Archives of Oral Biology 97 (2019) 67–71

Contents lists available at ScienceDirect

Archives of Oral Biology

journal homepage: www.elsevier.com/locate/archoralbio

Effects of articular disc or condylar cartilage resection on mandibular growth in young rats

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ARTICLE INFO

Keywords:
Resection
Articular disc
Condylar cartilage
Mandibular growth

ABSTRACT

Objective: This study was aimed to compare the effects of articular disc and condylar cartilage resection on mandibular growth in Sprague Dawley rats.

Design: Eighty-four male Sprague Dawley rats (age = 4 weeks) were grouped according to the following procedures: group A (n = 21), exclusive surgical exposure of articular disc and condylar cartilage; group B (n = 21), exclusive surgical resection of articular disc; group C (n = 21), exclusive surgical resection of condylar cartilage; group D (n = 21), surgical resection of both articular disc and condylar cartilage. All surgery was performed in unilateral. One rat was killed in each group immediately after the surgery. Hematoxylin and eosin (H&E) staining was used to confirm the completely removal of the disc or cartilage. Five rats in the four groups were sacrificed in 1, 3, 6, and 9 weeks post-operation. The heights and lengths of the mandibles were measured and analyzed statistically.

Results: The mandibular height of group D (5.01 ± 0.25 mm) was statistically lower than group A (5.59 ± 0.17 mm) at 1 week post-operation. The height of group C (5.62 ± 0.26 mm) was significantly lower than group A (6.27 ± 0.31 mm) 3 weeks after surgery. The height of group B (6.38 ± 0.36 mm) was significantly lower than group A (6.95 ± 0.10 mm) 6 weeks after surgery. At 9 weeks post-operation, the mandibular heights in groups B, C, and D were lower than group A, group D was lower than group C, and group C was lower than group B. The lengths of the mandibles were not significantly decreased until 9 weeks post-operation in group D.

Conclusions: The increase in mandibular height was interfered after either articular disc or condylar cartilage was resected, and mandibular height deficiency likely occurred earlier and more severely when cartilage was resected. However, the increase in mandibular length was barely interfered when either articular disc or condylar cartilage was resected.

1. Introduction

Mandibular deformity is related to previous trauma to the temporomandibular joint (TMJ). Clinical studies have revealed that prepubertal trauma can be considered an etiologic factor for the development of mandibular asymmetry (Sjursen, Legan, & Werther, 1999; Skolnick, Iranpour, Westesson, & Adair, 1994).

Condylar cartilage and TMJ disc both play an important role in mandibular growth (Dimitroulis, 1997). Condylar cartilage can provide a strong and flexible provisional supportive framework at a relatively high growth rate. The adaptive remodeling of condylar cartilage was initiated from chondrogenesis and finalized with osteogenesis. This ability is implicated in embryonic and postnatal growth. Condylar cartilage injury may induce significant damages to mandibular growth and result in mandibular deformity (Copray, Dibbets, & Kantomaa, 1988; Feng, Li, He, Yang, & Qiu, 2012; Pirttiniemi, Peltomaki, Muller, & Luder, 2009).

Meanwhile, The articular disc regulates the condylar biomechanical environment in the TMJ and affects mandibular growth. Injury or resection of articular disc can impede the normal growth of the ramus and result in the asymmetry of the mandible (Toledo, Cavalcanti, Correa, & Luz, 2014). This may result from primary influence on condyle growth (Legrell, Reibel, Nylander, Horstedt, & Isberg, 1999) or by secondary loss of condyle mass due to degenerative cartilage breakdown (Legrell & Isberg, 1999; Li & Li, 2012; Toledo et al., 2014).

However, the effect of resecting condylar cartilage or articular disc

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https://doi.org/10.1016/j.archoralbio.2018.10.005
Received 8 June 2018; Received in revised form 24 September 2018; Accepted 4 October 2018
0003-9969/

on mandibular growth has yet to be compared. A suitable animal model is urgently necessary to better understand the different role on the development of mandible between resection of disc and cartilage. This study aimed to compare the different effects on mandibular growth in young rats between resecting condylar cartilage and articular disc.

2. Materials and methods

2.1. Surgical procedures

Eighty-four 4-week-old male Sprague Dawley rats were fed with rodent feed. They were divided into the following four groups: sham operated (group A, n = 21), disc resection (group B, n = 21), cartilage resection (group C, n = 21), and both disc and cartilage resection (group D, n = 21). The study was approved by the Peking University Biomedical Ethics Committee (Approval no. LA2014235).

The rats were anesthetized by intraperitoneally injecting 400 μl/100 g of 2% pentobarbital sodium. A 1 cm pre-auricular incision was made on the right side. The parotid tissues were lifted, and the masseter muscle was blunt-dissected. The joint capsule was opened and the condyle was exposed below the zygomatic arch. The disc and condylar cartilage of group A were exposed but were still intact. In group B, the articular disc and associated attachments were resected by scalpel and forceps. In group C, the condylar cartilage was resected with a scalpel. In group D, both disc and cartilage were resected. The incision was closed by suturing in layers.

One rat was killed in each group immediately after the surgery. Whole heads of rats were dissected and collected. Next, the samples were fixed in 4% paraformaldehyde (PFA) and demineralized in 0.5 M ethylenediaminetetraacetic acid (EDTA) for 2 weeks. Subsequently, the samples were embedded in paraffin and cut with a thickness of 5 μm for regular hematoxylin and eosin (H&E) staining. The histological analysis was used to conform that the disc or cartilage had been resected.

All animals were fed a soft diet for the first 5 days after surgery and a solid diet thereafter. Five rats in groups A, B, C, and D were killed at 1, 3, 6, and 9 weeks after the operation (Furstman, 1966). The mandibles were isolated and fixed in 4% paraformaldehyde (Table 1). The body weight was measured before surgery and 1, 3, 6, and 9 weeks after surgery, which was used as an indicator of general growth.

2.2. Mandible measurements

The mandible was split into two halves along the median sagittal plane, and radiographic images were taken on the operated sides in each group using a standard dental X-ray machine (70 kV, 7 mA; Minray, Soredex, Finland). The exposure time was 0.12 s. The X-ray tube was directed toward the TMJ area perpendicular to the sagittal plane of the specimen.

Table 1
The animal groups in the study.

Groups	Numbers of animals					Total
	Immediately after surgery	1 week	3 weeks	5 weeks	9 weeks	
Sham operated group	1	5	5	5	5	21
Disc resection group	1	5	5	5	5	21
Cartilage resection group	1	5	5	5	5	21
Disc and cartilage resection group	1	5	5	5	5	21
Total	4	20	20	20	20	84

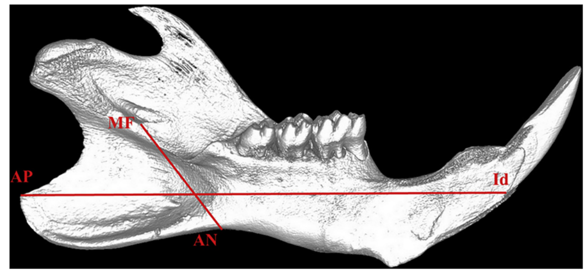

Fig. 1. Landmarks of mandible measurements.
Id, the most anterior limit of the lower bone insertion of the incisor.
AP, the apex of angular process peculiar to the rodent mandible.
MF, the most inferior and posterior point of the mandibular foramen.
AN, the most superior point of the convexity of the lower border of the mandible.

The specimens were trimmed, and the soft tissue was removed to clearly expose each anatomical landmark. Mandibular length and height were measured. Measurements were collected by an electronic digital caliper (0.02 mm resolution) with reference to the following anatomic landmarks (Fig. 1): Id-AP, the distance from the infradentale (Id) to the angular process (AP) representing the mandibular length. MF-AN: the distance from the mandibular foramen (MF) to the antegonial notch (AN) representing the mandibular height. Measurements were repeated thrice, and the mean was subjected to statistical analysis. The investigator measuring the mandible was blinded to the groupings of the experiment.

2.3. Statistical analysis

Data were statistically analyzed using SPSS version 20.0 for Windows. Twenty cases were selected randomly, and the same investigator repeated the measurements at least 2 weeks apart to assess the reliability of the method. Paired *t* test was performed to assess the systematic error. Dahlberg formula (Dahlberg, 1940) was considered to calculate the random error.

Paired *t* test was performed to evaluate the differences between means for the right and left sides in each group. One-way ANOVA was conducted to verify the possible differences among the four concomitantly compared groups. Bonferroni's multiple comparison test was carried out to identify the groups that differed from the sham operated group.

3. Results

Paired *t* test assessing the systematic error revealed that no significant difference at $p = 0.05$. The random error of linear measurement varied from 0.15 mm to 0.20 mm.

The body weights in the group B, C, and D were similar to those in the group A, with no significant differences during the experimental period. Thus, resection of disc and cartilage had no substantial influence on general growth (refer to Mendeley Data: https://doi.org/10.17632/r4j864ysth.4).

The histological results definitively proved that the disc or cartilage had been resected (Fig. 2). The means of the mandibular height are presented in Fig. 3. The heights of the mandible on the operated sides were significantly smaller than those on the contralateral sides 1 week after the operation except in group A. The mandibular heights on the operated sides differed significantly among the four groups (Fig. 4). The mandibular heights in group D (5.01 ± 0.25 mm) were significantly smaller than in group A (5.59 ± 0.17 mm) 1 week after the surgery, in group C (5.62 ± 0.26 mm) were significantly smaller than in group A (6.27 ± 0.31 mm) 3 weeks after the surgery, and in group B (6.38 ± 0.36 mm) were significantly smaller than in group A

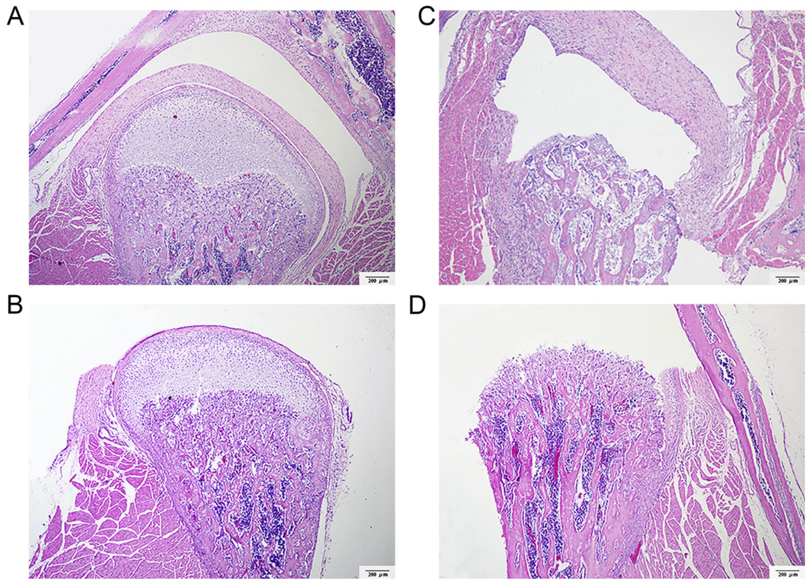

Fig. 2. The histological analysis immediately after the surgery in different groups: A. Sham operated group, B. Disc resection group, C. Cartilage resection group, D. Disc and cartilage resection group.

(6.95 ± 0.10 mm) 6 weeks after the surgery. At 9 weeks after the surgery, the mandibular heights in groups B, C, and D were all significantly smaller than in group A. Moreover, the mandibular heights were significantly smaller in group C (condylar cartilage resected) than in group B (disc resected).

The mean values of the mandibular length are presented in Fig. 5. A significant difference between the operated and contralateral sides was not observed until 6 weeks after the operation. When comparing mandibular length among groups, the results showed little difference (Fig. 6).

Lateral radiographs clearly showed that the degenerative condylar changes occurred 1 week later once the condylar cartilage was resected, while occurred 3 weeks later if only the disc was resected (Fig. 7).

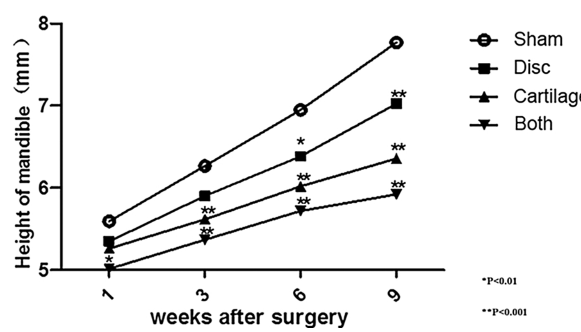

Fig. 4. Bonferroni's multiple comparison test was conducted to determine the groups that differed from the sham operated group in terms of mandibular height at $^{*}P < 0.01$ and $^{**}P < 0.001$.

4. Discussion

In this study, the roles of the disc and cartilage in mandibular development were compared. Either resection of disc or cartilage resulted in the asymmetry of the mandible and mainly affect the mandibular height. Cartilage resection caused more severe mandibular asymmetry than disc resection, and also the asymmetric effect attributed to cartilage resection occurred earlier.

In the growth stages, condylar cartilage was traditionally considered

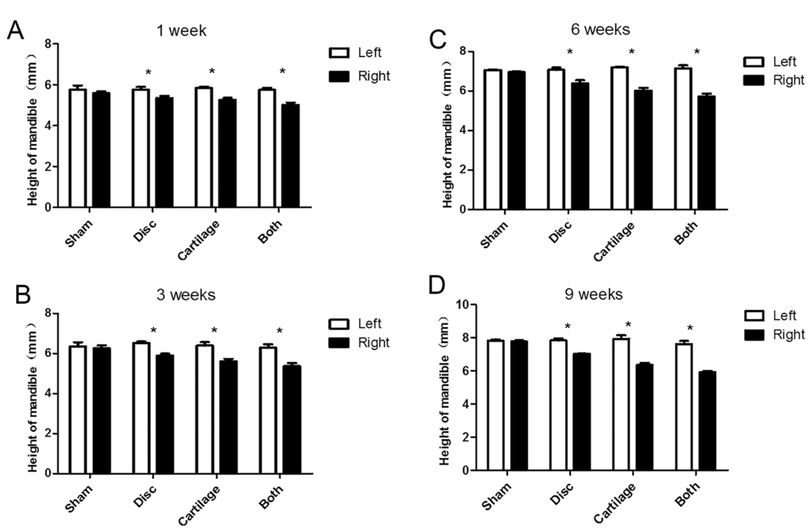

Fig. 3. Linear measurement of mandibular height. Paired *t* test was performed to identify the difference between sides at $^{*}P < 0.05$.
Sham, sham operated group; Disc, disc resection group; Cartilage, cartilage resection group; Both, disc and cartilage resection group (the same as below).

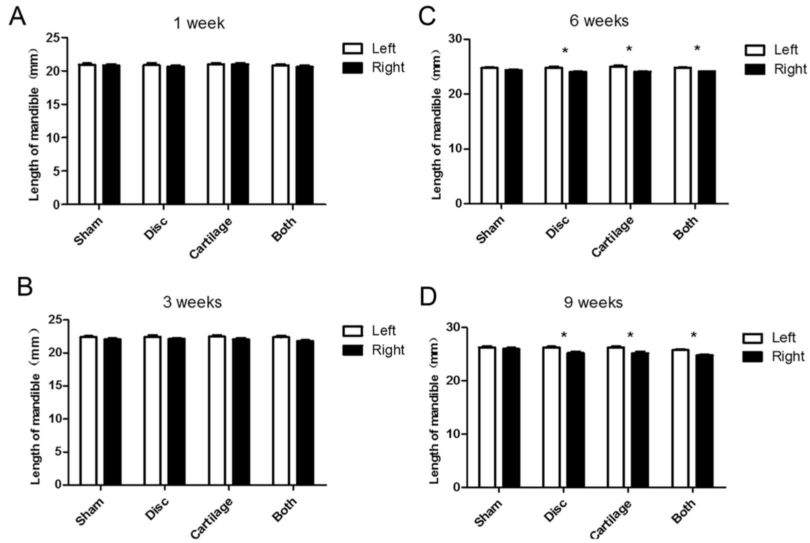

Fig. 5. Linear measurement of mandibular length. Paired t test was performed to identify the difference between sides at $^{*}P < 0.05$.

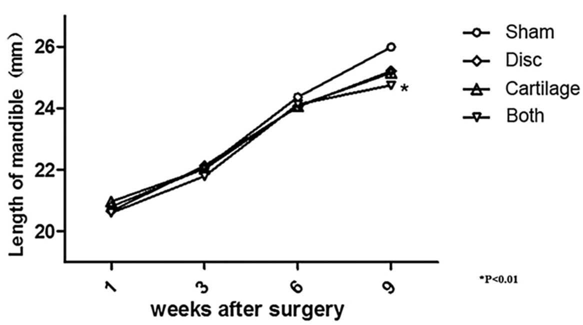

Fig. 6. Bonferroni's multiple comparison test was carried out to determine the groups that differed from the sham operated group in terms of mandibular length at $^{*}P < 0.01$.

as a development center of the condylar process (Copray et al., 1988), and its growth and adaptive remodeling consists of two processes: chondrogenesis and endochondral bone formation. The cartilage surface is covered by a thin layer of fibrous tissue in which there are undifferentiated mesenchymal cells (Shen & Darendeliler, 2005). The mesenchymal cells constantly differentiate into chondrocytes, which proliferate and then progressively mature into hypertrophic cells. The transition from chondrogenesis to osteogenesis is a process in which hypertrophic chondrocytes and matrices are degraded and are replaced by bone (Owtad, Park, Shen, Potres, & Darendeliler, 2013; Shen & Darendeliler, 2005). This process results in the growth of the mandibular condyle and lengthens the mandibular ramus. The progenitor cells in the superficial layer of the cartilage were removed and the transition from chondrogenesis to osteogenesis was disrupted when the cartilage of condyle was resected. Therefore, the decrease of mandibular height was observed.

The important role of articular disc during condylar growth has been well reported. Legrell et al has revealed that a reduction of ramus height and mandibular length in growing rabbits can be induced by disk displacement at a stage before the development of degenerative changes (Legrell et al., 1999). This finding points to a primary adverse influence on mandibular growth. On the other side, discectomy or non-reducing disc displacement can induce articular cartilage degeneration in TMJ, which were strongly associated with ipsilateral mandibular growth (Bryndahl, Warfvinge, Eriksson, & Isberg, 2011; Xu et al., 2009). This secondary cartilage degeneration could affect chondrogenesis and endochondral bone formation, resulting to the asymmetry of the mandible. Besides, The articular disc is crucial in the regeneration of a damaged condyle. After condylectomy in Wistar rats aged 4 weeks, functional appliance promoted mandibular growth and regeneration of the condyle 1 week after surgery. After 8 weeks, the shape and cartilage of the condyle were equivalent to a normal condyle (Fujita et al., 2013; Hayashi et al., 2014). However, when TMJ disc was resected (condylectomy + discectomy), regeneration of the cartilage was not observed with the use of the functional appliance (Hayashi et al., 2014). This study suggested that resection of the articular disc

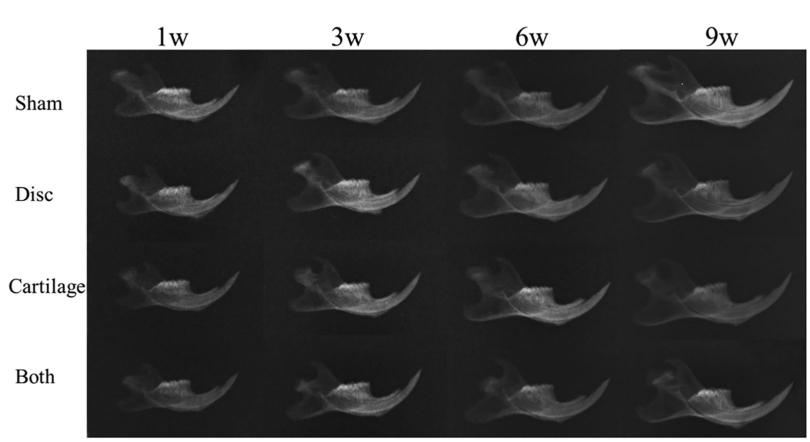

Fig. 7. Mandible radiograph showed the changes in condylar height and contour at 1, 3, 6, and 9 weeks after operation in each group.

could influence regeneration of condylar cartilage and mandibular growth.

In this study, the asymmetry appeared earlier in group C than that in group B. This finding confirmed that the deleterious effect of cartilage resection was likely more direct. Furthermore, cartilage resection caused worse outcomes than disc resection did. This result indicated that remodeling during cartilage resection was more difficult than that during disc resection. The mandible radiograph showed that degenerative condylar changes occurred earlier in group C than in group B, and this finding was consistent with the measurement results.

In previous studies, a specific reference point is typically selected from the condyle to measure the mandibular height (Holwegner, Reinhardt, Schmid, Marx, & Reinhardt, 2015; Hu et al., 2012; Teixeira, Teixeira, & Luz, 2006; Toledo et al., 2014). In our study, mandibular foramen was selected. This point was kept away from the surgical site, and this method could reduce the measurement errors caused by cartilage resection.

Although the height of the ramus is reduced because of degenerative lesions, the length of the mandible is slightly affected or unaffected. Besides the condylar process, the posterior surface of the ramus and the coronoid process are also principal sites of mandibular growth (Mani, 2010). The ramus increasingly grows through endochondral replacement at the condyle accompanied by surface remodeling, whereas the body of the mandible grows longer by the periosteal apposition of a new bone on its posterior surface. Therefore, disc and cartilage resection affects the growth of mandibular length to a less extent than ramus height does. In this study, the mandibular length was not significantly different in the right side in group B or in group C from that of group A.

In group D, the growth of the ramus height was still observed, although both cartilage and disc were resected. This finding can be explained on the basis of functional matrix theory of growth proposed by Moss and Salentijn (1969) and Moss (1997). According to this theory, the major determinant of maxilla and mandibular growth is the enlargement of nasal and oral cavities, which grow in response to functional requirements. This theory also states that the cartilages of the nasal septum and mandibular condyle are unimportant growth determinants. Therefore, the results of the last group are consistent with functional matrix theory to a certain extent.

5. Conclusions

The growth of mandibular height was interfered after articular disc or condylar cartilage was resected. Mandibular height deficiency likely occurred earlier and more severely when condylar cartilage was resected. However, the growth of mandibular length was barely interfered when either articular disc or condylar cartilage was resected.

Author contributions

S.C. contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, and drafting the article. L.H.H. and L.Z. contributed to the conception and design of the study, acquisition of data, and critically revising the manuscript. E.X and Y.H. contributed to the conception and design of the study, analysis and interpretation of data, and critically revising the manuscript. Y.Z. contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, and critically revising the manuscript. All authors have read and approved the final article.

Funding

This study was supported by the Youth Fund of Peking University School and Hospital of Stomatology (grant number PKUSS20160106).

Conflict of interest

None of the authors has any potential conflicts of interest to declare.

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