The Effect of Autologous Meniscal Fragment Implantation on Meniscus Regeneration Results from Synergic Effects of Meniscal Matrix and Living Chondrocyte Implantations

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Introduction: Poor healing capacity of the meniscus tissue often dictates removal of the damaged tissue, making meniscectomy the most common treatment for meniscal injury [1]. However, the loss of meniscal tissue results in secondary osteoarthritis. Currently, multiple strategies have been reported for meniscal repair, including allografts, biologic scaffolds, and tissue regeneration [2-4]. However, their utility still remains unknown. Recently, we have reported that implantation of autologous meniscal fragments wrapped with a fascia sheath into the donor site meniscal defect significantly enhanced fibrocartilage regeneration in vivo in the defect at 12 weeks after implantation in the rabbit, and proposed a novel strategy for meniscal repair [5]. That is the intraoperative meniscal fragment implantation made from the resected meniscus. Then, we have to ask a following question: Which component in the grafted meniscal fragments enhances fibrocartilage regeneration in vivo among the native meniscal matrix or the living chondrocytes? To distinguish the effects of the 2 components, we have conducted the present study, in which we have compared the effect of the meniscal fragments with living chondrocytes to the effect of implantation of the meniscal matrix necrotized by the freeze-thaw treatment using liquid nitrogen [6]. We hypothesized that the effect of autologous meniscal fragment implantation on meniscus regeneration results from synergic effects of meniscal matrix and living chondrocyte implantations.

Methods: A total of 75 Japanese White rabbits were used. In each animal, an anterior one-third of the right medial meniscus was resected. Then, the animals were divided into the following 3 groups of 25 rabbits each. In Group I, the defect was covered with a rectangle of fascia from the left thigh, trimmed to 10 x 12 mm. In Group II, the resected meniscus was fragmented into small pieces (0.5x0.5x0.5mm), which were then grafted into the defect. The defect with the meniscal fragments was then covered with a rectangular fascia in the same manner as Group I. In Group III, the resected meniscus was fragmented into small pieces, and underwent the freeze-thaw treatment using liquid nitrogen and saline solution 3 times in order to kill the chondrocytes. Then, the necrotized fragments were grafted into the defect, and covered with a rectangular fascia in the same manner as Group I. In each group, 5 rabbits were used for histological evaluation at 3, 6, and 12 weeks after surgery, and 5 rabbits were used for biomechanical evaluation at 6, and 12 weeks after surgery. In each period, morphological observations were performed in the animals immediately after sacrifice. Tissue dimensions of the regenerated tissue in the defect were determined in both the morphological and histological observations [7]. Histological findings of the regenerated tissue observed with the hematoxylin and eosin, Safranin-O, and Toluidine-blue staining methods, by 12 weeks after surgery, were compared to those of the non-treated fragments. This fact suggested that implantation of the living chondrocytes enhances the fibrocartilage regeneration effect of the native meniscal matrix implantation. Thus, the present study showed that the meniscal matrix implantation. This study demonstrated, first, that implantation of the frozen-thawed meniscal fragments significantly enhances fibrocartilage regeneration in vivo in the defect. Secondly there were significant differences in the histological and biomechanical evaluations between the implantation effects of the native meniscal matrix and the living chondrocytes. As for clinical relevance, this information is important to establish a potential novel therapy to repair a large defect after a meniscectomy in the near future.

Results: In Groups I, the defect was incompletely filled with thin fibrous tissues even at 12 weeks, while a cartilage tissue rarely regenerated in the tissue. In Group II, all defects except for one were completely filled with thick fibrocartilage tissues, which were richly stained with the Safranin-O and Toluidine-blue staining methods, by 12 weeks. In Group III, defects were almost filled with thin fibrocartilage tissues at 12 weeks. The gross observation score of Groups II and III were significantly greater (p=0.0018 and p=0.0205) than that of Group I at 12 weeks. The histological score of the cartilage regeneration of Group II was significantly greater than that of Groups I and III at 12 weeks (p=0.0001 and p=0.0043, respectively), while Group III was significantly greater (p=0.0070) than that of Group I at 12 weeks. The width and the cross-sectional area of the regenerated tissue of Groups II were significantly greater (p=0.0186) than that of Group I at 12 weeks. In the biomechanical evaluation at 12 weeks, the maximal load of the regenerated tissues were significantly greater (p=0.0002 and p=0.0293, respectively) in Group II than in Groups I and III, while Group III was significantly greater (p=0.0164) than Group I. The linear stiffness of the regenerated tissues were significantly greater (p=0.0014 and p=0.0205, respectively) in Group II than in Groups I and III at 12 weeks.

Discussion: This study demonstrated, first, that implantation of the frozen-thawed meniscal fragments significantly enhances fibrocartilage regeneration in vivo in the defect. Secondly there were significant differences in the histological and biomechanical evaluations between the implantation effects of the frozen-thawed fragments and the non-treated fragments. This fact suggested that implantation of the living chondrocytes enhances the fibrocartilage regeneration effect of the meniscal matrix implantation. Thus, the present study showed that the meniscus regeneration induced by the autologous meniscal fragment implantation results from synergic effects of implantation of the native meniscal matrix and the living chondrocytes. As for clinical relevance, this information is important to establish a potential novel therapy to repair a large defect after a meniscectomy in the near future.


Significance: This study has clarified a mechanism of the effect of the autologous meniscal fragment implantation.