Chapter 7

Voice profile after type I or II laser cordectomies for T1a glottic carcinoma

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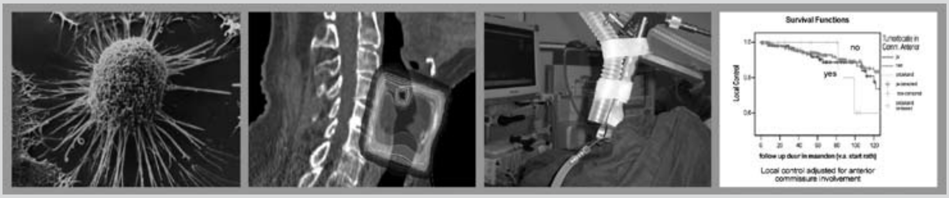

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Introduction

Carbon dioxide endoscopic laser surgery (henceforth laser surgery) is an established treatment modality for superficial T1a midcord glottic carcinoma. Although no randomized trial has yet been performed, from retrospective data local control rates can be considered at least comparable to those for radiotherapy (1). In addition to other benefits (lower cost and shorter treatment time), laser surgery as a primary treatment option should theoretically also lead to lower laryngectomy rates as it allows for additional resections and the added possibility of radiotherapy in the case of recurrent disease, although to our knowledge no study has as of yet been published to prove this.

However, the use of laser surgery in T1 glottic carcinoma is still largely restricted to superficial T1a midcord carcinomas. Dutch guidelines advocate the use of laser surgery only in lesions that are removable by a subepithelial or subligamental resectrion (type I or II, ELS classification). In larger lesions, radiotherapy still is the primary treatment. An important reason for this strategy is the uncertainty over post-operative voice quality in larger resections. The expected post-operative voice quality therefore plays a major role in deciding on a treatment strategy.

Several studies have investigated voice quality after laser surgery. Although overall voice quality has generally been found to be good, there is still uncertainty among surgeons as to the type and severity of voice disability that patients can expect. Possibly this is because many reports are of small, non-consecutive and/or poorly described patient series. In addition, the voice analysis methods that are used lack uniformity, reliability and validity. The European Laryngological Society (ELS) concluded already in 2000 that there is no single voice analysis method that adequately describes both voice function and quality and that the assessment of disordered voices thus needs to be multidimensional. They therefore implemented a basic protocol (2;3). This protocol evaluates three aspects of the voice: quality, function and performance and is composed of the following:

Quality:
- perceptual analysis (grade, roughness, breathiness of the GRBAS-scale)
- acoustics (jitter, shimmer, Fo-range and softest intensity)

Function:
- stroboscopy (closure, regularity of vibration, mucosal wave and symmetry)
- aerodynamics (phonation quotient)

Performance
- subjective rating by patient (Voice Handicap Index [VHI])

Although several studies have since then implemented aspects of this protocol (4-7), it is still often used incompletely and the various components of the protocol are mostly reported separately, without looking at their (possible) interaction. Also, there is some discrepancy between the reports as to the characteristics of the lasered voices in auditory perception. The aim of our study was therefore to determine if we could define a “typical” voice in terms of auditory perception for patients treated with laser surgery (type I or II cordectomies) for T1a midcord glottic carcinoma. Secondly, we aimed to investigate to which extent any of the other ELS parameters where related to this “typical” voice, hopefully forming one integrated voice profile for use as a guide in patient counseling and as a base of comparison in further studies of voice outcome.

Patients and method

Patients

From October 1996, patients with early glottic cancer (Tis/T1) with single, mid-cord lesions not extending into the anterior commisure are primarily offered carbon dioxide endoscopic laser excision at our institution, as opposed to the earlier standard treatment of radiation therapy. Because this was a study where the procedures administered were all part of standard clinical voice evaluation, the study was exempted from institutional review board approval. For most patients the appointment coincided with one of their routine follow-up appointments. Before surgery, all patients are staged by direct laryngoscopy and have biopsy proven squamous cell carcinoma. Laser surgery is performed only on mid-cord lesions when estimated that at least a 2-mm margin within the affected cord can be obtained either by a subepithelial or subligamental resection. This is in accordance with the Dutch National Guidelines for T1 glottic carcinoma and corresponds to a type I or II cordectomy according to the ELS classification (8;9). The final decision to perform laser surgery is therefore made during direct laryngoscopy. The surgical technique consists of an en bloc resection with sampling of margins when deemed necessary.

For this study, all 72 T1a lesions treated with laser surgery since the introduction of the technique at our institution in October 1996 were reviewed. Deceased patients (n=9), patients with recurrent (n=3) or residual disease requiring further treatment (n=12) and patients who had undergone additional vocal cord surgery for benign lesions (n=6) were excluded In 2000, 15 patients had already participated in the evaluation of their current voice quality according to the standard protocol used in our clinic for voice evaluation, closely resembling that of the ELS (data not published). In 2007, the remaining patients were contacted and asked to undergo the same protocol. Of the total 42 patients eligible for the study, 5 declined to participate, all due to unrelated health or social problems. As a result, voice quality was evaluated in 37 consecutive patients with primary T1a glottic carcinoma, treated by either a subepithelial or subligamental resection, corresponding to a type I or type II cordectomy as described by the ELS. The 2000 and the 2007 data were pooled and presented for evaluation in a random, blinded manner. The data from 2000 were thus re-evaluated for this study.

Voice quality, function and performance: multidimensional protocol

Stimulus material and procedure

Speech material was recorded on the same equipment for both groups. All speech material was recorded in a sound treated room, using a Dynamic Røde NTI Microphone, a Behringer Ultragain pre-amplifier and a Sony DTC-ZE 700 DAT recorder. The mouth-to-microphone distance was kept constant at 20 cm. Speech material for the perceptual analysis consisted of a standard, phonetically balanced Dutch text ("80 dappere fietsers") with a neutral content that was read aloud – at a comfortable level – by each subject, and recorded. Subjects were also asked to sustain a vowel, /a/, for as long as possible after maximal inspiration, and at spontaneous, comfortable pitch and loudness. The better of two attempts was used for further analysis Vital Capacity (VC: the volume change at the mouth between the position of full inspiration and complete expiration) was measured using a hand-held spirometer.

Perceptual analysis: GRBAS (quality)

Perceptual analysis of voice quality was done using the GRBAS-rating scale, based on the work of Isshiki 1969 (10). Running speech samples were presented in random order. A panel of six experienced listeners familiar with the GRBAS-system rated all the speech samples by consensus. In those instances where the judges rated voice quality differently, consensus was reached through re-evaluation and discussion.

Acoustics and aerodynamics (quality and function)

Analyses were performed on a stable, 2-second mid-section of the sustained /a/. The following parameters were measured in PRAAT, software for acoustic analyses (11): the average fundamental frequency (in Hz); percentage jitter; percentage shimmer and the harmonics to noise ratio. Although recommended in the ELS protocol, softest intensity and Fo-range was not analyzed as it had not been recorded in all patients. Aerodynamic measures consisted of the maximum phonation time (MPT) in seconds, the vital capacity (VC), and phonation quotient (VC/MPT in mL/s).

Videostroboscopy (function)

Videostroboscopy was performed using a Wolf rigid endoscope (Model 4450) and a Wolf stroboscope (Model 5012) by an experienced laryngologist. The endoscope was connected to a Sony camera (Model DXC-101P) and a Panasonic video recorder (Model NV-L25HQ). Speakers were asked to sustain /i/ at a comfortable pitch and loudness. A panel of six experienced raters judged the following parameters by consensus: glottic closure, mucosal wave, symmetry, non-vibrating parts and supraglottic involvement. These parameters, some of which are included in the ELS protocol (12), are a selection of the parameters advocated by Hirano and Bless, 1993 and were rated along these general lines.

Subjective rating: Voice Handicap Index (performance)

Evaluation of voice impairment experienced by patients was performed using a validated Dutch version of the Voice Handicap Index (VHI) (13). A total score of 15 points or more out of a possible 120 is taken to indicate voice impairment in daily life (13;14). The patients completed the questionnaires (unaided by the investigators).

Statistical methods

The Fisher's exact test of association was used to test the difference in various subgroups of the patient population, and for correlations with dichotomous variables. The student's t-test was used to test differences between means. Associations were tested with Pearson's correlation. A strong correlation was defined as having a correlation coefficient larger than 0.8.

Results

Patient characteristics are listed in table 1. Average follow-up was calculated in months from the date of treatment. All patients entered into the study agreed to participate in the self-assessment of voice quality. However, 3 patients declined to participate in the acoustic, aerodynamic and stroboscopic evaluation due to the perceived discomfort associated by them with the examinations. Therefore, for acoustic, aerodynamic and stroboscopic analyses there were 34 patients. Furthermore, 3 patients failed to fully complete the VHI questionnaire resulting in 34 patients being available for evaluation.

Voice assessment (multidimensional protocol)

Auditory perception: GRBAS (quality)

The types and severity of the dysphonia found in GRBAS evaluation are shown in table 2 and 3. In total, 65% of the voices were rated as dysphonic. Breathiness was found in (59%)

Table 1 | Patient characteristics.

Patient characteristic	
n	37
mean age (years)	67
range (years)	38-81
Female (n)	5
smokers / ex-smokers**	33
mean FU* (months)	34
range FU (months)	6-83

Abbreviation: * FU, follow-up from date of diagnosis
** ex-smokers defined as > 10 years ago

Table 2 | Type of voice pathology in GRBAS evaluation (in panel of 6 experience raters by consensus).

GRBAS	Laser	
type of pathology	n=34*	%
No pathology	12	35%
Roughness	5**	15%
Breathiness	20	59%
Both roughness and breathiness	4	12%
Asthenia	11	32%
Strain	6	18%

* three patients declined to participate in perceptual analysis
** of which 2 intermittent only

Table 3 | Sseverity of perceptual quality in GRBAS evaluation (in panel of 6 experience raters by consensus).

GRBAS grade of perceptual quality	Laser	
	n=22*	%**
Overall Grade		
1 (mild)	15	68
2 (moderate)	6	27
3 (severe)	1	5
Roughness		
1 (mild)	3	60
2 (moderate)	0	0
3 (severe)	0	0
intermittent	2	40
Breathiness		
1 (mild)	13	65
2 (moderate)	6	30
3 (severe)	1	5
Asthenia		
1 (mild)	9	82
2 (moderate)	2	18
3 (severe)	0	0
Strain		
1 (mild)	4	66
2 (moderate)	1	17
3 (severe)	1	17

* pathological voices only
** percentage patients with that particular perceptual characteristic

of patients, followed by asthenia (32%), strain (18%) and roughness (15%), in which 2 out of the 5 cases were intermittent. As for the severity of the dysphonia, overall grade was most commonly classed as mild (68%) compared to moderate (27%) or severe (5%) (table 3). The mean overall grade for dysphonia was 1.4. The resulting perceptual profile for dysphonic voices (normal voices excluded) is portrayed in figure 1. It shows the mean score on the GRBAS with the standard deviation. As can be seen from the profile, the grade was largely determined by the component of breathiness. Consequently, breathiness was the only parameter that showed a strong correlation with grade (Pearson's correlation coefficient 0.94, $p<0.001$ as opposed to roughness 0.34 $p=0.052$, asthenia 0.46 $p=0.07$ and strain 0.43 $p=0.012$). The perceptual analysis was plotted against the length of follow-up (<=2 years or >2 years) (figure 2). This showed that the average grade for the dysphonia was lower after 2 years although this was not statistically significant (1.15 versus 0.71, Student's t-test $p= 0.13$). This was because a normal voice was (grade =0)

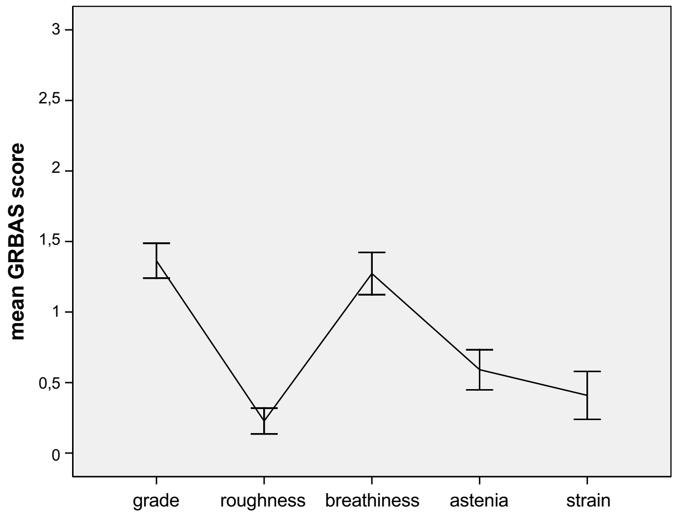

Figure 1 | Perceptual profile (GRBAS): mean with standard deviation in type I / II cordectomy voices (midcord T1a glottic carcinoma).

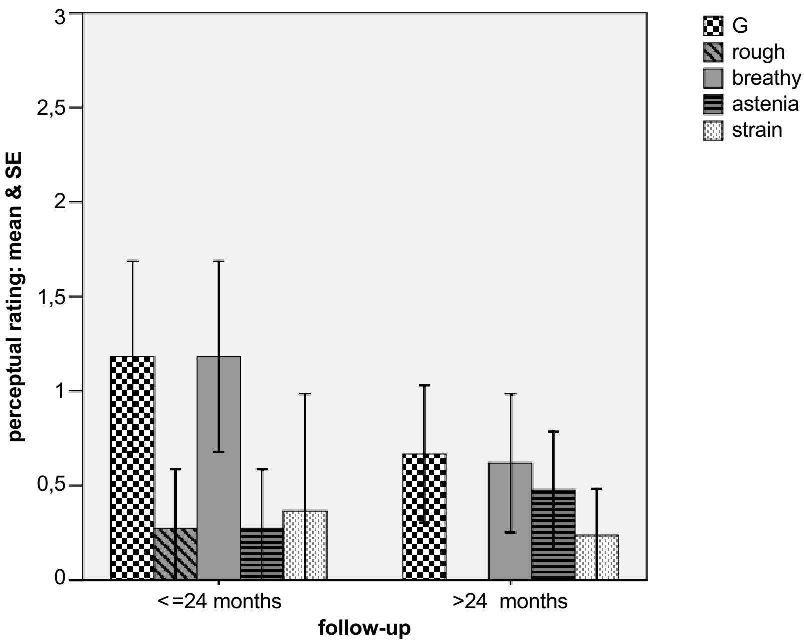

Figure 2 | The average rating (GRBAS-profile) relative to follow-up

Student's t-test for grade <=24 months (n=14) versus >24 months (n=20) p=0.13

was more common in patients with more than 2 years of follow-up, suggesting that some voices may normalize after time, although the difference did again not reach statistical significance (Fisher's exact test p=0.08).

Subjective rating: Voice Handicap Index (performance)
The total score on the voice handicap was normal (<15) in more than half of the patients (n=19, 56%). The mean score of 19 was slightly elevated. However, the distribution of the scores was skewed as the median of 13 score was lower than the mean. This indicates that the voice handicap for most patients was minimal with a minority of the patients being more severely affected. When plotted against the length of follow-up the average VHI score decreased after the first year from a mean value of 28 to 17, both in the second year and after. However, the decrease did not reach statistical significance (student t-test between <=12 months and 13-24 months p= 0.27).

Agreement between Voice Handicap (performance) and GRBAS (quality)
We also investigated, in the whole group (n=31 as 3 patients declined to participate in the acoustic evaluation and a further 3 did not complete the VHI correctly), the measure of agreement between the patients' perception of their voice impairment and the perception of voice quality as rated by experienced listeners in perceptual analysis. Trained listeners considered 65% (n=22) of voices deviant (grade >0) whereas the VHI showed that only 44% (n=15) of patients felt that they experienced significant physical, functional and/or emotional consequences of voice impairment (VHI>15). Seventy-six percent of patients with a normal VHI were judged to have some degree of deviant voice quality in perceptual analysis. In contrast, 43% of patients with an increased VHI were judged to have a normal voice (table 4). In line with this, the correlation between the VHI score and the severity of perceptual voice quality was weak (Pearson's correlation coefficient = 0.365, p=0.04, figure 3).

Acoustic (quality) and aerodynamic analysis (function)
Average values for the different acoustic and aerodynamic parameters together with two separate sets of reference values and correlations with the grade (GRBAS) and total VHI

Table 4 | Cross-table showing relationship between VHI and grade in perceptual analysis (normal versus increased; n=31 see text).

	Grade normal (=0)	Grade increased (1-3)
VHI normal (=<15)		
n	4	13
%	24%	76%
VHI increased (>15)		
n	6	8
%	43%	57%

Abbreviation: VHI, voice handicap index
Fisher's exact test p=0.44

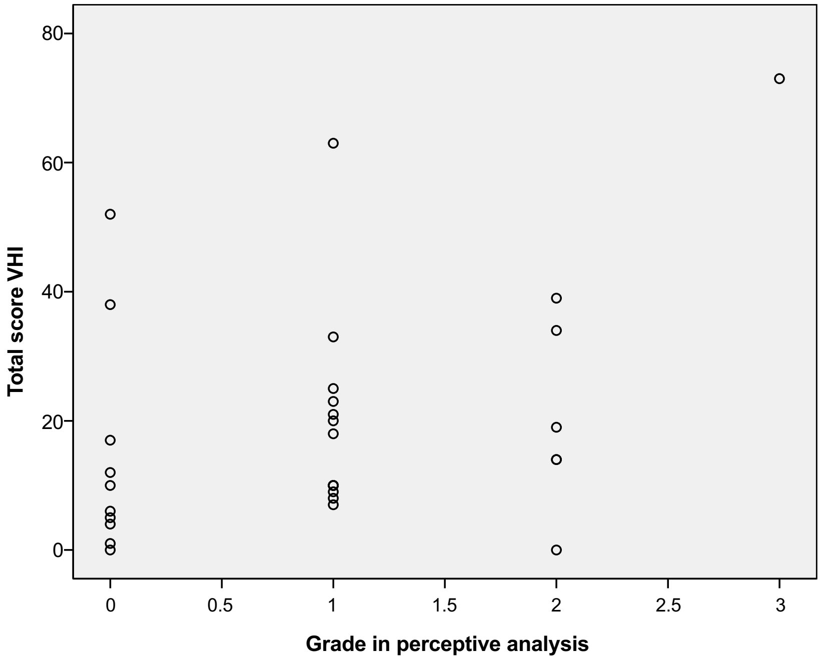

Figure 3 | Correlation between total score in the VHI and grade in perceptual analysis
Pearson's correlation coefficient 0.365, p=0.04

score are shown in table 5. The pitch perturbation measures % jitter, % shimmer and HNR which are associated with roughness and breathiness in literature, were all only slightly elevated compared to normal reference values. All correlations between acoustic parameters and grade were weak (see table 5).

Videostroboscopy (function)

Three patients declined to participate in the stroboscopic exam. In a further 7 patients the exam was not, or only partially, assessable. Videostroboscopy showed abnormal patterns of vibration in all patients but 1 (table 6). More than half of the patients (62%) had incomplete closure of the vocal folds. The symmetry and the vibratory pattern of the laser treated vocal fold was normal in only 1 patient (3%). Twenty-two (65%) patients had a reduced mucosal wave (including 5 patients with only a partially vibrating vocal fold) and in 6 patients (17%) it was absent. There were signs of ventricular compensatory activity in 17 (59%) patients. The percentage of patients with incomplete closure (n=18, 62%) corresponded to the number of patients judged to have breathiness in the GRBAS evaluation (59%). However, the two subpopulations did not completely overlap. Four out of 17 assessable patients (24%) judged to be breathy had complete closure in the stroboscopic exam. However, the chi-square test did show a trend for an association between breathiness and incomplete closure (p=0.57).

Table 5 | Average values for acoustic parameters with reference values (normal) and Pearson's correlation coefficients for GRBAS and total VHI score.

Acoustic/Aerodynamic Parameter	n=34*	normal 1	normal 2	g
Fox males	136	Appr 120	–	0.414
Fox females	209	Appr 220	–	0.484
jitter%	0.57%	<0.4	0.23–2.97	0.391
shimmer%	4.60%	<3.8	0.91 -6.71	0.187
HNR (dB)	17.26	>=20	–	-0.494
vc (ml)	2985	–	932-6300	-0.068
mpt (s)	34	–	9-43	-0.421
vc/mpt (mL/s)	87.8	–	75-379	0.418

Abbreviations: VHI, voice handicap index; Fox, mean fundamental frequency; HNR, harmonics to noise ratio; vc, vital capacity; MPT, mean phonation time; vc/mpt, phonation quotient
normal 1: values derived from Praat manual
normal 2: range found for 68 normal voices (26)
g (correlation coefficient for grade)
* three patients declined to participate in acoustic and aerodynamic analysis

Table 6 | Stroboscopic evaluation (by panel of 6 experience raters and consensus obtained)

Parameter Stroboscopy	Laser	
	n=34#	%
Closure		
complete	11	32%
incomplete*	18	53%
not assessable	5	15%
Symmetry		
symmetric	1	3%
asymmetric	26	76%
not assessable	7	21%
Mucosal wave		
normal on lasered side	1	3%
reduced on lasered side	22	65%
absent** on lasered side	6	17%
not assessable	5	15%
None-vibrating parts***		
yes	11	32%
no	21	63%
not assessable	5	15%
Ventricular activity		
yes	17	50%
no	12	35%
not assessable	5	15%

3 patients declined to take part in stroboscopic evaluation
* incomplete = any incomplete closure pattern
** absent = totally absent over entire fold
*** non-vibrating parts = non-vibrating segment somewhere on fold

Discussion

In this study we investigated if we could define a "typical" lasered voice in terms of auditory perception for patients with a type I or II resection for T1 midcord glottic carcinoma. Secondly, we investigated to which extent any of the other ELS parameters where related to this typical voice for patients with T1a glottic carcinoma treated with superficial laser resections (type I/II). We found that a third of our patients (35%) had a normal voice, whereas 65% had some degree of dysphonia in analysis by trained listeners (GRBAS). The grade of the deviation for the whole group was mild (mean grade 0.9). When normal sounding voices were excluded the mean grade in the remaining patients rose to 1.4. Therefore, although still relatively mild, deviation may have been underreported in earlier studies that include all patients in the outcome. As for the perceptual profile it was characterized mainly by breathiness followed by asthenia and strain. Standard deviations were small, indicating that the profile was representative for our population (fig 1). Breathiness was the dominant feature of our population and was in turn associated with incomplete closure. This is in line with a pathophysiological model in which tissue loss due to laser resection causes incomplete closure which in turn is related to breathiness (15). It may, however, be difficult to accurately judge closure in the stroboscopic exam. Especially as recordings often consist of only a few cycles and closure may vary from cycle to cycle.

Compared to similar studies in literature (table 7) it is interesting to see that roughness, not breathiness was the dominant feature in two Italian studies (4;5) A possible explanation for this might be that qualitative measures of voice such as roughness may also be influenced by culture. Our classification of roughness does not include "vocal fry". The reason is that vocal fry is classed as a physiological mode of vibration, just as chest voice or falsetto are different modes of vibration. However, in other studies it may have been classed as roughness (16;17).

The overall grade of the dysphonia in these two studies was also lower than in our population. This may well be explained by a proportion of "normal" voices included in these results. Our results are more in line with those of a recent study by Roh (7) who also found a predominance of breathiness, although these results may also be "diluted" by normal voices.

Table 7 | VHI and GRBAS in earlier studies.

Author	G	R	B	A	S	VHI
Peretti (5) 2003 type I/II*	0.8	0.8	0.2	0.04	0.0	-
Ledda (4) 2006 type I/II*	0.8	1.0	0.6	0.8	0.6	-
Roh 2007 (7) type I/II	1.5	1.2	1.4	-	1.3	11
Sjögren (this study) type I/II	1.4	0.1	1.3	0.6	0.4	19

Abbreviation: VHI, voice handicap index
*mean calculated for type I + type II values

As for the relationship between auditory perception and the other ELS aspects, the overall associations were poor. The impairment as experienced by patients was mild, indicated by only a slight elevation of VHI scores (mean=19, median 13). This handicap was highest in the first year after surgery and decreased after that, although as the decrease did not reach statistical significance we can again not exclude the possibility that this was due to chance. It is interesting that higher values were found for the VHI in several forms of benign voice pathology in two recent studies (18;19). Van Gogh found a VHI of around 40 for vocal fold paresis, structural lesions and edema. Brouwers found a VHI of 48.9 for a heterogeneous population with benign voice disorders. After treatment, this decreased to 28.3, which is still higher than in our population. We believe that this is (partly) due to an adaptation mechanism that may be stronger in cancer patients than in patients with benign voice/vocal fold disorders. This is illustrated by the outcome in a recent study by Roh where patients rated as a grade 2.7 (severe dysphonia) after a type IV resection reported a voice handicap of only 27 (out of 120).

Another important observation in this study was that trained listeners considered 65% (n=22) of voices deviant (grade >0) whereas the VHI showed that only 44% (n=15) of patients felt that they experienced significant physical, functional and/or emotional consequences of voice impairment (VHI>15). Furthermore, the correlations between the severity (grade) of the perceptual voice deviation and the VHI score were found to be weak (0.365). Illustrating this, one patient who reported no handicap (VHI <15) was judged as having a severe dysphonia (grade 3), whereas another patient who reported an increased voice handicap of 35 was judged to have no dysphonia (grade 0) in perceptual analysis. This illustrates that the amount of physical, functional and/or emotional voice impairment experienced by the individual patient is not necessarily related to the amount of dysphonia perceived by others. The VHI therefore provides important complimentary information to the other dimensions of voice assessment showing that the patient's perception of his or her handicap is probably governed by several other factors than the physical limitations created by the laser surgery alone. For instance, that the VHI is high in a minority of patients, regardless of perceptual rating, may partly be explained by the fact that patients with routine voice use can have significantly lower VHI scores than those with more intensive vocal demands (20). We believe additional instruments such as the Illness Perception Questionnaire (21) may offer more insight into the perception of voice impairment, or the lack thereof. Given that the amount of voice handicap experienced is generally low and unrelated to ratings of dysphonia implicates that it might be possible to perform more extended resections (with poorer perceptual outcome without substantially increasing the impairment experienced by most patients), thereby gaining the advantages of laser surgery over radiotherapy in larger T1 orT2 lesions discussed in the introduction. Ultimately the challenge will be to identify patients with increased risk of reporting voice impairment, regardless of perceptual rating, after treatment.

The values in acoustic analysis were all only slightly elevated from normal reference values. It must however be realized that the range for acoustic values in normal patients are large as can be seen form the second set of reference values in table 5. There is therefore a considerable overlap in acoustic parameters between the “perceptually” normal population and patients with mild dysphonia, which has also been shown by Ma and Yiu (22). Furthermore, research by Kreiman and Gerratt suggests that jitter and shimmer are not useful as independent indices of voice quality, because of listeners’ insensitivity and inability to isolate these pitch perturbation measures as separate dimensions in the overall pattern of perceived aperiodicity (23). Because of this and because these pitch perturbation measures give information about pitch variability and do not explain other sources of noise, such as turbulent airflow or nonlinear movement of vocal fold tissue adequately, a detailed acoustic profile of the laser treated voice was not judged to be meaningful. Non-linear measures more appropriate for this purpose are being developed and may prove better suited in the future (24;25).
Despite 35% of voices being normal in perceptual analysis and even 47% being judged as normal in self-evaluation, videostroboscopy showed dysfunction in all patients but one, with incomplete closure in 62% of the patients and reduced mucosal wave in all assessable patients but one. This illustrates that not all structural anomalies have a clinical impact.

In summary, 65% of patients treated with a type I or II laser resection for T1a midcord glottic carcinoma have dysphonia in auditory perceptual analysis. The typical laser treated voice is dominated by mild breathiness. Correlations between auditory perception and other parameters are weak. We therefore conclude that stroboscopy, VHI, perceptual and acoustic analyses measure separate, but complimentary aspects of the disordered voice, and these outcomes do not form one integrated voice profile. Indeed, the ELS introduced their own guideline for the current multidimensional voice assessment protocol with this caution: “it is not to be considered as the ultimate way to basically assess the voice”. The ELS therefore stated that further research work is needed and that “new and more sophisticated measurements or evaluation techniques are to be encouraged”. For example, acoustic parameters need to be identified that adequately describe disordered voice production. Also, given the poor inter- and intrarater reliabilities associated with both stroboscopy and perceptual rating, different assessment or rating approaches will have to be developed, so that voice professionals can establish clinically relevant, integrated voice profiles for use in patient counseling and clinical outcome studies.

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