Is there a relationship between sella turcica calcification and thyroid cartilage calcification? A random study using lateral cephalometric radiography

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SUMMARY

Thyroid cartilage changes begin in the second decade of life with the horn of the thyroid cartilage, and spread throughout the individual's lifetime to other cartilage plates. However, the objective of the present study is to assess if there is an association between thyroid calcification (TC) and sella turcica bridging (STB). Forty patients, 11 men and 29 women, aged between 40 and 62 years with a mean age of 48.6 years were studied. The sample inclusion criteria of this study were age in the fourth decade, no craniofacial deformities, no history of craniofacial surgical intervention, good-quality lateral cephalometric radiographs, and good visualization of the sella turcica (ST). A total of 40 registered patients were included in the assessment of calcification of the thyroid cartilage. Of these, 75% presented with thyroid calcifications, and 25% did not. Data on sex was available for all 40 registered patients. A total of 72.5% were female, and 27.5% were male. While in a comparison between calcification of the thyroid and calcification of the sella turcica, no statistical relationship was observed between the two variables. Thyroid cartilage calcification could be considered a normal part of the ageing process, while STB could appear on lateral radiographs due to superimposition of the anatomical structures. In this study, we found no relationship between thyroid cartilage calcification and STB, and a larger patient sample is required for evaluating calcification of the thyroid and STB.

Keywords: Sella turcica bridging – Thyroid cartilage calcification – Lateral cephalometry

INTRODUCTION

Lateral radiography, introduced by Broadbent in 1931, has played an essential role in orthodontic assessment and treatment planning (Durão et al., 2015). The main goals of lateral cephalometric radiography (LCR) are to provide detailed views of the patient's skeletal, dental, and soft-tissue morphology, to evaluate skeletal maturation and to assess a patient's progressive response to treatment. The sella turcica (ST) is an essential structural reference in cephalometric

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analysis. A sellar point is determined from this structure, usually located at the centre of the ST, and is considered an essential landmark in cephalometric studies (Shatyanarayana et al, 2013). The ST is a saddle-shaped bony structure located anatomically on the intracranial surface of the body of the sphenoid bone (Kaya et al., 2021). Radiographically, the size of the ST can be assessed through either linear or various area and volume measurement methods. Usually, it ranges from 4 to 12 mm in the vertical dimensions and 15 to 16 mm in the anteroposterior dimensions (Kaya et al., 2021).

The hypophysis is located within this anatomical space. Any change in the size of the ST is more frequently associated with pathology; thus, the relationship between dimensional and morphological variations in the ST and various syndromes and disorders, skeletal patterns (Alkofide, 2007; Meyer-Marcotty et al., 2010), and dental anomalies has been investigated in previous studies using lateral radiography. Axelsson et al. (2004) and Acevedo et al. (2021), distinguished five different morphological variations for the ST: STB, double floor contour, oblique anterior wall, pyramidal shape of the dorsum sella (DS), and irregularity in the posterior (DS). These structures may fuse and form osseous bridges due to an abnormal development of the anterior and posterior walls of the clinoid processes (Leonardi et al., 2011; Scribante et al., 2017). On LCR, many crucial anatomic structures can be observed, such as the laryngeal cartilage, in which ossification and calcification have been investigated widely since 1882 (Aramaki et al., 2017). When ossification begins with the lamina or cornua, the thyroid cartilage is visible on lateral cephalometric and lateral neck radiographs (Mupparapu et al., 2005). The thyroid cartilage is made up of hyaline cartilage, as well as other structures such as cricoid and arytenoid cartilage; the hyaline cartilages calcify and ossify as part of the ageing process (Aramaki et al., 2017). These changes begin in the second decade of life with the horn of the thyroid cartilage, and spread throughout the individual's lifetime to other cartilage plates (Aramaki et al., 2017; Garvin, 2008; Tabatabaee et al., 2020). The present study aims to evaluate the relationship between STB and calcification of the thyroid cartilage.

MATERIALS AND METHODS

This study included 40 patients, 11 men and 29 women, aged between 40 and 62 years with a mean age of 48.6 years. The sample inclusion criteria of this study were age in the fourth decade, no craniofacial deformities, no history of craniofacial surgical intervention, good-quality lateral cephalometric radiographs, and good visualization of the sella turcica. The cephalometric measurements were realized using Dolphin software 11.95.67 and performed by one observer with six years of orthodontic experience. On lateral radiography and after radiograph calibration, a series of specific cephalometric analysis measurements were conducted after identifying the following anatomical structures: nasion (N), sella (S), sella diameter (from the tuberculum sella (TS) to the DS), deepest point of the sella floor (SF), farthest point on the inner sellar wall (SW), most anterior point of the hyoid bone, base of the styloid process, glossal point, A point, pogonion point (Pg), anterior nasal spine (ANS) and posterior nasal spine (PNS) (Fig. 1). The intersection of the palatal plane with the S-N plane, the perpendicular distance between A point and the S-N plane, the perpendicular distance between Pg and the S-N plane, and the plane formed by the stylohyoid, styloglossal, and hyoidglossal planes were evaluated. A total of 14 values were evaluated from lateral radiography. Through radiograph assessment, scores were assigned for bridging of the sella turcica (no bridging = 0, partial bridging = 1, complete bridging = 2) (Fig. 1) and calcification of the thyroid cartilage (no calcification = 0, calcification = 1) (Fig. 2).

This study was conducted in accordance with the ethics defined in the Declaration of Helsinki, and approval was obtained from the research ethics committee of the Instituto Asturiano de Odontología (Ref. IAO-21-0621).

Informed consent was obtained from all subjects and/or their legal guardian(s).

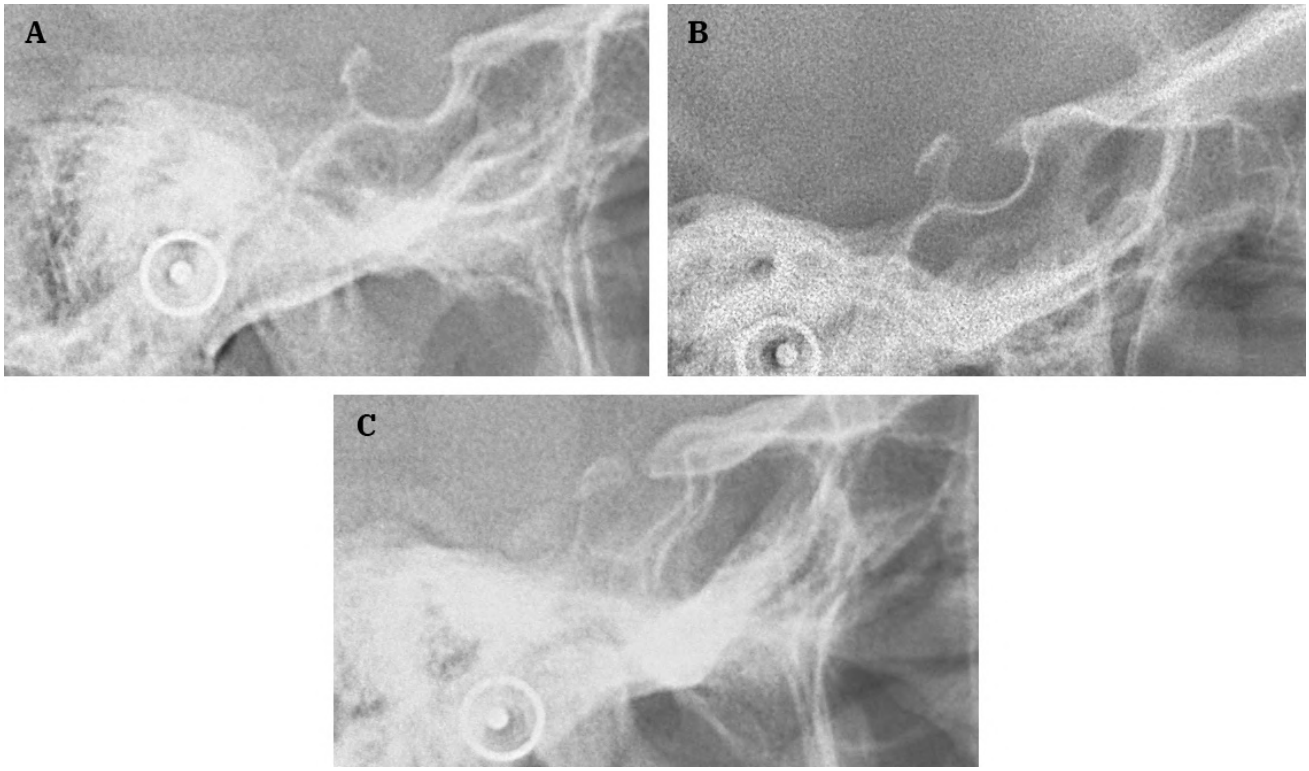

Fig. 1.- Sella Turcica and thyroid cartilage classification. **A**- Sella Turcica non bridging. **B-** Patient with partial Sella turcica bridging. **C-** Sella turcica with complete bridging.

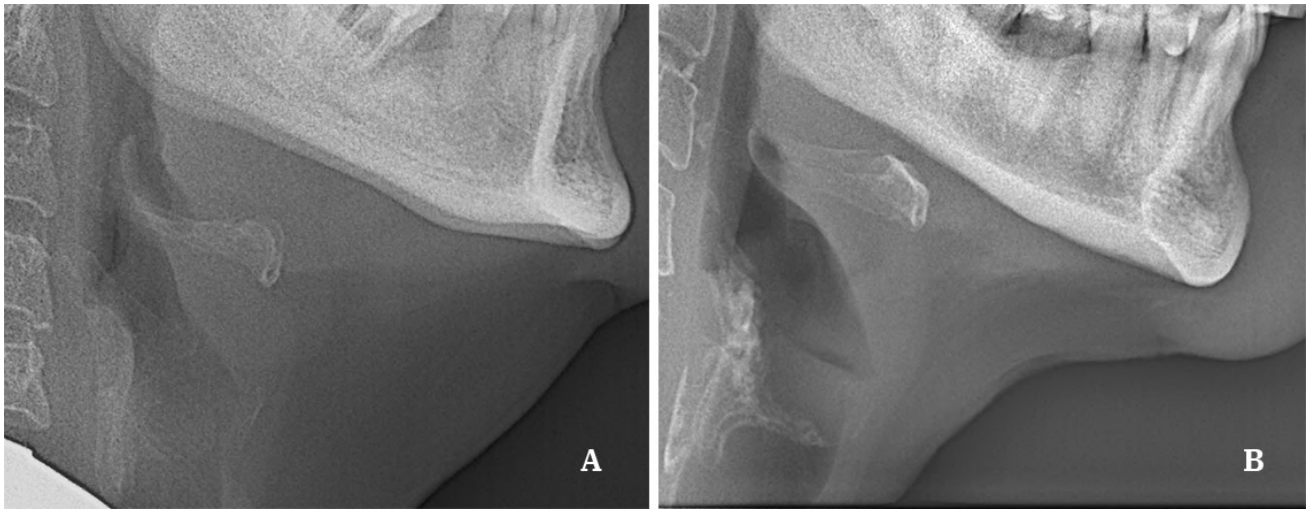

Fig. 2.- Thyroid cartilage classification. **A-** Thyroid cartilage calcification. **B-** Thyroid cartilage with no calcification.

Statistical study

Quantitative variables are described as the mean and standard deviation, and qualitative variables are described as the absolute and relative frequencies. The Pearson or Spearman correlation coefficients were calculated with significance testing depending on whether the normality hypothesis was verified. The relationships between qualitative variables were evaluated with Pearson's or Fisher's chi-square test depending on whether the hypothesis about expected frequencies was fulfilled. The differences in quantitative variables between two groups were assessed using Student's t test or the Wilcoxon test for independent samples, depending on whether the normality was verified.

Table 1. Summary values for the measured quantitative variables.

	n	Median	SD	Percentile (%)				
				0	25	50	75	100
Age	40	48.65	6.11	32.00	45.00	48.00	53.00	62.00
Long	40	8.88	2.42	3.00	7.00	8.50	11.00	15.00
Sella turica depth	40	8.72	1.52	6.00	8.00	9.00	10.00	13.00
Diam	40	11.93	1.80	6.00	11.00	12.00	13.00	15.00
SN-A	40	55.75	4.73	50.00	52.00	55.00	60.00	68.00
SN-Pg	40	105.58	10.29	59.00	100.00	105.00	111.25	120.00
SN	40	67.12	3.74	60.00	65.00	66.00	69.25	75.00
Palatine plane angle	40	9.62	2.65	4.00	7.75	10.00	12.00	16.00
Stylohyoid distance	40	80.20	8.95	63.00	74.75	75.60	86.50	100.00
Styloglossal distance	40	94.17	6.17	82.00	90.00	95.00	98.00	108.00
Hyoglossal distance	40	36.08	5.53	20.00	38.00	38.00	40.25	50.00

Finally, linear models were constructed to study whether calcification influenced the variables collected, adjusting for sex and age.

The level of significance used was 0.05. Statistical analysis was carried out using the R program (R Development Core Team), version 3.6.3. Entries to include in the bibliography (R and libraries used):

- R Core Team (2020). A: Language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.
- Corrplot. Taiyun Wei and Viliam Simko (2017). R package corrplot: Visualization of a correlation matrix (Version 0.84).

RESULTS

A summary of the measured quantitative variables is presented below: the number of available data, mean, standard deviation, zero percentile or minimum value, 25th percentile or first quartile, 50th percentile or median, 75th or third percentile, quartile, and 100th percentile or maximum value (Table 1).

A total of 40 registered patients were included in the assessment of calcification of the thyroid cartilage. Of these, 75% presented with thyroid calcifications, and 25% did not (Table 2).

Table 2. Calcification or no calcification of the thyroid cartilage variable.

	Frequency	%
Calcification	10	25
No calcification	30	75
Total	40	100

Data on sex were available for all 40 registered patients. A total of 72.5% were female, and 27.5% were male (Table 3).

Table 3. Patient sex classification.

	Frequency	%
Male	11	27.5
Female	29	72.5
Total	40	100

Moreover, in a comparison between calcification of the thyroid and calcification of the sella turcica, no statistical relationship was observed between the two variables (Fisher's test, p value = 0.135) (Table 4).

Table 4. Calcification of the thyroid and calcification of the sella turcica.

	n	%	n	%
No	6	60.00	9	30.00
Yes	4	40.00	21	70.00

To determine whether the behaviour of the depth from the sella turcica to the SF differs between sexes, various comparisons were made, as detailed in the table. Given that the normality hypothesis was not rejected for all modalities (Shapiro–Wilk test: Male, p value = 0.111; Female, p value = 0.067) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.97), the hypothesis of equality of population means cannot be rejected (Student's t test, p value = 0.824) (Table 5).

Table 5. The depth from the sella turcica to the SF and patient sex.

	n	Mean	Median	SD	P25	P75
Male	11	8.64	9.00	1.50	7.50	9.00
Female	29	8.76	9.00	1.55	8.00	10.00

To determine whether the behaviour of the anteroposterior maximum diameter of the TS to the most posterior point of the sella turcica differs according to sex, various comparisons were conducted, as detailed in the table. Given that the normality hypothesis was rejected for some of the modalities (Shapiro–Wilk test: Male, p value = 0.312; Female, p value = 0.039) and the reduced sample size, the hypothesis that the averages are equal cannot be rejected (Wilcoxon test, p value = 0.547) (Table 6).

Table 6. Anteroposterior maximum diameter of the TS to the most posterior point of the sella turcica and patient sex.

	n	Mean	Median	SD	P25	P75
Male	11	11.82	12.00	1.47	11.00	12.50
Female	29	11.97	12.00	1.94	11.00	13.00

Furthermore, to determine if the behaviour of the perpendicular SN-distance differs according to sex, various tests were conducted, as detailed in Table 7. Given that the normality hypothesis was rejected for some of the modalities (Shapiro–Wilk test: Male, p value = 0.01; Female, p value = 0.001) and the reduced size of the sample, the hypothesis that the averages are equal can be rejected (Wilcoxon test, p value <0.001).

Table 7. The perpendicular SN-distance differs according to sex.

	n	Mean	Median	SD	P25	P75
Male	11	70.45	70.00	3.33	68.00	12.50
Female	29	65.86	66.00	3.08	64.00	13.00

Likewise, to determine whether the S-N distance differs according to sex, various tests were conducted, as detailed in Table 8 below. Given that the normality hypothesis was not rejected for all modalities (Shapiro–Wilk test: Male, p value = 0.276; Female, p value = 0.246) and the hypothesis of equality of the two population variances (F test of variances, p value = 0.704), the hypothesis of equality of population means can be rejected (Student's t test, p value <0.001).

Table 8. The S-N distance and patient sex.

	n	Mean	Median	SD	P25	P75
Male	11	91.73	90.00	6.34	90.00	95.00
Female	29	75.83	75.00	5.03	74.00	78.00

To determine wheher the behaviour of the stylogenian distance differs according to sex, various tests were conducted, as detailed in Table 9. Since the hypothesis of normality was not rejected for all modalities (Shapiro–Wilk test, Male, p value = 0.228; Female, p value = 0.379) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.159), the hypothesis of equality of population means can be rejected (Student's t test, p value = 0.001).

Table 9. The stylogenian and patient sex.

	n	Mean	Median	SD	P25	P75
Male	11	99.00	98.00	3.87	95.50	101.00
Female	29	92.34	92.00	5.92	90.00	95.00

To determine whether the behaviour of age differs according to the TCscore, various tests were conducted, which are detailed in Table 10. Considering the sufficient sample size and the

result of the normality test (Shapiro–Wilk test, no thyroid calcifications: p value = 0.043), the hypothesis that the means are equal can be rejected (Wilcoxon test, p value = 0.042).

Table 10. The thyroid calcification and no calcification.

	n	Mean	Median	SD	P25	P75
No thyroid calcification	10	51.50	53.00	4.25	48.50	53.75
Thyroid calcification	30	47.70	46.50	6.40	44.25	51.00

Moreover, to determine whether the behaviour of the depth from the sella turcica to the SF differs according to the TCscore, various tests were conducted, as detailed in Table 11. Considering the sufficient sample size, that the hypothesis of normality was not rejected in all modalities (Shapiro–Wilk test, no thyroid calcifications: p value = 0.119) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.893), the hypothesis of equality of population means cannot be rejected (Student's t test, p value = 0.374).

Table 11. The depth from the sella turcica to the SF differs according to the thyroid calcification score.

	n	Mean	Median	SD	P25	P75
No thyroid calcification	10	9.10	9.00	1.45	9.00	9.75
Thyroid calcification	30	8.60	8.50	1.54	8.00	9.75

To determine whether the behaviour of the ante-post maximum diameter TS- most posterior point differs according to the thyroid calcification score, various tests were conducted, as detailed in Table 12. Considering the sufficient sample size, that the hypothesis of normality was not rejected for all modalities (Shapiro–Wilk test, no thyroid calcifications: p value = 0.151) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, 12 p values = 0.384), the hypothesis of equality of population means can be accepted (Student's t test, p value = 0.076).

To determine whether the behaviour of the stylohyoid distance differs according to the thyroid calcification score, various tests were conducted, as detailed in Table 13. Considering the sufficient sample size, that the hypothesis of normality was not rejected for all modalities (Shapiro–Wilk test, no thyroid calcifications: p value = 0.136) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.103), the hypothesis of equality of population means can be rejected (Student's t test, p value <0.001).

Table 12. Ante-post maximum diameter TS- most posterior point according to the thyroid calcification score.

	n	Mean	Median	SD	P25	P75
No thyroid calcification	10	12.80	13.00	1.40	12.00	13.00
Thyroid calcification	30	11.63	12.00	1.85	11.00	13.00

Table 13. Stylohyoid distance according to the thyroid calcification score.

	n	Mean	Median	SD	P25	P75
No thyroid calcification	10	88.60	92.50	9.94	8000	95.99
Thyroid calcification	30	77.40	75.00	6.69	74.00	82.25

To determine whether the behaviour of the greater anteroposterior DS-TS length differs according to the sella turcica calcification score, various comparisons were conducted, as detailed in Table 14. Given that the normality hypothesis was not rejected for all modalities (Shapiro–Wilk test: No, p value = 0.216; Yes, p value = 0.217) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.402), the hypothesis of equality of population means can be rejected (Student's t test, p value <0.001).

Table 14. Anteroposterior DS-TS length according to the sella turcica calcification score.

	n	Mean	Median	SD	P25	P75
No	15	10.73	11.00	2.19	10.00	11.50
Yes	25	7.76	8.00	1.81	7.00	9.00

To determine whether the depth from the maximum anterior-posterior diameter of the

TS to the most posterior point of the TS differs according to the calcification of the sella turcica, various comparisons were conducted, as detailed in Table 15. Since the hypothesis of normality was rejected for some of the modalities (Shapiro–Wilk test: No, p value = 0.287; Yes, p value = 0.025), and the reduced sample size, the hypothesis that the averages are equal can be rejected (Wilcoxon test, p value = 0.018).

Table 15. The maximum anterior-posterior diameter of the TS to the most posterior point of the TS differs according to the calcification of the sella turcica.

	n	Mean	Median	SD	P25	P75
No	15	12.80	13.00	1.52	12.00	13.50
Yes	25	11.40	11.00	1.78	11.00	12.00

To determine whether the behaviour of the stylogenian distance differs according to the calcification of the sella turcica, various tests were conducted, as detailed in the table 16. Given that the normality hypothesis was not rejected for all modalities (Shapiro–Wilk test: No, p value = 0.645; Yes, p value = 0.559) and that the hypothesis of equality of the two population variances was not rejected (F test of variances, p value = 0.372), the hypothesis of equality of population means can be rejected (Student's t test, p value = 0.026).

Table 16. The stylogenian distance according to the calcification of the sella turcica.

	n	Mean	Median	SD	P25	P75
No	15	96.93	95.00	6.58	95.00	101.00
Yes	25	92.52	93.00	5.38	90.00	96.00

DISCUSSION

The lateral cephalometric radiograph provides a specialized lateral skull view that allows clinicians to investigate facial type, growth pattern, the relationship of the jaw and teeth and the anatomy of the anatomical positioning of cervical vertebral hyoid bone and, on occasion, the laryngeal cartilage. After adolescence, human thyroid cartilage typically undergoes terminal differentiation and mineralization (Kirsch et al., 2000). Most of the previously cartilaginous human skeletal elements ossify by this point, and the epiphyseal disks close (Kirsch et al., 2000). In both sexes, ossification begins at the posterior border, the lower margin and the inferior horn of the thyroid cartilage (Mupparapu et al., 2002). Most male thyroid cartilage ossifies by approximately age 70, but female cartilage never completely ossifies, leaving the ventral half cartilaginous (Mupparapu et al., 2002). When ossification of the thyroid cartilage is seen on a lateral cephalometric radiograph at a young age, further imaging with ultrasound (US), computerized tomography (CT) or magnetic resonance imaging (MRI) may help rule out parathyroid adenomas (Mupparapu et al., 2002).

The degree and frequency of thyroid cartilage ossification are lower in females than in males, especially in the anterior aspect. However, the degree and frequency of cricoid calcification are also lower in females than in males (Mupparapu et al., 2002). For both sexes, however, the degree of ossification of the thyroid and cricoid increases with age. Furthermore, ossification begins in the posterior region of the thyroid cartilage in both sexes at 18 to 20 years. According to the present study, a higher incidence of thyroid cartilage was observed in females than in males; this phenomenon could be related to many factors, such as hormonal factors, especially for women in the fourth decade of life, a history of hyperthyroidism or a previous history of cancer.

STB is described as calcification of the clinoid processes without apparent clinical signs, and symptoms should be considered a standard variant of sella turcica anatomy (Scribante et al., 2017; Baidas et al., 2018). Moreover, Suleyman et al. (2019), believed that STB could be considered a developmental anomaly. Bridging of the sella turcica can be induced by a variety of factors, the most common of which is the appearance of fusion between the anterior and posterior structures on lateral radiography due to superposition of the structures despite the absence of genuine bone fusion (Suleyman et al., 2019).

Several 2D radiographic studies have investigated the phenomena of STB. Müller (1952) reported an incidence of 3.8%, while Cederberg et al. (2003), reported an incidence of 8% in a study of

225 subjects. Furthermore, Jewett (1920) reported an incidence of 13% in a study of 100 normal subjects. The increased frequency of complete bridging on lateral cephalometric radiography can be partly explained by the 2D view provided, which makes it difficult to discriminate between true STB and the appearance of fusion between the clinoid process because of radiographic superimposition (Acevedo et al., 2021). Through this study, 37.5% of subjects showed no STB, 57.5% of subjects showed partial STB, and 5% showed complete STB. Our results coincide with other surveys. A study conducted by Cederberg et al. (2003), on 255 patients showed that the percentage of partial sella turcica calcification was 68.8% on lateral radiographs.

The objective of this study was to assess whether there was a relationship between thyroid cartilage calcification and STB. However, the results of statistical analysis showed that there was no relationship between these structures.

Additionally, statistical analysis revealed that regarding the anterior-posterior dimension (DS-TS) of the sella turcica, there was no relationship with sex (P value = 0.358). Similarly, we found that there was no relationship between the depth of the sella turcica sex (P value = 0.824). However, an analysis of the stylohyoid distance and sex showed a significant relationship in women (P value = 0.06) but not in men (p value = 0.2).

Whether age plays a role in calcification remains controversial; thus, the pathologies that occur in the human body have been assessed in many studies in terms of the relationship with age. In this study, we also evaluated the relationship between age and calcification of the thyroid cartilage. Statistical analyses showed a significant relationship between age and TC (p value = 0.04). This result coincides with other studies, which indicate that calcification of the thyroid cartilage starts in the 25th year and that by the 65th year, the cartilage has become completely ossified (Mupparapu et al., 2005). Furthermore, a significant result was obtained when we compared calcification of the thyroid cartilage and stylohyoid and stylogenic calcification (p value = 0.01, P value = 0.01), respectively.

Due to the lack of studies on the relationship between calcification of both the sella turcica and thyroid cartilage, a large sample size and advanced radiographic techniques such as CBCT are required to fully evaluate both structures. This study was limited by the patient sample size and the radiographic 2D technique used in this study. Thyroid cartilage calcification could be considered a normal part of the ageing process, while STB could appear on lateral radiographs due to superimposition of the anatomical structures. In this study, we found no relationship between thyroid cartilage calcification and STB, and large patient sample is required for evaluating calcification of the thyroid and STB.

AUTHORS' CONTRIBUTIONS

Andrea Garrido analysed the data and carried out the work; Alaa Alsafadi directed the structure; Iván Menéndez performed the literature review; Ramón Cobo provided, as an otolaryngologist, knowledge of thyroid calcification, cephalometry and sella turcica, Teresa Cobo conceived the idea and the development approach.

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