Evaluation of the upper airway growth patterns based on cervical vertebral maturation in Japanese: A cross-sectional study

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Article

Keywords:

Posted Date: April 20th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1505014/v1

Abstract

This study aimed to calculate standard values of the cross-sectional area of the upper airway, evaluate the upper airway growth patterns, and assess the usefulness of the cervical vertebral maturation stage (CVMS) for growth assessment. Patients (n = 400) who visited the orthodontic clinic of Tokyo Medical and Dental University Dental Hospital were randomly selected. They were classified into five groups according to the CVMS. Lateral cephalometric radiographs were obtained before treatment to measure the upper airway. Changes in the cross-sectional area of the airway during growth were analyzed by calculating the standard values for each cervical age group to further elucidate the growth pattern using the CVMS. Differences between males and females were also compared, and patients (40 each) were randomly selected from each group. The reliability of CVMS was confirmed by the weighted kappa coefficient (κ). The intra- and inter-evaluator agreement—κ—both showed almost perfect agreement. We found that the upper airway growth spurt occurs between CVMS II-III and CVMS III-IV in males at CVMS II-III in females. This study elucidated the gender-related growth patterns of the upper airway using cervical spine age. CVMS classification was a reliable indicator in assessing the naso- and oropharynx growth and development.

Introduction

Respiration is a vital physiological function for mammals in which the air flows into the lungs through the airway.

Human growth and breathing are closely related. Previous reports have shown that obstructive sleep apnea (OSA) in children can cause dental malocclusion, abnormal maxillofacial growth modification, physical developmental disorders, emotional anxiety, and learning disabilities.[1–4] OSA is widely recognized as an adult disease but its prevalence in children is reported to be approximately as high as 3%.[5]

Enlarged adenoids and tonsils in children sometimes obstruct the upper airway (UA) and worsen OSA symptoms.[6–8] Based on the growth and development of lymphoid tissue in the body, Scammon et al.[9] reported that lymphoid tissue in the body overgrows to 200% of its original size and then regresses to 100% by adulthood. Based on this analogy, treatment strategies in various medical fields have been taken based on the assumption that the size of lymphoid tissue will eventually decrease after puberty. Therefore, it is believed that the growth curve of the adenoid and tonsils is the same as that of Scammon's lymphoid growth curve, although the sizes of adenoids and tonsils have not been measured over time. However, our group reported that, contrary to the conventional theory, the pharyngeal and palatine tonsils grow slowly, without excessive increase or decrease during the ages of 6–20 years.[3]

In general, under the same lung suction conditions, airflow is reduced if the UA is stenotic, but increased if it is wide. In terms of improving the breathing environment during growth, it is reasonable to use orthodontic treatment techniques to promote physiological growth of the maxilla and mandible, which play a role in determining the UA size, or to use surgical procedures to enlarge the UA by removing hypertrophied adenoids and tonsils in combination with jaw surgery.

In a previous study, we reported maxillary and mandibular growth patterns in the Japanese population using cephalometric analysis based on cervical vertebral maturation and demonstrated that cervical vertebral maturation stages (CVMS) was a useful method for assessing growth in patients undergoing orthodontic treatment.[10] However, there are few reports on the UA growth in the Japanese population.

Therefore, the purpose of this study was to (1) calculate standard values of the cross-sectional area of the UA, (2) evaluate the UA growth pattern, and (3) assess the usefulness of the CVMS for UA growth assessment.

Methods

A cross-sectional study was conducted by random sampling from patients who visited the Orthodontic clinic at Tokyo Medical and Dental University (TMDU) Dental Hospital.

This cross-sectional study was approved by the Ethics Committee of TMDU Dental Hospital (D2021-026). Before participation in the study, informed consent was obtained from patients and their guardians.

The patients were Japanese and aged between 6 and 20 years. Overall, 4000 patients were assigned random coefficients, and the sample to be measured was randomly selected.[11]In addition, random sampling was repeated until the sample size in each group (n = 40) was achieved.[11] Finally, 400 patients participated in this study and were assigned to 5 male and 5 female groups (CVMS I-V) based on the CVMS[12] (Fig. 1). The exclusion criteria were patients with syndromes that could affect maxillofacial morphology. Sample size was calculated using G*Power software (latest version: 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). A priori sample size estimation, performed at a 5% significance level ($\alpha = 0.05$) and 80% power, revealed that a minimum of 40 patients per group was required.

We traced the initial lateral cephalometric radiographs. The trace was plotted and measured using WinCeph ver.9 (Rise Corp., Tokyo, Japan) software. Measurement points are shown in Fig. 2. Variables measured on each lateral cephalometric radiograph are shown in Table 1. All lateral cephalometric radiographs were obtained according to international standards, and the UA dimensions were measured using the same method as in the previous reports[2,3,10] (Fig. 2). The measurement was performed three times by one investigator (AM), and the average value was used as the measured value, but the evaluation was verified by another investigator (TI). Restoration extraction was performed using the bootstrap method with 1,000 iterations to predict the population[3]. The measurement error in each measured value was calculated using Dahlberg's formula[13]. For group comparisons, the Kruskal–Wallis test was used, and the Steel–Dwass test was used for multiple comparisons ($p < 0.05$). In addition, the weighted kappa coefficient was calculated based on the degree of intra-evaluator and inter-evaluator agreement to verify the reliability of the CVMS. The intra-evaluator agreement was based on two CVM staging performed by one evaluator (AM) at 3-week intervals. The degree of agreement between the evaluators was based on the CVM evaluation determined by each of the two evaluators (AM and TI). SPSS version 25 (Statistical Package of Social Sciences, Chicago, IL, USA) was used for statistical analysis.

Table 1
Definitions of measurements variables. Symbol

Symbol	Description	Definition
S	Sella	The midpoint of the pituitary fossa
N	Nasion	The most anteroinferior point of frontal nasal suture
A	Point A	The deepest point on the curvature of the surface of the maxillary bone between ANS and the alveolar crest of the maxillary central incisor
B	Point B	The deepest point of the curved part of the mandibular alveolar process point
ANS	Anterior Nasal Spine	The cutting edge of anterior nasal spine
PNS	Posterior Nasal Spine	The cutting edge of the posterior nasal spine
Ar	Articulare	Drafting intersection of mandibular process posterior margin and external skull base
Go	Gonion	Plotting intersection of the tangents of the mandibular ramus and body
Pog	Pogonion	The most prominent point of the mandibular chin ridge

Results

Area comparisons

The average cross-sectional area of the UA in males was 1,144.16 ± 205.88 mm^2 in the CVMS I group, 1,148.82 ± 203.61 mm^2 in the CVMS II group, 1,357.84 ± 235.67 mm^2 in the CVMS III group, 1,642.78 ± 261.52 mm^2 in the CVMS IV group, and 1,662.05 ± 222.66 mm^2 in the CVMS V group. There was a significant increase in the UA in CVMS V compared to CVMS I. There was a significant increase in CVMS III compared to CVMS II and in CVMS IV compared to CVMS III (Fig. 3).

On the other hand, the average cross-sectional area of the UA in females was 1,071.29 ± 204.92 mm^2 in the CVMS I group, 1,112.43 ± 99.56 mm^2 in the CVMS II group, 1,260.83 ± 210.66 mm^2 in the CVMS III group, 1,344.69 ± 162.51 mm^2 in the CVMS IV group, and 1,327.93 ± 107.32 mm^2 in the CVMS V group.

There was a significant increase in the UA in CVMS V compared to CVMS I. There was a significant increase in the UA in CVMS III compared to CVMS II (Fig. 4). There were significant differences in the timing of the UA growth pattern between males and females (Fig. 3,4).

The κ coefficient for the degree of intra-evaluator agreement was 0.88, and the κ coefficient for the degree of inter-evaluator agreement was 0.85, both showing almost perfect agreement.

The measurement error for the cross-sectional area of the UA was 3.14 mm^2, as calculated using Dahlberg's formula, which was a sufficiently negligible error[13].

Discussion

The findings of this study indicate that the size of the airway increases with growth in both males and females. For growing patients with large adenoids and tonsils who complain of snoring or OSA, medical doctors and dentists explain to them that the sizes of the adenoids and tonsils decrease as they grow because the adenoids and tonsils are lymphoid tissue. However, our recent report showed that the adenoids and tonsils themselves do not rapidly regress with growth. In other words, it should be explained that "the adenoids and tonsils appear large relative to the airway, but as the airway grows in size, the relative respiratory environment improves."

When evaluating growth spurts of various organs of an individual, the patient's chronological age as well as height, weight, and physiological age are used. Cervical spine age is one of the indicators of physiological age like carpal roentgens.[14–17] We recently reported growth and development curves of the maxilla and mandible using cervical spine age.[10] The maxilla and mandible were reported to grow in both sexes. The airway also showed an almost similar trend of growth over time. This may indicate that the airway may enlarge anteriorly and inferiorly, similar to how the maxilla and mandible do.

The study showed that the cross-sectional area of the UA grows gradually and has a growth spurt between CVMS II-III and CVMS III-IV in males. It is known that the maxillary bone in males grows anteriorly and inferiorly, indexed by chronological age.[18] Our recent report suggested that anteroposterior growth of the maxilla between CVMS II-III reflects the timing of the maxillary growth spurt, which may be the reason for the enlargement of the airway between CVMS 2–3 in males.[10] The mandible, like the maxilla, grows anteriorly and downward, indexed by chronological age.[18] In our previous reports, males were reported to have a growth spurt in mandibular depth and length between CVMS III-IV.[10] We considered that anteroinferior movement of the lingual dorsum caused by the anterior migration of the lingualis muscle was associated with the anteroinferior growth of the mandibular alveolar bone (the chin spine), which enlarged the UA.[19, 20] It was suggested that the UA in males grows significantly when the maxilla and mandible grow.

It has been shown that the cross-sectional area of the UA grows gradually in females and that there is a growth spurt period between CVMS II-III. In our previous study, there was no clear growth spurt in anteroposterior maxillary length in females between CVMS 2–3.[10] However, it is also known that the maxillary and mandibular bone in females grows anteroinferiorly, indexed by chronological age.[18] The reason for the growth spurt between CVMS II-III in the female UA may be the particularly downward movement of the maxillary bone alongside the enlargement of the UA.

Based on the present results and our recent reports, we found that there was an association between UA growth and jaw growth and that the timing of the growth spurt was more accurate when CVMS was used as an indicator.[18] Orthodontists often use functional appliances, such as the twin block (TB) or the maxillary protracting appliance (MPA), for patients with retrognathia and/or maxillary hypoplasia who are in their growth spurt to promote maxillo-mandibular growth.[21] We believe that our results further support the previous reports that the functional appliances used in orthodontic treatment, such as TB or MPA, promote not only maxilla-mandibular growth but also UA growth.[18, 22, 23] The results of the present study clarified the timing of the growth spurt of the maxilla, mandible, and UA. The findings reveal the best time to use the functional appliance, which can significantly improve the treatment's effectiveness. Therefore, orthodontists should consider both occlusion and breathing environment in the treatment plan to ensure that the patient gains benefits.

One limitation of this study is that it was a cross-sectional survey, making it difficult to evaluate the continuous growth of the same individual. It would be desirable to conduct a longitudinal study and judge the results of both cross-sectional and longitudinal studies from multiple perspectives. However, it may be unethical to take cephalometric images of patients not undergoing orthodontic treatment for the study. In addition, the growth of the airway of patients undergoing orthodontic treatment would not reflect the natural growth pattern of the airway. Therefore, it is difficult to conduct a continuous longitudinal study of individuals. However, cross-sectional surveys are widely used to obtain standardized values because there are fewer individual differences and a larger number of subjects compared to longitudinal surveys.[2, 24] It is also widely accepted that growth patterns can be determined from these results. The method and results of this study are considered to be the best available at present. Second, we used 2-dimensional lateral cephalometric radiography, but there was no concern about additional radiological exposure because lateral cephalometric radiography is a routine examination in orthodontic diagnosis and treatment. Moreover, standardized lateral cephalometric radiographs are highly reproducible because the source-to-subject-to-film distance is kept strictly constant. The head position is also fixed. This allows the orthodontist to superimpose the cephalometric radiography within millimeters for the treatment/growth assessment of the patients.[25–27] A previous study reported that evaluation of the 2-dimensional upper airway area by lateral cephalometric analysis correlated well with the 3-dimensional upper airway assessment, and it could be used as a screening test to predict the airway volume by computed tomography.[28]

In conclusion, the standard values of the UA were calculated, and gender-related UA growth patterns in the Japanese population were clarified according to sex. Moreover, the CVMS is a useful method for the UA growth assessment in Japanese patients.

Declarations

Author Contributions

T.I designed and summarized this study and wrote the main manuscript text. A.M performed data extraction and analysis, and. E.K advised on statistical analysis. T.O reviewed and revised the manuscript and approved the final manuscript as submitted. All authors read and approved the final version of the manuscript.

Data availability statements

Additional Information

Competing interests

The authors declare no competing interests.

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Figures

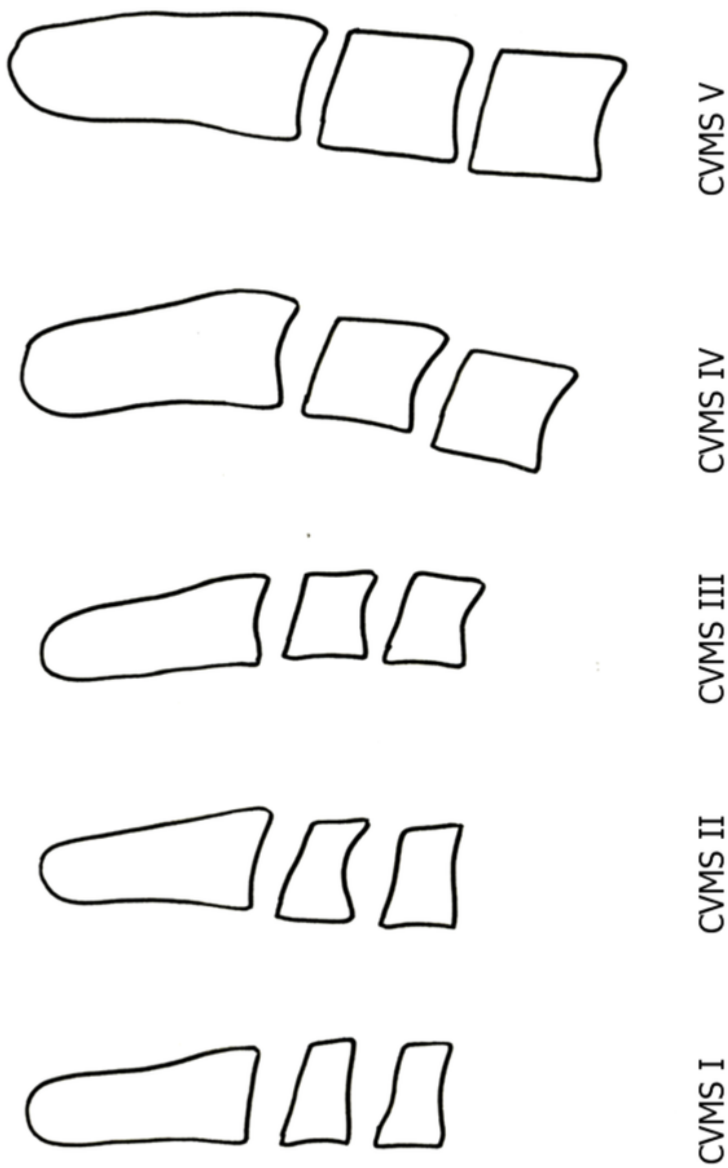

Figure 1

Definitions of CVMS. CVMS I: the lower borders of three vertebrae are flat. CVMS II: Concavities at the lower borders of both C2 and C3 are present. CVMS III: Concavities at the lower borders of C2, C3, and C4 are present. CVMS IV: At least one of the bodies of C3 and C4 is squared in shape. CVMS V: At least one of the bodies of C3 and C4 is rectangular vertical in shape.

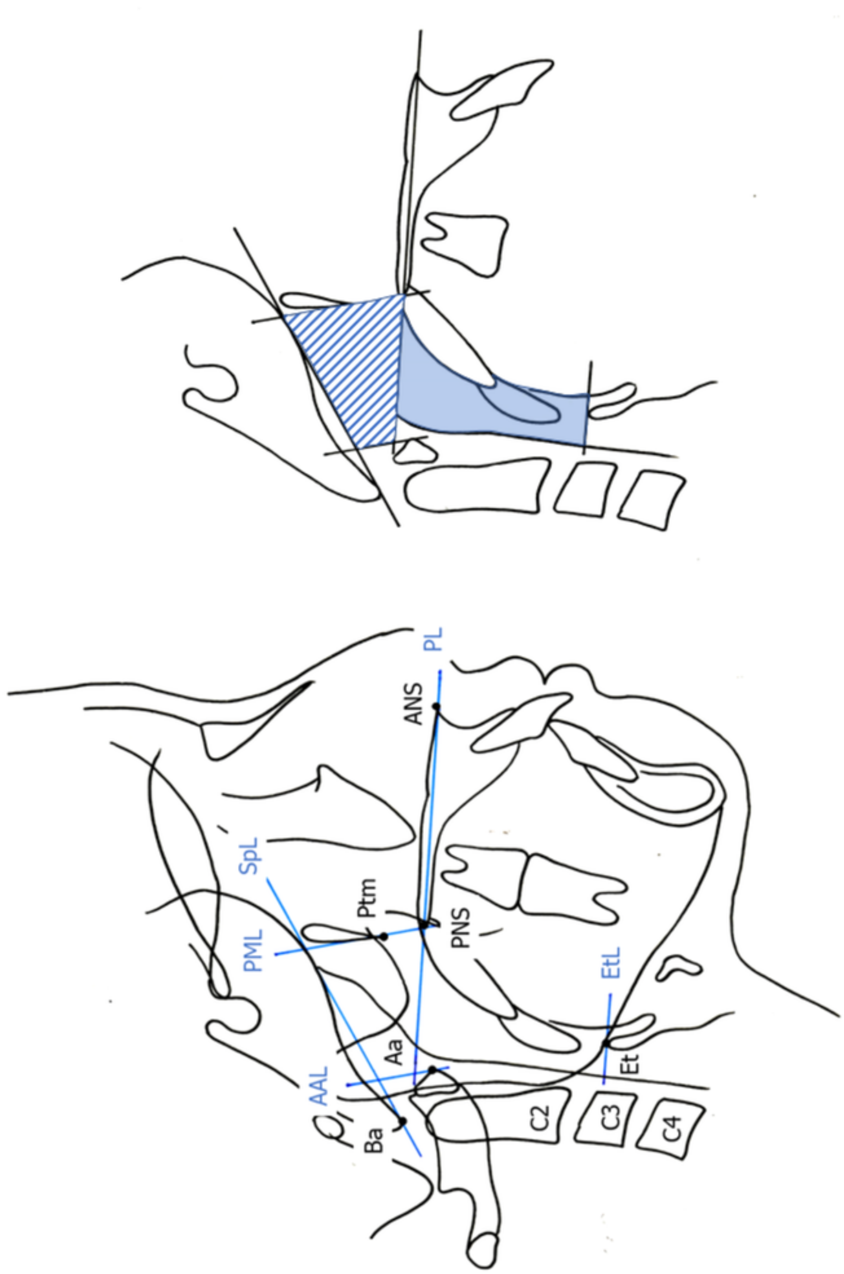

Figure 2

Cephalometric landmarks used to construct the two linear measurements and angular measurements analyzed in this study. Linear parameters: ANS-PNS; Distance between ANS and PNS, Ar-Go; Distance between Articulare and Gonion, Go-Pog; Distance between Gonion and Pogonion. Angular parameters: FMA; Mandibular plane to Frankfort-Horizontal plane, SNA; Sella-Nasion to Point A, SNB; Sella-Nasion to Point B.

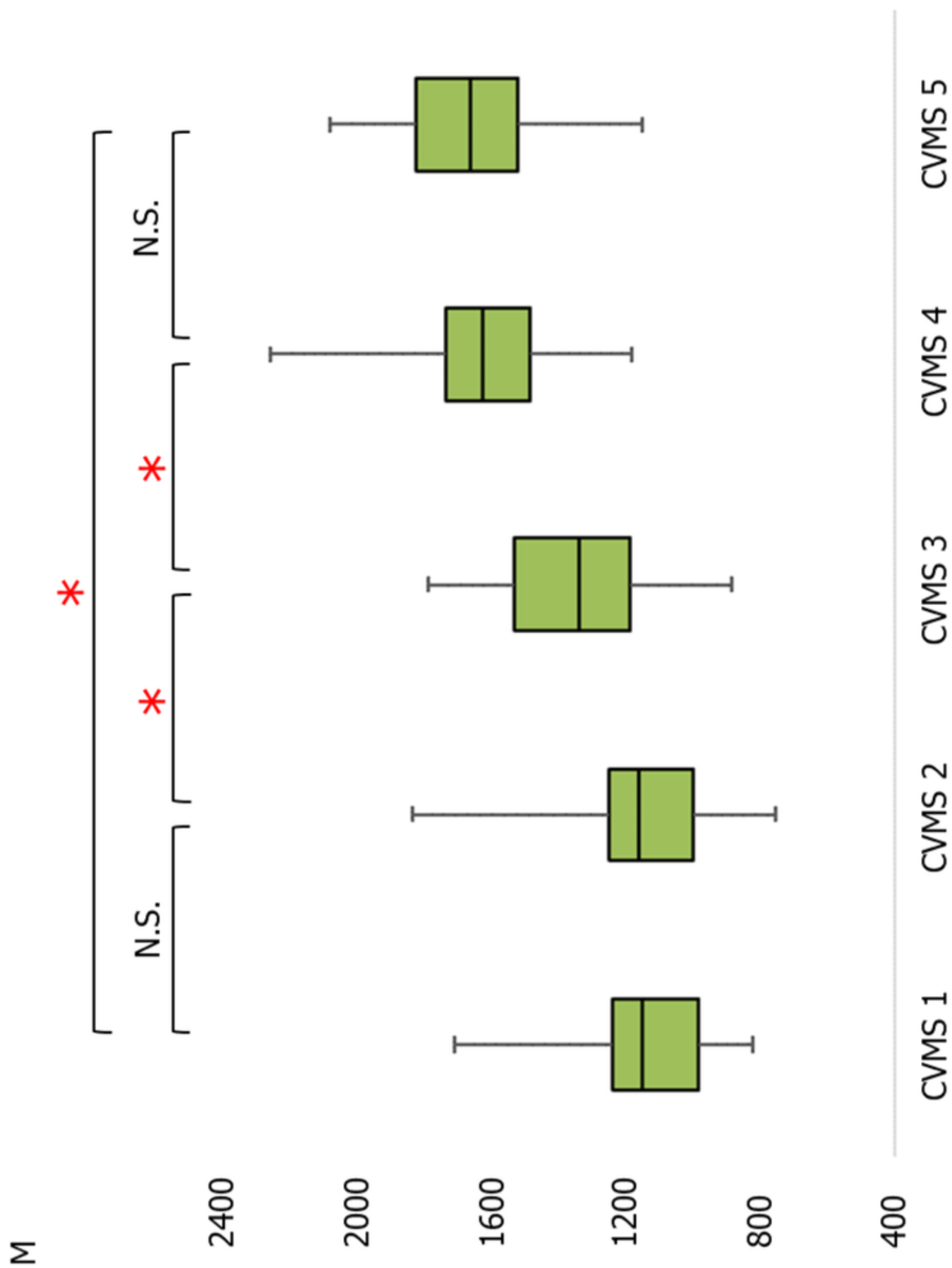

Figure 3

The average values for the airway in males (*p<0.05).

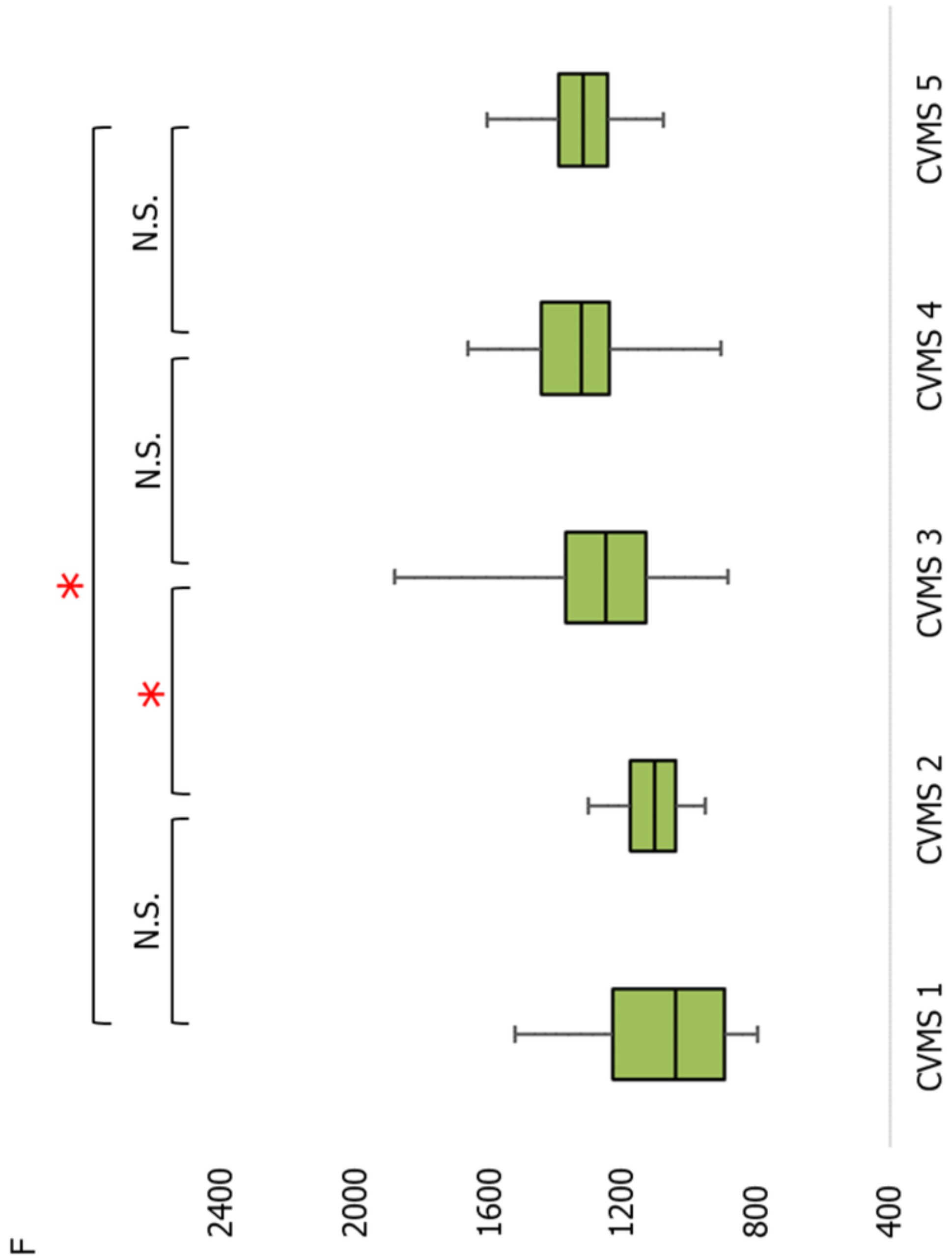

Figure 4

The average values for the airway in females (*p<0.05).