# The Expanding Role of Semaglutide: Beyond Weight Loss to Cardiovascular Outcomes in Clinical Practice

**Usman Mustafa**

1st Year MBBS, Islamabad Medical and Dental College, Islamabad, Pakistan

***Key points:***

- Introduction
- Mechanism
- Clinical Evidence and Cardiovascular Outcomes
- Conclusion

## Introduction

The global rise in obesity has contributed to increasing rates of cardiovascular disease and diabetes, creating a major burden on healthcare systems.[1] Obesity is an important cardiovascular risk factor, leading to growing interest in pharmacological treatments such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs).[2]

GLP-1 RAs are used in the management of obesity and related metabolic conditions. They promote insulin secretion, reduce appetite, and improve glucose control. Common drugs in this class include liraglutide and semaglutide, while tirzepatide acts on both GLP-1 and GIP receptors.[2]

Semaglutide is available in oral and injectable formulations and has a half-life of approximately one week. In addition to improving blood glucose levels and reducing body weight, semaglutide has been associated with improvements in cardiovascular risk factors such as blood pressure. Clinical studies have also demonstrated cardiovascular benefits in people with overweight or obesity.[1,8] Although generally well tolerated, semaglutide can cause adverse effects, particularly gastrointestinal symptoms, which may lead to treatment discontinuation in some patients.[3]

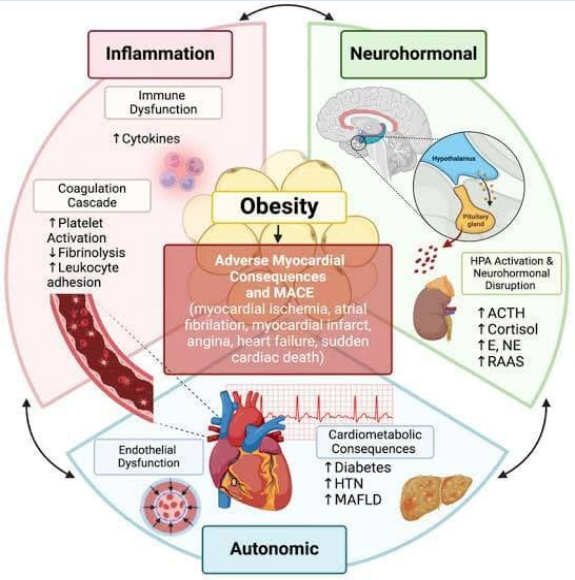



**Figure 1:** *Obesity-driven mechanisms of cardiovascular disease: inflammation, neurohormonal activation, endothelial dysfunction, and autonomic imbalance.*[2]

## Mechanisms

Semaglutide 2.4 mg is a long-acting GLP-1 receptor agonist administered once weekly. It was approved in the United States for chronic weight management in 2021 and has demonstrated substantial weight loss when combined with lifestyle modification.[4]

Obesity involves complex genetic, environmental, metabolic, and neurohormonal factors, with excess visceral adipose tissue playing an important role. GLP-

1 receptor agonists such as semaglutide help regulate appetite, glucose metabolism, and energy balance, while also producing beneficial effects on body weight and other metabolic risk factors.[5]

Semaglutide improves cardiovascular health mainly through its effects on glucose control, body weight, blood pressure, and other cardiovascular risk factors. It increases glucose-dependent insulin secretion and suppresses glucagon release, improving both fasting and postprandial glucose levels.[3] Semaglutide has also been associated with reductions in major adverse cardiovascular events (MACE), supporting its role in reducing cardiovascular risk in people with obesity or diabetes.[1,8]

## Clinical Evidence and Cardiovascular Outcomes

The SELECT trial included 17,604 adults with overweight or obesity who were at high cardiovascular risk. Treatment with semaglutide significantly reduced major adverse cardiovascular events (MACE) compared with placebo. Benefits were also seen in patients with heart failure, with a lower risk of heart failure-related outcomes (HR 0.79; 95% CI 0.64–0.98) and cardiovascular death (HR 0.76; 95% CI 0.59–0.97).[1]

Other randomized trials of oral and injectable semaglutide have also shown cardiovascular benefits. A meta-analysis found that semaglutide reduced cardiovascular mortality (RR 0.76; 95% CI 0.58–0.98) and the need for coronary revascularization (RR 0.68; 95% CI 0.52–0.88).[7] These findings suggest that semaglutide may lower cardiovascular risk in addition to its effects on weight and blood glucose control.

## Conclusions

Recent clinical trials have shown that semaglutide and other GLP-1 receptor agonists can provide cardiovascular benefits beyond weight loss. Semaglutide has been associated with reductions in major cardiovascular events and may therefore have an important role in cardiometabolic disease management.[8]Although longer-term studies are needed to further confirm these benefits, current evidence supports semaglutide as a promising treatment for reducing cardiovascular risk in appropriate patients.[1,7]

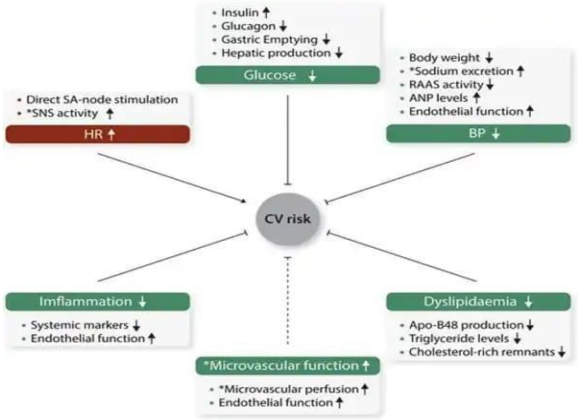



**Figure 2:** *The direct and indirect effect of GLP-1R on the heart and vessels* [8]

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