Regeneration of the Neocondyle After Free Fibular Flap Reconstruction of the Mandibular Condyle

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Purpose: Shifting of the flap position after condylar reconstruction with free fibular flaps is known to occur, but its long-term effects on postoperative esthetic outcomes have not been sufficiently reported. Therefore, in this study, we evaluated the long-term morphologic stability of the free fibular flap neocondyle.

Patients and Methods: This was a retrospective cohort study. The primary outcome variables were neocondyle regeneration and neocondyle position including the distance between the glenoid fossa and the initial neocondyle (Fo-Co), the distance between the glenoid fossa and the stable neocondyle (Fo-Co'), and shifting of the neocondyle (defined as the distance between the stable neocondyle and the initial neocondyle). The primary predictor variable was time. The other variables were age, gender, diagnosis, and number of fibular segments. Correlation analysis between the predictor variables and outcome variables was performed.

Results: The sample was composed of 26 patients (11 male and 15 female patients) with a mean age of 31 years. Diagnosis and number of fibular segments were significantly associated with Fo-Co and Fo-Co' ($P < .05$). Among the 26 patients, only 11 showed neocondyle regeneration at follow-up (group A) whereas 15 did not (group B). Neocondyle regeneration was significantly associated with patient age ($P < .01$). Stable Fo-Co and stable time were significantly associated with neocondyle regeneration ($P < .05$). The mean stable time was significantly shorter in group A (3.64 ± 1.12 months) than in group B (6.67 ± 3.85 months) ($P < .05$), and the mean Fo-Co' was significantly shorter in group A (13.65 ± 3.94 mm) than in group B (20.68 ± 8.87 mm) ($P < .05$).

Conclusions: The possibility of neocondyle regeneration is higher in pediatric patients than in adults. Neocondyle regeneration could result in the movement of the neocondyle toward the glenoid fossa with a shorter stable time, which could improve neocondyle repositioning. Repositioning of the neocondyle with free fibular flaps for mandibular condyle defects is a self-adaption process for temporomandibular joint function.

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Mandibular reconstruction is a challenge in oral and maxillofacial reconstructive surgery, which aims to achieve the best possible functional and esthetic outcomes. Free fibular flaps were initially used for mandibular reconstruction by Hidalgo[1] in 1989. Because the free fibular flap has several advantages, including a long pedicle length, a wide vessel diameter, and the ability to incorporate skin, muscle, and bone components, the flap has become highly reliable and popular in mandibular reconstruction.[2,3] The temporomandibular joint (TMJ), located between the mandibular condyle and the temporal glenoid fossa, is one of the most complex joints in the body.[4] TMJ disorders may cause impaired speech, eating difficulties, facial disfigurement, airway compromise, and psychological stress.[5] Mandibulectomy including the condyle could be warranted because of osteomyelitis, trauma, and tumors. Several techniques have been used to reconstruct mandibular condyles, including autogenous costochondral graft, autogenous coronoid process graft, distraction osteogenesis, vertical ramus osteotomy, total alloplastic joint prosthesis, and vascularized free tissue transfer for reconstruction. Large mandibular defects benefit from transfer of vascularized tissue such as fibular bone, iliac crest, or scapula.[6] For large mandibular defects including the condyle, the attachment of muscles and fibers around the mandibular ramus and condyle is cut off. By using vascularized tissue transfer, we can rebuild the anatomy of the mandibular ramus and condyle but cannot maintain an appropriate condyle-disc relationship during mandibular movements. Without the attachment of muscles and fibers, the position of the neocondyle with vascularized tissue transfer can only be determined using anterior titanium plate fixation between the transferred bone and the residual mandible. With clinical observation, postoperatively, the free fibular flap neocondyle and miniplates tend to shift after initial placement. In fact, the postoperative function of such neocondyles has not been well documented in the literature.

The purpose of this study was to evaluate the long-term stability of the free fibular flap neocondyle for mandibular condyle defects. The hypothesis on which this research was based was that the neocondyle would move toward the glenoid fossa postoperatively. The specific aim of the study was to evaluate the long-term morphologic stability of the free fibular flap neocondyle.

Patients and Methods

STUDY DESIGN

To address the research purpose, we designed and implemented a retrospective cohort study. The study population was composed of patients who had undergone mandibulectomy including the condyle for benign or malignant tumors and mandibular reconstruction with free fibular flaps at the Peking University School and Hospital of Stomatology between January 2013 and June 2015. Guiding elastics were used postoperatively until the occlusion was stable. Typically, the patient used guiding elastics for 2 to 4 weeks. During the first month after the operation, the patient was only allowed liquid and semisolid food. The inclusion criteria were *1)* stable occlusion before and after surgery, *2)* a unilateral mandibular defect including the condyle, and *3)* fixation of the free fibula with miniplates.

STUDY VARIABLES

The primary predictor variable was time, and the other study variables included age, gender, diagnosis, and number of fibular segments. The primary outcome variables were neocondyle regeneration and neocondyle position including the distance between the glenoid fossa and the initial neocondyle (Fo-Co), the distance between the glenoid fossa and the stable neocondyle (Fo-Co'), and shifting of the neocondyle (defined as the distance between the stable neocondyle and the initial neocondyle). The "stable time" was defined as the postoperative period in which there was no additional remodeling and movement of the neocondyle.

DATE COLLECTION METHODS

We retrospectively reviewed all postoperative maxillofacial computed tomography (CT) scans (with a slice thickness of 1 mm) for each patient. In all cases, the postoperative scans were taken at 3-month intervals during the first year after the operation. Postoperative CT data were imported into ProplanCMF (Materialise, Leuven, Belgium), which allowed creation of 3-dimensional (3D) virtual models of the maxillofacial skeleton. Such 3D virtual reconstruction was used to evaluate postoperative morphologic changes in the neocondyle.

Navigation software (iPlan, version 3.0; Brainlab, Feldkirchen, Germany) was used to measure the position of the reconstructed gonion and condyle. The same coordinate system was set up in the navigation system, wherein the line between the bilateral infraorbital edges was considered the x-axis and that between the anterior and posterior nasal spine was considered the y-axis; the line perpendicular to the x- and y-axes was considered the z-axis (Fig 1). Three-dimensional virtual models of the maxillofacial skeleton and mandible from every postoperative CT scan for every patient were imported into the same coordinate system. The coordinate position of the glenoid fossa was marked. The positions of several reconstructed

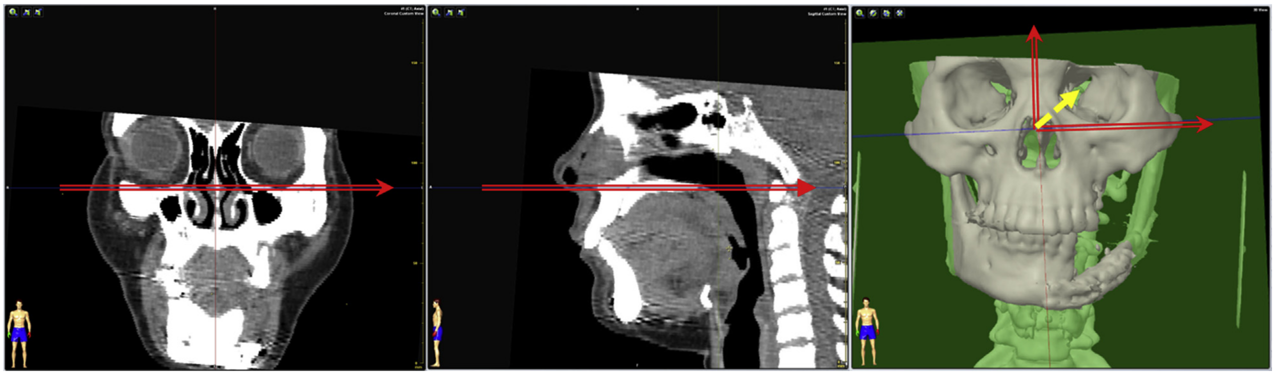

FIGURE 1. The same coordinate system for all patients was set up in the navigation system: The line between the bilateral infraorbital edges was used as the x-axis, the line between the anterior and posterior nasal spine was regarded as the y-axis, and the line perpendicular to the x-and y-axes was the z-axis. *Red arrow* in left panel is the line between the bilateral infraorbital edge; *red arrow* in middle panel is the line between the anterior and posterior nasal spine; *red* and *yellow arrows* in right panel is the coordinate system.

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mandibles were registered with the residual mandible. The coordinate positions of the reconstructed gonion and neocondyle at different time points were acquired using this method. Shift inclinations of the neocondyle in the x-, y-, and z-axes were acquired using 3D coordinates of the primary neocondyle minus those of the stable neocondyle. Distances between the glenoid fossa and the primary or stable neocondyle (Fo-Co or Fo-Co') at different time points could be calculated (Fig 2). The stable time for the postoperative position of the neocondyle and the regeneration situation of the neocondyle could be confirmed from the images (Fig 3).

Surgery, which was essentially the same for each patient, was performed with the patient under general anesthesia with nasotracheal intubation. On the basis of the location of the lesion, the mandible was exposed through a submandibular approach with or without a lower lip-splitting incision, and the TMJ disc was carefully preserved in all patients. After resection of the mandible, the free fibular flap was harvested, shaped, and fixed to the residual mandible with miniplates. The distal fibular segment was shaped as the neocondyle and placed in the glenoid fossa. The same chief surgeon (X.P.) performed tumor resection and mandibular reconstruction in every patient.

DATA ANALYSIS

A single, nonblinded biomedical engineer performed all linear measurements. The Kaplan-Meier method was used to estimate time to neocondyle regeneration. Cox hazard ratios were used to identify factors associated with outcome variables. Correlation analysis between the primary predictor and other predictor variables and the primary outcome variables was performed using SPSS software (version 17.0; SPSS, Chicago, IL).

This study received the ethical approval of Peking University School and Hospital of Stomatology (approval No. PKUSSIRB-201522051). Furthermore, the protocol was in keeping with the tenets of the Declaration of Helsinki.

Results

This retrospective case series involved 26 patients (11 male and 15 female patients) with an average age of 31 years (range, 8 to 72 years) who underwent surgical resection of tumors (benign in 21 and malignant in 5) (Table 1). In most patients, the primary tumor was an ameloblastoma (n = 13, 50%), the primary vein for anastomosis was the facial vein (n = 10, 38.5%) or external jugular vein (n = 15, 57.7%), and the primary artery for anastomosis was the facial artery (n = 25, 96.2%). All free fibular flaps survived after surgery without any complications. The Kaplan-Meier method was used to estimate time to neocondyle regeneration (Figs 4, 5).

Among the 26 patients, 11 showed regeneration at follow-up whereas 15 did not. Regeneration of the neocondyle was significantly related to patient age ($P < .01$); the rate of neocondyle regeneration was significantly higher in patients aged 18 years or younger (9 of 11) than in those older than 18 years (2 of 15) ($P < .01$). The mean Fo-Co values for all patients at 1 month after surgery and after the stable time were 19.86 ± 7.46 mm and 17.71 ± 7.93 mm, respectively, with no significant difference. The tumor diagnosis and the number of fibular segments were significantly associated with Fo-Co and Fo-Co' ($P < .05$). Patients were divided into 2 groups according to neocondyle regeneration: those with regeneration at follow-up (group A, n = 11) and those without regeneration (group B, n = 15) (Table 2). Fo-Co' and the stable time were significantly associated with neocondyle regeneration ($P < .05$).

FIGURE 2. Measurement of distance between glenoid fossa and initial neocondyle (Fo-Co) and distance between glenoid fossa and stable neocondyle (Fo-Co'). *Green arrows* are the three dimensional positions of the initial and stable condyle. *Red arrows* are distance between glenoid fossa and initial neocondyle (Fo-Co) and distance between glenoid fossa and stable neocondyle (Fo-Co').

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Group A patients were followed for 6 to 42 months (mean, 18.5 months). The mean stable time for the neocondyle and reconstructed gonion position was 3.64 ± 1.12 months. The mean Fo-Co and Fo-Co' were 18.24 ± 4.17 mm and 13.65 ± 3.94 mm, respectively. The mean Fo-Co' was significantly shorter than the mean Fo-Co ($P < .05$). The mean Fo-Co' could be divided into 3 distances in the x-, y-, and z-axes: 4.69 ± 2.36 mm, 7.53 ± 4.47 mm, and 9.35 ± 3.45 mm, respectively. The distance in the x-axis was shorter than the distances in the y- and z-axes ($P < .1$) (Table 2).

Group B patients were followed for 9 to 51 months (mean, 24.4 months). The mean patient age was 42.9 years (range, 14 to 72 years). The stable time for the neocondyle and reconstructed gonion position was 6.67 ± 3.85 months. The mean Fo-Co and mean Fo-Co' were 21.04 ± 9.12 mm and 20.68 ± 8.87 mm, respectively, with no significant difference ($P > .05$). The mean Fo-Co' could be divided into 3 distances in the x-, y-, and z-axes: 6.39 ± 5.27 mm, 13.11 ± 6.57 mm, and 10.58 ± 7.50 mm, respectively. The distance in the x-axis was shorter than the distances in the y- and

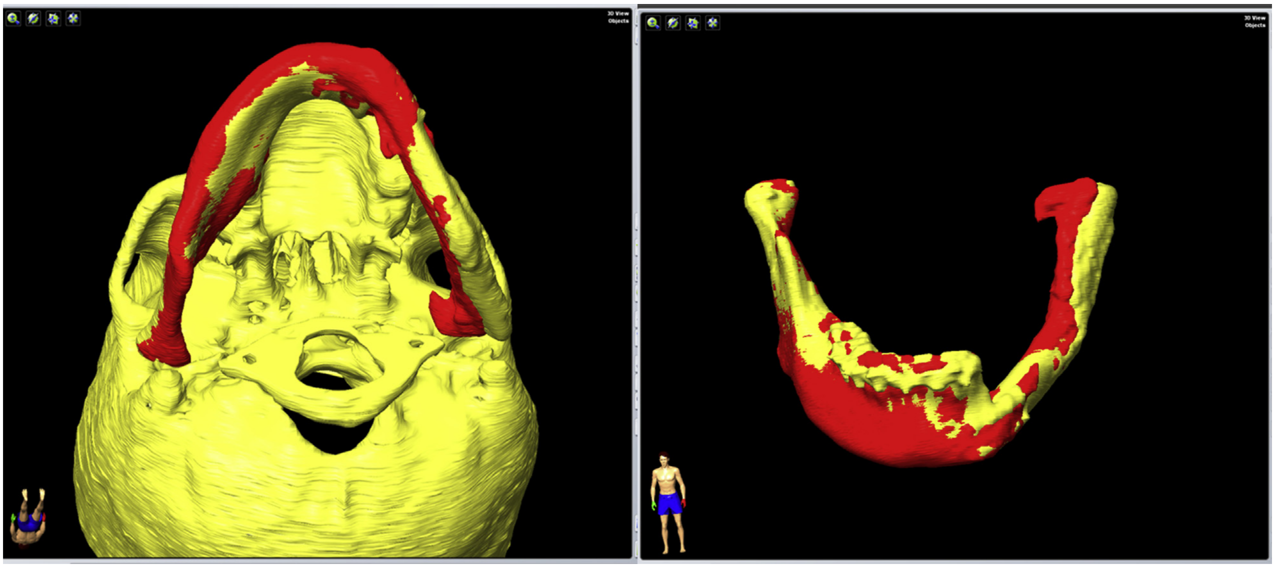

FIGURE 3. Registration between primary neomandible and stable neomandible to show regeneration of neocondyle.

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z-axes ($P < .1$). A negative or positive value for the condyle shift in the x-, y-, and z-axes, that is, to the right or left of the tumor lesion, could indicate the direction of movement of the repositioned neocondyle. On analysis of shift inclinations of the neocondyle in the x-, y-, and z-axes, it always moved from lateral to medial in the x-axis and from posterior to anterior in the y-axis.

The stable time for the neocondyle and reconstructed gonion position in group A was shorter than that in group B ($P < .05$). Moreover, the mean Fo-Co' at the stable time in group A was shorter than that in group B ($P < .05$) (Table 2).

Discussion

The purpose of this study was to evaluate the long-term stability and function of the free fibular flap neocondyle for mandibular condyle defects to examine the hypothesis that the neocondyle moves toward the glenoid fossa. The specific aims of the study were to estimate the relationship between postoperative morphologic changes in the neocondyle and age, gender, diagnosis, site, anastomotic vessels, and neocondyle repositioning. We found that postoperative morphologic changes in the neocondyle could influence its repositioning. In addition, neocondyle regeneration could guide its movement toward the glenoid fossa with a shorter stable time, which could improve neocondyle repositioning. Without neocondyle regeneration, neocondyle movement occurs from the lateral to medial direction along the x-axis and from the posterior to anterior direction along the y-axis.

In this study, all patients underwent mandibular defect reconstruction including the condyle with free fibular flaps. In our technique, the distal fibula end was rounded and shaped to form a neocondyle. Maintaining the fibular flap in the glenoid fossa can be a surgical challenge with functional complications including malocclusion and joint hypomobility. The neocondyle position is 3D, as it is dependent on the spatial relation between the fibular segments and the remaining mandible. Malpositioning of the neocondyle will result in TMJ dysfunction. Computer-aided design/computer-aided manufacturing and surgical navigation technology help define the exact dimensions of the reconstruction during surgery. Intermaxillary fixation is used to fix the distal fibula end into the glenoid fossa. However, by use of just 2 miniplates between the anterior fibular segment and residual mandible, direct suspension of the flap in the fossa is difficult and unstable postoperatively. For group B patients without condylar regeneration, the neocondyle always moved from lateral to medial in the x-axis and from posterior to anterior in the y-axis. We thought unilateral fixation of the fibular flap was not enough to keep the neocondyle stable. Because of swelling of soft tissues on the operative side, 1 month after surgery, the neocondyle exhibited lateral deviation. During surgery, the masseter and medial and lateral pterygoid muscles were cut off. Owing to dysfunction of the muscles, morphologic atrophy of the muscles led to an imbalance in inside and outside neocondyle pressure, thereby leading to movement in the x-axis. Moreover, because of resection of the mandibular ramus and coronoid process, the neocondyle had enough space to move forward. Meanwhile, soft and hard tissues behind the condyle were not affected much during

Table 1. DESCRIPTIVE STATISTICS OF STUDY SAMPLE

	Data
N	26
Gender	11 M and 15 F
Mean age, yr	31.9 ± 18.6
Diagnosis	21 benign and 5 malignant
Mean No. of fibular segments	2.38 ± 0.64
Neocondyle regeneration rate	11 of 26
Mean Fo-Co, mm	19.86 ± 7.46
Mean Fo-Co', mm	17.71 ± 7.93
Mean condyle shift, mm	10.21 ± 6.82
Mean stable time, mo	6.54 ± 5.10

Abbreviations: F, female; Fo-Co, distance between glenoid fossa and initial neocondyle; Fo-Co', distance between glenoid fossa and stable neocondyle; M, male.

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surgery, and this is why the neocondyle always moved from posterior to anterior in the y-axis. Early mobilization is crucial to the function of the TMJ, which also influences the position of the neocondyle. For group A patients with condylar regeneration, the distal fibula moved toward the temporomandibular fossa. In contrast to group B, the regenerated condyle in the fossa guided the distal fibula to move toward the fossa with a shorter stable time. After the stable time of the neocondyle, it continued to grow just as the residual mandible did. The temporomandibular disc was preserved in all cases. This point also may influence postoperative recovery of normal function, although few studies are available to support this assumption.

In a study in which 11 patients underwent condylar resection without disc removal and reconstruction of the distal fibula end, bone remodeling was observed.[7] In fact, disc preservation and molding of the end of the fibular graft seem to be responsible for good outcomes in terms of function. Lee et al[8] thought that if the disc requires resection, then precise fibula positioning with a planned 1-cm gap and postoperative range-of-motion exercises with guided elastics can provide an appropriately positioned and functional condylar reconstruction. A retrospective series of 6 patients with postoperative radiographic control showed displacement of the neocondyle, which was situated anterior to the eminence without functional limitations during the follow-up period.[9] In our research, the disc of every patient was reserved, and hence, Fo-Co included the thickness of the disc, which indicated that the neocondyle moved within a small range in all patients. We thought that neocondyle migration was an adaptive process between the neocondyle and surrounding structures, which could avoid TMJ dysfunction.

TMJ is a diarthrosis between the mandibular condyle and the glenoid fossa of the temporal bone. Its movement comprises both ginglymus and arthrodial movement, permitting a gliding motion in forward and backward directions. The condylar neck and head are composed of corticocancellous bone of varying thickness. The disc of the condyle is composed of fibrocartilage that articulates with the glenoid fossa.[10] Suspensory capsular ligaments, joint capsule limitation, and muscular attachment to the condylar head

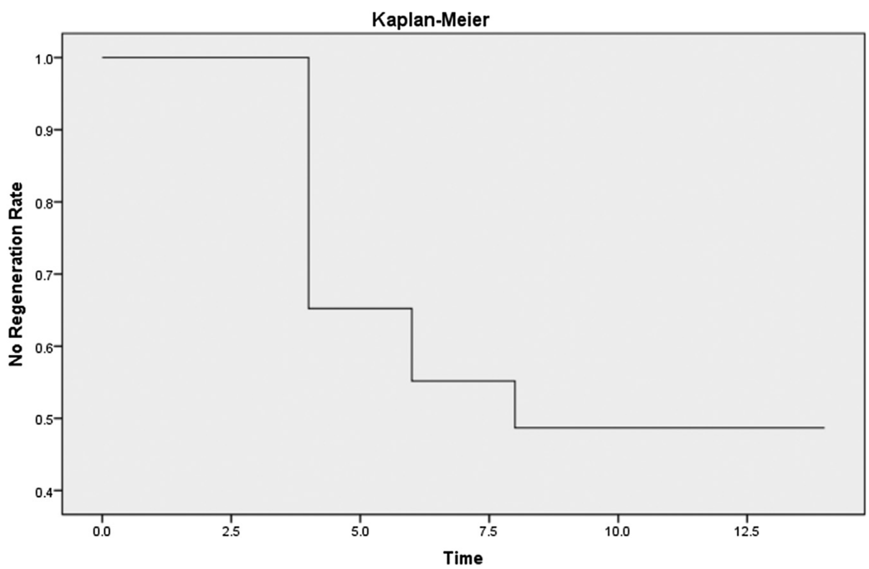

FIGURE 4. Survival analysis for estimation of time to neocondyle regeneration.

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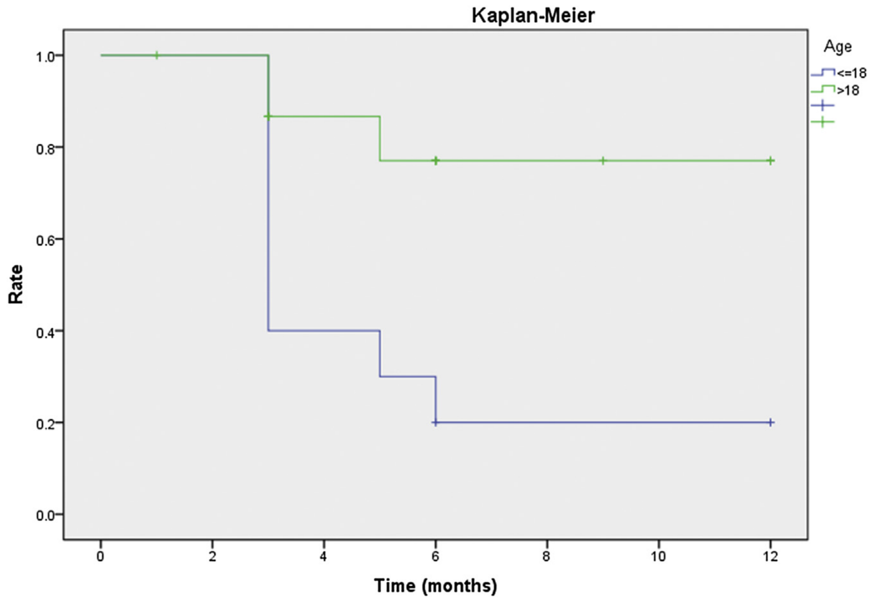

FIGURE 5. Kaplan-Meier analysis of association between age and neocondyle regeneration.

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and neck permit condylar movement within a certain range. Limitations of mandibular condylar reconstruction are related to TMJ dysfunction.[11] Options for condylar reconstruction include prosthetic materials and vascularized free flaps. However, application of prosthetic materials may result in postoperative complications such as plate fracture and wearing of the condylar head through the glenoid fossa. From the biological and anatomic perspective, costochondral grafts are similar to the condyle and can promote growth of the maturing skeleton and also cause unpredictable cartilage overgrowth.[10] When vascularized fibular flaps are used for mandibular condylar reconstruction, 3 condylar management strategies are used, of which 1 is used for condylar resection and 2 are used for condylar preservation.[12] The first is the fibula substitute condyle technique, whereby the distal fibula end is shaped and placed into the glenoid fossa. This method is suitable for mandibular defects that include the condyle. The narrow tubular shape and dense cortical structure of the substitute condyle are mostly similar to those of the native condyle. Moreover, vascularized bone grafts have numerous additional advantages, including the ability to resist infection and the ability to survive in irradiated recipient sites.[8] The second strategy is combined resection of the nonvascularized condyle head and distal fibula end. The third is a condyle preservation method in which the condylar head is preserved and the fibula is connected with the remaining condylar head.[13]

Table 2. COMPARISON OF FIBULAR FLAP PARAMETERS BETWEEN GROUPS A AND B

	Group A	Group B	*P* Value
Mean age, yr	17 ± 3.90	42.87 ± 17.46	<.001
Mean Fo-Co, mm	18.24 ± 4.17	21.04 ± 9.12	.354
Mean Fo-Co', mm	13.65 ± 3.94	20.68 ± 8.87	.013
Mean condyle shift, mm	10.82 ± 4.15	9.77 ± 8.38	.706
Mean stable time, mo	3.64 ± 1.12	6.67 ± 3.85	.010

Abbreviations: Fo-Co, distance between glenoid fossa and initial neocondyle; Fo-Co', distance between glenoid fossa and stable neocondyle.

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Ankylosis can be a severe complication of nearly any surgical procedure involving the TMJ. Condyle malposition can result from poor intraoperative positioning or long-term postoperative tissue resorption. Several studies have shown that the vascularized fibula end is placed into the glenoid fossa with the reconstruction plate between the fibula and the residual mandible. In a retrospective study including 17 patients, 2 patients experienced fibular head displacement from the fossa and 3 patients complained of persistent postoperative trismus.[14] In a series of 6 patients, González-García et al[9] reported a good appearance and good function, but 1 patient experienced postoperative temporo-fibular ankylosis, which could have been a result of imprecise placement of the fibular graft. Lee et al[8] attributed the ankylosis or trismus that occurred in these 2 series to imprecise placement of the neocondyle to re-create the joint.

Compared with their study, we used traditional methods with miniplates during surgery without any ankylosis or trismus. Miniplate fixation, introduced by Hidalgo,[1] is thought to be associated with greater malleability, a lower facial profile, a decreased operative time, and a decreased risk of disruption of the vascular pedicle.[15] In 1989, Kennady et al[16] suggested that reconstruction plates were associated with stress shielding and disuse osteoporosis. Miniplates and reconstruction plates are regarded as the gold standard for mandibular reconstruction.

For a mature condyle reconstruction with free fibular flaps, if the reconstruction plate is used for fixation, the surgeon should ensure that the neocondyle is located in the glenoid fossa, without an opportunity to improve the position of the neocondyle. The neomandible should be adequately stable to finish implantation during or immediately after surgery. In this study, miniplates were used to fix the mandible and fibula so that the neocondyle could be easily adjusted in the glenoid fossa during surgery. In addition, miniplates could provide mobility of the neocondyle for the adaptive process, which could avoid postoperative complications. After the stable time, patients using miniplates could undergo delayed implantation.

The question of whether reconstruction plates could be used for an immature facial skeleton remains controversial. The growth potential of the reconstructed mandible may be driven from the residual mandible, the fibular flap, or both. In general, the condyle is considered the most important and reliable growth center for the entire mandible. The reconstruction plate is fixed across the residual mandible and fibular flap, but this can impede mandibular growth. Therefore, removal of the reconstruction plate completely or partially should be conducted as soon as possible. Thus, given the limitation of fibular and mandibular growth, miniplates were the first choice.

Condylar reconstruction remains a mainstream treatment option. Experimental condylectomy in animals showed that the mandible can maintain its growth potential and that the condyle can regenerate after surgery.[17] Our results in this study supported condylar reconstruction as well. Regeneration of the neocondyle was significantly related to patient age ($P < .05$). The mean age of the 11 patients with regeneration at follow-up was 17.00 ± 3.90 years. The stable time for the neocondyle position was 3.4 ± 1.3 months, which is the rapid growth period, depicting a strong growth potential after reconstruction. After this period, the neocondyle and the residual mandible grew synchronously. Rather than a growth center, the condyle is more widely accepted as a growing site that can adjust to changes in other parts of the face.

Our study is the first to propose strategies for repositioning of a free fibular flap neocondyle for regeneration of the neocondyle. Neocondyle regeneration could result in its movement toward the glenoid fossa with a shorter stable time, and this could improve neocondyle repositioning. Without neocondyle regeneration, neocondyle movement occurs from the lateral to medial direction along the x-axis and from the posterior to anterior direction along the y-axis. Because this study was a retrospective cohort study, it was not possible to obtain detailed information about the function of the neocondyle and affected TMJ.

Neocondyle regeneration is significantly related to patient age. The initial position of the neocondyle is out of the glenoid fossa. Regeneration of the neocondyle could guide its movement toward the glenoid fossa with a shorter stable time, which could improve neocondyle repositioning. Without neocondyle regeneration, the neocondyle moves from the lateral to medial direction along the x-axis and from the posterior to anterior direction along the y-axis. Repositioning of the neocondyle with free fibular flaps for mandibular condyle defects is a self-adaption process for TMJ function. Mandibular condyle reconstruction using free fibular flaps with miniplates is feasible without complications. The next logical step is a prospective evaluation to truly assess the changes that occur in the function of the neocondyle and TMJ and determine which factors affect outcomes.

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