Rewriting The Scar: Emerging Antifibrotic Therapies in Heart Failure and Post-MI Remodeling

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Background:

Cardiac fibrosis is a key pathological feature of both heart failure and adverse ventricular remodeling following myocardial infarction (MI). It contributes to diastolic and systolic dysfunction, arrhythmogenesis, and long-term morbidity. While traditional pharmacological agents such as the renin-angiotensin-aldosterone system (RAAS) inhibitors exert indirect antifibrotic effects, recent advances have identified novel pathways and agents that may allow for direct modulation of fibrotic remodeling. This has opened the door to a new therapeutic era focused on disease modification at the myocardial tissue level.

Aim and objectives:

To explore and summarize the emerging landscape of antifibrotic pharmacotherapies targeting cardiac fibrosis, with particular emphasis on their potential application in heart failure and post-MI remodeling.

Methods:

A comprehensive literature search was conducted using **PubMed**, **Embase**, and **ClinicalTrials.gov** up to **March 2025**. Keywords included "cardiac fibrosis," "antifibrotic therapy," "Finerenone," "pirfenidone," "TGF-beta inhibitors," and "galectin-3 inhibitors." The search yielded **326 articles**, from which **72 studies** were selected after removing duplicates and screening titles and abstracts for relevance. Inclusion criteria encompassed preclinical and clinical studies evaluating pharmacological agents with direct antifibrotic mechanisms in cardiovascular disease. Following full-text review, **18 studies** met the inclusion criteria: **8 preclinical**, **6 early-phase human trials**, and **4 large-scale clinical trials**.

Result:

Among these, Finerenone, a non-steroidal mineralocorticoid receptor antagonist, has demonstrated significant cardiovascular benefits. The FIDELIO-DKD and FIGARO-DKD trials reported reductions in heart failure hospitalizations and attenuation of cardiac remodeling in patients with chronic kidney disease and type 2 diabetes. Pirfenidone, an antifibrotic agent approved for idiopathic pulmonary fibrosis, has shown potential in mitigating myocardial fibrosis in preclinical models, though clinical data in cardiac patients remain limited. Emerging therapies targeting galectin-3 and TGF-β pathways have exhibited promising results in early-phase studies, demonstrating reductions in myocardial fibrosis markers and improvements in ventricular compliance. However, these agents have yet to be incorporated into standard clinical practice pending further validation in large-scale trials.

Conclusion:

Cardiac fibrosis is a modifiable component of heart failure and post-MI remodeling. The development of targeted antifibrotic pharmacotherapy marks a significant paradigm shift from symptomatic management to disease-modifying strategies. Finerenone and other emerging agents offer promising therapeutic potential, especially in high-risk populations such as those with heart failure with preserved ejection fraction (HFpEF) and post-infarction left ventricular dysfunction. Future studies are warranted to validate their efficacy in diverse clinical settings and to explore their integration into guideline-directed medical therapy.

Keywords:

cardiac fibrosis, heart failure, post-myocardial infarction, Finerenone, antifibrotic therapy, ventricular remodeling