

INPLASY

The Use of Extracellular Vesicles in Achilles Tendon Repair: A Systematic Review

INPLASY202430019

doi: 10.37766/inplasy2024.3.0019

Received: 05 March 2024

Published: 05 March 2024

Corresponding author:

Varun Kasula

v_kasula0902@email.campbell.edu

Author Affiliation:

Duke University School of Medicine:
Department of Orthopedic Surgery.

Kasula, V¹; Padala, V²; Gupta, N³; Doyle, D⁴; Bagheri, K⁵; Anastasio, A⁶; Adams, S⁷.

ADMINISTRATIVE INFORMATION

Support - Duke University School of Medicine: Department of Orthopedic Surgery.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202430019

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 March 2024 and was last updated on 05 March 2024.

INTRODUCTION

Review question / Objective Can extracellular vesicle-based treatment augment and enhance wound healing in Achilles tendon pathologies?

Rationale Achilles tendon injuries are common musculoskeletal disorders that can lead to long-term disability and reduced quality of life. While several treatment modalities have been explored, emerging research suggests that extracellular vesicles (EVs) and exosomes, small membrane-bound vesicles secreted by various cell types, may play a pivotal role in the healing of Achilles tendon injuries. This proposed systematic review aims to comprehensively analyze the existing literature to assess the therapeutic potential of EVs and exosomes in Achilles tendon injury healing.

Condition being studied The condition/s being studied are Achilles tendon pathologies.

METHODS

Search strategy A database search was conducted in October 2023 in PubMed, Scopus, and Embase using various combinations of the terms including: "Achilles tendon, Achilles tendon repair, Achilles tendon surgery, extracellular vesicle, extracellular vesicle, exosome, exosomes, microvesicle, microvesicles, ectosome, ectosomes, apoptotic body, apoptotic bodies." No restrictions or filters will be enforced on the searches.

Participant or population This is a systematic review of in vivo animal studies. So the subjects being studied mainly consists of rats, mice, rabbits, etc.

Intervention The intervention group are the animal groups that received the extracellular vesicle treatment.

Comparator The comparator includes the negative control groups (i.e. injections of saline or phosphate-buffered saline, surgical repair only, or no treatment at all) and/or the positive control groups (i.e. injections of mesenchymal stem cells without extracellular vesicles, etc.).

Study designs to be included All studies that evaluate the effect of extracellular vesicle-based treatment on Achilles tendon pathologies in in vivo animal models will be included.

Eligibility criteria Studies must be a full-text papers (i.e. no abstracts, posters, presentations, etc.). They also must be published in a peer-reviewed journal and provide primary data (i.e. no review papers, etc.).

Information sources Electronic databases are the primary intended information source. If any data/information was missing or unclear, the primary authors of the paper in question were contacted to retrieve it.

Main outcome(s) The outcome measures that were considered in this review include: Type of EV used and cell source
Mechanism of induced injury (i.e. surgical vs. non-surgical) to Achilles tendon
Mechanism of delivery of EV to injury site
Experimental and control groups of each included study
Overall reported results of each included study
Proposed mechanisms by which EVs influence wound healing
Histologic and biomechanical analysis of Achilles tendon pathology.

Quality assessment / Risk of bias analysis The SYRCLE risk of bias tool was used. The SYRCLE tool was utilized to conduct a rigorous quality assessment of the included in vivo studies. It consists of 10 different parameters and an overall risk of bias score. The quality assessment was completed by 2 independent reviewers, and all conflicts were resolved by a third independent reviewer.

Strategy of data synthesis There was great heterogeneity that existed within the study designs and outcome measurement protocols in the included studies, thus rendering a meta-analysis not possible. A narrative synthesis of the data was separated by 3 different sections: (1) General information of the included studies (i.e. authors, animal model, type and source of EVs, etc.); (2) Information regarding study design (i.e. experimental groups, control groups, mechanism

of induced injury & EV delivery, etc.); (3) Outcome measurement information (i.e. overall results, proposed mechanisms, histologic & biomechanical analysis, etc.).

Subgroup analysis None planned.

Sensitivity analysis None planned.

Language restriction The search was only done in English, but no language restrictions were placed on published papers.

Country(ies) involved United States.

Keywords Achilles tendon; extracellular vesicle; exosome; mesenchymal stem cell; wound healing; collagen; microRNA; tenocyte; extracellular matrix; inflammation; macrophage polarization.

Contributions of each author

Author 1 - Varun Kasula - Author 1 conceptualized the project, worked on data search and extraction, and drafted the manuscript.

Email: v_kasula0902@email.campbell.edu

Author 2 - Vikram Padala - Author 2 worked on the data search and extraction process and helped with drafting the manuscript.

Email: tup54382@temple.edu

Author 3 - Nithin Gupta - Author 3 helped with conceptualization of the project, created the figures, helped develop the selection criteria, and helped with the risk of bias assessment process.

Email: n_gupta0210@email.campbell.edu

Author 4 - David Doyle - Author 4 helped with writing the manuscript.

Email: doyle2dm@cmich.edu

Author 5 - Kian Bagheri - Author 5 helped with the risk of bias assessment and editing the manuscript.

Email: k_bagheri1204@email.campbell.edu

Author 6 - Albert Anastasio - Author 6 helped with guidance and also editing the manuscript.

Email: albert.anastasio@duke.edu

Author 7 - Samuel Adams - Author 7 helped with guidance and also editing the manuscript.

Email: samuel.adams@duke.edu