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

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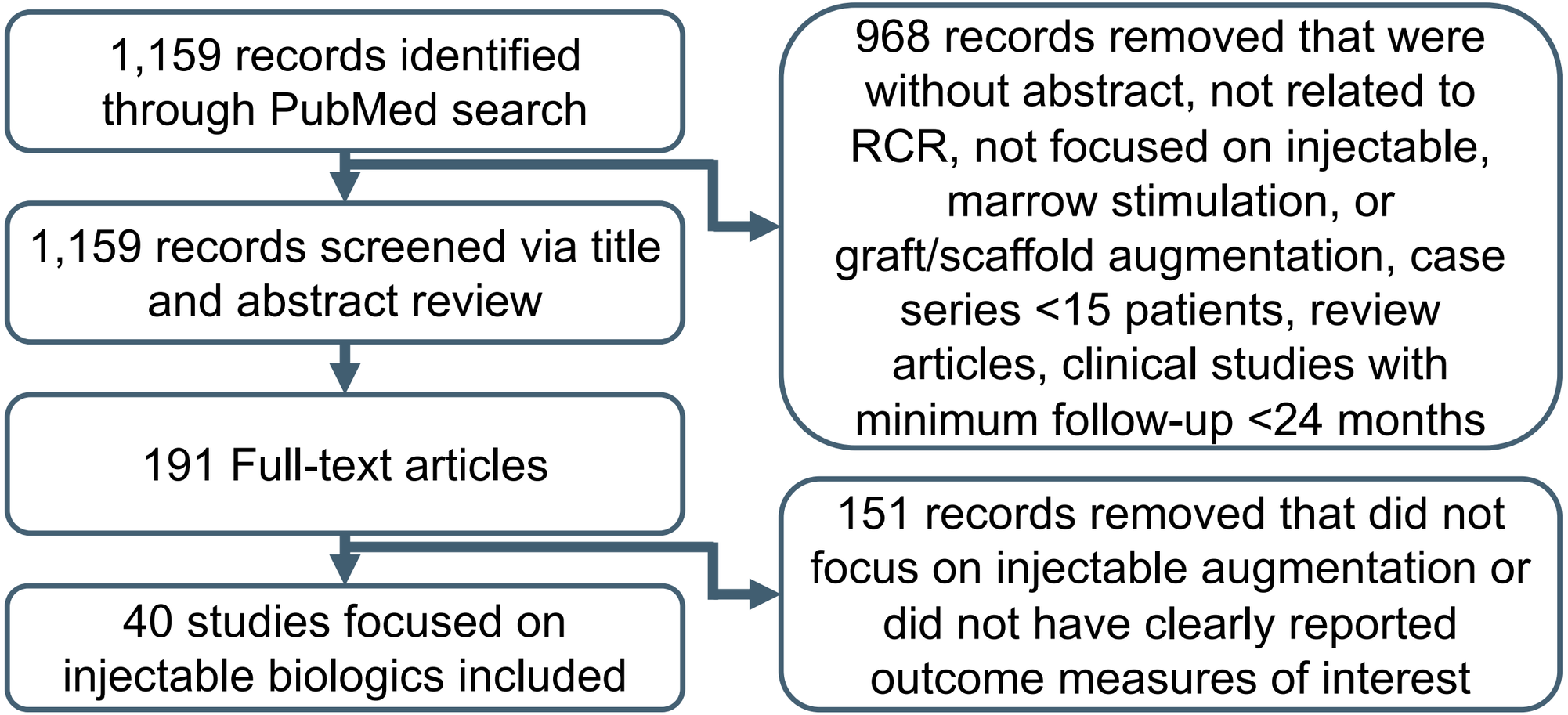
A total of 40 studies focused on injectable biologics were included in our analysis.



Twenty-nine preclinical studies were evaluated, covering a wide range of targets.

Overview

- **Twenty-nine preclinical studies were identified in total**; 16 (55%) were performed in a rat model, 11 were conducted in rabbits (38%), 2 in mice (7%)
- **No injectable was found to have a negative effect** on outcomes in the preclinical setting
- 55.2% of preclinical injectables demonstrated **increased load-to-failure**; 37.9% demonstrated **improved collagen quality and/or quantity**

Growth Factors
(8 studies)

- **Significant increase in load-to-failure** for all growth factors except TGF-β3 + adipose-derived stem cells and erythropoietin

Marrow/Adipose SCs
(10 studies)

- Demonstrated both **greater load-to-failure** and **reduced fatty infiltration**
- **No BMSCs** provided lasting collagenous improvements

Other Biologics
(11 studies)

- Includes rPTH, melatonin, and HA
- Botulinum toxin and rPTH **did not demonstrate improvement in outcomes**

HA: hyaluronic acid; TGF-β3: Transforming Growth Factor-β3; rPTH: Recombinant parathyroid hormone; BMSC: Bone marrow-derived mesenchymal stem cell.

Clinical studies, focused on PRP, showed significant heterogeneity in outcomes.

Overview

- **Eleven clinical studies** (10 PRP, 1 ADSC) were identified in total
- The studies were found to have **low risk of bias** per Newcastle-Ottawa Scale and Cochrane Risk of Bias assessment tool

Platelet-Rich Plasma (PRP)

(10 studies)

- **Significant heterogeneity**; multiple trials failed to demonstrate improvement in clinical or radiographic outcomes
- Three PRP studies (Barber 2011, Pandey 2016, Liu 2021) demonstrated **reduced retear rates** in PRP group vs control

Adipose-derived Mesenchymal SCs

(1 study)

- A matched-cohort study demonstrated the a **lower retear rate** in the intervention group (14.3%) vs. control (28.5%) at 28-month follow-up ($p < 0.001$)
- **No significant differences** in **range of motion or patient-reported outcomes**

ADSC: Adipose-derived mesenchymal stem cells

Key Takeaways

1. Approximately 83% of preclinical experiments demonstrated a **positive biomechanical or histologic effect**; **no negative effect** was seen by biologic injectable augmentation

2. **Significant heterogeneity in outcomes** exists in clinical literature exploring PRP with multiple trials failing to demonstrate any significant improvement in clinical or radiographic outcomes

3. **Delivery and preparation methods** of PRP may significantly alter outcomes and **tear size** may play a critical role in deciding utilization of PRP

4. Adipose-derived mesenchymal stem cells (MSCs) have demonstrated an **overall positive effect** in the preclinical setting and a **decreased retear rate** versus controls in a matched cohort study

PRP: Platelet-Rich Plasma

Limitations

- **Select injectables without strong evidence in RCR**, but which do affect the supraspinatus tendon, were excluded from our review; however, they **may still warrant attention**.
- **Significant variability** in preparation and source of injectable biologics coupled with a **small sample size** of clinical studies which may contribute to **heterogeneity of outcomes**.
- Outcomes of PRP studies have a **high fragility index** and thus require further study to develop a clearer picture of PRP effectiveness in RCR

PRP: Platelet-Rich Plasma

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