Evaluation of the Effects of Guided Bone Regeneration and Periosteum on Newly Formed Bone in a Distraction Gap

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Abstract: We determined the causes of bone resorption within a distraction gap and determined whether it could be prevented via guided bone regeneration during distraction. Another goal was to determine the effect of periosteum in bone healing in a distraction gap.

Twelve sheep mandibles were bilaterally distracted. One side of the 6 sheep mandibles formed the control group; the other side was the study group, from which the periosteum was excised and distraction was performed. In the other 6 sheep, on the study side, guided bone regeneration was applied with distraction; on the other study side, guided bone regeneration was applied, and the periosteum was excised at the distraction. At the end of a 1-week latent period, all subjects were distracted 10 mm (1 mm/d), and we waited 3 months for consolidation. At the end of this period, all animals were killed, and radiologic evaluations of the newly formed bone within the distraction gap were conducted.

The surface area of the regenerating bone in the membrane groups was significantly higher than in the groups without a membrane. However, no additional effect of the periosteum on the bone surface area was observed. No significant difference between the groups in densitometric values was observed.

Concomitant use of guided bone regeneration with distraction osteogenesis may be the optimal way to generate a flat bone surface within a distraction gap.

Key Words: Distraction osteogenesis, membrane, guided bone regeneration, periosteum

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The concept of extending bones by distraction osteogenesis is well known and has recently been successfully applied by many surgeons in orthopedics and maxillofacial surgery. Although this procedure is easy and effective and has few complications, many questions about it have not yet been answered.

One problem with distraction osteogenesis is the possibility of having less new bone regeneration than is needed in the bone segment and thus having a concave bone surface at the distraction site. Studies have shown that this problem may occur because of soft tissue invasion into the distraction gap or because of periosteum damage.[1]

Our study concerned the prevention of soft tissue invasion into the distraction gap by using membranes to increase the quality and amount of newly regenerated bone. Thus, we used membranes that were rigid and soluble and that could be fixed to one of the distracted segments and moved in the distraction gap. It was expected that we would obtain increased bone volume, and a smooth bone surface that was not concave. Moreover, the parameters of the study were extended to determine the effect of periosteum on bone regeneration in the distraction gap. To our knowledge, this is the first experimental study in which the distraction procedure was performed synchronously with guided tissue regeneration, in which a structurally rigid, but movable, membrane was used.

The aim of this study was to determine the causes of bone resorption within the distraction gap and to determine whether it could be prevented by guided bone regeneration during distraction. We also sought to determine the effect of the periosteum on bone healing in the distraction gap.

MATERIALS AND METHODS

Twelve mature sheep were used for the study under veterinary supervision. The protocol for the experiment was approved by the Animal Care and Use Committee. The animals were divided into 4 study groups, and a bilateral mandibular distraction osteogenesis procedure was applied to all animals.

One side of 6 mandibles that were distracted bilaterally was classified as group 1 and the other side as group 2. The other 6 mandibles were classified on 1 side as group 3 and the other side as group 4. The groups were treated as follows:

Group 1: Six sheep hemimandibles were distracted; these constituted the control group.

Group 2: The other side of the mandibles was also distracted, and the periosteum (15 × 20 mm) was excised at the osteotomy line.

Group 3: Six hemimandibles were distracted and a resorbable membrane was fixed to the anterior bone segment with resorbable pins so that the membrane would move in the distraction gap.

Group 4: The same procedures were performed as in group 3. In addition, the periosteum (15 × 20 mm) on the osteotomy line and at the distraction area was excised.

Distractors were specially designed and fabricated for sheep mandibles. Distractor pins were designed to allow the membrane to slide in the distraction gap and not to damage the inferior alveolar nerve.

Sheep were anesthetized with an intramuscular injection of xylazine (Rompun 2%; Bayer, Istanbul, Turkey) and ketamine hydrochloride (Ketalar; Eczacibasi-Warner Lambert, Istanbul, Turkey). The animals were given antibiotics and analgesics intraoperatively and for 5 days thereafter.

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FIGURE 1. Extraoral approach and osteotomy line.

All surgical procedures were carried out under aseptic and antiseptic conditions. Animals were fed a soft diet after the operation. After a latent period of 7 days, the mandibles were distracted for 10 days at a rate of 1 mm/d. The surgery area and that around of the pins was irrigated with an antiseptic solution until the end of the distraction procedure.

Surgical Method

The edentulous mandible was exposed after an extraoral incision, and an osteotomy was performed anterior to the first premolar area (Fig. 1). The inferior alveolar nerve was preserved while performing the osteotomies. Before full separation of the bone segments, the distractor was temporarily fixed to the bone. Then, the distractor was removed, and full separation of the bone segments was performed. To ensure full separation, we observed free movement of the bone segments. After that, the distractor was fixed with bicortical pins. Until this point, the same procedures were performed in all groups. In addition, in group 2, the periosteum was excised on the osteotomy line (15 × 20 mm; Fig. 2). In group 3 after fixation of the distractor, a resorbable membrane (Inion Ltd, Tampare, Finland) was applied on the osteotomy line and fixed with resorbable pins to the anterior fragment so that it would slide in the distraction gap (Fig. 3). In group 4, resorbable membranes were applied, as in group 3. In addition, the periosteum on the osteotomy line was excised (15 × 20 mm). The wounds were closed primarily with 3-0 vicryl suture (Fig. 4).

In all groups, the same distraction procedure was performed. After 7 days of neutral fixation, gradual distraction was started at a rate of 1 mm/d and was continued for 10 days; each sheep underwent 10 mm of distraction osteogenesis. After 3 months of the consolidation phase, all animals were killed, and mandibles were removed. To assess the radiodensitometry and regeneration areas, the harvested bones were scanned by computed tomography. Axial sections of the middle part of the regeneration areas were chosen for the radiologic evaluation. For densitometric evaluation, we used 2 different points from the cortex and medullary bone and took the average of those values for statistical analyses (Fig. 5). The area measurements were hand drawn at the computer with the same sections, and a software program measured the regeneration areas (Fig. 6).

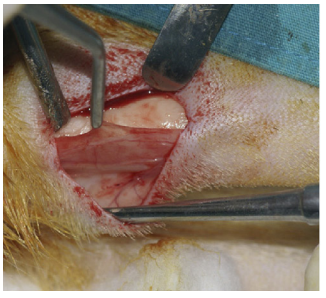

FIGURE 2. Periosteum at the osteotomy line.

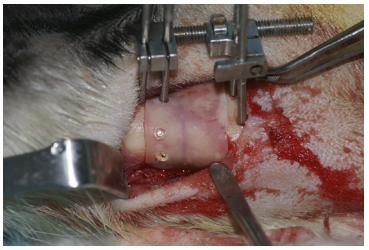

FIGURE 3. Resorbable membrane that fixed with resorbable pins to the anterior fragment.

FIGURE 4. Distractor after being applied to the mandible.

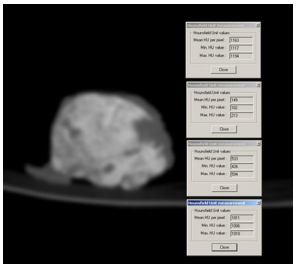

FIGURE 5. Axial section of the distraction area and densitometric measurements.

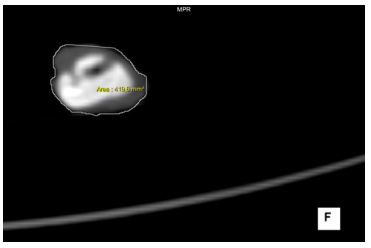

FIGURE 6. Area measurements of the distraction region.

FIGURE 7. Radiologic view of the distraction area.

The average bone mineral density and area measurement values were compared using the Kruskal-Wallis test.

RESULTS

Macroscopic Findings

After the surgery, an infection developed around the pin in 1 mandible of the control group. This was treated with antibiotics and a wound dressing.

All of the mandibles were lengthened sufficiently. We observed inferior vectoral deviation in 3 mandibles.

In the third month of the consolidation period, 4 distractors collapsed, but we did not eliminate these mandibles from the study because we considered the elapsed time to have been sufficient for mineralization of the distraction gap.

At the end of third month of the consolidation period, complete bone healing was observed in all animals. Distraction gaps were surrounded with cortical bone. In addition, the distraction gap was visualized radiographically (Fig. 7).

Area and Densitometric Measurements

Statistical values are given in Table 1. No statistically significant densitometric difference was observed among the groups. In the area measurements, no statistically significant difference was found between the groups in which no membrane was used (groups 1 and 2) and those in which a membrane was used (groups 3 and 4, $P > 0.05$). All other group comparisons (groups 1 and 3, groups 1 and 4, groups 2 and 3, groups 2 and 4) revealed statistically significant differences in area measurements ($P < 0.05$). The amount of new bone was greater in groups 3 and 4 than in groups 1 and 2.

DISCUSSION

Distraction osteogenesis had become an alternative to classic reconstructive surgery and orthognathic surgery by stimulating new bone formation mechanically at the distraction gap.[2,3] Ilizarov[4] explained that applying gradual tension forces on living tissues stimulates new tissue regeneration. Distraction osteogenesis, which has been widely used in maxillofacial surgery, such as augmentation of the alveolar ridge and midface advancement, has many advantages over conventional osteotomies.[5] On the other hand, distraction osteogenesis has some disadvantages, such as longer treatment time.

Another problem is the occurrence of concave bone defects at the distraction gap. In particular, in the literature are many clinical and experimental reports of patients with atrophic bones—vertical alveolar defects that had preprosthetic augmentation with distraction osteogenesis.[6–8] Augmentation of alveolar bone with vertical distraction was first reported by Block et al[9] in a dog mandible. Chin and Toth[10] published the first clinical report. Recently, vertical alveolar distraction has become popular in augmentation of atrophic alveolar bones before implant placement. However, as mentioned before, concave bone defects at the distraction area can cause fenestrations and dehiscence at implant surfaces. Few studies about this have been reported, and most did not examine reasons for or solutions to this problem.

Chiapasco et al[11] compared the efficiency of distraction osteogenesis and guided bone regeneration. They used autogenous bone grafts and guided bone regeneration in one group and distraction osteogenesis in another group to examine augmentation of atrophic alveolar bones. After the augmentation procedures, implants were placed in the augmented alveolar bones. According to their results, bone resorption was greater with the guided bone regeneration technique than with distraction osteogenesis. In addition, they suggested that both techniques could be used for the augmentation of the atrophic alveolus but that distraction osteogenesis had a better prognosis in the long term. In our study, we used the 2 techniques together (guided bone regeneration with distraction osteogenesis) and obtained promising results.

Because of the advantages of distraction osteogenesis, Klug et al[1] performed distraction in 10 patients having insufficient vertical alveolar height. Although all patients had sufficient vertical alveolar height at the end of the distraction procedures, concave bone defects occurred at the vestibular side of the first 6 patients. For this reason, Klug et al applied titanium membranes in the distraction gap of the last 4 patients to prevent the invasion of the soft tissues into the distraction gap. At the end of the consolidation period, they removed the membranes and distractors and they encountered a smooth surface at the vestibular side of the distraction area. Concave bone defects that occurred because of invasion of soft tissues into the gap were also reported by Block et al.[9]

Concave bone defects can be the result of faster invasion of fibroblasts than of osteogenic cells into the distraction gap. It can also be the result of fibrotic healing at the distraction gap that was distracted at a high ratio. Theoretically, placing a membrane in the distraction gap prevents fibroblast invasion and provides time for osteogenic cells to fill in the gap.[12] Elshahat et al[12] reported a study about preventing fibrotic tissue occurrence in the distraction gap with a high distraction ratio in 14 rabbits. They applied the distractor to 7 rabbits and waited for a 7-day latent period. Then, they began distraction at a rate of 2 mm/d. They performed the same procedure in the other 7 rabbits and then placed a collagen membrane above the osteotomy line. After 4 weeks of consolidation time, they observed osteogenesis in the distraction gap in both groups, but more bone formation had occurred in the membrane group. They concluded that new bone in the distraction gap took the shape of the collagen membrane, and the membrane prevented soft tissue

TABLE 1. Statistical Values of Densitometric and Area Measurements

	Group 1	Group 2	Group 3	Group 4	*P*
Density	876.5 (164.00–1145.00)	917.0 (803.00–1016.00)	731.5 (623.00–1120.00)	837.50 (715.00–1232.00)	>0.05
Area	367.5 (310.20–431.60)	361.8 (308.70–471.20)	**515.35 (419.60–676.00)**	**535.9 (442.00–626.90)**	<0.05*

Values are presented as median (minimum–maximum).
*Values in bold face were significantly higher than the other values.

invasion. On the other hand, early bone mineralization and higher bone density were seen in the group that was distracted without a membrane. The reason for the higher density bone formation in that group was explained by the periosteum's effects on mineralization and bone formation. These authors did not observe fibrosis in the group distracted without a membrane. They explained that if the periosteum was not damaged during the operation, it acted as a natural membrane for guided bone regeneration. They recommended that a membrane be used when the periosteum was damaged or distraction was to be applied at a high distraction ratio. Garcia et al[13] performed 17 alveolar distractions in 12 patients. They mentioned the same problem and suggested that concave bone defects could cause fenestration and dehiscence around implants. They suggested guided tissue regeneration as a treatment.

Although concave bone defects are seen frequently, only a few studies about them have been reported. Some have pointed out the importance of the periosteum's effect on bone healing in the distraction gap. Kojimoto et al[14] distracted 27 rabbit tibias. They excised the periosteum at the osteotomy line from one group of rabbits, and in the other group, the tibial endosteum was extracted, but the periosteum was preserved. No problem arose with callus formation in endosteum-extracted group. On the other hand, they observed deformities, callus formation, and tibia lengthening in the excised periosteum group. Thus, they suggested that protecting the periosteum was more important than a carefully performed corticotomy.

The effect of the periosteum in cartilage regeneration and bone formation has been reported previously.[15] Kano et al[16] excised the periosteum from 3 patients, whereas they were extracting mandibular wisdom teeth. They applied tension forces to the periosteum with a specially designed device, and they observed increased osteogenic and angiogenic growth factors due to the tension forces. Schmidt et al[17] performed periosteal distraction in rabbits and then conducted histologic examination and histomorphometric analyses of the distraction area. Eventually, on postoperative days 28, 35, 42, and 56, the experimental site showed an increase in the number of osteoblasts, collagen fibers parallel to the distraction vector, islands of osteoblasts surrounded by newly formed bone, and maturation of bone.

In our study, we did not see any significant difference in bone formation between the periosteum-distracted groups and the no-periosteum-distracted groups (groups 1 and 2 versus groups 3 and 4). According to our study, the endosteum was apparently more important than the periosteum in distraction osteogenesis. Although it is well known that guided tissue regeneration hinders the relationship between bone defect and periosteum, many reports have indicated successful treatment of bony defects with guided tissue regeneration. Likewise, our study showed that the periosteum was apparently not the most important factor in the formation of bone in the distraction gap. In our study, in the competition in bone regeneration between the periosteum and endosteum, the outcome was in favor of the endosteum. In our study, endosteal blood cells were sufficient to support the increased mechanical loading.

A few studies have examined the importance of the periosteum in distraction osteogenesis, and they have suggested that the periosteum should be protected in the operation. However, especially during a dissection with a periosteal elevator or ecarteur, the saw and distractor devices can damage the periosteum. Generally, surgeons ignore periosteal damage and pay attention to other aspects of the distraction procedure. As a result, concave bone defects can occur, and additional bone grafts may be required. However, other studies have shown that even when the periosteum is preserved perfectly, concave bone defects can occur because the newly regenerated bone does not exactly follow the bone segments.

In conclusion, during distraction osteogenesis, concave bone defects can occur, although the periosteum is preserved perfectly. Our study shows that this problem can be addressed with guided bone regeneration. However, this is not to say that the periosteum is unimportant in distraction osteogenesis. If guided tissue regeneration is not used in the operation, preserving the periosteum's integrity is important for the success of the distraction.

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