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Impact of GLP-I Receptor Agonists on Psoriasis and Cardiovascular Comorbidities: A Narrative Review

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Abstract: Psoriasis is an immune-mediated skin disease known to be associated with a higher risk of cardiometabolic comorbidities such as hypertension, myocardial infarction, and stroke. GLP-1 receptor agonists (GLP-1RAs) are medications approved to treat type 2 diabetes mellitus and obesity and have been reported to improve psoriasis. As more psoriasis patients start GLP-1RAs for approved indications, it is of interest to understand the impact of GLP-1RAs on both psoriasis and associated cardiovascular risk. In this review, we examine the effect of GLP-1RAs on psoriasis and cardiovascular comorbidities—defined as hypertension, stroke, and myocardial infarction. The majority of case reports and prospective cohort studies found GLP-1RAs improved psoriasis, while two randomized controlled trials showed conflicting results. For cardiovascular disease, most studies found GLP-1RAs reduced systolic blood pressure, total stroke, and myocardial mortality. These results suggest that GLP-1RAs may be a particularly promising treatment for psoriasis patients with diabetes or obesity comorbidities, offering both cardioprotective benefits and potential improvement in psoriatic symptoms.

Keywords: skin disease, oxidative stress, hypertension, stroke, myocardial infarction

Introduction

Psoriasis is an immune-mediated disease affecting 125 million people worldwide and is characterized by both skin inflammation and systemic comorbidities. Up to one-third of psoriasis patients develop psoriatic arthritis, and patients with psoriasis also have an increased risk of cardiometabolic diseases and increased cardiovascular mortality.^{1,2} Furthermore, previous studies have demonstrated a close relationship between psoriasis and type 2 diabetes mellitus (T2DM).³ As a result, physicians are recommended to perform comprehensive annual screenings to monitor psoriasis patients for not only psoriatic arthritis but also cardiovascular diseases such as stroke, hypertension, and myocardial infarction (MI).¹

Glucagon-like-peptide-1 receptor agonists (GLP-1RA) have recently garnered increased media attention and research interest due to their weight loss properties and utilization as an effective T2DM treatment.⁴ Their mechanism of action for T2DM and weight loss involves stimulating insulin secretion through GLP-1 receptor agonism.⁵ While commonly associated with the pancreas, these receptors are located throughout the body in various locations, such as the kidneys, brain, and heart.⁵ With a wide distribution of receptors, the effects of GLP-1RAs are multifocal and shown to have a beneficial impact on neurologic, degenerative, and vascular diseases.⁶ A potential beneficial effect on psoriasis has also been suggested, but the mechanism behind this improvement is not fully understood.^{6–8}

Previous reviews have examined the effect of GLP-1RAs on psoriatic skin disease in hopes of better defining this relationship.^{9,10} In this review, we analyze studies on GLP-1RAs in psoriasis and cardiovascular disease, which we define

as hypertension, stroke, and myocardial infarction. The combined effect of GLP-1RAs on skin and cardiovascular disease could be particularly beneficial for patients with psoriasis and warrants further research.¹

Materials and Methods

We conducted a narrative review using two PubMed (Medline) searches, one for psoriasis and one for associated cardiovascular diseases. The search terms used for psoriasis included 1) “GLP-1” and ‘psoriasis’ 2) “semaglutide” and ‘psoriasis’ 3) “liraglutide” and “psoriasis” and 4) “glucagon-like peptide-1” and “psoriasis” and was limited to English-language articles. The search terms for cardiovascular disease included 1) “GLP-1” or “glucagon like peptide” or “semaglutide”[Title] and “hypertension”[Title] 2) “GLP-1” or “glucagon like peptide” OR “semaglutide”[Title] and “stroke”[Title] and 3) “GLP-1” or “glucagon like peptide” or “semaglutide”[Title] and “myocardial infarction”[Title] and was limited to meta-analyses in the English language. Following review by the authors, 14 articles related to the use of GLP-1RAs and their impact on psoriasis, and 11 meta-analyses related to their impact on cardiovascular disease were included in this review. We utilized the Critical Appraisal Skill Program (CASP) checklist to review all studies except for meta-analyses ([Supplemental Tables 1](#) and [2](#)). The CASP review revealed that most studies were of reasonable quality with limitations identified in the length of follow up and generalizability of the results due to the small sample sizes. Psoriasis studies included controlled clinical trials, case reports, case series, prospective cohort studies, meta-analyses, and randomized control trials that analyzed the impact of GLP-1RAs in humans. Cardiovascular disease studies included meta-analyses only in humans. Studies excluded in both reviews included reviews and articles using animal models. All duplicate articles were excluded. One additional cardiovascular disease paper on liraglutide was included in the review.

Results

Psoriasis

Initial interest in the effects of GLP-1RAs on psoriasis came from a series of six case reports demonstrating an improvement in psoriasis in patients treated with various GLP-1RAs ([Table 1](#)). Of these six psoriasis patients, three were treated with liraglutide, two with semaglutide, and one with exenatide.^{11–16} Four patients had T2DM and two had insulin resistance, while three patients were obese. Five out of six cases reported reduction of the psoriasis area and severity index (PASI) score and/or physician’s global assessment (PGA) after treatment with GLP-1RAs ranging from 3 to 12 months.^{11–16} In one case, the patient had a 98.3% improvement in PASI score following treatment with semaglutide, and in another case, a patient previously non-responsive to acitretin had an improvement in PASI with liraglutide and acitretin in combination.^{13,15} Furthermore, the metabolic benefit of GLP-1RAs was demonstrated in these patients with psoriasis, with five out of six cases reporting a reduced body weight or body mass index (BMI) and four out of six studies reporting reduced glycated hemoglobin ([Table 1](#)).^{11–13,15,16} There was only one case report that documented a worsening of psoriasis and the development of topical resistance following the initiation of liraglutide. Following discontinuation of liraglutide, the patient showed improvement in their psoriasis.¹⁴

We next reviewed one case series and three prospective cohort studies that examined the impact of GLP-1RAs in a total of 23 patients with psoriasis and T2DM ([Table 1](#)). In all of these studies, patients treated with GLP-1RAs had clinical improvement, with significantly reduced PASI scores.^{17–20} The mechanism behind this improvement was analyzed in two studies, with one study demonstrating a decrease in dermal T cells, IL-17, and epidermal thickness and another showing inhibition of invariant natural killer T cell (iNKT) cytokine secretion.^{19,20} Beyond clinical and cellular improvement, many of these studies also examined changes in the patient-reported Dermatology Life Quality Index (DLQI) following treatment with GLP-1RAs. Three studies reported a significant reduction in DLQI scores, demonstrating a positive effect on quality of life.^{17,18,20} Moreover, three of these four studies reported improvement in these psoriasis patients’ lipid profiles, glycated hemoglobin, or body mass index, indicating metabolic improvement in addition to skin improvement ([Table 1](#)).

We identified two randomized controlled trials (RCTs) investigating the effects of GLP-1RAs on psoriasis outcomes compared to placebo ([Table 1](#)). In the two RCTs performed, there were mixed findings. An RCT conducted in China of 11 psoriasis patients with T2DM treated with liraglutide vs 13 psoriasis patients treated with acitretin, calcipotriol, and oral diabetes medications for 12 weeks showed superior improvement in the liraglutide group for PASI and DLQI, and significant reductions

Table I Review of Studies Investigating the Impact of GLP-IRAs on Psoriasis

Author	Year	PMID	Population	Study Design	Patients	Psoriasis and QoL Impact	Metabolic and Other Impact
Case Report							
Buyschaert et al ¹¹	2012	22227407	France	Case report	61 y.o male with T2DM, HTN, HLD treated with metformin, sulphonylureas, and exenatide	>6.9-point reduction in PASI and discontinuation of topical PsO treatment after 12 months of treatment with exenatide	Reduction in CRP levels, body weight, and glycated hemoglobin after 12 months of treatment with exenatide
Costanzo et al ¹²	2021	34463640	Italy	Case report	73 y.o Caucasian male with obesity, T2DM and COPD treated with metformin and new start semaglutide	25.2-point reduction in PASI and 23-point reduction in DLQI after 16 weeks of treatment with semaglutide	Reduction in glycated hemoglobin, BMI, and fasting glucose level after 16 weeks of treatment with semaglutide
Faurshou et al ¹⁶	2014	22160246	Denmark	Case report	59 y.o male with T2DM, HTN, HLD, MI treated with an increased metformin dose, decreased insulin dose, and new start liraglutide	Reduction in itch and 2-point reduction PGA after 12 weeks of treatment with liraglutide	Reduction in glycated hemoglobin and body weight after 12 weeks of treatment with liraglutide
Malavazos et al ¹³	2023	37551923	Italy	Case report	50 y.o Caucasian female with obesity, T2DM treated with semaglutide	Reduction in PASI by 8 points, DAPSA by 23 points, and DLQI by 15 points after 16 weeks of treatment with semaglutide	Reduction in glycated hemoglobin, body weight, triglycerides, and LDL cholesterol after 10 months of treatment with semaglutide
Nowowiejska et al ¹⁴	2023	37415553	Poland	Case report	34 y.o female with insulin resistance treated with liraglutide	Paradoxical worsening of PsO after 8 weeks of treatment with liraglutide	No discussion on metabolic impact
Reid et al ¹⁵	2013	23834125	Ireland	Case report	54 y.o male with obesity, insulin resistance and melanoma previously treated with acitretin was treated with liraglutide and acitretin in combination	6.6-point reduction in PASI and 13-point reduction in DLQI after 12 months of treatment with liraglutide	Reduction in body weight after 12 months of treatment with liraglutide
Prospective Cohort Studies and Case Series							
Ahern et al ¹⁷	2013	22691169	Ireland	PCS	PsO patients with T2DM and obesity treated with liraglutide n=7	Significant reduction in median PASI by 1.8 points (p=0.03) and median DLQI by 4 points (p=0.03) after 10 weeks of treatment with liraglutide	Significant increase in circulating iNKT cell number and significant reduction in glycated hemoglobin and fasting triglyceride to HDL-cholesterol ratio after 10 weeks of treatment with liraglutide
Buyschaert et al ¹⁸	2014	24506139	UK	Case series	PsO patients with T2DM on exenatide n=1 and liraglutide n=6	Significant reduction in mean PASI by 2.8 points (p=0.04), skin expression levels of IL-17, dermal $\gamma\delta$ T-cell numbers, and improvement in skin histopathology after 16–20 weeks of treatment	Significant reduction in glycated hemoglobin after 16–20 weeks of treatment
Hogan et al ¹⁹	2011	21744074	Ireland	PCS	PsO patients with T2DM and obesity on liraglutide n=2	1.7-point mean reduction in PASI and significant reduction in iNKT cell number in psoriatic plaques after 6 weeks of treatment with liraglutide	Significant increase in circulating iNKT cells; GLP-1 dose-dependent inhibition of iNKT cell cytokine secretion (but not cytolytic degranulation in vitro) and reduction in body weight after 6 weeks of treatment with liraglutide

(Continued)

Table 1 (Continued).

Author	Year	PMID	Population	Study Design	Patients	Psoriasis and QoL Impact	Metabolic and Other Impact
Xu et al ²⁰	2019	30844468	China	PCS	PsO patients with T2DM on liraglutide n=7	Significant reduction in mean PASI by 13.5 points (p=0.03) and mean DLQI by 17.7 points (p=0.001); improvement in skin histopathology after 12 weeks of treatment with liraglutide	Significant reduction in glycated hemoglobin, BMI, waist circumference, and fasting c-peptide after 12 weeks of treatment with liraglutide
Randomized Control Trials and Meta-Analysis							
Chang et al ²¹	2022	33934692	N/A	Meta-analysis	PsO patients with T2DM on liraglutide n=32	Significant 4.33 standardized mean difference in PASI (p=0.01) following liraglutide treatment; no significant difference between DLQI following treatment.	Significantly lower plasma glucose following liraglutide treatment; no significant difference between BMI and glycated hemoglobin following treatment.
Faurschou et al ²²	2015	25139195	Denmark	RCT	Obese, glucose-tolerant PsO patients on liraglutide n=11 vs placebo n=9	No significant difference in change in PASI and DLQI between two groups after 8 weeks	Significant reduction in bodyweight, cholesterol, and fasting plasma glucose in liraglutide-treated patients compared to placebo after 8 weeks; no significant difference in high sensitivity CRP levels between two groups after 8 weeks
Lin et al ²³	2022	32962477	China	RCT	PsO patients with T2DM on liraglutide n=11 vs control n=13	Higher reduction in PASI and DLQI in treatment group (mean reduction of 12.32 and 18.18, respectively) compared to control group (mean reduction of 6.15 and 8.54, respectively) after 12 weeks; decreased skin expression levels of IL-17, IL-23, and TNF along with improvement in skin histopathology	Higher reduction in weight, BMI, waist circumference, and fasting c-peptide in treatment group after 12 weeks; no significant difference in glycated hemoglobin or fasting blood glucose levels between two groups after 12 weeks
Sun et al ²⁴	2023	36623489	China	Meta-analysis	PsO patients receiving hypoglycemic agents; GLP-1RA studies included n=32	34% of patients taking GLP-1RAs achieved a PASI75 and had a 3.14 mean reduction in PASI score and no significant improvement in DLQI	4.93 mean reduction in weight, 1.59 mean reduction in BMI, and 0.62 mean reduction in glycated hemoglobin in patients treated with GLP-1RAs

Abbreviations: GLP-1RA, Glucagon-like-peptide-1 receptor agonists; MI, myocardial infarction; PASI, psoriasis area and severity index; PGA, physician's global assessment; T2DM, type 2 diabetes mellitus; iNKT, invariant natural killer T cells; DLQI, dermatology life quality index; RCTs, randomized controlled trials; PsO, psoriasis; CRP, c-reactive protein; PCS, prospective cohort study; HTN, hypertension; HLD, hyperlipidemia; COPD, chronic obstructive pulmonary disease; BMI, body mass index; DAPSA, disease activity for psoriatic arthritis; QoL, quality of life; PMID, PubMed Identifier; LDL, low-density lipoproteins; HDL, high-density lipoproteins.

in the expression of IL-23 and IL-17 in psoriatic skin.²³ However, an RCT conducted in Denmark in glucose-tolerant psoriasis patients found no significant difference in improvement in PASI or DLQI following eight weeks of treatment with liraglutide (n=11) compared to placebo (n=9).²² Finally, Sun et al and Chang et al both meta-analyzed Ahern et al, Buyschaert et al, Faurschou et al, and Xu et al and found a significant reduction in PASI following treatment with a GLP-1RA, but no significant change in DLQI.^{21,24}

Cardiovascular Comorbidities

While the definition of cardiovascular disease is broad, in this review, we define it as hypertension, stroke, and myocardial infarction.

Hypertension is a common comorbidity in psoriasis and two meta-analyses analyzed the effects of GLP-1RAs on blood pressure (Table 2).²⁵ In a paper by Zhao et al, liraglutide was compared to placebo regarding its effects on systolic

Table 2 Summary of Meta-Analyses Investigating the Impact of GLP-IRAs on Cardiovascular Diseases Known to Be Psoriasis Comorbidities. These Were Defined as Hypertension, Stroke, Myocardial Infarction, and Stroke

Author	Year	PMID	Trials Included	Methods	Background Diseases of Trial Participants	Findings
Hypertension						
Sun et al ²⁷	2015	26358202	60 RCTs	Patients with T2DM treated with GLP-IRAs n=12,016	Not discussed for individual studies	Significant reduction in SBP, increase in heart rate, and no significant incident of HTN.
Zhao et al ²⁶	2019	30616638	18 RCTs	Patients with T1DM, T2DM, and metabolic syndrome treated with GLP-IRAs=13,662	10 studies included patients with T2DM 5 studies included patients with metabolic syndrome 2 studies included patients with T1DM 1 study included patients with prediabetes 16 studies had an investigational group with an average BMI >30	Significant reduction in SBP in patients treated with liraglutide.
Myocardial Infarction						
Huang et al ⁷	2017	28286967	6 RCTs	Patients with T2DM and normoglycemia treated with GLP-IRAs n=800	None of the studies had a treatment group with an average BMI >30 Total of 31.4% patients had dyslipidemia	Significant improvement in left ventricular ejection fraction in patients treated with liraglutide and reduction in infarct size in acute myocardial infarction patients undergoing percutaneous coronary intervention.
Stroke						
Barkas et al ²⁸	2019	30629331	5 RCTs	Patients with T2DM treated with GLP-IRAs n= 42,358	Average baseline BMI in all five studies was >30 63.3% had history of MI 18.5% had history of stroke 20.5% had history of PAD 18.8% had history of heart failure	Significant reduction (13%) in total stroke.
Bellastella et al ²⁹	2020	31813360	7 CVOTs	Patients with T2DM treated with GLP-IRAs n=56,004	76.4% of patients had baseline statin use The reported weight loss was not associated with stroke	Significant reduction (16%) in total stroke.
Benn et al ³⁰	2021	33765180	48 RCTs total	Normoglycemic and hyperglycemic patients treated with 8 glucose-lowering drugs n=200,695	6.3% of patients had T2DM Average BMI of all participants was 25.4, ranging from 23.0–28.3 Average LDL of all participants was 123.52 mg/dl, ranging from 100.36–150.54 mg/dl	Significant reduction in ischemic stroke risk ratio (0.85).
Kim et al ³¹	2024	38273787	79 RCTs total	Patients with T2DM treated with SGLT-2 inhibitors and GLP-IRAs n=206,387	Not discussed for individual studies	Lower risk of total stroke in GLP-IRA treated patients compared to placebo in pair-wise meta-analysis. No significant reduction in total stroke in GLP-IRA treated patients compared to placebo in network meta-analysis.
Li et al ³²	2023	36462459	19 RCTs total	Patients with T2DM treated with SGLT-2 inhibitors, DPP-4 inhibitors, and GLP-IRAs n= 155,027	Mean BMI of patients in GLP-IRA studies was 32.2 29.6% of patients had a history of stroke across 7 studies	Significant reduction (16%) in total stroke.

(Continued)

Table 2 (Continued).

Author	Year	PMID	Trials Included	Methods	Background Diseases of Trial Participants	Findings
Wei et al ³³	2022	36545339	8 RCTs	Patients with T2DM treated with GLP-IRAs n= 60,081	Across 8 studies, mean BMI of patients in each study was 32.1 and 76.7% of patients had a history of cardiovascular disease	Significant reduction in total stroke (17%) and ischemic stroke (17%) but not hemorrhagic stroke.
Stroke and Myocardial Infarction						
Malhotra et al ³⁴	2020	32246253	8 RCTs	Patients with T2DM treated with GLP-IRAs n=56,251	Across 8 studies, mean BMI of patients in each study was 32.1 In 5 RCTs, 18.4% of patients had a history of stroke In 5 RCTs, 62.9% of patients had a history of MI In 4 RCTs, 21.9% of patients had a history of PAD	Significant reduction in total stroke (16%), major adverse cardiovascular events (13%), cardiovascular mortality (12%) and all-cause mortality (12%).
Sinha et al ³⁵	2019	30794833	13 RCTs total	Patients with T2DM treated with SGLT-2 inhibitors, DPP-4 inhibitors, and GLP-IRAs n=124,877	79.1% of patients had established cardiovascular disease	Significant reduction in cardiovascular death (12%), stroke (13%), and combined stroke and myocardial infarction (11%), but no significant reduction myocardial infarction alone or heart failure.

Abbreviations: GLP-IRA, Glucagon-like-peptide-1 receptor agonists; MI, myocardial infarction; T2DM, type 2 diabetes mellitus; T1DM, type 1 diabetes mellitus; RCTs, randomized controlled trials; CVOT, cardiovascular outcome trial; SBP, systolic blood pressure; SGLT-2, sodium-glucose cotransporter-2; DPP-4, dipeptidyl peptidase-4; HTN, hypertension; BMI, body mass index; PAD, peripheral artery disease; LDL, low-density lipoproteins; PMID, PubMed Identifier.

blood pressure (SBP) and diastolic blood pressure (DBP). They found that when used for less than a year, liraglutide resulted in a significant decrease in SBP but had no significant effect when used for over a year. They also demonstrated that liraglutide had a dose-dependent effect on DBP, significantly reducing DBP when used at a higher dose but slightly increasing it at a lower dose.²⁶ Comparatively, Sun et al compared liraglutide, exenatide, dulaglutide, and albiglutide to placebo as well as to other diabetes therapies, including insulin and sulfonylureas and found that overall, GLP-IRAs significantly reduced SBP, but only exenatide significantly decreased DBP.²⁷

For MI and adverse cardiovascular events (Table 2), GLP-IRAs were found to be beneficial. Malhotra et al found significant reductions in major cardiovascular adverse events, cardiovascular mortality, and all-cause mortality among patients treated with GLP-IRAs. Sinha et al reported a significant decrease in cardiovascular death and MI when combined with stroke, but not for MI alone.^{34,35} Additionally, it was also found that patients treated with exenatide and liraglutide had a significant increase in heart rate.²⁷ In patients who had already had a myocardial infarction, it was found that GLP-IRAs significantly reduced infarct size in patients undergoing percutaneous coronary intervention, and liraglutide resulted in significant improvement in left ventricular ejection fraction.⁷ Despite this, there was no significant reduction in heart failure in the one meta-analysis that studied this cardiovascular outcome.³⁵

Finally, most meta-analyses focused on risk reduction in total stroke, non-fatal stroke, and fatal stroke in patients treated with GLP-IRAs (Table 2). Six of the studies found a significant decrease in total stroke, and four of these studies also found a significant reduction in non-fatal stroke but no significant change in fatal stroke.^{28,29,32–35} Some studies focused on defining strokes in terms of ischemic or hemorrhagic, with Benn et al finding a significant reduction in ischemic stroke risk ratio based on GLP-IRAs reducing plasma glucose levels.³⁰ Wei et al found that there was a significant reduction in risk of ischemic stroke in patients with T2DM treated with GLP-IRAs but no reduction in hemorrhagic stroke.³³ Compared to other diabetes medications, Sinha et al found that dipeptidyl peptidase-4 inhibitors and sodium-glucose cotransporter-2 inhibitors had a neutral effect on risk of stroke, while GLP-IRAs significantly reduced stroke (13%).³⁵ Finally, one paper found no significant risk reduction in total stroke when performing a network meta-analysis but did find an associated decrease in total stroke in the pair-wise meta-analysis.³¹

Discussion

Based on this review, GLP-1RAs might have a beneficial effect on psoriasis but larger randomized studies are needed. Case reports and prospective cohort studies suggested benefit for psoriasis, while two small RCTs showed conflicting results with one study demonstrating skin improvement following GLP-1RAs in patients with T2DM after 12 weeks, and the other showing no effect in glucose-tolerant patients after a shorter timeframe of 8 weeks.^{22,23} GLP-1RAs may help improve psoriatic skin disease by increasing peripheral iNKT cells and decreasing plaque-associated iNKT cytokine production.^{8,17,19} Moreover, GLP-1RAs improve not only psoriatic symptoms and quality of life but also metabolic and inflammatory features that are known risk factors for cardiovascular disease, such as a reduction in body weight, which was found in 12 of the 14 included psoriasis studies (Table 1). Previous research has shown that visceral adipose tissue correlates with vascular inflammation in psoriasis, and myeloid cell count correlates with established atherosclerosis and insulin resistance.^{36,37} The mechanism of improvement may be related to a reduction in visceral adipose tissue and monocyte proinflammatory responses and adhesion to vascular endothelium following treatment with GLP-1RAs.^{38,39}

Limitations of the reported psoriasis studies include relatively small sample sizes, which limits the generalizability of these results, with the majority of reported patients being male and the race and ethnicity of the patients infrequently noted. Furthermore, the length of the GLP-1RA treatment period varied from study to study, ranging from 6 weeks up to 12 months, with variable follow up periods. This heterogeneity makes interpretation of treatment effects and outcomes more complex.

In large meta-analyses, the benefits of GLP-1RAs on cardiovascular diseases in patients with T2DM are clear. While not effective in reducing DBP, they have a positive effect on decreasing SBP, myocardial mortality, and risk of total stroke.^{26,27,33,34} Moreover, in the recently reported SELECT trial involving 17,604 obese or overweight patients with preexisting cardiovascular disease but without T2DM, weekly semaglutide was shown to be superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke (Hazard ratio, 0.80; 95% CI 0.72 to 0.90; $P < 0.001$).⁴⁰ Thus, GLP-1RAs have beneficial cardiovascular effects in patients with either T2DM or obesity.

The mechanism behind the beneficial impact of this therapeutic agent on psoriasis may be similar in myocardial mortality and stroke, with GLP-1RAs increasing signaling in survival pathways, resulting in decreased oxidative stress and apoptosis in the ischemic tissue.⁷ This also correlates with the findings that the risk of hemorrhagic stroke was not decreased by GLP-1RAs.³³ While the mechanism underlying the increase in cardiovascular disease in psoriasis patients is not fully understood, the primary hypothesis is related to systemic inflammation and oxidative stress.^{2,41} The reduction in oxidative stress and apoptosis in this tissue following GLP-1RAs may be particularly beneficial in treating these comorbidities in psoriasis patients with increased oxidative stress markers.⁴¹ Additionally, other metabolic and inflammatory markers, such as BMI and glycated hemoglobin, showed improvement in psoriasis patients treated with GLP-1RAs (Table 1).^{1,18,24}

Clinicians treating psoriasis patients may want to work with primary care providers to discuss the use of GLP-1RAs in psoriasis patients with concurrent T2DM or obesity due to the positive effects on associated cardiovascular comorbidities. This may be particularly important in light of recent evidence demonstrating that many primary care providers are unaware of the increased cardiovascular risk in patients with psoriasis and that both dermatologists and rheumatologists are prone to prescribe drugs such as statins to patients with psoriasis.^{42,43} While the results on psoriasis improvement seem to be mixed, many patients report either an improvement in the PASI or DLQI or a neutral effect, with only one case of psoriasis worsening.^{13,14,16} With the increasing interest in these medications, further studies should be conducted to determine their precise effects on psoriasis and its comorbidities.

Despite these knowledge gaps in skin disease, recent research demonstrating the beneficial impact of GLP-1RAs on major cardiovascular events, chronic kidney disease, T2DM, and obesity warrants their consideration for use in psoriasis patients with T2DM for their overall positive health impacts.^{44,45} As with any new therapies, side effects in GLP-1RAs such as diarrhea, vomiting, abdominal pain, and pancreatitis must be balanced against the benefits.^{1,46}

Conclusion

This review analyzes the effects of GLP-1RAs on both psoriasis and cardiovascular comorbidities, including hypertension, stroke, and myocardial infarction. The positive impact of GLP-1RAs is demonstrated in multiple large-scale studies

of cardiovascular diseases, suggesting their possible utility in treating these comorbidities in psoriasis patients. As interest in these medications grows, further randomized clinical trials are needed to examine their effects on psoriasis.

Abbreviations

GLP-1RA, Glucagon-like-peptide-1 receptor agonists; MI, myocardial infarction; PASI, psoriasis area and severity index; PGA, physician's global assessment; T2DM, type 2 diabetes mellitus; iNKT, invariant natural killer T cells; DLQI, dermatology life quality index; RCTs, randomized controlled trials; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; CASP, Critical Appraisal Skill Program.

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References

1. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *JAMA*. 2020;323(19):1945–1960. doi:10.1001/jama.2020.4006
2. Xue K, Shao S, Fang H, et al. Adipocyte-derived CTRP3 exhibits anti-inflammatory effects via LAMP1-STAT3 axis in psoriasis. *J Invest Dermatol*. 2022;142(5):1349–1359.e8. doi:10.1016/j.jid.2021.09.027
3. Wan MT, Shin DB, Hubbard RA, Noe MH, Mehta NN, Gelfand JM. Psoriasis and the risk of diabetes: a prospective population-based cohort study. *J Am Acad Dermatol*. 2018;78(2):315–322.e1. doi:10.1016/j.jaad.2017.10.050
4. Ozempic for weight loss: does it work, and what do experts recommend? Cultivating-health. Available from: <https://health.ucdavis.edu/blog/cultivating-health/ozempic-for-weight-loss-does-it-work-and-what-do-experts-recommend/2023/07>. Accessed May 7, 2024.
5. Muscogiuri G, Cignarelli A, Giorgino F, et al. GLP-1: benefits beyond pancreas. *J Endocrinol Invest*. 2014;37(12):1143–1153. doi:10.1007/s40618-014-0137-y
6. Lee YS, Jun HS. Anti-inflammatory effects of GLP-1-based therapies beyond glucose control. *Mediators Inflamm*. 2016;2016:1–11. doi:10.1155/2016/3094642
7. Huang M, Wei R, Wang Y, et al. Protective effect of glucagon-like peptide-1 agents on reperfusion injury for acute myocardial infarction: a meta-analysis of randomized controlled trials. *Ann Med*. 2017;49(7):552–561. doi:10.1080/07853890.2017.1306653
8. Faurischou A, Pedersen J, Gyldenløve M, et al. Increased expression of glucagon-like peptide-1 receptors in psoriasis plaques. *Exp Dermatol*. 2013;22(2):150–152. doi:10.1111/exd.12081
9. Matwiejuk M, Mysliwiec H, Jakubowicz-Zalewska O, Chabowski A, Flisiak I. Effects of hypolipidemic drugs on psoriasis. *Metabolites*. 2023;13(4):493. doi:10.3390/metabo13040493
10. Al-Badri MR, Azar ST. Effect of glucagon-like peptide-1 receptor agonists in patients with psoriasis. *Ther Adv Endocrinol Metab*. 2014;5(2):34–38. doi:10.1177/2042018814543483
11. Buysschaert M, Tennstedt D, Preumont V. Improvement of psoriasis during exenatide treatment in a patient with diabetes. *Diabetes Metab*. 2012;38(1):86–88. doi:10.1016/j.diabet.2011.11.004
12. Costanzo G, Curatolo S, Busà B, Belfiore A, Gullo D. Two birds one stone: semaglutide is highly effective against severe psoriasis in a type 2 diabetic patient. *Endocrinol Diabetes Metab Case Rep*. 2021;2021. doi:10.1530/EDM-21-0007
13. Malavazos AE, Meregalli C, Sorrentino F, et al. Semaglutide therapy decreases epicardial fat inflammation and improves psoriasis severity in patients affected by abdominal obesity and type-2 diabetes. *Endocrinol Diabetes Metab Case Rep*. 2023;2023(3). doi:10.1530/EDM-23-0017
14. Nowowiejska J, Baran A, Flisiak I. The first case of the exacerbation of psoriatic skin lesions after liraglutide. *Pol Arch Intern Med Published Online*. 2023. doi:10.20452/pamw.16527
15. Reid CT, Tobin AM, Ahern T, O'Shea D, Kirby B. Liraglutide in combination with Acitretin for severe recalcitrant psoriasis. *Br J Dermatol*. 2013;169(1):230–231. doi:10.1111/bjd.12380
16. Faurischou A, Knop FK, Thyssen JP, Zachariae C, Skov L, Vilsbøll T. Improvement in psoriasis after treatment with the glucagon-like peptide-1 receptor agonist liraglutide. *Acta Diabetol*. 2014;51(1):147–150. doi:10.1007/s00592-011-0359-9
17. Ahern T, Tobin AM, Corrigan M, et al. Glucagon-like peptide-1 analogue therapy for psoriasis patients with obesity and type 2 diabetes: a prospective cohort study. *J Eur Acad Dermatol Venereol*. 2013;27(11):1440–1443. doi:10.1111/j.1468-3083.2012.04609.x
18. Buysschaert M, Baeck M, Preumont V, et al. Improvement of psoriasis during glucagon-like peptide-1 analogue therapy in type 2 diabetes is associated with decreasing dermal $\gamma\delta$ T-cell number: a prospective case-series study. *Br J Dermatol*. 2014;171(1):155–161. doi:10.1111/bjd.12886

19. Hogan AE, Tobin AM, Ahern T, et al. Glucagon-like peptide-1 (GLP-1) and the regulation of human invariant natural killer T cells: lessons from obesity, diabetes and psoriasis. *Diabetologia*. 2011;54(11):2745–2754. doi:10.1007/s00125-011-2232-3
20. Xu X, Lin L, Chen P, et al. Treatment with liraglutide, a glucagon-like peptide-1 analogue, improves effectively the skin lesions of psoriasis patients with type 2 diabetes: a prospective cohort study. *Diabet Res Clin Pract*. 2019;150:167–173. doi:10.1016/j.diabres.2019.03.002
21. Chang G, Chen B, Zhang L. Efficacy of GLP-1rA, liraglutide, in plaque psoriasis treatment with type 2 diabetes: a systematic review and meta-analysis of prospective cohort and before-after studies. *J Dermatol Treat*. 2022;33(3):1299–1305. doi:10.1080/09546634.2021.1882658
22. Faurschou A, Gyldenløve M, Rohde U, et al. Lack of effect of the glucagon-like peptide-1 receptor agonist liraglutide on psoriasis in glucose-tolerant patients – a randomized placebo-controlled trial. *J Eur Acad Dermatol Venereol*. 2015;29(3):555–559. doi:10.1111/jdv.12629
23. Lin L, Xu X, Yu Y, et al. Glucagon-like peptide-1 receptor agonist liraglutide therapy for psoriasis patients with type 2 diabetes: a randomized-controlled trial. *J Dermatol Treat*. 2022;33(3):1428–1434. doi:10.1080/09546634.2020.1826392
24. Sun X, Cai X, Liu L, et al. Effect of different types of hypoglycemic medications on psoriasis: an analysis of current evidence. *Dermatology*. 2023;239(2):299–313. doi:10.1159/000528026
25. deShazo RA, Secrest AM, Armstrong AW, Duffin KC. Addressing hypertension in patients with psoriasis: review and recommendations. *J Psoriasis Psoriatic Arthritis*. 2020;5(4):129–138. doi:10.1177/2475530320936373
26. Zhao X, Huang K, Zheng M, Duan J. Effect of liraglutide on blood pressure: a meta-analysis of liraglutide randomized controlled trials. *BMC Endocr Disord*. 2019;19(1):4. doi:10.1186/s12902-018-0332-5
27. Sun F, Wu S, Guo S, et al. Impact of GLP-1 receptor agonists on blood pressure, heart rate and hypertension among patients with type 2 diabetes: a systematic review and network meta-analysis. *Diabet Res Clin Pract*. 2015;110(1):26–37. doi:10.1016/j.diabres.2015.07.015
28. Barkas F, Elisaf M, Milionis H. Protection against stroke with glucagon-like peptide 1 receptor agonists: a systematic review and meta-analysis. *Eur J Neurol*. 2019;26(4):559–565. doi:10.1111/ene.13905
29. Bellastella G, Maiorino MI, Longo M, et al. Glucagon-like peptide-1 receptor agonists and prevention of stroke systematic review of cardiovascular outcome trials with meta-analysis. *Stroke*. 2020;51(2):666–669. doi:10.1161/STROKEAHA.119.027557
30. Benn M, Emanuelsson F, Tybjærg-Hansen A, Nordestgaard BG. Impact of high glucose levels and glucose lowering on risk of ischaemic stroke: a Mendelian randomisation study and meta-analysis. *Diabetologia*. 2021;64(7):1492–1503. doi:10.1007/s00125-021-05436-0
31. Kim JS, Lee G, Park KI, Oh SW. Comparative effect of glucose-lowering drugs for type 2 diabetes mellitus on stroke prevention: a systematic review and network meta-analysis. *Diabetes Metab J*. 2024;48(2):312–320. doi:10.4093/dmj.2022.0421
32. Li J, Ji C, Zhang W, Lan L, Ge W. Effect of new glucose-lowering drugs on stroke in patients with type 2 diabetes: a systematic review and Meta-analysis. *J Diabetes Complications*. 2023;37(1):108362. doi:10.1016/j.jdiacomp.2022.108362
33. Wei J, Yang B, Wang R, et al. Risk of stroke and retinopathy during GLP-1 receptor agonist cardiovascular outcome trials: an eight RCTs meta-analysis. *Front Endocrinol*. 2022;13:1007980. doi:10.3389/fendo.2022.1007980
34. Malhotra K, Katsanos AH, Lambadiari V, et al. GLP-1 receptor agonists in diabetes for stroke prevention: a systematic review and meta-analysis. *J Neurol*. 2020;267(7):2117–2122. doi:10.1007/s00415-020-09813-4
35. Sinha B, Ghosal S. Meta-analyses of the effects of DPP-4 inhibitors, SGLT2 inhibitors and GLP1 receptor analogues on cardiovascular death, myocardial infarction, stroke and hospitalization for heart failure. *Diabet Res Clin Pract*. 2019;150:8–16. doi:10.1016/j.diabres.2019.02.014
36. Rivers JP, Powell-Wiley TM, Dey AK, et al. Visceral adiposity in psoriasis is associated with vascular inflammation by 18F-fluorodeoxyglucose positron-emission tomography/computed tomography beyond cardiometabolic disease risk factors in an observational cohort study. *JACC Cardiovasc Imaging*. 2018;11(2):349–357. doi:10.1016/j.jcmg.2017.08.014
37. Manyak GA, Patel NH, Dey AK, et al. Abdominal visceral adiposity is associated with coronary artery plaque lipid-rich necrotic core partly mediated by bone marrow uptake of 18F-FDG positron emission tomography/computed tomography in psoriasis. *J Invest Dermatol*. 2022;142(7):2030–2033.e1. doi:10.1016/j.jid.2021.10.031
38. Liao C, Liang X, Zhang X, Li Y. The effects of GLP-1 receptor agonists on visceral fat and liver ectopic fat in an adult population with or without diabetes and nonalcoholic fatty liver disease: a systematic review and meta-analysis. *PLoS One*. 2023;18(8):e0289616. doi:10.1371/journal.pone.0289616
39. Bloch O, Blatt A, Appel MY, et al. Coronary atherosclerosis severity is closely associated with decreased GLP-1R positivity among CD16+ pro-inflammatory and patrolling monocyte subsets. *Atheroscler Plus*. 2021;46:15–19. doi:10.1016/j.athplu.2021.10.001
40. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389(24):2221–2232. doi:10.1056/NEJMoa2307563
41. Dobrică EC, Cozma MA, Găman MA, Voiculescu VM, Găman AM. The involvement of oxidative stress in psoriasis: a systematic review. *Antioxidants*. 2022;11(2):282. doi:10.3390/antiox11020282
42. Berna-Rico E, Abbad-Jaime de Aragon C, Garcia-Aparicio A, et al. Cardiovascular screening practices and statin prescription habits in patients with psoriasis among dermatologists, rheumatologists and primary care physicians. *Acta Derm Venereol*. 2023;103:adv5087. doi:10.2340/actadv.v103.5087
43. Barbieri JS, Beidas RS, Gondo GC, et al. Analysis of specialist and patient perspectives on strategies to improve cardiovascular disease prevention among persons with psoriatic disease. *JAMA Dermatol*. 2022;158(3):252–259. doi:10.1001/jamadermatol.2021.4467
44. Vlado P, Tuttle Katherine R, Peter R, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N Engl J Med*. 2024;391(2):109–121. doi:10.1056/NEJMoa2403347
45. Wilding John PH, Batterham Rachel L, Salvatore C, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989–1002. doi:10.1056/NEJMoa2032183
46. Liu L, Chen J, Wang L, Chen C, Chen L. Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: a real-world disproportionality study based on FDA adverse event reporting system database. *Front Endocrinol*. 2022;13. doi:10.3389/fendo.2022.1043789

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