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RETROPALATAL AND RETROGLOSSAL AIRWAY COMPLIANCE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Abstract

Objectives—We hypothesized that preferential retropalatal as compared to retroglossal collapse in patients with obstructive sleep apnea was due to a narrower retropalatal area and a higher retropalatal compliance. Patients with a greater retropalatal compliance would exhibit a recognizable increase in negative effort dependence (NED).

Methods—Fourteen patients underwent upper airway endoscopy with simultaneous recordings of airflow and pharyngeal pressure during natural sleep. Airway areas were obtained by manually outlining the lumen. Compliance was calculated by the change of airway area from end-expiration to a pressure swing of $-5\text{cmH}_2\text{O}$. NED was quantified for each breath as $[\text{peak inspiratory flow} - \text{flow at } -5\text{cmH}_2\text{O}]/[\text{peak flow}] \times 100$.

Results—Compared to the retroglossal airway, the retropalatal airway was smaller at end-expiration ($p < 0.001$), and had greater absolute and relative compliances ($p < 0.001$). NED was positively associated with retropalatal relative area change ($r = 0.47$; $p < 0.001$).

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DISCLOSURE STATEMENT

Drs. Marques, Genta, and Messineo declare no conflicts of interest. Dr. Taranto received personal fees as a consultant for Novion Pharmaceuticals and Cambridge Sound Management outside the submitted work. Dr. Sands received personal fees as a consultant for Cambridge Sound Management and Nox Medical outside the submitted work. Dr. Azarbarzin received personal fees as a consultant for Somnifix outside the submitted work. Dr. Wellman received personal fees as a consultant for Bayer, Somnifix, Cambridge Sound Management and Nox Medical outside the submitted work. Dr. White is the Chief Scientific Officer for Philips Respironics and is a consultant to Night Balance.

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Conclusions—Retropalatal airway is narrower and more collapsible than retroglossal airway. Retropalatal compliance is reflected in the clinically-available NED value.

Keywords

Upper airway; compliance; obstructive sleep apnea; respiratory physiology

1. INTRODUCTION

Obstructive sleep apnea (OSA) is caused by pharyngeal collapse during sleep and is associated with adverse health outcomes (7, 17). Pharyngeal collapse can occur at the retropalatal level (soft palate), retroglossal level (tongue base), oropharyngeal lateral walls, and/or hypopharynx (epiglottis). Retropalatal collapse occurs more commonly (80–95%) than retroglossal collapse (40–55%) among OSA patients (16, 22, 23). The reasons for the preferential collapse of the retropalatal airway are not totally understood.

Previous imaging studies in OSA patients using optical coherence tomography during wakefulness have shown that the retropalatal airway is narrower than the retroglossal airway (24). Additionally, endoscopic imaging during general anesthesia, in which airway collapse was produced by a gradual reduction in CPAP, has shown that the retropalatal space is narrower and collapses completely at a higher pressure than the retroglossal space (9). However, retropalatal and retroglossal within-breath compliances during phasic breathing in sleeping OSA patients have not been compared.

In addition to a lack of information about phasic airway narrowing in OSA, it is not known how much airway compliance (measured endoscopically) translates into the within-breath airflow changes that are a hallmark of flow-limited inspiration in OSA (5, 14, 15). The reduction from peak to mid-inspiratory airflow during inspiratory flow limitation is commonly known as “scooping” or more formally “negative effort dependence (NED)”, and is easily recognized from inspection of the airflow shape during polysomnography. Given the association between cross-sectional area and airflow, we hypothesized that NED would reflect the compliance of the airway. To test these concepts, OSA patients were evaluated with upper airway endoscopy and simultaneous measurements of airflow and pharyngeal pressure during natural sleep.

2. METHODS

2.1. Subjects

Patients with a previous diagnosis of OSA were invited to participate in the study. The age range was 21 to 70 years. Subjects were excluded if they had heart failure, diabetes, or renal insufficiency, or if they were taking medications that could affect upper airway muscle function. The study was approved by the Institutional Review Board at Brigham and Women’s Hospital. Written informed consent was obtained from all patients before participation in the study.

2.2. Instrumentation

The participants were instrumented with electrodes for sleep staging: electroencephalography (C4-A1, O2-A1), left and right electrooculography, and submental electromyography. After topical application of a decongestant (oxymetazoline 0.05%) and anesthetic (lidocaine 4%), a 5-French pressure catheter (Millar Instruments, Houston, TX) and a 2.8 mm-diameter pediatric bronchoscope (model BFXP-160F, Olympus, Tokyo, Japan) were passed through 2 sealed ports in a nasal mask. The catheter and the bronchoscope were then inserted through the left and right nostrils, respectively. The tip of the pressure catheter was placed at the level of the epiglottis. Subjects breathed via the nasal mask that was connected to a pneumotachometer (Hans-Rudolph, Kansas City, MO) and differential pressure transducer (Validyne, Northridge, CA) to measure airflow. Physiological signals and endoscopic videos were synchronized and saved using Spike 2 software (Cambridge Electronic Design, Cambridge, England). Electroencephalography, electrooculography, and electromyography data were sampled at 125 Hz. Pressure and flow data were captured at a sampling frequency of 500 Hz. Endoscopic images were sampled at 30 frames/second.

2.3. Protocol

The subjects were asked to sleep supine with the neck in a neutral position. The bronchoscope's tip was initially placed in the velopharynx above the palate. In this position, several sequences of flow-limited breaths (lack of increase in flow despite decreasing pharyngeal pressure) were recorded. The endoscope was then advanced to the oropharynx to observe the oropharyngeal and hypopharyngeal structures (Figure 1) under the same conditions. The position of the scope was adjusted if necessary to provide a clear view of both pharyngeal levels and to keep the entire lumen in the field of view.

2.4. Data analysis

Periods of NREM sleep during stable flow limitation at atmospheric pressure without arousals were considered for analysis (1). Sequences were discarded if the endoscopic image quality was not satisfactory (e.g. presence of secretions or insufficient view of the airway circumference).

Retropalatal and retroglossal images at three time points were captured for luminal area determination: 1) at the end of expiration, 2) at a pharyngeal pressure swing of $-5\text{cmH}_2\text{O}$, 3) and at the peak negative inspiratory pressure. Retropalatal and retroglossal luminal areas were obtained by manually outlining the airway lumen using computer software (Image Processing Toolbox, Matlab, Natick, MA). Image distortion caused by the wide-angle endoscopic lens was digitally corrected before analysis. For each image, the software provided an area in pixels (Figure 2). The pharyngeal pressure catheter was used as a reference to convert pixel number to absolute area, as previously described (10). Briefly, the catheter diameter in each endoscopic image was manually measured in number of pixels at the level of the airway luminal outline (Figure 2). Area in pixels was then converted to mm^2 using the conversion factor obtained with the known catheter diameter. Retropalatal and retroglossal airway absolute compliance was calculated as the change in luminal area/ luminal pressure swing using the formula: $([\text{luminal area at end-expiration}] - [\text{luminal area$

at a pharyngeal pressure swing of $-5\text{cmH}_2\text{O}/5\text{cmH}_2\text{O}$). Relative compliance was calculated as the percent change in luminal area/luminal pressure swing. The same pressure swing of $-5\text{cmH}_2\text{O}$ was used for all calculations to control for the driving pressure through the airway. Minus $5\text{cmH}_2\text{O}$ was chosen to guarantee that a minimum comparable pressure swing was achieved at both pharyngeal levels during flow limitation. NED was calculated for each breath included in the analysis using the formula: $([\text{peak inspiratory flow}] - [\text{flow at a pharyngeal pressure swing of } -5\text{cmH}_2\text{O}]/\text{peak inspiratory flow}) \times 100$.

2.5. Definition of compliance

The strictest definition of compliance of a structure (upper airway) is the change in volume per change in extraluminal minus intraluminal pressure. We consider three factors in our definition: First, we note that we use the term “compliance” in reference to the *cross-sectional compliance*; conceptually, the cross-sectional area dominates the effect on airflow obstruction. Second, we inherently take the extraluminal pressure to be equal to zero (i.e. atmospheric pressure outside the body) in our calculations; however, we acknowledge that opposing pharyngeal dilator muscle forces act during inspiration to partially maintain area for any given intraluminal pressure (theoretically, by achieving negative local extraluminal pressure). Thus, our measure of compliance, which is based on intraluminal pressure alone, is not a pure measure of pharyngeal tissue properties (e.g. under hypotonic conditions), but rather a reflection of the *effective compliance* observed during spontaneous breathing in sleep; it is this effective compliance that we consider is most relevant to the manifest pharyngeal obstruction. Our approach here is congruent with approaches to measure arterial compliance (4, 26). Third, our measure is intentionally a dynamic measure, intended to capture effects on the time scale of the respiratory cycle, and may therefore be different to steady-state values. Rather than use the term *dynamic effective cross-sectional compliance*, we use the term *compliance* for ease of communication.

2.6. Statistical analysis

Descriptive values are presented as the mean $\pm$ standard deviation (SD) or the median [interquartile range] for continuous variables. Normal distribution was tested using the Shapiro-Wilk test. A Mann-Whitney U test was used for comparisons between peak inspiratory flow, the change in luminal areas and compliances at each pharyngeal level. Inspiratory time and peak negative pressure of retropalatal and retroglottal breaths were compared using a t-test. A Spearman rank order test was performed for correlation analyses between retropalatal and retroglottal luminal area changes and NED. Data analysis was performed using SPSS statistical software (version 20, SPSS Inc., Chicago, IL), and statistical significance was considered when the p value was <0.05 .

3. RESULTS

Fourteen OSA patients (age 51 ± 5 years; 9 men and 5 women) were studied. Subjects' characteristics are presented in Table 1. We analyzed a total of 228 flow-limited breaths at the retropalatal level (16 ± 8 breaths per subject) and 142 flow-limited breaths (10 ± 6 breaths per subject) at the retroglottal level all during supine NREM sleep (Table 2).

3.1. Retropalatal and retroglossal luminal area and compliance

We assessed the luminal area of both pharyngeal levels at the end of expiration, at a pharyngeal pressure of $-5\text{cmH}_2\text{O}$, and at the peak negative inspiratory pressure. An example of airflow, pharyngeal pressure, and both retropalatal and retroglossal endoscopic views from a representative subject are shown in Figure 3. With a progressive reduction in pharyngeal pressure— from end-expiration ($0\text{cmH}_2\text{O}$), to $-5\text{cmH}_2\text{O}$, and then peak negative pressure ($-11.4 \pm 6\text{cmH}_2\text{O}$) — retropalatal luminal area fell markedly from $19.2 [23.9] \text{ mm}^2$ to $5.1 [9.1] \text{ mm}^2$, and finally $1.6 [2.2] \text{ mm}^2$. By contrast, the retroglossal luminal started from $55.0 [30.7] \text{ mm}^2$ and fell modestly to $43.5 [25.9] \text{ mm}^2$, and finally $33.2 [27.3] \text{ mm}^2$. On average, we found that the retropalatal luminal area was significantly smaller than the retroglossal luminal area at all three time points analyzed ($p < 0.001$) (Figure 4).

For the entire group, retropalatal airway absolute compliance was slightly higher than retroglossal airway compliance (3.2 ± 2.1 vs $2.1 \pm 1.8 \text{ mm}^2/\text{cmH}_2\text{O}$, $p < 0.001$). More notably, the percent reduction in the retropalatal luminal area from end expiration ($0\text{cmH}_2\text{O}$) to a pharyngeal pressure swing of $-5\text{cmH}_2\text{O}$ was greater than the percent reduction in the retroglossal luminal area ($63\% \pm 16$ vs $17 \pm 13\%$, $p < 0.001$); thus, retropalatal *relative compliance* was therefore substantially higher than retroglossal relative compliance (11.9 ± 3.3 vs $3.2 \pm 2.4 \text{ %}/\text{cmH}_2\text{O}$, $p < 0.001$).

In 9 out of 14 patients, the absolute retropalatal compliance was greater than the retroglossal compliance. Figure 5 shows individual graphs of three representative patients. In all patients, the retropalatal luminal area at end expiration was smaller than the retroglossal area, and in most cases it was approximately half as large. Of the patients studied, six were judged to have a “posteriorly located tongue” at end expiration, meaning the tongue base was touching or pushing against the epiglottis at end expiration. In the other, eight patients, the tongue was “anteriorly located” during end expiration, meaning it was not touching the epiglottis and the vallecula was clearly visible. Nevertheless, in both of these groups the retropalatal area was smaller than the retroglossal area at all phases of the respiratory cycle, including at peak negative inspiratory pressure. The retropalatal luminal area in the patients with posteriorly located tongue was $26.8 \pm 11.8 \text{ mm}^2$, whereas in the patients with an anteriorly located tongue, it was $27.2 \pm 16.2 \text{ mm}^2$ ($p = 0.9$).

3.2. NED and compliance correlation

NED was positively associated with the percent change of retropalatal luminal area from end-expiration to a pressure swing of $-5 \text{ cmH}_2\text{O}$ ($r = 0.47$; $p < 0.001$), as shown in Figure 6. This suggests that NED may be a surrogate marker for retropalatal airway compliance. However, the same did not appear to be true for the retroglossal airway, since we found that NED was negatively correlated with the percent change in retroglossal luminal area ($r = -0.17$; $p = 0.03$). Finally, according to the classification described in a previous work (6) six patients in this study had tongue-related obstruction defined by a posterior displacement of the tongue narrowing both the velopharynx and oropharynx, four patients had isolated palatal collapse and, three patients had collapse at the pharyngeal lateral walls. Patients with posteriorly located tongue were found to have a small amount of NED compared to the

patients with an anteriorly located tongue ($6 \pm 5\%$ vs $17.5 \pm 10\%$, $p=0.02$). This finding is consistent with our previous work (6).

4. DISCUSSION

The major findings of the current study were:

1. The retropalatal airway was narrower than the retroglossal airway at all pharyngeal pressures, including end-expiration, $-5\text{cmH}_2\text{O}$, and peak negative pharyngeal pressure.
2. Both absolute and relative retropalatal airway compliance were higher than retroglossal airway compliance.
3. NED was more closely associated with the dynamic reduction in retropalatal than retroglossal luminal area.

Our findings suggest that the higher vulnerability of the retropalatal airway to collapse is because it is both narrower and more compliant than the retroglossal airway. In addition, dynamic retropalatal airway narrowing is reflected in the inspiratory airflow shape (NED).

4.1. Retropalatal and retroglossal luminal areas

Our results agree with previous studies conducted during wakefulness showing that the retropalatal airway has the smallest cross sectional area in both awake normal subjects and patients with sleep disordered breathing (3, 20). Schwab et al. analyzed pharyngeal images obtained from MRI performed in a group of 68 awake subjects, including both normal controls and OSA patients (20). They found that in all subjects the minimum cross-sectional area was in the retropalatal segment. Furthermore, computational fluid dynamics has also shown that the retropalatal region forms the most severe constriction within the pharynx in OSA patients (3). However, these studies were performed in awake subjects when pharyngeal muscle activation is known to be greater. Under general anesthesia, when pharyngeal muscle activity is diminished, Isono et. al. showed in 57 individuals that the maximum retropalatal area was smaller than the maximum retroglossal area (9). However, airway collapse in this study was achieved by a gradual reduction in CPAP, whereas our study examined the impact of the natural dynamic swings in inspiratory negative pressure on airway collapse.

Additionally, previous studies have shown that the retropalatal airway narrows more than the retroglossal airway from wakefulness to sleep (2, 21). Trudo et al. studied 15 normal subjects with MRI and showed a larger reduction in retropalatal versus retroglossal airway volume and area from wakefulness to sleep. However, only normal subjects were studied, and MRI provided only a static evaluation of the airway that was not synchronized to the respiratory cycle. In another study, Borek et al. compared retropalatal and retroglossal airway dimensions from wakefulness to sleep in OSA patients using drug-induced sleep endoscopy and found that the mean reduction in the retropalatal airway area was 84% compared to 39% in the retroglossal airway. However, again there are some methodological differences between this paper and our study. First, Borek and colleagues calculated percent change in the upper airway caliber from wake to sleep. This is a relative change in area, and

thus values can be influenced by the starting size of the airway (small airways appear to have a greater compliance than large airways). Also, it was not a within-breath measurement and thus did not capture the dynamics during natural breathing. Moreover, propofol may influence upper airway collapsibility differently than sleep (8). In the current study we assessed absolute luminal areas using endoscopic images synchronized with the airflow signal during natural sleep. Nevertheless, our current findings, along with these previous studies, suggest that retropalatal area is smaller than retroglossal area across a broad range of conditions.

4.2. Retropalatal and retroglossal compliances

A handful of previous studies have examined pharyngeal compliance. Rowley et al compared changes in retropalatal and retroglossal cross-sectional area from wakefulness to sleep in two separate studies (18, 19). In the first study, they performed upper airway endoscopy in 8 normal subjects during wakefulness and natural sleep. Compliance was defined as the slope of the regression line of the retropalatal cross-sectional area versus pharyngeal pressure. They demonstrated that the retropalatal airway compliance during NREM sleep was significantly greater than the compliance during wakefulness. In another study, they analyzed the *retroglossal* airway compliance using a similar methodology in 10 normal subjects; they found no significant difference between the retroglossal compliance during NREM sleep and wakefulness. These studies showed that the retropalatal, but not the retroglossal, compliance increased from wakefulness to sleep. These previous studies are in line with our observations of an increased compliance from wakefulness to sleep. However, in both studies, only normal subjects were included. Additionally, the pharyngeal compliance measurements were made over a very small range of pharyngeal pressures (-1 to $+1$ cmH₂O) during eupneic breaths. In our study, we evaluated the luminal area changes at both pharyngeal levels in OSA patients during inspiratory flow limitation over a range of 5cmH₂O of pharyngeal pressure.

4.3. Negative effort dependence

NED or “scooping” is a key feature of inspiratory flow limitation in OSA patients (14, 25). Previous work by our group showed that a low NED (absence of scooping) is a predictor of a posteriorly located tongue (6). The present study extends our previous observations by demonstrating that NED is associated primarily with the reduction in retropalatal, as opposed to retroglossal, luminal area. That is, greater NED is a recognizable manifestation of a greater retropalatal contribution to airflow obstruction in OSA. This finding provides the physiological framework for developing tools to discriminate between retropalatal and retroglossal contributions to OSA. Distinguishing between retropalatal and retroglossal airway collapse has implications for responses to therapies such as oral appliance therapy and pharyngeal surgery (11, 13).

4.4. Limitations

This study has several limitations. First, the use of the pressure catheter as a reference to convert dimensions into absolute area may contribute a degree of measurement uncertainty as it relies on subjective assessment of the catheter diameter in the endoscopic images. However, this methodology has been used previously (12, 18) and was considered adequate

for making comparisons between the two pharyngeal levels. We note that our measures of percent luminal area change did not rely on precise catheter diameter assessment. Regardless, the differences in diameter between the retropalatal and retroglossal regions were quite large. Second, luminal area calculations may be affected by movement of the scope and difficulty defining the plane of measurements. To avoid this, only images without change in the relationship of the scope to anatomic landmarks in different planes were analyzed. Third, luminal area measurements from endoscopic images may also be subject to image distortion and amplification of the wide view lenses, as well as the ability to accurately detect the edge of the airway lumen. To minimize this, we corrected for lens distortion (Matlab function “lensdistort”, available online at the Matlab Central File Exchange), and only images in which the airway lumen was clearly visible were analyzed. Fourth, we acknowledge that the pharyngeal pressure swing at the retropalatal level may be smaller than at the epiglottic region (where the pharyngeal pressure catheter was located). However, retropalatal compliance could be even greater if the pharyngeal pressure swing at the retropalatal level had been measured. Fifth, a pressure swing of $-5\text{cmH}_2\text{O}$ for luminal area and NED calculations was used in order to standardize the measurements for comparison, which may have underestimated NED. Finally, due to the invasiveness of the study, the sample size was small. Nevertheless, the 14 subjects represented a variety of collapse sites/mechanisms and the outcomes were clear and reached strong statistical significance.

5. CONCLUSION

In conclusion, the retropalatal airway is narrower and more collapsible than the retroglossal airway. Additionally, patients with a more pronounced retropalatal compliance exhibit a greater NED (“scooping” of inspiratory airflow); this finding paves the way for personalized interventions based on non-invasive recognition of the site of collapse in OSA.

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Highlights

- Retropalatal luminal area is smaller than retroglossal area at end-expiration.
- Retropalatal airway is more dynamically-compliant than retroglossal airway.
- Negative effort dependence is associated with inspiratory retropalatal narrowing.

Figure 1.
Example of endoscopic views of retropalatal and retroglossal airway with anatomic landmarks identified.

Figure 2.

Examples of retropalatal (A) and retroglossal (B) images showing the airway luminal outline. The catheter diameter was measured at the same plane of the luminal outline. The white images on the right highlight the airway lumen from which the number of pixels were counted. Luminal areas were calculated by converting the area in pixels to mm^2 using the conversion factor obtained with the known catheter diameter.

Figure 3.

Raw data of a representative subject showing the larger reduction of the retropalatal area proportionally to the retroglossal area for the same negative pharyngeal pressure swing. The arrows indicate the retropalatal and the retroglossal luminal areas at end-expiration (Pharyngeal pressure=0 cmH₂O) and at a pharyngeal pressure swing of -5 cmH₂O. This subject's absolute retropalatal compliance was 1.8 mm²/cmH₂O and the retroglossal was 1.0 mm²/cmH₂O.

Figure 4.

Retropalatal luminal area was smaller than the retroglossal luminal area at all pharyngeal pressures, including end-expiration, $-5\text{cmH}_2\text{O}$, and peak negative pharyngeal pressure ($p < 0.001$). The black dots represent the median luminal area from all breaths at retropalatal level analyzed at each time point (end-expiration, pharyngeal pressure swing of $-5\text{ cmH}_2\text{O}$ and peak negative pressure). The red squares represent the median luminal area from all breaths at retroglossal level analyzed at each time point. The bars represent the interquartile ranges.

Figure 5.

Individual graphs of three representative subjects showing the absolute luminal area reduction from end-expiration to a pharyngeal pressure swing of -5 cmH₂O. Each black dot represents one breath at the retropalatal level both at end-expiration and at a pharyngeal pressure swing of -5 cmH₂O. Each red square represents one breath at the retroglossal level both at end-expiration and at a pharyngeal pressure swing of -5 cmH₂O. Subject A's absolute retropalatal compliance was 8.2 mm²/cmH₂O and the retroglossal was 1.8 mm²/cmH₂O ($p < 0.001$). Subject B's absolute retropalatal compliance was 3.7 mm²/cmH₂O and the retroglossal was 1.8 mm²/cmH₂O ($p = 0.01$). Subject C's absolute retropalatal compliance was 1.8 mm²/cmH₂O and the retroglossal was 1.0 mm²/cmH₂O ($p = 0.02$).

Figure 6.
NED was correlated with the retropalatal relative luminal area change (from end-expiration to a pharyngeal pressure swing of 5 cmH₂O).

Table 1

Subjects' characteristics.

Parameters	Values
Age (years)	51 ± 5
Sex (% men)	64
Body mass index, BMI (kg/m ²)	35 ± 6
Neck circumference (cm)	42 ± 4
Apnea-hypopnea index, AHI (events/hour)	56 ± 32
Supine apnea-hypopnea index, AHI (events/hour)	61 ± 31

Data presented as mean ± standard deviation.

Table 2

Comparisons of breaths selected for analysis at the retropalatal and retroglossal levels

	Retropalatal breaths (n=228)	Retroglossal breaths (n=142)	p value
Peak inspiratory flow, L/s	0.25 [0.14]	0.26 [0.21]	0.265
Inspiratory time, sec	1.7 ± 0.3	1.6 ± 0.4	0.100
Peak negative pressure, cmH ₂ O	-11.9 ± 6	-10.5 ± 5	0.050
End-expiratory area, mm ²	19.2 [23.9]	55.0 [30.7]	<0.001
Pressure swing of -5 cmH ₂ O area, mm ²	5.1 [9.1]	43.5 [25.9]	<0.001
Peak negative pressure area, mm ²	1.6 [2.2]	33.2 [27.3]	<0.001
Absolute compliance, mm ² /cmH ₂ O	3.2 ± 2.1	2.1 ± 1.8	<0.001
Relative compliance, %/cmH ₂ O	11.9 ± 3.3	3.2 ± 2.4	<0.001

Data presented as mean ± standard deviation or median [interquartile range].