JCN Open Access ORIGINAL ARTICLE
pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2021;17(2):283-289 / https://doi.org/10.3988/jcn.2021.17.2.283

Sex Differences in Obstructive Sleep Apnea by Bioelectrical Impedance Analysis

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Background and Purpose Obesity is known of one of the risk factors for obstructive sleep apnea (OSA). Although body mass index (BMI) can be an indicator for obesity, it does not represent the actual body composition of fat or muscle. We hypothesized that bioelectrical impedance analysis (BIA) can help analyze the fat and muscle distributions in males and females with OSA.

Methods This study screened subjects who visited the Department of Neurology, Samsung Medical Center, Seoul, Korea due to sleep disturbances with symptoms suggestive of OSA from December 2017 to December 2019. All subjects underwent overnight type I polysomnography (PSG) and BIA.

Results PSG and BIA were completed in 2,064 OSA patients who had an apnea-hypopnea index (AHI) of ≥5/hour (77.1% males and 22.9% females). The females had remarkably higher fat indicators and lower muscle indicators. The AHI was significant correlated with all BIA parameters in all OSA patients: body fat mass (ρ=0.286, p<0.001), percentage body fat (ρ=0.130, p<0.001), visceral fat area (VFA) (ρ=0.257, p<0.001), muscle mass (ρ=0.275, p<0.001), and skeletal muscle mass (SMM) (ρ=0.270, p<0.001). The correlations in males were similar to those in all patients, where those in females were not. In females with OSA, all of the BIA fat indicators were correlated with AHI, whereas the muscle indicators were not. Adjusting age and BMI when analyzing the SMM/VFA ratio showed a strong correlation in males with OSA (p=0.015) but not in females with OSA (p=0.354).

Conclusions This study has revealed that the body composition of fat and muscle has different patterns in OSA patients. The SMM/VFA as measured using BIA is the factor most significantly associated with AHI in males but not in females after adjusting for age and BMI.

Key Words sleep apnea, obstructive, bioelectrical impedance, body compositions.

Received November 30, 2020
Revised February 2, 2021
Accepted February 2, 2021

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INTRODUCTION

Obstructive sleep apnea (OSA) involves repetitive episodes of the partial or complete obstruction of the upper airway during sleep.[1-3] This results in hypoxemia, increased respiratory effort, and frequent arousals during sleep. The physiologic changes in OSA increase the risks of cerebrovascular disease, cardiovascular disease, metabolic syndrome, and other diseases. Among factors associated with reduction of the resting pharynx size or increased airway collapsibility, obesity is the most important risk factor for OSA. Other factors are higher age, male sex, abnormal craniofacial morphology, nasal obstruction, genetic factors, and endocrine abnormalities such as thyroid disorders.[3]

The body mass index (BMI) calculated by dividing the body weight by the square of the height represents an estimated measurement of body fat and the body fat mass (BFM) that is used as an obesity indicator. A normal BMI is between 18.5 and 22.9 kg/m^2, a BMI of 23.0 to 24.9 kg/m^2 indicates overweight, and a BMI of ≥25 kg/m^2 indicates obesity in Korea. However, BMI has limitations in assessing the actual body composition because it does not accurately reflect the true body fat composition,[4-6] and hence may underestimate obesity-related risks for patients with normal BMI.[7]

Accurate obesity assessments need to be based on body composition measurements, including measurements of body fat and body muscle.[8-11] Bioelectrical impedance analysis (BIA) is an easy, convenient, and widely used method for analyzing the body composition. It measures various aspects of the body composition including BMI and the muscle and fat distributions. The reproducible results have shown high accuracies and strong correlations with dual-energy X-ray absorptiometry assessments of body fat.[12,13] However, the relationships between OSA and parameters measured by BIA have not been well investigated. There have been attempts to screen OSA in type 2 diabetes mellitus patients using BIA,[14] with results indicating that the body muscle-to-fat ratio as measured with BIA can be used to screen for OSA.

OSA is more prevalent in males, which is largely explained by sex hormones.[15] Sleep apnea in females exhibits different trends depending on their menopausal state,[3,16] with it tending to be less severe in premenopausal females and females receiving hormone replacement treatment than in untreated postmenopausal females.[15,17-19] However, males tend to have a higher mean body weight, free fat mass, and neck circumference (NC) compared with females,[20] and hence there may be distinctive differences in the body composition between the sexes aside from the hormonal state.

This study aimed to determine the relationship between OSA severity and body composition using BIA measurements, and further determine differences therein between males and females.

METHODS

Study population and study protocol

We analyzed subjects who visited the Department of Neurology, Samsung Medical Center, Seoul, Korea due to sleep disturbances with symptoms suggestive of OSA. The subjects were consecutively enrolled from December 2017 to December 2019. We selected patients with suspected symptoms of OSA by self-reported or witnessed snoring or apnea during sleep, morning headache, dry mouth, or excessive daytime sleepiness. Those who had OSA-compatible symptoms with oropharyngeal examination findings and completed overnight type I polysomnography (PSG) and BIA were included in the study. Subjects who were diagnosed with OSA according to criteria of the American Academy of Sleep Medicine (AASM) were finally enrolled.[21] We excluded subjects who were aged ≤18 years, who could not remain standing to have an elementary body composition test, and who did not undergo PSG and BIA. Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the Human Ethics Review Committee of Samsung Medical Center (protocol registration system ID: 2019-01-051).

Polysomnography

All subjects underwent overnight type I PSG. PSG was conducted using six-channel electroencephalography, two-channel electrooculography, and a minimum of four-channel electromyography for the chin, intercostals muscles, right and left anterior tibialis, sleep stages, arousals, apneas/hypopneas, and rapid-eye-movement sleep without atonia as analyzed manually according to the AASM criteria. PSG was conducted by PSG technicians, with the obtained data reviewed by certified sleep specialists. Apnea was defined as decrease of >90% in the thermistor-based airflow in the presence of continued respiratory effort lasting at least 10 seconds. Hypopnea is defined as a decrease of >30% in the nasal pressure signal lasting for at least 10 seconds, accompanied by a decrease of ≥3% in oxygen saturation or an arousal. The apnea-hypopnea index (AHI) is a ratio of the sum of apnea and hypopnea episodes to the total hours of sleep, with the values used to divide subjects into normal (AHI<5), mild (5≤AHI<15), moderate (15≤AHI<30), and severe (AHI≥30) groups.

Measurement of body composition

The human body is composed of water, protein, fat, and minerals, which have different bioelectrical impedances.[22] BIA using the InBody770 device (Biospace, Seoul, Korea) was applied when subjects visited for PSG investigations. This analyzer uses a direct segmental multifrequency BIA method to investigate the body composition using 30 impedance measurements at 6 frequencies (1, 5, 50, 250, 500, and 1,000 kHz) on each arm, each leg, and the trunk. BIA is an easy and noninvasive method; after 3 hours of fasting, the subject empties their bladder and then holds the detection handles and remains stationary, with data being obtained automatically. The parameters consisted of weight, BMI, BFM, percentage body fat (PBF), segmental BFM, visceral fat area (VFA), muscle mass (MM), skeletal muscle mass (SMM), segmental MM, and skeletal muscle mass index. Segmental means were obtained for parameters measured on each limb (right arm, right leg, left arm, and left leg).

Measurement of anthropometric parameters

Segmental circumferences were measured using a flexible plastic measuring tape. The head circumference was measured at 2.5 cm above the ears, at 7.5 cm above the eyebrows, and at the middle of the occipital bone. NC was measured from the level just below the laryngeal prominence perpendicular to the axis of the neck. The waist circumference (WC) was measured horizontally at the midline between the costal margin and iliac crest. The hip circumference (HC) was measured at the widest part of the hip. The waist-to-hip ratio (WHR) was calculated as WC/HC. Segmental circumferences including both arms and legs were measured at the midpoint of the upper arm and 5 cm below the top of the inner leg.

Statistical analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 22.0, IBM Corp., Armonk, NY, USA). Categorical variables are given as numbers and percentages, and continuous variables are given as mean± standard-deviation values. In univariate analyses, the χ^2 test or Fisher's test was used for comparisons of categorical variables. Student's *t* test or the Mann-Whitney U test was used for comparing continuous data between two groups, while one-way analysis of variance (ANOVA) or the Kruskal-Wallis test was performed when more than two groups were compared. Correlation analysis was performed using Spearman's rank correlation coefficient. In multivariate analyses, ANOVA with a general linear model was used to investigate the differences in BIA measurements with adjustment for confounders in different sexes. A probability value of $p<0.05$ was considered statistically significant.

RESULTS

Baseline clinical characteristics of the study patients

This study initially enrolled 2,616 subjects who had sleep disturbances with suspected symptoms of OSA. Among them, 26 subjects who were younger than 18 years and 111 who

Table 1. Characteristics of obstructive sleep apnea patients according to sex

	Total (*n*=2,064)	Males (*n*=1,591)	Females (*n*=473)	*p* (males vs. females)
Age, years	54.0±13.9	52.6±14.0	58.8±12.2	<0.001
Anthropometric measurements				
Height, cm	167.8±8.8	171.1±6.4	156.6±6.4	<0.001
Weight, kg	75.3±15.0	79.1±13.7	62.6±12.0	<0.001
BMI, kg/m²	26.6±4.3	27.0±4.1	25.5±4.7	<0.001
NC, cm	37.1±3.4	38.0±2.7	33.8±3.5	<0.001
WC, cm	89.7±11.9	91.4±11.6	83.7±10.6	<0.001
HC, cm	100.3±7.3	101.7±6.8	95.8±7.1	<0.001
Waist-to-hip ratio	0.89±0.06	0.90±0.06	0.87±0.06	<0.001
Polysomnography				
AHI, *n*/hour	33.0±23.2	35.8±23.5	23.8±19.6	<0.001
Mild	525 (25.4) 9.6±2.9	330 (20.7) 9.7±2.9	195 (41.2) 9.4±2.8	0.142
Moderate	614 (29.7) 21.8±4.3	456 (28.7) 21.9±4.3	158 (33.4) 21.6±4.4	0.444
Severe	925 (44.8) 53.8±19.0	805 (50.6) 54.3±18.6	120 (25.4) 50.1±21.0	0.025
Total arousal index, *n*/hour	29.4±16.7	31.5±17.3	22.0±11.9	<0.001
Respiratory arousal index, *n*/hour	21.4±18.5	24.1±19.2	12.5±11.9	<0.001
BIA				
BFM, kg	21.7±8.5	21.4±8.5	22.6±8.6	<0.010
PBF, %	28.4±7.5	26.4±6.4	35.2±7.1	<0.001
VFA, cm²	96.7±40.3	92.7±38.2	110.2±44.2	<0.001
MM, kg	50.6±9.6	54.4±7.0	37.6±4.9	<0.001
SMM, kg	29.8±6.2	32.3±4.5	21.4±3.1	<0.001
SMM/VFA, kg/cm²	0.36±0.17	0.40±0.17	0.23±0.10	<0.001

Data are mean±standard deviation or *n* (%) values.
AHI: apnea-hypopnea index, BFM: body fat mass, BIA: bioelectrical impedance analysis, BMI: body mass index, HC: hip circumference, MM: muscle mass, NC: neck circumference, PBF: percentage body fat, SMM: skeletal muscle mass, VFA: visceral fat area, WC: waist circumference.

had inappropriate sleep data were excluded. PSG and BIA were completed in 2,479 patients, of which 2,064 [1,591 males (77.1%), 473 females (22.9%)] were finally enrolled in the study analysis after excluding 415 (169 males, 246 females) who had AHI <5/hour.

The severity of OSA in the 2,064 patients was as follows: 525 (25.4%) mild (5≤AHI<15/hour), 614 (29.7%) moderate (15≤AHI<30/hour), and 925 (44.8%) severe (AHI≥30/hour). The other baseline characteristics along with the PSG and BIA results are presented in Table 1. The enrolled patients were aged 54.0±13.9 years and had an AHI of 33.0±23.2/hour and a BMI of 26.6±4.3 kg/m^2. The BIA results were PBF=28.4±7.5%, VFA=96.7±40.3 cm^2, and MM=50.6±9.6 kg.

Anthropometric measurements and PSG results according to sex

There was a preponderance of males in the study (*n*=1,591, 77.1%). The sex differences in the anthropometric measurements and PSG findings are presented in Table 1. Male patients were significantly taller and heavier than female patients, with higher BMI, along with significantly higher values of NC, WC, HC, and WHR. PSG revealed that the AHI and the respiratory arousal index were higher in male patients than in female patients. The sex differences were only significant in the severe-OSA group.

Sex differences in BIA results

The BIA results were also revealed significant sex differences in the muscle and fat distributions. The females with OSA had remarkably higher fat indicators and lower muscle indicators than did the males with OSA. The BFM, PBF, and VFA were significantly higher in females than in males (21.4±8.5 kg vs. 22.6±8.6 kg, $p<0.01$; 26.4±6.4% vs. 35.2±7.1%, $p<0.001$; and 92.7±38.2 cm^2 vs. 110.2±44.2 cm^2, $p<0.001$). But, the MM, SMM, and SMM/VFA were significantly higher in males than in females (54.4±7.0 kg vs. 37.6±4.9 kg, $p<0.001$; 32.3±4.5 kg vs. 21.4±3.1 kg, $p<0.001$; and 0.40±0.17 kg/cm^2 vs. 0.23±0.10 kg/cm^2; $p<0.001$) (Table 1).

Body composition analysis and Spearman's rank correlation analysis for AHI

In Spearman's rank correlation coefficient analysis, all BIA measurements were significantly positively correlated with AHI (Table 2): BFM (ρ=0.286, $p<0.001$), PBF (ρ=0.130, $p<0.001$), VFA (ρ=0.257, $p<0.001$), MM (ρ=0.275, $p<0.001$), and SMM (ρ=0.270, $p<0.001$). However, the correlations varied with sex, with their significance being was greater in males. The correlations were consistently seen in the males with OSA, whereas for the females with OSA, BIA for all of the fat measurements revealed significant positive correlations with AHI, but not for the following muscle measurements: MM, SMM, right leg MM, and left leg MM. Further analysis of SMM/VFA revealed negative correlations in all patients, male OSA patients, and female OSA patients.

Table 2. Simple correlations between AHI and anthropometric or BIA parameters

	Total (*n*=2,064)	Males (*n*=1,591)	Females (*n*=473)
BMI	0.370*	0.361*	0.302*
NC	0.371*	0.305*	0.272*
Chest circumference	0.370*	0.305*	0.261*
WC	0.356*	0.320*	0.260*
HC	0.358*	0.313*	0.240*
Right arm circumference	0.376*	0.332*	0.280*
Left arm circumference	0.377*	0.332*	0.283*
Right leg circumference	0.317*	0.270*	0.176*
Left leg circumference	0.316*	0.270*	0.171*
BIA			
BFM	0.286*	0.331*	0.271*
Right arm BFM	0.246*	0.321*	0.273*
Left arm BFM	0.246*	0.320*	0.267*
Trunk BFM	0.307*	0.335*	0.278*
Right leg BFM	0.250*	0.318*	0.251*
Left leg BFM	0.245*	0.315*	0.249*
PBF	0.130*	0.304*	0.277*
VFA	0.257*	0.333*	0.292*
MM	0.275*	0.166*	0.077
SMM	0.270*	0.160*	0.064
Right arm MM	0.308*	0.212*	0.171*
Left arm MM	0.310*	0.212*	0.184*
Trunk MM	0.300*	0.201*	0.141†
Right leg MM	0.247*	0.130*	0.018
Left leg MM	0.245*	0.126*	0.004
SMM/VFA	-0.111*	-0.302*	-0.278*

*$p<0.001$, †$p<0.05$.
AHI: apnea-hypopnea index, BFM: body fat mass, BIA: bioelectrical impedance analysis, BMI: body mass index, HC: hip circumference, MM: muscle mass, NC: neck circumference, PBF: percentage body fat, SMM: skeletal muscle mass, VFA: visceral fat area, WC: waist circumference.

Multiple regression analysis of correlations between AHI and BIA parameters

Considering the presence of multicollinearity, multiple regression analysis was performed with selected parameters (Table 3, Fig. 1). After adjusting for covariates, age, sex, and BMI, and SMM/VFA were related to AHI in all of the enrolled OSA patients (Model 1). Similar findings were obtained in males with OSA (Model 2). However, in the females, after adjusting confounding factors of age, sex and BMI, SMM/VFA was no longer associated with AHI (Model 3).

Table 3. Results of multivariate regression analysis of AHI

Variable	Model 1 (R^2=0.218)		Model 2 (R^2=0.162)		Model 3 (R^2=0.210)	
	Beta (95% CI)	*p*	Beta (95% CI)	*p*	Beta (95% CI)	*p*
Age	0.012 (0.001 to 0.014)	<0.001	0.011 (0.008 to 0.013)	<0.001	0.017 (0.012 to 0.023)	<0.001
Sex, male	0.467 (0.361 to 0.551)	<0.001	Males only		Females only	
BMI	0.062 (0.054 to 0.071)	<0.001	0.064 (0.053 to 0.075)	<0.001	0.064 (0.048 to 0.081)	<0.001
SMM/VFA	-0.289 (-0.520 to -0.058)	0.014	-0.309 (-0.557 to -0.061)	0.015	0.393 (-0.440 to 1.226)	0.354

Model variables included demographics (age and sex) and BMI.
AHI: apnea-hypopnea index, BMI: body mass index, CI, confidence interval, SMM: skeletal muscle mass, VFA: visceral fat area.

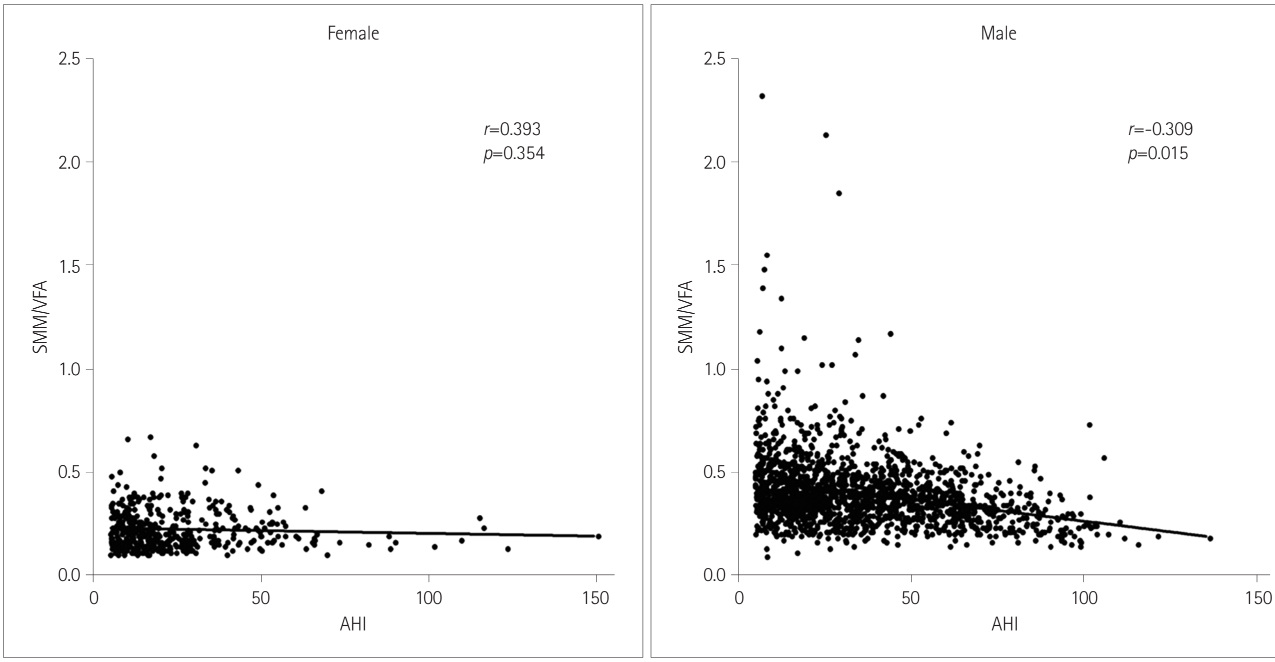

Fig. 1. Ratio of SMM to VFA according to the AHI in female and male patients with OSA. After adjusting confounding factors, SMM/VFA was significantly related to AHI in all OSA patients and in male OSA patients, but not in female OSA patients. AHI: apnea-hypopnea index, OSA: obstructive sleep apnea, SMM: skeletal muscle mass, VFA: visceral fat area.

DISCUSSION

OSA is a repetitive upper airway obstruction, and parameters associated with airway narrowing contribute as risk factors. Obesity is the most important risk factor, and BMI has been a good indicator. However, performing meticulous assessments of individual patients are problematic. More accurate assessments of body composition can be achieved using computed tomography, magnetic resonance imaging, dual-energy X-ray absorptiometry, and BIA,[12,13] and BIA has been found to be a convenient and cost-effective method. To our best knowledge, this is the first large cross-sectional study to analyze the BIA results in OSA patients, including assessments for different sexes in the Korean population.

The incidence of OSA is higher in males than in females (4% vs. 2%).[23,24] Several factors contribute to the male predominance in the prevalence of OSA, including the anatomic size, collapsibility, and resistance of the upper airway, hormonal changes, different clinical presentation, and tolerance of symptoms.[25] Moreover, the body composition (especially the fat distribution) varies between males and females, with females generally having a higher PBF. In the present study, the males with OSA had higher BMI, WC, MM, and SMM, but lower BFM, PBF, and VFA than did the females with OSA. The correlation analysis revealed that fat and muscle parameters were correlated in all of the OSA patients, with a similar pattern in males. However, in females the fat parameters were correlated with OSA severity whereas the muscle parameters were not.

Previous studies have revealed that visceral fat accumulation is associated with OSA.[26,27] Another study demonstrated that the primary type of fat associated with OSA is visceral adiposity in males but global adiposity in females.[28] A VFA assessment using computed tomography indicated that despite similar BMI and WC, males had larger VFA and more-severe OSA than females, with an independent association.[29]

The present study found that AHI was positively correlated with BFM, PBF, and VFA in both females and males, with the correlations being stronger in males.

This study also revealed significant differences in muscle parameters between males and females with OSA. Male OSA patients exhibited significant correlations with MM, SMM, and segmental MM, whereas females with OSA showed correlations only for the trunk, right- and left arm MM, and not for any other muscle indicators. One study has investigated the associations between OSA and skeletal muscle measurements using computed tomography, and found positive correlations between muscle parameters and AHI.[30] In our study, while visceral fat had similar patterns in males and females with OSA, the muscle parameters exhibited patterns that differed with sex. The significance of this finding was further supported after adjusting for age and BMI, with SMM/VFA being significantly negatively correlated in males but not in females. Certain parameters of the body composition were significantly correlated in males with OSA but not in females.

BIA assessments have previously been used in OSA, but mostly with a focus on analyzing the overnight fluid shift.[31,32] OSA patients have a higher baseline fluid content in both legs, and their overnight shifts may aggravate airway narrowing during sleep as compared with non-OSA subjects.[31] Only one study has investigated the body composition using BIA in OSA patients with diabetes mellitus, and the results suggested that the muscle-to-fat ratio obtained by BIA can be used to screen for OSA in patients with inadequately controlled type 2 diabetes mellitus: the area under the curve was 0.70 ($p<0.001$).[14] Our study further revealed that the ratio between muscle and fat is different in OSA patients of different sexes.

This study had some limitations. First, this was a cross-sectional observation study, and so it could not reveal the exact causative relationships between OSA and BIA parameters. However, we were able to report apparent associations. Second, we did not compare BIA data with data from other assessments. Computed tomography and magnetic resonance imaging are the gold standards for quantitative assessments of fat or muscle, and so future studies are needed to confirm the accuracy of BIA data. Third, we did not distinctly analyze data on the menopause status of females, despite hormonal effects being important in OSA. Fourth, our population was restricted to males and females living in Korea, and so the results might not be applicable to other populations.

In conclusion, this study has revealed significant sex differences in the body composition of fat and muscle in OSA patients. The ratio of SMM to VFA as measured by BIA could be the most significant factor that is negatively associated with AHI in males but not in females with OSA after adjusting for age and BMI.

Author Contributions

Conceptualization: all authors. Data curation: Jae Rim Kim, Pamela Song. Formal analysis: Jae Rim Kim, Pamela Song. Investigation: all authors. Methodology: all authors. Validation: Pamela Song, Eun Yeon Joo. Supervision: Pamela Song, Eun Yeon Joo. Writing—original draft: Jae Rim Kim, Pamela Song. Writing—review & editing: all authors.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Acknowledgements

This study was supported by Samsung Medical Center Grant #(OTC1190671).

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