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# Airway Measurements in Rheumatoid Arthritis Using Lateral Cephalometric Radiographs: Does It Predict OSA

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## ABSTRACT

*Introduction: Obstructive Sleep Apnea (OSA) is common among Rheumatoid Arthritis (RA) patients, likely due to their increased anatomical obstruction of the upper airway during sleep.*

*Aim: The aim of this study was to determine the association between cephalometric data of the upper airway in RA patients and their risk of OSA.*

*Materials and methods: The study was conducted on 60 adults with RA followed at rheumatology clinics at a university hospital, from June 2017 to September 2018. The demographic details of the patients, were collected through a personal interview. All patients were then assessed for the risk of OSA using the Berlin questionnaire and then underwent Polysomnography (PSG) to confirm the diagnosis of OSA. Finally, each patient underwent lateral cephalography for cephalometric data acquisition.*

*Results and discussion: The demographic characteristics showed a female predilection of 93.3%, a mean age of 49.90 ± 13.52 years, and a mean BMI of 33.12 ± 9.17 kg/m$^2$. Thirty-seven (61.7%) participants were at low risk and 23 (38.3%) were at high risk of OSA based on the Berlin questionnaire. However, only 42 patients underwent diagnostic PSG, 29 of whom (69%) were found to have OSA. The cephalometric scores of patients with OSA and those without OSA were not significantly different. Similarly, the correlation between the cephalometric data and the risk of OSA was not significant.*

*Conclusion: The cephalometric area of the upper airway was not significantly correlated with OSA. Hence, cephalometry is not reliable for predicting the risk of OSA in RA patients.*

**Key words:** Sleep apnea, Rheumatoid arthritis, Cephalometric area, Risk

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## INTRODUCTION

Obstructive Sleep Apnea (OSA) is characterized by recurrent upper airway obstruction at single or multiple levels during sleep due to both anatomical and non-anatomical reasons. This can lead to pauses in breathing during sleep, micro arousals, daytime sleepiness, and fatigue. Moreover, OSA has been shown to be an independent risk factor for adverse cardiovascular outcomes, including myocardial infarction, stroke, and hypertension [1]. The overall prevalence of OSA in the general population measured by an Apnea-Hypopnea Index (AHI) ≥ 5 events/h, ranges from 9% to 38% and is greater for older individuals, males, and those with a higher Body Mass Index (BMI) [2]. The prevalence of OSA in the Saudi general population has been estimated to be 8.8% [3]. Worse still, we recently demonstrated that the prevalence of OSA (AHI ≥ 5 events/h) among Rheumatoid Arthritis (RA) patients was 58.1%, whereas the prevalence of moderate to severe OSA (AHI ≥ 15) was 22.9% [4]. This concurs with the findings of reading, who reported that 50% of RA patients were at high risk for OSA based on the Berlin questionnaire [5].

OSA is linked to anatomical characteristics such as the morphology of the maxilla and mandible, location of the hyoid, thickness of the wall, length of the airway, and size of the tongue [6]. Variations in the morphology of the maxilla and mandible are the most prevalent traits, and OSA is commonly linked to a mandibular deficit and a shorter, tapered and narrower maxilla [7]. Although the

higher prevalence of OSA among patients with RA is not fully understood, studies have linked OSA in RA patients to Retrognathia. RA patients are at risk of airway obstruction, particularly when the Temporo Mandibular Joints (TMJs) are involved [8]. The involvement of the TMJs as a result of the reduced ramus height and the downward and backward rotation of the mandible may explain the high prevalence of OSA among RA patients [9]. The effects of the narrowing and obstruction of this crucial area are important in the field of craniofacial orthodontics [10]. Redlund-Johnell concluded that approximately three-quarters of 400 RA patients had severe TMJ destruction that could lead to upper airway obstruction due to acquired retrognathia. Based on these findings, it has been suggested that patients with RA and TMJ involvement are likely to have OSA.

Many investigations, such as cephalometry, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), fluoroscopy, fluoroscopic MR, and somnofluoroscopy, can be used to examine the craniofacial skeletal anomalies and features of the oropharyngeal soft tissues [6]. Although cephalometry only provides a two-dimensional picture, it is a basic and economical evaluation approach that exposes patients to less radiation than CT.

Hence, the measurement of the cross-sectional area of the upper airway using cephalometric analysis may help in the early identification of RA patients at risk of OSA. The aim of this study was to investigate the potential relationship between the upper airway area using simple measurements from cephalometric radiographs in RA patients with and without OSA. The hypothesis of this study was that RA patients with OSA would have narrower upper airway spaces than non-OSA patients. This may explain the high prevalence of OSA among these patients.

## MATERIALS AND METHODS

This cross-sectional study was performed on a target group of patients with RA aged >18 years at the rheumatology clinic of King Abdulaziz University Hospital in Jeddah from June 2017 to September 2018. All patients fulfilled the American College of Rheumatology/European League against Rheumatism (ACR/EULAR 2010) classification criteria [11]. Patients with other connective tissue diseases and overlap syndrome were excluded from the study. The study protocol was approved by the research and ethics committee of King Abdulaziz University Hospital.

### Screening

At this stage, all patients over the age of 18 years visiting the rheumatology clinics were interviewed individually by trained physicians. Detailed personal data and medical histories were collected, the OSA risk was evaluated by the Berlin Questionnaire, and daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS).

### Procedures

All patients were then offered to undergo a diagnostic sleep study using full Polysomnography (PSG). They then underwent cephalometry at the dental clinic of the same institution.

### Instruments

**Berlin questionnaire:** This widely used and reliable questionnaire consists of 11 self-reported items used to identify people at high risk for OSA. These questions are related to snoring, daytime sleepiness, and obesity or high blood pressure, three types of apnea signs and symptoms. The questionnaire was created to help clinicians quickly determine OSA risk factors, and it has been validated in patients aged 18 and older [2]. The scoring procedure includes evaluating "yes or no" replies as well as Multiple Choice Questions (MCQs). "Yes" earns one point in the "yes or no" questions, while the two responses that correlate to the highest degree of apnea each earn one point in the MCQs. If an individual earns two or more points in categories one and two, a higher risk is indicated. When a respondent's blood pressure is high or their BMI is more than 30 $kg/m^2$, they are judged to be at high risk based on the category three questions.

**Epworth Sleepiness Scale (ESS):** The ESS is a widely used, standardized and validated questionnaire for determining the amount of daytime sleepiness [12]. The ESS enables respondents to assess their chances of dozing off in eight distinct scenarios or activities that most individuals face in their everyday lives on a four points scale. The results of all eight questions are then added together to provide a score ranging from 0 to 24, which is used to determine the respondent's average sleep propensity in those eight scenarios. A score <10 is categorized as normal, and a score ≥ 10 is considered indicative of Excessive Daytime Sleepiness (EDS).

**Cephalometry:** Written informed consent was obtained from each patient before obtaining lateral cephalometric radiographs at the same centre. Cephalometry was performed for all participants in the study. Upper airway measurements were obtained using a millimetre ruler and lateral cephalometric radiographs. The picture elements (pixels) were converted to square millimetres, and a polygon tool was used to obtain the airway area. Measurements were performed using the lateral cephalogram. The measured upper airway area was described as the area from the origin of the retro-palatal region to the bottom of the epiglottis; this is a simple measurement of the neck soft tissue thickness. All airway measurements were performed by a single examiner under the same conditions using ImageJ® software (National Institute of Health image, public domain).

**Polysomnography (PSG):** The presence of OSA was confirmed with PSG performed with a SOMNO medics plus (SOMNO Medics, Randersacker, Germany) and consisting of continuous recordings from the following: surface leads for Electroencephalography (EEG), electrooculography, electromyography (submental and bilateral anterior tibialis muscles), electrocardiography,

nasal pressure, nasal and oral airflow (thermocouple), chest and abdominal impedance belts for respiratory muscle effort, pulse oximetry for oxygen saturation and pulse rate, a tracheal microphone for snoring and body position sensors for sleep position. PSG records were scored manually according to the American Academy of Sleep Medicine (AASM) 2012 scoring manual [13]. Registered polysomnographic technologists were assigned to manually score the data from these PSG studies. The average number of apnea and hypopnea events per hour of sleep, *i.e.,* the AHI, was then calculated. Subjects with an AHI <5 were considered normal, while subjects with an AHI ≥ 5 were categorized as having OSA.

### Statistical analysis

Statistical analysis was performed using IBM Statistics Program for Social Science (SPSS) software version 22.0. The independent Student's t test was used to assess the differences between the continuous variables, and the Pearson *chi-square* test was used to assess the differences in categorical variables between the participants with a higher and lower risk of OSA. A bar graph was drawn to illustrate the differences between the means of the cephalometric data of the participants with a higher and lower risk of OSA. A binary logistic regression test was conducted to find the association between the cephalometric data and the risk of OSA and between the cephalometric data and the confirmed OSA cases, and scatter plots were constructed to plot the corresponding data. Spearman's correlation test was performed to determine whether any relation existed between the risk of OSA based on the Berlin Questionnaire scores and the actual incidence of OSA based on the AHI score.

## RESULTS

### Patient characteristics

Demographic characteristics, details of the cephalometric data and the risk of OSA based on Berlin score and the numbers of patients with OSA based on PSG for the entire study population are summarized in Table 1. Among the 60 RA patients, most (93.3%) were female. The mean age of the participants was 49.90 ± 13.52 years (range: 19-88 years), and the mean BMI was 33.12 ± 9.17 kg/$m^2$. On assessment of the risk of OSA using the Berlin score, 37 (61.7%) participants were at low risk, whereas 23 (38.3%) were at high risk. Furthermore, only 42 subjects agreed to undergo diagnostic sleep studies, *i.e.,* polysomnography. According to an AHI ≥ 5, of the 42 patients, 29 (69%) were diagnosed with OSA. The mean cephalometric area of the upper airway was 485.11 ± 143.38 $mm^2$.

**Table 1: Demographic characteristics of the participants.**

| Characteristics | Mean ± SD |
|---|---|
| Age | 49.90 ± 13.52 |
| BMI | 33.12 ± 9.17 |
| Cephalometric Area | 485.11 ± 143.38 |
| | N (%) |
| Sex | |
| Female | 56 (93.3) |
| Male | 4 (6.7) |
| Risk of OSA | |
| Low risk | 37 (61.7) |
| High risk | 23 (38.3) |
| OSA (AHI >5) | |
| Non-OSA | 13 (31.0) |
| Confirmed OSA | 29 (69.0) |

### Comparison of demographic characteristics with the risk of OSA

All demographic characteristics were compared between the participants with low/high risk for OSA. There were no significant differences observed among any of the characteristics between the groups (Table 2).

**Table 2: Comparison of demographic characteristics between the risks of sleep apnea.**

| | Low risk | High risk | P value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| Age | 47.43 ± 13.12 | 53.87 ± 13.47 | 0.073 |

| | | | |
|---|---|---|---|
| BMI | 32.92 ± 10.48 | 33.44 ± 6.76 | 0.831 |
| Cephalometric Area | 463.32 ± 110.97 | 520.17 ± 181.38 | 0.185 |
| | Low Risk | High Risk | P value |
| | N (%) | N (%) | |
| | Sex | | |
| Female | 35 (94.6) | 21 (91.3) | 0.619 |
| Male | 2 (5.4) | 2 (8.7) | |

BMI: Body Mass Index, Statistically significant P value less than 0.05.

### Variation in the cephalometric data between the participants with low and high risk of OSA

There was no significant difference between the mean cephalometric area among the individuals with low and high risk of OSA (463.32 ± 110.97 and 520.17 ± 181.38, respectively; P=0.185), as illustrated in Table 2.

### Variation in the cephalometric data between the participants with confirmed OSA and non-OSA

The mean cephalometric area among the non-OSA patients and those confirmed with OSA was 476.72 ± 102.12 and 475.79 ± 125.95, respectively. This difference was not significant, as shown in Table 3.

**Table 3: Differences in cephalometric areas among the participants with confirmed OSA and non-OSA.**

| | Non-OSA | OSA | P Value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| Cephalometric Area | 476.72 ± 102.12 | 475.79 ± 125.95 | 0.982 |

### Association of cephalometric data with the risk of OSA

The association between the Berlin score and the cephalometric area of the participants was not significant (P=0.143), with a log odds ratio of 1.003 (95% Confidence Interval (CI)=0.999-1.007). The variance was 5% ($R^2$) with the risk of sleep apnea, and the classification accuracy was 66.7% (Table 4).

### Association of cephalometric data with OSA

The association between the diagnosis of OSA and the cephalometric area of the participants was not significant

(P=0.981), with an odds ratio of 1.000 (95% CI=0.994-1.006). The variance was 0% ($R^2$) with the risk of sleep apnea, and the classification accuracy was 69% (Table 4).

**Table 4: Results of binary logistic regression test for determining the association of cephalometric area with risk of OSA and actual OSA based on AHI scores.**

| Variable | $R^2$ | Accuracy | P value | Odds Ratio | 95% CI |
|---|---|---|---|---|---|
| Cephalometric Area with Risk of OSA (Berlin) | 0.05 | 66.7 | 0.143 | 1.003 | 0.999-1.007 |
| Cephalometric Area with Actual OSA (AHI) | 0.000019 | 69 | 0.981 | 1 | 0.994-1.006 |

## DISCUSSION

This cross-sectional study investigated the association between upper airway area and OSA in RA patients. We found that there was no clear association between the upper airway area, as measured using the cephalometric technique, and the risk of OSA. Accordingly, measuring the upper airway area using cephalometry did not help in predicting OSA in this group of patients.

The prevalence of OSA among the Saudi Arabian population was reported to be 8.8% on average, with males (12.8%) affected more often than females (5.1%) [3]. In the Western world, this prevalence is 15% among males and 2 to 5% among females [14]. These prevalence rates are similar in Asia and the western world despite differences in BMI. Hence, the craniofacial morphology of Asia's population might be the contributing factor to the

higher prevalence rates of OSA among Asians [15]. OSA was found to be much more prevalent among RA patients than among healthy individuals. In a study conducted by Reading [5], 50% of the participants with RA were at high risk of OSA. In a similar study, Mustafa found that 37% of the participants with RA were at high risk of OSA. Recently, we reported that 58% of RA patients had OSA with an AHI of 5 or greater, while 22% had moderate to severe OSA [4]. The current study also confirmed this high risk of OSA among RA patients, as 38.3% of the RA patients were at risk of OSA.

As expected, patients with RA have the same risk factors for OSA as the general population, including age, obesity and sex [3]. Many studies in the literature have considered obesity as the main risk factor for OSA [7]. This is due to fat accumulation around the region of obstruction and the increased thickness of pharyngeal walls as well as the para-pharyngeal fat pads, which promote obstruction of the upper airway [16]. Nevertheless, in the current study, obesity as measured by the BMI did not seem to play a role since patients with a higher risk of OSA had a BMI of 33.44 ± 6.76, while those with a lower risk of OSA had a mean BMI of 32.92 ± 10.48; this difference was not statistically significant. Similarly, age was not a risk factor in our study since there was no significant difference in age between the 2 groups (Table 2). Furthermore, the majority of RA patients in the current study were female. However, this is related to the nature of the disease, which may in turn be related to genetic and hormonal factors that lead to a female propensity [4]. The data in the literature clearly show that females are at greater risk of developing RA than males and are also associated with more active disease and worse joint destruction [17].

However, as discussed before, RA patients are at higher risk of OSA than the general population, which may be related to anatomical abnormalities seen in the former group. These abnormalities are related to micrognathia and retrognathia, resulting from destruction of the TMJ, as well as occipito-cervical lesions. In 1983, Davies and Iber first reported the presence of OSA caused by micrognathia in a patient with RA [18]. This report was followed by several case reports linking OSA with RA due to micrognathia. Subsequently, Redlund-Johnell [8] studied 400 patients with RA and found that 70% of those with severe arthritic TMJ destruction had episodes of upper airway obstruction. Sugahara [19] also reported that RA is an indirect risk factor for OSA caused by TMJ damage. Shoda [20] examined the prevalence of OSA in patients with RA and occipito-cervical lesions using a portable monitoring device and found that 23 patients (79%) had OSA. Moreover, studies have reported that the oropharynx is commonly affected or observed to be narrower in patients with OSA than in healthy participants [21]. In a study conducted by Abramson [22], reduced airway dimensions and an increased airway length were observed in patients with OSA. Hence, TMJ involvement in RA may lead to significant acquired anatomical narrowing and a reduced area of the upper airways. There are multiple indicators that might be utilized to detect upper airway obstruction in patients with OSA, including nasopharyngeal size, soft palate size, and length and area of the upper airway [23]. Bader reported that patients with RA have narrower upper airways as measured on lateral cephalometric radiographs than non-RA patients (means 479.7 $mm^2$ versus 516.7 $mm^2$). This may partially explain the high prevalence of OSA among patients with RA [24].

In the current study, however, we failed to show a difference in this upper airway area, described as the area from the origin of the retro-palatal region to the bottom of the epiglottis, between RA patients with and without OSA. It is conceivable that having RA would lead to some degree of narrowing in the upper airway and hence predispose these patients to OSA. This may explain the poor association between the size of the upper airway area and OSA in our RA population, as all RA patients probably had a narrowed pharynx (Table 4). Therefore, narrowing of the upper airway in RA may contribute to the high prevalence of OSA, although likely not as a sole factor. Additionally, the methodology used to evaluate the narrowing of the upper airways may explain the negative findings in our study relative to other studies. This proposed explanation is supported by previous studies on OSA patients. Yucel [25] used cephalometric measurements and reported a narrower cross-sectional area of the oropharynx in patients with severe OSA than in patients with mild/moderate OSA and healthy individuals ($P<0.05$). Similar results were observed in a study conducted by Polo [26]. Who conducted a CT study and revealed that patients with OSA had a reduced air space at the oropharyngeal level.

This study has certain limitations, including the relatively small number of patients, its single-cantered nature and the fact that only RA patients were included with no control healthy group; therefore, outcomes were not compared between RA patients and healthy individuals. In addition, in our study, lateral cephalography was used to quantify the area of the upper airway; however, 3D CT would have been more accurate.

## CONCLUSION

Patients with RA were observed to have a high prevalence of OSA. Cephalometric analysis could be useful in determining the risk of OSA. However, there was no significant association between the cephalometric area of the upper airway and the risk of OSA. Based on the current study results, cephalometry cannot be employed to predict the risk of OSA in patients with rheumatoid arthritis.

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