Natural Extracellular Matrix Grafts for Rotator Cuff Repair

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The results of open or arthroscopic repair of the rotator cuff vary widely in the literature. The factors that have been shown to affect outcome relate to the technique of surgery, the size of the tear, the quality of the tissue and age of the patient, the chronicity of the tear, the degree of muscle atrophy, and the degree of tendon retraction. In many cases, the size of the tear is correlated with the degree of tendon retraction, muscle atrophy, and loss of tissue quality. Postoperative care influences outcome and is dependent upon the length and type of protection in the first 6 weeks after surgery, as well as the progression of the rehabilitation program from passive range of motion through active motion and resistance exercises. The larger and more chronic the tear, the more likely the patient will benefit from an abduction brace or pillow and a slower progression of the rehabilitation program.

Despite our understanding of the factors that affect surgical outcome, a high percentage of larger tears fail to heal after either open or arthroscopic repair. Here, we must make a clear distinction between clinical and anatomical outcome. Historically, it was thought that good clinical outcomes could be achieved despite the persistence of a rotator cuff defect. Although many patients with persistent defects [as noted on magnetic resonance imaging (MRI), arthrography, or ultrasonography] have favorable clinical outcome when compared to their preoperative, patient-oriented, functional outcome scores, their objective (strength) and subjective (pain, functional activities and satisfaction) results are even better when the tear either partially or completely heals after surgery. Therefore, our goals for rotator cuff repair should include improvement in subjective scores and strength as well as a healed tendon. Hence, strategies to enhance the biological potential of the rotator cuff tendon to heal must be developed and investigated.
18.1. Biological Enhancement of Rotator Cuff Repair

Methods to enhance the biological potential of tendons to heal include the use of cell therapy, growth factors, gene delivery systems, and biological scaffolds. A thorough review of each of these methods is beyond the scope of this chapter. However, each will be discussed briefly here.

Mesenchymal progenitor cells (MPCs) are known to differentiate into a variety of cell phenotypes and are essential for natural wound healing. Accordingly, autologous or allogeneic MPCs can be obtained from bone marrow, blood, or adipose tissue, and can be culture expanded and delivered to a tendon repair site to enhance healing. Animal studies using MPCs delivered in collagen gel or poly-lactide-co-glycolide acid (PLGA) scaffolds to patellar or Achilles tendon defects have demonstrated improvements in the mechanical properties of the repair tissue compared to natural repair. Further, if MPC constructs are first mechanically conditioned in culture, such as allowing contracture around a suture, the resulting improvement in repair biomechanics is even more substantial. In addition, cell therapy using autologous tenocytes was shown to enhance flexor tendon repair in an avian model. Currently, cell therapy is used clinically for the effective treatment of skin wounds; however, its use has not been documented for rotator cuff (or any) tendon repair in humans to date.

A recent review article describes the roles of five growth factors that are known to be involved during tendon healing. These include insulin-like growth factor-I (IGF-I), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF). All five are markedly upregulated following tendon injury and are active at multiple stages of the healing process. These molecules or members of their superfamilies [such as cartilage-derived morphogenetic protein-2 (CDMP2) or osteogenic protein-1 (OP-1), members of TGF-β superfamily], have been explored in animal models as therapeutic agents to increase the efficacy and efficiency of tendon and ligament healing. Results demonstrate that exogenous application of these growth factors into the wound site (either singly or in combination) can improve the efficacy and efficiency of tendon or ligament healing. The challenges that remain in using growth factor therapies include attaining specific and sustained delivery of growth factors to target cells and determining optimal spatial and temporal delivery strategies. In addition, we must better understand how growth factors work together with one another and other molecules in the repair site. Clearly, growth factor therapies will require rigorous investigation in preclinical and clinical trials before they could become practical for general clinical use.

Using gene therapy, it is possible to increase the cellular production of certain proteins (such as growth factors) that are important for tendon healing. The feasibility of gene transfer to normal and injured tendon and ligaments has been demonstrated in animal models. Gene therapy