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CLINICAL STUDY

Motor features of voluntary cough following partial laryngectomy for glottal carcinoma

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Abstract: *Background:* Aspiration and respiratory tract infections are commonly observed in patients following conservative laryngeal surgery such as supracricoid laryngectomy with cricohyoidopexy (CHP). Since laryngeal closure is important for cough effectiveness, we hypothesised that CHP reduced cough intensity by affecting the cough motor pattern.

Methods: In ten male patients with laryngeal cancer eligible for CHP, we assessed the intensity of maximum voluntary cough (MVC) prior to and 2 months after surgery. Cough intensity was indexed in terms of both the peak amplitude of the integrated electromyographic activity of abdominal muscles (IEMGp) and the ratio of IEMGp to the duration of the expiratory ramp during cough (TEC), i.e. the rate of rise of IEMG activity (IEMGp/TEC). For each cough effort, the duration of the compressive phase (CP), the cough peak flow (CPF), the time elapsed from the onset of cough to CPF (TTP) and their ratio, i.e. the volume acceleration (VA), were also evaluated.

Results: CHP did not affect IEMG-related variables; in contrast, it reduced ($p<0.01$) CPF, CP and lengthened ($p<0.05$) TTP values. In consequence, cough VA values after CHP were consistently lower than in control condition.

Conclusions: Supracricoid laryngectomy with CHP alters the intensity of voluntary cough as indexed by flow-related variables. This may reduce cough efficiency and facilitate the onset and/or persistence of chest infections *(Tab. 2, Fig. 1, Ref. 22).* Full Text in free PDF *www.bmj.sk.*

Key words: cough, supracricoid laryngectomy, cricohyoidopexy, electromyography, airflow.

The cough motor pattern consists of three phases: an initial inspiratory phase, during which the glottis opens and the inspiratory muscles draw air into the lungs; a compressive phase, during which the glottis tightly closes and air is compressed within the lung, and an expulsive phase with glottal opening and subsequent, sudden expulsion of air (1–5).

Previous human studies (6, 7) have shown that, compared to control subjects, laryngectomised patients display a similar cough peak flow (6, 7), a lengthened time to cough peak flow [6], and a consequently reduced volume acceleration (7), both during voluntary (6, 7) and reflex cough efforts (7). These alterations in cough motor pattern and intensity may account, at least in part, for the association between total laryngectomy and subsequent respiratory complications, particularly aspiration and respiratory tract infections (8). Although respiratory complications are also common following conservative (or partial) laryngeal surgery (9), there seem to be no previous studies aimed to investigate the pattern and intensity of cough following this type of surgery.

We hypothesised that also partial laryngeal surgery has an impact on cough motor mechanisms and may therefore affect cough intensity. We set out to investigate the impact of conservative excision of the larynx on the motor pattern and intensity of voluntary cough, since objective evaluation of this type of cough has been reported (10) to predict the risk for aspiration.

Methods

Patients

Ten male patients, aged 47–78 years (mean 65.7 years), with a diagnosis of squamous cell laryngeal carcinoma participated in the study. According to the American Joint Committee for Cancer staging classification (11), two patients were classified as T1N1M0, while the remaining 8 patients were T2N1M0. None of them had previously received radiation therapy to the neck. All patients reported a previous smoking history; however, they had refrained from smoking soon after the disease had been diagnosed, i.e 1–3 months before inclusion in the study. Individual informed consent was obtained after detailed explanations of the procedures, but not of the purposes, of the study.

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Surgical procedure

All patients underwent the well-established CHP (12, 13). This surgical procedure consists of resecting the thyroid cartilage, the paraglottic space, the pre-epiglottic space, and the whole epiglottis, whereas the hyoid bone, the cricoid cartilage, and one or two arytenoid cartilages are preserved (12, 13). The reconstruction of the larynx is made by suturing the cricoid to the hyoid bone (12, 13). The attitude toward the arytenoid cartilage varied according to the preoperative laryngeal motility and the intraoperative assessment of the exact tumor extent (13). In the present study, four patients had the arytenoid on the tumor side resected, while in the remaining 6 patients both arytenoids were spared. An ipsilateral neck dissection sparing the accessory nerve, jugular vein, sterocleidomastoid muscle and resecting nodes was performed in 8 patients; the remaining 2 patients underwent bilateral neck dissection.

Experimental recordings and protocol

Most of the experimental procedures have been fully described elsewhere (7, 14, 15). All participants breathed through a No. 4 Fleisch pneumotachograph and a flow transducer (HP47304; Hewlett and Packard, Palo Alto, CA). The accuracy of the pneumotachograph-transducer assembly had preliminarily been assessed by using a calibration device similar to that developed by Petusevsky et al (16) and capable of generating high flow rates (range 0–7.5 l/s) by explosive decompression of air contained in a metal cylinder. Maximal voluntary cough (MVC) efforts were obtained by repeatedly encouraging each participant to cough as forcefully as possible as in a strong attempt at clearing of the airways. The lung volume at which these expulsive efforts were commenced was not controlled.

The force of expiratory muscles was measured by means of a portable pressure transducer (Spirovis, Cosmed, Italy) as the maximal static expiratory pressure (PEmax), i. e., the highest pressure generated by a patient against the closed airway and sustained for at least 1 s after a full inhalation to near total lung capacity (17). Patients were connected to the transducer by wearing a mouthpiece and a noseclip; during these measurements their cheeks and floor of the mouth were supported with the palm of the hands by an investigator. In all instances, participants were vigorously urged to exhale as hard as possible for the entire maneuver which lasted at least 4 s.

During PEmax manoeuvres and MVC efforts, the electromyographic (EMG) activity was recorded from the abdominal muscles using surface Ag-AgCl electrodes positioned 3 cm apart along the line of right obliquus externus fibers, with the lower medial electrode 10–20 mm lateral to the edge of the rectus sheath and just above the level of the umbilicus. The EMG activity recorded with these electrodes during cough was considered to reflect the activation of the obliquus externus muscle, as well as the activity of deeper abdominal muscles with minimal contamination of the EMG signal by the rectus abdominis electrical activity (14). The EMG signals were amplified, bandpass filtered, full wave rectified, and passed through a „leaky“ integrator (low-pass resistance *x* capacitance filter, time constant 50 ms) to obtain the so-called “integrated” EMG activity (IEMG). Prior to MVC recordings, participants were asked to change their posture and to simulate events such as throat-clearing; the IEMG wave forms evoked by these manoeuvres were compared with those recorded during voluntary coughing for differentiation.

All patients were studied on two different experimental sessions, the first (control condition) ~1 week before CHP and the second 58–65 days after the surgical procedure. During each experimental session, routine pulmonary function tests were performed in all participants. Reference values were taken from Morris et al (18). After completion of pulmonary function tests, patients were comfortably seat on a dentist’s chair provided with head- and arm-rests; they were repeatedly reminded to relax and breathe normally with as constant a pattern as possible. After few minutes of rest they were requested to perform 8–10 MVC manoeuvres, each separated by a ~10-s interval, during which both the expiratory flow and abdominal IEMG activity were recorded. Three to five reproducible (coefficient of variation less than 5 %) PEmax maneuvers were also performed. For each participant the recording were carefully inspected and all unsatisfactory samples were discarded.

Data collection and analysis

From the flow signals generated during each maximum cough effort, we measured the rate of cough peak flow (CPF), the time elapsed from the onset of cough to cough peak flow (TTP), and the duration of compressive phase (CP), i. e. the time elapsed between the end of the inspiratory phase and the onset of the subsequent expiratory phase. The ratio of CPF on TTP, i.e. the volume acceleration (VA), was subsequently calculated. During PEmax and for each MVC, the peak of IEMG activity ($IEMG_P$) and the duration of the rising phase of that activity (T_{EC}) were also measured. Since measurements of IEMG amplitudes recorded in different experimental session cannot reliably be used for within- and between-subject comparisons without adequate processing (7, 14, 15), all $IEMG_P$ values recorded in each participant during PEmax manoeuvres and MVC were expressed as a fraction of the highest $IEMG_P$ value recorded throughout each experimental session. The highest $IEMG_P$ value was attained during PEmax. The normalized $IEMG_P$ values, expressed as relative units, were subsequently used for all analyses. The ratio of $IEMG_P$ to T_{EC} ($IEMG_P/T_{EC}$), i.e. the rate of rise of IEMG activity, were subsequently calculated. In each subject, the static expiratory maneuver showing the highest PEmax value, expressed as a percentage of subject’s predicted value (17), was selected for analysis.

Comparisons between lung function variables observed during preoperative evaluation and after CHP were performed by the paired Wilcoxon test. The same statistical procedure was used to compare flow- and IEMG-related variables recorded before and after CHP. Reported data are means±SD, unless otherwise stated. In all instances, p<0.05 was taken as significant.

Tab. 1. Mean values (±standard deviation) of forced vital capacity (FVC), forced expiratory volume at 1 sec (FEV1), forced expiratory flow between 25 and 75 % of FVC (FEF25-75), peak expiratory flow (PEF) and maximal expiratory pressure (PEmax) recorded in control conditions (C) and after supracricoid partial laryngectomy with cricohyoidopexy (CHP).

	FVC		FEV1		FEF25-75		PEF		PEmax	
	l	%	l	%	l/s	%	l/s	%	cmH2O	%
C	3.80 (0.73)	96.82 (18.03)	2.81 (0.62)	90.55 (16.77)	2.14 (0.81)	69.25 (23.21)	7.99 (1.40)	97.73 (15.64)	133.8 (12.22)	101.82 (8.52)
CHP	3.47 (0.88)*	88.45(17.21)*	2.55 (0.72)*	82.82 (18.51)*	1.58 (0.74)*	50.75 (21.86)*	6.29 (1.22)#	80.27 (15.56)#	123.4 (15.82)	92.82 (12.86)

% – percent of predicted value; * – p<0.05; # – p<0.01

Tab. 2. Mean values (±standard deviation) of IEMG-related variables (peak amplitude of the integrated abdominal electromyographic activity during both PEmax and cough, IEMGp; time duration of the expiratory IEMG ramp during cough, TEC; rate of rise of IEMG activity during cough, IEMGp/TEC) and flow-related variables (cough peak flow, CPF; compressive phase, CP; the duration of time to cough peak flow, TTP; volume acceleration, VA) recorded in control conditions (C) and 2 months after supracricoid partial laryngectomy with cricohyoidopexy (CHP).

	IEMG-related variables				Flow-related variables			
	PEmax	MVC			MVC			
	IEMGp (RU)	IEMGp (RU)	TEC (s)	IEMGp/TEC	CPF (l/s)	CP (s)	TTP (ms)	VA (l/s2)
C	0.83 (0.35)	0.80 (0.18)	0.22 (0.11)	3.81 (0.26)	4.71 (1.25)	0.25 (0.09)	35.12 (9.2)	140.89 (45.2)
CHP	0.85 (0.55)	0.81 (0.39)	0.23 (0.10)	3.68 (0.84)	3.97 (0.93)*	0.02 (0.06)#	48.25 (7.1)*	82.22 (14,34)#

RU – relative units; MVC – maximum voluntary cough; * – p<0.05; # – p<0.01

Results

Respiratory function data recorded during preoperative assessments and after CHP are summarized in Table 1. Forced expiratory flows recorded after CHP were significantly ($p<0.05$) lower than the corresponding values obtained in control conditions (Tab. 1); in contrast, PEmax values recorded during preoperative conditions and after CHP were similar (Tab. 1).

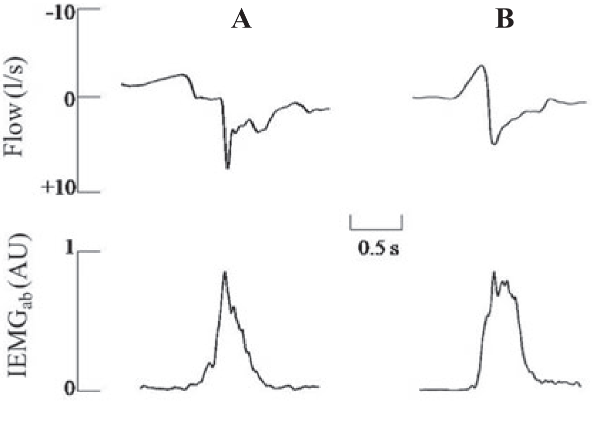

Fig. 1. Representative, original recordings of airflow and integrated electromyographic activity (IEMG) of the abdominal muscles obtained during maximal voluntary coughing in pre-operative condition (left panels) and after supracricoid partial laryngectomy with cricohyoidopexy (right panels). Compared with preoperative, control condition, patient commonly displayed absence of compressive phase and a reduction of cough peak expiratory flow during intense cough efforts voluntarily produced.

As reported in Table 2, mean values of $IEMG_P$ recorded after CHP during both PEmax manoeuvres and MVC did not significantly differ from the corresponding values obtained in control conditions. Similarly, mean values of T_{EC} and IEMGp/T_{EC} recorded during MVC in control conditions did not significantly differ from those obtained after CHP (Tab. 2). In contrast, CHP caused a significant reduction ($p<0.01$) in mean CPF and CP values (Tab. 2). In most patients (n=8, 80.0 %), CHP actually led to disappearance of CP (Fig. 1). Furthermore, after CHP, TTP values were significantly ($p<0.05$) longer than in control conditions (Tab. 2). Thus, cough VA values (i.e., the ratio of cough peak flow to the corresponding time to peak) after CHP turned out to be consistently lower than those observed in pre-operative conditions. Representative original recordings of cough expiratory flow and IEMG activity obtained in control condition and after CHP are reported in the figure.

Discussion

The novel and important finding of this study is that intensity of voluntary cough, when indexed in terms of cough peak expiratory flow, and volume acceleration, is reduced after supracricoid partial laryngenctomy with CHP. In contrast, the simultaneously recorded abdominal IEMG activity is unaffected by the surgical procedure. Of note, values of spirometric variables (i.e. the forced vital capacity, the forced expiratory volume at 1 sec, the forced expiratory flow between 25 and 75 % of forced vital capacity, and the peak expiratory flow) recorded during a forced expiration were similarly reduced.

In most animal species and in humans, the larynx is implicated in complex behavioral and homeostatic functions, such as respiration, swallowing, voice production and coughing. As for the cough reflex, several animal studies have investigated the temporal relationships between the pattern of activation of the intrinsic laryngeal muscles (i.e. the posterior cricoarytenoid abductor muscle, and the thyroarytenoid and lateral cricoarytenoideus adductor muscles) and the ongoing mechanical events (1, 19, 20). These studies indicated that, at the laryngeal level, coughing requires control of the glottis by a well-coordinated sequence of activation of both abductor and adductor laryngeal muscles (1, 19, 20). More precisely, during the inspiratory phase of cough, contraction of the abductor muscle reduces upper airway resistance and, along with diaphragm activation, promotes inspiratory flow. During the subsequent compressive phase, the laryngeal adductor muscles close the glottis, while the abductor display minimal activity. During the expulsive phase of cough the abductor muscle of the larynx is recruited while the adductors are suppressed (1, 19, 20). These phenomena would open the glottis and, along with the activation of expiratory muscles, promote expulsion of air from the lungs. Interestingly, a previous study (21) performed in humans confirmed that during volitional cough laryngeal adductor muscles are active during the compressive phase of cough, and that adduction occurs immediately following inspiration to close off the upper airway and raise intrapulmonary pressure. Furthermore, as in the animal studies (1, 19, 20), the posterior cricoarytenoid muscle activates for vocal fold abduction at the onset of the expulsive phase of cough (21). Taken together, these observations emphasize the role of the larynx and, consequently, the importance of its anatomical and functional integrity in the genesis of motor pattern of coughing.

The CHP is an alternative to radiation therapy, near total and total laryngectomy in selected cases of glottal carcinoma (12, 13). This procedure is considered as a conservative surgical laryngeal technique, as it preserves physiological rehabilitation of speech, swallowing, and respiration without a permanent tracheostomy (12, 13). However, like total laryngectomy, this organ-preservation surgery is frequently associated with postoperative complications, including swallowing disfunction, aspiration and airway infections (9). In the present study we investigated the motor pattern of voluntary cough efforts in patients who underwent conservative surgery of the larynx. From the cough flow tracing, we measured or calculated several variables that may be relevant for assessing the intensity of a cough effort. We found that, after CHP, loss of the compressive phase occurred, i.e. the functional aspect that differentiates cough from other respiratory expulsive manoeuvres (1). In addition, the cough peak flow rate decreased, along with a lengthening of the time required to achieve the cough peak flow. In consequence, volume acceleration decreased markedly. The impairments in these airflow-related variables observed during voluntary coughing, along with the finding of a reduced peak expiratory flow during forced expiration, observed in our patients after CHP, cast doubts on the assumption that conservative surgery of the larynx has no major impact on patients' airway clearing capacity (22); rather, the observed phenomena support the possibility of an impaired cough motor response after CHP. A weakened expulsive capacity of cough after CHP may facilitate the spreading of an initial airway infection and partly accounts for the occurrence of postoperative respiratory complications in these patients.

The results of the present study also indicate that, during voluntary cough, the peak and rate of rise of the integrated IEMG activity recorded after CHP were similar than those in control conditions. This finding is in keeping with previous observations obtained in our laboratory showing that, in patients with total laryngectomy, IEMG activity recorded during voluntary cough is similar to that observed in normal subjects (7). These findings indicate that the central command from to the respiratory muscles is unaffected by partial laryngectomy, and that the reduction in flow-related variables must be due to local (laryngeal) changes which prevent full expression of muscle force dictated by respiratory muscle activation. It may be hypothesized that in the absence of a fully functional larynx leading to partial and/or short lasting upper airway closure, optimization of the force-length-velocity relationship of the expiratory muscles fails, even in the presence of adequate muscle activation (4). In consequence, the resulting expiratory flow of voluntary cough is reduced compared pre-operative conditions. In addition, the presence of airway obstruction after CHP, as documented by the reduction in forced expiratory flows, also accounts for the decrease in CPF, and index which is well known to be affected not only by the force of the expiratory muscles, but also by the airway patency.

In conclusion, the findings suggest that patients who underwent conservative surgery of the larynx have an impaired cough motor pattern. This, along with the well known swallowing disturbances, may account for the onset and/or persistence of airway infections. Further investigations are required to clarify if the alterations of cough intensity and motor pattern induced by CHP persists beyond two months after surgery, and, perhaps more importantly, to assess their influences on the patients' quality of life and frequency of occurrence of airway complications.

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