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Autologous fat transplantation to the velopharynx for treating mild velopharyngeal insufficiency: A 10-year experience[☆]

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KEYWORDS

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Abstract *Background:* For the last two decades, autologous fat transplantation has been used to treat mild velopharyngeal insufficiency (VPI); however, there is still disagreement about its effectiveness. The aim of the study was to evaluate the procedure by using speech analysis and magnetic resonance imaging (MRI).

Patients and methods: This is a prospective study of 47 non-syndromic patients with mild VPI who underwent autologous fat transplantation to the velopharynx between 2006 and 2015. Thirty-two patients had a cleft palate, all of which had been repaired before fat transplantation. Eight patients developed VPI after adenotonsillectomy, one after uvulo-palatoplasty and six had VPI of unknown etiology. Twelve patients underwent two procedures of fat transplantation.

Preoperative and 1-year postoperative audio recordings were blinded for scoring independently by three senior speech therapists on a five-point scale.

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Preoperative and 1-year postoperative MRIs were obtained during phonation, measuring the velopharyngeal distance and the velopharyngeal gap area. Correlations between the speech outcomes and MRI were calculated.

Results: Audible nasal emission was the only speech parameter that improved significantly postoperatively ($p = 0.005$). A significant reduction in both velopharyngeal distance ($p < 0.005$) and the gap area ($p < 0.005$) was found after treatment. A significant improvement in the mobility of the velum was observed after treatment ($p = 0.03$). There was no significant correlation between speech outcomes and MRI.

Conclusions: Autologous fat transplantation for the treatment of mild VPI, although significantly reducing audible nasal emission, made no significant improvement in hypernasality or nasal turbulence. No complications were observed.

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Introduction

Velopharyngeal insufficiency (VPI) is an incomplete closure between the soft palate and the nasopharynx during speech causing hypernasality, audible nasal emission, weak pressure consonants, and nasal turbulence.

Speech assessment, nasopharyngoscopy, and videofluoroscopy are the standard tools used to investigate and classify VPI. On the basis of the size and pattern of the VPI and its etiology, different treatment paths are taken.

To decrease the velopharyngeal gap and restore normal speech, the surgical treatments of VPI can be divided into procedures that advance the pharyngeal wall closer to the soft palate (i.e., pharyngoplasties) and those that lengthen the soft palate (e.g., Furlow palatoplasty, palatal pushback, buccal flap, and palate re-repair).^{1,2} Although these procedures are effective at resolving VPI, they are not free from complications. Pain, bleeding, and obstructive sleep apnea can be observed in the immediate postoperative phase, especially after pharyngeal flap and sphincteroplasty.^{3,4} Therefore, in the case of mild VPI, these procedures could be considered to be an overtreatment. In the last two decades, autologous fat transplantation, considered to be a less invasive and burdensome operation for the patient, has been used to treat persistent mild VPI.⁵⁻¹⁶

Because of the small number of subjects and the relative difficulties of investigating fat longevity, many studies recommended caution when considering the effectiveness of fat transplantation to the velopharynx for treating VPI and suggested further research.^{7,9,10,12} There is still a lack of consensus on which patient categories may obtain the most benefit and which criteria should be followed when choosing this procedure.

The present study included a larger subject sample than that has been previously reported^{10,12} and may help to answer some of these questions.

Furthermore, VPI is a condition that affects not only speech but also many psychosocial aspects of a patient's life. The authors had previously emphasized the importance of investigating patient's subjective evaluation, and they had demonstrated, by using a validated questionnaire, the improvement of VPI-related quality of life after fat transplantation.¹⁷ For this reason, investigating objective assessments in a larger subject sample may help to complete the

evaluation of fat transplantation for the treatment of mild VPI.

The aim of the present study was to assess the effect of autologous fat transplantation on speech and velopharyngeal closure and to examine associations between the two outcome variables.

The study's secondary objective was to compare patients with and without cleft in terms of speech outcomes and magnetic resonance imaging (MRI).

Patients and methods

As a standard protocol, all the patients were preoperatively assessed in a multidisciplinary clinic by the senior cleft surgeon (CF) and speech therapists. Speech was evaluated, and the movement of the lateral pharyngeal walls and soft palate was examined by oral inspection during phonation /a/, and by nasopharyngoscopy. Based on the perceptual speech evaluation, oral inspection, and nasopharyngoscopy, the need for surgical treatment was determined.

Inclusion criteria for the study were as follows: (1) borderline to mild hypernasality for which conventional pharyngoplasty was excluded as a treatment option; (2) small but consistent velopharyngeal gap as demonstrated by nasopharyngoscopy during phonation; and (3) nonsyndromic patients.

Patients with palatonasal fistulae or an unoperated submucous cleft palate were excluded. A medial deviation of the internal carotid artery, identified on the preoperative MRI or on intraoperative ultrasound, would be a direct contraindication to autologous fat transplantation to the posterior pharyngeal wall.¹⁵ One should be particularly careful when considering patients with the 22q11.2 deletion syndrome for fat transplantation to the posterior pharyngeal wall, as an estimated 49-55% of these patients are reported to have a medial deviation of at least one internal carotid artery.¹⁸

Patients

A total of 48 patients with mild VPI underwent autologous fat transplantation to the velopharynx between 2006 and 2015. One patient, who had previously undergone surgical

Table 1 Demographic and clinical characteristics ($N = 47$). Data are presented as mean (SD), unless otherwise stated.

	Mean (SD)
Number of fat transplantations	1.23 (0.43)
Total volume fat injected, mL	5.96 (1.55)
Volume fat injected velum + palatopharyngeal arches, mL	4.22 (1.40)
Volume fat injected posterior pharyngeal wall, mL	1.75 (0.97)
Age at first fat transplantation, median (range)	11.11 (5.5-50.5)
Sex, number (%)	
Male	24 (51)
Female	23 (49)
Diagnosis, number (%)	
No cleft	15 (32)
Submucous cleft palate	5 (11)
Isolated cleft palate	12 (25)
Complete cleft lip and palate	15 (32)
Second fat transplantation, number (%)	12 (25)
Pharyngeal flap prior to fat transplantation, number (%)	4 (8)
Pharyngeal flap after fat transplantation, number (%)	6 (13)

and radiotherapeutic treatment of a pharyngeal cancer, was excluded from the analysis of the present study, leaving a total of 47 patients (24 males and 23 females). The descriptive data of the population study are presented in [Table 1](#).

Thirty-two patients (68%) had a cleft palate, all of which had been repaired before fat transplantation. Five of these patients had a submucous cleft palate that was surgically repaired at 10-12 years of age. The remaining 27 patients had an overt cleft palate (\pm cleft lip) repaired at 12-15 months of age. Fifteen patients were born with no cleft pathology, of which eight had developed VPI after adenotonsillectomy and one after uvulopalatopharyngoplasty. Six patients had VPI of unknown etiology.

Four patients (8%) had undergone a superior pharyngeal flap before the autologous fat transplantation.

Patients had a median age of 11.1 years (range 5.5-50.5 years) at the first fat transplantation.

In 12 patients (25%), a second fat transplantation procedure was undertaken with a mean time of 2.6 years between the first and the second operation.

Additionally, data from the 3-year follow-up speech investigation were reviewed in 36 of the 47 patients included in the study.

Autologous fat transplantation

The procedure was performed under general anesthesia with oral intubation. Fat was harvested from the thigh medially or from the periumbilical area through a small incision after the donor site had been infiltrated with local anesthetic (0.8 mg/mL^{-1} lidocaine + 0.001 mg/mL^{-1}

Table 2 Speech variables and rating scales for perceptual speech analysis.

Hypernasal resonance/hyponasal resonance/audible nasal emission/weak pressure consonants/nasal turbulence

(0) = Not Present

(0.5) = Borderline

(1) = Mild and Consistent

(2) = Moderate and Consistent

(3) = Severe and Consistent

adrenaline). The harvesting was performed with liposuction under light negative pressure, as described by Coleman.¹⁹ The harvested fat was placed in a microcentrifuge (IEC Medilite 6, Asheville, NC, USA) and centrifuged at 3000 rpm (1200 g) for 3 min to separate blood and liquid fat from fat cells. Exposure to ambient air and time from harvesting to injection were minimized.^{20,21} The pharynx was inspected and palpated, and a Doppler ultrasound assessment (Intra-operative Probe, Resterilizable 8 MHz, Huntleigh Technology Plc, Cardiff, UK) was performed to exclude vessels at the site of injection.¹⁵ The fat cells were injected orally into the recipient sites with a 1-mL syringe connected to a blunt-tipped cannula curved approximately 90° at the tip, and a handle (High Pressure Handle 27,200, Karl Storz, Tuttlingen, Germany). Fat rolls were placed into the midline of the posterior pharyngeal wall, superficial to the prevertebral fascia, into the midline and lateral parts of the velum and into the palatopharyngeal arches bilaterally. An almost equivalent procedure was performed in the patients who had a pharyngeal flap with fat injections placed posterosuperior to the base of the flap in the posterior pharyngeal wall. As shown in [Table 1](#), the mean total volume of fat injected was 5.96 mL. A mean of 1.75 mL was injected into the posterior pharyngeal wall, and a mean of 4.22 mL was injected into the velum and palatopharyngeal arches combined. In eight patients (17%), small vessels were found at the planned recipient site during Doppler assessment of the posterior pharyngeal wall. The fat injection was made only in the velum in these patients. Prophylactic intravenous antibiotic (cefalotin, 30 mg/kg body weight, in one dose) was given at the time of anesthetic induction. Patients were discharged on the first postoperative day.

Speech analysis

Pre- and 1-year postoperative audio recordings were blinded for perceptual scoring rating independently by three trained listeners from the speech therapy group.

In those patients who underwent two fat transplantations, only the last speech assessment was chosen for comparison. Hypernasality, hyponasality, nasal turbulence, audible nasal emission, and weak pressure consonants were scored on a five-point scale ([Table 2](#)). Speech samples were phonetically balanced for the Norwegian language. For assessment of hypernasal resonance, single words with high vowels were used, whereas for assessment of hyponasal resonance, single words with nasal consonants were used.²² The assessment was made primarily on highly vulnerable

speech sounds, that is, pressure consonants and fricatives. The word list included words with consonants in which the speech sound is most distinctly articulated and not influenced by the phonetic context. Reading of single words and repetition of sentences were recorded (Coomber 393 tape recorder, London, UK and microphone AKG C1000S, Vienna, Austria; audio software Audacity, Dominic Mazzoni, sound-card Edirol UA-25, Shizuoka, Japan and microphone AKG c520, Vienna, Austria) for analysis.

MRI examination

Preoperative and 1-year postoperative MRIs were performed in 36 patients (76.6%). Eleven patients did not undergo the procedure or had incomplete MRI. MRIs were obtained during vocal rest and during phonation /i/ with the patient in the supine position.

All MRI investigations were performed with a 1.5 Tesla MRI scanner (Magnetom Sonata, Siemens, Erlangen, Germany) with an eight-channel head array coil. A T1 gradient echo two-dimensional sequence was performed in the sagittal and the axial planes. Acquisition parameters were equivalent to those in our previous studies.^{10,12} A senior consultant radiologist measured the velopharyngeal distance and the velopharyngeal gap area during phonation on a diagnostic workstation (Sectra PACS IDS 5 11.4 P1, Sectra Imtec AB, Linköping, Sweden). The velopharyngeal distance was defined as the shortest distance between the velum and the posterior pharyngeal wall, which was not always midsagittal, as some patients produced an asymmetric velopharyngeal closure. The area between the velum and pharynx, that is, the velopharyngeal gap area, was measured in the axial plane parallel to the hard palate.

The location of the internal carotid arteries could easily be defined without the use of contrast, thereby excluding a medialized internal carotid artery and reducing the risk of intravascular fat injections. None of the 36 patients who underwent MRI were found to have a unilateral or bilateral medialization of the internal carotid artery(ies).

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences version 21.0 (SPSS Inc., Chicago, IL, USA). Agreement statistics were performed with the user-developed package kappaetc by Stata (StataCorp LP, College Station, TX, USA).²³ Inter- and intrarater reliability between the three speech therapists was measured using percent agreement and Gwet's AC.²⁴ Both methods were linearly weighted for disagreement.

A paired sample *t*-test was used to compare pre- and postoperative results. The mean values from all three speech therapists' perceptual scorings were reported. The Cohen's *d* effect size for paired samples was also calculated. The Spearman rank correlation coefficient (ρ) was calculated to analyze the correlation between the difference in the pre- versus postoperative velopharyngeal distance/gap area during phonation and the effect of surgery on speech. *P*-values <0.05 were considered to be significant.

Results

The velopharyngeal distance and the gap area during phonation and vocal rest are presented in Table 3. In those patients who underwent two MRI investigations because of two surgical procedures, only the last MRI result was taken into consideration for the analysis of the data. When comparing pre- and 1-year postoperative MRI during phonation, a significant reduction of both the mean velopharyngeal distance, from 3.75 to 1.93 mm ($p < 0.005$), and the velopharyngeal gap area, from 45.91 to 31.91 mm² ($p < 0.005$), was found after treatment. No change was found comparing pre- and 1-year postoperative results in vocal rest. A medium effect size after treatment was calculated for the velopharyngeal distance ($d = 0.77$); a small effect size after treatment was calculated for the velopharyngeal gap area ($d = 0.39$).

Analysis of pre- and postoperative speech parameters is presented in Table 4.

Based on the Altman Benchmark Scale, the strength of agreement between raters (interrater) was "very good" (0.81-0.93) using the percent agreement and "good" (0.60-0.91) for the Gwet's AC (Table 5). Intrarater reliability on 33% of the material was "very good" (0.80-1.00) using the percent agreement and "good" (0.60-1.00) for the Gwet's AC.

Hypernasality did not change significantly 1-year postoperatively ($p = 0.08$); hypernasality improved in 21 patients (44.8%), deteriorated in 13 (27.6%) patients, and remained unchanged in 13 (27.6%) patients. Weak pressure consonants improved in 17 patients (36.2%), deteriorated in 10 (21.3%), and remained unchanged in 20 (42.5%). Hyponasality improved in 10 (21.3%) patients, deteriorated in 14 (29.8%) patients, and remained unchanged in 23 (48.9%) patients. Nasal turbulence improved in 21 patients (44.8%), deteriorated in 13 (27.6%) patients, and remained unchanged in 13 (27.6%) patients. Audible nasal emission was the only parameter that improved significantly after treatment ($p = 0.005$); it improved in 21 (44.8%) patients, deteriorated in 8 (17%) patients, and remained unchanged in 18 (38.2%) patients. A medium effect size after treatment was calculated for audible nasal emission ($d = 0.54$).

To examine the study's second aim, outcome measures in patients with cleft palate ($n = 32$) were compared to the rest of the group (Table 6). Results showed a significant improvement of audible nasal emission ($p = 0.02$) but no significant change in hypernasality ($p = 0.08$). Hyponasality, weak pressure consonants, and nasal turbulence did not change significantly ($p > 0.33$). MRI outcomes during phonation showed a significant reduction in the velopharyngeal distance and a reduction of the velopharyngeal gap area for both patient groups.

Spearman correlation analysis showed no correlation between the change of the velopharyngeal distance or the velopharyngeal gap area during phonation and the change of any of the speech parameters ($\rho < 0.28$; $p > 0.24$).

Finally, we compared the difference between the velopharyngeal distance in vocal rest and in phonation (movement of velum and pharyngeal wall) preoperatively and postoperatively (Table 7). A significant improvement of the velopharyngeal movement was observed ($p = 0.03$), with a small effect size ($d = 0.31$).

Table 3 Velopharyngeal distance and gap area measured by MRI; mean (SD).

	During phonation /i/			During vocal rest		
	Preoperative	Postoperative	p-value	Preoperative	Postoperative	p-value
Velopharyngeal distance in sagittal plane (mm)	3.75 (2.33)	1.93 (2.40)	<0.005*	8.96 (3.29)	8.95 (3.33)	0.99
Velopharyngeal gap area in axial plane (mm ²)	45.91 (40.32)	31.91 (31.08)	<0.005*	147.67 (67.97)	142.42 (81.51)	0.69

* Statistically significant.

Table 4 Perceptual speech analysis of pre- and postoperative audio recordings; mean (SD).

	Preoperative	Postoperative (1-year)	p-value
Hypernasality	0.52 (0.37)	0.42 (0.36)	0.08
Hyponasality	0.15 (0.36)	0.10 (0.16)	0.39
Audible nasal emission	0.26 (0.26)	0.14 (0.18)	0.005*
Weak pressure consonants	0.22 (0.23)	0.21 (0.29)	0.82
Nasal turbulence	0.41 (0.46)	0.31 (0.34)	0.13

* Statistically significant.

No complications (e.g., infection, hematoma, and emboli) were observed in patients intra- or postoperatively. There were no reported symptoms of nasal airway obstruction or sleep apnea during the postoperative observation period or at the postoperative follow-up consultations. Minimal or no postoperative pain was reported by the patients. Four patients with cleft palate and two with no cleft pathology underwent pharyngeal flap surgery after fat transplantation due to persistent VPI. At the 3-year follow-up investigation ($n=36$), only these six patients had undergone a secondary pharyngoplasty.

Discussion

VPI surgery aims to improve voice resonance and speech intelligibility by restoring a satisfying closure of the velopharyngeal sphincter. The present study illustrates the authors'

Table 5 Inter-rater reliability, calculated as percent agreement and with Gwet's AC1 for each of the variables between the three raters; coefficient (standard error).

Variable	Percent agreement	Gwet's AC1
Hypernasality (preoperative)	0.85 (0.02)	0.68 (0.04)
Hypernasality (postoperative)	0.81 (0.02)	0.60 (0.06)
Hyponasality (preoperative)	0.93 (0.02)	0.91 (0.03)
Hyponasality (postoperative)	0.83 (0.04)	0.78 (0.06)
Audible nasal emission (preoperative)	0.84 (0.02)	0.72 (0.05)
Audible nasal emission (postoperative)	0.87 (0.02)	0.81 (0.04)
Weak pressure consonants (preoperative)	0.84 (0.02)	0.74 (0.05)
Weak pressure consonants (postoperative)	0.85 (0.02)	0.76 (0.05)
Nasal turbulence (preoperative)	0.86 (0.02)	0.72 (0.06)
Nasal turbulence (postoperative)	0.88 (0.02)	0.78 (0.04)
Mean	0.86	0.75

experience with the technique of autologous fat transplantation to the velopharynx for a period of 10 years, analyzing preoperative and 1-year postoperative results of speech and MRI.

In our cohort of 47 patients with mild VPI who were operated on with this procedure, audible nasal emission im-

Table 6 Pre- and postoperative results of MRI/Speech parameters of patients with and without cleft palate; mean (SD).

	Patients with Cleft Palate			Patients Without Cleft Palate		
	Preoperative	Postoperative	p-value	Preoperative	Postoperative	p-value
Velopharyngeal distance in sagittal plane (mm)	3.72 (2.52)	2.14 (0.24)	< 0.0005*	3.82 (1.94)	1.45 (2.42)	0.03*
Velopharyngeal gap area in axial plane (mm ²)	49.17 (44.53)	34.00 (32.32)	0.02*	38.80 (29.79)	27.36 (29.15)	0.01*
Hypernasality	0.60 (0.37)	0.48 (0.35)	0.08	0.28 (0.26)	0.31 (0.41)	0.78
Hyponasality	0.19 (0.42)	0.10 (0.16)	0.33	0.03 (0.08)	0.08 (0.13)	0.21
Audible nasal emission	0.32 (0.29)	0.16 (0.20)	0.02*	0.14 (0.19)	0.12 (0.19)	0.78
Weak pressure consonants	0.28 (0.25)	0.26 (0.32)	0.68	0.11 (0.20)	0.18 (0.30)	0.46
Nasal turbulence	0.47 (0.52)	0.38 (0.35)	0.35	0.25 (0.30)	0.22 (0.41)	0.74

* Statistically significant.

Table 7 Difference from vocal rest to phonation of velopharyngeal distance and gap area measured by MRI; mean (SD).

	Preoperative	Postoperative	<i>p</i> -value
Difference between velopharyngeal distance from rest to phonation on sagittal plane (mm)	5.19 (3.65)	6.36 (3.89)	0.03*
Difference between velopharyngeal gap area from rest to phonation on axial plane (mm ²)	101.72 (67.41)	100.94 (76.25)	0.95

proved significantly, and a moderate effect size was observed. Hypernasality did not reach statistical significance.

Of the 47 patients who underwent the procedure, 36 patients had completed pre- and postoperative MRI, and a significant reduction in both velopharyngeal distance and gap area was found.

Kummer et al.²⁵ described how hypernasality may not be proportionate to the dimensions of the velopharyngeal gap when the velopharyngeal gap area is small, as it is in borderline to mild VPI. Instead nasal turbulence, described as a result of the friction and bubbling that are produced when the airstream is forced through a small velopharyngeal gap, may represent the typical stigma of a borderline VPI.²⁵⁻²⁷ Although improvement of nasal turbulence was found in 21 (44.8%) patients, it did not change significantly when calculating mean scores.

When performing subgroup analysis, we still found a significant improvement in audible nasal emission, while no improvement was found in the noncleft group. This finding supports the notion that fat transplantation to the velopharynx may be particularly beneficial in patients with cleft palate. This may be partially explained by autologous fat reducing fibrosis in scar tissue and improving its elastic properties.²⁸ In this case, a fat graft could regain the pliability of a scarred velum (secondary to previous palate repair) and increase its mobility.^{7,9,12} Fat transplantation may not only “fill the gap” between velum and pharynx during phonation but also lead to a reduction of fibrosis and an improvement of velar elevation, noticeable when injected into a cicatricial levator veli palatini muscle. This may also explain why the reduction of the velopharyngeal distance, when examined with MRI, was found only during phonation. To support this hypothesis, a significant improvement in the difference in movement between vocal rest and phonation was found; it seems that the soft palate becomes more mobile and better able to rise against the pharyngeal wall after fat transplantation.

A reduction in the velopharyngeal space observed by MRI did not match an equivalent improvement in speech. In fact, no correlation between pre- and postoperative MRI changes during phonation and any change in speech parameters was found. An improvement of an objective value, such as gap size, does not always correlate with an improvement in speech values. Thus, even if there is significant reduction of the velopharyngeal space, in some patients, a complete velopharyngeal closure is not reached, making the speech still compromised because of air leakage to the nose. The smaller the gap, the more difficult it will be to find a correlation between images and speech assessments, as previously discussed.²⁵

Numerous studies^{5-8,29} have described improvement in nasal resonance after autologous fat transplantation, but,

as Bishop et al. stated in a review,¹⁴ studies tend to use different scales of measurement, complicating comparisons between outcome measures. A strength of the current study is that it was based on standardized methods already used in our previous studies on fat transplantation to the velopharynx:^{10,12} a similar scale as the one described by Harding et al.³⁰, and audio recordings blinded and scored independently by three senior and specialized speech therapists. In addition, calculations of inter-rater reliability demonstrated good agreement between them. Gwet’s AC has methodologically been shown to provide a more stable inter-rater reliability coefficient than Cohen’s Kappa and has been recommended for inter-rater reliability analysis.³¹ Linear weighting of disagreement took the ordinal data structure of the scoring system into account and was therefore used for all the reliability coefficient estimations.

As discussed in our previous studies and as part of a clinical protocol,^{10,12} only candidates with VPI of borderline to mild degree have been treated with this technique. The preoperative direct view of the velopharyngeal sphincter during nasopharyngoscopy had to show a relatively small central gap, usually with characteristic protrusion of saliva during phonation, as described by Witzel.³²

In our patients, unlike in the study by Cantarella et al.⁹, fat injection to the lateral pharyngeal walls was avoided due to the risk of intravascular fat embolism. The routine of performing MRI (without contrast) preoperatively aims to not only assess the velopharyngeal gap but also identify major vessels in the posterior pharyngeal wall. In addition, Doppler ultrasound assessment was performed intraoperatively to exclude small vessels at the site of injection¹⁵. None of the patients who undertook MRI had a medialized carotid artery, but in eight (17%) of our patients, small vessels were detected by Doppler ultrasound in the posterior pharyngeal wall, and fat injection was limited to the soft palate. The efficiency of fat injection in the soft palate only is unknown to us. As the latter group is too small for performing a subgroup analysis, a larger study, preferably a randomized trial, would be the best method to answer this question. Perhaps in the future, using a more sophisticated ultrasound probe that would be able to discern small vessels from the surrounding tissue with millimeter-capacity, we will be able to inject fat into the typical risk zones of the lateral pharyngeal walls. At the same time, the risk of increasing hyponasality (in 29.8% of our patients) and of obstructive sleep apnea (OSA) has to be taken into consideration. In a recent study, Phua et al.³³ raised concerns about the safety of the procedure, as three of their patients developed severe OSA after fat transplantation. Phua et al. injected fat graft also in the lateral pharyngeal walls, and the patients who developed OSA had syndromes associated with hypotonia (velocardiofacial syndrome, ulnar-mammary

syndrome, and pituitary dysfunction requiring growth hormone replacement). As previously described, an important criterion in our study is the exclusion of syndromic patients.

Unfortunately, there is a highly variable percentage of fat reabsorption after autologous fat transplantation.^{34,35} No studies have calculated the percentage of fat reabsorption in the velopharynx; in many studies, however, the procedure had to be repeated more than once.^{6,16,36} Piotet et al.¹⁶ suggested that transplanted fat was stable 3 months after surgery. They performed multiple fat transplantations in 64% of the patients, highlighting the need for multiple fat grafts to reach an optimal result. In our study, only twelve (25%) patients received a second fat transplantation, with a relatively long average time of 2.6 years (range, 1.5-5.6 years) between each procedure. Six of 47 patients (12.7%) underwent a superior pharyngeal flap after fat transplantation, but only two of them had previously undergone a second fat transplantation. Thus, it is important to inform the patients and their parents about the possibility of a second fat transplantation to achieve optimal speech results.

Finally, in our study, 36 of the 47 patients had 3 years of follow-up or longer. Only six of those patients had to undergo a secondary pharyngoplasty. This may suggest the stability of the fat transplant over time.

Limitations of the study

A limitation of the study is the relatively small sample size, especially considering that the patients had speech impairment of borderline to mild degree. This may have influenced the results and made it more difficult to detect a significant improvement in speech. Nasometry scores may be added as a supplementary speech outcome in future studies, thereby giving more strength to our results. Neither intelligibility test nor patient perceived outcome was used in the present study. However, as mentioned above, the authors had previously described a significant improvement of VPI-specific quality of life after fat transplantation by using a validated questionnaire including 25 of the present study's 47 patients.¹⁷

Conclusion

The present study included a larger subject sample than that evaluated in previous studies of the treatment of VPI with autologous fat transplantation to the velopharynx. Audible nasal emission improved one year after autologous fat transplantation, while hypernasality did not change significantly when scored by three blinded speech therapists. MRI results showed significant improvement in the velopharyngeal distance/gap area during phonation 1 year postoperatively.

The velopharyngeal sphincter became more mobile after the procedure, and this may support the hypothesis of fat grafting decreasing fibrosis.

Even though autologous fat transplantation is not meant to substitute pharyngoplasties, only less than 15% of the patients needed a secondary pharyngoplasty.

Preoperative MRI and Doppler ensure procedural accuracy and are important safety methods to exclude vessels at the site of injection.

Autologous fat transplantation to the velopharynx may be used as an alternative treatment option in non-syndromic cleft palate patients with borderline to mild degree of VPI. The study highlights the difficulties in evaluating the procedure in treating patients with borderline to mild VPI. Its effectiveness in completely resolving VPI remains uncertain. More studies are required to confirm or refute our results and to help standardize inclusion criteria and methods of evaluation for this procedure. We recommend that patients should be monitored closely in a trial setting and be consented appropriately with regard to the outcome of the existing studies.

Ethical approval

The study was approved by the [Regional Ethics Committee of South-Eastern Norway](#); reference 2014/2139A.

Conflict of interest statement

None.

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