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Transoral radiofrequency of the terminal branches of the recurrent nerve in the treatment of adductor spasmodic dysphonia: our experience over 11 patients

S. Beyaert[1] · G. Delahaut[1] · J. Ambroise[2] · G. Lawson[1] · V. Bachy[1] · S. Hassid[1] · L. Delacroix[1] · M. Remacle[3] · S. Van der Vorst[1]

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Abstract

Purpose Spasmodic dysphonia (SD) or laryngeal dystonia is as a rare vocal disorder characterized by involuntary action-induced endolaryngeal contraction. In the last decade, botulin toxin injection has become the standard treatment in adductor spasmodic dysphonia necessitating repetitive injections. The purpose of this study is to analyze retrospectively data from patients treated with the minimal-invasive transoral radiofrequency-induced thermotherapy (RFITT) of the terminal branches of the recurrent nerve.

Methods Between 2009 and 2015, 11 patients (six females and five males aged from 32 to 91 years) with adductor SD were treated with RFITT. Pre-operative and post-operative vocal assessments (VHI-30, GRBASI, and acoustic-aerodynamics measurements), number of surgical revisions, delay between procedures, and post-operative complications were recorded. Statistical analyses were carried out on the first vocal assessment performed 2–8 weeks after the first procedure.

Results Based on available data from ten patients, voice handicap index (VHI) showed improvement with a mean value of −17.7 points (p-value ($p$val) = 0.014, adjusted p-value (adj $p$val) = 0.21); instability has also revealed improvement in six patients ($p$val = 0.05, adj $p$val = 0.31). Four patients underwent only one procedure including one patient showing still long-term beneficial results after 5 years of follow-up. Other patients required one to three new procedures with an average time between procedures of 15.3 months. Over 24 surgeries performed on a total of 11 patients, one definitive treatment-related severe adverse event was reported.

Conclusion Thanks to long-lasting effect, repetitive treatments are less frequent compared to botulin toxin therapy. In our opinion, RFITT is a promising alternative to botulin toxin as a second-step procedure in case of toxin resistance or patient's lack of compliance.

Keywords Spasmodic dysphonia · Thermotherapy · Radiofrequency

Purpose

Spasmodic dysphonia (SD) or laryngeal dystonia is defined as a rare vocal disorder (14/100,000) which mainly affects women aged 30–50 characterized by involuntary action-induced endolaryngeal contraction. This disease has still unclear multifactorial pathogenesis like environmental, genetic, and brain abnormalities (basal ganglia) [1–4]. It can occur in three forms, adductor (ADSD), abductor (ABSD) or mixed. ADSD (± 90% of all cases) affects the thyro-arytenoid (TA) and lateral crico-arytenoid muscles, resulting in a harsh and strain-strangled voice with voice breaks. ABSD is affecting the posterior crico-arytenoid muscle (± 10%) and causes or induces weak and breathy voices [3, 4]. In the

S. Beyaert and G. Delahaut contributed equally to this work.

✉ G. Delahaut
gilles.delahaut@chuuclnamur.uclouvain.be

1 Department of ENT and Head and Neck Surgery, Université catholique de Louvain, CHU UCL Namur, Avenue du Dr Gaston Therasse 1, 5530 Yvoir, Belgium

2 Institut de Recherche Expérimentale et Clinique (IREC), Centre de Technologies Moléculaires Appliquées, Université Catholique de Louvain, Brussels, Belgium

3 Department of ENT and Head and Neck Surgery, Centre Hospitalier Luxembourg, Luxembourg, Luxembourg

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last decade, botulin toxin injection has become the standard treatment in ADSD. The main disadvantages are the recurrence of symptoms necessitating repetitive injections every 3–6 months [5–7], clinical resistance to the toxin [8], and the cost of treatment. To improve patient's quality of life and to obtain a long-term vocal control, the development of other options is needed. Different surgical alternatives were developed to avoid intrinsic laryngeal muscles hyperadduction, including relaxation thyroplasty, laryngeal nerve crush, recurrent laryngeal nerve resection, or thyro-arytenoid myoto/myectomy [3–9].

The purpose of this study is to present our experience with the minimal-invasive transoral radiofrequency-induced thermotherapy (RFITT) of the terminal branches of the recurrent nerve in the treatment of adductor spasmodic dysphonia as described by Remacle and al [9] and to analyze retrospectively the data of 11 patients.

Materials and methods

Procedure

As described by Remacle et al. [9], this surgery is performed under general anesthesia in three steps. The patient, not curarized, is placed in supine position, ventilated by high-frequency jet ventilation through a laryngoscope under suspension. First of all, the vocal fold is tested with a stimulator connected with a laryngeal needle to find the area of maximal contraction for minimal stimulation (Fig. 1a). This stimulation zone is generally located anterolaterally to the vocal process of the arytenoid cartilage (Fig. 1b). Second, thermotherapy is performed with Celon® laryngeal probe (Fig. 1c) in the identified area at 10 W power. The generator automatically controls the delivered energy, preventing overheating of the vocal folds and subsequent excessive scars. The energy delivery is controlled by a foot pedal activated by the surgeon. Finally, the vocal fold contraction test is repeated. Vocal fold stimulation threshold must be higher than the initial testing and, if possible, not respond to an electrostimulation of 5 mA. One or two additional thermotherapies may be required to achieve the desired effect, which corresponds to the denervation of the terminal branches of the recurrent nerve resulting in paresis of the thyro-arytenoid muscle.

The procedure is an ambulatory surgery and lasts around 20 min. Postoperative care requires 2 days voice rest, antibiotics, and corticosteroid inhalations. Painkillers are rarely necessary.

The choice of the first vocal fold to be treated is made by the surgeon: the vocal fold with the most hyperadduction demonstrated on simple phonation during the pre-operative fibroscopy is chosen for RFITT. No additional investigation (EMG, radiological imagery, …) is requested. For surgical revisions, we propose to perform a new surgery only after complete healing of the first surgery and to perform it always on the contralateral vocal fold. If the fibroscopy shows complete healing and if the patient requests a new procedure, the decision to re-operate is made by mutual agreement between the patient, the surgeon, and the speech therapist, decision also based on monitoring of voice parameters (VHI and GRABSI in particular).

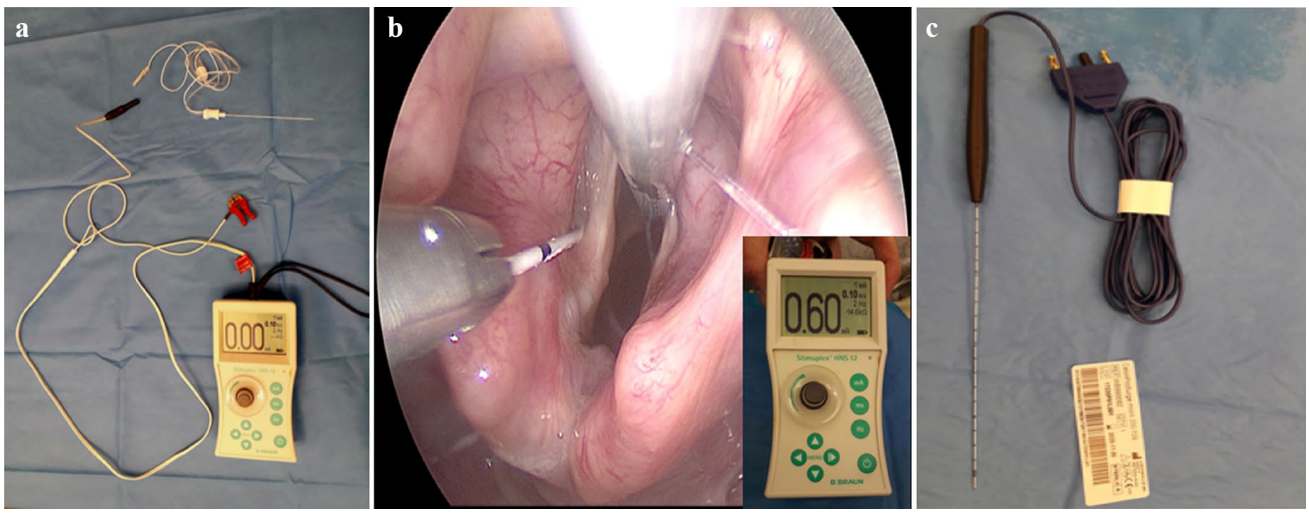


Fig. 1 **a** Electrostimulator. **b** Laryngeal electrostimulator producing minimal vocal fold movement at a stimulation of 0.60 mA. **c** Celon ProSurge micro 200-T09. First, the vocal fold is tested with a stimulator to find the area of maximal contraction for minimal stimulation, generally located anterolaterally to the vocal process. Second, thermotherapy is performed with Celon® laryngeal probe in the identified area at 10 W power. Finally, the vocal fold contraction test is repeated, and the threshold must be higher than the initial testing corresponding to the denervation of the terminal branches of the recurrent nerve

Each surgery in the present study was performed by experienced head and neck surgeons (Lawson G. and Remacle M.).

Population

We report the evolution of 11 consecutive patients (six females and five males aged from 32 to 91 years) with adductor spasmodic dysphonia; six were previously treated by botulin toxin therapy and six were treated with speech therapy (Table 1). All patients were diagnosed for ADSD by a phoniatrician or a laryngologist. All received laryngeal radiofrequency procedures between 2009 and 2015. The selection criteria for this surgery were informed consent, resistance to repeated injections of botulin toxin, patient's demand for a therapeutic option with longer effects, and easy access to the glottic plane. We recorded all pre-operative and post-operative vocal assessments, number of surgical revisions, delay between procedures, and post-operative complications. We statistically analyzed the vocal results after the first procedure in all patients but 1, due to a loss of data.

Vocal assessment

Pre-operative and post-operative vocal assessments included Hirano's scale (GRABSI), Voice Handicap index (VHI)-30 questionnaire, [5, 10] and acoustic-aerodynamics measurements (maximum phonation time, minimum intensity, maximum intensity, minimum frequency, maximum frequency, phonation quotient, estimated subglottic pressure, jitter, and shimmer) performed by speech therapists specialized in voice therapy. The acoustic-aerodynamics measurements were performed with the digital analyzer Kay Elemetrics Model CSL 4150B and the phonatory aerodynamic system PAS 6600. VHI was considered as the most accurate endpoint for our report. Postoperative examination was performed 2–8 weeks after the surgical procedure.

Statistical methods

All statistical analyses were performed on R v4.1.0. To assess the impact of the operation, mixed-effects models were built for each outcome by including a patient random effect and the operation as a fixed effect. The Student's *t* test was used for pairwise comparisons of the data. Considering that multiple outcomes were assessed, Benjamini–Hochberg method was used for multiple testing corrections. An adjusted p-value < 0.05 was considered statistically significant.

Results

Vocal assessments

Based on the vocal assessment available on 10 patients (Table 1), VHI showed a tendency to improve with a mean value of −17.77 points (Fig. 2) [p-value ($p$val) = 0.014, adjusted p-value (adj $p$val) = 0.21]. Instability has also shown a trend toward improvement (Fig. 3) ($p$val = 0.05; adj $p$val = 0.31) with six patients having a lower instability after the first procedure. All other subjective and objective

Table 1 Population characteristics and clinical data (VHI, instability, number of revisions, and complications)

Patient ID	Sex	Age	Previous treatment	Preoperative VHI	Postoperative VHI*	Preoperative instability	Postoperative instability*	Number of revisions	Postoperative complications**
1	F	66	Botox + speech therapy	55	44 (6)	2	2 (6)	1	None
2	F	91	Botox	32	39 (2)	3	3 (2)	3	None
3	F	65	Speech therapy	109	98 (8)	0	1 (8)	3	None
4	F	41	Botox + speech therapy	74	38 (2)	2	1 (2)	1	Postoperative pain
5	F	51	NA	96	58 (3)	3	1 (3)	0	None
6	M	63	Botox	71	59 (8)	3	2 (8)	2	Vocal fold hematoma
7	F	64	Speech therapy	66	40 (8)	3	2 (8)	0	None
8	M	32	NA	95	46 (8)	1	0 (8)	0	None
9	M	53	Botox	68	59 (8)	NA	1 (8)	1	Vocal fold hematoma
10	M	34	Speech therapy	57	63 (NA)	1	0 (NA)	0	Vocal fold hematoma
11	M	36	Botox + speech therapy	69	NA	2	NA	2	Desinsertion of the vocal ligament

*Weeks between the first surgery and the first vocal assessment

**On all performed interventions

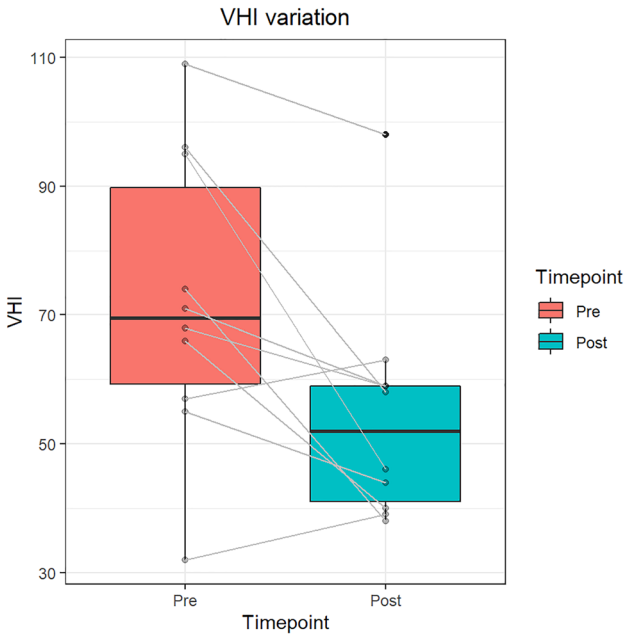
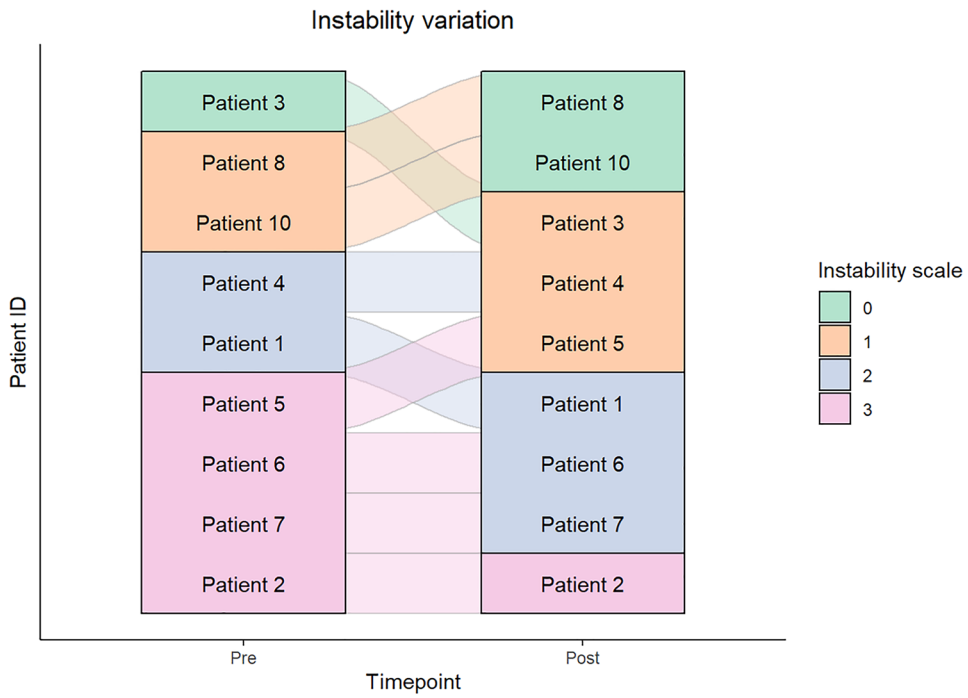


Fig. 2 VHI-30 variation assessed 2–8 weeks after the first surgery

measurements investigated were not significantly modified after the procedure such as grade ($pval = 0.097$; adj $pval = 0.31$), roughness ($pval = 0.100$ adj $pval = 0.306$), breathiness ($pval = 0.246$; adj $pval = 0.57$), strength ($pval = 0.102$; adj $pval = 0.31$), maximum phonation time ($pval = 0.99$; adj $pval = 0.99$), minimum intensity ($pval = 0.76$; adj $pval = 0.88$) and maximum intensity ($pval = 0.30$; adj $pval = 0.57$), minimum frequency ($pval = 0.89$; adj $pval = 0.96$) and maximum frequency ($pval = 0.46$; adj $pval = 0.63$), phonation quotient ($pval = 0.35$; adj $pval = 0.57$), estimated subglottic pressure ($pval = 0.75$; adj $pval = 0.88$), jitter ($pval = 0.38$; adj $pval = 0.57$), and shimmer ($pval = 0.31$; adj $pval = 0.57$). Asthenia was not investigated, because it remained at 0 for all patients before and after surgery (Table 2).

In addition, further analyses were conducted to check the impact of variables on VHI and the need of revisions. There was no significant variation in age between patients with a single surgery and patients with one or more revisions ($pval = 0.12$) (Fig. 4a). By dividing our cohort by the median age (median age: 58 years), younger patients showed a significant variation in VHI ($pval = 0.034$), while older patients showed just a non-significant variation ($pval = 0.057$) (Fig. 4b). The difference between the two populations was probably related to the small number of patients in our cohort, and a larger number of patients included would probably have led to significant results in both populations. Moreover, no significant VHI variation was found between < 58 years vs > 58 years old for pre- and post-surgery VHI values ($pval = 0.46$ and 0.80, respectively) (Fig. 4c). Analysis of the VHI variation post- vs pre-surgery, by separating our cohort in two populations with patients having more than one surgery or not showed that patients having a new RFITT have a significant variation in VHI ($pval = 0.043$), while patients

Fig. 3 Instability evolution assessed 2–8 weeks after the first surgery



Rating scale: 0=normal; 1=slight; 2=moderate; 3=severe

Table 2 Results of the pre- and post-surgery vocal assessments performed after the first RFITT procedure

	Pre				Post				*p*-Value	Adjusted *p*-value
	Mean	Median	SD	Range (min–max)	Mean	Median	SD	Range (min–max)		
VHI	72.30	69.50	22.71	32–109	54.4	52.0	22.71	38–98	0.014	0.21
Grade	2.22	2.00	NA	1–3	1.5	1.0	NA	1–3	0.097	0.30
Roughness	0.44	0	NA	0–2	0.90	1.00	NA	0–2	0.100	0.30
Breathiness	1	1	NA	0–2	0.2	0.0	NA	0–1	0.246	0.57
Asthenia	0	0	NA	0–0	0	0	NA	0–0	NA	NA
Instability	2	2	NA	0–3	1.3	1.0	NA	0–3	0.05	0.30
Strained	1.875	2.00	NA	0–3	1.2	1.5	NA	0–3	0.102	0.30
Jitter (%)	3.5	2.1	2.81	0.56–8.10	4.718	3.39	4.64	0.60–16–40	0.383	0.57
Shimmer (%)	11.24	10.45	7.82	2.20–23.38	8.70	6.45	4.97	2.86–17.00	0.315	0.57
I_{min} (dB)	63.70	62.50	6.97	55–77	64.60	62.50	10.63	53.00–85.00	0.765	0.88
I_{max} (dB)	102.10	103.00	7.35	91–114	99.10	101.00	8.81	80–109	0.298	0.57
Freq min (Hz)	125.36	126.50	40.86	69–174	122.80	119.8	32.54	73–174	0.894	0.95
Freq max (Hz)	472	453	127.74	247–659	437	415	103.93	246–587	0.460	0.63
Phonatory quotient (mL/s)	347.02	367.05	208.73	69–733	811.60	305.20	1301.31	136–4420	0.348	0.574
Intraoral pressure (cm H_2O)	14.18	12.18	9.76	5.70–37.28	14.79	11.04	8.26	5.25–29.16	0.748	0.88

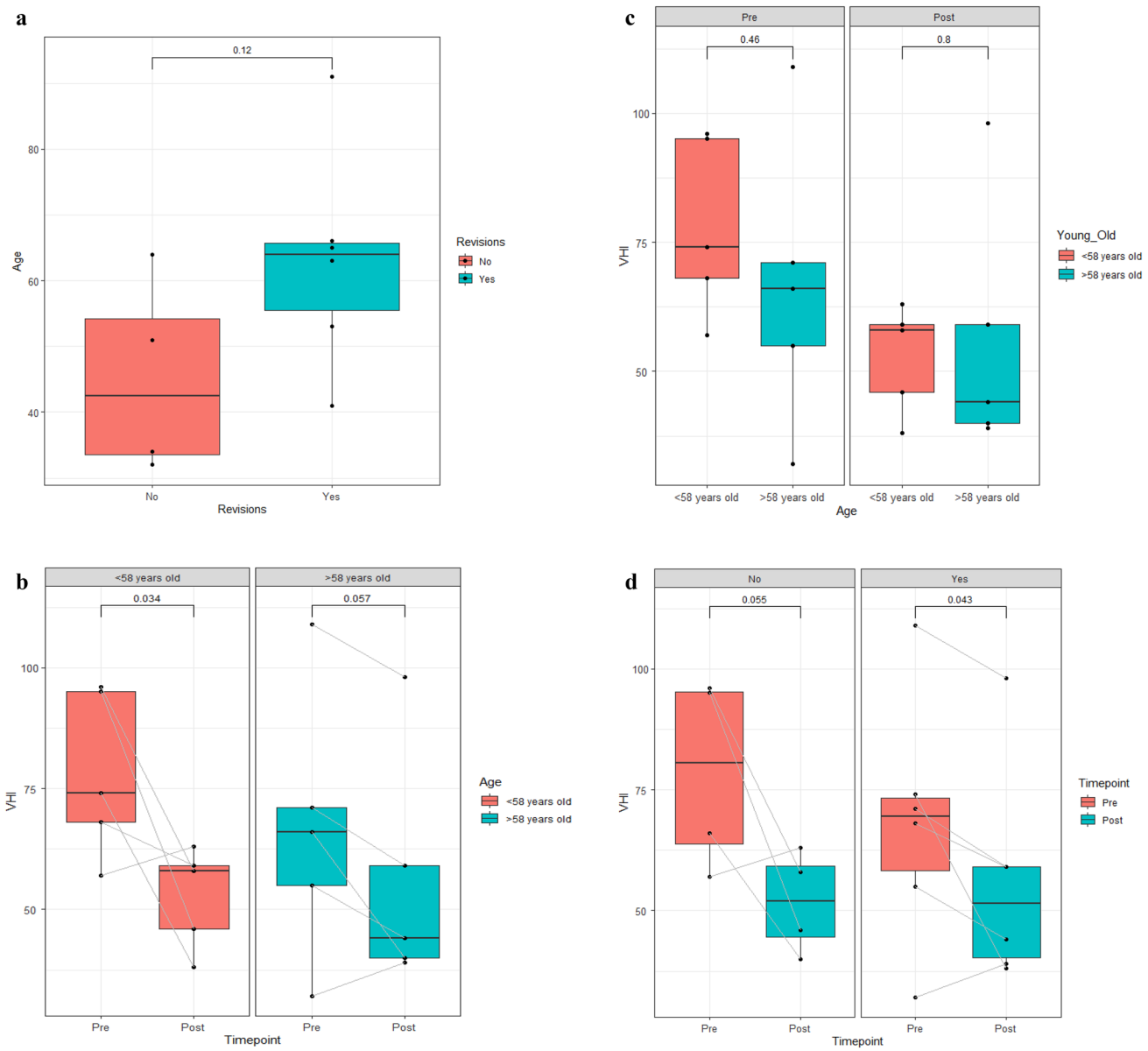


Fig. 4 **a** Age variation between patients with a single surgery and patients with one or more revisions. **b** VHI-30 variation assessed 2–8 weeks after the first surgery by separating our cohort by the median age. **c** Comparison of VHI-30 within the same timepoint between our cohort separated by median age. **d** VHI-30 variation assessed 2–8 weeks after the first surgery by separating our cohort by the presence of revision or not

without revision show just a non-significant variation ($p$val = 0.055) (Fig. 4d). Again, the difference between the two populations is probably related to the small number of patients in our cohort. A larger number of patients included would probably have led to significant results in both populations.

Furthermore, no significant association was found between exposure to previous treatment (botox and/or speech therapy) and the need for revision surgery, assessed by Fisher's exact test (p-value = 0.13).

Surgical revision and delay between procedures

Four patients underwent one procedure to achieve satisfactory result. Three patients underwent one surgical revision and four patients needed two or three additional revisions with an average delay of 15.3 months between procedures (min–max: 4–32 months; median value: 11 months, CI 95% 9.18–21.43) on a total of 24 procedures (See Table 1).

Revision surgery was indicated in case of recurrence or unsatisfactory results (i.e., disappointing outcome for the

patient, objectified by the surgeon, speech therapist, and vocal assessment). In these cases, first revision was performed on the contralateral vocal fold. In all cases, complete healing after the first surgery was achieved before considering surgical revision.

Postoperative complications

Over the 24 procedures, transient vocal fold paresis was obtained as expected, but no significant change in aerodynamic and acoustics measurements was observed. No swallowing disorders were reported after the procedure. Three patients had transient hematoma of the vocal fold and only one patient complained of post-operative pain. One patient developed a severe complication, resulting in significant dysphonia. This patient underwent a total of three surgeries, the first surgery being on the left vocal fold, the second, performed 32 months later on the same left vocal fold, and a third surgery performed 8 months later on the right vocal fold. Only four vocal assessments were available for this patient: At baseline (VHI-30 = 69; G2 R1 B0 A0 S0 I2; phonatory quotient = 397 mL/s), 2 weeks after the second surgery (VHI-30 = 50; G1 R0 B0 A0 S1 I1; phonatory quotient = 351 mL/s) and 2 weeks (VHI-30 = 94; G3 R2 B1 A0 S2 I1; phonatory quotient = 1739 mL/s) and 3 months (VHI-30 = 92; G2 R1 B1 A1 S2 I0; phonatory quotient = 748 mL/s) after the third surgery.

After his third operation, the fibroscopy showed scar atrophy at the level of the vocal processes with glottic gap associated with a decrease in vocal power with perforation of the vocal folds with complete disinsertion of the vocal ligament on the right and partial on the left; good surface mucosal mobility, no paresis in adduction and abduction.

Discussion

Nowadays, the standard treatment for spasmodic dysphonia in its adductory form remains the injection of botulinum toxin into the thyro-arytenoid muscle. This procedure aims to suppress the hyperadduction of the vocal folds [2, 3]. Although this technique has been statistically proven effective [3, 4, 11], the transient effects' duration and the need to repeated injections every 3–6 months have a significant impact on patients' quality of life [5–7, 12]. Some patients may also develop toxin resistance necessitating the development of alternative treatment plans.

Other authors have published different surgical technique inspired by the RFITT, as described by Kim et al. [13]. The goal of the authors is to ablate portions of the TA without affecting innervation. The major technical difference is the ablation of both TA muscles simultaneously, whereas in our study, we treated one vocal fold at a time. The voice outcome at 2 months reported by the authors seems to be similar, with a significant decrease in VHI-30 and strained voice ($p$val < 0.05). No information regarding grade, roughness, instability, breathiness, and asthenia variation is given. However, Kim et al. [13] noted significant variations in aerodynamic parameters, such as global resistance and mean flow rate, even lasting 12 months for the mean flow rate. Such significant variations in aerodynamic parameters were not found in our retrospective study at 2 months, possibly indicating the less-invasive nature of our procedure. Finally, the duration of effectiveness of the procedure reported by the authors seems to be around 1 year, compared to our analysis where the median time between two revisions was 15.3 months including one patient showing still long-term beneficial results after 5 years of follow-up. However, in our study, the data were collected retrospectively, and a prospective study is needed to make conclusions.

The radiofrequency of the terminal branches of the recurrent laryngeal nerve has the advantage of being a simple, rapid, rapidly effective and minimally invasive technique. Due to the small number of patients, adjusted p-value showed no significative improvement in VHI and instability after the first vocal assessment. However, this small retrospective analysis shows interesting results with an average decrease in VHI of 17.7 points and with a trend to improve voice instability at the first evaluation, carried out between 2 and 8 weeks post-op. Indeed, 8 out of 10 evaluable patients were satisfied with the functional results after the first intervention (by considering an improved post-operative VHI compared to baseline). Furthermore, four patients required only one intervention: one patient benefit from long-term results with 5-year follow-up; the other three patients were lost to follow-up after their first vocal assessment. Seven patients required 1 to 3 surgical revisions, with an average delay of 15.3 months between the procedures, which could be considered as a major increase over the 3–6-month interval between botox injections. In addition, no significant changes in aerodynamic and acoustics measurements, or swallowing disorders were observed, showing that RFITT is safe regarding laryngeal functions.

According to the clinical response, a revision surgery may be necessary either to improve the results either because of symptoms recurrence. For those patients, the second surgery is performed on the contralateral vocal fold after total healing of the first surgery, to avoid complication such as bilateral palsy and subsequent dyspnea and/or aspiration. Temporary and insufficient result may be explained by an insufficient destruction of nerve fibers during the procedure leading to distal reinnervation of the recurrent nerve in the TA muscle. Another hypothesis, proposed by Juliëtta et al. [5], suggests the development of an overcompensation of other intrinsic adductor muscles, such as the lateral cricothyroid muscle, linked to a central activation underlying the

dystonia phenomenon. However, we do not propose pre- or post-operative EMG due to the invasiveness of EMG, similar to a botox injection.

In our experience, some patients show an excellent functional response after one or two procedures, while others show poor or no result despite several surgical revisions, suggesting that there are both responders and non-responder patients. Therefore, we have never proposed a fourth surgical revision considering the low benefit expected. Moreover, we have not found any predictive sign for non-responders patients.

Out of a total of 24 performed surgeries, one patient showed a major long-term complication with significant vocal consequences related to the desinsertion of the vocal ligament after a second procedure on the same vocal fold. This complication was difficult/impossible to anticipate and we did not find any pre-operative clinical signs that could explain such an outcome. This is why, we now propose to perform a new surgery only after complete healing of the first surgery and to perform it always on the contralateral vocal fold to avoid future complications. No other long-term adverse effects were observed or reported and patient's satisfaction was achieved in most of the cases.

In our setting, this surgical procedure can be proposed as a second-step procedure in the treatment of adductor spasmodic dysphonia for patients resistant to botulin toxin injections and for patients looking for a longer lasting solution.

Conclusion

Transoral radiofrequency-induced thermotherapy of the recurrent nerve terminal branches is a feasible and effective procedure. Thanks to long-lasting effect, repetitive treatments are less frequent compared to botulin toxin therapy. In our opinion, it is a promising alternative to botulin toxin as a second-step procedure in case of toxin resistance or patient's lack of compliance. Further multicentric prospective studies involving a larger number of patients are necessary to demonstrate its clinical benefits and clarify its place among the current therapeutic panel of spasmodic dysphonia.

Author contributions Conceptualization: [GD]; methodology: [GD, SB, and JA]; formal analysis and investigation: [GD, SB, and JA]; materials: [GL, VB, MR, SVdV, LD, and SH]; writing—original draft preparation: [SB] writing—review and editing: [GD and SVdV], and Supervision: [SVdV]. One participating author is member of the editorial board of the present journal.

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Declarations

Conflict of interest The authors have no relevant financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of CHU UCL Namur, site Godinne (76/2020).

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