

A randomized prospective controlled study of acoustical measures of laryngopharyngeal reflux

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Introduction

- With high speed films it has been possible to document treatment effect of Laryngopharyngeal reflux in a randomized controlled way.
- The statistical difference was significant comparing subjective complains related to oedema of the arytenoids regions. Acoustical differences and EGG changes were not found in a statistical overview.

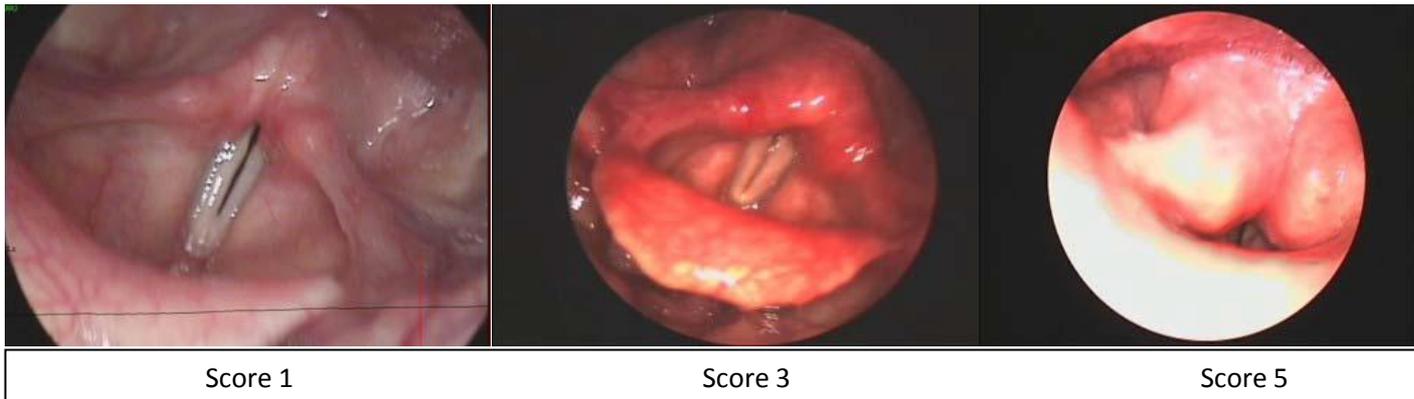
- The aim of this prospective randomized study was to try to find out how acoustical analysis with the Multi dimensional voice program by Laryngograph Ltd. on sustained tones as well as reading of a text seemed not to be sufficient, in **documenting treatment effect of acoustical voice related laryngopharyngeal reflux.**
- Laryngopharyngeal reflux might not influence the speaking voice, related to the fundamental frequency. Further studies should be made on the singing voice.

Material

- All participating patients had signed a written consent, which was scanned and stored in the database. Patients were randomized into three groups of treatment with lifestyle guidance as for Gastroesophageal reflux, lifestyle correction + proton pump inhibitors (esomeprazole) 1 tablet daily 40 mg and a group with supplementary alginate 1 tablet after the evening meal.
- All the included patients were aged 18 or over.
- The required symptom duration for inclusion was at least 2-4 weeks. Each participating patient had, as minimum, three subjective complaints of Laryngopharyngeal reflux. The objective findings of inter-arytenoid oedema, documented with high speed films, was also required for the inclusion to the study. It was based on a visual scale 1-5.
- *Avoid the following acid provoking food: smoking, fatty and smoked food, coffee, chocolate, spices, strong alcohol (alcohols containing a lot of tannins), acidic fruits and juices. No food after 9:00 pm, avoid over eating. You should sleep with your head high. Singers should avoid eating just before a concert.*

FIGURE 1

Visual scores of oedema of the arytenoid regions on highspeed films (score 1 normal arytenoids, score 3 most often seen oedema at the first examination, score 5 nearly closed larynx due to arytenoid oedema).



The specific Laryngopharyngeal reflux symptoms were:

- Hoarseness or a problem with your voice
- Clearing your throat/excess throat mucus or postnasal drip
- Difficulty swallowing food, liquids, or pills (dysphagia)
- Coughing after you ate or after lying down, troublesome or annoying cough
- Breathing difficulties or choking episodes (larynx spasms and hick up)
- Sensational of something sticking in your throat or lump in your throat (globules)
- Heartburn, chest pain, indigestion or stomach acid coming up, pain or burning feeling in the throat.

Method

- The Multi-Dimensional Voice Program (MDVP by Laryngograph Ltd.) was combined with the subjective complaints and the high speed films (Wolf Ltd. 4000 pictures/sec. for 2 sec.), and all parameters were stored in the software program based FileMaker Pro 8.5. The high speed films were recorded with the standard equipment from Wolf Ltd.
- The Multi-Dimensional Voice Program was used for sustained tones and reading of a standard text measuring fundamental frequency (Fo), intensity (dB), and electroglottograms with percent variation and irregularity measuring the percentage of laryngeal cycles which have bigger cycle-to-cycle changes than a threshold. (Fx 3% threshold, Qx 6 % threshold).
- *The sustained tones were “ah” in the patient’s spontaneous speech area and the standard text: “the North wind and the Sun”. The measurements were made in the ear- nose- throat clinic with background noise between 50-60 dB. Storage was made in the MDVP software program and analyses filed together with the analyses of all other parameters online.*

Sample size consideration for the prospective randomized controlled study

- A total of 49 patients were needed in the group of lifestyle correction, lifestyle correction + proton pump inhibitor and the third group with supplementary alginate, to obtain a power of 90% in a two-group, one-sided, *t*-test to detect a difference of 20% under the assumption that the true difference was 5% and that the standard deviation was 25%.
- Based on this general consideration and taking into account, possible drop out and evaluation of multiple endpoints, a total of 237 patients were randomized in the study.

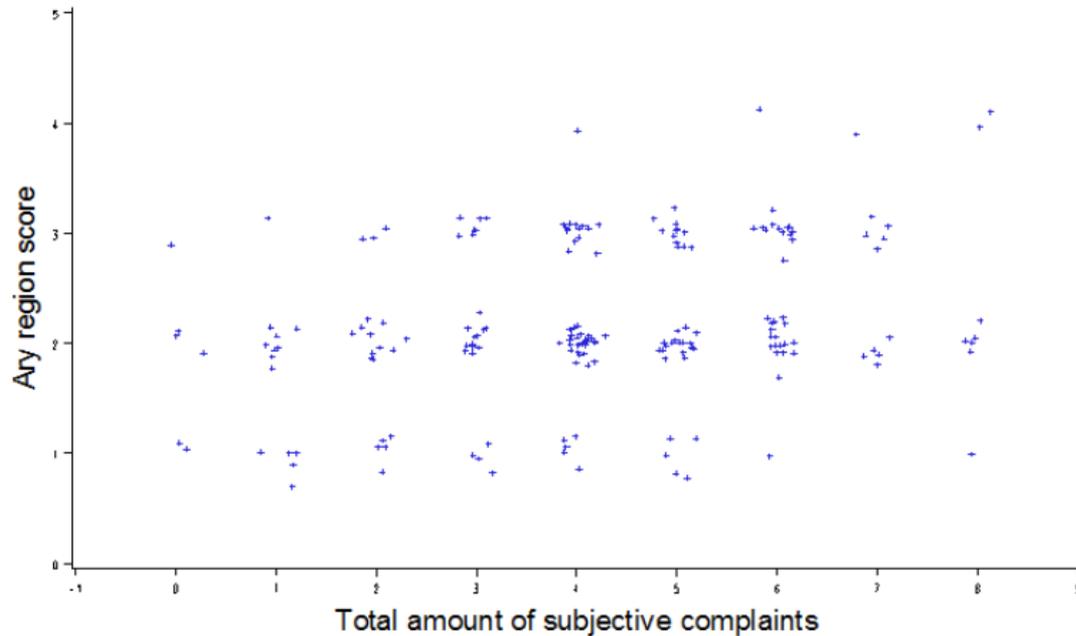
Statistical analysis

- Each numerical week 2, endpoint was evaluated in an analysis of covariance including baseline value as covariate and treatment group as fixed effect. This included subjective complains, interarytenoids oedema scores on high speed films and acoustical analysis.
- **For each endpoint the hypotheses were tested:**
 1. An **effect** of treatment of laryngopharyngeal reflux based on acoustical analysis, subjective complaints and high speed films.
 2. A **difference** between treatment group of lifestyle guidance and lifestyle guidance and added treatment with the proton pump inhibitor esomeprazole 40 mg, one tablet at night against the two sided alternative that there is a difference.
 3. A **difference** between treatment group of lifestyle guidance and lifestyle guidance combined with esomeprazole 40 mg and alginate, 1-2 chewing tablets after the evening meal against the two sided alternative that there is a difference.

Missing values were analyzed as such and no imputation was made, which means that missing data were not included in the analysis.

Figure 2

Our earlier study showed a statistical significant correlation between subjective complaints and oedema of the arytenoid region.



Data are filtered (added noise) to show all data points
Spearman correlation: 0.280 | 95% CI: [0.149;0.410]

Scatter plot of the total amount of subjective complaints (abscissa) versus oedema of the inter-arytenoid region, week 2 (ordinate). Data are filtered (added noise) to show all data points. (Spearman Correlation 0.280 | 95% CI [0.149;0.410]).

Results

- The mean age of the population was 42 years, divided in the three groups.
- In the lifestyle group there were 22 males and 56 females.
- In the lifestyle + PPI group there were 17 males and 53 females.
- In the lifestyle + PPI + alginate there were 26 males and 64 females.
- The statistical analysis showed that the differences between the three treatment groups were negligible, therefore the three treatments groups have been collapsed in the following analyses.

TABLE 1

The arytenoids region edema visual score is compared with acoustical and electroglottographical measurements (EGG): sustained tones and reading of a standard text. With MDVP on a sustained tone (Fo) a significant less shimmer and irregularity was found after the second week. This was also the case for fundamental frequency variation (Fo) during reading of a standard text. Statistical output from ANCOVA - variables not transformed. (See also table 2).

parameter	First consultation			Second consultation					Third consultation				
	N	Mean	SD	N	Mean	SD	Mean change	95% CI	N	Mean	SD	Mean change	95% CI
Arytenoids region, average visual score edema (of 1-5)	237	2.71	0.69	196	2.19	0.70	-0.52	[-0.60; -0.43]	147	1.96	0.72	-0.77	[-0.88; -0.66]
MDVP sustained - Tone /ah/ Jitter (%) Hz	234	2.81	8.31	192	2.02	5.73	-0.77	[-1.59; 0.04]	143	2.55	6.93	-0.31	[-1.47; 0.85]
MDVP sustained - Tone /ah/ Shimmer (%) dB	232	9.35	8.04	191	7.76	4.38	-1.37	[-1.94; -0.79]	144	7.96	4.56	-1.41	[-2.16; -0.65]
MDVP sustained- Tone /ah/ Qx (%) EGG	234	46.39	8.60	191	46.45	7.19	0.25	[-0.59; 1.09]	143	47.08	7.59	0.63	[-0.49; 1.75]
MDVP sustained- Tone /ah/ Qx (%) irregularity EGG	232	25.17	22.25	190	23.74	21.94	-2.10	[-4.87; 0.68]	144	23.30	20.16	-3.92	[-7.03; -0.80]
MDVP – Reading text Fundamental frequency variation (%) Hz	235	10.73	9.20	194	9.43	7.64	-1.18	[-2.21; -0.15]	144	9.51	8.29	-1.92	[-3.28; -0.55]
MDVP – Reading text Intensity variation (%) dB	233	16.23	4.91	193	15.26	4.13	-1.02	[-1.54; -0.49]	145	15.77	4.27	-0.80	[-1.49; -0.10]
MDVP - Reading variation of Qx (%) EGG	235	47.68	6.03	193	47.81	5.75	0.35	[-0.30; 1.00]	145	47.51	5.86	0.10	[-0.72; 0.92]
MDVP - Reading variation of Qx (%) irregularity EGG	234	41.74	14.81	193	40.58	15.08	-1.07	[-2.99; 0.85]	144	37.89	15.65	-4.52	[-6.89; -2.14]

Supplementary table

Parameter	First consultation		Second consultation			Third consultation		
	N	Mean (SD)	N	Mean (SD)	Mean change [95% CI]	N	Mean (SD)	Mean change [95% CI]
Reading								
Frequency (%)	235	10.73 (9.20)	194	9.43 (7.64)	-1.18 [-2.21; -0.15]	144	9.51 (8.29)	-1.92 [-3.28; -0.55]
Intensity (%)	233	16.23 (4.91)	193	15.26 (4.13)	-1.02 [-1.54; -0.49]	145	15.77 (4.27)	-0.80 [-1.49; -0.10]
Qx (%)	235	47.68 (6.03)	193	47.81 (5.75)	0.35 [-0.30; 1.00]	145	47.51 (5.86)	0.10 [-0.72; 0.92]
Qx % irregularity	234	41.74 (14.81)	193	40.58 (15.08)	-1.07 [-2.99; 0.85]	144	37.89 (15.65)	-4.52 [-6.89; -2.14]
Sustained tone /ah/								
Jitter (%)	234	2.81 (8.31)	192	2.02 (5.73)	-0.77 [-1.59; 0.04]	143	2.55 (6.93)	-0.31 [-1.47; 0.85]
Shimmer (%)	232	9.35 (8.04)	191	7.76 (4.38)	-1.37 [-1.94; -0.79]	144	7.96 (4.56)	-1.41 [-2.16; -0.65]
Qx (%)	234	46.39 (8.60)	191	46.45 (7.19)	0.25 [-0.59; 1.09]	143	47.08 (7.59)	0.63 [-0.49; 1.75]
Qx % irregularity	232	25.17 (22.25)	190	23.74 (21.94)	-2.10 [-4.87; 0.68]	144	23.30 (20.16)	-3.92 [-7.03; -0.80]

TABLE 2

	Spearman correlation	P-value
SPEAD - Tone /ah/ Jitter (%)	0.11841	0.1065
SPEAD - Tone /ah/ Shimmer	0.14999	0.0416*
SPEAD - Tone /ah/ Qx (%)	0.05220	0.4792
SPEAD - Tone /ah/ Qx pct irregularity	0.22148	0.0025**
SPEAD - Reading Frequency (%)	0.17048	0.0190*
SPEAD - Reading Intensity (%)	-0.01763	0.8107
SPEAD - Reading Qx (%)	-0.10627	0.1466
SPEAD - Reading Qx pct irregularity	0.08721	0.2340

Spearman correlation of acoustical measurements to arytenoids, after two weeks

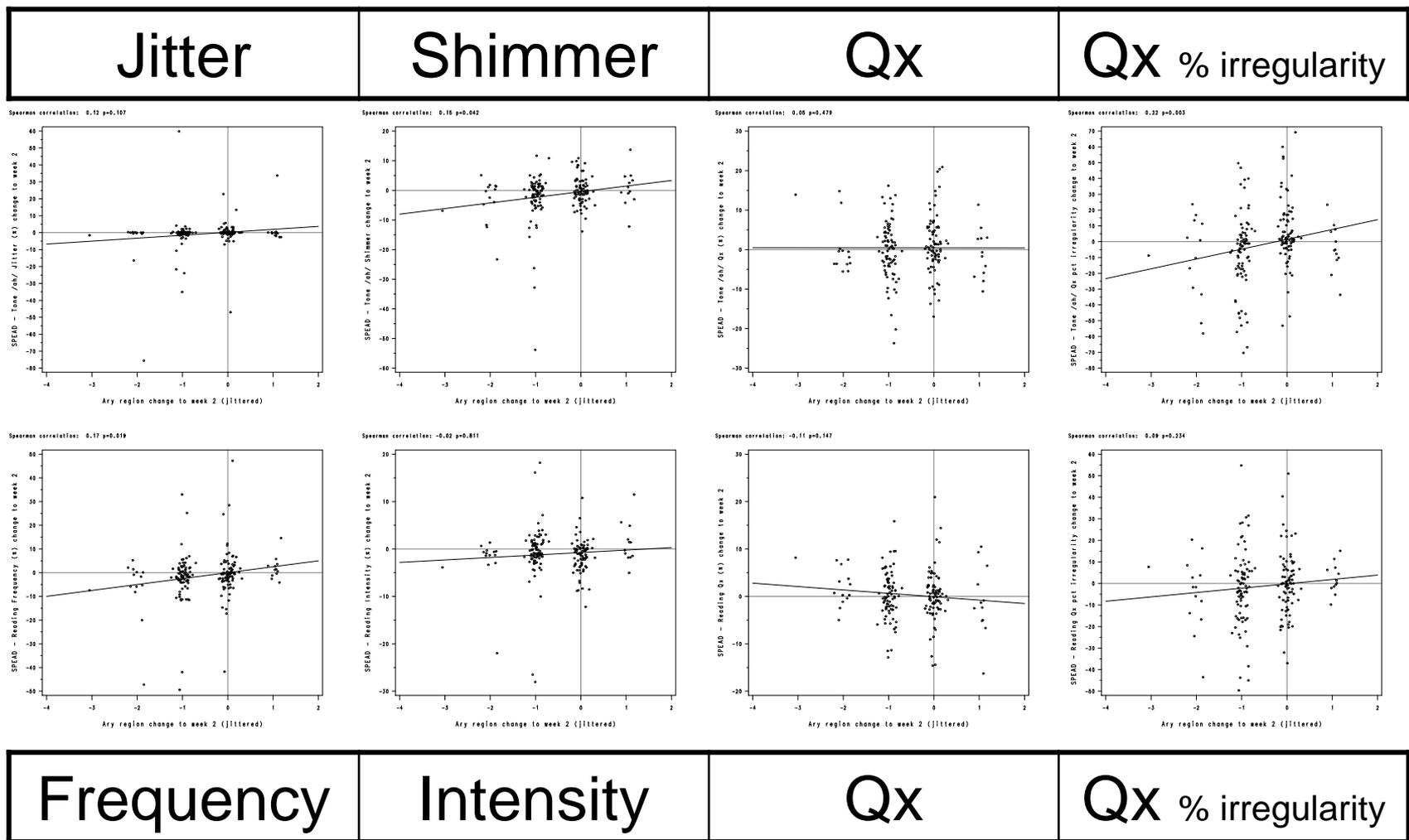
* Statistically significant on 5% level, ** significant on 1% level

- In Figure 3 scatter plots are presented for the changes from the first and second examination after two weeks.
- Both sustained tones and reading of standard text are presented.
- The scatter plot shows the variation could be depending mostly on a few apparent deviant results.

Figure 3

Tone

Reading



Discussion

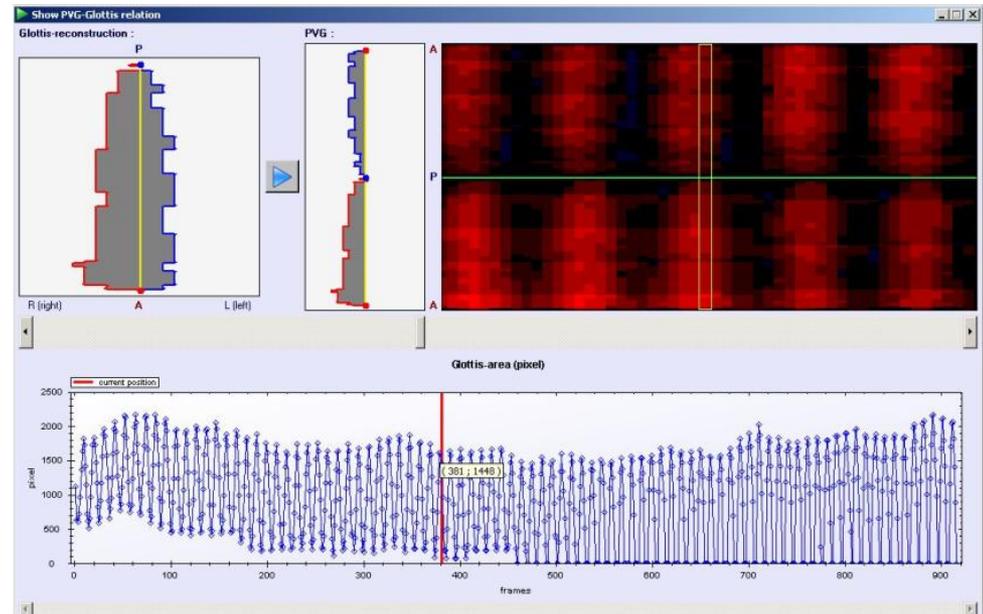
- A randomized controlled trial of Laryngopharyngeal reflux treatment with acoustical, statistical analysis with Multi dimensional voice program by Laryngograph Ltd., was carried out using sustained tones (Fo) and reading of a standard text.
- The acoustical measures of voice in patients with laryngopharyngeal reflux did not show differences that had statistical prognostic value.
- This is in contrast with the earlier shown correlation between the arytenoid regions swallowing and the subjective complaints in our earlier paper useable for prognostics of treatment aspect.

- The glottis analysing tools online on high-speed films for vocal fold dynamics for each vocal cord with the Phonovibrogram can be used statistically in the future together with many parameters of sustained tones as shown in one of our patients (Table 3).
- The use of arytenoid oedema on high speed films, visual score 1-5, seems in this study for treatment of Laryngopharyngeal reflux to be better as a prognostic parameter than acoustical analysis.
- In the future it will be possible to evaluate the oedema of arytenoid areas with light and narrow band imaging as well as optical coherence tomography as a supplementary diagnostic factor.

TABLE 3

One of our patients with a set-up on line from Glottal Analysis Tools with high speed films (Döllinger et al.). An increased control with contrast ensures accurate segmentation, and the area is calculated in each vocal fold cycle. This also ensures accurate jitter, shimmer and quotients.

Jitt(%)	5,048				
HNR(dB)	11,098				
Shim (%)	0,542				
		Mean	Std	Min	Max
ClosingQuotient(CQ)	0,4149	0,0602	0,2727	0,5455	
AsymmetrieQuotient	0,4872	0,0721	0,3333	0,5833	
Stiffness	Left	0,4919	0,1902	0,254	0,9897
Stiffness	Right	0,4769	0,1664	0,2625	0,8411



Thank you for your attention

Union of the European Phoniaticians

