

The Prospect Science of Meniscus Preservation

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Meniscus Injury

The meniscus plays a role in stabilizing (secondary) knee joints by load transmission and reducing the contact stresses on knee joint cartilage. Meniscal tear more commonly involves the young patient and may be associated with ligament injuries. Meniscal injury also can be associated with some congenital anomaly. The meniscus injury treatment is challenging and most commonly treated with excision.

Excision of the meniscus is associated with poor clinical outcomes, and high chance of early cartilage degeneration. Current meniscus repair techniques are still associated with common re-admission for surgery and poor clinical outcomes. To improve the patient-reported outcomes, the current basic research project should focus on enhancing meniscus healing and replacing meniscus tears.

The Option for Meniscus Preservation Meniscus repair

Meniscus repair still will be the primary option for meniscal preservation. However, repairing a torn meniscus is not always easy. Some complex tears are sometimes difficult to repair, technically demanding, and more commonly associated with poor outcomes. Challenges in meniscus repair also can be associated with the availability of the proper suture material/implants.

Meniscal Auto/Allograft

Meniscus transplantation could be one option to preserve the joint. Autografts derived from the fat pad, tendon, cartilage, periosteum, synovial flap, and perichondrium have been reported for the reconstruction of the meniscus.⁶ However, satisfactory results were rarely reported.

Therefore, autograft transplantation is not a popular procedure until recently. Allograft transplantation of the meniscus is now one of the treatment options for the case which subjected for partial/total meniscectomy.⁷

This procedure is mostly performed in a developed country with a widespread availability of the tissue bank. Recent systematic review and meta-analysis study showed the outcome of allograft meniscus transplantation to have around 80% of 5-10 years survival rate and around 50% of > 10 years survival rate.

Tissue Engineering

Meniscus tissue engineering is a combination of cells (stem cells), extracellular matrix, and biologic stimuli (growth factors). The goal in tissue engineering could be an in vivo implantation of the acellular matrix and homing of cells.

Another option also could be performed by in vitro cell seeding on the matrix followed by maturation in vivo.



Cell-Free Therapy

There are two kinds of cell-free meniscal scaffolds currently in clinical use. This method is called the meniscus scaffold replacement (MSR). The collagen meniscus implant or 'CMI' (Ivy Sports Medicine, Lochhamer, Germany) and the polyurethane-based, also known as 'ACTIFIT' (Orteq Bioengineering, London, UK) have been used in a clinical setting in European countries.⁹

A recent systematic review comparing the use of ACTIFIT and CMI on 658 patients at > 3 years follow-up. Outcome failure was found in 6.7% of patients receiving CMI and 9.9% of patients receiving the ACTIFIT scaffold. The failure rate itself ranged from 0% to around 30% amongst the included studies.

The study's conclusion showed that patients might have a better clinical outcome with the use of both scaffolds, mainly when high tibial osteotomy or anterior cruciate ligament reconstruction is performed as a combined procedure.

Cell-Based Therapy

Enhancement of meniscus regeneration with the use of mesenchymal stem cells (MSCs) have been widely studied recently. Several tissues, including bone marrow, adipose, and synovium can be the source of MSCs. MSCs capable of differentiating into several differentiated cell, including chondrocytes, adipocytes, osteoblasts, etc. The significant efficacy of MSCs in enhancing meniscus repair and regeneration have been reported by several studies.¹¹

However, many of those studies were conducted in vitro or in vivo with animal subjects. Several studies (Case report/case series) of human stem cells injection for enhancement of human meniscus repair have been reported with promising outcome.

A combined strategy with the use of tissue engineering and MSCs is also an emerging field from a clinical view. A very recent study that combine the polyurethane meniscal scaffold with MSCs for meniscal regeneration has been reported. A comparative study of an acellular scaffold repair compared to a combination of MSCs and meniscal scaffold was performed.¹⁴

The author noted a significant clinical and radiological improvement in the compared groups. However, they conclude that the addition of MSC to the scaffold had no significant difference. Further human in vivo study with a larger subject is needed to prove the good potential clinical application of stem cells in meniscus regeneration.

The Prospect

The use of endogenous stem/progenitor cells for meniscus repair/regeneration is still one of the issues of debate. Several current research findings revealed that endogenous stem/progenitor cells might be responsible for the healing process of the meniscus after injury. However, additional growth factors/cytokines are still needed to initiate the cell proliferation, differentiation, and maturation at the site of meniscus injury. Cell-free strategies with the recruitment of the endogenous progenitor/stem cells, which enhance meniscal repair, are a promising method for treating meniscus injury.

References

- 1. Tapasvi, S. Lateral meniscus tears in ACL injured knee. *The Hip and Knee Journal*. 2021 (2)1: 5-21.
- 2. Santoso A, Poetera CY, Marindratama H, Anugrah JY, Anwar IB, Sibarani TSMHS. Both medial and lateral bucket-handle meniscus tears associated with chronic ACL injury: A rare presentation of triple-PCL sign. *Int J Surg Case Rep.* 2021 Oct;87:106413.
- 3. Santoso A, Praditya ES, Nagieb M, Aribowo GP, Anwar IB, Sibarani T. Symptomatic Discoid Meniscus: A Case series. *The Hip and Knee Journal*. 2021, (2)1: 50-53
- 4. Di Matteo B, Moran CJ, Tarabella V, Viganò A, Tomba P, Marcacci M, Verdonk R. A history of meniscal surgery: from ancient times to the twenty-first century. *Knee Surg Sports Traumatol Arthrosc.* 2016 May;24(5):1510-8.
- 5. Smith JH, Houck DA, Kraeutler MJ, McCarty EC, Frank RM, Vidal AF. "Doctor, What Happens After My Meniscectomy?". *J Bone Joint Surg Am.* 2019 Nov 6;101(21):1965-1973. doi: 10.2106/JBJS.19.00082. PMID: 31567671.



- 6. Liu C, Toma IC, Mastrogiacomo M, Krettek C, von Lewinski G, Jagodzinski M. Meniscus reconstruction: today's achievements and premises for the future. *Arch Orthop Trauma Surg.* 2013 Jan;133(1):95-109. doi: 10.1007/s00402-012-1624-2. Epub 2012 Oct 18. PMID: 23076654.
- 7. Southworth TM, Naveen NB, Tauro TM, Chahla J, Cole BJ. Meniscal Allograft Transplants. Clin Sports Med. 2020 Jan;39(1):93-123. doi: 10.1016/j. csm.2019.08.013. PMID: 31767113.
- Bin SI, Nha KW, Cheong JY, Shin YS. Midterm and Long-term Results of Medial Versus Lateral Meniscal Allograft Transplantation: A Meta-analysis. *Am J Sports Med.* 2018 Apr;46(5):1243-1250. doi: 10.1177/0363546517709777. Epub 2017 Jun 13. PMID: 28609637.
- 9. Pereira H, Fatih Cengiz I, Gomes S, Espregueira-Mendes J, Ripoll PL, Monllau JC, Reis RL, Oliveira JM. Meniscal allograft transplants and new scaffolding techniques. *EFORT Open Rev.* 2019 Jun 3;4(6):279-295. doi: 10.1302/2058-5241.4.180103. PMID: 31210969; PMCID: PMC6549113.
- 10. Houck dA, kraeutler mJ, Belk Jw, mccarty ec, Bravman Jt. Similar clinical outcomes following collagen or polyurethane meniscal scaffold implantation: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2018;26:2259–2269.

- 11. Guo W, Xu W, Wang Z, Chen M, Hao C, Zheng X, Huang J, Sui X, Yuan Z, Zhang Y, Wang M, Li X, Wang Z, Peng J, Wang A, Wang Y, Liu S, Lu S, Guo Q. Cell-Free Strategies for Repair and Regeneration of Meniscus Injuries through the Recruitment of Endogenous Stem/Progenitor Cells. Stem Cells Int. 2018 Jul 12;2018:5310471. doi: 10.1155/2018/5310471. PMID: 30123286; PMCID: PMC6079391
- 12. Dai TY, Pan ZY, Yin F. In Vivo Studies of Mesenchymal Stem Cells in the Treatment of Meniscus Injury. *Orthop Surg.* 2021 Dec;13(8):2185-2195. doi: 10.1111/ os.13002. Epub 2021 Nov 8. PMID: 34747566; PMCID: PMC8654668
- 13. Jacob G, Shimomura K, Krych AJ, Nakamura N. The Meniscus Tear: A Review of Stem Cell Therapies. *Cells.* 2019;9(1):92. Published 2019 Dec 30. doi:10.3390/cells901009
- 14. Olivos-Meza A., Pérez Jiménez F.J., Granados-Montiel J., Landa-Solís C., Cortés González S., Jiménez Aroche C.A., Valdez Chávez M., Renán León S., Gomez-Garcia R., Martínez-López V., et al. First Clinical Application of Polyurethane Meniscal Scaffolds with Mesenchymal Stem Cells and Assessment of Cartilage Quality with T2 Mapping at 12 Months. *Cartilage*. 2019 doi: 10.1177/1947603519852415