QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

apcz.umk.pl/QS Nicolaus Copernicus University in Toruń

Cite as: MAŁEK, Martyna, DENKIEWICZ, Aleksandra, DENKIEWICZ, Karolina, PACHULSKA, Klaudia, DOROSZ, Weronika, PODOLAK, Maja, NAWRACAJ, Michał, MIŁKOWSKA, Maria, BARTCZAK, Julia and SOSIŃSKI, Piotr. Glucagon-like peptide-1 receptor agonists in metabolic dysfunction-associated steatotic liver disease: a narrative review. Quality in Sport. 2026;60:72834. https://doi.org/10.12775/QS.2026.60.72834

ARTICLE TIMELINE

Received: 29.05.2026. Revised: 20.06.2026. Accepted: 20.06.2026. Published: 26.06.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines: Medical Sciences; Health Sciences.

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Nauki medyczne; Nauki o zdrowiu.

Glucagon-like peptide-1 receptor agonists in metabolic dysfunction-associated steatotic liver disease: a narrative review

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Abstract

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most common chronic liver diseases worldwide and is strongly linked to obesity and type 2 diabetes mellitus. Glucagon-like peptide-1 (GLP-1) receptor agonists have gained attention because of their hepatoprotective and cardiometabolic effects.

Aim: This narrative review summarizes current evidence on GLP-1 receptor agonists in the treatment of MASLD and metabolic dysfunction-associated steatohepatitis (MASH).

Materials and methods: A literature review was conducted using PubMed, Scopus and Google Scholar. Included studies comprised clinical trials, randomized controlled trials, meta-analyses, review articles and international guidelines published between 2021 and 2025.

Results: Evidence suggests that GLP-1 receptor agonists, especially semaglutide and liraglutide, reduce hepatic steatosis, insulin resistance, body weight and inflammatory activity in patients with MASLD or MASH. Several studies demonstrated improvements in liver histology and non-invasive fibrosis markers, although antifibrotic effects were less consistent in advanced cirrhosis. These agents also improved glycemic control and cardiovascular risk factors, with an acceptable safety profile.

Conclusions: GLP-1 receptor agonists appear to be a promising therapeutic option for MASLD and MASH. However, further long-term randomized studies are required to confirm their effects on fibrosis and liver-related outcomes.

Keywords: MASLD, MASH, GLP-1 receptor agonists, semaglutide, liraglutide, obesity, insulin resistance, liver fibrosis

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), reflects an updated nomenclature emphasizing the close relationship between hepatic steatosis and metabolic dysfunction. The terminology evolved from NAFLD to Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) and finally to MASLD following the 2023 Multi-Society Delphi Consensus, aiming to provide a more accurate and positive definition of the disease associated with obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome. [1, 2]

MASLD includes a spectrum of liver disorders ranging from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, cirrhosis, and hepatocellular carcinoma [3]. MASH was previously referred to as non-alcoholic steatohepatitis (NASH).

MASLD represents a rapidly growing global health burden, currently affecting approximately 38% of the adult population worldwide, with prevalence expected to exceed 55% by 2040. The disease is strongly associated with obesity and T2DM, particularly in rapidly developing regions, including Asia and the Middle East, where prevalence rates continue to rise. MASLD is also becoming a leading cause of liver-related morbidity and mortality, including hepatocellular carcinoma and cirrhosis, which highlights its increasing public health significance. [4]. Cardiovascular disease remains the leading cause of death in patients with MASLD. Numerous cohort studies and meta-analyses have demonstrated that MASLD is an independent risk factor for major adverse cardiovascular events, including coronary heart disease, stroke, heart failure, arrhythmias, and cardiovascular death. The risk increases with fibrosis severity and MASH progression [5].

MASLD is strongly associated with obesity, insulin resistance, and T2DM, which are considered major drivers of disease progression and extrahepatic complications. Current management is based primarily on lifestyle modification, including dietary changes, physical activity, and weight reduction. However, maintaining long-term weight loss remains difficult in clinical practice. Current guidelines recommend at least 5–10% body weight reduction to improve steatosis and liver inflammation, while greater weight loss may be needed to improve fibrosis. Despite the increasing prevalence of MASLD, approved pharmacological options remain limited, particularly for advanced disease stages [6, 7].

Due to the close relationship between MASLD, obesity, and T2DM, incretin-based therapies, particularly GLP-1 receptor agonists, have gained attention as potential therapeutic options. Although current guidelines do not yet recommend GLP-1 receptor agonists as formal MASH-targeted therapies because of limited phase III histological evidence, these agents are considered safe in patients with MASLD and are widely used for the treatment of obesity and T2DM. Their effects on body weight, insulin sensitivity, cardiometabolic risk factors, and hepatic steatosis make them promising candidates for future MASLD management strategies [3].

The aim of this review is to summarize current evidence regarding the role of GLP-1 receptor agonists in the treatment of MASLD, with particular emphasis on their metabolic, hepatic and cardiovascular effects.

2. Materials and methods

A literature search was conducted using PubMed, Scopus, and Google Scholar databases. The following keywords: “MASLD”, “MASH”, “NAFLD”, “GLP-1 receptor agonists”, “semaglutide”, “liraglutide”, and “tirzepatide” were used. Clinical trials, randomized controlled trials, meta-analyses, review articles, and international guidelines published in English between 2021 and 2025 were included. Landmark studies published before 2021 were also considered if they were highly relevant to the topic. Animal studies, conference abstracts, case reports, editorials, duplicate publications, and articles not directly related to MASLD or GLP-1 receptor agonists were excluded from the review.

3. Results

3.1 Pathophysiology of MASLD

Insulin resistance plays an important role in the pathophysiology of MASLD and strongly links the disease with obesity and type 2 diabetes. Under normal physiological conditions, insulin regulates glucose and lipid metabolism. In MASLD, however, insulin signaling becomes impaired, especially in adipose tissue, causing increased lipolysis and an excessive release of free fatty acids into the circulation. These fatty acids are then taken up by the liver, where they promote lipid accumulation. In parallel, hyperinsulinemia promotes hepatic lipid synthesis while failing to adequately suppress glucose production, which further worsens metabolic imbalance [8].

As a result, hepatic metabolism becomes dysregulated due to an excess supply of substrates. The liver receives fatty acids from adipose tissue and carbohydrates from the gut. These substrates are increasingly converted into lipids through enhanced *de novo* lipogenesis driven by glucose, fructose, and amino acids. This leads to progressive triglyceride accumulation within hepatocytes, leading to hepatic steatosis [9].

Hepatic steatosis reflects an imbalance between lipid acquisition and disposal. While lipid input and synthesis are increased, pathways responsible for lipid clearance, such as very-low-density lipoprotein (VLDL) secretion and fatty acid oxidation, are insufficient. Although mitochondrial β-oxidation may initially rise as a compensatory mechanism, persistent metabolic overload ultimately results in mitochondrial dysfunction, oxidative stress, and hepatocellular injury, promoting inflammation and disease progression [9,10].

3.2. Mechanisms of action of GLP-1 receptor agonists

GLP-1 receptor agonists exert their metabolic effects through a combination of central and peripheral mechanisms. They promote weight loss primarily by reducing caloric intake and modulating energy balance. Their action within the central nervous system (CNS) enhances satiety, decreases meal size, and delays gastric emptying, which contributes to reduced energy consumption. Appetite regulation involves both homeostatic and reward pathways, as GLP-1 signalling stimulates anorexigenic neurons while also influencing mesolimbic circuits, reducing both hunger-driven and hedonic food intake [8].

In addition to their effects on body weight, GLP-1 receptor agonists improve insulin sensitivity and glucose homeostasis. They enhance glucose-dependent insulin secretion and suppress glucagon release, leading to increased peripheral glucose uptake and reduced hepatic glucose production. These processes help counteract insulin resistance and are partly mediated through regulation of transcription factors such as sterol regulatory element-binding protein 1c (SREBP-1c) and carbohydrate-responsive element-binding protein (ChREBP) [8,11].

A key mechanism underlying their hepatoprotective effects is the modulation of hepatic lipid metabolism. GLP-1 receptor agonists reduce hepatic fat accumulation through both indirect and direct pathways. Weight loss decreases the influx of free fatty acids to the liver, while direct hepatic effects include suppression of *de novo* lipogenesis, increased fatty acid oxidation, reduced VLDL production, and improved lipid handling in adipose tissue. Together, these processes lead to reduced triglyceride accumulation and improvement in hepatic steatosis [8,11].

In addition, GLP-1 receptor agonists exhibit anti-inflammatory properties. They reduce levels of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin 6

(IL-6), and C-reactive protein (CRP), and reducing hepatic inflammation and lipotoxic stress, which may contribute to slowing disease progression [8,11].

These mechanisms are reflected in clinical findings. As shown in the analyzed study, GLP-1 receptor agonists significantly reduced liver fat content (SMD −0.72, $p < 0.0001$) and increased the likelihood of achieving substantial hepatic fat reduction (≥30% and ≥70%). Notably, these effects appeared independent of weight loss, suggesting a direct influence on intrahepatic lipid metabolism, likely through reduced lipogenesis and enhanced lipid clearance [10].

3.3. Effects of GLP-1 receptor agonists on hepatic steatosis

Several clinical studies have demonstrated that GLP-1 receptor agonists might significantly reduce hepatic fat accumulation in patients with MASLD/MASH. In a randomized placebo-controlled trial conducted by Flint et al., semaglutide decreased liver steatosis assessed by magnetic resonance imaging-proton density fat fraction (MRI-PDFF). A reduction in hepatic fat content was observed as early as week 24 and was maintained throughout the study period. Moreover, a substantially higher proportion of patients treated with semaglutide achieved at least a 30% reduction in liver fat content compared with placebo. In contrast, the change in liver stiffness assessed by magnetic resonance elastography (MRE) did not differ significantly between the semaglutide and placebo groups after 48 weeks. Semaglutide therapy was also associated with reductions in liver fat volume, body weight, and visceral adipose tissue, suggesting a beneficial effect on both hepatic steatosis and metabolic profile. [12]

Armstrong et al. demonstrated that 48-week treatment with liraglutide improved liver histology in patients with biopsy-proven NASH. Histological improvement was defined as the resolution of active steatohepatitis, including the disappearance of hepatocyte ballooning, without worsening of fibrosis. Hepatocyte ballooning is considered a hallmark of active steatohepatitis and reflects ongoing hepatocellular injury and inflammation. In addition to histological outcomes, the study also assessed changes in steatosis, inflammation, fibrosis, insulin resistance, liver enzymes, and metabolic parameters, highlighting the multidimensional effects of GLP-1 receptor agonists in patients with MASLD/MASH. [13]

In the study conducted by Newsome et al., semaglutide treatment was associated with a reduction in disease activity in patients with biopsy-confirmed NASH. A significant proportion of semaglutide-treated patients achieved a reduction in the NAFLD Activity Score (NAS), which assesses steatosis, lobular inflammation, and hepatocyte ballooning. Specifically, NAS reduction was observed in 83% of patients treated with semaglutide 0.4 mg compared with 44% in the placebo group. These findings suggest that the treatment may improve not only hepatic steatosis but also hepatocellular injury and inflammatory activity. Furthermore, treatment resulted in substantial reductions in liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as well as biomarkers of hepatocyte injury such as cytokeratin-18 apoptosis biomarkers M30 and M65 (CK-18 M30 and CK-18 M65). Additionally, patients receiving semaglutide experienced significant weight loss, which is strongly associated with improvement in hepatic steatosis. [14]

Overall, current evidence suggests that GLP-1 receptor agonists may reduce hepatic steatosis through combined metabolic, anti-inflammatory, and hepatoprotective effects.

3.4. Effects on liver fibrosis and histological outcomes

Liver fibrosis is considered one of the strongest predictors of liver-related and overall mortality in patients with MASLD/MASH. Therefore, improvement in fibrosis has become one of the major therapeutic goals in clinical trials evaluating GLP-1 receptor agonists.

In the LEAN trial, Armstrong et al. investigated whether liraglutide could improve liver histology and prevent fibrosis progression in patients with biopsy-confirmed NASH. The study was designed as a multicentre, double-blind, randomized placebo-controlled phase II clinical trial. The primary endpoint was the resolution of active steatohepatitis without worsening of fibrosis after 48 weeks of treatment. Liver fibrosis was assessed using the Kleiner fibrosis scoring system (F0–F4) and the modified Ishak score (F0–F6). The authors highlighted that effective therapy for NASH should be able not only to reduce hepatic steatosis and inflammation, but also to prevent the progression of fibrosis, which is one of the major predictors of liver-related complications and mortality. [13]

In the ESSENCE trial, Sanyal et al. demonstrated that semaglutide significantly increased the likelihood of liver fibrosis regression in patients with biopsy-confirmed MASH and stage F2–F3 fibrosis. Histological assessment was performed using the NASH Clinical Research Network (NASH CRN) scoring system, which includes evaluation of both disease activity (NAS) and liver fibrosis stage on a scale from F0 to F4.

Improvement in liver fibrosis without worsening of steatohepatitis was achieved in 36.8% of patients treated with semaglutide compared with 22.4% in the placebo group, whereas resolution of steatohepatitis without worsening of fibrosis was observed in 62.9% and 34.3% of patients, respectively. Importantly, simultaneous fibrosis regression and resolution of steatohepatitis were observed in 32.7% of patients receiving semaglutide.

In addition to histological assessment, the authors also analyzed non-invasive markers of fibrosis, including the enhanced liver fibrosis (ELF) score, procollagen type III peptide (PRO-C3), liver stiffness assessed by transient elastography (FibroScan), and FibroScan-AST (FAST) score. All assessed parameters improved during semaglutide therapy, suggesting a potential reduction in active fibrogenesis and slowing of disease progression. The authors emphasized that fibrosis regression has major clinical importance, as advanced fibrosis is associated with an increased risk of cirrhosis, liver failure, and liver-related mortality. [15]

Loomba et al. evaluated that the effects of semaglutide on histological outcomes were evaluated in patients with NASH-related compensated cirrhosis (F4). Histological assessment was performed using the NASH Clinical Research Network (NASH CRN) scoring system. Despite significant improvements in metabolic parameters, liver enzymes, and hepatic steatosis assessed by magnetic resonance imaging–proton density fat fraction (MRI-PDFF), semaglutide did not significantly improve fibrosis regression or NASH resolution compared with placebo. Improvement in fibrosis without worsening of NASH was observed in 11% of semaglutide-treated patients compared with 29% in the placebo group. However, semaglutide significantly reduced liver fat content and decreased PRO-C3 levels, suggesting attenuation of active fibrogenesis despite the absence of measurable histological fibrosis regression. These findings may indicate that advanced cirrhosis represents a stage of liver disease that is less responsive to the antifibrotic effects of GLP-1 receptor agonists. [16]

In the study conducted by Flint et al., despite achieving a significant reduction in hepatic steatosis, semaglutide did not demonstrate a significant improvement in liver stiffness

compared with placebo. Fewer patients on semaglutide had worsening of liver stiffness, which could be indicative of potential slowing of fibrosis progression. Such results suggest that fibrosis regression may be more difficult to achieve than reduction of hepatic steatosis and more likely needs a longer period of therapy.

It was found that magnetic resonance elastography (MRE) might not be sensitive enough to detect subtle changes in fibrosis in patients with less severe liver disease. Furthermore, decrease in hepatic steatosis in this phase likely precedes measurable fibrosis regression and contributes to slowing further progression of fibrosis. [12]

3.5. Metabolic and cardiovascular benefits

Metabolic dysfunction is a central component of the pathogenesis and progression of MASLD/MASH. Therefore, obesity therapeutics, insulin resistance, dyslipidemia, and cardiovascular risk factors may offer substantial clinical benefits beyond improvement in liver histology alone. Numerous studies have demonstrated that GLP-1 receptor agonists not only reduce hepatic steatosis, but also improve glycemic control, promote weight loss, and favorably affect cardiovascular and metabolic parameters in patients with MASLD/MASH.

Alkhouri et al. demonstrated that semaglutide therapy, both as monotherapy and in combination with cilofexor and/or firsocostat, resulted in significant improvements in metabolic parameters in patients with NASH. The study found significant body weight reduction, between 7% and 9.6% after 24 weeks of treatment, with improvement in glycemic control, such as reduction in fasting plasma glucose and HbA1c levels. Similar benefits were observed in patients with type 2 diabetes, where HbA1c was reduced by up to 1.7%.

In addition, the treatment with semaglutide improved several cardiovascular and metabolic risk markers such as triglycerides, total cholesterol, and LDL cholesterol. Reductions in inflammatory biomarkers, for example CRP, and hepatocyte apoptosis marker CK-18 M30 were also identified. Combination therapy was associated with greater reduction in liver fat, ALT/AST levels, and MRI-PDFF despite similar body weight reduction in all treatment groups.

The authors pointed out that improvement in metabolic dysfunction may be an important consideration in patients with MASLD/MASH. However, cardiovascular disease is one of the leading causes of mortality in this population. [17]

Mantovani et al., in a comprehensive meta-analysis of 13 randomized controlled trials involving 1811 patients with MASLD/MASH, showed that GLP-1 receptor agonists result in substantial metabolic benefits besides their hepatoprotective ones. Treatment with GLP-1 receptor agonists was associated with significant reduction in body weight (approximately 4.5 kg) and HbA1c levels (−1.3%) versus placebo or reference therapy. In addition, GLP-1 receptor agonist therapy significantly decreased serum liver enzyme levels, such as ALT, AST, and GGT.

These agents significantly reduce the risk of overall mortality as well as cardiovascular and renal complications in patients with type 2 diabetes and obesity, which is particularly important because cardiovascular disease remains the leading cause of death in patients with MASLD/MASH. [18]

GLP-1 receptor agonist therapy was associated with a significantly greater reduction in body mass index (BMI) and a larger decrease in fibrosis-4 (FIB-4) index compared with physical activity alone. GLP-1 receptor agonists improve insulin sensitivity, reduce *de novo* lipogenesis. They have anti-inflammatory effects, and decrease lipotoxicity. In addition to such mechanisms beneficially affecting MASLD progression, they may also help to reduce the cardiovascular risk.

The authors additionally noted that GLP-1 receptor agonists may represent an important adjunct to lifestyle modification, especially in daily clinical practice, where maintaining long-term weight reduction through lifestyle changes alone is often challenging. [19]

Similar conclusions were presented by Wydeheft et al., who emphasized that GLP-1 receptor agonists and dual GLP-1/GIP agonists provide substantial metabolic and cardiometabolic benefits, including significant weight reduction and improvement in obesity-related complications, although careful long-term monitoring remains necessary, particularly in vulnerable patient populations. [20]

Incretin-based therapies may improve metabolic parameters and reduce hepatic fat accumulation in patients with MASLD/MASH. [21]

3.6. Safety and adverse effects

GLP-1 receptor agonists are generally considered safe and well tolerated in patients with MASLD/MASH. Across multiple clinical trials, the most common adverse effects were gastrointestinal symptoms. Most adverse events occurred at mild to moderate in severity and mainly during dose escalation.

The most commonly reported adverse effects associated with semaglutide therapy were gastrointestinal symptoms, including nausea, vomiting, diarrhea, constipation, and upper abdominal pain. Another effect that was also often observed and likely contributed to body weight reduction was decreased appetite. Despite the gastrointestinal adverse events, treatment discontinuation due to adverse effects remained low, reflecting an overall favorable tolerability profile. [12]

No cases of hepatic decompensation were observed in patients with NASH-related compensated cirrhosis. Hepatic and renal function parameters remained stable throughout treatment. These results indicate semaglutide acceptable tolerability even in patients with advanced liver disease. [16]

The incidence of acute pancreatitis was similar in the semaglutide and placebo groups; fatal adverse events were rare and did not clearly associate with treatment. The gradual dose-escalation regimen, consistent with conventional clinical practice, allowed for long-term therapy with good tolerability and without the emergence of new safety signals. [15, 22, 23]

Romero-Gómez et al. assessed the effect of semaglutide therapy on health-related quality of life (HRQoL) and patient-reported outcomes in biopsy-proven NASH patients. Semaglutide treatment showed significant improvements in the physical component of HRQoL, specifically in aspects such as bodily pain, vitality, physical functioning, and social functioning. Importantly, large semaglutide-induced weight loss did not appear to impair physical function or muscle functioning.

The authors emphasized that improvement in quality of life might be another significant additional benefit of GLP-1 receptor agonist therapy, particularly in patients with MASLD/MASH, in whom fatigue, reduced physical functioning, and impaired daily activity are common clinical problems. [24]

A summary of the major clinical studies evaluating GLP-1 receptor agonists in patients with MASLD/MASH is presented in Table 1.

Table 1. Summary of clinical studies evaluating GLP-1 receptor agonists in patients with MASLD/MASH

Study (year)	Drug	Population	Duration	Main hepatic outcomes	Metabolic benefits
Flint et al. (2021) [12]	Semaglutide	Patients with NAFLD (Semaglutide n=44; placebo n=23)	48 weeks	↓ liver fat (MRI-PDFF); no significant fibrosis improvement	↓ body weight; ↓ visceral fat; ↓ HbA1c
Armstrong et al. (2016) [13]	Liraglutide	Patients with biopsy-proven NASH (liraglutide n=26; placebo n=26)	48 weeks	Resolution of steatohepatitis without worsening fibrosis; disappearance of hepatocyte ballooning	↓ insulin resistance; ↓ body weight; ↓ ALT/AST
Newsome et al. (2021) [14]	Semaglutide	Patients with biopsy-confirmed NASH (semaglutide 0.4 mg n=82; placebo n=80)	72 weeks	↓ NAS score; ↓ steatosis; ↓ lobular inflammation; ↓ hepatocyte ballooning	↓ ALT/AST; ↓ body weight; ↓ CK-18 M30 and CK-18 M65
Sanyal et al. (2025) [15]	Semaglutide	Patients with biopsy-defined MASH and F2–F3 fibrosis (semaglutide n=534; placebo n=266)	72 weeks	Fibrosis regression; resolution of steatohepatitis; ↓ ELF score; ↓ liver stiffness; ↓ FAST score; ↓ PRO-C3	↓ body weight; ↓ HbA1c; ↓ HOMA-IR; improved lipid profile; ↓ hs-CRP
Loomba et al. (2023) [16]	Semaglutide	Patients with biopsy-confirmed NASH-related compensated cirrhosis (F4) (semaglutide n=47; placebo n=24)	48 weeks	No significant fibrosis regression; ↓ liver fat; ↓ PRO-C3	↓ body weight; ↓ HbA1c; ↓ fasting plasma glucose; ↓ triglycerides; ↓ VLDL cholesterol; ↓ ALT, AST, GGT; ↓ hs-CRP

↑, increased; ↓, decreased; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK-18 M30 and CK-18 M65, cytokeratin-18 fragments M30 and M65 (biomarkers of hepatocyte apoptosis and cell death); ELF score, Enhanced Liver Fibrosis score; FAST score, FibroScan-AST score; HbA1c, glycated hemoglobin; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; hs-CRP, high-sensitivity C-reactive protein; MRI-PDFF, magnetic resonance imaging–proton density fat fraction; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; PRO-C3, procollagen type III peptide; VLDL, very low-density lipoprotein

4. Discussion

The beneficial effects of GLP-1 receptor agonists in MASLD/MASH may be related to the central role of insulin resistance in disease pathogenesis. Insulin resistance drives up free fatty acid delivery to the liver and promotes *de novo* lipogenesis, leading to hepatic steatosis.

Through enhanced insulin sensitivity, decreased body weight, and improving glycemic control, GLP-1 receptor agonists may reduce hepatic lipid accumulation and restore metabolic balance. Reduced hepatic fat content can reduce oxidative stress, hepatocellular injury, and

inflammation, which could explain the improvements in steatosis, NAS score, and liver enzymes identified in clinical trials.

Moreover, histological markers of disease activity in several studies improved, including steatohepatitis resolution and reduction in NAS score. Although the antifibrotic effects of GLP-1 receptor agonists appear less consistent, particularly in advanced cirrhosis, improvements in non-invasive fibrosis markers and liver stiffness may suggest attenuation of active fibrogenesis and slowing of disease progression. These findings indicate that GLP-1 receptor agonists may provide both hepatoprotective and systemic metabolic benefits in patients with MASLD/MASH.

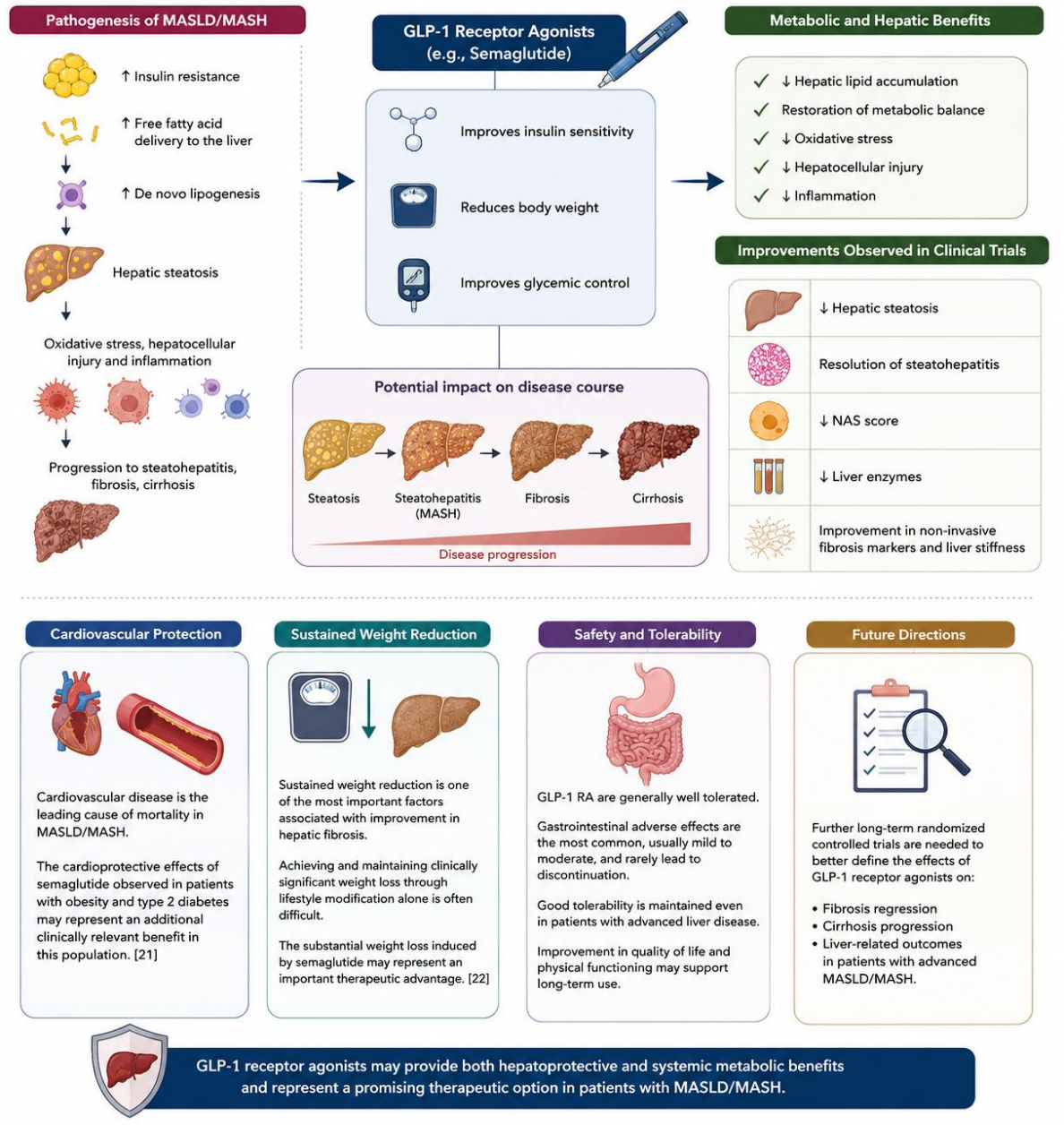
Since cardiovascular disease remains the leading cause of mortality in patients with MASLD/MASH, the cardioprotective effects of semaglutide observed in patients with obesity and type 2 diabetes may represent an additional clinically relevant benefit in this population. [25]

Sustained weight reduction is considered one of the most important factors associated with improvement in hepatic fibrosis in patients with MASLD/MASH. Yet it is often difficult to obtain and maintain clinically meaningful weight loss via lifestyle change in routine clinical practice. Therefore, the remarkable weight loss induced by semaglutide may provide a significant therapeutic advantage. [26]

Overall, recent data indicated that GLP-1 receptor agonists show a favorable safety and tolerability profile in patients with MASLD/MASH, including those with advanced liver disease. Gastrointestinal adverse effects are the most common treatment-related events. They are usually mild to moderate in severity and rarely lead to treatment discontinuation. Moreover, its favorable effects on quality of life and physical functioning may enhance the long-term clinical use of GLP-1 receptor agonists in this patient group.

Nevertheless, more long-term randomized controlled trials are needed to better define the effects of GLP-1 receptor agonists on fibrosis regression, cirrhosis progression, and liver-related outcomes in patients with advanced MASLD/MASH.

Figure 1. Potential mechanisms and clinical effects of GLP-1 receptor agonists in patients with MASLD/MASH.



5. Conclusions

In summary, GLP-1 receptor agonists are a promising therapeutic option in patients with MASLD/MASH due to their multidimensional metabolic, hepatoprotective, and cardiometabolic actions. Current evidence indicates that these agents can decrease hepatic

steatosis, improve insulin resistance and glycemic control, contribute to substantial weight reduction, and decrease inflammatory activity, while also giving potential benefits in liver histology and fibrosis progression. Importantly, GLP-1 receptor agonists have a favorable safety profile and may additionally reduce cardiovascular risk, which is even more important considering that cardiovascular disease remains the leading cause of death in patients with MASLD/MASH. Nevertheless, further large-scale long-term randomized controlled trials are required to better define how these measures affect fibrosis regression, cirrhosis progression, and liver-related clinical outcomes.

Disclosure

Author Contributions

Conceptualization: [MM], [AD]

Methodology: [PS], [JB]

Check: [KD], [MN], [MM]

Investigation: [MM], [AD]

Data curation: [PS], [MM], [AD]

Writing - rough preparation: [MMi]

Writing - review and editing: [MP]

Visualization: [AD], [KP]

Project administration: [WD]

Funding

This research received no external funding.

Data Availability Statement

Not Applicable.

Conflicts of Interest

The authors declare no conflict of interest.

Acknowledgments

In preparing this work, the authors used ChatGPT (OpenAI) for language editing assistance and generation of the graphical illustration. After using this tool, the authors reviewed and edited the content as needed and accepted full responsibility for the substantive content of the publication.

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