Reviewer #1:

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.

Dear reviewer,
We sincerely appreciate your valuable suggestions and agree with them. Specifically, we have changed the title to: "Current and Novel Therapies for Patients with Coexisting Heart Failure with Reduced Ejection Fraction and Non-Alcoholic Fatty Liver Disease: A Comprehensive Review."

2. Please change the word emphasize in the 3rd last line of the abstract to emphasis.

Dear reviewer, we agree with your suggestion. We changed the word to "emphasis".

3. Suggestion changing the heading Pathophysiology to Pathophysiology linking NAFLD with cardiovascular disease and HFrEF

Dear reviewer, we agree with your suggestion. We changed the word to "Pathophysiology linking NAFLD with cardiovascular disease and HFrEF".

4. The references in the manuscript are currently all shown as subscripts- please change to the format needed for the journal.

Dear reviewer, thanks for the information. We changed the references to the journal's format.

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.

Dear reviewer, we appreciate and agree with your suggestion. We added the following information regarding NAFLD and HFpEF:
"The association between HF and NAFLD has similar processes in both HFpEF and HFrEF patients, which are mediated by inflammatory and fibrosis processes. The pathophysiological relationship between NAFLD and HFpEF is attributable, at least in part, to the secretion of adipokines and proinflammatory cytokines such as leptin that at the level of liver tissue, have a profibrotic activity, and in the heart produce cardiac hypertrophy and endothelial dysfunction. Other important factors are TNF-A and IL-6 which contribute to hepatocyte injury and NAFLD, while damaged hepatocytes release IL-33 which promotes the profibrotic effect. In the heart, IL-33 is released in response to myocardial fiber stretch".

6. Suggest adding a figure showing NAFLD by imaging and histology.

Dear reviewer, thank you for your suggestion. Unfortunately, we don't have any available NAFLD imaging or histology to submit in the paper. Thank you

Reviewer#2:

1.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.

Dear reviewer,
Thank you for your valuable suggestion. We greatly appreciate your feedback and have made the necessary revisions to the table in order to provide more precise information. We have ensured that the table clearly illustrates the similarities in treatments between NAFLD and HFrEF.

Furthermore, we have carefully reviewed and modified the conclusion to ensure accuracy regarding HFrEF and NAFLD. The updated conclusion is as follows:

"Heart failure with reduced ejection fraction is a major public health problem worldwide. Additionally, due to the rising numbers of obesity and associated comorbid conditions such as diabetes mellitus and metabolic syndrome, NAFLD has also become a common condition. Multiple recent studies have shown a strong association between HF, specially the HFrEF subtype, and NAFLD. Although there are multiple proposed pathophysiologic mechanisms, most of them have as a common factor the development of systemic inflammation. To date, several non-pharmacological, pharmacological, and surgical interventions have been studied in patients with concomitant HFrEF and NAFLD and so far evidence shows potential benefits of dietary changes; certain medications, such as ACEi, ARB, MRA, and SGLT-2i; and bariatric surgery. However, there is still a lack of robust data and well designed clinical trials investigating other drugs or novel therapies that could have a benefit on both of these conditions and improvement in outcomes."

Once again, we would like to express our gratitude for your insightful input, which has greatly contributed to the improvement of our manuscript.

2. Additionally, the current referencing style, where the reference number is placed at the end of the sentence with subcription, seems odd. It would be good to double-check if this referencing style is suggested by the publisher.

Dear reviewer, we appreciate your suggestion. We changed the references according to the journal's format.

Reviewer #3:

1.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 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.

Dear reviewers, we agree and appreciate your suggestion. We have added to the paper the following information regarding potential biomarkers and gene therapy:

¨Fibroblast growth factor 21 (FGF21) is a hormone that plays an important role in regulating metabolic pathways. This hormone was mainly produced by the liver and its signaling was found to be associated with NAFLD pathogenesis. Additionally, FGF21 also regulates lipid and glucose metabolism which are correlated with cardiovascular disease and heart failure. In summary, FGF21 might be a potential biomarker for prognosis prediction or treatment target in future. However, further studies are required to identify the precise role of this¨