Update on Biologics in the Treatment of Rotator Cuff Disease

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Rotator cuff disease is the most common condition affecting the shoulder, causing significant pain and functional impairment in the adult population. Improvements in arthroscopic instrumentation and suture anchor technology have allowed the development of stronger constructs with multiple suture configurations, allowing repair of large and massive tears through minimally invasive means. However, although repair instrumentation and techniques have improved, healing rates have not. A high failure rate remains for large and massive rotator cuff tears. The next frontier in the management of rotator cuff disease is biologic augmentation to facilitate healing following repair.

The biology of the patient and the tendon remains a notable factor in rotator cuff healing. Repair efforts are negatively affected by decreased vascularity with normal aging, increased collagen fragility, muscle atrophy, and fatty infiltration of the chronically torn tendon. Surgical techniques to enhance the biology of the repair site and improve mechanical stability should be used whenever possible. Recognizing the tear pattern and performing an anatomic, tension-free repair provides the best chance for success. Microfracture of the healing bed of the greater tuberosity[1] and the use of vented suture anchors allow marrow contents from the humerus to bathe the repair site and facilitate healing. These surgical techniques can be used by the surgeon during any repair and may improve rotator cuff healing rates for large and massive tears.

The use of medications in the postoperative period may facilitate tendon healing to bone. Matrix metalloproteinases (MMPs) play a role in the pathophysiology of rotator cuff disease. Doxycycline has anticatabolic effects and blocks the destructive action of MMPs. Bedi et al[2] demonstrated that administration of oral doxycycline reduced MMP activity and enhanced healing at the enthesis following rotator cuff repair in a rat model. Doxycycline has the added benefit of protecting against infection with *Propionibacterium acnes*, which may inhibit healing of the rotator cuff. Chechik et al[3] showed that atorvastatin had a beneficial effect on the repaired rotator cuff, increasing the biomechanical strength of the repair through a cyclooxygenase-2–dependent mechanism.

Platelet-rich plasma (PRP) may be a safe adjuvant to rotator cuff repair; however, current studies have reported mixed results and have not shown improvement in healing rates or functional outcomes. Hoppe et al[4] recently showed that platelet-released growth factors heighten tenocyte proliferation and promote synthesis of the extracellular matrix to enhance healing of rotator cuff tendon in a laboratory culture medium. More clinical studies are necessary to determine the efficacy of PRP injections for rotator cuff disease.

Several papers presented at the 2013 Annual Meeting of the American Academy of Orthopaedic Surgeons demonstrated the use of biologics to facilitate healing in animal models. Angeline et al[5] showed that low vitamin D levels negatively af-

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fect early healing at the rotator cuff repair site in a rat model. Morikawa et al[6] presented that deficiency of SOD1, an antioxidant enzyme, induced degeneration and reduction of mechanical properties in the rotator cuff tendon. Biologic augmentation has shown success in the knee, as well. Strauss et al[7] showed that intra-articular injection of growth hormone demonstrated improvement in the gross and histologic appearance of repair tissue in the treatment of focal articular cartilage lesions, and Figueroa et al[8] reported that the addition of mesenchymal stem cells and a collagen scaffold aided in regeneration of the anterior cruciate ligament. The addition of these biologics may be on the horizon in surgical repair in the shoulder.

Gulotta and colleagues[9,10] have shown in several studies that mesenchymal stem cells can augment rotator cuff healing in a rat model. Oh et al[11] won the Neer Award for their 2013 paper on the use of adipose-derived stem cells (ADSCs). The authors injected ADSCs into the rotator cuff repair site in a rabbit model with simulated chronic subscapularis tears. The tendon-repair group with ADSCs demonstrated better healing compared with controls, superior muscle action potentials, higher load to failure in biomechanical testing, and less fatty degeneration by histologic examination. The authors concluded that the local administration of ADSCs might improve tendon healing and decrease muscle atrophy and fatty degeneration following rotator cuff repair.

Studies such as these pave the way for the future use of biologics in orthopaedic surgery. Continued research and advancements in biologic augmentation will likely improve healing rates and patient outcomes following rotator cuff repair.

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