

Original Article

Comparison of ^{99m}Tc -MDP SPECT qualitative vs quantitative results in patients with suspected condylar hyperplasia[☆]D.F. López Buitrago^{a,*}, J. Ruiz Botero^a, C.M. Corral^b, A.R. Carmona^c, A. Sabogal^a^a Universidad del Valle, Cali, Colombia^b Egresada, Universidad del Valle, Cali, Colombia^c Centro de medicina nuclear Gamanuclear, Cali, Colombia

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ABSTRACT

Objective: To compare qualitative vs quantitative results of Single Photon Emission Computerised Tomography (SPECT), calculated from percentage of ^{99m}Tc -MDP (methylene diphosphonate) uptake, in condyles of patients with a possible clinical diagnosis of condylar hyperplasia.

Materials and method: A retrospective, descriptive study was conducted on the ^{99m}Tc -MDP SPECT bone scintigraphy reports from 51 patients, with clinical impression of facial asymmetry related to condylar hyperplasia referred by their specialist in orthodontics or maxillofacial surgery, to a nuclear medicine department in order to take this type of test. Quantitative data from ^{99m}Tc -MDP condylar uptake of each were obtained and compared with qualitative image interpretation reported by a nuclear medicine expert.

Results: The concordances between the 51 qualitative and quantitative reports results was established. The total sample included 32 women (63%) and 19 men (37%). The patient age range was 13–45 years (21 ± 8 years). According to qualitative reports, 19 patients were positive for right side condylar hyperplasia, 12 for left side condylar hyperplasia, with 8 bilateral, and 12 negative. The quantitative reports diagnosed 16 positives for right side condylar hyperplasia, 10 for left side condylar hyperplasia, and 25 negatives.

Conclusions: Nuclear medicine images are an important diagnostic tool, but the qualitative interpretation of the images is not as reliable as the quantitative calculation. The agreement between the two types of report is low (39.2%, Kappa = 0.13; $p > 0.2$).

The main limitation of quantitative reports is that they do not register bilateral condylar hyperplasia cases.

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Comparación de resultados cualitativos vs. cuantitativos de ^{99m}Tc -MDP SPECT en pacientes con sospecha clínica de hiperplasia condilar

RESUMEN

Palabras clave:

Asimetría facial

Hiperplasia condilar

Gammagrafía ósea

Tomografía computarizada de emisión por fotón único

Objetivo: Comparar el resultado de los informes cualitativos de la tomografía computarizada de emisión por fotón único (SPECT), con los resultados cuantitativos, calculados a partir del porcentaje de captación del radiofármaco ^{99m}Tc -MDP (metilendifosfonato), en cóndilos de pacientes con sospecha clínica de hiperplasia condilar.

Materiales y método: Estudio retrospectivo, descriptivo realizado en 51 pacientes con impresión clínica de asimetría facial y sospecha de hiperplasia condilar, remitidos a un centro de medicina nuclear para realizarles gammagrafía ósea-SPECT por el especialista en ortodoncia y/o cirugía maxilofacial. Se obtuvieron los datos cuantitativos del porcentaje de captación del radiofármaco ^{99m}Tc -MDP en ambos cóndilos, y se compararon con el informe cualitativo generado por el médico nuclear en cada uno de los sujetos.

Resultados: Se estableció la concordancia entre 51 informes cualitativos y sus resultados cuantitativos. Del total de la muestra, 32 eran mujeres (63%) y 19 hombres (37%). La edad de los pacientes estaba en un rango de 13–45 años (21 ± 8 años). Según los informes cualitativos 19 pacientes fueron positivos para hiperplasia condilar derecha, 12 para izquierda, 8 bilaterales y 12 negativos. Según los resultados cuantitativos, 16 fueron positivos para hiperplasia condilar derecha, 10 izquierdos y 25 negativos.

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Conclusiones: Las imágenes de medicina nuclear son una importante herramienta diagnóstica, pero la interpretación cualitativa de la imagen no es tan confiable como la determinación cuantitativa. Los informes cualitativos concuerdan con los resultados cuantitativos de la prueba SPECT ^{99m}Tc -MDP, en un bajo porcentaje (39.2%, kappa = 0.13; $p > 0.2$).

La principal limitación del método cuantitativo es que no registra casos de hiperplasia condilar bilateral.

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Introduction

Cranio-mandibular diagnosis is based on paraclinical examinations, anamnesis and the clinical findings. Condylar hyperplasia can be unilateral (UCH), or both mandibular condyles can be affected. It is characterised by exaggerated and progressive growth, which causes secondary facial asymmetry or mandibular prognathism.¹ Therefore, diagnosis begins with the clinical detection of facial asymmetry, correlation with intraoral occlusal features and with radiographic and/or tomographic findings.² According to the patient's age and the progression of asymmetry, nuclear medicine scintigraphic examinations of the bone are requested, either planar bone scan or single photon emission computed tomography (SPECT), to determine if there is elevated radiopharmaceutical uptake of the by mandibular condyle cells,¹ which would indicate the presence of increased osteoblastic activity.

The results of the scintigraphy can be reported qualitatively or quantitatively; the level of radiopharmaceutical uptake in the mandibular condyle in suspected UCH is compared to the contralateral and to a reference anatomical structure, which would give information about relative activity or inactivity.

When hyperplasia in an active state is confirmed, the indicated therapeutic approach to prevent progression and the development of severe facial asymmetry is a high condylectomy (consisting in a 5–6 mm osteotomy of the condylar head, where the centre of condylar growth is found) followed by orthodontic treatment, either to compensate the secondary asymmetry left by the hyperplasia or to decompensate the asymmetry. In this case a second surgery will be needed to correct the sequelae and improve facial aesthetics.^{1–3}

The planar bone scintigraphy is sensitive (85%) but poorly specific (67%),² compared to SPECT. In a previous study by López and Corral,⁴ in 61 patients, SPECT was found to be better capable of detecting hyper-uptake in the condylar tissue, compared to planar, therefore indicating a greater sensitivity regarding cellular hyperplasia in the condylar (52.46% detected cases, vs. 13.1% detected with planar bone scintigraphy).

Accepting that SPECT⁵ is the scintigraphic test of choice it is important to bear in mind that a positive diagnosis does not necessarily mean condylar hyperplasia, since this result may be due to an increase in cellular bone metabolism for other reasons such as inflammation, neoplasm, trauma, infection or even a normal growth spurt.⁶ Therefore, variables that lead to error in the interpretation of the scintigraphic results must be minimised.⁷

The SPECT radioactivity counts for each of the condyles are determined from the region of interest (ROI). The ROI is defined from a transaxial slice of each condyle in which the radioactive counts of the reference bone structure (clivus) can also be obtained. Consequently, radioactive counts per minute data are not relevant because due to dependence on the average life of the radioisotope and other variables that are compensated in the calculation process.⁸

Studies such as those by Hodder et al.,⁹ and Fahey et al.,⁵ show that the difference in the percentage uptake between condyles in patients with suspected UCH is greater than 10%, therefore if the difference between the condyles, for the uptake of the radiopharmaceutical does not exceed 10%,^{8–10} the result is accepted as high

uptake, but is not accepted as positive for UCH, the percentage uptake in a condyle with suspicion of active UCH must be above 55%^{4,9,11} with respect to the contralateral. Logically, the diagnosis of bilateral condylar hyperplasia cannot be based on this threshold.

The aim of this investigation was to retrospectively analyse bone scintigraphy studies with ^{99m}Tc -MDP (methylene diphosphonate) of patients with facial asymmetry and clinical suspicion of condylar hyperplasia, comparing qualitative and quantitative SPECT data using the percentage of uptake in the condyles.

Materials and methods

This study meets the requirements of biomedical research according to the Declaration of Helsinki 1964 and was approved by the Institutional Committee of Human Research Ethics of our university (Act 008 of 2015).

The SPECT bone scintigraphy scans and qualitative nuclear medicine reports of 51 patients were analysed.

The 32 women and 19 men between 13 and 45 years of age had been referred to the nuclear medicine centre by orthodontic or maxillofacial specialists due to a clinical diagnosis of facial asymmetry with suspicion of active condylar hyperplasia. Patients with a history of arthritis, autoimmune disease, condylar trauma, previous condylar surgery, or condylar tumour were excluded from the study.

High-resolution scintigraphic images were obtained, by means of a low energy collimator, 3 h after the intravenous administration of 740 MBq (20 mCi) of ^{99m}Tc -MDP. The static lateral projection of the head was obtained with a matrix of 256 × 256 and 700 000 counts per projection. For the tomographic images, a 64 × 64 matrix was used with a rotation of 360° every 15 s. The condyles and clivus, the anatomical reference structure, can be visualised on the same axis of the transaxial plane. Coronal and sagittal sections were obtained for further analysis of the images.

All recorded data were obtained through the Segami computer system (Segami Corporation) and pre-calibrated Mirage software, which does not require a direct operator.

All qualitative reports (Fig. 1) were issued by 2 nuclear physicians based the SPECT images obtained at the same nuclear medicine centre from the visual scale of colours ranging from the warmest (higher uptake) to the less warm (lower uptake). The quantitative reports (Fig. 2) express percentage uptake using the following formula:

$$\begin{aligned} &\% \text{ uptake of condyle of study} \\ &= \frac{\text{counts of condyle of study}}{\text{counts of condyle in study} + \text{contralateral condyle}} \times 100 \end{aligned}$$

Statistical analysis

For the description of demographic characteristics of the sample, mean ± standard deviation and range were calculated. The Kendall kappa concordance coefficient was calculated to establish the degree of agreement between the qualitative and quantitative reports (% uptake in each condyle). In the concordance calculation it was essential not to include bilateral cases as it was known in

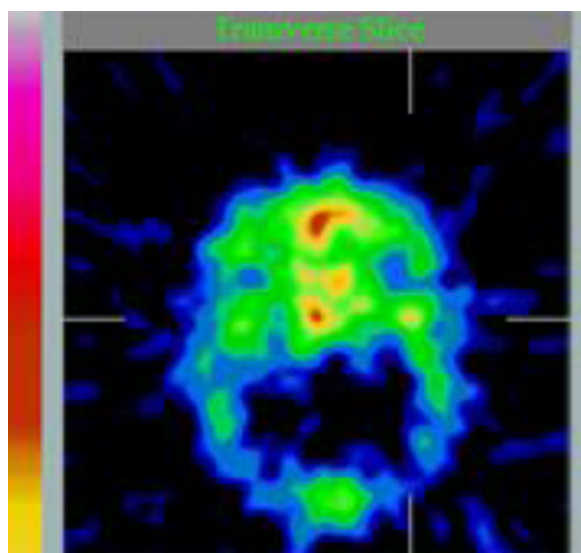


Fig. 1. Visual interpretation of the SPECT-transaxial slice.

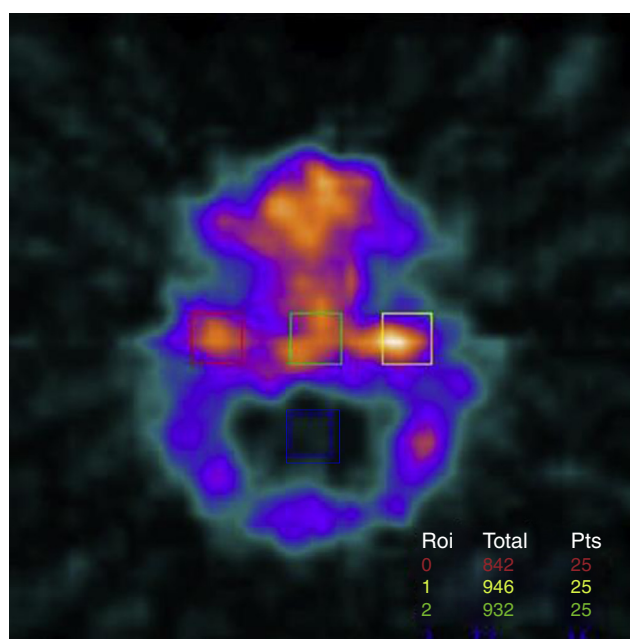


Fig. 2. Quantitative method – ROI fixed to obtain number of radioactive accounts for each condyle, clivus which is the reference structure and background accounts.

Table 1
Demographic description of the sample.

Sex	n	%
Male	19	37
Female	32	63
Total	51	100

advance that the quantitative report does not detect them. Differences by sex and by laterality were analysed using the Chi-squared test. The level of significance was set at $p = 0.05$.

Results

The qualitative and quantitative data of the total sample were compared (Table 1 and Fig. 3). According to the qualitative reports,

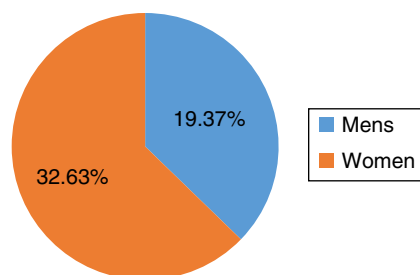


Fig. 3. Distribution of the sample by gender.

Table 2
Diagnostics for each test type.

	Qualitative	Quantitative	Quali %	Quant %
Right hyperplasia	19	16	37.25	31.30
Left hyperplasia	12	10	23.53	19.6
Bilateral	8	0	15.7	0
Negative	12	25	23.52	49
Total	51	51	100	100

19 patients were positive for right condylar hyperplasia, 12 for left, 8 bilateral and 12 negative. According to the quantitative results, 16 were positive for right condylar hyperplasia (% uptake ≥ 55), 10 left, 0 bilateral and 25 negative (Table 2 and Fig. 4).

The distribution of the diagnoses by sex does not show a statistically significant association ($\chi^2 p = 0.11$). There was discordance between qualitative and quantitative data in seven cases (13.7%): there were 8 cases (15.7%) that were considered as diagnosed as bilateral in the qualitative tests, 7 of them were negative according to quantitative analysis.

The percentage of concordance between the two methods to report the diagnosis was 39.2% and Cohen's kappa concordance coefficient was not acceptable ($k = 0.13$; $p > 0.2$). Concordance is acceptable if it is $> 70\%$ and $k > 0.5$ so we concluded that the two methods were not concordant.

The total distribution of the results of the 51 patients shows that there was a positive concordance regarding the side of the hyperplasia between both reports in only 12 patients (23.53%) and in 8 patients (15.69%) there was negative concordance. In 16 patients conflicting results of one negative and one positive test were recorded (31.37%) and in 7 cases (13.73%) there was no concordance on the side of the hyperplasia between the two reports.

In 8 patients (15.69%), the qualitative report shows bilateral hyperplasia, whereas in the quantitative interpretation (when expressed in percentage and taking a difference between both condyles greater than 10% as indicator of hyperplasia) did not allow to define bilaterality of the disease (Fig. 2). According to both methods of diagnostic interpretation, the most frequent condylar hyperplasia is right unilateral and there is no gender difference in diagnoses ($p = 0.11$).

Discussion

The use of diagnostic tests such as bone SPECT with ^{99m}Tc -MDP,^{12,13} which offer a quantitative evaluation of the relative bone metabolic activity at the level of the mandibular condyle, allows the clinician to approach the diagnosis and treatment decisions in relation to the clinical conditions when faced with condylar hyperplasia.

It is common for clinicians to rely only on the qualitative results, the visual interpretation of the images interpreted by the nuclear physician,^{14–16} without using the ROI based mathematical formula

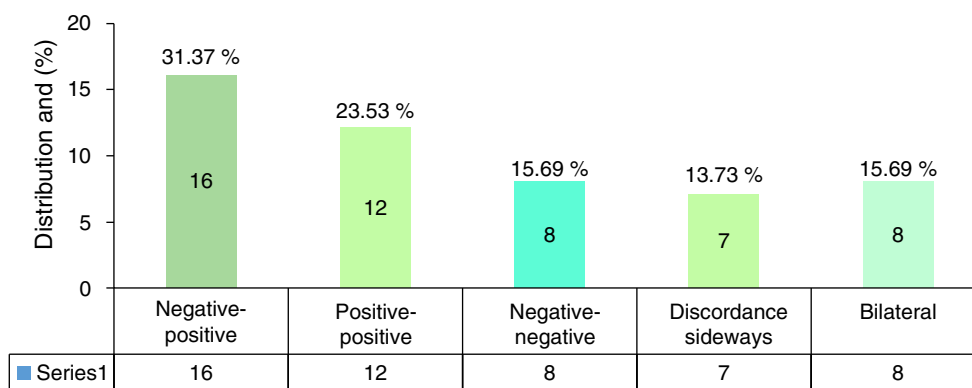


Fig. 4. Distribution of results.

which provides a percentage of radiopharmaceutical uptake per condyle.^{17,18}

These numerical data may be more accurate than simple subjectivity, eliminating human error.¹⁹ Therefore, the creation of a clear protocol which includes requesting the scintigraphic test obtaining quantitative reports would aid the correct diagnosis of condylar hyperplasia and therapeutic decision making process.

The quantitative technique seems to be less sensitive but more specific than qualitative, we see 25 negative cases (49%) versus 12 (23.5%) qualitatively diagnosed negative cases. However it is not possible to calculate sensitivity/specificity because false negative and false positive statistics cannot be determined due to the lack of a gold standard test available; although there is a histopathological test, it cannot confirm or exclude condylar hyperactivity.²

The studies accept as a decision limit a difference of 10% or more in the percentage of radiopharmaceutical uptake between the two condyles, as indicative of UCH.¹⁹

Hodder et al.,⁹ in the United Kingdom carried out a study in which the percentage uptake of patients with facial asymmetry and who were suspected to have active UCH exceeded 10%, whereas in the control group, patients who underwent the bone scan for other reasons, there was not a single case where the difference between the two condyles was greater than 6%.

Likewise, in an Iranian study, Kajan et al.,¹⁸ performed scans on 38 patients with no clinical suspicion of condylar hyperplasia, finding that in these patients, considered as healthy, the difference in the maximum percentage uptake did not exceed the 6.2%, with an average of 2.1%.

In Boston, Fahey et al.,⁵ sample of 32 healthy subjects, found that the maximum difference between the two condyles for the radiopharmaceutical percentage uptake was 6.7%.

On the other hand, Wen et al.,¹⁹ in China, performed SPECT on 105 patients with suspected UCH and 44 controls, finding an average in the difference in uptake between the condyles, with suspected hyperplasia of 18%, whereas for the controls the average distribution of radioactivity in both condyles was uniform and symmetrical, with no percentage differences.

It is common, as these previous studies demonstrate, that there be percentage differences in the uptake of the radiopharmaceutical between healthy condyles, which can be explained by differences in the cellular activity of the condylar head in patients with normal TMJ and in the absence of other diseases different from hyperplasia.^{20,21} This may be due to variations in the growth and remodelling of the condylar tissues, possibly due to causes that affect the joint mechanics or the functional position of the mandible (i.e. mandibular laterognathism) or due to even to methodological differences.^{22–24} However if the differences do not exceed 10%, they cannot be interpreted as indicative of condylar hyperplasia; hence here lies the diagnostic risk of not delivering the

numerical data in the interpretation of the scintigraphic test. Not only do these values have diagnostic value, but they also serve as a guide for the treatment of patients with UCH. Elbaz et al.²⁵ and Wolford et al.,²⁶ propose therapeutic algorithms for the management of UCH, based on clinical and radiographic findings: the severity of the asymmetry and the positive result of the SPECT, provided that the suspicious condyle has a percentage of uptake of 10% or more compared to the contralateral. The present study shows that the two methods (qualitative versus quantitative) are not comparable and indicates that the qualitative method is inaccurate, subjective, not specific and with possible variability in interpretation between the two evaluators, whereas the quantitative method is more accurate. Additionally, as reported by Karssemakers et al.,²⁰ there is an excellent inter-evaluator agreement for the quantitative SPECT test when using the same ROI of the condylar image in patients with suspected UCH. The qualitative result could lead to errors in the therapeutic decision, such as a failure to provide treatment in a false negative diagnosis and unnecessarily treat a false positive.

One limitation of this study is that it did not evaluate inter-observer agreement in qualitative reports, as in this case the reports were done by the institution's two nuclear medicine physicians who emitted one single report. Additionally, it would be of great importance to establish from the histopathological test of patients submitted to high condylectomy, the specificity and the sensitivity of both tests, since according to histopathological criteria the condylar hyperplasia is divided into active and inactive. Active condylar hyperplasia is characterised by the increase in the osteoblastic bone metabolism with undifferentiated mesenchymal cells present, followed by a layer of hypertrophic cartilage with chondrocytes resting on the trabecular bone and whose calcification rate seems to be above the normal ranges by capturing the radiopharmaceutical of the scintigraphy.²⁷ Inactive condylar hyperplasia is when activity has finished and normal metabolic rate is observed. This limitation means it is not possible to establish relative operation curves with cut-off values other than 10%. Therefore, further studies are needed in this area.

The main limitation of the quantitative method is that it does not detect cases of bilateral condylar hyperplasia.

In summary, this study shows that the qualitative results do not concur with the quantitative results of the SPECT test. With such a low percentage of concordance (39.2%, kappa = 0.13, $p > 0.2$) the probability of erroneous diagnoses in patients with clinical suspicion of condylar hyperplasia is high.

Conclusions

The use of nuclear medicine imaging procedures is an important diagnostic tool, but the qualitative assessment of the image is not as reliable as the quantitative one.

The results of this study suggest the quantitative method should be used, as the qualitative method is less reliable.

Conflict of interests

The authors declare no conflict of interest.

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