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Impact of bilateral nasal polyposis on the interoptic and interzygomatic distance

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Abstract

Purpose To identify and determine variations on eye distance in patients with bilateral nasal polyposis (BNP) compared to a healthy control group.

Methods This is a case–control study that included 20 BNP patients and 40 healthy controls. We included all patients with BNP confirmed by pathology and a computed tomography scan. A healthy control group was admitted, filtered by the exclusion criteria of nasal polyposis, craniofacial malformations, and encephalocele. Paranasal sinus CT scans were performed in all participants, and two measures were evaluated, the interoptic (soft tissue) and the interzygomatic (bone structure) distances.

Results A total of 20 BNP subjects, 13 (65%) male and 7 (35%) female, with a mean age of 38.8 years, and 40 healthy controls, 16 (40%) male and 24 (60%) female with a mean age of 43.2 years, were included. The mean interoptic distance was 69.7 mm (71.9 mm men, 66.4 mm women) and interzygomatic distance was 103.1 mm (104.5 mm men, 100.6 mm women). A significant increase of the interoptic ($p < 0.001$) and interzygomatic ($p < 0.002$) measurements was found in patients with polyposis compared to the controls. In the receptor operative curve analysis, the interoptic distance had an area under a curve of 96% and the threshold that maximizes the sensitivity and specificity was 59.85 mm (sensitivity 90%, specificity 95%, PPV 90%, NPV 95%).

Conclusions An increase in ocular and orbital distances was identified in patients with BNP. Polyposis may be identified by measuring eye separation. The established cut point distance identifies patients that may benefit from follow-up. Further research in this study line is suggested.

Keywords Hypertelorism · Nasal polyposis · Interoptic · Interzygomatic · Facial dysmorphism

Introduction

Nasal polyposis is an increasing health problem that is present in 2–5% of the general population. This condition affects men more than women in a 2–3:1 ratio. Polyps may develop due to a chronic inflammatory process of the nasal mucosa, producing rhinorrhea, nasal obstruction, and olfactory alterations [1, 2]. It has been associated with different syndromes and may present up to 36% in patients with aspirin intolerance, 20% in cystic fibrosis, and 7% in asthma [3–5].

Woakes [6] first described a syndrome that associated chronic inflammation of the nasal mucosa, broadening of the nasal vault increasing eye distance, myxomatous tissue growth, and bone necrosis. Wentges [7] defined this

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syndrome as the presence of nasal polyposis, hyperplastic deformation of the nasal pyramid, and periosteal resorption with bone fibrosis.

Greig defined the increase in the distance between both eyes as ocular hypertelorism and used the interpupillary (soft tissue) distance to evaluate it [8]. Teisser noted that various eye abnormalities increased the interpupillary distance, but not necessarily between the orbits. He described the term orbital hypertelorism, in which the bony structure distance is increased, therefore, decreasing the distance between the lateral epicanthi and the auditory meatus [9]. Orbital hypertelorism is not considered a pathology, but a craniofacial characteristic that may be present in diverse diseases [10].

At the time of the research, little evidence of a relationship between both phenomena was found. The main purpose of our study is to determine variations in eye separation of bilateral nasal polyposis (BNP) patients compared to healthy controls.

Patients and methods

We included all patients diagnosed with BNP confirmed by histopathology. The patients were referred by the Department of Otolaryngology-Head and Neck Surgery of the University Hospital of the Autonomous University of Nuevo Leon in Monterrey, Mexico, to the Radiology Department of the same clinic for a paranasal sinuses computed tomography (CT) scan from January 2013 to June 2016.

The inclusion criteria for the subjects were a biopsy-confirmed BNP diagnosis analyzed by a head and neck specialized pathologist and a paranasal sinuses CT scan performed in the institution. Forty healthy controls with CT scans filtered by the exclusion criteria of nasal polyposis, craniofacial malformations, and encephalocele were included. All patients had between 1 and 5 years with obstructive nasal symptoms and a grade 2–3 of the Lildholdt endoscopic nasal polyposis classification [11]. All subjects, including the control group, were Hispanic and lived in northeastern Mexico. The research protocol was approved by the local Research and Ethics Committee with the registry key OT16-00001.

Once the subjects were enrolled, we evaluated two different measurements in the CT scans. To standardize the image in assessment, we selected an axial slice where the optic papilla and the crystalline were present in all CT scans. The interoptic distance was defined as the length between the entrance of both optic nerves to the eyeball, the optic papilla. The interzygomatic distance is the length between the anterior margin of the frontal process of both zygomatic bones at the plane of the optical nerves, as shown in Fig. 1.

We define measure or measurement as the anatomical structure in evaluation and distance as the numerical value of separation in millimeters.

The CT scans were obtained with a Discovery 690 General Electric Tomograph. Slices were performed at 0.625 mm with an interspace of 0.6 mm, using Bone Plus technique for paranasal sinuses.

Sample size was calculated for a two-group *t* test with a 1:2 case–control ratio, a 0.05 significance level and a power of 0.8, resulting in 20 and 40 subjects each. Comparisons between the study groups were made using a Mann–Whitney *U* Test for non-parametric data. Permutation test were used in non-normal distributed variables. We used a logistical regression with tenfold cross validation, reporting area under a curve (AUC), receptor operative curve (ROC), sensitivity, specificity, positive predictive value and negative predictive

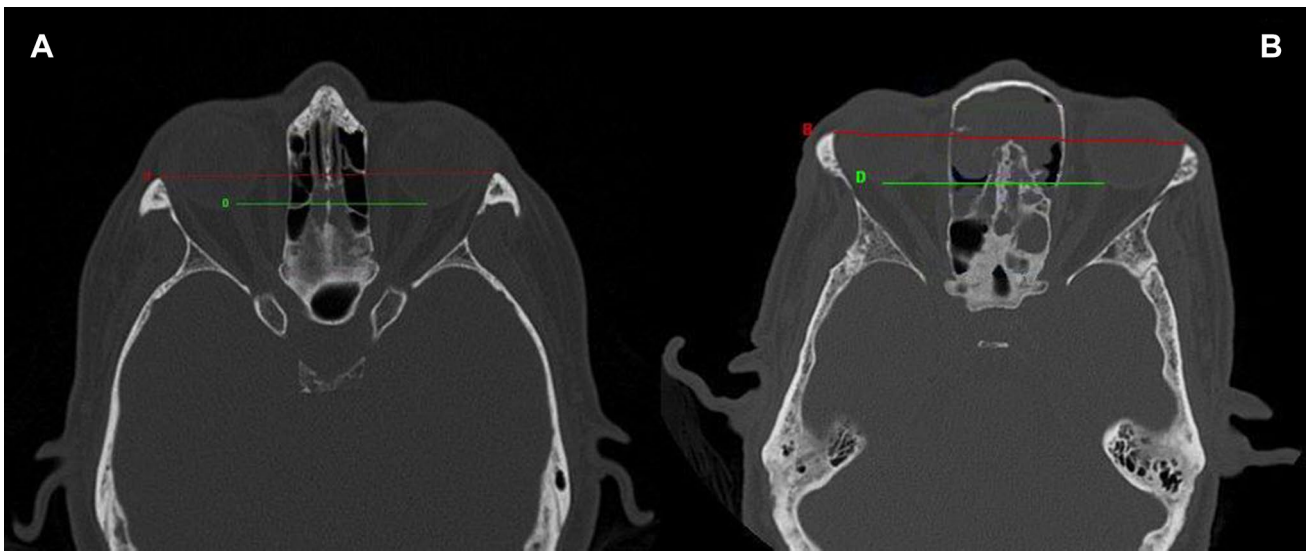

Fig. 1 Interoptic and interzygomatic distances measured in CT scans of nasal polyposis patients and healthy controls

value. A p value ≤ 0.05 was considered statistically significant. The analysis was performed with the R 3.4.0 software (R Foundation for Statistical Computing, Vienna, Austria) for Windows 10.

Results

A total of 20 BNP subjects, 13 (65%) male and 7 (35%) female, with a mean age of 38.8 years, and 40 HC, 16 (40%) male and 24 (60%) female with a mean age of 43.2 years, were included. Age and gender were distributed homogeneously among BNP study subjects and in healthy controls.

The interoptic distance of the BNP group varied from 56.6 to 89.1 with an average of 69.7 mm (71.9 in men and 66.4 in women) and from 95 to 112.2 with an average of 103.1 mm (104.5 in men and 100.6 in women) in the interzygomatic distance. The control group varied from 50 to 65.5 with an average of 54.7 mm (56.5 in men and 53.6 in women) in the interoptic distance and from 91.8 to 105.5 with an average of 97.2 mm (99.7 in men and 95.9 in women) in the interzygomatic distance.

There is a significant increase in the distances of the interoptic and interzygomatic measurements in patients with BNP compared to the HC, as shown in Table 1.

We divided the subjects into groups of men and women due to the difference in the facial morphology involving the size and sexual characterization. Interoptic and interzygomatic distances in women were statistically increased in patients with BNP with a $p = 0.03$ and 0.002, respectively. In men, both distances were significantly higher in the BNP subjects compared to HC, with a $p < 0.001$ in interoptic and $p = 0.004$ in interzygomatic distance.

We chose the two best logistic regression models, based in the lowest Akaike information criteria (AIC). The independent variable of the first model was the interoptic distance (odd 1.57; CI 0.09, 27.05; $p < 0.001$), with an accuracy of 93% in cross validation, and for the second model, the interzygomatic distance (odd 1.42; CI 1.17, 1.72; $p < 0.001$) with an accuracy of 78% in cross validation. When adjusting by gender, interoptic distance model held significance in men but not in women, and the interzygomatic model held significance in both.

In the receptor operative curve (ROC) analysis, the interoptic distance had AUC of 96%, and the threshold that maximizes the sensitivity and specificity was 59.85 mm (sensitivity 90%, specificity 95%, positive predictive value 90%, negative predictive value 95%) as shown in Fig. 2. However, 56.6 mm maximizes sensitivity at 100% (with a specificity of 75%) and 65.85 mm maximizes specificity at 100% (with a sensitivity of 55%). For the interzygomatic distance, the AUC was 84%, the threshold that maximizes the sensitivity and specificity was 100.6 mm (sensitivity 85%, specificity 77%, positive predictive value 65%, negative predictive value 91%) as shown in Fig. 3. However, 94.7 mm maximizes sensitivity at 100% (with a specificity 32%) and 105.6 mm maximizes specificity at 100% (with a sensitivity of 20%).

Discussion

The main finding of this study is the identification of a significant increase of eye separation between patients with BNP and healthy controls.

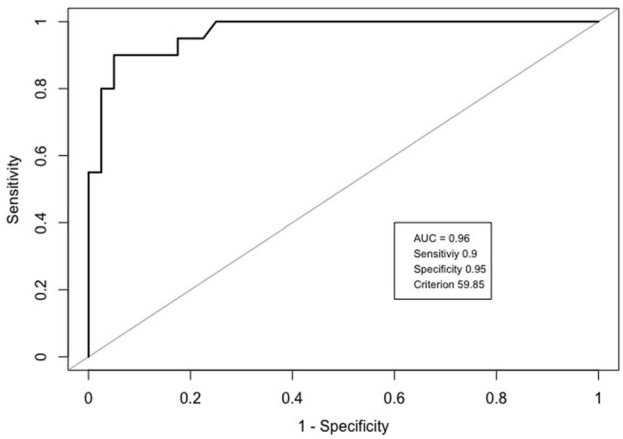

Fig. 2 Interoptic distance ROC curve analysis

Table 1 Average and standard deviation difference in interoptic and interzygomatic distance between bilateral nasal polyposis patients and healthy controls

	Bilateral nasal polyposis (standard deviation) $n = 20$	Healthy controls (standard deviation) $n = 40$	p value
Interoptic distance average	69.7 mm (±11.1)	54.7 mm (±3.1)	0.001
Male	72.0 mm (±11.4)	56.8 mm (±3.8)	< 0.001
Female	65.4 mm (±11.1)	53.6 mm (±2.1)	0.03
Interzygomatic distance average	103.1 mm (±4.1)	97.2 mm (±3.9)	0.002
Male	104.5 mm (±4.3)	99.7 mm (±3.7)	0.004
Female	100.6 mm (±2.9)	95.5 mm (±3.2)	0.002

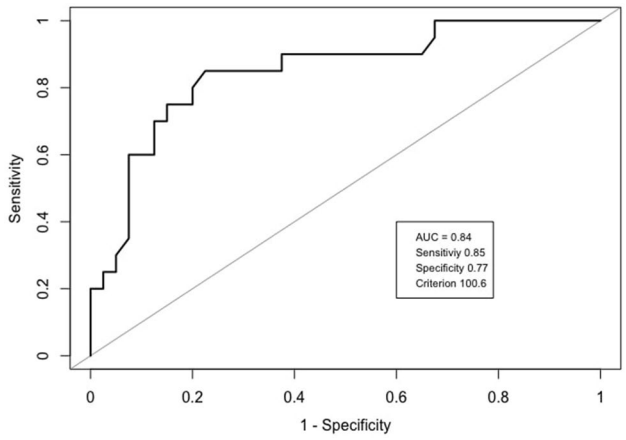

Fig. 3 Interzygomatic distance ROC curve analysis

A study performed by Ural et al. found no association between true hypertelorism (which they define as the increased distance of bone structures) and nasal polyposis. This contrasts with our results, which suggest that both phenomena are present in these patients. In the same study, they conclude that there is a difference not in bone, but in adjacent soft tissue structures. They state that the distance between the medial canthi is significantly increased among patients with nasal polyposis compared to controls. Our study confirms these results; we observed a significant increase in the interoptic distance (soft tissue measurement) and identified the association between nasal polyposis and ocular hypertelorism [12].

As the literature states, there is a difference in the concept of ocular and orbital hypertelorism. The ocular term involves soft tissue and orbital bone structures. In this study, we found a statistical increase in distances involving both, bone and soft tissue structure measurements in BNP patients. The reason for this phenomenon is unknown, although different authors suggest that it may be caused by inflammation of the lacrimal sac and nasolacrimal duct due to recurrent subclinical sinusitis [12, 13]. Weber et al. explain that an expansion of the nasal and paranasal cavities develops in addition to a thinning of the bony walls, increasing the distance between the orbits and producing hypertelorism [14].

Although a specific pathophysiology is not clear, the novel finding of this study reveals an increased eye separation (bone and soft tissue structures) in patients with nasal polyposis. To our knowledge, this is the first work to study both phenomena and determine a specific cut point to identify nasal polyposis. For an optimal follow-up scheme, subjects will be followed with a complete otolaryngologic physical examination.

Conclusion

An increase in interoptic and interzygomatic distances was identified in patients with bilateral nasal polyposis. The best sensitivity (90%) and specificity (95%) to identify bilateral nasal polyposis is 59.4 mm interoptic distance. An evaluation of facial dysmorphisms in this population is recommended. We encourage more research teams to continue to work in this subject to identify the pathophysiology of this phenomenon and to determine an optimal follow-up scheme in these patients. Further research in this study line is suggested.

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Compliance with ethical standards

Conflict of interest The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. There is no conflict of interest. Neither the research nor the authors received a specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval The research protocol was approved by the local Research and Ethics Committee with the registry key OT16-00001.

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