Chaudhari, M., Zelko, I., Lorkiewicz, P., Hoetker, D., Doelling, B., Brittian, K., Bhatnagar, A., Srivastava, S., & Baba, S. P. (2023). Metabolic pathways for removing reactive aldehydes are diminished in atrophic muscle during heart failure. *Journal of Cardiac Failure*. https://doi.org/10.21203/rs.3.rs-3621159/v1

Definitions

- **Reactive Aldehydes:** Harmful chemicals formed during oxidative stress that can damage cells.
- **Atrophic Muscle:** Muscle that has shrunk or weakened.
- **Heart Failure:** A condition where the heart cannot pump blood effectively.
- **Aldehyde Dehydrogenase (ALDH2):** An enzyme that helps remove harmful aldehydes.
- **Histidyl Dipeptides (Carnosine and Anserine):** Compounds in muscles that help neutralize harmful substances.
- **Transverse Aortic Constriction (TAC):** A surgical method used to create heart failure in animal studies.
- **Oxidative Stress:** Damage caused by free radicals, which are harmful molecules that can harm cells.

Key Findings

- Heart failure causes muscle wasting and increases harmful reactive aldehydes in muscles.
- Enzymes and compounds that remove these harmful aldehydes are reduced in atrophic muscles during heart failure.
- Muscle-protecting compounds like carnosine are decreased in the muscles of heart failure mice.

Introduction

This study looks at how heart failure leads to muscle wasting and damage. The researchers focus on how heart failure increases harmful chemicals in muscles and decreases the body's ability to remove these chemicals, leading to muscle shrinkage and weakness.

Main Content

Background

Heart failure is a condition affecting many people and can lead to muscle wasting, a serious complication that reduces a patient's strength and quality of life. Muscle wasting in heart failure is caused by several factors, including oxidative stress, which produces harmful chemicals called reactive aldehydes. These aldehydes damage muscle cells, leading to atrophy. Normally, the body uses certain enzymes and

compounds to remove these harmful substances, but this study investigates how these processes are affected in heart failure.

Objectives

The main goal of the study was to understand how heart failure affects the metabolic pathways that remove reactive aldehydes from muscle tissue. The researchers wanted to see if these pathways are diminished in atrophic muscle during heart failure.

Methods

- **Participants:** Male wild-type mice were used for the study.
- **Procedure:** Mice were subjected to a heart failure model using transverse aortic constriction (TAC) surgery. After 14 weeks, their muscle tissues were analyzed.
- **Measurements:** The study measured muscle weights, levels of harmful aldehydes, enzymes like ALDH2, and protective compounds like carnosine and anserine using techniques like Western blotting and LC/MS-MS.

Results

- **Muscle Wasting:** Mice with heart failure had decreased body and muscle weights, indicating muscle wasting.
- **Increased Aldehydes:** Higher levels of harmful aldehydes (HNE and acrolein) were found in the muscles of heart failure mice.
- **Decreased Protective Pathways:** The enzyme ALDH2 and the compounds carnosine and anserine were significantly reduced in the muscles of heart failure mice. This reduction hampers the muscle's ability to remove harmful aldehydes, contributing to muscle damage and atrophy.

Conclusion

The study shows that heart failure leads to muscle wasting by increasing harmful chemicals in the muscles and decreasing the body's ability to remove these chemicals. Enzymes and compounds that protect muscles are reduced, leading to greater muscle damage. These findings highlight the need for further research into therapies that can boost these protective pathways and prevent muscle wasting in heart failure patients.

Word Count: 488