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Do GLP-1 Drugs Provide Key Weight-Loss Benefit?

Popular GLP-1 drugs can help many people shed significant weight, but they may fall short in delivering a key benefit essential for long-term health: improving heart and lung fitness, University of Virginia researchers caution in a new paper.

The team emphasises that weight loss from GLP-1 drugs offers clear health benefits for people with obesity, type 2 diabetes, and heart failure, including better blood-sugar control, short-term improvements in heart and kidney outcomes, and survival benefits. However, to ensure patients gain the full cardiovascular and respiratory benefits of weight loss over time, doctors may need to recommend exercise programmes, nutrition support, or complementary medications alongside GLP-1 therapy.

While GLP-1 medications help patients lose fat, they also lead to a loss of fat-free mass, including muscle, which accounts for 40-50% of fat-free mass. Studies indicate that 25-40% of the weight lost with GLP-1 therapy is from fat-free mass, a far steeper decline than the typical 8% loss per decade due to ageing.

To better understand the long-term consequences, study researchers reviewed current data on GLP-1 drugs and their effects on cardiorespiratory fitness (CRF), a measure of how efficiently the body uses oxygen during exercise. CRF is a powerful predictor of cardiovascular and all-cause mortality and reflects the combined performance of the heart, lungs, blood vessels, and muscles.

Patients with obesity often have low CRF, sometimes due to inadequate muscle mass or because fat infiltrates muscle, reducing its quality. CRF is a strong predictor of mortality risk across a wide range of populations. A study of nearly 400,000 individuals worldwide found that CRF was a far better predictor of mortality risk than weight alone. Once CRF was accounted for, body weight no longer predicted death risk. This is why understanding the impact of GLP-1 drugs on CRF is so important.

The researchers found that while GLP-1 drugs improve certain measures of heart function, these benefits do not translate into meaningful improvements in VO2max, the gold-standard measure of CRF. Although some small studies suggest that exercise may help improve VO2max in patients on GLP-1 therapy, these studies lacked strong controls, and larger, rigorous trials are needed.

The researchers conclude that while GLP-1 drugs significantly reduce body weight and body fat, they also cause substantial lean mass loss without clear evidence of improving CRF. This could negatively impact metabolic health, frailty, and lifespan, they warn, underscoring the need for further research to optimise patient outcomes. They also highlight promising developments, such as monoclonal antibodies in clinical pipelines that may help offset lean muscle loss in the future.

It's important for patients using GLP-1 drugs to discuss strategies to preserve muscle mass with their healthcare providers. The American Diabetes Association recommends screening for malnutrition and low muscle mass before starting these medications, alongside ensuring adequate protein intake and regular exercise. There is also a need to study whether exercise during GLP-1 therapy can preserve or even improve VO2max, ensuring patients get the full health benefits of their weight loss.

Source: University of Virginia Health System
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