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Evaluation of the Pharyngeal Airway Using Computational Fluid Dynamics in Patients with Acromegaly

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Objectives: Perioperative airway management may be particularly challenging in patients with acromegaly undergoing trans-sphenoidal pituitary surgery (TSS). Management for airway obstruction is required prior to pituitary surgery to minimize perioperative hypoxia. The purpose of this retrospective study was to evaluate airway obstruction by simulation of computational fluid dynamics (CFD) using computed tomography (CT) images in patients who had undergone TSS.

Methods: CT images of the nasopharyngeal airways of patients with acromegaly (n = 5) or nonfunctional pituitary adenoma (n = 6) undergoing TSS from April 2012 to January 2017 were used to construct these airways in three dimensions. Estimated airflow pressure and velocity in the retropalatal airway (RA), oropharyngeal airway (OA), and hypopharyngeal airway (HA) were simulated using CFD.

Results: Estimated pharyngeal airflow pressure in the HA, OA, and RA was significantly greater in patients with acromegaly than in those with nonfunctional pituitary adenomas whereas the estimated pharyngeal airflow velocity was significantly impaired only in the RA of patients with acromegaly. Minimum postoperative SpO_2 both within 3 hours and from 3 to 12 hours after the end of anesthesia was significantly lower in the patients with acromegaly. Additionally, estimated volume of tongue and pharyngeal airflow pressure in the HA, OA, and RA correlated with minimum postoperative SpO_2.

Conclusion: Pharyngeal airflow pressure estimated from CT images is high in patients with acromegaly, and these values correlate with postoperative minimum values for SpO_2. Preoperative evaluation of CT images by CFD can predict difficulty in airway management and perioperative hypoxia.

Key Words: Acromegaly, pharyngeal airway, computational fluid dynamics, computed tomography.
Level of Evidence: 4.

INTRODUCTION

Anatomic abnormalities in the upper airways of patients with acromegaly can restrict spontaneous breathing. Obstructive sleep apnea (OSA) is strongly associated with acromegaly, occurring in up to 70% of individuals, and is a result of obstruction at the laryngeal level caused by hypertrophy of supraglottic soft tissue, including the tongue, soft palate, epiglottis, and aryepiglottic folds, or decreased vocal fold mobility.[1] Chung et al. recently reported that 5.0% of patients undergoing trans-sphenoidal pituitary surgery (TSS) have the comorbidity of OSA and that OSA is independently associated with increased risks of postoperative tracheostomy and hypoxemia after TSS.[2] Although the incidence of airway-related postoperative complications has not been established, Munish et al. have reported that patients with high-risk OSA according to the American Society of Anesthesiologists checklist have a higher incidence of postoperative hypoxia (16.8% vs. 10.2%), defined as one or more instances of pulse oximetry values of <90% on 2–3 L/min oxygen by nasal cannula, and more frequently require tracheal reintubation (4.9% vs. 0.9%) than do matched controls with low-risk OSA.[3,4]

Additionally, prognathism caused by bony thickening of the mandible creates difficulties in management of the airways of patients with acromegaly. In a prospective study of 128 patients with acromegaly, Schmitt et al. found that 20% of those assessed as having Mallanpati Class 1 or 2 were difficult to intubate[5] and that approximately 50% of "difficult-to-intubate patients" had been initially assessed as having Mallampati Class 1 or 2.[6] These findings indicate that conventional preoperative assessment of airways is frequently insufficient to predict difficult airway management and that patients with acromegaly undergoing surgery are at greater increased risk of perioperative compromise of the airway than expected. Furthermore, nasal respiration is obstructed by nasal packing to achieve hemostasis after TSS.

In patients with OSA, severity of apnea is reportedly correlated with the constricted area of the pharyngeal airway (PA) and rate of narrowing during forced inspiration.[7]

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A study evaluating differences between patients with acromegaly and healthy individuals in craniofacial characteristics, upper spine, and PA morphology demonstrated that patients with acromegaly had smaller dimensions at the nasal, uvular, and mandibular pharyngeal levels and at the narrowest point of their pharyngeal airway spaces than healthy controls.[8] These findings suggest that constriction at the PA may not be accurately evaluated preoperatively in patients with acromegaly. Furthermore, Isono et al. estimated closing pressures from cross-sectional images of the pharynx obtained by endoscopy and found that patients with acromegaly have a high incidence of both OSA and central sleep apnea and that those with sleep-disordered breathing have higher closing pressures at both the velopharynx and oropharynx,[9] implying that the cause of airway constriction differs between patients with acromegaly and individuals with ordinary sleep apnea.

Recently, construction of three-dimensional (3D) images by computational fluid dynamics (CFD) has been used to evaluate ventilation conditions in the PA.[10] Wootton et al. performed CFD using magnetic resonance imaging (MRI) and found that the decrease in pressure from the choanae to the minimum cross section (where tonsils and adenoids constrict the pharynx) was significantly correlated with the obstructive apnea–hypopnea index in children with OSA,[11] suggesting that preoperative airway assessment using CFD methods can predict difficulties in airway management and perioperative hypoxia. Therefore, we assessed constriction of the PA in patients with acromegaly undergoing TSS by simulation with CFD using computed tomography (CT) images to calculate pharyngeal pressure and velocity and investigated the relationship between the simulated ventilation conditions and postoperative decreases in oxygen saturation in patients with and without acromegaly.

MATERIAL AND METHODS

Patients

This retrospective study was performed in accordance with the Declaration of Helsinki and with the approval of the Medical Ethics Committee of Kagoshima University Faculty of Medicine.

CT images of the neck and head regions of patients who had been diagnosed as having acromegaly (acromegaly, n = 5) or nonfunctional pituitary adenomas (control, n = 6), undergoing TSS in the Departments of the Cranial Nerve Surgery at Kagoshima University Hospital from April 2012 to January 2017 were used in this study. Patients with CT images showing complete airway obstruction, complications of thyroid disease, or for whom CT images from the nasopharyngeal to supraglottic levels had not been obtained were excluded from this study.

Perioperative Supply of Oxygen

The fraction of inspiratory oxygen was maintained between 0.4 and 0.5 during surgery and increased to 1.0 from the end of surgery until tracheal extubation. After extubation, 3 L/min oxygen was supplied via a facial mask until 3 h after the end of anesthesia. Oxygen saturation was monitored by pulse oximeter (SpO_2) until 12 h after the end of anesthesia in all patients. For 3 h after the end of anesthesia, 3 L/min oxygen was supplied via a facial mask.

Analysis of CT images

CT images using a 64-slice CT medical imaging system (Aquilion PRIME; Toshiba Medical Systems, Tochigi, Japan) with 0.6 mm slice thickness were obtained preoperatively in all patients in this study. The cross-sectional images were reformatted in multiple planes and used to generate 3D images of the nasopharyngeal airway, as previously reported.[12] Image processing was performed with Philips DICOM Viewer 3.0 (Philips Medical System Nederland B.V., Best, the Netherlands).

Simulation of Pharyngeal Airway Ventilation Conditions

Volume-rendering software (Intage Volume Editor; Cybernet, Tokyo, Japan) was used to generate 3D volume data for the tongue and PA. Using mesh-morphing software (DEP Mesh Works/Morpher; Idaj, Kobe, Japan), the 3D models were subsequently converted to a smoothed model without losing the patient-specific shape of the airway. CFD was used to simulate ventilation of the PA models as follows (Fig. 1).[13,14] The models were exported to fluid dynamics software (Phoenics; CHAM-Japan, Tokyo, Japan) in stereolithographic format, and the fluid was assumed to be Newtonian, homogeneous, and incompressible. Elliptic-staggered equations and a continuity equation were used in the analysis. The CFD of the PA models was analyzed under the following conditions:

volumetric flow rate; 400 cm^3/s (body weight 40–50 kg), 500 cm^3/s (body weight 51–60 kg), 600 cm^3/s (body weight 71–80 kg)

no-slip condition at the wall surface

300 iterations to calculate mean values.

Convergence was judged by monitoring the magnitude of the absolute residual sources of mass and momentum, normalized to their respective inlet fluxes. Iteration was continued until all residuals fell below 0.2%. Simulation of estimated airflow pressure and velocity was performed at the retropharyngeal airway (RA), oropharyngeal airway (OA), and hypopharyngeal airway (HA).[10]

Statistics

Values are presented as the mean ± standard deviation (SD). An unpaired t-test or the Mann–Whitney U test was used to detect intergroup differences, depending upon the data distribution. Correlations between SpO_2 and airway pressure, and airway velocity were assessed using the Spearman rank correlation coefficient. All statistical analyses were conducted using GraphPad Prism software (version 6.0; GraphPad Software, La Jolla, CA, USA). $P < .05$ was considered to denote statistical significance.

RESULTS

There were no significant differences in clinical characteristics between the control and acromegaly group (Table I). Although the volume of the tongue was significantly larger in patients with acromegaly than in control patients (P = .001), the PA volume did not differ between these groups. There were consistently no differences in diameter or width of the RA, OA, or HA between the acromegaly and control groups. Despite the absence of differences in two-dimensional parameters of morphological structures in the PA, the estimated airway pressure was significantly higher in patients with acromegaly than in controls throughout the PA; RA (P = .024), OA (P = .032), and HA (P = .023) (Table II). The estimated velocity in the RA was consistently

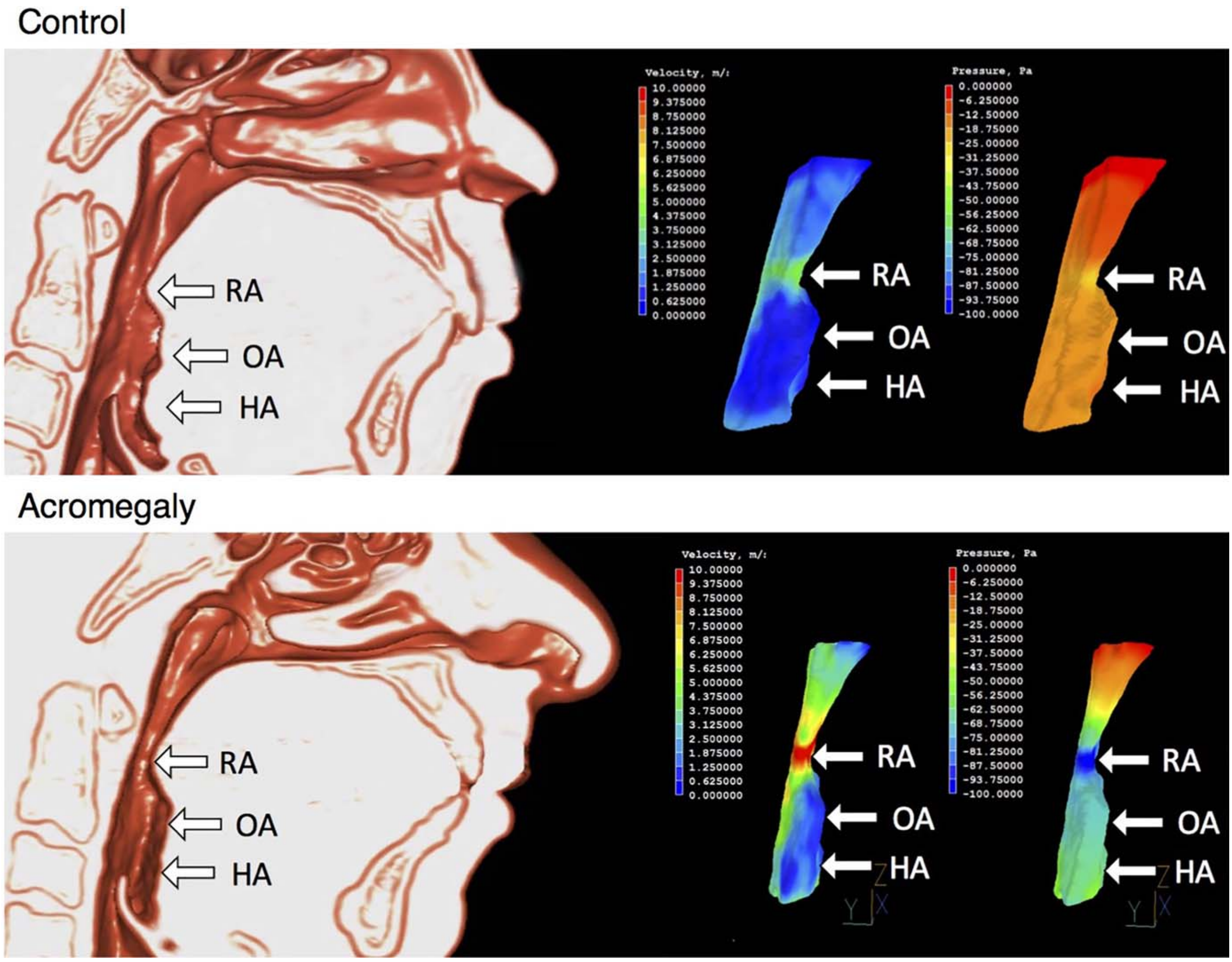

Fig. 1. Example of simulated pharyngeal airway ventilation using computational fluid dynamics (CFD) in control patients (top) and patients with acromegaly (bottom).

significantly higher in patients with acromegaly than in control patients (P = .041); however, the differences in velocity in the OA and HA between the acromegaly and control groups were not statistically significant. The minimum SpO_2 both within 3 hours and from 3 to 12 hours after the end of anesthesia was significantly lower in patients with acromegaly than in control patients (P = .04 and P = .01, respectively) (Table III). Minimum SpO_2 was measured when breathing room air in all patients. Additionally, estimated pharyngeal airflow pressure at the HA, a site proximal to the glottis and lower respiratory tract, was significantly correlated with the minimum SpO_2 postoperatively ($R = 0.52$, P = .01) (Fig. 2). Similarly, correlations were detected between the postoperative minimum SpO_2 and volume of the tongue ($R = 0.45$, P = .03) and the airflow pressure at the RA ($R = 0.45$, P = .02) and OA ($R = 0.56$, $P < .01$).

TABLE I.
Patient Characteristics.

	Acromegaly (n = 5)	Control (n = 6)	*P* value
Height (cm)	167.5 ± 10	158.1 ± 12	.13
Weight (kg)	65.4 ± 13	58.4 ± 11	.67
BMI	23.2 ± 2	23.6 ± 2	.79
Age (y)	48 ± 17	56 ± 15	.67
Sex (M/F)	2/3	2/4	.99

Data are expressed as mean ± SD.
BMI = body mass index; SD = standard deviation

DISCUSSION

In this study, we found that negative pharyngeal pressure estimated by a CFD method using preoperative CT images was higher in all regions of the PA, including the RA, OA, and HA, in patients with acromegaly and correlated with the minimum postoperative SpO_2 (Table I, Fig. 2). Since neither the diameter, width, or volume of the PA (RA, OA, and HA) differed between patients with acromegaly and controls (Table II), our findings indicate the difficulty in predicting airway obstruction from the PA structure as shown on CT images without

TABLE II.
Simulated Volume, Pressure, and Velocity of the Pharyngeal Airway.

		Acromegaly (n = 5)	Control (n = 6)	*P* value
Diameter (mm)	RA	9.82 ± 2.15	12.17 ± 4.20	.32
	OA	14.90 ± 4.36	15.27 ± 2.75	.86
	HA	14.58 ± 5.03	16.38 ± 2.11	.63
Width (mm)	RA	20.34 ± 4.79	23.23 ± 5.21	.37
	OA	29.96 ± 8.36	25.08 ± 6.07	.29
	HA	30.38 ± 6.14	30.80 ± 2.36	.65
Volume (cm^3)	Tongue	138.5 ±15.61	87.73 ±19.99	<.001
	PA	10.16 ± 3.67	10.35 ± 4.81	>.99
Pressure (Pa)	RA	− 62.4 ± 34.9	− 21.2 ± 12.7	.024
	OA	− 46.6 ± 22.6	− 19.8 ± 11.6	.032
	HA	− 44.9 ± 21.5	− 18.2 ± 9.9	.023
Velocity (m/s)	RA	8.8 ± 4.8	4.1 ± 1.7	.041
	OA	3.1 ± 1.0	2.9 ± 1.2	.420
	HA	2.7 ± 0.8	2.3 ± 1.0	.251

Data are expressed as mean ± SD.
HA = hypopharyngeal airway; OA = oropharyngeal airway; RA = retropalatal airway; SD = standard deviation.

estimating airflow pressure in patients with acromegaly (Table II, Fig. 2) as discussed previously.[15] Additionally, the volume of the tongue was larger in patients with acromegaly (Table II) and correlated with minimum postoperative SpO_2 (Fig. 2). It has been suggested that the anatomical imbalance of the upper airway observed in patients with OSA is attributable to having a larger tongue for a given maxillomandibular size.[16] However, both soft tissue hypertrophy and anatomical alteration appear to contribute to the increased incidence of hypoxia in patients with acromegaly and OSA.[17] Given that we estimated PA pressure independent of the influence of tongue volume in our study, both anatomical imbalance of the upper airway and PA narrowing synergistically induce pharyngeal airway obstruction after surgery, resulting in development of postoperative hypoxia in patients with acromegaly after TSS.

Difficulties in airway management, such as in laryngoscopy and intubation, have frequently been reported in patients with acromegaly. However, preoperative evaluation by assessing extended Mallampati score (EMS) or modified Mallampati classification (MMP) has reportedly failed to predict difficult perioperative airway management in patients with acromegaly.[18] In one study of patients undergoing TSS, the cohort with OSA had significantly higher rates of acromegaly (17.1% vs. 6.4%; $P < .001$) than those without OSA[19]. Meta-analysis of the association between OSA and postoperative outcome has revealed that OSA is associated with higher odds of desaturation (odds ratio [OR] 2.27), reintubation (OR 2.05), and transfer to the ICU (OR 2.81).[20]

In this study, only the patients with acromegaly had undergone polysomnography, OSA having been diagnosed when the number of episodes of apnea or hypopneas per hour of sleep (ie, apnea–hypoxia index [AHI] > 5). All five patients in the acromegalic group had been diagnosed as having OSA. Soft tissue swelling and hyperplasia of connective tissue and higher collapsibility along the PA is expected in individuals with acromegaly. In a study using fiberoptic nasopharyngoscopy with the Muller maneuver (FNMM), MRI, and with 3D elaboration, it was found that the uvula and tongue base were the main sites of obstruction according to FNMM. Uvular diameters obtained by MRI imaging correlated with the severity of upper airway collapse as assessed by FNMM. Narrowing and a smaller total volume of upper airways were identified by 3D-MRI in patients with severe OSA[17], suggesting a possible correlation between the severity of OSA and perioperative airway collapse in patients with acromegaly.

Additionally, Saeki et al. have reported that the oxygen desaturation index, which is defined as the number/hour of oxygen desaturation episodes exceeding 4% from the base line, is worse in patients with acromegaly than in those without it during nasal packing after TSS.[21] The most serious complication of TSS is injury to the carotid artery and resultant massive bleeding.[22] Patients with acromegaly may have atypical bony and vascular anatomy, including “kissing” carotid arteries, that necessitate reconsideration of the surgical approach or plan to ensure safe tumor removal.[23] This suggests that patients with acromegaly have a higher risk of airway-related adverse events caused by postoperative bleeding as well as by airway constriction than those without acromegaly.

It is therefore likely that postoperative sleep-disordered breathing and acute respiratory failure resulting in oxygen desaturation occur frequently in patients with acromegaly, consistent with the lower SpO_2 both within 3 hours and from 3 to 12 hours after the end of anesthesia in patients with acromegaly than in those without it (Table III). Although the anatomical morphology and causes of airway constriction appear to differ between individuals with acromegaly and those with ordinary sleep apnea, postoperative minimum SpO_2 was significantly correlated with PA pressure regardless of the presence or absence of acromegaly in our study (Fig. 2). These results are consistent with a previous study's findings that the severity of OSA in children is strongly correlated with pressure changes at the sites of obstruction of the pharyngeal airway,[11] suggesting that airflow pressure in the PA simulated by a CFD method using nasopharyngeal CT images may predict postoperative hypoxia. Additionally, the correlation between airway pressure and postoperative minimum SpO_2 may indicate that postoperative hypoxia is attributable mainly to airway obstruction,

TABLE III.
Oxygen Saturation in the Perioperative Period.

	Acromegaly	Control	*P* value
Pre-SpO_2 (%)	98.2 ± 0.4	98.3 ± 0.8	.35
Post-ope SpO_2 (%)			
0–3 h	95.8 ± 3.6	99.2 ± 0.8	.04
3–12 h	94.4 ± 0.9	96.3 ± 1.6	.01

Data are expressed as mean ± SD. Pre-SpO_2; the oxygen saturation before the induction of anesthesia. Post-SpO_2; the lowest oxygen saturation after the end of anesthesia.
SD = standard deviation

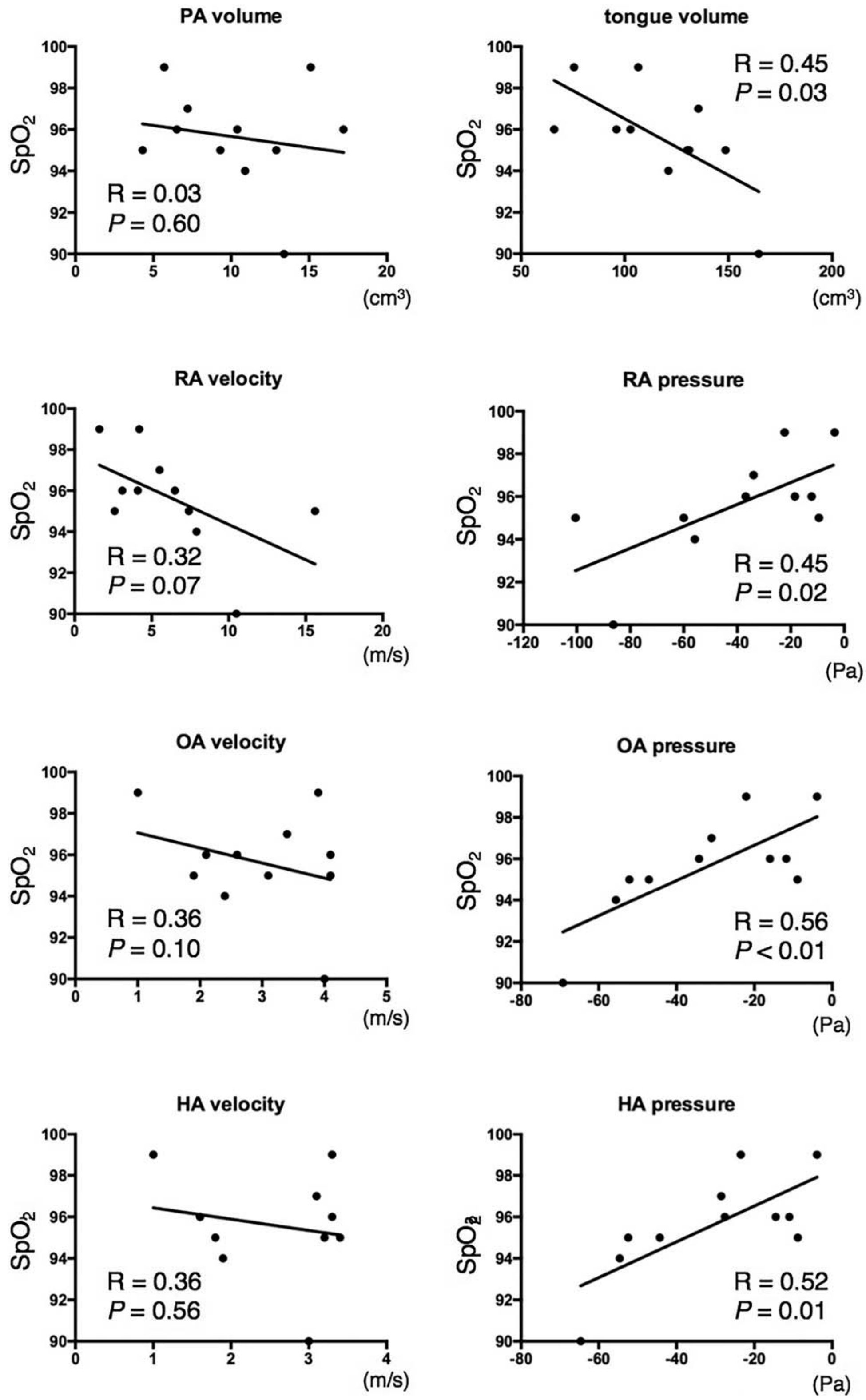

Fig. 2. Correlation between estimated minimum postoperative SpO_2 and estimated airway variables between 3 hours and 12 hours after the end of anesthesia.

rather than central apnea, including opioid-induced apnea. However, the absence of postoperative complications such as respiratory arrest due to a central mechanism might have been due to the small sample size in this study. Further investigation is required to evaluate whether simulated airflow pressure correlates with perioperative adverse events and outcomes.

Airway obstruction can occur in the nasal, retropalatal, and retroglossal/hypopharyngeal regions; patients with OSA undergoing surgery reportedly have multiple levels of obstruction.[24] In patients with active acromegaly, AHI scores are reportedly significantly correlated with HA space, this being defined as the lowest extent of the hard palate as seen on MRI images. This space is highly variable, depending on factors such as respiratory movement, patient arousal, and tongue position.[25] One limitation of our study is that, because it was retrospective, we had no data on head position or respiration at the time of CT scanning.

Despite significant differences in airflow pressure between patients with acromegaly and control patients in all segments of the PA (RA, OA, and HA), the velocity was significantly greater only in the RA, the narrowest site in the PA (Fig. 1), but not in the OA or HA (Table II). This is consistent with the markedly greater airway constriction observed in the RA region than in the OA and HA in both groups of patients (Fig. 1). It is also consistent with a report of a study using 3D CFD simulation of the upper airway of OSA that found that both maximum airflow velocity and lowest negative pressure occur in the narrowest portions of the velopharynx, that is the retropalatal airway.[26] However, the possibility that the phase of respiration, such as inspiration/expiration, and movement of the glottis during the CT scan alter airflow resistance cannot be excluded.

In conclusion, we here demonstrated that the volume of the tongue and airflow pressure in the PA is greater in patients with acromegaly than in those without it and correlates with postoperative minimum SpO_2. Not only patients with acromegaly undergoing TSS but also those patients with other surgical procedures general anesthesia can develop postoperative adverse events such as apnea. Fluid analysis of the PA using preoperative CT images may be useful for perioperative airway management in patients with acromegaly undergoing general anesthesia.

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