

Age-Dependent Histological Morphotypes in Mandibular Condylar Hyperplasia: A Preliminary Report

Morfotipos Histológicos Dependientes de la Edad en la Hiperplasia Condilar Mandibular: Informe Preliminar

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SUMMARY: Mandibular condylar hyperplasia or hyperactivity (CH) is characterized by excessive growth of the mandibular condyle, causing functional and esthetic disturbances. Its histopathological basis remains controversial, as features traditionally described in CH have also been reported in non-hyperplastic condyles. This pilot study aimed to set the basis for defining histological morphotypes of CH in relation to patient age and comparing them with a cadaveric control. An observational, retrospective pilot study was conducted on condyles excised from seven patients (17–55 years) with unilateral CH treated by condylectomy between 2017 and 2018. As a single non-CH comparative sample, two condyles from a 65-year-old fresh cadaver were included. Specimens were processed for paraffin-embedded hematoxylin–eosin staining. Two blinded observers reviewed slides assessing cartilage thickness, subchondral cortical bone, trabecular orientation, and cartilage islands. Three morphotypes were identified: juvenile (<20 years), with thick proliferative layer, cartilage islands, thin vertical trabeculae, and absent cortical bone; transitional (20–27 years), with thinner proliferative layer, fewer cartilage islands, discontinuous cortical bone, and heterogeneous trabeculae; and adult (≥28 years), with loss of proliferative layer, scarce cartilage, thick trabeculae in multiple orientations, and continuous cortical layer. Control condyles resembled the adult morphotype but showed focal cartilage penetration and possible osteophyte formation. These findings suggest age-dependent morphotypes in CH, which may often represent adaptive remodeling rather than a purely pathological process.

KEY WORDS: Mandibular Condyle; Hyperplasia; Temporomandibular Joint.

INTRODUCTION

The head of the mandibular condylar process (commonly known among clinicians as “mandibular condyle”) is one of the anatomical components of the temporomandibular joint (TMJ). The mandibular condyle undergoes dynamic changes throughout life. It becomes a mature osteoarticular structure by endochondral ossification during growth and plays a fundamental role in adaptive remodeling in response to mechanical stimuli (Nickel *et al.*, 2018). Mandibular condylar hyperplasia (also known as “condylar hyperactivity”; CH) is a condition

characterized by an abnormal and disproportionate growth of the mandibular condyle, leading to facial asymmetry, occlusal changes, and oro-facial functional alterations (Villanueva-Alcojol *et al.*, 2011). Despite its well-described clinical signs, the etiology and pathophysiology of CH are not yet fully understood. Traditionally, diagnosis has been based on clinical, imaging, and in some cases, histopathological criteria, the latter being subject to debate due to the low specificity of the histological features (Vásquez *et al.*, 2016).

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The histopathology of excised condyles in CH patients has historically been interpreted as a reflection of the proliferative state of its cartilage layer, with classifications such as that of Slootweg and Müller (1986), which distinguished histological types according to the presence of proliferative cell layers (Slootweg & Müller, 1986). However, later studies have reported similar patterns in condyles of subjects without CH, calling into question the diagnostic validity of these criteria (Saridin *et al.*, 2010; Espinosa *et al.*, 2021). In parallel, Wolford *et al.* (2014) proposed an etiological classification, not broadly used in clinical practice, that recognized multiple causes of CH, including neoplastic, hormonal, and functional factors.

An alternative hypothesis is that CH may correspond to adaptive responses to increased or asymmetric functional loads rather than a nosological entity. This concept is supported by animal models in which masticatory overload induced morphological and histological condylar changes without evidence of structural pathology (Chen *et al.*, 2009; Balanta-Melo *et al.*, 2018; Toro-Ibacache, *et al.*, 2025a). At the cellular level, it has been described that mechanical stimulation generates an osteogenic response mediated by sustained shear stress (Daegling *et al.*, 2021) and by molecular muscle–bone crosstalk (Buvinic *et al.*, 2021), reinforcing the adaptive theory. Otherwise, it has been proposed that histological features such as proliferative cartilage, chondrogenic islets, or irregular trabeculation may not reflect active hyperplasia but condylar remodeling at different stages (Villanueva-Alcojol *et al.*, 2011). Furthermore, Espinosa *et al.* (2023) have shown that single-photon emission computed tomography (SPECT) may over- or underestimate condylar activity. At the same time, Gray *et al.* (1990) highlight the lack of correlation between imaging activity and histology.

This preliminary study proposes the concept of age-dependent Condylar Morphotypes in CH, defined as a range of histological patterns that vary with biological age, as opposed to a set of histological findings defining CH. By analyzing a series of CH condyles diagnosed with CH and comparing them with those from a cadaveric sample, we describe histological condylar morphotypes and evaluate their association with patient age. CH may often represent an adaptive condition expressed differently among ages rather than a specific pathological entity.

MATERIAL AND METHOD

Ethical Approval. All procedures were approved by the Research Ethics Committee of the Metropolitan North Health Service of Chile (No. 086/2024) and the study was conducted by the Helsinki Declaration of 1975, as revised in 2000.

Cadaveric samples were obtained and processed in accordance with ethical guidelines for the use of human anatomical material.

Study Design. An observational, retrospective case series pilot study of human resected condyles was conducted. We compared them with the condyles of a single non-CH.

We included seven resected mandibular condyle samples coming from patients (range 17- 55 years old), diagnosed with unilateral CH and treated by proportional condylectomy at the Maxillofacial Surgery Unit of Hospital San José between 2017 and 2018 (Santiago, Chile) (Tousidonis *et al.*, 2025). Two mandibular condyle samples resected by the proportional technique from a 65-year-old fresh cadaveric male donor were used as the single non-CH comparative sample. The donor was considered non-CH because of his facial symmetry and maintenance of vertical dimension by the presence of bilateral posterior maxillo-mandibular teeth. The donor surgery was performed according to the protocols of the Department of Anatomy and Legal Medicine of the Universidad de Chile.

Technical Protocol. Resected condyles were fixed in 10 % formalin, decalcified in EDTA-based solution (Osteosoft, Merck KGaA, Darmstadt, Germany), and subsequently embedded in paraffin blocks. Histological sections of 5 µm thickness were obtained and stained with hematoxylin-eosin (H&E).

Two independent observers (JPB and VTI), blinded to the clinical diagnosis and patient age, re-evaluated the slides for this work under a transmitted-light optical microscope. Considering clinical relevance, the current use of previous histopathological classifications of CH patients, and developmental anatomy criteria, we qualitatively evaluated the thickness of the total articular cartilage and of the hypertrophic (deep) cartilage layer, the presence of subchondral cortical bone, trabecular bone characteristics (thickness, orientation), and the presence of cartilage islands within bone trabeculae

RESULTS

Table I summarizes the histological characteristics of the seven condyles analyzed.

Based on the histological criteria evaluated, three predominant histological morphotypes were defined according to age range: juvenile, transitional, and adult (Fig. 1).

Two cases of 17- and 19-year-olds showed the juvenile morphotype. They exhibited a thick proliferative

Table I. Characterization of condyles with hyperplasia and controls.

Cases	Sex	Age (Years)	Affected Side	Condylar Cartilage Thickness	Greater thickness condylar cartilage (mm)	State of Fibrous Articular Layer	Hypertrophic Cartilage Layer	Bone Penetration of Cartilage Layer	Presence of Subchondral Cortical Bone	Bone Trabeculae
1	M	17	Left	Uniform Thickness	0,63	Continuous	Uniform Thickness	Trabecular Bone	Not	Thin and Vertical Organization
2	M	19	Left	Not Uniform Thickness	0,51	Discontinuous	Uniform Thickness with localized thickening	Trabecular Bone	Not	Thin and Vertical Organization
3	M	22	Right	Uniform Thickness	0,6	Detachment by artifactual separation	Not Uniform Thickness	Subchondral Cortical Bone	Yes	Thick and organized in different directions
4	M	27	Right	Not Uniform Thickness	0,49	Detachment by artifactual separation	Uniform Thickness	Absent	Yes	Thin and Vertical Organization
5	F	28	Left	Uniform Thickness	0,26	Detachment by artifactual separation	Uniform Thickness	Absent	Yes	Thin and Vertical Organization
6	F	29	Left	Not Uniform Thickness	NA	Discontinuous	Uniform Thickness with localized thickening	Subchondral Cortical Bone	Yes	Thick and organized in different directions
7	F	55	Right	Not Uniform Thickness	0,49	Continuous	Absent	Absent	Yes	Thick and organized in different directions
C1 (L)	M	65	Left	Uniform Thickness	0,69	Continuous	Uniform Thickness with localized thickening	Subchondral Cortical Bone	Yes	Thick and organized in different directions
C2 (R)	M	65	Right	Uniform Thickness	1,07	Continuous	Uniform Thickness with localized thickening	Subchondral Cortical Bone	Yes	Thick and organized in different directions

C1 (L): Left Control Condyle, C2 (R): Right Control Condyle, F: Feminine, M: Masculine, NA: Not Available.

layer, a thick hypertrophic cartilage layer, numerous cartilage islands within thin and vertically oriented bone trabeculae, and the absence of subchondral cortical bone (Fig. 1).

The transitional morphotype was observed in two cases of 22 and 27-year-olds. They showed a reduction in the thickness of the proliferative layer, a still present hypertrophic cartilage layer, and a few cartilage islands located within bone trabeculae. In this morphotype a subchondral cortical bone layer, with variable thickness, was observed. Bone trabeculae show heterogeneous thickness and orientations (Fig. 1).

The adult morphotype was observed in three samples from individuals aged 28, 29, and 55 years old. They featured the absence of the proliferative cartilage layer, scarce cartilaginous tissue in bone, and a thick, mature subchondral layer of cortical bone (Fig. 1).

The two control condyles samples obtained from the 65-year-old donor exhibited thick and homogeneous articular cartilage and the absence of a proliferative layer. These features were similar to those observed in the 55-year-old adult morphotype case. Interestingly, we observed localized cartilage penetration into the trabecular bone in both control samples, as observed in the young morphotype (Fig. 2).

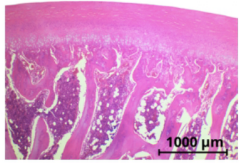
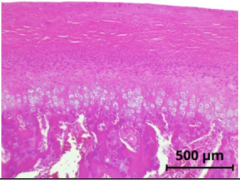
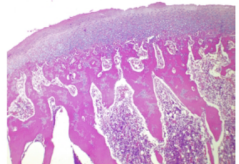
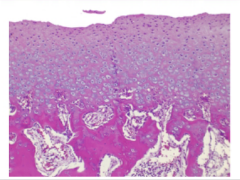
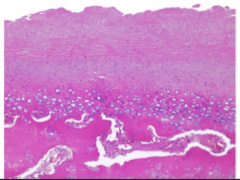
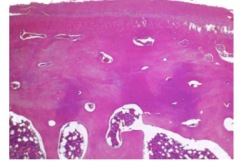
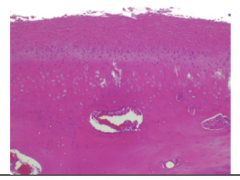
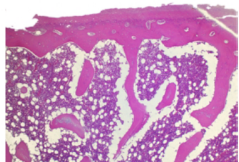
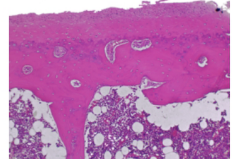
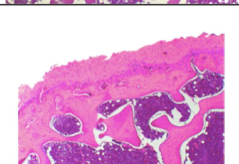
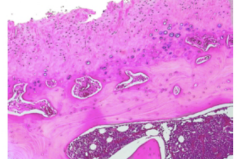
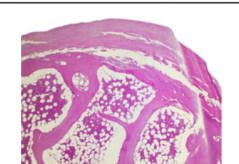
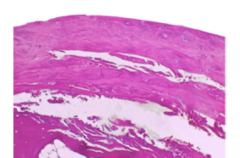
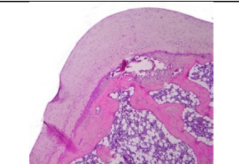
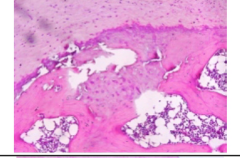
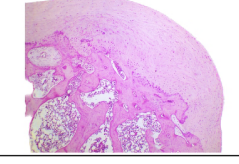
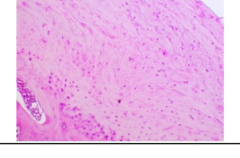
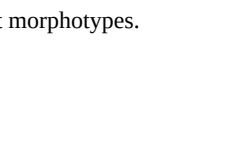
Condylar Hyperplasia Cases	Age	4x	10x	Morphotype
	17 y.o.			Juvenile
	19 y.o.			
	22 y.o.			Transitional
	27 y.o.			
	28 y.o.			Adult
	29 y.o.			
	55 y.o.			
				
Normal Condyles (Control)	65 y.o. (L)			
	65 y.o. (R)			

Fig. 1. Age-dependent morphotypes.

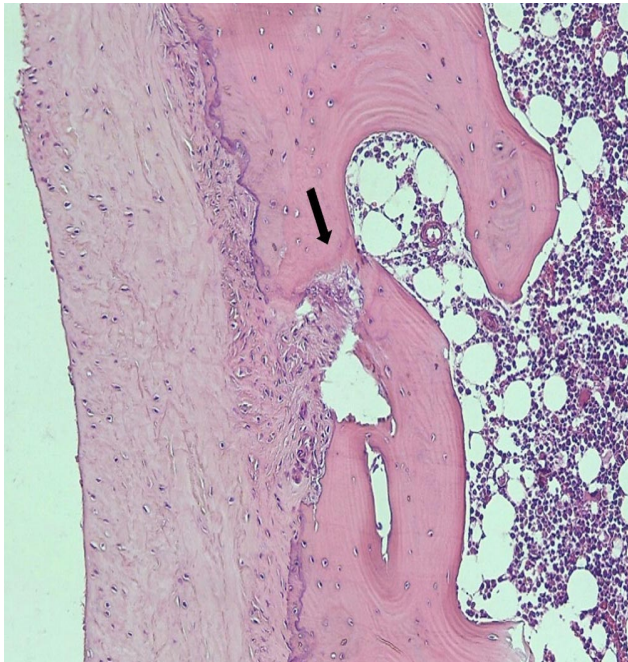


Fig. 2. Right control condyle with localized thickening of hypertrophic cartilage and penetration (arrow) into the thickness of the subchondral cortical bone

DISCUSSION

Our findings support the hypothesis that resected CH samples show age-dependent gradient changes (Fig. 3). The

condyles of CH patients appear to transition from a juvenile morphotype characterized by a thick proliferative and hyperplastic cartilage layer, absent subchondral cortical bone, and thin vertically oriented trabeculae with cartilage islands; to an adult, “mature” morphotype lacking proliferative and hyperplastic cartilage, featuring a defined subchondral cortical bone layer, and thick organized trabeculae. This adult morphotype resembles the non-CH samples suggesting that condyles in adult asymmetric patients may undergo adaptive remodeling of osteo-cartilaginous tissues rather than a pathological process.

The remodeling of cartilage and bone under mechanical demands is a physiological process that allows structural tissue and organ-level adaptation to withstand their loading scenario. The mandibular surface of the TMJ in humans (Koolstra & Van Eijden, 2005) and some mammals undergoes mainly compressive stress and strain during mastication (Ravosa *et al.*, 2007). Experimental work on rodents and primates has shown that mechanical stimuli such as orthopedic mandibular advancement (Owtad *et al.*, 2013), masseter unilateral paralysis (Balanta-Melo *et al.*, 2018) and soft diet (Chen *et al.*, 2009) showed that the cartilage and bone of the condyles are augmented, decreased and reorganized in response to the changing loading conditions. These studies support the idea of TMJ’s adaptive capacity. On the other hand, sustained, significant overload in time would cause degenerative changes (i.e., matrix alteration and chondrocyte apoptosis) at the TMJ cartilage (Ravosa *et al.*, 2007).

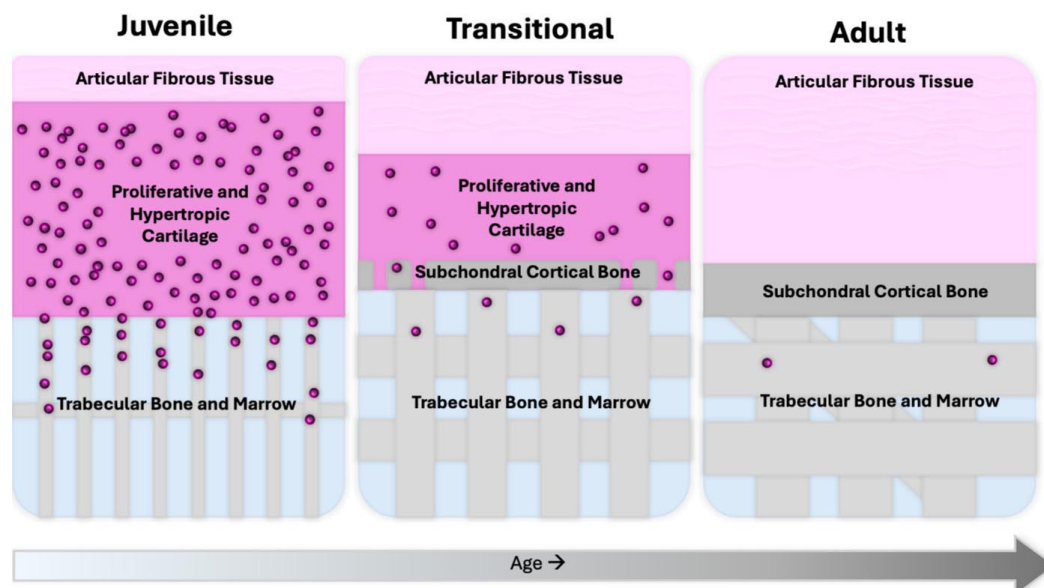


Fig. 3. Schematic representation of the proposed three morphotypes: juvenile, transitional, and adult. The figure illustrates the progressive organization of the condylar fibrocartilage and subchondral bone with age, from a diffuse proliferative cartilage with thin trabeculae (juvenile) to a well-defined subchondral cortical layer and organized trabeculae (adult).

Age is relevant to the adaptation capacity of the mandible. Chewing efficiency decreases with age (Peyron *et al.*, 2004), and more chewing cycles are needed for bolus formation. Likewise, bone has a reduced capacity to sense and respond to functional demand in older humans (Zhang *et al.*, 2024). Therefore, during somatic growth, the TMJ would have an increased capacity to react and respond to alterations in chewing conditions (which could explain the higher incidence of CH in younger individuals). Older individuals can also adapt in a more limited manner, which agrees with the histological features of the adult morphotype, which is quite similar to that of the control individual. Although our preliminary study has a reduced sample size, the histological findings result agree with Slootweg & Müller (1986) and Espinosa *et al.* (2021) in the suggested age dependence of the histologic findings. However, there is a large variability observed in the control samples of other studies, questioning the diagnostic specificity of the “CH features” (Vásquez *et al.*, 2016; Espinosa *et al.*, 2021). A large sample size of cases and adequate controls (in age, functional, and metabolic status), which are difficult to find, is an aim for future research.

However, why could CH be the product of an asymmetric mandibular response? Chewing in humans is an intrinsically asymmetric process, in both muscle activation and generated forces (Buvinic *et al.*, 2021). During this process, the TMJ surfaces are mainly subjected to compressive stress and strain (Toro-Ibacache, *et al.*, 2025b), and these strains are not symmetrical in magnitude even when the biting scenario is symmetrical (Toro-Ibacache & O’Higgins, 2016; Toro-Ibacache, *et al.*, 2025b). This can be attributed to the intrinsic anatomical asymmetry of the craniofacial skeleton and the craniomandibular muscles. Espinosa *et al.* (2019) showed in a group of unilateral CH-diagnosed individuals that their mandibles are not only bilaterally asymmetric but also have a wide shape range, in several cases similar to that of non-clinically asymmetrical mandibles. An asymmetric structural adaptation can be the result of individual factors, such as occlusal plane inclination (Chen *et al.*, 2009; Toro-Ibacache, *et al.*, 2025b), presence of occluding posterior teeth (Kotanlı *et al.*, 2024), or even sex, since women are more affected by CH and TMJ disorders, which has been linked to hormonal factors (Raijmakers *et al.*, 2012). Further research is thus needed that considers such possibilities.

The results of this pilot study may contribute with data to establish a morphological baseline in CH cases, which can be further strengthened to support clinical decision-making regarding surgical intervention when functional alterations have not yet been addressed. It is important to emphasize that histology must be integrated with clinical and imaging data, avoiding therapeutic decisions based solely on histology (Espinosa *et al.*, 2019). Limitations of this

preliminary study include its small sample size, retrospective nature, and absence of imaging and molecular analyses. Future research should focus on multicenter studies with matched cases and controls, incorporating histomorphometry, molecular analyses, biomechanical modeling, and longitudinal follow-up to confirm and expand these findings.

CONCLUSION

We qualitatively described histological changes in CH samples identifying juvenile, transitional, or adult morphotypes. Our findings suggest CH may represent an adaptive recapitulation of juvenile morphotypes in adulthood in response to functional loading, supporting CH as an adaptive condition rather than a pathological entity. These preliminary results require cautious interpretation. Future studies should include larger, multicenter cohorts with well-characterized controls and standardized histological, molecular, and biomechanical analyses.

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RESUMEN: La hiperplasia o hiperactividad condilar mandibular (HCM) se caracteriza por un crecimiento excesivo del cóndilo mandibular, que causa alteraciones funcionales y estéticas. Su base histopatológica sigue siendo controvertida, ya que características tradicionalmente descritas en la HCM también se han observado en cóndilos no hiperplásicos. Este estudio piloto tuvo como objetivo establecer las bases para definir los morfotipos histológicos de la HCM en relación con la edad del paciente y compararlos con un grupo control cadavérico. Se realizó un estudio piloto observacional y retrospectivo en cóndilos extirpados de siete pacientes (17–55 años) con CH unilateral tratados mediante condilectomía entre 2017 y 2018. Como muestra comparativa única sin CH, se incluyeron dos cóndilos de un cadáver embalsamado de 65 años. Las muestras se procesaron para tinción con hematoxilina-eosina incluidas en parafina. Dos observadores cegados revisaron las láminas evaluando el grosor del cartílago, el hueso cortical subcondral, la orientación trabecular y las islas de cartílago. Se identificaron tres morfotipos: juvenil (<20 años), con capa proliferativa gruesa, islas de cartílago, trabéculas verticales delgadas y ausencia de hueso cortical; transicional (20–29 años), con capa proliferativa más delgada, menos islas de cartílago, hueso cortical discontinuo y trabéculas heterogéneas; y adultos (≥30 años), con pérdida de la capa proliferativa, cartílago escaso, trabéculas gruesas en múltiples orientaciones y capa cortical continua. Los cóndilos de control se asemejaban al morfotipo adulto, pero presentaban penetración focal del cartílago y posible formación de osteofitos. Estos hallazgos sugieren morfotipos dependientes de la edad en la hiperplasia cóndilomandibular, que a menudo representan una remodelación adaptativa más que un proceso puramente patológico.

PALABRAS CLAVE: Cóndilo mandibular; Hiperplasia; Articulación temporomandibular.

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