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Randomized trial of nasal surgery for fixed nasal obstruction in obstructive sleep apnoea

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Short title: Nasal surgery and obstructive sleep apnoea

Abstract

Although nasal surgery has limited efficacy in obstructive sleep apnoea treatment, some patients experience improvement. This study tested the hypothesis that post-surgery improvement is associated with increased nasal breathing epochs.

Forty-nine OSA patients [mean apnoea-hypopnoea index (AHI) 30.1±16.3 events·h^{-1}] with symptomatic fixed nasal obstruction due to deviated septum were randomly assigned to either septoplasty (surgery group; 27 patients) or sham surgery (placebo group; 22 patients). Breathing route was examined during overnight polysomnography.

Patients of the placebo group were non-responders, whereas in the surgery group, 4 patients were responders (14.8%) and exhibited considerable increase of nasal breathing epochs (epochs containing ≥3 consecutive phasic nasal signals), and 23 patients were non-responders presenting modest increase of nasal breathing epochs ($p<0.001$). The change in AHI was inversely related to the change in nasal breathing epochs ($R^2=0.775$; $p<0.001$); responders exhibited among the greatest increases in nasal breathing epochs. Baseline nasal breathing epochs were positively related to percent change in AHI ($R^2=0.610$; $p<0.001$). Responders had among the lowest baseline nasal breathing epochs; a cut-off value of 62.4% of total sleep epochs best separated (100% sensitivity, 82.6% specificity) responders/non-responders.

Nasal surgery rarely effectively treats obstructive sleep apnoea. Baseline nasal breathing epochs can predict the surgery outcome.

Keywords: apnoea-hypopnoea index; nasal breathing epochs; nasal surgery; obstructive sleep apnoea.

Introduction

In humans the nose normally accounts for about half of the total respiratory resistance to airflow [1]. During sleep, nasal obstruction can provoke an increase in airflow resistance upstream, promoting more negative intraluminal pressure in the pharynx and predisposing to pharyngeal occlusion [2]. Thus, experimentally induced nasal obstruction triggers the generation of obstructive apnoeas, and allergic rhinitis elicits both sleep fragmentation and obstructive sleep apnoea (OSA) [3, 4].

Despite the relationship between nasal obstruction and OSA, the therapeutic role of improving nasal airway patency on OSA severity remains a point of conjecture [5]. In fact, administration of intanasal corticosteroids has been shown to improve sleepiness and reduce the apnoea-hypopnoea index in patients with OSA and rhinitis [6], whereas several uncontrolled trials examining the impact of surgical correction of deviated nasal septum on OSA severity provided inconsistent and rather disappointing results [7]. The reasons for this limited efficacy of the surgical correction of nasal obstruction are unclear [8]. Interestingly, within these trials, there were OSA patients who experienced polysomnographic and symptomatic resolution following nasal surgery [7, 9].

The importance of breathing route (oral or nasal) in upper airway obstruction during sleep has been well documented. Indeed, the present authors demonstrated a potent correlation between oral/oro-nasal breathing epochs and the number of apnoeas and hypopnoeas [10], and forced mouth breathing has been shown to exert a profound influence on OSA severity [5]. Accordingly, the change in breathing route induced by increased nasal resistance could by itself contribute to the increase in the frequency of sleep-related breathing disorders [11, 12]. Consequently, the surgical reversal of nasal obstruction and prevention of the ensuing shift to oral breathing has prompted FITZPATRICK *et al* to make the plausible speculation that the breathing route before and after nasal surgery might be a determinant of the surgical outcome [5, 13].

Therefore, the purpose of this study was to examine the effectiveness of surgical correction of nasal obstruction on alleviating OSA through a randomized placebo-controlled trial (sham surgery) and to investigate whether the breathing route before and after surgery is associated with the outcome of nasal surgery. Our hypothesis was that patients with OSA who respond to nasal surgery by reducing the number of apnoeas-hypopnoeas might exhibit preoperatively decreased proportion of

nasal breathing epochs, and thus, greater potential for increasing them postoperatively in comparison with patients with OSA who do not benefit from nasal surgery.

Methods

Study subjects

Fifty-one consecutive subjects who referred to the Center of Sleep Disorders of "Evangelismos" General Hospital of Athens for suspected sleep disordered breathing were recruited. The enrolment criteria were: 1) nasal septum deviation with or without inferior turbinal hypertrophy, as assessed by clinical examination and flexible fiberoptic nasopharyngoscopy along with nasal resistance values exceeding normal limits at baseline (symptomatic fixed nasal obstruction), 2) apnoea/hypopnoea index greater than 5 events·h^{-1} at baseline, 3) no upper or lower respiratory tract disease, including a history of nasal allergy, 4) no recent surgery involving upper airway, 5) no use of medications known to influence nasal resistance (antihistamine, decongestants, etc), and 6) no history of any neuromuscular or cardiovascular disease. Exclusion criterion was considered the treatment of OSA with continuous positive airway pressure (CPAP) during the course of the study.

Using a table of random numbers, subjects were randomized to either the surgery group or the placebo group (sham surgery). The subjects of the placebo group were offered nasal surgery at the end of the study. One otolaryngologist performed all operations under topical anaesthesia. Due to long waiting lists for both diagnosis and treatment with CPAP (3 to 4 months in the latter situation in our hospital), the CPAP treatment in all patients included in the study, if needed, was delayed only for a period similar to that in which CPAP treatment would normally have been provided.

Prior to enrolment to the study, each participant provided informed consent, which included writing in a chart, "On entering this study, I realize that I may receive placebo surgery. I further realize that this means that I will not have nasal surgery. This placebo nasal surgery will not benefit OSA". The study protocol was approved by the hospital ethics committee.

Study protocol

Sleep studies were performed one month or less before (baseline study) and three to four months after surgery. Each subject reported to the sleep laboratory between 9 and 10pm. Nasal resistance was measured in upright seated and supine

positions. A full-night diagnostic polysomnography with concomitant monitoring of the breathing route during sleep was then performed, usually from midnight to 7am.

Rhinomanometry

For each subject, nasal resistance to airflow was measured during wakefulness first in the upright seated position and then in supine position by active anterior rhinomanometry (PDD-301/r, Piston, Budapest, Hungary) using a standard protocol [10].

Polysomnographic methods

A full-night diagnostic polysomnography (EMBLA S7000, Medcare Flaga, Iceland) was performed in each subject. To determine the stages of sleep an electroencephalogram (with four channels, C4-A1, C3-A2, O2-A1, O1-A2), electro-oculogram and electromyogram of the submentalis muscle were obtained. Arterial blood oxyhemoglobin was recorded with the use of a finger pulse oximeter. Thoracoabdominal excursions were measured qualitatively by respiratory effort sensors [XactTrace belts featuring Respiratory Inductive Plethysmography (RIP), Medcare Flaga, Iceland] placed over the rib cage and abdomen. Snoring was detected with a vibration snore sensor and body posture with a body position sensor. Airflow was monitored using an oral thermistor (oral flow sensor, Medcare Flaga, Iceland) placed in front of the mouth and a nasal cannula/pressure transducer (21in/53cm, Medcare Flaga, Iceland) inserted in the opening of the nostrils and linked to independent channels, as previously described [10]. All variables were recorded with a digital acquisition system (Somnologica 3.3, Medcare Flaga, Iceland).

Surgery group

All patients underwent submucous resection of the deviated nasal septum; in most patients (18/27) submucous resection of the bilateral inferior turbinates was also performed. Nasal packing was removed on the second postoperative day and routine saline nasal irrigation and debridement were performed. Postoperatively, none of the patients experienced any complication.

Placebo group (sham surgery)

To ensure blinding, a standard submucosal resection of the nasal septum was simulated. After the infiltration of the nasal septum with 10ml lidocaine 1% containing epinephrine 1:200000 the surgeon asked for all instruments and manipulated the nose as if submucosal resection was being performed. The patients remained in the operating room for the same amount of time required for the surgery

group. Patients spent the night after the procedure in the hospital and were cared for by nurses who were unaware of the treatment group assignment. Nasal packing was removed on the second postoperative day and routine saline nasal irrigation and debridement were performed.

End points and definition of treatment response

The primary end point was the reduction in apnoea-hypopnoea index (AHI) in the surgery group *versus* the control group. In this context, treatment success was defined as a postoperative AHI of less than 15 events·h^{-1} along with at least 50% decrease from the baseline AHI (responders) [14]. Treatment failure was defined as a postoperative AHI of more than 15 events·h^{-1} and/or a decrease of AHI from baseline less than 50% (non-responders). A complete response was defined as a reduction in AHI to 5 events·h^{-1} or less (normalization of AHI). Secondary end point-was daytime sleepiness assessed by the Epworth sleepiness scale score.

Analysis

Sleep stage was scored manually in 30-s epochs [15]. Obstructive respiratory events were scored using standard criteria [16, 17]. Route of breathing was evaluated by using the oral and nasal sensor signals to classify each 30-s epoch as nasal, oral or oro-nasal based on the predominant breathing route, and was expressed in % total sleep epochs (TSE), as previously described [10]. Cross-contamination between the oral and nasal channel was meticulously excluded by regular testing during polysomnographic calibration. Thus, we asked subjects to breathe normally and exclusively through the nose for 30 s and subsequently through the mouth for another 30 s in both supine and right lateral postures so that we could verify that each sensor was activated exclusively. We continuously checked sensors during the recording to avoid dislodgement. All measurements were analyzed by a single investigator to ensure consistency and all polysomnographies were scored by a single experienced sleep technologist and subsequently reviewed by the same investigator, who was blinded to the patient's group identity.

The minimum sample size was calculated based on 80% power and a two-sided 0.05 significance level using the Statistica 7.0 statistical program. Sample size capable to detect a change of 10 events·h^{-1} for AHI after surgery was estimated using mean baseline value of AHI 36 events·h^{-1} and the same standard deviation before and after surgery (14 events·h^{-1}) which were obtained from a previous study [18]. The critical sample size was estimated to be 24 patients. Data are presented as mean ± SD,

unless otherwise specified. Baseline difference between groups concerning age was tested by unpaired t-test. Two-way analysis of variance (ANOVA) with repeated measures was used for variable comparisons between groups before and after surgery, followed by the Scheffé test for *post-hoc* analyses as appropriate. Linear regression analysis was performed using the least square method. Diagnostic performance of baseline nasal breathing epochs to distinguish responders from non-responders to surgery was expressed as the area under the receiver operating characteristic curve. A value of 1.0 indicates perfect discrimination. Cut-off value achieving the best combination of sensitivity and specificity was calculated as the maximum difference between sensitivity and (1- specificity). A p value of < 0.05 was considered to indicate statistical significance.

Results

Of the 51 patients (39 men) initially fulfilling the inclusion criteria, eligible for further analysis were considered 49. Two patients dropped out because of willingness to begin CPAP therapy. There were 27 subjects randomly assigned to the surgery group and 22 subjects to the placebo group. Baseline characteristics were similar in these two study groups (table 1). There was no change in body mass index after surgery or sham surgery. Nasal resistance decreased in both seated and supine positions ($p<0.001$) in the surgery, whereas remained unchanged in the placebo group.

Apnoea-hypopnoea index

AHI remained unchanged after surgery or sham surgery (table 1). Based on our pre-study endpoints and definitions of treatment response, 23 patients of the surgery group (85.2%) were treatment failures (non-responders), whereas 4 patients (14.8%) were treatment successes (responders; table 2, fig. 1). Only one patient of the surgery group (3.7%) presented complete response. AHI decreased in responders and increased in non-responders ($p<0.001$, two-way ANOVA; table 2). All patients of the placebo group were treatment failures (fig. 1).

Epworth Sleepiness Scale

Epworth score was the same in patients of the surgery and placebo group at baseline and decreased after treatment only in the surgery group (table 1). Baseline Epworth score was lower in non-responders than in responders, and decreased after nasal surgery only in responders ($p<0.001$; table 2). Individual values of Epworth

score, along with nasal resistance and AHI of patients of the surgery group, are contained in table 3.

Nasal and oral/oro-nasal breathing epochs

Baseline proportion of nasal and oral/oro-nasal breathing epochs did not differ in patients of the surgery and placebo group, but after surgery nasal breathing epochs increased and oral/oro-nasal breathing epochs decreased in the surgery group, whereas they remained unchanged in the placebo group ($p<0.05$; table 1). Baseline oral/oro-nasal breathing epochs were lower and nasal breathing epochs were higher in non-responders than respective baseline in responders (table 2). Most importantly, baseline nasal breathing epochs could discriminate responders from non-responders; the area under the receiver operating characteristic curve was 0.924 ± 0.054 (mean ± standard error), and the cut-off value of nasal breathing epochs at baseline that best separated (100% sensitivity and 82.6% specificity) responders from non-responders was 62.4% of total sleep epochs (fig. 2). Individual values of nasal breathing epochs at baseline and after surgery in responders and non-responders are also illustrated in figure 2. Nasal breathing epochs increased, whereas oral/oro-nasal breathing epochs decreased in both groups, but they changed in a significantly greater degree in responders than in non-responders ($p<0.001$; fig. 3). The change in nasal breathing epochs after surgery was inversely related to the change in AHI ($R^2=0.775$, $p<0.001$; fig. 4); responders exhibited the greatest increases in nasal breathing epochs after surgery. Finally, baseline nasal breathing epochs were positively related to the percent change in AHI ($R^2=0.610$, $p<0.001$; fig. 5).

Discussion

The main findings of this randomized controlled trial of surgical correction of fixed nasal obstruction in obstructive sleep apnoea were that: 1) nasal surgery does not influence apnoea-hypopnoea index; only 15% of patients experienced significant reduction in apnoea-hypopnoea index (responders) and only 4% of patients had a complete response (normalization of AHI); 2) the change in AHI after surgery was inversely related to the change in nasal breathing epochs, so that the increase in nasal breathing epochs explained 77.5 % of variance of the decrease in AHI; responders exhibited among the greatest increases in nasal breathing epochs after surgery; 3) baseline nasal breathing epochs were positively related to the percent change in AHI after surgery, so that lower baseline nasal breathing epochs explained 61.0 % of

variance of the percent decrease in AHI after surgery; responders had among the lowest baseline nasal breathing epochs; and 4) baseline nasal breathing epochs with a cut-off value of 62.4 (% total sleep epochs) separated responders from non-responders with 100% sensitivity and 82.6% specificity.

The present study is the first to examine the role and prove the rare efficacy of nasal surgery in the treatment of OSA in a randomized controlled with sham surgery setting. In fact, in the absence of a control group any result obtained by previous trials may have been attributed not only to the intrinsic effect of the surgical procedure but also to either the natural history of the condition or the independent placebo effect [19]. In general, previous studies were prospective pre- and post-surgery comparisons [7, 9, 18, 20, 21] or retrospective case series [22, 23], the surgical procedures they employed were heterogeneous [7, 20, 21], and often objective assessment of nasal resistance was not performed in all patients [18, 21, 22]. In particular, in an analysis of nine of them, 18% of patients achieved response defined by a postoperative AHI of less than 20 events·h^{-1} along with at least 50% decrease from the baseline AHI [7], a finding modestly better than that of the present study (15% of our patients fulfilled this definition of response); combining this results with the findings of our study, it appears that septoplasty with or without bilateral inferior turbinate resection has indeed a limited role in the management of sleep-disordered breathing. However, the role of nasal surgery in facilitating the initiation of CPAP therapy is unequivocal [20], since it has been proven that postoperatively the continuous positive airway pressure needed to reverse OSA is significantly reduced [21].

In respect to the role of nasal breathing epochs, the present study can have important ramifications for clinical practice. That is because nasal surgery has a significantly variable effect on OSA ranging from complete resolution to severe aggravation and, thus the ability of baseline nasal breathing epochs to predict therapeutic response is of paramount importance. This inconsistent effect of nasal surgery on OSA is not novel [7], but is in line with the assumption that pharyngeal collapsibility is sensitive to alterations in upper airway anatomy through both local mechanical factors and neuromuscular tone changes [24, 25]. Hence, it appears that nasal surgery should be avoided in OSA patients with nasal obstruction when baseline proportion of nasal breathing epochs is more than ~ 62 % of total sleep epochs (fig. 2). In this context, although the association between nasal obstruction and the proportion of nasal breathing is intuitively obvious [5], a moderate increase in nasal resistance

may not induce a decrease in nasal breathing but a "through high nasal resistance" breathing pattern [13]. Similarly, OHKI *et al* concluded that in normal subjects very high resistive load is needed to be added to the nasal breathing circuit to provoke a shift to pure mouth breathing [26]. These observations give credence to the contention that nasal resistance is only important to the point where it exceeds a certain threshold and triggers the shift to oro-nasal breathing. Therefore, as nasal resistance in the present study was equal in responders and non-responders at baseline, it is plausible to suggest that responders had lower threshold than non-responders, thereby presenting decreased proportion of nasal breathing epochs for a given value of nasal resistance. Moreover, the increase in nasal breathing epochs postoperatively might also be a surrogate for reduced mouth opening. Indeed, the latter has been convincingly associated in previous studies with sleep disordered breathing through many causal pathways [10].

It is noteworthy that several lines of evidence support the argument that mouth breathing induced by nasal obstruction facilitates the induction of apnoeas [5, 10, 11]. FITZPATRICK *et al* documented a marked increase in OSA severity in mouth breathing as compared to nasal breathing, the normal pathway for ventilation during sleep [5, 11]. Moreover, the proportion of oral and oro-nasal breathing epochs has been shown to be positively related to the severity of sleep disordered breathing [10]. The results of the current study add weight to the same argument demonstrating that surgical reversal of nasal obstruction improves OSA only when it succeeds in restoring the preponderance of nasal breathing epochs postoperatively.

Patients who underwent nasal surgery, in contrast to those who underwent sham surgery, experienced a significant reduction in the level of daytime sleepiness (table 1). Yet, this improvement was confined in responders, whereas in non-responders Epworth score remained unchanged (table 2). The improvement observed in daytime somnolence may be related not only to the improvement in sleep apnoea severity but also to a relief of nasal discomfort associated with nasal obstruction. Indeed, CRAIG *et al* documented that reducing nasal congestion with topical corticosteroids in patients with allergic rhinitis improved subjective sleep quality [27].

Some methodological issues require consideration in the current study. Foremost, it is a short-term study with a follow-up period ranging from 3 to 4 months. It is possible that the longer-term effect of relieving nasal obstruction on OSA severity might be different. Nonetheless, VERSE *et al* reviewing the outcome of nasal

surgery as a treatment for OSA in nine studies where the follow-up period varied from 1 to 44 months failed to discern any trend towards sleep apnoea severity improvement with longer follow-up [28]. Moreover, the study was adequately powered to detect an improvement in AHI of 10 events·h^{-1}, because any less improvement is unlikely to be clinically relevant. Thirdly, nasal resistance was measured in seated and supine positions using anterior rhinomanometry alone. Anterior rhinomanometry requires minimal cooperation and, thus has increased reproducibility and negligible failure rate, although posterior nasal malformations cannot be determined. Nonetheless, posterior rhinomanometry was performed in all patients, but the results were not always acceptable. However, thanks to flexible fiberoptic nasopharyngoscopy the possibility of posterior nasal malformations was convincingly eliminated and, accordingly the results of posterior rhinomanometry were omitted from further analysis. Fourthly, the instrumentation of nasal cannula/pressure transducer and oral thermistor to detect airflow presents some drawbacks that have been thoroughly discussed previously [10]. Although these devices are non-obtrusive and easily tolerated, they cannot quantify ventilation, partly because their signal-flow relationship is non-linear resulting in underestimation of nasal ventilation and overestimation of oral ventilation, especially at low flows [29, 30]. Therefore, it would be possible that oral only breathing may still have a nasal component, and any detection of oral only breathing might actually be scarce. Therefore, the frequency of oral only breathing epochs could be overestimated in the present study, although it was already rarely encountered. Finally, although sensor dislodgement from the nares or from the mouth was meticulously checked by the technician on duty, it is possible that slight deviations in thermistor position may not have been completely avoided, and this may have then resulted in nasal airflow contamination of the oral signal.

In conclusion, this randomized controlled study provided evidence that nasal surgery is not in general effective in the treatment of obstructive sleep apnoea, as only ~15% of patients presented a postoperative AHI of less than 15 events·h^{-1} along with at least 50% decrease from baseline AHI and only 4% of patients presented a complete polysomnographic resolution. However, the proportion of nasal breathing epochs preoperatively can accurately delineate the subgroup of patients that can benefit from nasal surgery. Further studies are needed to confirm prospectively the performance of the cut-off point of baseline nasal breathing epochs detected in the present study to predict surgery outcome.

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Table 1. Anthropometric data, nasal resistance values and polysomnographic parameters at baseline and after surgery in the surgery and placebo groups.

	Surgery group (n=27)		Placebo group (n =22)	
	Baseline	After surgery	Baseline	After sham surgery
Age, y	39.0±7.5		37.6±8.8	
Male sex, %	63.0		59.1	
Body mass index, $kg \cdot m^{-2}$	30.4±3.2	31.0±3.6	29.9±3.5	30.3±3.5
Apnoea-hypopnoea index, $events \cdot h^{-1}$	31.5±16.7	31.5±18.2	30.6±13.8	32.1±14.3
Nasal Resistance seated, $cmH_2O \cdot L^{-1} \cdot s$	4.2±0.9	2.0±0.6**	4.0±0.8	4.0±0.7
Nasal Resistance supine, $cmH_2O \cdot L^{-1} \cdot s$	4.5±1.0	2.4±0.5**	4.4±0.8	4.4±0.7
Average oxygen saturation, %	94.3±1.1	94.5±1.4	95.0±1.1	95.0±1.0
Mean duration of apnoea-hypopnoea, s	23.2±3.7	23.7±3.0	22.0±2.4	22.1±2.5
Epworth Sleepiness Scale Score	13.4±2.9	11.7±3.4**	13.7±4.4	12.5±3.7
Sleep time in supine posture, min	151.5±102	153.0±92.7	148.2±99.1	153.2±96.7
Nasal breathing epochs % TSE	71.4±13.2	84.0±6.0**	74.1±11.8	74.3±10.6
Oral breathing epochs % TSE	3.5±3.8	1.3±1.3*	3.6±2.7	3.3±2.3
Oro-nasal breathing epochs % TSE	25.1±10.0	14.8±5.4**	22.3±9.2	22.4±8.4

Data are presented as mean ± SD. TSE: total sleep epochs. *: $p<0.05$ versus baseline; **: $p<0.01$ versus baseline.

Table 2. Anthropometric data, nasal resistance values and polysomnographic parameters at baseline and after surgery in the responders and non-responders.

	Responders (n=4)		Non-responders (n=23)	
	Baseline	After surgery	Baseline	After surgery
Age, yrs	36.3±5.9		39.4±7.8	
Male sex, %	75.0		60.9	
Body mass index, $kg \cdot m^{-2}$	27.8±4.3	28.0±4.3	30.9±2.9**	31.5±3.3
Apnoea-hypopnoea index, $events \cdot h^{-1}$	31.0±21.3	8.1±4.0*	31.6±16.8	35.6±16.5*
Nasal Resistance seated, $cmH_2O \cdot L^{-1} \cdot s$	4.3±0.7	1.8±0.3*	4.2±0.9	2.1±0.6*
Nasal Resistance supine, $cmH_2O \cdot L^{-1} \cdot s$	4.8±0.7	2.3±0.2*	4.5±1.0	2.4±0.6*
Average oxygen saturation, %	95.1±1.0	96.1±0.9	94.2±1.0	94.2±1.2
Mean duration of apnoea-hypopnoea, s	22.3±2.5	23.1±3.6	23.4±3.5	23.6±3.2
Epworth Sleepiness Scale Score	16.0±3.6	11.8±5.0*	13.0±2.6**	11.7±3.2
Sleep time in supine posture, min	157.3±69.9	155.8±76.2	150.1±100.1	151.9±97.2
Nasal breathing epochs % TSE	53.1±6.8	89.6±4.1*	74.6±11.3$^{\#}$	83.0±5.8*
Oral breathing epochs % TSE	8.5±5.1	1.1±1.4*	2.6±2.9$^{\#}$	1.3±1.3*
Oro-nasal breathing epochs % TSE	38.4±3.7	9.3±2.7*	22.8±8.7$^{\#}$	15.7±5.2*

Data are presented as mean ± SD. TSE: total sleep epochs. *: $p<0.05$ versus baseline; **: $p<0.05$ versus baseline of the responders; $^{\#}$: $p<0.001$ versus baseline of the responders.

Table 3. Individual values of nasal resistance, apnoea-hypopnoea index, and Epworth Sleepiness Scale scores of patients of the surgery group, at baseline and after surgery.

Patient No	Baseline NR	After surgery NR	Baseline AHI	After surgery AHI	Baseline ESS	After surgery ESS
1	5,3	2,1	51,7	8,3	19	17
2	3,7	2,3	10,6	2,3	12	7
3	3,9	2,1	13,2	17,9	11	9
4	4,2	2,6	65,7	79,8	18	16
5	3,7	1,1	42,0	26,7	13	10
6	5,0	2,2	21,8	10,9	19	15
7	3,8	2,2	47,6	29,9	15	10
8	3,6	2,1	48,8	26,7	14	11
9	5,1	2,5	39,9	10,7	14	8
10	4,0	2,6	22,3	29,9	16	16
11	5,9	2,7	44,1	58,7	14	14
12	6,3	1,9	40,2	55,1	15	14
13	6,9	2,4	21,6	34,8	10	9
14	6,2	2,7	6,4	19,9	8	5
15	5,1	1,9	7,3	16,8	9	10
16	4,1	1,9	14,5	14,4	10	7
17	3,5	1,9	11,5	26,8	13	12
18	4,8	2,3	19,6	28,8	14	13
19	3,7	2,5	23,5	31,3	16	16
20	4,2	2,7	36,7	48,8	15	16
21	3,7	2,0	41,1	49,9	14	12
22	4,3	2,3	23,4	33,2	15	14
23	3,5	2,0	37,8	27,2	14	13
24	3,4	2,1	54,5	56,4	13	15
25	4,40	3,30	31,00	30,70	11	11
26	5,00	3,60	56,20	52,30	11	9
27	5,50	3,70	18,10	22,20	9	7

NR: Nasal Resistance in supine posture; AHI: Apnoea-hypopnoea index; ESS: Epworth Sleepiness Scale. Patients numbered 1, 2, 6 and 9 fulfilled the criteria for treatment success (responders).

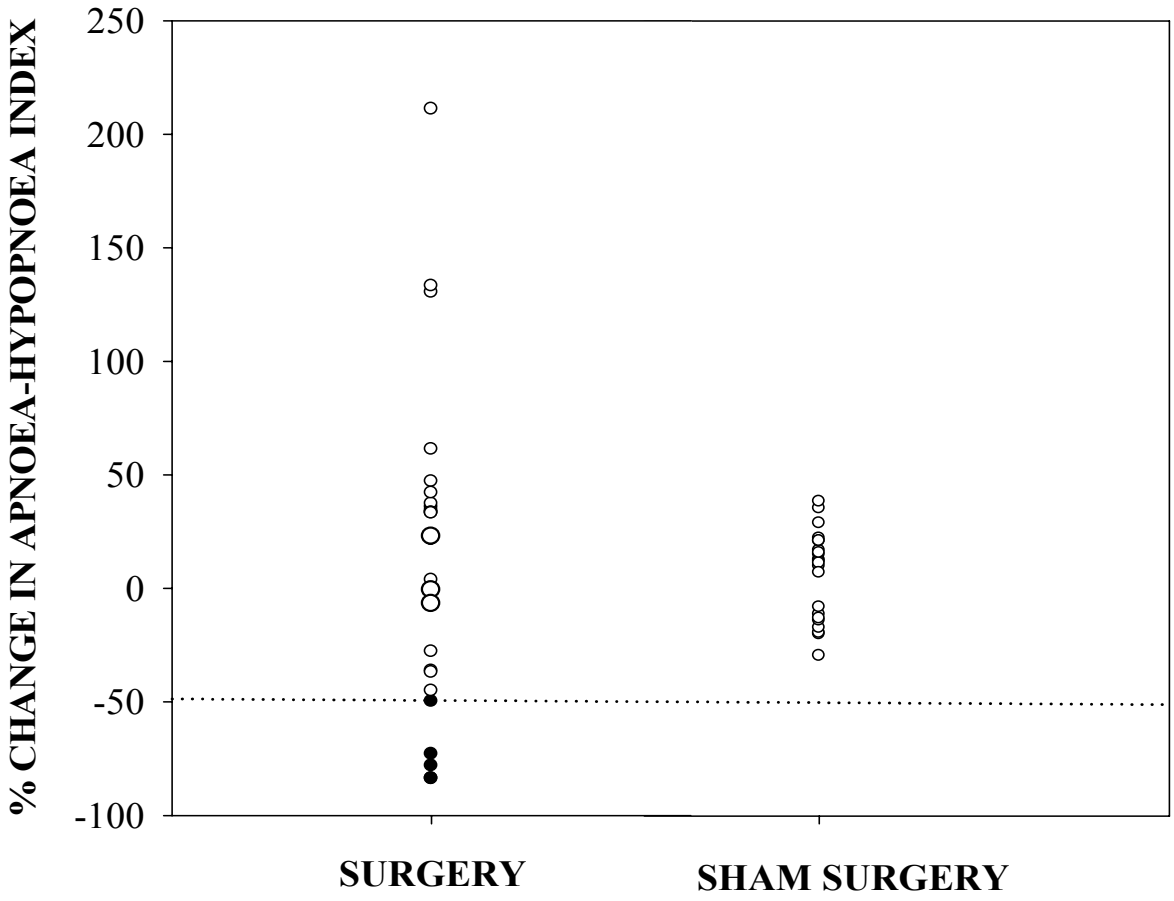

Figure 1. Percent change of apnoea-hypopnoea index in patients of the surgery group [responders (•) and non responders (°)] and the placebo group (sham surgery) [non responders (°)]. Dotted horizontal line: limit of % change in apnoea-hypopnoea index after surgery compared to baseline (-50%). This limit along with postoperative apnoea-hypopnoea index of less than 15 events·h^{-1} was used to define treatment response.

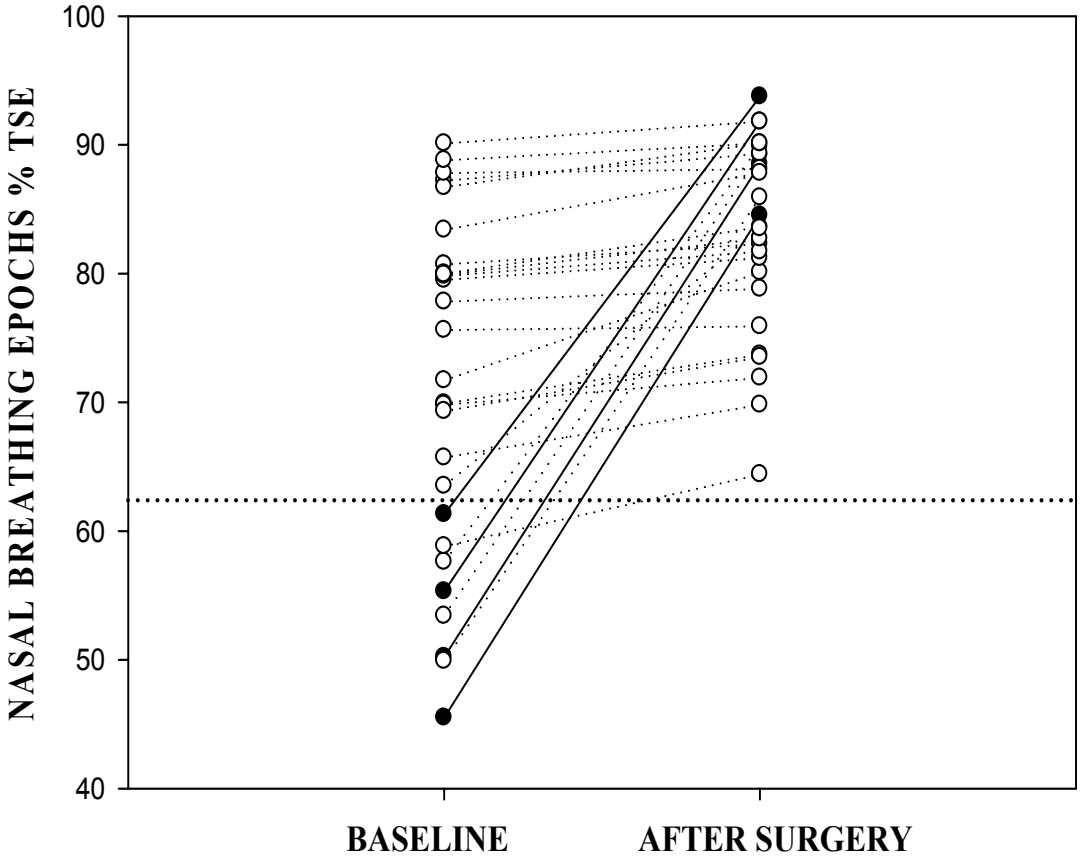

Figure 2. Nasal breathing epochs at baseline and after surgery in responders (●) and in non responders (○). Dotted horizontal line: cut-off value of baseline nasal breathing epochs (62.4% TSE) with maximum diagnostic discrimination of response to surgery (100% sensitivity and 82.6% specificity). TSE: total sleep epochs.

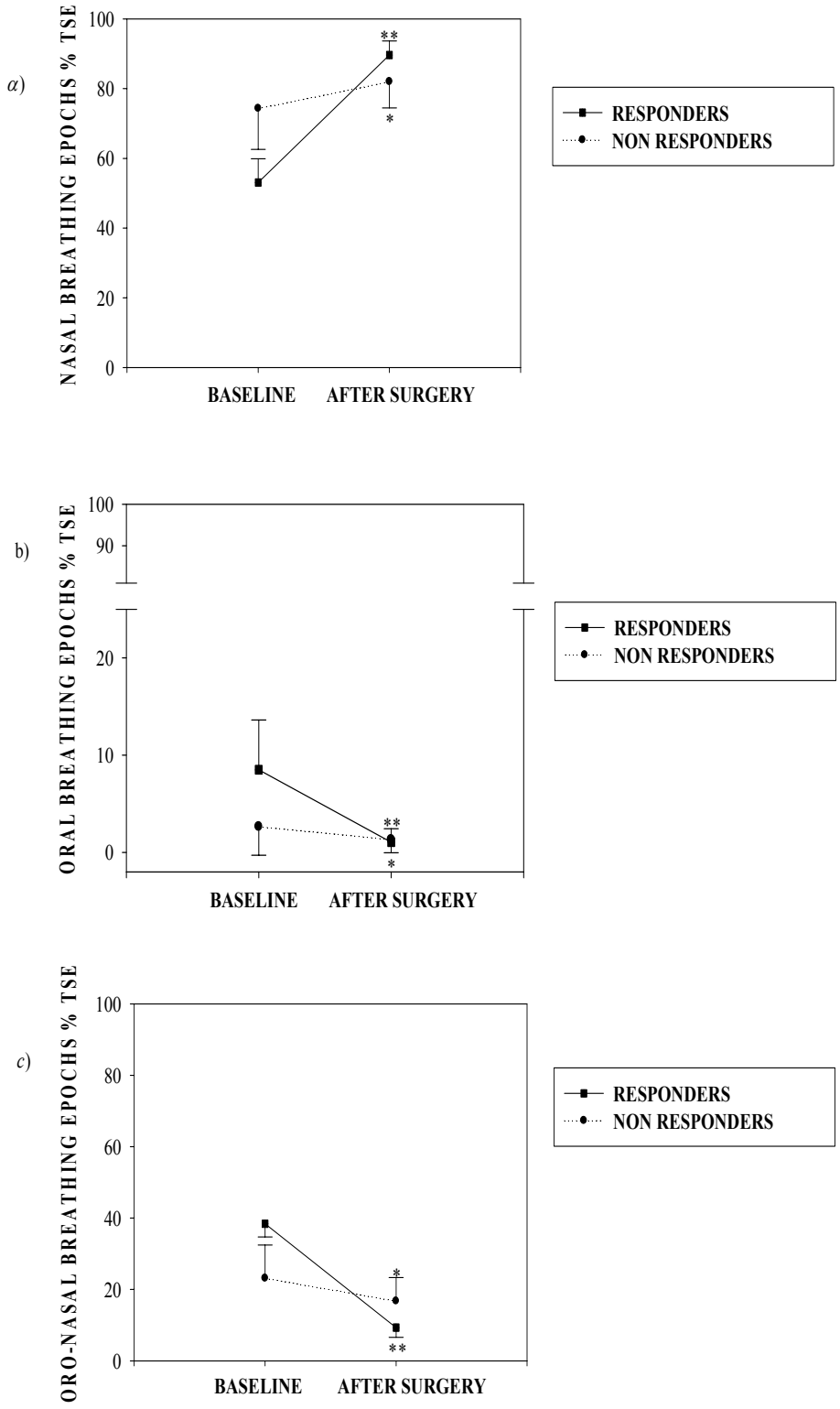

Figure 3. Occurrence of a) nasal, b) oral, and c) oro-nasal breathing epochs at baseline and after surgery. Data are presented as mean ± SD. *: $p<0.05$ *versus* baseline. **: $p< 0.001$ *versus* baseline. TSE: total sleep epochs.

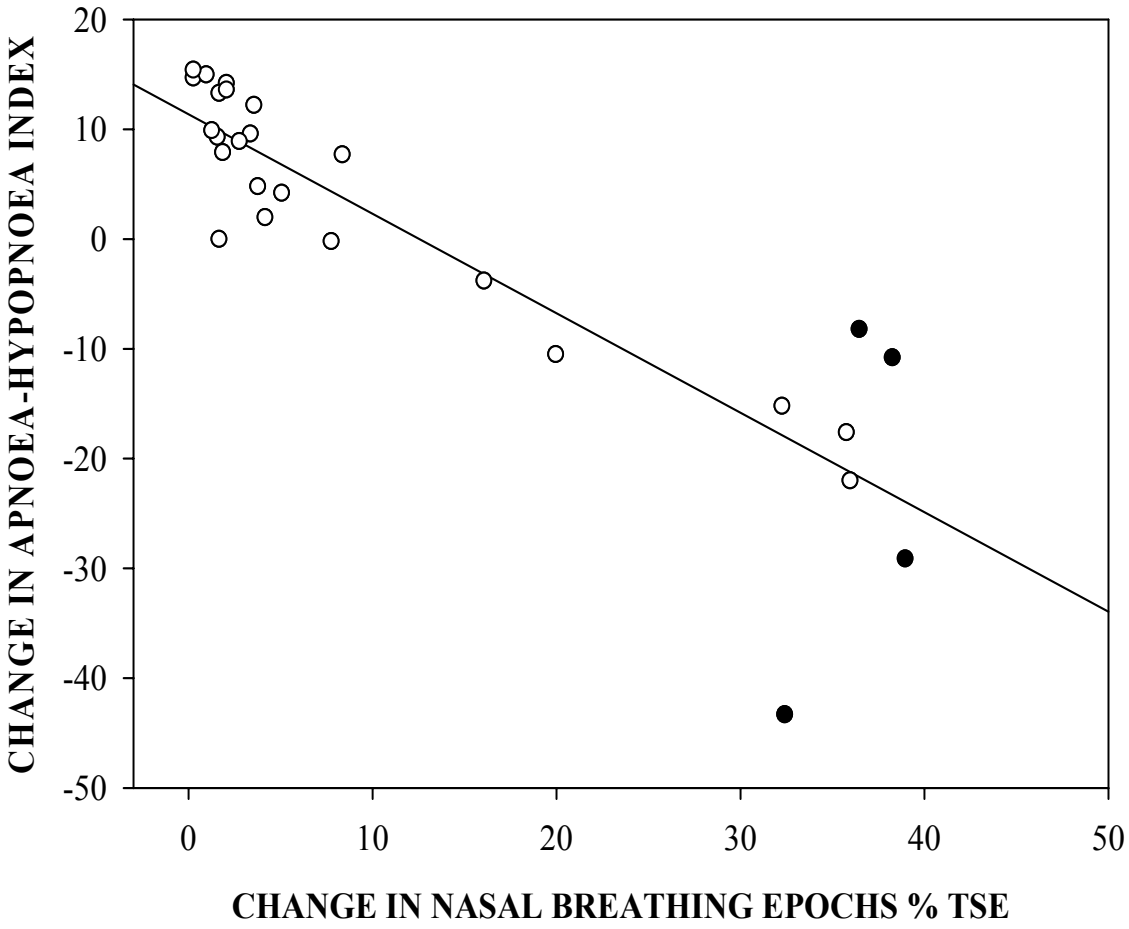

Figure 4. Relationship between the change in nasal breathing epochs % TSE and the change in apnoea/hypopnoea index before and after surgery in responders (●) and in non-responders (°). Solid line: linear regression line (R^2=0.775; p<0.001). TSE: total sleep epochs.

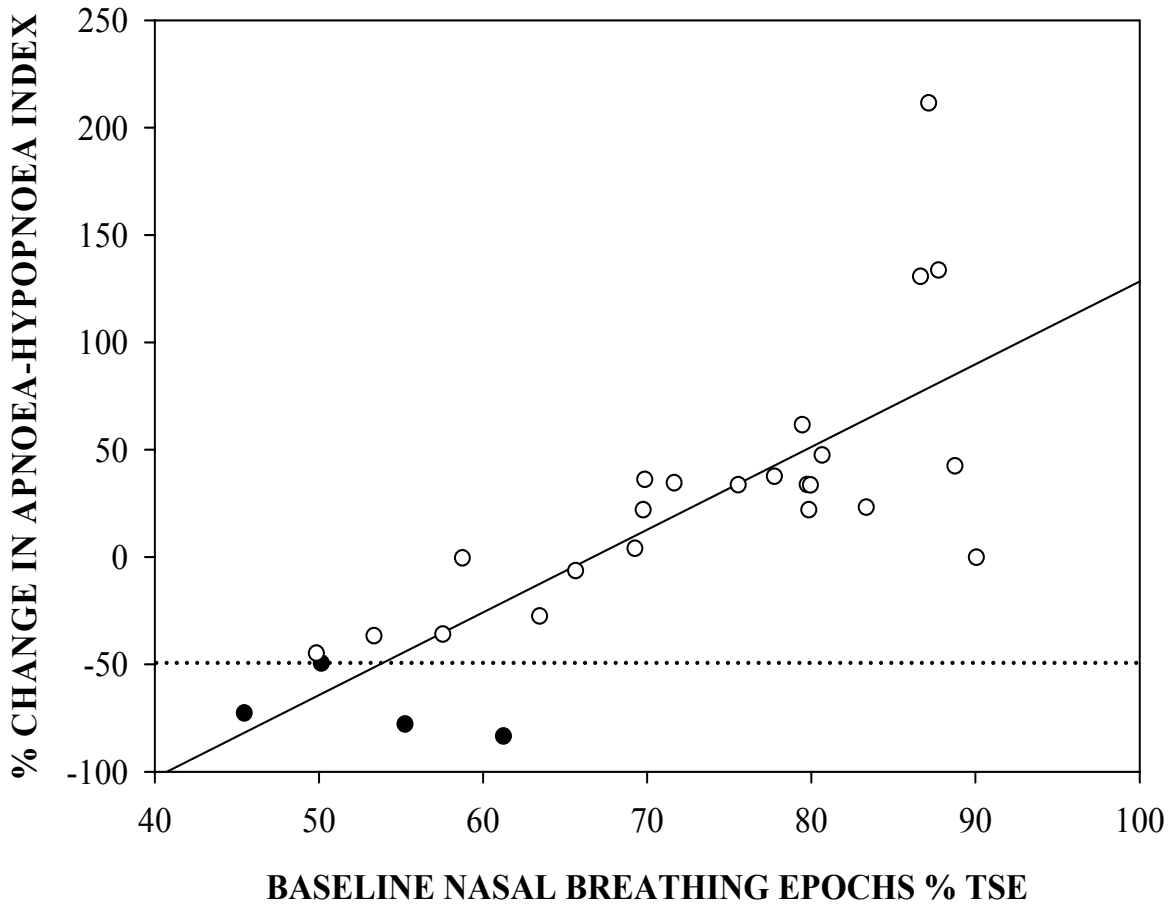

Figure 5. Relationship between the baseline (before surgery) nasal breathing epochs and the percent change in apnoea-hypopnoea index before and after surgery in responders (•) and in non-responders (°). Solid line: linear regression line (R^2=0.610; p<0.001). Dotted horizontal line: limit of % change in apnoea-hypopnoea index after surgery compared to baseline (-50%). This limit along with postoperative apnoea-hypopnoea index of less than 15 events·h^{-1} was used to define treatment response.