

Diode laser treatment in therapy-resistant allergic rhinitis: impact on nasal obstruction and associated symptoms

Philipp P. Caffier · Hans Scherer · Konrad Neumann ·
Sven Lück · Harald Enzmann · Andreas Haisch

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Abstract The ideal treatment in severe obstructive allergic rhinitis unresponsive to standard therapy is lacking. This study aimed to evaluate the efficacy of endonasal corrective laser surgery in perennial (pAR) and seasonal (sAR) allergic rhinitis. Forty subjects (20 pAR, 20 sAR) underwent videoendoscopic diode laser surgery. Examinations were performed preoperatively and at follow-ups 1, 12, and 24 months after surgery, including objective parameters (rhinomanometry, videoendoscopy, allergy tests) and subjective visual analog scales (evaluation of surgery, satisfaction, allergic symptoms). Of all patients, 95% received inferior turbinate, 40% septal, and 15% middle turbinate surgery. Postoperatively, two subjects showed considerable residual symptomatology (95% response rate). Throughout follow-up, objective rhinomanometry and subjective scores for nasal obstruction, rhinorrhea, sneezing, itching, and overall satisfaction improved significantly with time ($p < 0.0005$). The improvement was greatest for nasal obstruction, initially higher in pAR but more sustained in sAR. After 2 years, 30% sAR and 40% pAR subjects had been receiving pharmacotherapy due to recurrent symptoms. The allergic condition remained unchanged (skin and in-vitro tests). Outpatient endonasal diode laser surgery appears to be effective, safe and well tolerated for treating otherwise

therapy-resistant pAR and sAR, providing long-lasting symptom reduction with complete stop or decreased use of antiallergics.

Keywords Allergic rhinitis · Perennial · Seasonal · Therapy resistance · Diode laser surgery

Introduction

Allergic rhinitis (AR) represents one of the most common global health problems with seriously increasing incidence over the last decades [1, 2]. More than 600 million sufferers worldwide make AR currently the most prevalent allergic disorder, affecting up to 30% of adults and 40% of children [3–6]. AR is defined as IgE-mediated inflammation of nasal mucous membranes after exposure to specific extrinsic proteins in sensitised individuals [7]. Pathophysiologically, binding of inhaled allergens to specific IgE antibodies leads to mast cell and basophil activation [8]. This causes immediate and delayed release of various mediators including histamine and leukotrienes, which attract inflammatory cells from the peripheral circulation [9–11]. The resulting symptoms typically include nasal obstruction, rhinorrhea, sneezing, and itching.

Based on timing and periodicity of symptoms, AR can be classified as perennial (pAR) or seasonal (sAR). Although effective treatments exist, both types often remain undiagnosed and not correctly treated [12], which may involve substantial individual and general consequences, such as progression to more significant secondary or comorbid diseases like asthma (“allergic march”), considerable impairment of quality of life, and major negative impact on healthcare costs and economic productivity [13, 14]. Despite clear diagnostic and therapeutic guidelines

P. P. Caffier (✉) · H. Scherer · S. Lück · H. Enzmann · A. Haisch
Department of Otorhinolaryngology, Head and Neck Surgery,
Charité - University Medicine Berlin,
Campus Charité Mitte, Charitéplatz 1,
10117 Berlin, Germany
e-mail: philipp.caffier@charite.de

K. Neumann
Institute for Medical Informatics, Biometry and Epidemiology,
Charité - University Medicine Berlin,
Campus Charité Mitte, Charitéplatz 1,
10117 Berlin, Germany

from the WHO (World Health Organisation), EAACI (European Academy of Allergology and Clinical Immunology), and GA²LEN (Global Allergy and Asthma European Network), the ideal strategy for severe cases with treatment incompliance, intolerance, or poor response to standard therapy is still missing [15]. Therapy resistance frequently results in a multitude of ineffective treatment attempts or risky long-term application of topical decongestants and systemic corticosteroids [16]. Patients often try to alleviate their misery by self-adjusting their treatment regimen because of deterioration or lack of efficacy and bothersome side-effects [17]. In these cases, alternative approaches are needed to provide symptom relief and to avoid the side-effects of unsuccessful pharmacotherapy.

Deficiencies of many older trials on surgical intervention in AR patients are related to the following facts: (1) operations were done in pAR only (questionable value for severe sAR), (2) predominance of non-laser methods, (3) treatment of inferior turbinates only, (4) focus on the major symptom nasal obstruction, (5) lack of long-term results, and (6) firstly inclusion of patients with hypertrophic turbinates and afterwards looking for associated allergies. However, inferior turbinate hypertrophy is normally not associated with allergy-related rhinorrhea, sneezing, and itching. Thus, our approach was vice versa: to check the history and current allergic condition at the beginning, followed by investigation of the nasal cavity.

Instead of using laser surgery as a successful anti-obstructive treatment for inferior turbinate hypertrophy only, we wanted to more comprehensively help desperate patients from our allergy consultancy, who presented with severe AR and a history of treatment incompliance, intolerance, or poor response to standard anti-allergic therapy. The goal of our prospective study was to evaluate the 2-year efficacy of laser-based, corrective, endonasal septum and turbinate surgery in improving the whole AR symptomatology: not only nasal obstruction but also rhinorrhea, sneezing, and itching. To examine further new aspects, our results were compared between the otherwise therapy-resistant pAR and sAR subgroup.

Materials and methods

Study design

After local topical anesthesia, study patients underwent outpatient corrective diode laser surgery for reduction of allergy-associated hyperplastic turbinates and removal of obstructing septal pathologies. Clinical assessment and data collection were performed before surgery and at follow-ups 1, 12, and 24 months postoperatively, including objective parameters (rhinomanometry, endonasal videoendoscopy,

allergy diagnostic tests) and subjective visual analog scales for evaluation of surgical procedure, postoperative satisfaction, and allergic symptoms. The recurrent need of conventional relief medication used during the follow-up period was another outcome measure. The results for pAR and sAR patients were analyzed separately and discussed in comparison between both groups.

Subjects

Forty consecutive study participants (20 pAR, 20 sAR) were recruited from the allergy consultancy of Charité University ENT outpatient clinic in Berlin, Germany. Selection criteria included a positive medical history with present subjective complaints, confirmed diagnosis of AR (skin and in-vitro blood tests), incompliance, intolerance, or poor response to conservative standard treatments including failed specific immunotherapy and insufficient prolonged antiallergic pharmacotherapy ≥ 2 years, and written informed consent. Exclusion criteria were the coexistence of acute bacterial infection, nasal polyps, massive septal deviation unsuitable for endonasal laser application, symptoms not resulting from IgE-mediated inflammation (e.g., vasomotor rhinitis, rhinitis medicamentosa, hormonal rhinitis related to pregnancy), patients with positive sensitization but inappropriate clinical symptomatology, and any concurrent complementary or alternative treatment (e.g., acupuncture).

All sAR patients presented during the individual allergy season and asked for immediate help. Hence, laser surgery was conducted at baseline when patients suffered from allergic complaints. Because they showed severe allergic symptoms lasting for more than 4 weeks, postoperative control 1 month post-interventional represented the surgery-related short-term results, and not improvement due to the end of the individual allergy season. Since sAR is by definition a periodic disease, the impact on clinical symptomatology at long-term follow-up after 1 and 2 years was once again evaluated during the allergy season and compared to the symptoms of previous years.

Laser surgery

A semiconductor diode laser (Lumenis, Dreieich, Germany) with the following settings was used: wavelength $\lambda=830$ nm, continuous-wave, output power 5 W. The laser light was applied in contact mode via a soft bending, plastic-clad silica fiber (600- μ m core diameter) guided through a three-channel applicator sheath according to Scherer [18], including canals for the laser fiber, suction, and the rigid 25°-optic rhinoscope (Wolf, Knittlingen, Germany). Coupled to a videoendoscopic camera, the surgical procedure was conducted directly via a large-format LCD screen and then digitally recorded onto hard disc.

Preoperatively, topical anesthesia and decongestion were applied using cotton pads imbibed with 0.5% tetracaine and 0.1% naphazoline (50/50 mix) for about 10 min, followed by endonasal brushing using cotton applicators soaked with 5% lidocaine hydrochloride gel for about 3 min. Videoendoscopic surgery was performed in supine position after nasal anesthesia and pre-blackening of the tip of the laser fiber. Hyperplastic inferior turbinates were treated with two parallel posteroanterior mucosal cuts at their mediobasal parts (blanching around the fiber) with optional delivery of laser spots to the hyperplastic head. Middle turbinate pathologies were reduced by laterobasal vaporization in hyperplasia, or ablation of the lateral wall in concha bullosa. Concerning septal deformities, basal crests were vaporized by drawing the fiber repeatedly over the protruding tissue, spines, or crests were resected via caudocranial cuts at their septal basis. In contrast to the gentle surface coagulation of soft tissue (low power, continuous mode), hard tissue vaporization and dissection through the bone was performed in pulsed mode (high laser power, short exposure time, long intervals). After surgery, patients were put on nasal irrigation with saline, dexpanthenol ointment (Bepanthen; Bayer, Leverkusen, Germany), and naphazoline hydrochloride ointment (Siozwo; Febena, Cologne, Germany) for about 4 weeks. In case of septal and concha bullosa surgery, patients received prophylactic clindamycin hydrochloride capsules (Sobelin; Pfizer, Berlin, Germany) p.o. 300 mg t.i.d. (1-1-1) for about 5 days. Before discharge, routine postoperative observation period lasted for about 20 min.

Examination instruments

Videoendoscopy of nasal cavities was done for visual assessment to evaluate anatomic pathologies and indication for laser surgery. Preoperatively and during all follow-up visits, digital endoscopic photo- and video documentation was used for monitoring mucosal condition and visual objectification of treatment results.

Laboratory analysis of serum total and specific IgE levels as well as skin prick tests (SPT) were carried out to detect or confirm suspected allergen-specific IgE and to reveal changes of sensitization and reactivity before vs. after surgery. Specific IgE was analyzed using the ImmunoCAP FEIA system (Phadia, Freiburg, Germany) reported in kU/l and converted into RAST classes (0-6): class 0 (<0.35 kU/l); class 1 (0.35–0.69 kU/l); class 2 (0.70–3.49 kU/l); class 3 (3.50–17.49 kU/l); class 4 (17.50–49.99 kU/l); class 5 (50.00–99.99 kU/l); class 6 (≥ 100 kU/l). SPT were performed with commercially available allergen extracts (ALK-Abello, Wedel, Germany). Subjects were tested for a panel of 15 common inhalant allergens (pollen, dander, molds, and mites) which were applied to

the volar forearms and evaluated after 20 min. The allergen-induced ‘wheal and flare’ reaction’s diameter was measured according to the following established gradual classification: <3 mm (++); 3–5 mm (+++); > 5 mm (++++) . A wheal ≥ 3 mm in the presence of a positive histamine control and a negative isotonic sodium chloride control constituted a positive skin test result.

Visual analog scales (VAS) served to obtain and compare the pre-, intra-, and posttherapeutic subjective data. On a numeric scale from 0 to 10, patients had to evaluate their surgery-related pain and discomfort, postoperative satisfaction, and extent of allergic symptoms (nasal congestion, sneezing, itching, and rhinorrhea).

Rhinomanometry was used for assessment of nasal resistance from pressure–flow relationships because it is regarded as the most accurate measure of nasal airway patency [19]. Objective nasal congestion was quantified by active anterior rhinomanometry (Hortmann, Neckartenzlingen, Germany) under standardized conditions at a pressure of 150 Pa. Preoperative airflow curves were compared with postoperative measurements.

Statistics

All statistical tests and graphics were created using SPSS 16.0 statistical package (SPSS Inc., Chicago, IL) and SAS 9.1 (SAS Institute Inc., Cary, NC). For descriptive statistics, means $\pm$ SD, range, median, or quartile range were computed for all subjective and objective parameters depending on the distribution and scale of the measurements. Wilcoxon signed-rank tests and the paired *t* tests were performed to compare ordinal and metrically scaled data before and after laser surgery, respectively. Spearman’s correlation coefficients were determined to evaluate connections between subjective scores and objective measurements. The long-term longitudinal data analysis for the VAS scores was performed by a non-parametric ANOVA procedure as described in Brunner et al. [20]. The analysis was carried out by SAS macros provided by Brunner’s research group (<http://www.ams.med.uni-goettingen.de/de/sof/ld/makros.html>). The long-term longitudinal analysis for the metrical rhinomanometric data was done by repeated-measurements ANOVA. The level of significance was set at $\alpha=0.05$.

Results

Preoperative baseline data

Altogether, 40 patients aged 21 to 67 years (mean 40 ± 13 years) with confirmed diagnosis and fully documented data records entered laser therapy and complete follow-up evaluation. Study participants consisted of two groups: 20

pAR and 20 sAR subjects with comparable patient characteristics (e.g., sex ratio, age, sociodemographic criteria). All relevant baseline data are illustrated in Table 1. The mean duration of AR lasted 6 ± 3 years (range 2–18 years). All subjects experienced insufficient prolonged pharmacotherapy ≥ 2 years (e.g., antihistamines, leukotriene receptor antagonists, nasal corticosteroids). Decongestants were regularly applied by 11 pAR and 5 sAR subjects. Failed specific immunotherapy was reported by 5 pAR and 4 sAR patients. The overall response to preceding standard therapy revealed 62.5% of subjects with poor response (or unresponsive), 27.5% were incompliant, and 10% were intolerant.

Regarding current allergic complaints, nasal obstruction, rhinorrhea, sneezing, and itching were prevalent in all patients. Comparison of subjective VAS data in both AR groups did not disclose relevant distribution differences. Preoperative baseline values were highest for nasal obstruction, ranging from 4 to 10, with a median score of 7. The median VAS scores in pAR and sAR were 6 for rhinorrhea, 5 for sneezing, and 4 for nasal itching. Other common accompanying non-nasal symptoms were itchy eyes/throat/ears, eye-dropping, bronchial asthma, Eustachian tube dysfunction, and dull headaches.

The allergy tests showed that pAR was caused by house dust mites (HDM), moulds, or pets, while sAR patients

Table 1 Pretherapeutic patient characteristics. Data are expressed as number and percentage of subjects, unless otherwise noted

Characteristics	All patients (<i>n</i> =40)	pAR (<i>n</i> =20)	sAR (<i>n</i> =20)
Gender			
Male	19 (47.5%)	9 (45%)	10 (50%)
Female	21 (52.5%)	11 (55%)	10 (50%)
Age (years; mean $\pm$ SD)	40 $\pm$ 13	39 $\pm$ 13	42 $\pm$ 12
AR duration (years; mean $\pm$ SD)	6 $\pm$ 3	7 $\pm$ 4	6 $\pm$ 3
Response to standard therapy			
Poor response/ unresponsive	25 (62.5%)	13 (65%)	12 (60%)
Incompliant	11 (27.5%)	5 (25%)	6 (30%)
Intolerant	4 (10.0%)	2 (10%)	2 (10%)
Polysensitisation	34 (85.0%)	16 (80%)	18 (90%)
Predominant allergic sensitisation			
House dust mites	11 (27.5%)	11 (55%)	-
Tree pollen	8 (20.0%)	-	8 (40%)
Grass pollen	8 (20.0%)	-	8 (40%)
Moulds	5 (12.5%)	5 (25%)	-
Weed pollen	4 (10.0%)	-	4 (20%)
Pets	4 (10.0%)	4 (20%)	-
Appearance of nasal mucosa			
Pale, edematous, profuse rhinorrhea	31 (77.5%)	15 (75%)	16 (80%)
Beefy red, minimal rhinorrhea	9 (22.5%)	5 (25%)	4 (20%)
Endonasal pathologies			
Inferior turbinate hyperplasia	38 (95%)	19 (95%)	19 (95%)
Septal deformities (crests, spurs)	16 (40%)	9 (45%)	7 (35%)
Middle turbinate hyperplasia/concha bullosa	6 (15%)	4 (20%)	2 (10%)
AR-associated symptoms			
Nasal obstruction	40 (100.0%)	20 (100%)	20 (100%)
Rhinorrhea	40 (100.0%)	20 (100%)	20 (100%)
Sneezing	40 (100.0%)	20 (100%)	20 (100%)
Nasal itching	40 (100.0%)	20 (100%)	20 (100%)
Hyposmia	27 (67.5%)	15 (75%)	12 (60%)
Itchy eyes/throat/ears	26 (65.0%)	12 (60%)	14 (70%)
Epiphora	21 (52.5%)	10 (50%)	11 (55%)
Bronchial asthma	20 (50.0%)	8 (40%)	12 (60%)
Snoring	19 (47.5%)	10 (50%)	9 (45%)
Eustachian tube dysfunction	17 (42.5%)	8 (40%)	9 (45%)
Dull headaches	15 (37.5%)	9 (45%)	6 (30%)

were sensitised to tree, grass, or weed pollen. SPT and specific IgE revealed polysensitisation in 85% of subjects without group-specific differences. Regarding the particular predominant sensitisation with main clinical relevance, SPT displayed in both groups comparable wheal and flare reactions >5 mm diameter (++++). Mean baseline levels of allergen-specific IgE were similarly elevated, in sAR (median 25.7 kU/l, quartile range 14–40 kU/l) slightly higher compared to pAR subjects (median 19.1 kU/l, quartile range 12–41 kU/l). The detailed sensitisation-related serum concentrations are illustrated in Fig. 1. Converted into RAST scores, patients sensitised to HDM, moulds, tree or grass pollen yielded RAST classes ranging from 2 to 5; the median value was 4 (quartile range 3–4). Subjects with pet- or weed-sensitisation comprised only RAST class 3 and 4 (median 3.5). Mean baseline levels of total IgE were also increased, again slightly higher in sAR (median 458.3 kU/l, quartile range 346–638 kU/l) than in pAR patients (median 427.5 kU/l, quartile range 205–654 kU/l). There were no significant correlations between allergy test results (SPT wheal size, RAST class) and amount of nasal symptoms.

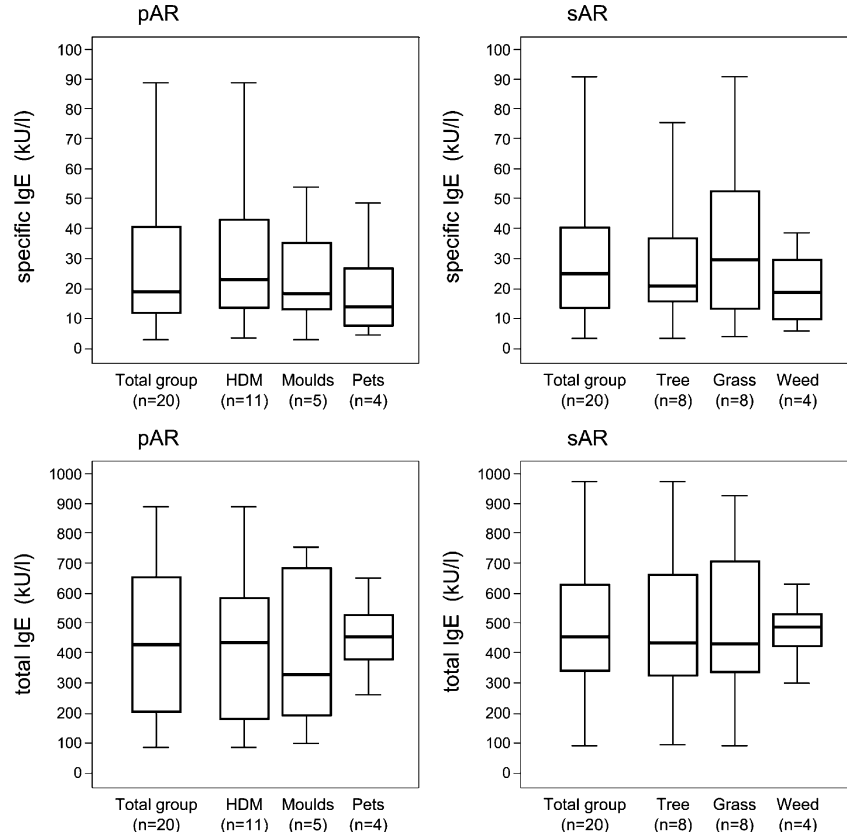
The nasal mucosa at first presentation was mainly pale, of bluish-grey color, and edematous (boggy) with profuse discharge. Videoendoscopic evaluation displayed the following obstructing endonasal pathologies: bilateral hyper-

plastic inferior turbinates in each 19 pAR and 19 sAR subjects, septal crests or spurs in 9 pAR and 7 sAR patients, and middle turbinate hyperplasia or concha bullosa in four pAR and two sAR subjects. Objective baseline rhinomanometry showed 282 ± 137 cm³/s mean total nose inspiration at 150 Pa (range 57–544 cm³/s), without significant differences ($p=0.659$) between pAR and sAR (292 ± 139 cm³/s vs. 272 ± 137 cm³/s).

Intra-, perioperative, and short-term results

According to the preoperative status, 95% of all patients (38/40) received inferior turbinate reduction, 40% (16/40) resection of septal deformities, and 15% (6/40) middle turbinate surgery. Figure 2 gives a typical impression of pretherapeutic endonasal pathologies, intraoperative diode laser treatment, and posttherapeutic videoendoscopic follow-up. For each side of the nose, the duration of laser treatment ranged from 4 to 17 min (mean 8 ± 4 min). In general, the surgical intervention was well tolerated. VAS resulted in very low scores for intraoperative pain (median 0, range 0–4) and discomfort (median 2, quartile range 0–3). In both groups, topical anesthetic preparation caused no relevant local or systemic side-effects. Most patients experienced temporary anesthesia-induced numbness of the upper front teeth, a feeling of slight endonasal pressure

Fig. 1 Preoperative group- and sensitisation-related serum concentrations of allergen-specific IgE (kU/l) and total IgE (kU/l) in pAR and sAR patients



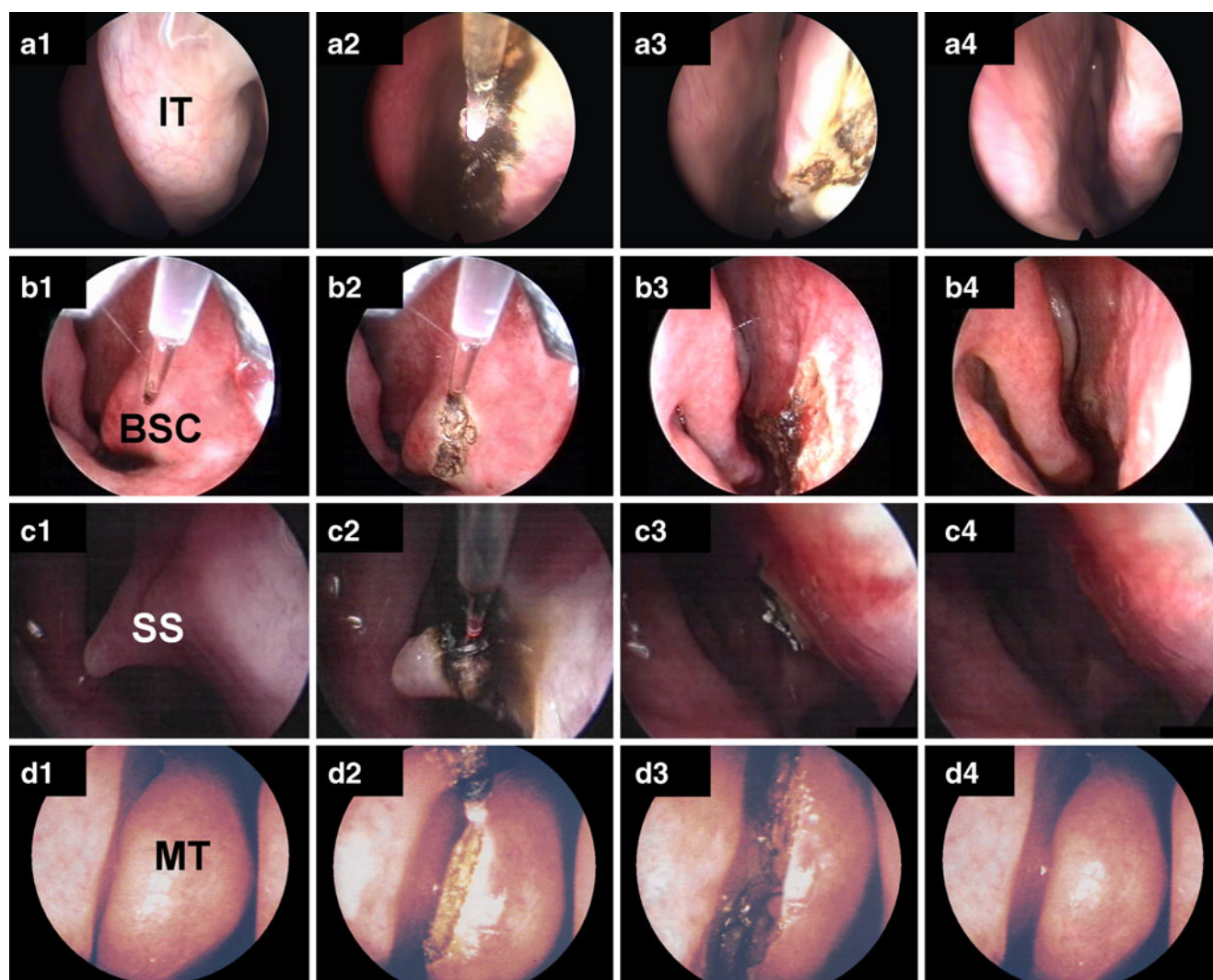


Fig. 2 Videoendoscopic recording of endonasal diode laser surgery in otherwise unresponsive AR. Examples for treatment of the following intranasal pathologies: **a** Hyperplastic inferior turbinate (IT; left side); **b** Anterior basal septal crest (BSC; right side); **c** Posterior septal spur

(SS; right side); **d** Hyperplastic middle turbinate (MT; left side). Photodocumentation was done before surgery (1), intraoperatively (2), directly after surgery (3), and during follow-up 2 years after laser treatment (4)

caused by the laser application system, and odor nuisance (“grill smell”) during laser vaporization. Painful laser-induced burning or stinging sensations were rarely observed and effectively treated by renewing topical anesthesia. There was no major bleeding requiring nasal packing, nor were there any other acute intra- or perioperative complications.

Concerning short-term results after 1 month, videoendoscopy showed an almost completed or advanced mucosal healing process. Crusting was decreased or already gone and the postoperative edema had disappeared in all subjects. Subjectively, 38 patients (19 pAR and 19 sAR) stated beginning improvement of general condition, especially of nasal obstruction, which was initially representing the cardinal and most compromising AR symptom. VAS confirmed highest reduction of median obstruction score

from 7 to 5 ($p < 0.0005$), which was more pronounced in pAR (median 4, quartile range 3–5) compared to sAR subjects (median 5, quartile range 4–5). These results were accompanied by smaller improvements (1 point each) for median rhinorrhea, sneezing, and itching scores (each $p < 0.0005$). Preliminary overall patient satisfaction was adequate (median 6, quartile range 6–7). Both patients without indication for inferior turbinate reduction reported unchanged or considerable residual symptomatology (95% overall response rate).

Postoperative results

Treatment outcome was evaluated at control visits 12 and 24 months after diode laser surgery. Videoendoscopy showed persisting widened nasal lumina in most cases

(Fig. 2). Throughout follow-up, subjective nasal symptoms in most patients decreased continuously with time. The VAS data confirmed the greatest improvement for nasal obstruction: The median score was reduced from 7 to 3 after 1 year with equal results after 2 years ($p<0.0005$). Reduction was similar in both groups until 12 months. At 24 months, the pAR group showed, in contrast to the sAR group, a slight reversion of that trend ($p=0.00001$). No significant general difference between pAR and sAR could be found ($p=0.561$). The other nasal symptoms showed smaller improvement without significant group-specific differences apart from rhinorrhea where VAS scores were slightly higher in the sAR group ($p=0.044$). Compared to baseline status, median VAS scores after 2 years were reduced for rhinorrhea from 6 to 4, for sneezing from 5 to 2, and for nasal itching from 4 to 2 (each $p<0.0005$). The reductions showed no group specific characteristics (no significant time group interaction). Detailed pre- and posttherapeutic box plots of subjective nasal symptom data for pAR and sAR subjects are depicted in Fig. 3. The overall patient satisfaction significantly improved with time ($p<0.0005$) and resulted for both AR groups similarly in high median satisfaction scores of 8 (quartile range 7–9) at the end of follow-up. Subjective improvement for ‘itchy eyes’ and other non-nasal allergic symptoms was limited and inconsistent.

Objective rhinomanometry at 150 Pa total nose inspiration revealed a significant mean ventilation increase from 282 ± 137 cm³/s (baseline) to 496 ± 140 cm³/s after 1 year and 485 ± 140 cm³/s after 2 years ($p<0.0005$). Regarding both patient groups, improvement after 1 year was considerably higher in pAR than in sAR subjects (533 ± 129 cm³/s vs. 459 ± 143 cm³/s). Two years postoperatively there was seen an opposite development: the mean improvement was slightly reduced in pAR but increased in sAR (490 ± 142 cm³/s vs. 480 ± 141 cm³/s). These differences were statistically not significant ($p=0.482$ for group effect and $p=0.618$ for group with time interaction). The maximum relative intraindividual change was a four-fold ventilation improvement in each 1 pAR and 1 sAR patient with bilateral inferior turbinate reduction and resection of obstructing septal deformities. The average intraindividual effect of endonasal laser surgery yielded significant airflow increases of 110% (1 year) and 106% (2 years), i.e., an approximately two-fold overall improvement compared to initial values. The differences between pre- and postoperative data and the 95% confidence intervals of expected values confirmed the significant lasting improvement of nasal ventilation, especially in patients with reduction of hyperplastic turbinates and accessory removal of interfering septal pathologies (Table 2). An AR subgroup analysis based on the different types of allergens was tried but did not lead to meaningful

results, because the sample sizes were too small. Rhinomanometry results were also consistent with the VAS data, which was proven by moderate correlations ($\rho=-0.552$, $p<0.0005$) between subjective obstruction scores and objective nasal airflow values at 150 Pa total nose inspiration before operation. No significant correlations could be found after 1 and 2 years as well as between the other VAS scores and the rhinomanometry results.

The allergic condition remained unchanged during the whole follow-up period. We observed no reduction of mean skin reactivity to skin prick tested allergen extracts. The in-vitro tests confirmed SPT results by showing that there were no significant differences in the serum levels of either specific or non-specific IgE pre- vs. postoperatively (data not shown). Comparison of pAR and sAR revealed no relevant differences or trends.

Altogether, 32 AR subjects (80%) after 1 year and 26 (65%) after 2 years established a stable non-medicated disease without relevant obstruction or other strongly compromising nasal symptoms. In contrast, 20% of all patients (four pAR, four sAR) had been taking on-demand medication during the first postoperative year due to recurrent allergic symptoms. After 2 years, 30% sAR (6/20) and 40% pAR (8/20) subjects had been receiving antiallergic pharmacotherapy. Conventional relief medication comprised topical nasal spray application of mometasone furoate (Nasonex; Essex Pharma, Munich, Germany), decongestants like xylometazolin hydrochloride (Otriven 0.1%, Novartis, Munich, Germany), and ipratropium bromide (Atrovent 0.03%, Boehringer, Ingelheim, Germany) in case of persisting heavy rhinorrhea. Most patients without pharmacotherapy stated that pursuing the non-medicated life reduced the burden of the disease.

Regarding the impact of co-variables on pAR and sAR outcome, no differences were found between the two patient groups. None of the other factors investigated (age, gender, AR duration, specific allergic sensitisation) had a significant influence on the diode laser treatment effectiveness.

Discussion

The established standard treatment of AR consists of four major components: patient education, environmental control measures and allergen avoidance, pharmacological management, and specific allergen immunotherapy [21–24]. Surgical care is not primarily indicated but may be recommended in comorbid or complicating conditions, such as chronic sinusitis, nasal polyposis, or anatomical abnormalities causing severe obstruction. However, the ideal strategy for severe pAR and sAR refractory to standard therapy is still lacking. This is the first study of

Fig. 3 Pre- and posttherapeutic subjective VAS data of nasal symptoms obstruction, rhinorrhea, sneezing, and itching in both patient groups. Box-plots display the median, quartiles, range of values covered by the data, and any outliers (*single dots*)

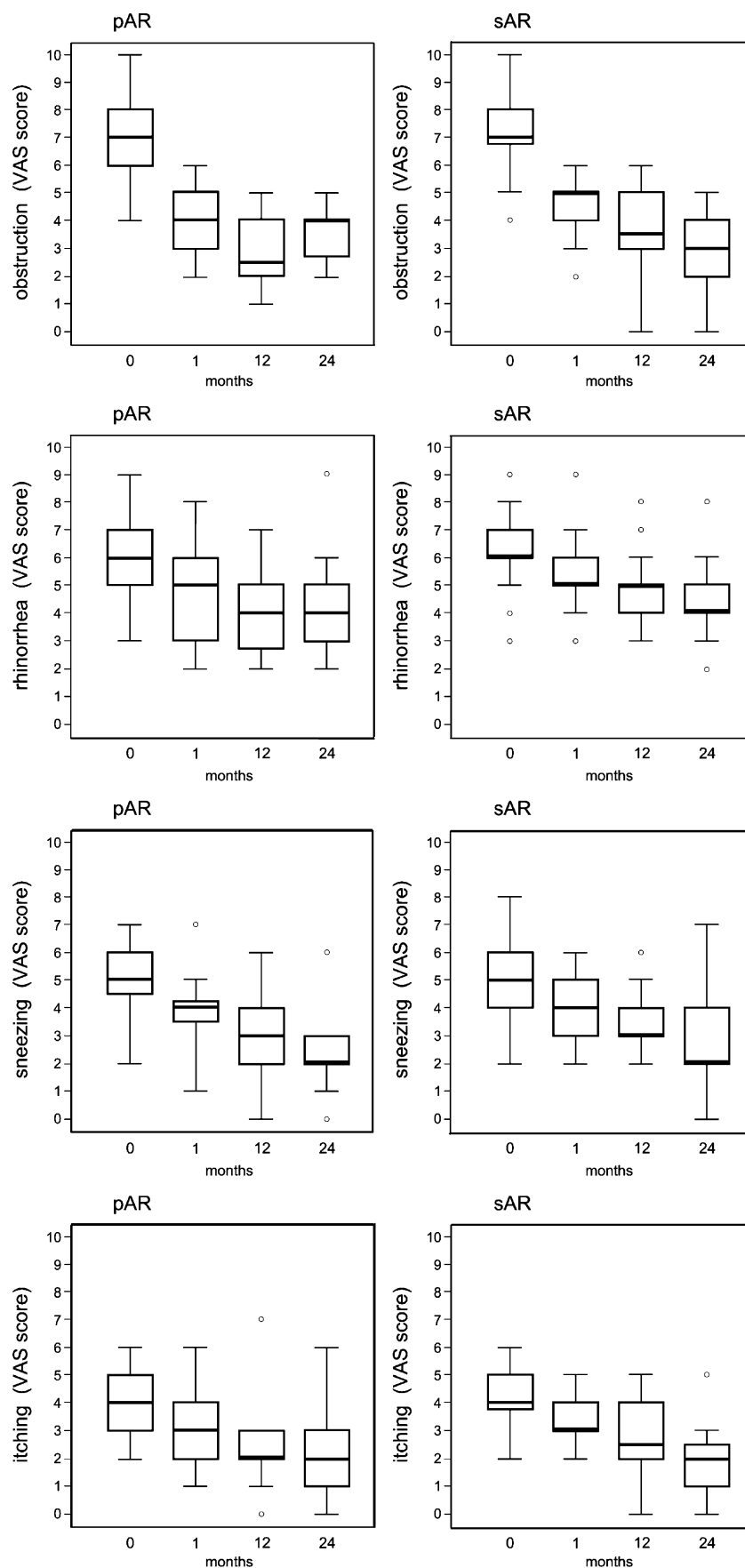


Table 2 Objective rhinomanometric improvement of nasal ventilation induced by endonasal diode laser treatment

Patient group	Therapeutic effect	Mean airflow differences (cm ³ /s)±SD		95% confidence interval for expected values	
		150Pa inspiration	150Pa expiration	150Pa inspiration	150Pa expiration
All patients (n=40)	Pre- vs. 1 year postoperative	214±109	200±107	(179, 249)	(166, 234)
	Pre- vs. 2 years postoperative	203±108	194±107	(169, 237)	(160, 229)
	1 vs. 2 years postoperative	-11±45	-6±46	(-26, 3)	(-21, 9)
pAR (n=20)	Pre- vs. 1 year postoperative	242±104	221±97	(193, 290)	(175, 266)
	Pre- vs. 2 years postoperative	199±99	182±95	(152, 245)	(138, 227)
	1 vs. 2 years postoperative	-43±32	-39±25	(-58, -28)	(-51, -27)
sAR (n=20)	Pre- vs. 1 year postoperative	187±110	180±115	(136, 239)	(126, 233)
	Pre- vs. 2 years postoperative	207±118	207±119	(152, 263)	(151, 262)
	1 vs. 2 years postoperative	20±33	27±38	(5, 36)	(9, 45)
Turbinate surgery (n=24)	Pre- vs. 1 year postoperative	175±111	162±110	(126, 225)	(110, 214)
	Pre- vs. 2 years postoperative	161±105	149±101	(119, 202)	(111, 188)
	1 vs. 2 years postoperative	-14±40	-13±37	(-30, 1)	(-27, 2)
Turbinate and septal surgery (n=16)	Pre- vs. 1 year postoperative	253±106	238±102	(202, 306)	(196, 279)
	Pre- vs. 2 years postoperative	248±113	235±117	(199, 297)	(180, 291)
	1 vs. 2 years postoperative	-5±44	-3±49	(-19, 10)	(-18, 12)

pAR/ sAR = perennial/seasonal allergic rhinitis; Pa Pascal

its kind demonstrating that endonasal corrective laser surgery may provide sustained effective reduction of all allergic nasal symptoms. In other words, diode laser septal and turbinate surgery increases the anatomical space of the common nasal ways rather than removes the allergic reaction, however this method seems to be clearly beneficial in otherwise therapy-resistant pAR and sAR.

Preoperatively, all baseline data were comparable in both patient groups. According to the literature, pAR and sAR may differ from more than only timing and periodicity of symptoms. Differences for persistent and intermittent AR were found for clinical features (e.g., symptom manifestation, age of onset, distribution of the disease, concomitance of asthma or another allergy) and diagnostic findings (e.g., rhinomanometric nasal airflow, skin reactivity to different aeroallergens, their interrelationship, covariation of sensitisation, level of total IgE antibodies) [25–29]. In general, histamine-induced sneezing, rhinorrhea and itching are often the pronounced symptoms in sAR. The key symptom of pAR is usually nasal obstruction, while sneezing and rhinorrhoea are often less troublesome than in sAR. In contrast, our results revealed that initial occurrence and strength of nasal symptoms in therapy-resistant pAR and sAR differed only marginally between groups. The cardinal and most compromising symptom was nasal obstruction due to pAR- and sAR-induced hyperplastic turbinates and septal pathologies. However, all patients had the typical allergy-associated endonasal symptom-complex (conditio

sine qua non): nasal obstruction, rhinorrhea, sneezing, and nasal itching. Therefore, also the clinical symptoms seen in sAR patients were primary related to AR, and not only to hypertrophic turbinate disease.

Diode laser treatment performed as an outpatient procedure under local anesthesia was well tolerated and showed promising long-lasting symptom relief in both patient groups. The improvement was greatest for nasal obstruction, initially higher in pAR but more sustained in sAR. However, objective rhinomanometric and subjective VAS data after 2 years showed a decline of therapeutic effect on nasal ventilation in pAR. Other studies concur with these findings, demonstrating a less pronounced and shorter-lasting effect in pAR compared to non-allergic rhinitis [30, 31]. Comparison to sAR has not been reported previously. Follow-up videoendoscopy confirmed increasing obstruction by showing slowly recurring growth of inferior turbinates in some pAR subjects. In contrast to sAR, the cavernous tissue tends to expand again, possibly because of the unchanged persistent allergic inflammation of the nasal mucosa [32]. Since patients continue to live in their familiar environment, including permanent contact with the individually relevant allergens, this may (especially in pAR) induce the recurrent hyperplasia of nasal turbinates. As shown in previous trials, our results demonstrate a significant relationship between the rhinomanometric degree of nasal airflow limitation and the severity of AR nasal symptoms [33].

The other nasal symptoms of rhinorrhea, sneezing, and itching also significantly improved, but without group-specific differences between pAR and sAR. In contrast, Sroka et al. [31] reported that the majority of their pAR patients, apart from nasal obstruction, did not experience any changes of these additional allergic symptoms after inferior turbinate laser treatment, indicating that the reason for the allergic reaction was not eliminated. However, our findings concur with those of other studies that showed postoperative improvement of all nasal symptoms in pAR [34–36]. Explaining histopathological examinations following surgery revealed that the lamina propria is occupied by fibrous tissues, and that the number of vessels and nasal glands in the turbinates decrease [36, 37]. Partial laser inferior turbinectomy is followed by a reduction in the number and activity of the glandular acini in the laser-treated areas [38]. The local destructive effect of laser energy on the glandular acini themselves, the surrounding cholinergic nerve fibers, and the afferent trigeminal fibers seems to explain the beneficial implications of laser surgery on secretory reflex, nasal pruritus, and generation of systemic sneeze reflex in suchlike treated AR [38–40].

With respect to immunological responses, we could not find any relevant therapy-related changes of the allergic condition in both patient groups' skin and in-vitro tests. However, Mori et al. [41] demonstrated a decrease in the allergic immune reaction after KTP-laser therapy, while Jovanovic and Dokic [32] could not prove a reduction of allergic mediators following Nd:YAG laser turbinectomy. An aggravating factor is that most pAR and sAR patients today are sensitised to more than one trigger [42]. According to our results, SPT and specific IgE revealed polysensitisation in 85% of subjects without group-specific differences. Clinically relevant polysensitisation with simultaneous impact of different allergens increases the intensity of allergic complaints [43]. Nevertheless, even though the underlying allergic condition remained unchanged, subjective appraisal after diode laser intervention referred to high overall satisfaction in the context of better well-being and improved quality of life.

Concerning surgical intervention, many different techniques have been described for relief of AR-associated nasal obstruction [31, 34, 35, 44]. The most commonly used procedures aim at volume reduction of hyperplastic inferior turbinates, which may be done via conventional surgery such as conchotomy, inferior turbinoplasty, lateral out-fracture, and turbinectomy. The main disadvantages of these techniques are a distinct risk of perioperative hemorrhage with necessity of nasal packing, uncontrolled mucosal damage with prolonged crusting or exposure of bone, and postoperative pain. Radical procedures like total

turbinectomy are obsolete, since they lead to ciliary destruction, atrophy of the mucous membrane, reduced humidifying capabilities of the nasal mucosa, and chronic infections. Vidian neurectomy and cauterization, which cut the parasympathetic and the major portion of the sympathetic supply to the nasal mucosa, were shown to abolish AR-induced hyperrhinorrhea but became obsolete too, owing to potentially serious complications like blindness and anosmia [45]. In contrast, our results confirmed that laser surgery offers the benefits of limited tissue trauma, rapid and bloodless operation, less postoperative edema, good spontaneous epithelialization of defects, less pain, and high patient acceptance under outpatient conditions. We used the diode laser because of various advantages over other laser systems successfully applied in endonasal surgery, i.e., excellent coagulation, good hemostatic and vaporization effects, flexible fiber-guided surgery, and preservation of deeper layers due to superficial tissue interaction (penetration depth 1–3 mm). Due to these favorable characteristics, no perioperative complications like bleeding or other serious adverse events were observed. Sometimes, vaporization of obstructing spurs and crests exposed their lower bony parts. In these cases, further irradiation and local heating up converted the bone into a white shining (“china-like”) fragile structure, which can be easily broken by using the laser fiber. This new structure seems to be biologically inert and well accepted by the mucosa during re-epithelialization. Granulation tissue in this area has not been observed. Altogether, accessory removal of interfering septal pathologies offered a supportive anti-obstructive benefit and may be superior over inferior turbinate surgery alone.

Conclusions

Outpatient endonasal corrective diode laser surgery appears to be an effective, safe and well-tolerated treatment option for otherwise therapy-resistant pAR and sAR. In both groups, all investigated nasal symptoms improved significantly, while the allergic condition remained unchanged (skin and in-vitro tests). Before considering endonasal laser surgery, our results suggest that patients should be divided into “blockers” vs. “sneezers and runners” [28]. Especially pAR and sAR “blockers” seem to benefit from laser treatment, resulting in long-lasting relief of nasal obstruction and improvement of accompanying nasal symptoms with complete stop or decreased use of antiallergic pharmacotherapy.

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