Evidence for Utilization of Injectable Biologic Augmentation in Primary Rotator Cuff Repair: A Systematic Review of Recent Data from 2010-2022

Abstract #151

Bono OJ, Jenkin B, Forlizzi J, Mousad A, Le Breton S, MacAskill M, Mandalia K, Mithoefer K, Ramappa A, Ross G, Shah SS

Investigation performed at New England Baptist Hospital

Disclosures

I (and/or my co- authors) have no financial interests to disclose related to this presentation

Background

Biologic healing remains a significant challenge as tendon tear recurrence is associated with clinical deterioration in the long term.

Injectable biologic augmentation has been hypothesized to improve tissue quality at the suture-tendon interface.

Purpose

To investigate the effect of injectable biologic supplementation in rotator cuff repair and to assess the quality and adherence to evolving reporting standards.

Preclinically, outcomes of interest included reported load-to-failure, load-to-gap, gap size, and stiffness; while clinically, they included healing rate and any patient reported outcome measures.

Methods

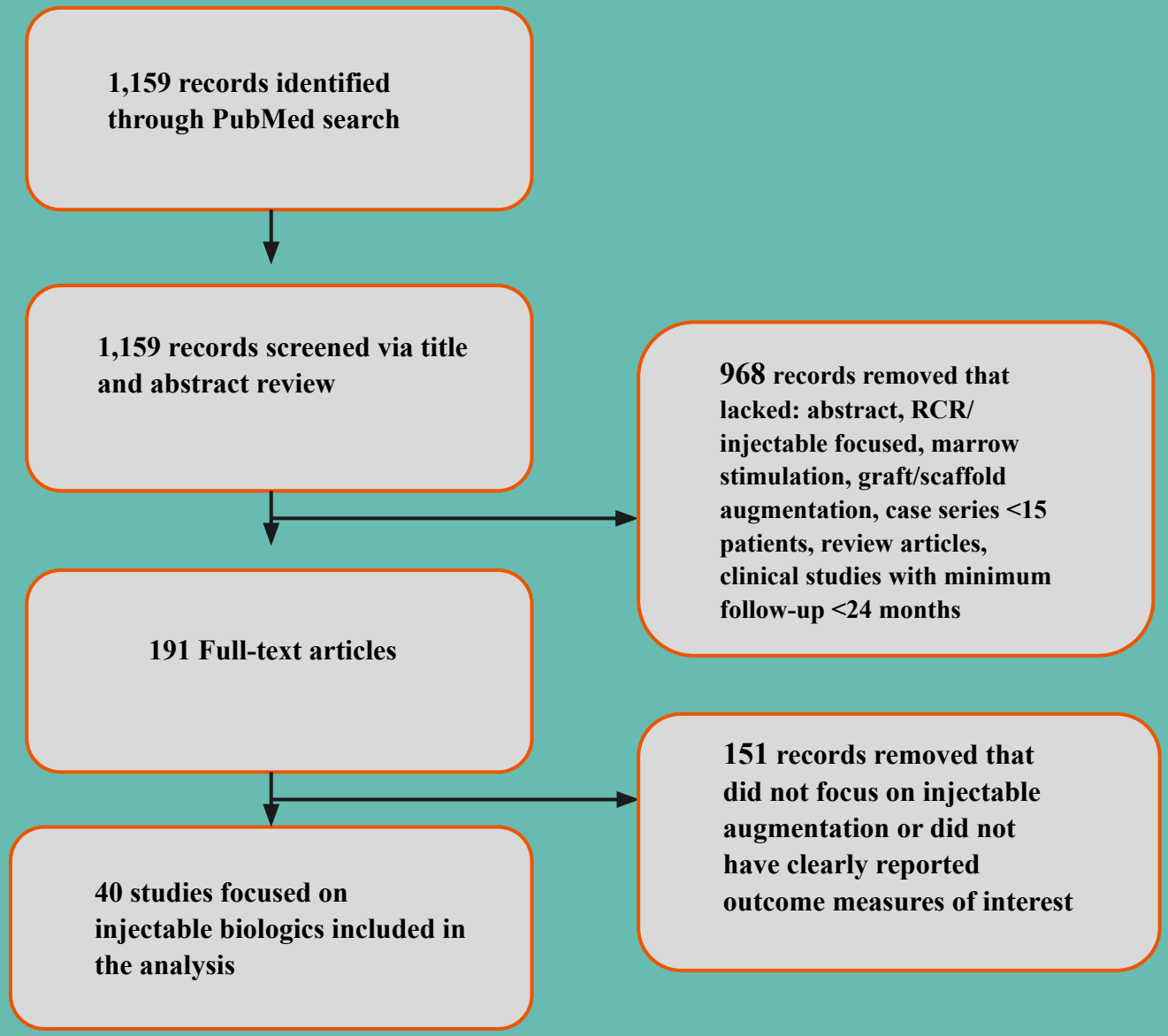
A systematic review was conducted following PRISMA guidelines.

Two reviewers performed relevant paper selection with a third arbitrating disputes.

Full text inclusion criteria were clinical studies focused on rotator cuff repair augmentation with clearly reported healing rate or any patient reported outcome measure, and preclinical studies with in vivo animal models and clearly reported load-to-failure, load-to-gap, gap size, or stiffness. Any studies that were not focused on injectable augmentation were excluded.

Assessment of quality, risk of bias, and adherence to relevant Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO) guidelines was performed for each clinical study.

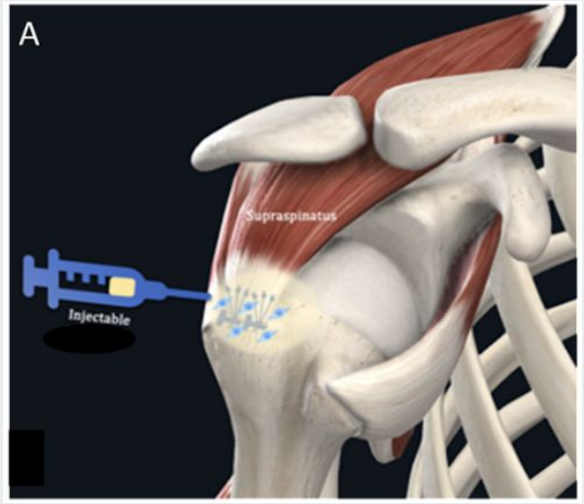
PRISMA Flowchart



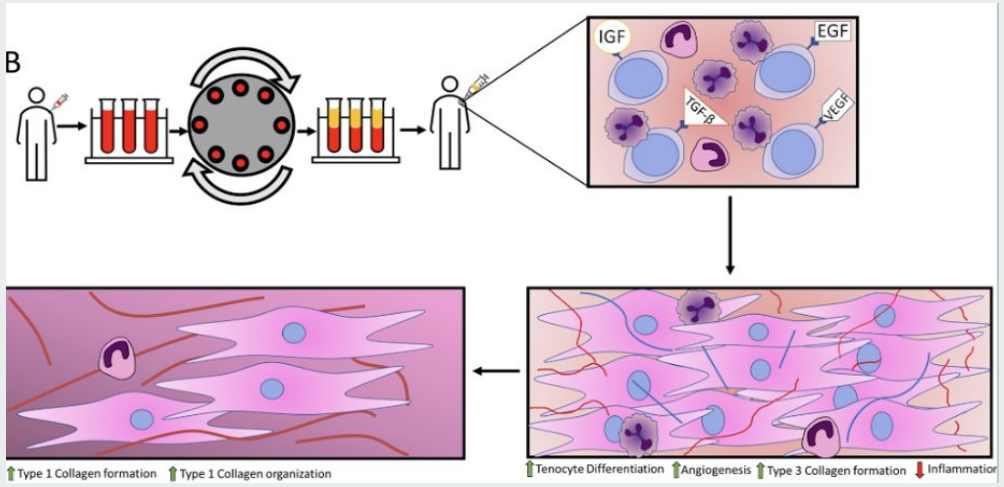
In total **40** studies, consisting of **29** preclinical (in vivo animal models) and **11** clinical, were included in the study.

Results

Injectables reported included growth factors (such as TGF- β3, erythropoietin), bone marrow- & adipose-derived mesenchymal stem cells (ADSC), and other agents (namely platelet-rich plasma (PRP) & hyaluronic acid).

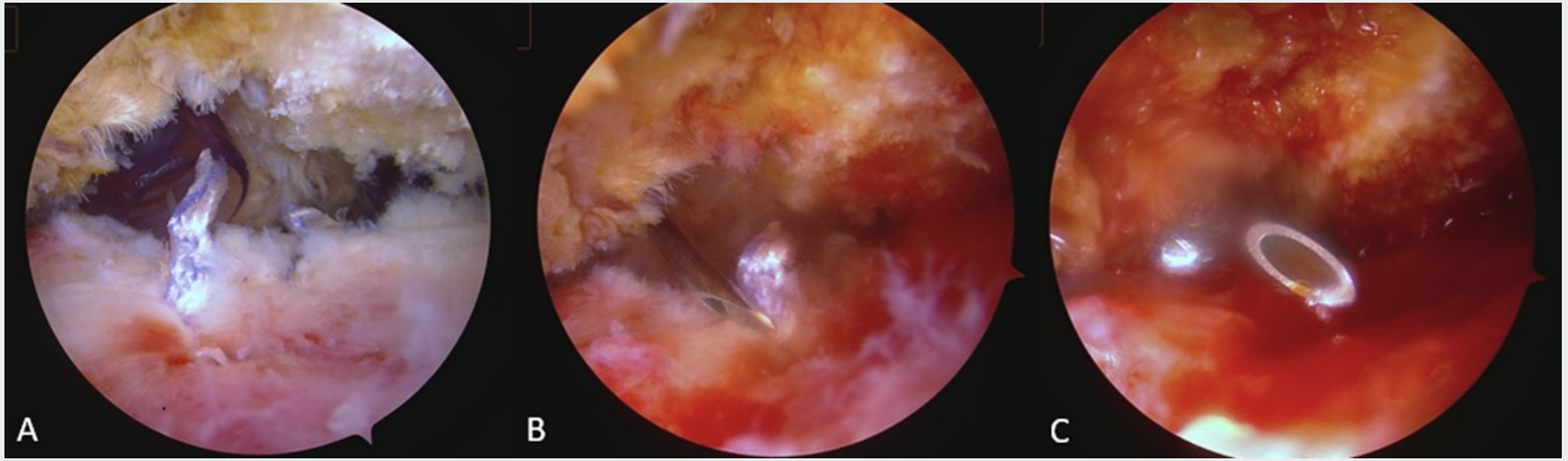


A: Depiction of injection of biologic into the site of rotator cuff repair.



B: PRP collection and injection into the repair site releasing growth factors that stimulate tenocyte differentiation and improved collagen quality and quantity.

Intraoperative Injection of Biologic Augment Following Rotator Cuff Repair



A: The rotator cuff repair site visualized by arthroscope.

B: Needle inserted into the site of the repair.

C: Injection of the biologic augment via the needle at the site of the repair.

Results

Twenty-nine preclinical studies were identified in total. Sixteen (55%) of the preclinical studies related to injectable biologics were performed in a rat model, eleven were conducted in rabbits (38%), two in mice (7%).

The most common findings for **preclinical** injectables were increased load-to-failure (16/29 studies, or 55.2%) and improved collagen histological quality (11/29 studies, or 37.9%).

Notably, no injectable was found to have a negative effect on outcomes in the preclinical setting.

Results

Clinically, all eleven clinical studies (10 PRP, 1 ADSC) indicated no adverse events with similar or improved patient-reported outcomes measures (PROMs) compared to control repairs.

(On average, the clinical studies adhered to 66% of relevant MIBO reporting guidelines and had low risk of bias)

In one study utilizing an innovative delivery technique, a concentrated PRP globule with fibrin matrix was shuttled over a suture to maintain concentrated PRP at the repair site and demonstrated a significant decrease in retears (P=0.03) on MRI evaluation at 31-month follow-up.

Results

A **matched cohort study** investigating augmentation with ADSCs demonstrated the retear rate was significantly lower in the ADSC augmented group than in the control repair group at 28-month follow-up ($P<.001$).

However, there were no significant differences in range of motion or patient-reported outcomes between groups.

Conclusions

Preclinically, a wide range of injectables has been investigated, with approximately 83% of studies demonstrating a positive biomechanical or histologic effect and no studies showing an overall negative effect.

Clinically, while there remains scant data at long term follow-up in favor of PRP, utilization of innovative delivery techniques may reduce the risk of arthroscopic washout of PRP and has been shown to potentially improve retear rates.

Further, ADSCs have been shown to reduce retear rates at 28-month follow-up, making ADSCs a promising injectable augment for RCR.

Discussion

Preclinically, a large variety of substances have been investigated, the majority of which led to improved repair constructs.

Notably, adipose- and bone marrow-derived stem cells and growth factors including TGF-β and FGF had positive effects in the preclinical setting.

Discussion

PRP and adipose-derived mesenchymal stem cells have been researched in the clinical setting with various technique improvements leading to improved patient outcomes.

Delivery of PRP may play an essential role. Both improving PRP preparation and utilizing various modes of PRP delivery such as fibrin gels show potential in improving RCR biologic injectable augmentation and should be further explored as methods to enhance patient outcomes.