this seems to be independently related to the stomal recurrence as showed by the logistic regression analysis, thus favouring the hypothesis of tumour cell implant at the tracheostomy site. Still, bulky tumours with subglottic involvement spread easily to the thyroid and paratracheal area, and this could explain most recurrences and not just the implant at the tracheostomy site (Condon, 1969; De Jong, 1969; Mantravadi *et al.*, 1981; Griebie and Adams, 1987). However, as implantation of exfoliated cells is a proven mechanism, irrigation of the operative site before closure and wide resection of the tracheostomy tract are mandatory. There are also arguments against performing emergency tracheostomy. The patients are prepared for operation in a hurry, and it can be argued that they do not give truly informed consent. Also, the histological diagnosis depends on a frozen section, the patient's general medical condition may be less than ideal, and psychological preparation may be poor (McCombe and Snell, 1991). In addition, accurate diagnosis of tumour extent is not possible, and neither is appropriate planning and performance of the operation. A definite indication for emergency tracheostomy can be uncontrolled haemorrhage from a large laryngeal cancer (Davis and Shapshay, 1980), a very rare form of presentation (none of our patients, and not reported in the series available, see Table I). Pre-operative radiotherapy has not proved to be

useful: only 2 of the 18 patients treated developed stomal recurrence, but 10 did recur locoregionally! (Breneman *et al.*, 1988).

One of our results looks controversial: the lack of association between stomal recurrence and the presence of lymph node metastases. In other words, the absence of cervical metastases is strongly related to peristomal relapse: only one out of 17 patients suffering recurrence at the tracheostomy site was found to bear metastatic neck nodes. In Montravadi's series, 58 per cent of the patients were found to bear neck metastases, but none of the tumours was subglottic, neck surgery consisted only in radical neck dissection on positive necks, and surprisingly, neither prior tracheostomy nor tumour size were related to stomal recurrence (Mantravadi *et al.*, 1981). Probably the absence of neck metastases in our series can be related to the site of the primary tumour (Fig. 4) and the type of neck dissection; our standard elective neck dissection does not include the paratracheal lymph nodes, and the stomal recurrences occurred more often on tumours with subglottic components. Barr *et al.* (1990) considered stomal recurrence to be part of a group of aggressive neck recurrences associated with more advanced disease before the laryngectomy. Weismann *et al.* (1979) reported similar results to ours, suggesting that stomal recurrences arise for heterogeneous causes. Certain events, such as preoperative tracheostomy, appeared more frequently than others in these patients, and no single factor or group of factors could explain all the recurrences.

The best treatment is prophylaxis, as surgical salvage is associated with significant morbidity and a poor success rate (Gluckman *et al.*, 1987): free surgical margins to avoid residual disease, wide resection of the tracheostomy tract, irrigation of the wound before closure with hypertonic solutions. If the tumour shows subglottic extension or evidence of deep infiltration, resection of the ipsilateral thyroid lobe—or total thyroidectomy—has been advocated (Harris and Butler, 1968; Harrison, 1971; Capella and Morello, 1978; Weismann *et al.*, 1979; Harrison, 1986; Lahoz *et al.*, 1989) as has dissection of the paratracheal lymph nodes (Harris and Butler, 1968; Harrison, 1971; Batsakis *et al.*, 1976; Capella and Morello, 1978; Weismann *et al.*, 1979; Harrison, 1986; Lahoz *et al.*, 1989). Manubrial resection helps the surgeon to clear adequately the paratracheal and upper mediastinal nodes, a technique with mininmal morbidity and no mortality (Harrison, 1990). The role of post-operative radiotherapy for the high risk patient will not be discussed.

Conclusion

Postlaryngectomy stomal recurrence is the most devastating late complication of laryngeal carcinoma. Its development is closely associated with subglottic extension, extralaryngeal spread of the primary tumour (T4) and prior tracheostomy. The origin of the stomal recurrence may be metastatic spread to the paratracheal and prelaryngeal lymph nodes, direct extension of the tumour and tumour seeding of the tracheostomy site. The best treatment is to avoid this dismal complication: patients showing subglottic involvement by the tumour should have prophylactic recurrent laryngeal lymphatic and superior mediastinal dissection, thyroidectomy and postoperative radiation therapy. There is also a rationale for irrigation of the operative wound with hypertonic solutions, as tumour cell implantation has proved to be a mechanism.

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