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A three-dimensional study of hemimandibular hyperplasia, hemimandibular elongation, solitary condylar hyperplasia, simple mandibular asymmetry and condylar osteoma or osteochondroma

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A R T I C L E I N F O

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A B S T R A C T

Purpose: To investigate the morphological features of hemimandibular hyperplasia (HH) in comparison to other condylar hyperplasia-associated asymmetries, including hemimandibular elongation (HE), solitary condylar hyperplasia (SCH), simple mandibular asymmetry (SMA) and condylar osteoma or osteochondroma (COS).
Materials and methods: A total of 31 HH, 9 HE, 6 SCH, 10 SMA and 10 COS patients were included in this study. Clinical documentation, panoramic radiography and computed tomography data were retrospectively reviewed. The three-dimensional measurements were performed on multi-planar reformation images and volume rendering images. The accuracy of the subjective radiological signs was evaluated using sensitivity, specificity and receiver operating curve analysis. Discriminant analysis was performed to generate predictive formulas using quantitative data.
Results: The condyles in HH were regularly or irregularly enlarged, with significantly enlarged anterior-posterior length [16.2/5.29 (mean/SD, mm) $P < 0.001$] and volume [5.3/2.9(mean/SD, cm^3) $P < 0.001$] compared to the normal values. The condyles in HE and SMA were normally shaped, and the quantitative measurements were within the normal range. The ramus heights in the HH patients [55.7/5.4(mean/SD, mm)] were enlarged in comparison to the contralateral side ($P < 0.001$) and normal values ($P < 0.001$). The ramus heights in the HE [52.4/7.1 (mean/SD, mm), $P < 0.001$] and SMA [50.3/5.0(mean/SD, mm), $P = 0.002$] patients were enlarged in the contralateral side comparison but were within the normal range. The mandibular body heights in HH were enlarged in the premolar [16.6/1.3 (mean/SD, mm), $P < 0.001$] and molar [24.8/1.4 (mean/SD, mm), $P < 0.001$] regions. The inferior convexity of the lower mandibular border and inferiorly displaced mandibular canal produced high specificity, sensitivity and area under the curve for the diagnosis of HH. Discriminant analysis could predict the diagnoses with a cross-validation accuracy rate of 85.7%.
Conclusions: HH is a distinct clinical entity characterized by enlargement of the condyle, ramus and mandibular body. The inferior convexity of the lower mandibular border and inferiorly displaced mandibular canal is accurate and specific for the diagnosis of HH. The condyles in HE are not hyperplastic. The term “condylar hyperplasia” alone cannot be used to refer to HH or HE.

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1. Introduction

Hemimandibular hyperplasia (HH) has been clearly defined in the classic contribution by Obwegeser and Makek in 1986 (Obwegeser and Makek, 1986) and in a further comprehensive review in 2001 (Obwegeser and Obwegeser, 2001). Typical HH is characterized by the three-dimensional enlargement of one side of the mandible; i.e., the enlargement of the condyle, the condylar neck and the ascending and horizontal rami. The anomaly terminates exactly at the symphysis of the affected side. Clinically, the increase in the vertical height of the middle and lower facial thirds on the affected side and downward-bowed mandibular lower border are the important features. The etiology is not clearly known, but it could be associated with genetic anomalies or accidents acquired during embryo development.

Hemimandibular elongation (HE) should be clearly differentiated from HH or condylar hyperplasia (CH). HE is characterized by a horizontal displacement of the mandible plus chin toward the unaffected side (Obwegeser and Makek, 1986). The mandibular body of both sides lies on the same level. HE can be unilateral or bilateral or occur together with HH.

There exist some controversies regarding the nomenclature of HH, HE and CH (Higginson et al., 2018; Nolte et al., 2016), and there have been many misused and unclear connotations in the use of diagnostic terms. The term “condylar hyperplasia” has been used to refer to several kinds of mandibular overgrowth with different condylar conditions (Higginson et al., 2018; Rushton, 1946; Broadway, 1958). Particularly, CH has been used to refer to both HH (Higginson et al., 2018) and HE (Nolte et al., 2016; Janakiraman et al., 2015) without distinction. Obwegeser and Makek stated that the term “condylar hyperplasia” should not be used to mean HH and HE. They also pointed out that there should be no condylar hyperplasia in HE (Obwegeser and Makek, 1986; Obwegeser and Obwegeser, 2001). CH should be used to refer to the hyperplasia of the condyle alone, which is called solitary condylar hyperplasia (SCH) (Obwegeser and Makek, 1986). These inconsistencies in the use of the diagnostic names can lead to confusion in scientific research.

Wolford classified CH into 4 types (Wolford et al., 2014a). CH Type 1 is an accelerated and prolonged growth aberration of the “normal” mandibular condyle growth mechanism, causing a predominantly horizontal growth vector, resulting in prognathism that occurs bilaterally (Type 1A) or unilaterally (Type 1B). CH Type 2 is the enlargement of the mandibular condyle caused by an osteochondroma, resulting in a predominantly vertical growth vector and condylar enlargement without (Type 2A) or with exophytic tumor growth (Type 2B). CH Type 3 includes other rare, benign tumors, and CH Type 4 includes malignant conditions. Wolford and Obwegeser share the same basic understanding of these diseases. Type 1 in Wolford's classification is compatible with HE, and Type 2 is compatible with HH (Wolford et al., 2014b).

These two diagnostic systems contain four benign clinical entities that are closely associated with but should be differentiated from CH, including HH, HE, SCH and condylar osteoma or osteochondroma (COS). Moreover, we often encounter some simple mandibular asymmetries (SMA) that cannot be indisputably classified as any of the well-known diseases. SMA should be considered as a common developmental asymmetry of the mandible rather than a pathological disease. High-quality evidence is still lacking to support the quantitative distinctions between these clinical entities (Higginson et al., 2018).

The aim of this study is to investigate the three-dimensional quantitative features of HH to make clear the distinctions between HH and other diseases that might be associated or confused with CH (HE, SCH, SMA and COS).

2. Materials and methods

2.1. Patients

A total of 66 patients who were diagnosed with mandibular asymmetry with the suspected overgrowth of a unilateral condyle or mandible in our hospital between January 2013 and December 2017 were included in this study. All patients underwent panoramic radiograph and spiral computed tomography (CT) scans for diagnostic evaluation. This study was approved by the Ethical Board of the Peking University Stomatology School and Hospital (PKUSSIRB-2012084).

2.2. Inclusion and exclusion criteria

The inclusion criteria for typical and severe HH were as follows: enlargement of the condyle, the condylar neck and the ascending and horizontal rami; anomaly terminated exactly at the symphysis of the affected side; inferior convexity of the lower mandibular border; inferiorly displaced mandibular canal. The inclusion criterion for mild HH was a mildly enlarged mandible with a slight inferior convexity of the lower border and/or an inferiorly displaced mandibular canal; the condyles might not be as remarkably enlarged as those found in typical HH (Fig. 1).

The inclusion criteria for HE were the elongation of one side of the mandible with displacement of the chin prominence to the other side; the elongation of the mandible terminated at the symphysis (Fig. 2A).

The inclusion criteria for SCH were hyperplasia of the condyle; a slight increase in the dimensions of the affected side; the chin slightly shifted to the unaffected side; no increase in mandibular body height (Fig. 2B). The inclusion criterion for COS was a large osseous exostosis protruding from the condyle (Fig. 2C). The inclusion criteria for SMA were asymmetry of the mandible existed but did not meet any of the above four or other well-known diagnoses; the condyles on bilateral sides were of different kinds of normal shape.

The exclusion criteria were as follows: bilateral enlargement of the mandible due to acromegaly or macrogonion; mandibular hyperplasia with soft tissue overgrowth; mandibular asymmetry due to hypoplasia of one side of the mandible.

Diagnostic consensuses were made by two experienced oral and maxillofacial radiologists who were blinded to the clinical information.

2.3. CT scan and imaging process

The maxillofacial region was scanned using a 16-row spiral computed tomography scanner (GE Optima, USA). The following scanning parameters were used: 200–380 mA (automatic exposure control); 120–140 kV; pitch: 1.625; field of view: 20 cm; reconstruction thickness: 1.25 mm. The consecutive axial images were reconstructed and stored in our picture archiving and communication system.

The Digital Imaging and Communications in Medicine (DICOM) data were imported into Mimics 14.11 software (Materialise Technologies, Leuven, Belgium) to be reconstructed and modeled to observe the three-dimensional morphology.

2.4. Diagnostic imaging evaluation

All images were evaluated by two oral and maxillofacial radiology specialists with more than 10 years of experience in consensus. The radiologists were blinded to the clinical

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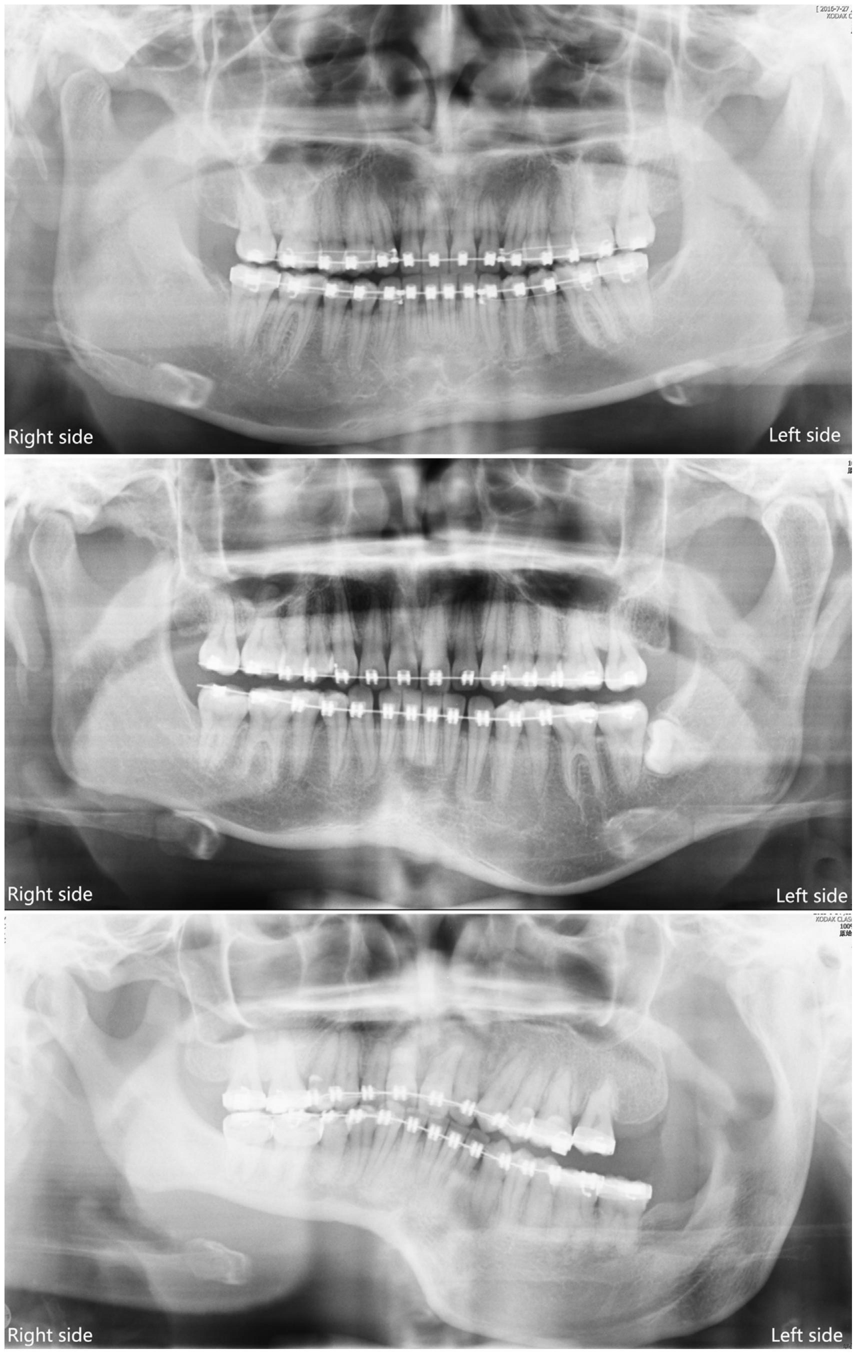

Fig. 1. A: Mild HH showing an inferior convexity of the lower mandibular border and a moderately inferiorly displaced mandibular nerve canal on the right side. B: Typical HH showing an enlargement of the mandible, which terminates exactly at the symphysis on the left side. Three-dimensional CT images of the same patient are presented in Fig. 4A, B. C: Severe HH showing the enlargement of the mandible, with a remarkable mandibular deformity on the left side.

information. The diagnostic confidence was divided into five levels for analysis.

The three-dimensional CT images of the mandible were segmented for suppositional observation to determine whether the condyle, ramus and mandibular body were enlarged. The mandibular canal was evaluated on panoramic radiography to determine whether its place was normal. The lower border of the mandibular body was evaluated on both CT and panoramic radiographs to determine whether an inferior convexity existed.

The condylar morphology of the affected side was evaluated to observe whether the condyle was enlarged and whether the shape was regular. Regular enlargement formed due to homogenous overgrowth in all directions left the condyle with an enlarged normal appearance. A local osseous exostosis could form on a regularly enlarged condyle. Enlargement with a deformed shape was defined as an enlarged condyle without a regular shape.

2.5. Quantitative measurements

The vertical height of the mandibular body was measured at each mandibular tooth site, and the average heights of the

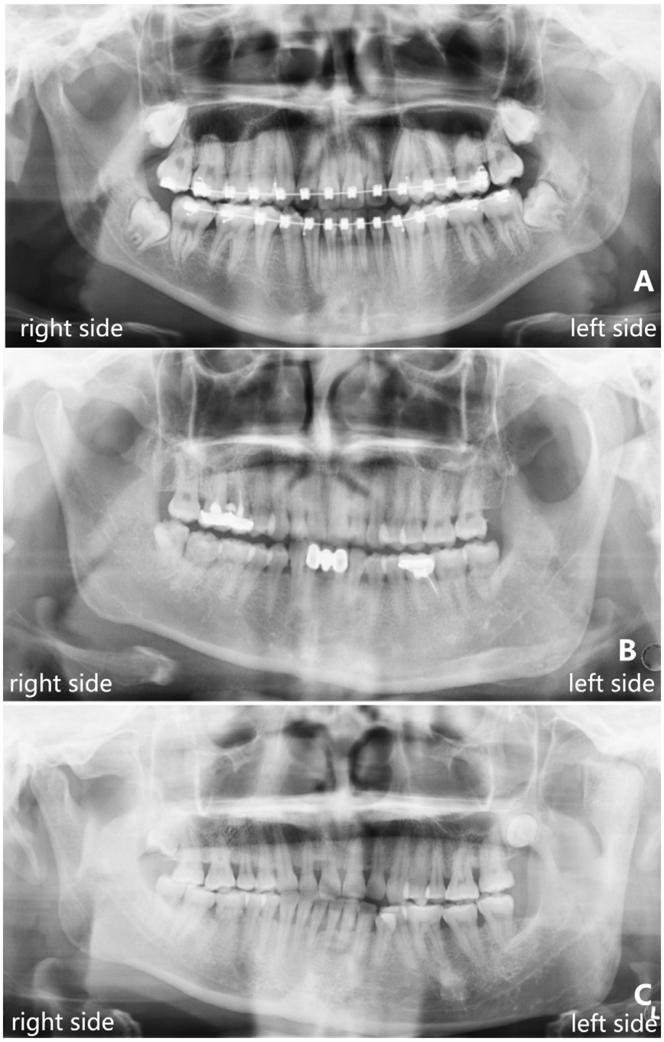

Fig. 2. A: HE showing the elongation of the right side of the mandible with displacement of the chin prominence to the left side. Three-dimensional CT images of the mandible of the same patient are presented in Fig. 4C, D. B: SCH showing an enlargement of the condyle on the left side without an enlargement of the ramus or body. Three-dimensional CT images of the mandible of the same patient are presented in Fig. 4E, F. C: COS showing a large osseous exostosis from the condyle with the deformation, without an enlargement of the ramus or body.

mental, premolar and molar regions were calculated (Fig. 3A). Horizontal mandibular body lengths were measured in segments, including incisor to canine, premolar region, molar region and total body length at the alveolar crest level (Fig. 3A). The linear horizontal width of the ramus and the length of the ramus were measured at the mandibular foramen level (Fig. 3B). The maximum anterior-posterior diameter of the condyle was measured on the three-dimensional images (Fig. 3C). The condylar height was measured from the sigmoid notch to the condylar top, parallel to the vertical long axis of the condylar neck (Fig. 3B). A central maxillary line was drawn along the anterior nasal spine and the midpoint of the nasal bones. A central mandibular line was drawn along the midpoints of the incisors and the mental region. The intersection angle of the maxillary and mandibular central lines was measured as the mandibular deviation angle (Fig. 3D).

The whole mandible was segmented into the condyle, ramus and body for volumetric measurements using the Mimics 11.0 software.

2.6. Validation assessment

Reproducibility was evaluated by two observers performing the linear and volumetric measurements on 10 patients; one observer performed all measurements twice. Variance components were estimated from these results; the intraobserver and interobserver variability were evaluated by calculating the correlation coefficients from the variance estimates. After determining the observer agreement, the whole study population was analyzed.

2.7. Statistical analysis

The means and standard deviations (SD) of the outcome variables were compared using Student's t-test. The normal distributions of the measurements were tested. The normal value ranges of the measurements were calculated with a one-sided method, using the data from the unaffected side of all patients. The measurement results of each group were evaluated in comparison to the normal ranges and the contralateral side measurement results of the unaffected side.

Bayes discriminant analysis was used to produce a scoring system. Discriminant analysis is a generalized statistical method that generates a suitable combination of features that separate or characterize two or more classes of objects. The principle of Bayes discriminant analysis is to generate corresponding functions for each classification. The quantitative measurement results of each sample are used to calculate predictive values using each function. The function that produces the largest predictive value indicates the classification to which the sample belongs. The accuracy of Bayes discriminant analysis of the cross-validation can be evaluated. All data were statistically analyzed using IBM SPSS version 19. A value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patients and radiological findings

Demographic information of the patients is listed in Table 1. Patients were divided into 5 groups: HH ($n = 31$), HE ($n = 9$), SCH ($n = 6$), SMA ($n = 10$) and COS ($n = 10$). The HH patients were classified into mild ($n = 10$), typical ($n = 10$) and severe ($n = 11$) types based on a subjective radiological evaluation.

The clinical characteristics, radiological findings and treatment protocols are also presented in Table 1. An enlarged condyle, enlarged ramus, rounded angle, inferior convexity of the inferior mandibular border, and inferiorly displaced mandibular canal were the main radiological findings of HH (Fig. 4A, B). HE presented mainly as an elongation of one side of the ramus (Fig. 4C, D). Enlarged condyles were also present in SCH (Fig. 4E, F) and COS (Fig. 5A, B), but the ramus and mandibular body changes were not remarkable in these two groups (Figs. 4E–F and 5A–B). SMA presented with unspecified mandibular asymmetry without condylar enlargement (Fig. 5C, D). The calculated sensitivity, specificity and AUC of the image findings for the diagnosis of HH are presented in Table 2.

3.2. Condyle morphology

Enlargement of the condyles was one of the most prominent features of HH (29/31) and SCH (6/6) in comparison to HE and SMA. The enlarged condyles could present a regular shape without a local exostosis (15/29) (Fig. 6A), regular shape with a limited exostosis (10/29) (Fig. 6B) or deformed irregular shape (4/29) (Fig. 6C) in HH (Table 1). The anterior beak, a bony protrusion from the medial pole of the condyle along the lateral pterygoid muscle, was a frequent

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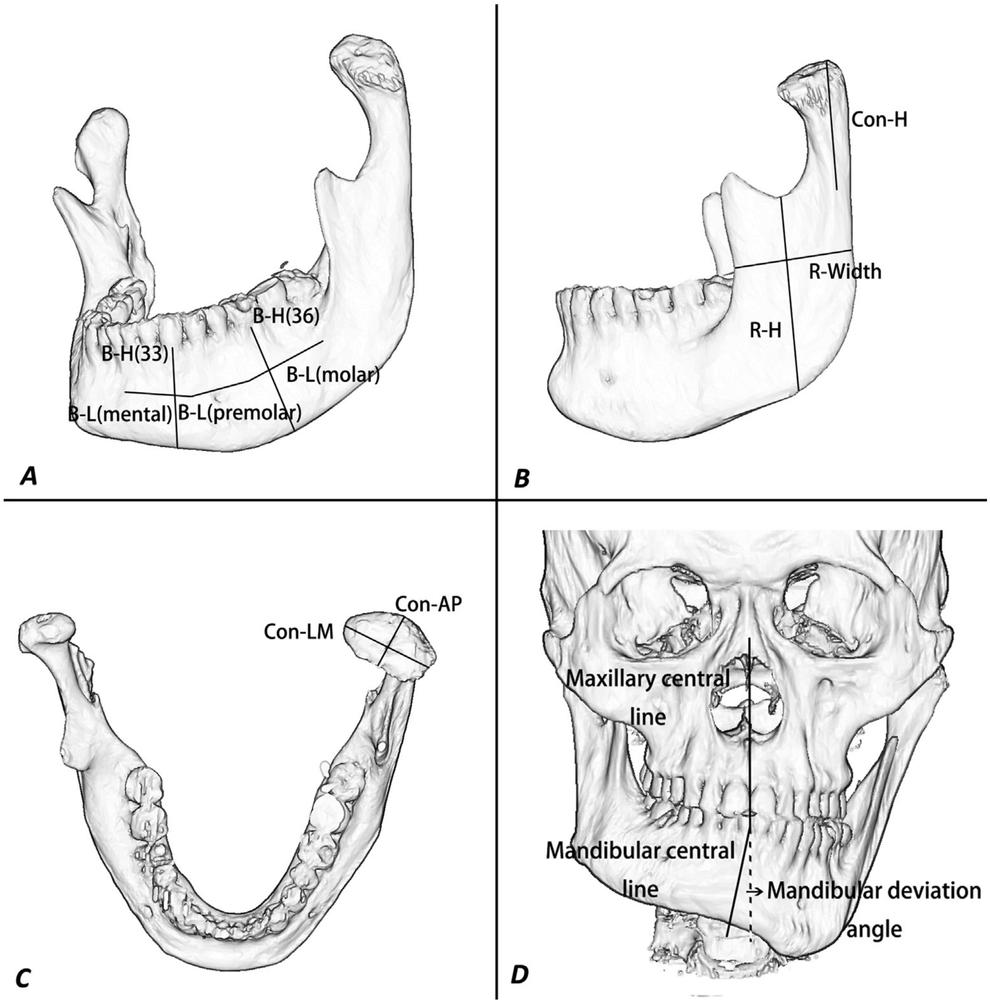

Fig. 3. Schematic drawings of the quantitative measurements.

Table 1
Clinical information and radiological features.

	HH			HE	SCH	SMA	COS
	Mild	Typical	Severe				
Gender (F/M)	9/1	8/2	4/7	**6/3**	5/1	7/3	6/4
Age (year)	22.5	23.6	28.1	23.2	29.1	26.4	23.7
Total number	10	10	11	9	6	10	10
Radiology Findings							
Enlarged condyle	8	10	11	1	6	0	4
Enlarged condyle with regular shape	6	3	6	1	3	0	0
Enlarged condyle with deformed shape	1	1	2	0	3	0	4
Enlarged condyle with local exostosis	1	6	3	0	3	0	0
Tumor-like exostosis	0	0	1	0	0	0	6
Anterior beak exostosis	1	3	2	0	0	0	0
Osteoarthrosis	1	3	5	0	2	1	0
Enlarged ramus	6	10	11	1	0	0	0
Rounded angle	5	10	11	0	0	0	0
Inferior convexity of the lower mandibular border	9	10	11	0	0	0	0
Inferiorly displaced mandibular canal	7	9	11	0	0	0	0
Treatment							
Condylectomy	3	9	6	1	5	0	9
Le Fort I osteotomy	5	9	7	8	6	4	0
Bilateral mandibular sagittal split	5	9	7	8	6	5	0
Genioplasty	5	7	7	8	5	5	0
No surgery	5	1	4	1	4	5	1

(F:Female; M:Male).

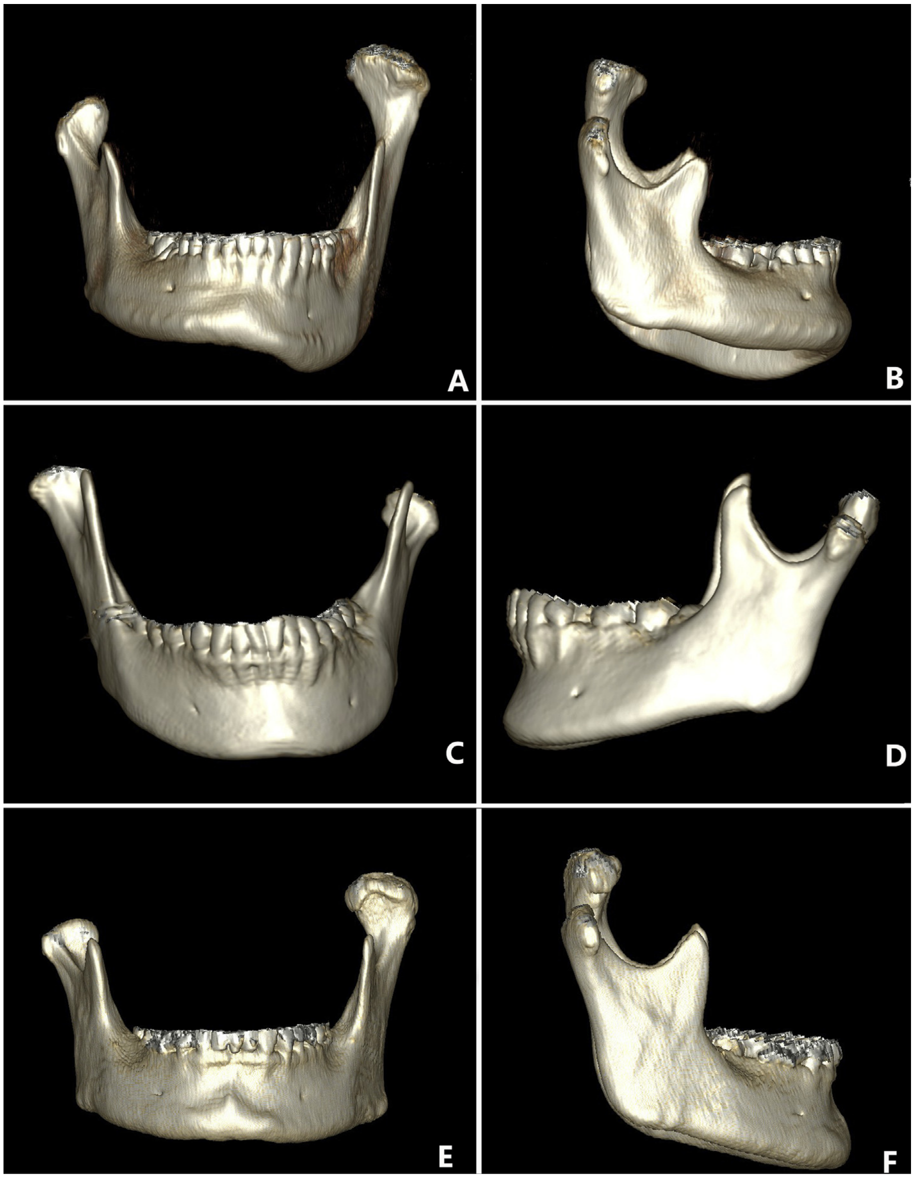

Fig. 4. (A, B) Frontal (A) and lateral suppositional (B) views of an HH mandible, showing the enlargement of the condyle, ramus and mandibular body. Note the remarkable and specific inferior convexity of the lower mandibular border. C–D: Frontal (C) and lateral suppositional (D) views of an HE mandible, showing that the condyle is not significantly enlarged but that the right side of the mandible is elongated. E, F: Frontal (E) and lateral suppositional (F) views of an SCH mandible showing only a remarkable enlargement of the condyle.

exostosis type (6 cases) in HH (Fig. 6B). The lateral pole was another frequent site for a local exostosis (4 cases) in HH.

Three out of 6 SCH cases were considered as a regular enlargement of the condyle without an exostosis. Two cases presented with a local exostosis from the lateral pole and one case with an exostosis from the top.

The condyles in HE (Fig. 4E, F) and SMA (Fig. 5C, D) showed asymmetric condylar morphology on two sides but were of a normal size and shape. Quantitative measurements also proved that although the condyles on the affected side showed a larger anterior-posterior diameter and volume compared with the unaffected side ($P < 0.05$), they did not extend beyond the normal range ($P > 0.05$) (Table 4). The condyles in COS presented with a large osseous exostosis from the top (2), anterior surface (2) or medial pole (2), or presented as a large, deformed condyle without a clear demarcation between the exostosis and the condyle (4).

3.3. Quantitative measurements

In HH patients, the anterior-posterior diameter ($P < 0.001$), the lateral-medial diameter ($P = 0.003$), the condylar height ($P < 0.001$) and the volume ($P < 0.001$) of the condyles on the affected side were significantly increased in comparison to the contralateral normal side and the normal value (Table 3). The height ($P < 0.001$) and the volume ($P < 0.05$) of the ramus on the affected side were significantly increased in comparison to the normal value and the contra-lateral normal side (Table 3). The mandibular heights of the mental ($P < 0.001$), premolar ($P < 0.001$) and molar ($P < 0.001$) areas were all significantly increased in comparison to the contralateral normal sides.

In HE patients, the most dramatic changes were observed on the heights of the ramus ($P < 0.001$) and the condyle ($P < 0.001$) (Table 4). The condyles in HE showed smaller size, especially the

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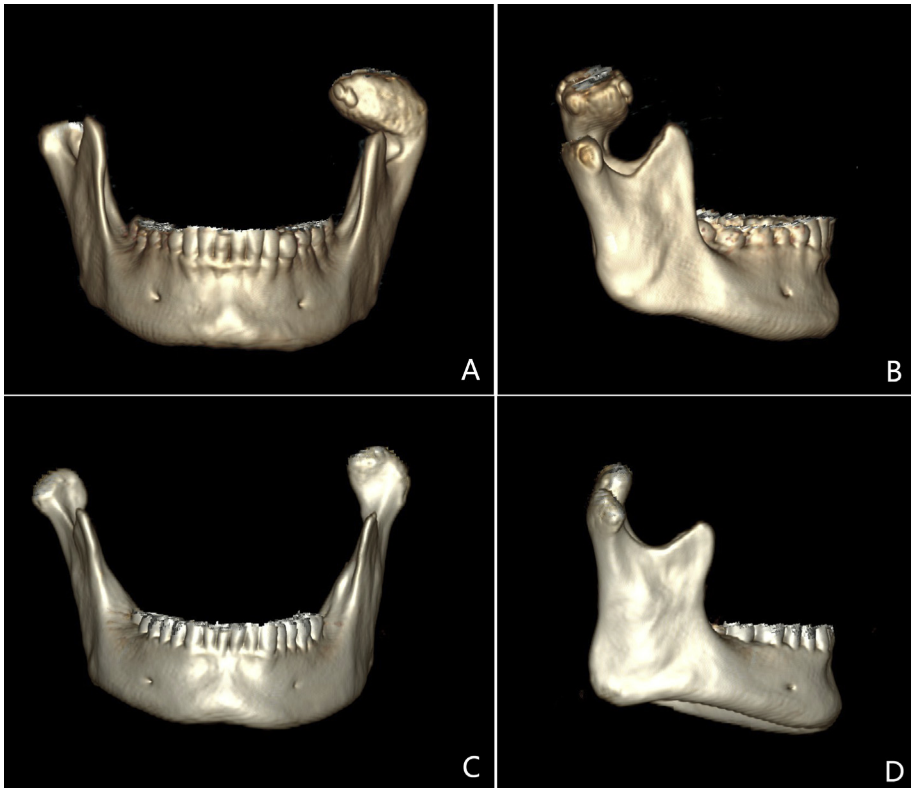

Fig. 5. A, B: Frontal (A) and lateral suppositional (B) views of a COS mandible showing a huge osseous tumor-like exostosis of the condyle. C, D: Frontal (C) and lateral suppositional (D) views of an SMA mandible showing simple mandibular asymmetry, which cannot be classified as any other well-known disease.

anterior-posterior diameter, in comparison to the condyles in HH. The mandibular body height, length and volumes showed no remarkable enlargement.

In SCH patients, the affected condyles showed significantly enlarged anterior-posterior diameter, height and volume (Table 4). The height of the ramus and mandibular body on the affected side showed slight but statistically significant enlargement in comparison to the contra-lateral normal side. The lengths of the mandibular body on the affected side showed no significant changes.

In SMA patients, the anterior-posterior and lateral-medial diameters, the vertical heights and the volumes of the condyles on the affect sides showed slight but statistically significant enlargement in comparison to the contralateral normal sides. The height of the ramus on the affected side showed slight but statistically significant enlargement ($P = 0.016$). The heights and lengths of the mandibular body on the affected side showed no significant enlargement (Table 4).

In COS patients, the anterior-posterior diameter ($P < 0.001$) and the volume ($P < 0.001$) of the condyles on the affected side showed remarkable and statistically enlargement in comparison to those of the contralateral side and normal value. The measurements of the ramus and the mandibular body showed no significant enlargement (Table 4).

The HH and HE patients showed larger mandibular deviation angle compared with SCH, SMA and COS patients (Tables 3–4).

Table 2
Accuracy of CT features for diagnosis of HH.

	Sensitivity	Specificity	AUC
Condyle features			
Enlargement of condyle	93.5%	54.4%	0.777
Enlarged condyle with regular shapge	48.4%	81.8%	0.666
Enlarged condyle with deformed shape	54.8%	72.7%	0.645
Local limited exostosis	48.4%	81.8%	0.633
Tumor-like exostosis	6.9%	52.7%	0.324
Anterior Beak exostosis	29.0%	100%	0.645
Osteoarthrosis	29.0%	90.9%	0.635
Ramus and body features			
Enlarged ramus	87.1%	97.0%	0.956
Rounded angle	83.9%	100%	0.965
Bowing inferior border	96.8%	100%	0.983
Inferiorly displaced canal	87.1%	100%	0.968

(AUC: area under the curve).

3.4. Discriminant analysis

The quantitative measurement results were used to generate an adjunctive differential diagnosis. Five discriminant formulas for five diseases were constructed as follows. The variables X_1 to X_{15} stand for the anterior-posterior diameter (X_1), medial-lateral diameter (X_2), vertical height (X_3) and volume of the condyle (X_4); the volume (X_5), horizontal width (X_6) and vertical height (X_7) of the ramus; the vertical heights of the mental (X_8), premolar (X_9) and molar (X_{10}) regions; the horizontal widths of the mental (X_{11}), premolar (X_{12}) and molar (X_{13}) regions; the volume of the body (X_{14}) and the mandibular deviation angle (X_{15}). The measurement variables of each patient were imported into five formulas for calculation. The formula that produced the largest predictive value signified the classification to which the patient belonged. The accuracy rate of cross-validation was 85.7% (Table 5).

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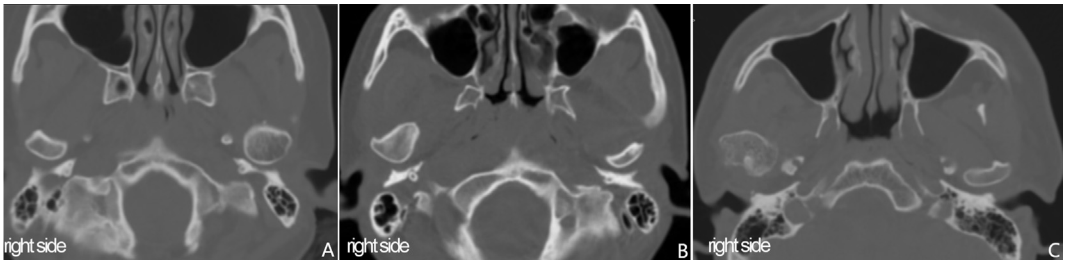

Fig. 6. Condylar morphologies in HH. A: The left condyle is regularly enlarged without an osseous exostosis. B: The right condyle is regularly enlarged with an anterior protruding beak. C: The right condyle is irregularly enlarged with a deformed shape.

4. Discussion

Terminology and classification consensus are of prime importance for a differential clinical diagnosis and treatment. There exists some confusion in regard to the term “condylar hyperplasia” (CH), which has been used to include several different clinical diseases, including HH, HE, SCH, SMA and COS, from the early publications to the present (Rushton, 1946; Norman and Painter, 1980; Wolford et al., 2009; Jones and Tier, 2012; Kyteas et al., 2017). These entities all present larger condyles on one side and asymmetry of the mandible but are of quite different pathological natures. The radiological quantitative data are provided in this study to support the differential diagnosis of these entities. We suggest that a practical differential diagnostic criterion and a widely accepted classification nomenclature for these entities is highly necessary.

Obwegeser and Wolford both made very clear definitions. The term “condylar hyperplasia” alone is inappropriate and inadequate in reference to any of these diseases. In Wolford's classification, CH Type 1 is compatible with HE (Wolford et al., 2009). Wolford further classified CH Type 1 into unilateral and bilateral types. Obwegeser also stressed the existence of bilateral HE, but he pointed out that HE never has an enlarged condyle, either clinically or radiologically, and that the architecture of the condyle is normal (Obwegeser and Makek, 1986; Obwegeser and Obwegeser, 2001). Although one side of the condyle is significantly larger than the contralateral side in HE, it is obviously incorrect to think that the larger condyle is hyperplastic (Obwegeser and Obwegeser, 2001). Our data also support that both linear and volumetric measurements of the condyles in HE are within the normal ranges. Furthermore, the condyles are not deformed, and no osseous exostosis exists in HE, which obviously differs from HH and SCH.

Wolford's classification of CH Type 2 is compatible with HH as described by Obwegeser. Typical HH exhibits very specific radiological signs, including an enlarged ramus, convexity of the mandibular inferior border, rounded angle, and inferiorly displaced mandibular canal. Severe HH exhibits more dramatic changes. There are also some mild or rudimentary types of HH (Obwegeser and Obwegeser, 2001), showing moderate or minor differences between the bilateral mandibles. According to our experience, very rudimentary HH can be easily confused with SMA. A noticeable change of increased distance between the apices of the molars and premolars on the affected side and inferior convexity of the mandibular lower border support the diagnosis of HH.

SCH has been defined by Obwegeser, but not specified by Wolford. One explanation is that SCH is truly much rarer than HH. SCH is characterized by an enlargement of the condylar head and/or neck without the involvement of the ramus and the body. Although the condylar enlargement and deformation is very similar to HH, the inferior convexity of the lower mandibular border and inferiorly displaced mandibular canal are always absent in SCH. We agree with Obwegeser that SCH should be differentiated from HH, because it is helpful for improving the understanding of the pathogenesis and the clinical management. Surgical treatment of SCH does not necessitate a contouring osteotomy of the inferior mandibular border (Obwegeser and Obwegeser, 2001). Sometimes SCH may be confused with condylar osteomas or osteochondromas developing from the top of the condyle; however, we strictly included cases with a very regularly enlarged condyle.

We use the term SMA to refer to a wide spectrum of generalized asymmetry of the mandible, which could be specified as any one of the diagnoses of HH, HE, SCH, COS or other well-known diseases. SMA is a developmental variant per se and may manifest as various degrees and forms of asymmetry. The condyles in SMA are also not hyperplastic. Although the condyle on the larger side of the mandible seems to be stronger, the condyles on both sides are morphologically and developmentally normal. A condylectomy could be obviated in both HE and SMA patients.

COS presents with a tumor-like osseous mass deriving from a normal condyle. In COS, a native condyle with a nearly normal-sized profile can be discerned. Except for the condylar region, the two sides of the mandible are of little difference. Quantitative measurement results also support this opinion. There is a special kind of COS featured by a huge osseous exostosis from the top of the condyle without a clear cortical demarcation from the native condyle, in which an enlargement of the condyle is seemingly obvious without the involvement of the ramus and the body. However, we think that it is better to consider this kind as COS rather than SCH, because the profile of a native normal condyle indicates that the exostosis should be a secondary disease rather than a developmental malformation.

Although Obwegeser and Makek's definitions of HH and HE have been gradually accepted and used by an increasing number of authors (Han et al., 2018), they have not been used consistently in all publications (Nolte et al., 2016). The first reason for this controversy is likely to be that the histopathological diagnosis does not play a prominent role in the diagnosis. The subjective imaging evaluation is the main basis for the diagnosis of this kind of disease. The second reason is that both HH and SCH are actually rare. HE is much more common and presents with a visually “hyperplastic” condyle. HE could be mistaken for condylar hyperplasia because the smaller condyle on the contralateral side could be easily used as normal control in individual case diagnosis. The last reason is that the deformation of the condyles in HH and SCH is very similar to that of a COS. Some cases of COS could be confused with condylar hyperplasia. The condyles in HH are often irregularly enlarged and deformed, with an anterior extending bony prominence called the “anterior beak” (Obwegeser and Obwegeser, 2001). This circumstance is common in HH and easily confused with COS; Wolford classified it as CH Type 2A with the description of osteochondroma

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Table 3
Three-dimensional quantitative measurements of the mandibles in mile, typical, severe and total HH patients.

	Normal value (Mean/SD)	Normal Upper Range	Mild HH(Mean/SD)			Typical HH(Mean/SD)			Severe HH(Mean/SD)			Total HH(Mean/SD)		
			Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2
Con-AP	6.8/1.4	9.6	14.7/4.6	6.7/1.2	0.002/0.002	15.8/5.4	6.8/1.2	<0.001/<0.001	19.2/3.6	6.4/1.5	<0.001/<0.001	16.2/5.2	6.6/1.3	<0.001/<0.001
Con-LM	17.5/2.4	22.2	16.8/2.9	17.6/2.3	0.607/0.708	19.5/2.8	17.7/2.2	0.051/0.015	22.9/4.7	17.7/2.4	0.003/0.005	20.1/4.1	17.8/2.2	0.003/0.003
Con-H	19.4/3.7	26.6	24.9/3.9	19.2/4.9	0.023/<0.001	27.4/2.5	20.0/3.0	<0.001/<0.001	34.3/6.9	20.1/3.5	<0.001/<0.001	28.9/6.0	20.3/3.8	<0.001/<0.001
Con-V	1.9/0.6	3.1	3.5/0.9	1.9/0.7	0.004/<0.001	4.6/1.3	1.8/0.5	<0.001/<0.001	7.8/3.5	1.9/0.7	<0.001/0.001	5.3/2.9	1.9/0.6	<0.001/<0.001
R–H	46.7/4.9	56.26	51.8/5.8	43.7/5.2	<0.001/<0.001	55.3/3.1	45.7/4.0	<0.001/<0.001	58.4/6.0	45.9/5.0	<0.001/<0.001	55.7/5.4	46.0/4.6	<0.001/<0.001
R-Width	32.2/2.96	38.0	29.8/3.4	31.2/2.8	0.292/0.636	32.4/2.8	31.1/2.3	0.206/0.274	31.3/4.6	30.7/4.0	0.694/0.355	31.2/3.6	32.1/3.1	0.133/0.153
R–V	8.5/2.5	13.4	9.7/3.2	8.7/2.0	0.012/0.076	10.6/2.4	8.6/1.1	0.003/0.061	10.8/3.1	7.5/2.1	0.002/0.079	10.7/2.8	8.5/1.8	<0.001/0.006
B-Mental-H	29.7/3.5	36.6	29.9/3.2	28.1/3.3	<0.001/0.561	30.8/3.4	28.3/3.0	<0.001/0.281	32.2/3.7	28.3/4.5	0.001/0.024	31.0/3.4	28.7/3.6	<0.001/0.045
B-premolar-H	29.5/3.5	36.4	31.8/3.6	27.4/3.3	0.025/0.661	33.4/2.5	28.3/3.1	0.070/0.556	34.8/3.1	29.0/4.8	0.003/0.435	28.5/3.7	27.1/3.0	<0.001/0.281
B-molar-H	27.8/3.0	33.7	30.7/2.7	25.8/3.6	<0.001/<0.001	33.0/1.6	27.4/2.5	<0.001/<0.001	33.8/3.5	26.6/3.1	<0.001/<0.001	32.8/2.8	27.1/3.0	<0.001/<0.001
B-Mental-L	17.6/1.7	20.9	17.1/1.5	17.3/1.5	0.264/0.633	18.7/1.3	17.9/1.4	0.022/0.056	19.8/1.0	18.2/1.0	0.010/<0.001	18.6/1.6	17.9/1.3	0.023/0.008
B-premolar-L	16.0/1.6	19.1	16.4/1.1	16.9/1.1	0.893/0.258	16.5/1.8	16.2/1.2	0.457/0.417	16.5/0.8	16.7/1.2	0.675/0.450	16.6/1.3	16.6/1.2	0.851/0.150
B-molar-L	25.1/1.3	27.6	24.0/1.4	24.9/1.1	0.671/0.480	24.7/1.9	25.1/1.6	0.561/0.475	25.1/0.9	25.9/1.3	0.096/0.954	24.8/1.4	25.3/1.4	0.126/0.444
B–V	23.5/4.3	31.93	25.4/4.6	22.9/4.7	<0.001/0.009	27.0/3.5	23.8/3.4	0.001/0.012	28.0/6.2	23.6/5.5	<0.001/0.004	27.4/4.8	23.9/4.5	<0.001/<0.001
Angle	–	–	5.4			8.7			15.9			9.9		

(Con:condyle; R:ramus; B:body; H:height; V: volume; L:length; M: normal mean; sd: standard deviation; Range: normal upper range; Angle: mandible deviation angle; AP: anterior-posterior; LM: lateral-medial; P^1: P value in comparison between the affected and the contralateral side; P^2: P value in comparison between the affected side and normal value; millimeter used in linear measurements; cm^3 used in volumetric measurements).

or exophytic tumor extension (Wolford et al., 2014a). From the three-dimensional observation, this condylar change could be seen as a restricted anterior extension of the medial pole. We think that this should be a form of functional adaptability due to distraction of the lateral pterygoid muscle rather than a tumor.

Quantitative measurements help reveal some striking features and differential points of these entities. Although the condyles in these entities are all visually and subjectively larger on the affected side, only the condyles in HH, SCH and COS extend beyond the upper range of the normal values. The condyles in HE and SMA could be considered as physiological asymmetry because the measurements do not support their enlargement in comparison to the normal values. The ramus and body in SCH show no quantitative differences between the two sides, which differentiates SCH from HH.

The pathogenic mechanism of HH remains unknown. In consideration that the condyle is the center of the major field of growth, it is reasonable to postulate that the condylar morphology is highly correlated with the growth status of the mandible. Factors such as vascular anomalies, trauma, endocrine and other factors have been taken into consideration (Olate et al., 2013; Eduardo et al., 2015). HH comes into being as a result of abnormal growth stimulation within the condyle. Resection of the affected condyle leads to the arrest of the abnormal growth (Norman and Painter, 1980). The stimulation mechanism of HH lies within the top layer of the condyle (Norman and Painter, 1980). Hyperactivity or hyperproduction of growth regulators lying within the fibrocartilaginous layer of the condyle affect either the longitudinal or the expansile growth of the same side of the mandible (Obwegeser and Makek, 1986).

Radionuclide examinations have been found to be a valuable tool in assessing the activity of condylar growth. The radionuclide uptake ratio of the bilateral condyles can be generated. An uptake difference above 10% is considered to be indicative of condylar hyperactivity (Yang et al., 2016; Wen et al., 2014). However, these examinations cannot be used as the gold standard due to unsatisfactory accuracy (Obwegeser and Makek, 1986; Alyamani and Abuzinada, 2012).

Because the condyle is regarded as the growth center for the mandible, whether a condylectomy should be performed to avoid postoperative recurrence is of importance. Deformed condyles with a cartilaginous or osseous exostosis outgrowth and increased radionuclide uptake ratio are candidates for a condylectomy (Rushton, 1946). The deformity progression can cease after a condylectomy in juvenile patients (Obwegeser and Makek, 1986; Bertolini et al., 2001). A condylectomy is also helpful for correcting facial asymmetry and reconstructing the temporomandibular joint (Sugawara et al., 2002; Lo et al., 2010; Singh et al., 2014; Kaya et al., 2007). Simultaneous orthognathic surgery and condylectomy could effectively correct the facial deformity (Han et al., 2018). Dissection of the mandibular nerve and osteotomy of the inferior border is sometimes needed in severe HH.

Three-dimensional technologies have been used to improve the diagnosis and treatment outcomes of mandibular deformities (Han et al., 2018; Hatamleh et al., 2017). Three-dimensional imaging, a computer-aided surgical plan and a navigation system, provide new and effective protocols for the accurate surgical correction of HH (Han et al., 2018; Eduardo et al., 2015; Hatamleh et al., 2017). A three-dimensional diagnosis is also of the utmost importance for surgical outcomes (Walters et al., 2013). The quantification of asymmetry could be useful for the evaluation of the degree of deformity and for monitoring disease progression (Nolte et al., 2016). Quantification also enables a classification of severity and provides insight into the pathogenesis and behavior of the disease.

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Table 4
Three-dimensional quantitative measurements of the mandibles in HE, SCH, SMA and COS patients.

	Normal value (Mean/SD)	Normal Upper Range	HE (Mean/SD)			SCH Mean/SD			SMA Mean/SD			COS Mean/SD		
			Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2	Affected	Normal	P^1/P^2
Con-AP	6.8/1.4	9.6	8.6/1.7	6.8/1.3	0.05/0.001	16.4/3.9	7.6/1.5	<0.001/<0.001	8.7/2.1	6.4/1.4	0.002/0.001	17.7/1.6	7.8/1.8	<0.001/<0.001
Con-LM	17.5/2.4	22.2	18.4/2.6	16.5/2.0	0.051/0.255	20.5/4.5	17.9/2.2	0.052/0.063	18.9/2.7	17.8/2.7	0.006/0.065	17.7/0.9	17.8/1.0	0.827/0.883
Con-H	19.4/3.7	26.6	24.4/2.8	18.7/2.1	<0.001/<0.001	31.8/6.1	20.4/2.8	<0.001/<0.001	22.7/4.5	17.3/5.1	0.002/0.015	23.8/2.9	18.2/1.8	0.008/0.023
Con-V	1.9/0.6	3.1	2.6/0.5	1.6/0.4	0.002/<0.001	5.6/2.4	2.1/0.5	0.001/0.001	2.6/0.7	1.5/0.6	0.001/0.001	4.0/0.7	2.1/0.2	0.007/<0.001
R–H	46.7/4.9	56.26	52.4/7.1	48.7/5.6	0.068/0.002	49.5/4.6	47.0/3.8	0.013/0.079	50.3/5.0	46.1/6.0	0.016/0.031	51.6/4.3	47.7/4.3	0.060/0.047
R-Width	32.2/2.96	38.0	32.3/3.8	31.1/3.1	0.173/0.940	31.9/2.6	32.6/2.3	0.089/0.803	33.1/3.5	32.8/3.7	0.823/0.430	31.9/1.6	33.1/2.7	0.237/0.874
R–V	8.5/2.5	13.4	9.3/2.9	8.9/2.6	0.365/0.780	8.4/1.3	9.8/4.8	0.377/0.495	9.5/2.1	8.9/2.3	0.360/0.561	9.9/2.5	9.7/2.5	0.006/0.488
B-Mental-H	29.7/3.5	36.6	32.4/3.1	31.7/3.1	0.100/0.017	31.4/2.8	30.6/2.6	0.016/0.095	29.6/3.3	28.9/3.3	0.008/0.941	29.9/1.4	29.4/2.1	0.290/0.607
B-premolar-H	29.5/3.5	36.4	31.9/3.2	31.7/3.2	<0.001/<0.001	32.5/1.9	30.4/2.2	0.036/0.009	30.3/3.3	28.9/3.6	0.004/0.258	31.3/2.5	30.4/1.7	0.149/0.088
B-molar-H	27.8/3.0	33.7	28.4/3.7	28.7/3.2	0.856/0.511	31.5/2.4	29.2/1.9	0.007/<0.001	28.5/3.8	27.2/3.3	0.017/0.459	30.6/2.1	28.8/2.5	0.015/0.060
B-Mental-L	17.6/1.7	20.9	18.9/1.6	17.8/1.5	0.014/0.036	16.8/1.7	16.7/1.8	0.837/0.156	17.8/1.1	17.5/1.4	0.373/0.667	18.1/2.8	17.1/4.0	0.204/0.578
B-premolar-L	16.0/1.6	19.1	15.7/2.6	16.6/2.2	0.291/0.694	15.7/1.4	15.4/1.7	0.167/0.396	15.2/1.6	16.1/2.0	0.752/0.116	16.8/0.9	15.3/1.3	0.546/0.380
B-molar-L	25.1/1.3	27.6	24.8/2.0	25.1/0.8	0.760/0.670	24.1/2.1	24.6/1.2	0.512/0.202	24.6/1.6	24.6/1.5	0.891/0.346	24.7/0.7	25.1/1.1	0.497/0.637
B–V	23.5/4.3	31.93	23.1/4.0	22.9/4.0	0.733/0.863	24.1/2.7	22.6/2.6	0.023/0.618	23.1/5.3	22.3/5.1	0.078/0.882	24.9/5.0	24.4/3.9	0.440/0.477
Angle	–	–	9.1						7.9				7.1	

(Con:condyle; R:ramus; B:body; H:height; V: volume; L:length; M: normal mean; SD: standard deviation; Range: normal upper range; Angle: mandible deviation angle; AP: anterior-posterior; LM: lateral-medial; P1: P value in comparison between the affected and the contralateral sides; P^2: P value in comparison between the affected side and normal value; millimeter used in linear measurements; cm^3 used in volumetric measurements).

Table 5
Three-dimensional quantitative measurements of the mandibles in HE, SCH, SMA and COS patients.

Patients	Discriminant Formulae
HH	$Y = -591.2 + 1.869X_1 - 3.392X_2 - 1.3X_3 + 0.002X_4 - 0.002X_5 + 6.505X_6 + 4.416X_7 + 5.381X_8 - 0.178X_9 + 9.671X_{10} + 8.0X_{11} + 9.29X_{12} + 15.2X_{13} - 0.011X_{14} - 3.162X_{15}$
HE	$Y = -597.9 + 1.227X_1 - 3.504X_2 - 1.9X_3 + 0.002X_4 - 0.002X_5 + 6.587X_6 + 4.696X_7 + 5.877_8 + 0.617X_9 + 8.265X_{10} + 8.754X_{11} + 7.959X_{12} + 15.8X_{13} - 0.012X_{14} - 3.107X_{15}$
SCH	$Y = -574.6 + 2.0X_1 - 3.050X_2 - 0.814X_3 + 0.002X_4 - 0.002X_5 + 6.447X_6 + 4.259X_7 + 5.022X_8 + 1.372X_9 + 8.733X_{10} + 7.423X_{11} + 9.232X_{12} + 14.84X_{13} - 0.012X_{14} - 3.409X_{15}$
SMA	$Y = -563.5 + 1.274X_1 - 3.199X_2 - 1.024X_3 + 0.001X_4 - 0.002X_5 + 6.443X_6 + 4.366X_7 + 5.304X_8 + 0.381X_9 + 8.888X_{10} + 8.291X_{11} + 7.782X_{12} + 15.49X_{13} - 0.012X_{14} - 2.959X_{15}$
COS	$Y = -605.6 + 2.346X_1 - 3.649X_2 - 1.642X_3 + 0.003X_4 - 0.002X_5 + 6.736X_6 + 4.315X_7 + 5.304X_8 + 0.979X_9 + 9.336X_{10} + 8.062X_{11} + 10.1X_{12} + 14.96X_{13} - 0.012X_{14} - 3.492X_{15}$

5. Conclusion

HH and SCH present with hyperplastic condyles with or without condylar deformation. Surgical excision could be considered for severely deformed condyles in HH or SCH. HE and SMA are caused by the imbalanced development of bilateral condyles. The condyles are not hyperplastic, and surgical excision is not necessary in HE and SMA. COS is a tumor or tumor-like disease, in which the condyle may sometimes mimic hyperplasia and necessitate excision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.08.001.

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