

PEER-REVIEW REPORT

Name of journal: *World Journal of Cardiology*

Manuscript NO: 85556

Title: Current and Novel Therapies for Patients with Coexisting Heart Failure with Reduced Ejection Fraction and Non-Alcoholic Fatty Liver Disease: A Comprehensive Review

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06312955

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Assistant Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: United States

Manuscript submission date: 2023-05-04

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-11 04:06

Reviewer performed review: 2023-05-17 12:17

Review time: 6 Days and 8 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors of this review have done an excellent job summarizing the non-pharmacological and pharmacological therapies available or being considered for patients with coexisting heart failure with reduced ejection fraction (HFrEF) and non-alcoholic fatty liver disease (NAFLD). Effective management of coexisting HFrEF and NAFLD requires addressing underlying risk factors and optimizing treatment for both conditions. Careful selection of medications for HFrEF is crucial to avoid worsening NAFLD, and vice versa. This comprehensive review provides valuable information on current treatment options for coexisting HFrEF and NAFLD, which can aid in the development of new therapeutic strategies in the near future. However, I have few comments to be addressed. Some notable genes have been identified to have a role in the pathophysiology of both HFrEF and NAFLD, providing potential targets for effective treatment in cases of coexistence. One such gene is FGF21, which has been



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found to be upregulated in both HFrEF and NAFLD with potential role in inhibiting oxidative stress, inflammation, obesity, cardiac hypertrophy and insulin resistance. Exploring the potential of targeting these genes for therapeutic purposes would be a fascinating and informative topic for a broader audience. It could shed light on novel approaches that could potentially benefit individuals with coexisting HFrEF and NAFLD. What about the common biomarkers for detecting HFrEF and NAFLD? Identifying reliable biomarkers can aid in the early detection, monitoring, and management of both conditions. Discussing common biomarkers for detecting HFrEF and NAFLD would be a valuable addition to the manuscript. It may provide valuable insights into the diagnostic aspects of coexisting HFrEF and NAFLD. Overall, implementing these suggestions would further improve the already well-structured and well-written review, increasing its accessibility and providing valuable information to a broader range of readers.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04051277

Position: Peer Reviewer

Academic degree: BSc, Doctor

Professional title: Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-05-04

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-18 01:16

Reviewer performed review: 2023-05-18 01:32

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

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Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review paper summarizes current and novel therapies for patients with coexisting heart failure with reduced ejection fraction (HFrEF) and non-alcoholic fatty liver disease (NAFLD). My major concern is that some sections, such as the table only mentioned for NAFLD) and conclusion even without the key work HFrEF/HFpEF. This creates a disconnect between the title and the content. Additionally, the current referencing style, where the reference number is placed at the end of the sentence with subscription, seems odd. It would be good to double-check if this referencing style is suggested by the publisher.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04322445

Position: Peer Reviewer

Academic degree: FRCP (C), MBBS, MD

Professional title: Professor

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: United States

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Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-18 08:58

Reviewer performed review: 2023-05-25 08:22

Review time: 6 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting review of the association of NAFLD and heart failure focusing mainly on HFrEF including the pathophysiological associations, overlapping comorbidities and other relationships with the intention of highlighting the association and looking at current evidence of treatment that can effectively treat both conditions. I think this is an important topic for a review and had a degree of novelty. It is generally well written but I have a few comments. 1. Suggest changing the title to: Current and Novel Therapies for Patients with Coexisting HFrEF and NAFLD: Where do we stand ? As this is a review looking overall at this association you could also consider the title : The association of NAFLD and HFrEF. A review. 2. Please change the word emphasize in the 3rd last line of the abstract to emphasis. 3. Suggestion changing the heading Pathophysiology to Pathophysiology linking NAFLD with cardiovascular disease and HFrEF 4. The references in the manuscript are currently all shown as subscripts- please



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change to the format needed for the journal. 5. Although you have focused on HFrEF and NAFLD I think a few lines under the heading of NAFLD and HFpEF will be of value. 6. Suggest adding a figure showing NAFLD by imaging and histology.