

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80261

Title: Management of metabolic-associated fatty liver disease: The diabetology perspective

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06008175

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-31 00:46

Reviewer performed review: 2022-11-02 06:17

Review time: 2 Days and 5 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input type="radio"/>] Yes [<input checked="" type="radio"/>] No



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**Peer-reviewer
statements**

Peer-Review: ☒ Anonymous ☐ Onymous

Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

This review described the management of the metabolic-associated fatty liver disease. Since MAFLD is a novel concept proposed in 2020, little is known about its management and more time will be needed for its establishment. Still, the review will help us understand the concept of MAFLD and develop future treatments.

PEER-REVIEW REPORT

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Manuscript NO: 80261

Title: Management of metabolic-associated fatty liver disease: The diabetology perspective

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03668558

Position: Editorial Board

Academic degree: MD

Professional title: Consultant Physician-Scientist, Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-06 07:45

Reviewer performed review: 2022-11-13 20:28

Review time: 7 Days and 12 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
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

This is a well written paper which offers an overview on current (pharmacological and not) treatments for patients with metabolic syndrome and metabolic associated liver disease (MAFLD). 1. The Authors said that, because of the interplay between MAFLD and diabetes, all patients with one of these conditions should be evaluated/monitored for the other. This point poses logistic issues. Who should monitor these patients? GP? Hepatologists? Diabetologists? This is an important point, in my opinion, since the number of potentially involved patients is very large. There could be many patients who are monitored/followed-up twice, and others that are not monitored at all. A comment would be valuable. 2. There are many therapies that have recently revolutionized the treatment of diabetes. Some of these (e.g., semaglutide) seem effective also in reducing fibrosis in patients with MAFLD. Moreover, these patients share often arterial hypertension, obesity, CKD and other metabolic diseases. What type of strategy the Authors suggest? Multidisciplinary consultation for an individualized treatment plan for all patients? for patients who fail first-line therapy? 3. What therapy (between SGLT2-i and GLP1-Ras) the Authors suggest as first line therapy in patients with diabetes and MAFLD? 4. What is the Authors' advice about bariatric surgery? Do they consider it after failure of weight loss or do they consider it earlier, in patients with MAFLD, Type 2 DM and BMI>35? 5. I congratulate the Authors for the section about pregnancy 6. HCC shares different characteristics in patients with MAFLD than in patients with different underlying etiologies. This point should be discussed more in depth, in my opinion. Minor - I suggest to add a brief definition of NASH, NAFLD, MAFLD, for the non-expert reader - Why SBP has been reported as the only complication of Portal hypertension

(Table)? - Liver transplantation in patients with MAFLD is an established therapeutic option. Nevertheless, high BMI, type-2 DM may deserve special attention in the setting of LT. A comment would be important.

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Manuscript NO: 80261

Title: Management of metabolic-associated fatty liver disease: The diabetology perspective

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05914775

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor, Lecturer

Reviewer's Country/Territory: Thailand

Author's Country/Territory: United Kingdom

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-06 05:37

Reviewer performed review: 2022-11-14 04:29

Review time: 7 Days and 22 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
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 type="checkbox"/> Minor revision <input checked="" 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
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SPECIFIC COMMENTS TO AUTHORS

Jeeyavudeen et al. extensively reviewed the management of MAFLD from the view of an endocrinologist. This review is updated and interesting for most readers. However, there were some considerations that the authors should be addressed. Major: 1. Due to the rapid growth of knowledge in this field. Please add the subheading of search strategies and the date of searching after the introduction part. 2. Page 6: Please review more information regarding the role of liver biopsy in those patients because liver biopsy may require intermediate to high-risk fibrosis patients or NASH diagnosis or exclude other coexisting diseases. 3. Currently, there are many dietary regimens to improve obesity and MAFLD. It's essential to review whether the type of diet affects the metabolic parameters, including the ketogenic, low carbohydrate, and the Mediterranean diet. Lastly, what regimen is suitable for this group of patients? 4. Besides exercise intervention, increased physical activity is helpful in those patients. Please review more information regarding the suggestion of increased physical activity, i.e., walking steps. 5. The exercise comprised two methods, including aerobic and resistance training. Please review more papers about these types of exercises. 6. In summary, lifestyle intervention is hard to achieve, but encouragement is necessary. Please explain more information about the method to improve compliance with lifestyle intervention. 7. Based on current evidence, pioglitazone is only used in patients with biopsy-proven NASH, especially with T2DM. Therefore, this sentence can misinterpret; "when there is evidence of NASH (raised transaminases and/or non-invasive tests)". Please modify the sentence. 8. Although bladder cancer risk had been reported from pioglitazone, the data is controversial. Please add more data about this risk. 9. Please add more data regarding



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the PIVENS study, which determined the efficacy of pioglitazone and vitamin E in patients with biopsy-proven NASH. Minor: 1. Please correct the term “metabolically-associated fatty live disease (MAFLD)” to “metabolic-associated fatty liver disease (MAFLD)” in the abstract and Core Tip. 2. Please remove liver failure from the keyword. The additional “obesity” and “NAFLD” keywords are appropriate and relevant to this review. 3. MAFLD is a new term that is not the same as NAFLD. Please substitute the “MAFLD” for “NAFLD” in the drugs used to manage MAFLD. 4. Please check the English style throughout the manuscript.

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Manuscript NO: 80261

Title: Management of metabolic-associated fatty liver disease: The diabetology perspective

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03446972

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Physician, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-08 05:09

Reviewer performed review: 2022-11-19 11:08

Review time: 11 Days and 5 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
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 checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input 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
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SPECIFIC COMMENTS TO AUTHORS

1. The global prevalence of obesity leads to various metabolic disorders, particularly metabolic-associated fatty liver disease (MAFLD) and type 2 diabetes mellitus (T2DM). As the diseases of metabolic syndrome, MAFLD and T2DM have similar pathogenesis. It is important for this review to summarize the management of MAFLD from a diabetologist's perspective. 2. This review concisely and coherently organized and presented the comprehensive management of MAFLD from the aspects of lifestyle intervention, drug treatment and surgical treatment. This article also summarized emerging concepts and the management of special populations with MAFLD, such as pregnant women, children and the elderly individuals. 3. At present, the treatment of MAFLD is still a world problem, because there are no drugs approved by the FDA for the management of the disease. Most of drugs for T2DM or others have not been recommended for MAFLD due to their efficacy and side effects. It is necessary to improve the knowledge of the personalized treatment options with targeted drugs on MAFLD. Further research is still urgent needed on novel therapies, including novel therapeutic and surgical approaches for MAFLD.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 03446972

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Physician, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-09-20

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-12-01 10:46

Reviewer performed review: 2022-12-01 10:51

Review time: 1 Hour

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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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<https://www.wjgnet.com>

statements

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

It is important for this review to summarize the management of MAFLD from a diabetologist's perspective. The authors have revised the manuscript in accordance with the peer-review report and the criteria for manuscript revision by authors.