

Title	Clinical application of endoscopic soft palate augmentation in the treatment of velopharyngeal insufficiency			
Author(s)	Isomura, E.T.; Matsukawa, M.; Yokota, Y. et al.			
Citation	International Journal of Oral and Maxillofacial Surgery. 2023, 52(8), p. 854-859			
Version Type	VoR			
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Int. J. Oral Maxillofac. Surg. 2021; xx: 1-6 https://doi.org/10.1016/j.ijom.2023.01.003, available online at https://www.sciencedirect.com



# Clinical Paper Cleft Lip and Palate

# Clinical application of endoscopic soft palate augmentation in the treatment of velopharyngeal insufficiency\*

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E. T. Isomura, M. Matsukawa, Y. Yokota, N. Tanaka, C. Sugiyama, K. Nohara: Clinical application of endoscopic soft palate augmentation in the treatment of velopharyngeal insufficiency. Int. J. Oral Maxillofac. Surg. 2021; xx: 1-6. © 2023 The Author(s). Published by Elsevier Inc. on behalf of International Association of Oral and Maxillofacial Surgeons. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Abstract. Velopharyngeal structure augmentation with the injection of autologous fat tissue into the nasal mucosa of the soft palate has been reported previously. However, as the injection points in the velopharyngeal space cannot be observed directly, these injections may be difficult to perform accurately. This report describes a new endoscope-assisted approach in which the materials for velopharyngeal structure augmentation are administered while observing the injection points directly, also enabling adjustment of the amount of material injected. A case series of five patients aged 8-16 years who underwent endoscopic soft palate augmentation under general anaesthesia is reported. Autologous fat tissue was injected into the nasal mucosa of the soft palate using a needle-type device of an endoscope, and the effects of the treatment were evaluated. The injections were performed successfully, and the velopharyngeal function was improved. This new technique of endoscopy-assisted augmentation was useful for the treatment of velopharyngeal insufficiency.

Keywords: Velopharyngeal insufficiency; Palate; Endoscopy; Nasopharynx; Subcutaneous fat. Abbreviations: VPI; velopharyngeal insufficiency; ESPAendoscopic soft palate aumgentation; BMI body mass index; MRImagnetic resonance imaging; BVPIborderline velopharyngeal insufficiency; VPC velopharyngeal complete closure; BCLP bilateral cleft lip and palate; UCLP unilateral cleft lip and palate.

Accepted for publication 10 January 2023 Available online xxxx

Post-palatoplasty, velopharyngeal insufficiency (VPI) is inevitable in a certain percentage of cleft palate cases, irrespective of the success of the surgery. 1,2 The main causes of VPI are inadequate or poor movement of the soft palate due to scarring, the short palate, and poor repair of the levator veli palatini muscle. In addition, some 22q11.2 deletion syndromes present with VPI because of inadequate soft palate muscle, including in patients who do not have a cleft palate.

Speech plays an important role in daily life, and speech disorders such as VPI reduce the patient's quality of life. Historically, a pharyngeal flap operation has been employed to manage

<sup>\*</sup> This article was presented in part at the Annual Meeting of the American Cleft Palate Craniofacial Association (ACPA 2021; April 28-May 2, 2021), the 66th Congress of the Japanese Society of Oral and Maxillofacial Surgeons (November 12-14, 2021), and the 14th International Cleft Congress (July 11–15, 2022).

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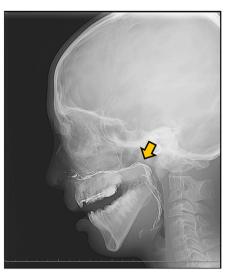


Fig. 1. Lateral X-ray images before injection. Lateral X-rays were used before injection to check where the levator veli palatini muscle would be elevated during vowel pronunciation, resulting in restenosis of the pharynx. A contrast medium applied through the nasal cavity made the nasal side of the levator veli palatini muscle clear.

VPI.<sup>2,4–7</sup> Velopharyngeal structure augmentation, which involves the injection of materials into the tissue around the velopharynx, has also been performed as a less invasive alternative to a pharyngeal flap operation; this procedure does not change the original structure of the pharynx.<sup>2,4–7</sup> However, the anatomical sites and injection materials used for augmentation have varied widely owing to a lack of standardized criteria, and their effects have also varied across institutions.<sup>8–19</sup>

The authors of the present study recently investigated the most effective injection approach for velopharyngeal structure augmentation in dogs.<sup>20,21</sup> Dogs naturally exhibit VPI, and the nasopharyngeal closure movement can be triggered by applying respiratory depression.<sup>2</sup> Taking advantage of this property, it was elucidated experimentally that the soft palate was a more effective injection site to reduce nasal air leakage than the posterior pharyngeal wall or bilateral pharyngeal walls. Furthermore, it was found that autologous fat tissue was the best material histologically compared with hyaluronic acid or collagen, because a part of the injected area showed increased muscle tissue. A method of injection into the nasal mucosa of the soft palate with a needle device and an endoscope to directly confirm the injection site was also proposed.<sup>21</sup>

The aim of this study was to report the technique of endoscopic soft palate augmentation (ESPA) using autologous fat injection in a series of five patients.

# Patients and methods

Five patients with a non-syndromic repaired cleft palate (age 8–16 years; three female and two male) underwent ESPA. All clinical protocols were reviewed and approved by the Clinical Ethics Committee of Osaka University Graduate School of Dentistry (approval number, H30-E30).

# Technique

Before ESPA, the degree of VPI was assessed endoscopically to identify the injection site and evaluate the gap. Lateral X-ray images were also used to check where the levator veli palatini muscle would be elevated during vowel pronunciation, resulting in restenosis of the pharynx (Fig. 1). Thereafter, ESPA was performed with the patient under general anaesthesia.

Subcutaneous fat was suctioned from the left femoral area with a cannula (60-ml monoject Toomey hub cannula; Tulip Medical Products, San Diego, CA, USA), because this is safer than abdominal fat suctioning in children with a relatively low body mass index (BMI) and low subcutaneous fat (Table 1, Fig. 2). The suctioned fat tissue was centrifuged at 800 rpm for 2 min to separate three layers: an upper layer comprising oil from crushed fat cells, a middle layer comprising fat cells, and a bottom layer comprising

blood, water, and lidocaine used for local anaesthesia. The middle layer was used as the injection material.

The autologous fat tissue was injected into the nasal mucosa of the soft palate using a needle-type device (ViziShot 2 FLEX 19-gauge suction biopsy needle; Olympus Medical Systems Corp., Tokyo, Japan) with an endoscope (Video Bronchoscope BF-1TQ290; Olympus Medical Systems Corp.). The device was first inserted through the nostril, and the fat tissue was then injected into the soft palate nasal mucosa at the back of the levator veli palatini muscle, while confirming the injection site in the anteroposterior direction with the C-arm and in the transverse direction with the endoscope (Figs. 3 and 4). During the injection of the fat tissue, the point of the levator veli palatini was pushed up from the oral cavity with a rod-shaped instrument to facilitate visualization of the point with endoscopy. The fat injection was performed until the soft palate lightly touched the posterior wall of the pharynx under endoscopic observation, with reference to the findings obtained on endoscopic images before surgery. Thus, the injection amount differed among patients, ranging from approximately 2 ml to 4 ml.

#### **Evaluation**

The following functional evaluations were performed before and at 1 month and 12 months after the operation: (1) magnetic resonance imaging (MRI) video recorded during speech vowels; (2) nasopharyngeal endoscopic observation during speech, with the findings classified as follows, depending on the modulation of the area of the velopharvngeal opening by movements of the velum and pharyngeal walls: VPI, substantially unclosed with a visible gap; BVPI, borderline with bubbling; and VPC, complete closure; (3) speech assessment by speech therapists with more than 10 years of experience, who evaluated the severity of the VPI and abnormal articulation by their own hearing during actual conversations with the patient.

# Results

The characteristics of the study participants are shown in Table 1. BMI in childhood is affected by the maturity rate and varies widely not only with age

Table 1. Patient characteristics.

Case No.	Age (years)	Sex	Cleft type	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )
1	12	M	BCLP	139.0	27.6	13.8ª
2	8	F	UCLP	124.0	20.8	13.4 <sup>a</sup>
3	8	F	UCLP	127.0	21.6	13.4 <sup>a</sup>
4	16	M	UCLP	160.9	48.4	18.7 <sup>b</sup>
5	14	F	BCLP	160.7	43.5	16.8°

BCLP, bilateral cleft lip and palate; F, female; M, male; UCLP, unilateral cleft lip and palate

<sup>&</sup>lt;sup>c</sup>BMI at the 3rd percentile.

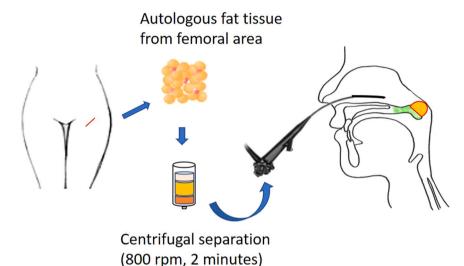


Fig. 2. Schematic diagram of endoscopic soft palate augmentation. Subcutaneous fat was suctioned from the left femoral area with a cannula. The suctioned fat tissue was centrifuged at 800 rpm for 2 min to separate three layers: an upper layer comprising oil from crushed fat cells, a middle layer comprising fat cells, and a bottom layer comprising blood, water, and lidocaine used for local anaesthesia. The middle layer was used as the material injected into the nasal mucosa of the soft palate using the needle-type device of the endoscope.

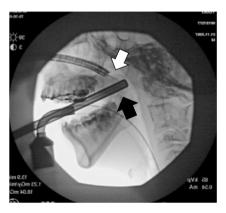


Fig. 3. C-arm image obtained during endoscopic soft palate augmentation. The device (white arrow) was inserted, and material was injected after confirming the injection point, which was pushed up from the oral side with a rod-shaped instrument (black arrow).

but also height, within the age groups. Therefore, only about 10–18 ml of fat tissue could be obtained, and there was no excess sample because the collected tissue was reduced to one-third after centrifugation. In case 2, as liposuction was not sufficient and no improvement in VPI was observed, the findings for this case were excluded from the analysis.

With the material injected using an endoscope, the injection site could be observed directly and the injection amount adjusted easily. The injections were performed successfully, and the restoration of velopharyngeal function was confirmed by the improvement in hypernasality on the day after the operation. Postoperatively there was pain in the thigh at the liposuction site, but the pain in the pharynx was mild, and

the patients could consume a semi-solid diet from the next day.

#### MRI video observation

The MRI findings obtained before ESPA showed that closure of the velopharyngeal sphincter required some effort (Fig. 5). In contrast, after ESPA, the soft palate appeared able to touch the velopharyngeal posterior wall more easily, and the injected fat tissue was visualized as a white lesion in the soft palate on MRI.

# Nasopharyngeal endoscopic observation

Nasopharyngeal fibrescopic observation showed some improvement in VPI during speech, except in case 2, in which little improvement was observed. For example, patient case 4 showed a space before ESPA, with BVPI–VPI apparent in vowels and BVPI apparent in consonants; however the space disappeared after ESPA, with velopharyngeal competence (VPC) appearing in vowels and consonants (Table 2, Fig. 6). The endoscope allowed concentration of the injection at the site where closure was insufficient before the operation.

Nasopharyngeal fibrescopic observation showed some improvement in VPI during speech in all cases except case 2, which showed little improvement in this evaluation.

# Speech assessment

Some improvement was observed in all cases in the speech assessments performed by the speech therapists, even if small. All cases showed a mild-to-moderate improvement aurally (Supplementary Material Table S1). These improvements in VPI were maintained for over 12 months, and further follow-up will be performed.

<sup>&</sup>lt;sup>a</sup>BMI below the 3rd percentile.

<sup>&</sup>lt;sup>b</sup>BMI between the 15th and 50th percentiles.

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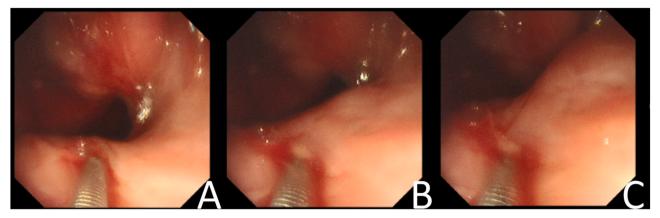


Fig. 4. Representative view of the endoscope during endoscopic soft palate augmentation. Autologous fat tissue was injected into the soft palate nasal mucosa after confirming the injection point in the transverse direction by endoscopy. (A) Before injection; (B) during injection; (C) after injection.

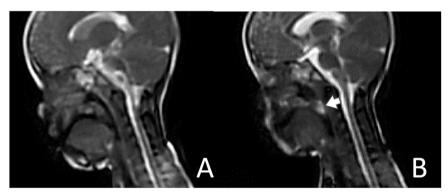


Fig. 5. Representative MRI scans during speech before (A) and after (B) endoscopic soft palate augmentation in case 4. After endoscopic soft palate augmentation, the injected fat tissue appeared as a white lesion (arrow) in the soft palate on MRI, and the patient's soft palate could touch the velopharyngeal posterior wall more easily.

Moreover, the patients showed no complications such as sleep apnoea or hyporhinolalia. One patient experienced mild paresthesia at the site of thigh liposuction, but this recovered to the extent that it was not noticeable in daily life within approximately 6 months.

## **Discussion**

Honjyo<sup>23</sup> reported that speech mislearning in early childhood makes later treatment difficult. Therefore, early treatment of VPI is important for patients

BMI in childhood is affected by the maturity rate and varies widely with age and height. The BMI of the included patients was compared with those of other Japanese children of the same sex and age, based on the BMI reference curves by height of Japanese children and adolescents aged 5–17 years obtained from the 2001 nationwide survey data.<sup>24</sup> Patients with a BMI below the 5th percentile were considered underweight, while those with a BMI between the 5th and 85th

percentiles were considered to have a healthy weight. Since all of the study patients, except patient case 4, were underweight, liposuction was difficult. In fact, liposuction was not sufficient in case 2.

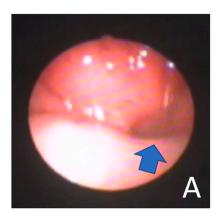
Fat injections can be used in children because this method can be repeated multiple times. Fat injections for the treatment of VPI can be performed at multiple locations, including the soft palate, lateral pharyngeal wall, and posterior pharyngeal wall. 8-19 Several studies have reported cases involving injection into the posterior pharvngeal wall because this site seems to be easier to inject than the other sites. However, MRI showed the nasopharyngeal closure plane to be on the back surface of the levator veli palatini muscle. Moreover, experimental evaluations suggested that the best injection site is the soft palate and that injections at this site are also suitable for the original anatomy.<sup>20</sup> Boneti et al.<sup>15</sup> reported fat injection into the soft palate transorally with a 17-gauge needle, but this approach may injure the levator veli palatini muscle itself, which is very close to the injection area.

ESPA was developed to address these considerations and appears to cause less damage to the levator veli

Table 2. Nasopharyngeal endoscopic observations (except case 2).

Case No.	Pre-operation		Post-operation (1 month)		
	Vowel	Consonant	Vowel	Consonant	
1	BVPI	BVPI-VPI	VPC	VPC-BVPI	
3	VPI	BVPI	BVPI	VPC-BVPI	
4	BVPI–VPI	BVPI	VPC	VPC	
5	BVPI–VPI	VPC-BVPI	BVPI–VPI	VPC-BVPI	

BVPI, borderline closure, bubbling is observed; VPC, complete closure; VPI, substantially unclosed, visible gap is present.



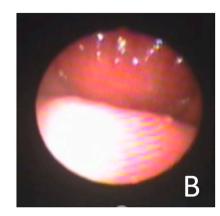


Fig. 6. Nasopharyngeal fibrescopic findings during speech before and after endoscopic soft palate augmentation (ESPA) in case 3. (A) Image obtained before ESPA showing the space on the right side during speech, demonstrating velopharyngeal insufficiency. (B) Image obtained after ESPA showing that the space disappeared, indicating that ESPA was successful in treating the velopharyngeal insufficiency.

palatini.<sup>21</sup> Currently, endoscopic technology is mainly being developed for use in gastrointestinal surgery, and there are various devices for this purpose. However, ESPA is slightly diffito perform with existing endoscopes and devices. With a thin endoscope that allows a device with a 19-gauge needle to pass into and be inserted through the nasal cavity of a child, the tip of the endoscope bends only in one direction to allow adjustment of the insertion site. In addition, the most suitable length of the needle device is 70 cm, and therefore adipose tissue remains in the device and is wasted as a result. Thus, it will be necessary to develop more appropriate endoscopes and devices in the future.

It has been reported that 30–70% of an autologous fat graft transplant is resorbed within a year, and therefore most of the patients require repeat fat injections. <sup>25–28</sup> In the present study, resorption of the fat grafts could not be determined. Furthermore there is no way to avoid the possibility of overinjection, but according to a systematic review by Nigh et al., <sup>18</sup> negative effects of over-injection are rare, and only one of 251 patients showed postoperative apnoea symptoms.

ESPA cannot replace the pharyngeal flap operation, because it can only improve mild-to-moderate VPI. However, it has several merits. First, ESPA can be performed during childhood, which is important for early speech therapy, even if a pharyngeal flap operation is necessary after maturation. Second, VPI after palatoplasty with Furlow's method can occur due to scarring of the

soft palate rather than shortness of the soft palate. In such cases, fat injection is more suitable than the velopharyngeal flap operation because it does not involve the extension of the soft palate. Finally, if VPI recurs after a pharyngeal flap operation, autologous fat tissue can be injected at the back of the velopharyngeal flap. At present, surgery for VPI is mainly performed through the velopharyngeal flap, but expansion of the surgical procedures with the use of ESPA is expected.

The results of this study were obtained over a short-term period, and multiple fat injections or the injection of adipose tissue-derived stem cells might be more suitable for a better long-term prognosis, as reported in breast reconstruction and fields. <sup>29,30</sup> Nevertheless, stem cell transplantation remains an expensive treatment option and requires multiple surgeries, which places a heavy burden on the patient. Moreover, with the establishment of the Regenerative Medicine Law in Japan, complicated procedures are required to perform stem cell transplantation; hence, this procedure is not easy to perform. New materials and technologies that replace these techniques are desired.

# **Funding**

This study was supported by Grants-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (Grant Number 21K10091). The funding organization had no role in the study design, in the collection,

analysis, and interpretation of the data, in the writing of the manuscript, or in the decision to submit the manuscript for publication.

# Competing interests

None

Acknowledgements. We wish to thank Dr Tadashi Sasai for taking the MRI video.

# Ethical approval

All clinical protocols were reviewed and approved by the Clinical Ethics Committee of Osaka University Graduate School of Dentistry (approval number, H30-E30).

## **Patient consent**

Consent was obtained from all patients.

# Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2023.01.003.

## References

- Naran S, Ford M, Losee JE. What's new in cleft palate and velopharyngeal dysfunction management? *Plast Reconstr Surg* 2017;139:1343e–55e. https://doi.org/ 10.1097/PRS.000000000003335
- Rogers C, Konofaos P, Wallace RD. Superiorly based pharyngeal flap for the surgical treatment of velopharyngeal insufficiency and speech outcomes. J Craniofac Surg 2016;27:1746–9. https:// doi.org/10.1097/SCS.00000000000003050
- 3. Filip C, Impieri D, Aagenæs I, Breugem C, Høgevold HE, Særvold T, Aukner R, Lima K, Tønseth K, Abrahamsen TG. Adults with 22q11.2 deletion syndrome have a different velopharyngeal anatomy with predisposition to velopharyngeal insufficiency. *J Plast Reconstr Aesthet Surg* 2018;71:524–36. https://doi.org/10.1016/j.bjps.2017.09.006
- Kogo M, Sakai T, Harada T, Nohara K, Isomura E, Seikai T, Otsuki K, Sugiyama C, Nakagawa K, Tanaka S. Our unified pharyngeal flap operation. *J Cleft Lip Palate Craniofac Anom* 2017;4:189–91. https://doi.org/10.4103/jclpca.jclpca\_82\_17
- Valnicek SM, Zuker RM, Halpern LM, Roy WL. Perioperative complications of superior pharyngeal flap surgery in children. *Plast Reconstr Surg* 1994;93:954–8.

# 6 Isomura et al.

- https://doi.org/10.1097/00006534-199404001-00009
- Aboloyoun AI, Ghorab S, Farooq MU.
   Palatal lifting prosthesis and velopharyngeal insufficiency: preliminary report.
   Acta Med Acad 2013;42:55-60. https://
  doi.org/10.5644/ama2006-124.71
- Orr WC, Levine NS, Buchanan RT. Effect of cleft palate repair and pharyngeal flap surgery on upper airway obstruction during sleep. *Plast Reconstr* Surg 1987;80:226–32. https://doi.org/10. 1097/00006534-198708000-00010
- Filip C. Response re: 'Autologous fat grafting for the treatment of velopharyngeal insufficiency: state of the art'. J Plast Reconstr Aesthet Surg 2014; 67:1155-6. https://doi.org/10.1016/j.bjps. 2014.02.001
- Filip C, Matzen M, Aagenæs I, Aukner R, Kjøll L, Høgevold HE, Abyholm F, Tønseth K. Speech and magnetic resonance imaging results following autologous fat transplantation to the velopharynx in patients with velopharyngeal insufficiency. Cleft Palate Craniofac J 2011;48:708–16. https://doi.org/10.1597/09-161
- Coleman SR. Structural fat grafting: more than a permanent filler. *Plast Reconstr Surg* 2006;**118**(Suppl):108S–20S. https://doi.org/10.1097/01.prs. 0000234610.81672.e7
- Leuchter I, Schweizer V, Hohlfeld J, Pasche P. Treatment of velopharyngeal insufficiency by autologous fat injection. Eur Arch Otorhinolaryngol 2010; 267:977–83. https://doi.org/10.1007/ s00405-009-1157-7
- Cantarella G, Mazzola RF, Mantovani M, Baracca G, Pignataro L. Treatment of velopharyngeal insufficiency by pharyngeal and velar fat injections.
   Otolaryngol Head Neck Surg 2011;
   145:401–3. https://doi.org/10.1177/0194599811411655
- Lau D, Oppenheimer AJ, Buchman SR, Berger M, Kasten SJ. Posterior pharyngeal fat grafting for velopharyngeal insufficiency. Cleft Palate Craniofac J 2013;50:51-8. https://doi.org/10.1597/11-038
- Cantarella G, Mazzola RF, Mantovani M, Mazzola IC, Baracca G, Pignataro L. Fat injections for the treatment of velopharyngeal insufficiency. *J Craniofac Surg* 2012;23:634–7. https://doi.org/10.1097/SCS.0b013e31824db85b

- Boneti C, Ray PD, Macklem EB, Kohanzadeh S, de la Torre J, Grant JH. Effectiveness and safety of autologous fat grafting to the soft palate alone. *Ann Plast Surg* 2015;74(Suppl 4):S190–2. https://doi.org/10.1097/SAP. 0000000000000000442
- 16. Filip C, Matzen M, Aagenæs I, Aukner R, Kjøll L, Høgevold HE, Tønseth K. Autologous fat transplantation to the velopharynx for treating persistent velopharyngeal insufficiency of mild degree secondary to overt or submucous cleft palate. *J Plast Reconstr Aesthet Surg* 2013;66:337–44. https://doi.org/10.1016/j.bjps.2012.11.006
- Leboulanger N, Blanchard M, Denoyelle F, Glynn F, Charrier JB, Roger G, Monteil JP, Garabedian EN. Autologous fat transfer in velopharyngeal insufficiency: indications and results of a 25 procedures series. *Int J Pediatr Otorhinolaryngol* 2011;75:1404–7. https://doi.org/10.1016/j.ijporl.2011.08.001
- Nigh E, Rubio GA, Hillam J, Armstrong M, Debs L, Thaller SR. Autologous fat injection for treatment of velopharyngeal insufficiency. *J Craniofac Surg* 2017; 28:1248–54. https://doi.org/10.1097/SCS. 00000000000003702
- Bishop A, Hong P, Bezuhly M. Autologous fat grafting for the treatment of velopharyngeal insufficiency: state of the art. *J Plast Reconstr Aesthet Surg* 2014;67:1–8. https://doi.org/10.1016/j.bips.2013.09.021
- Isomura ET, Nakagawa K, Matsukawa M, Mitsui R, Kogo M. Evaluation of sites of velopharyngeal structure augmentation in dogs for improvement of velopharyngeal insufficiency. *PLoS One* 2019;14:e0212752https://doi.org/10.1371/journal.pone.0212752
- Isomura ET, Matsukawa M, Nakagawa K, Mitsui R, Kogo M. Endoscopic soft palate augmentation using injectable materials in dogs to ameliorate velopharyngeal insufficiency. *PLoS One* 2020; 15:e0238646https://doi.org/10.1371/journal.pone.0238646
- Kogo M, Kurimoto T, Koizumi H, Nishio J, Matsuya T. Respiratory activities in relation to palatal muscle contraction. *Cleft Palate Craniofac J* 1992;
   29:174–8. https://doi.org/10.1597/1545-1569\_1992\_029\_0174\_rairtp\_2.3.co\_2
- 23. Honjyo I. Significance of nasopharyngeal closure in clef palate speech. (Japanese).

- *Pract Otol* 1967;**60**:865–81. https://doi.org/10.5631/jibirin.60.865
- Tokumura M, Nanri S, Kimura K, Tanaka T, Fujita H. Height-specific body mass index reference curves for Japanese children and adolescents 5–17 years of age. *Pediatr Int* 2004;46:525–30. https:// doi.org/10.1111/j.1442-200x.2004.01949.x
- Chajchir A, Benzaquen I. Liposuction fat grafts in face wrinkles and hemifacial atrophy. Aesthet Plast Surg 1986;10:115–7. https://doi.org/10.1007/BF01575279
- Guerrerosantos J, Gonzalez-Mendoza A, Masmela Y, Gonzalez MA, Deos M, Diaz P. Long-term survival of free fat grafts in muscle: an experimental study in rats. Aesthet Plast Surg 1996;20:403–8. https://doi.org/10.1007/BF02390315
- Leong DT, Hutmacher DW, Chew FT, Lim TC. Viability and adipogenic potential of human adipose tissue processed cell population obtained from pump-assisted and syringe-assisted liposuction. *J Dermatol Sci* 2005;37:169–76. https://doi. org/10.1016/j.jdermsci.2004.11.009
- Niechajev I, Sevćuk O. Long-term results of fat transplantation: clinical and histologic studies. *Plast Reconstr Surg* 1994; 94:496–506. https://doi.org/10.1097/ 00006534-199409000-00012
- Li K, Li F, Li J, Wang H, Zheng X, Long J, Guo W, Tian W. Increased survival of human free fat grafts with varying densities of human adipose-derived stem cells and platelet-rich plasma. *J Tissue Eng Regen Med* 2017;11:209–19. https://doi.org/10.1002/term.1903
- 30. Lin G, Wang G, Banie L, Ning H, Shindel AW, Fandel TM, Lue TF, Lin CS. Treatment of stress urinary incontinence with adipose tissue-derived stem cells. *Cytotherapy* 2010;**12**:88–95. https://doi.org/10.3109/14653240903350265

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