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Long Term Control of T2DM and Weight Through Roux-en-Y Gastric Bypass Surgery Versus Weight Loss Medication

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Abstract

•Type II diabetes mellitus (T2DM) affects hundreds of millions of individuals in the United States and prevalence is increasing.
•As a lifelong disease, interventions must be studied long-term.
•This project aims to compare long term efficacity of Roux-en-Y gastric bypass surgery and several antidiabetic medications that result in weight loss in type II diabetics who have failed to achieve goals through first line treatment of diet, exercise, and metformin.
•A literature review was completed using the electronic search database PubMed with a variety of MeSH terms and keywords.
•Research showed strong evidence that surgery was superior to medications in reducing HbA_{1C} and weight.
•Research also showed that the antidiabetic medications discussed decreased HbA_{1C} and weight superiorly to placebos and other classes of antidiabetic medications.
•Continued research that directly compares these medications over a longer interval of time is needed.
•*Keywords:* long term, gastric bypass, weight loss medication

Introduction

- T2DM is a lifelong disease characterized by disfunction of insulin secretion, resulting in elevated blood glucose levels that can damage organs all throughout the body (Galicia-Garcia et al. 2020).
- It is estimated to affect 463 million individuals and that number is rising (Galicia-Garcia et al. 2020).
- It is a multifactorial disease but is associated with obesity because it is believed that adipose tissue creates inflammatory mechanisms that lead to insulin resistance (Galicia-Garcia et al. 2020).
- Diagnosis and monitoring is often done using a blood test called glycated hemoglobin (HbA_{1c}) which serves as an objective measurement of glycemic control over a 2–3-month period.
- First line treatment is typically lifestyle changes through diet and exercise, as well as the medication metformin.
- The lifestyle changes are difficult to carry out, and many can not achieve control of their T2DM with first line treatment, so more intense medical interventions are often required.
- Options that can lower blood glucose and weight include Roux-en-Y gastric bypass surgery (RYGB) and medications such as the GLP-1 agonists semaglutide and liraglutide, and the SGLT2 inhibitors empagliflozin and dapagliflozin.

Statement of the Problem

- Since T2DM is a lifelong disease, the long-term efficacy of treatment options must be considered when determining treatment.
- Long term efficacy of RYGB surgery, semaglutide, liraglutide, empagliflozin, and dapagliflozin should be studied, looking at reduction of HbA_{1C} and weight loss as well as the adverse events associated with each intervention, to best determine treatment course.

Research Question

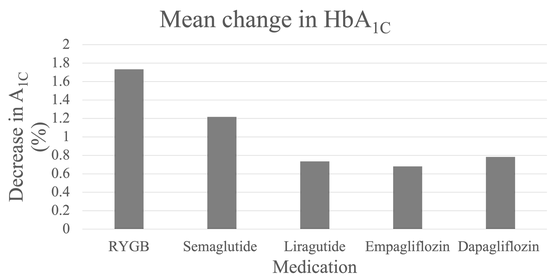
- In patients with type II diabetes mellitus (T2DM) who have failed to achieve blood glucose control through diet, exercise, and metformin, does Roux-en-Y gastric bypass surgery or addition of weight loss medication improve long-term HbA_{1c} more effectively?

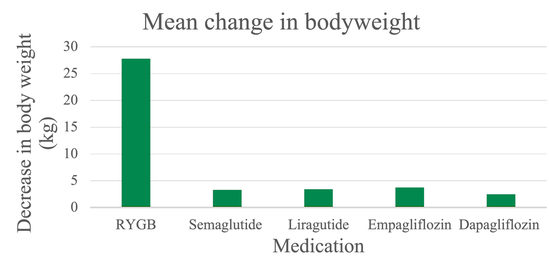
Literature Review

- Schauer et al. (2017) found that after 5 years, RYGB lowered HbA_{1C} by 2.1% and body weight by 23.2 kg on average, significantly more than intense medical therapy alone ($p = 0.003$, $p = 0.003$).
- Mingrone et al. (2021) found that patients who had RYGB saw HbA_{1C} reduced by 1.9% and body weight by 37.3 kg on average after 10 years, significantly more than the medical therapy group ($p = 0.0097$; $p < 0.0001$). They also required fewer diabetic medications and had fewer diabetes-related complications at the end of the study. The study also found:
  - Weight changes did NOT predict diabetes remission or relapse following the surgery.
  - Patients who did not go into remission in the first two years post-surgery did not do so at all in the 10-year period.
  - Highest risk for relapse was within first 5-years of surgery, risk declines significantly after 5 years.
- Pratley et al. (2019) found that after 52 weeks, patients taking oral semaglutide reduced HbA_{1C} by 1.2% and body weight by 4.3 kg, which is significantly more compared to liraglutide ($p = 0.0002$, $p = 0.0019$). Liraglutide reduced HbA_{1C} by 0.9% and body weight by 3.0 kg, which was more than the placebo's respective changes of -0.2% and -1.0 kg. Semaglutide treatment was discontinued due to adverse effects more often than liraglutide. Liraglutide decreased HbA_{1C} and bodyweight more rapidly than semaglutide.
- Rodbard et al. (2019) found that after 52 weeks, patients who took oral semaglutide saw significantly improved HbA_{1C} with a reduction of -1.3% compared to those who took empagliflozin who saw a reduction of -0.9% ($p < 0.0001$), however, there was no difference in weight loss with respective changes of -3.8 kg and -3.6 kg ($p= 0.6231$) unless discontinuation of therapy and use of rescue medication was statistically accounted for.
- Kohan et al. (2014) found that dapagliflozin 10 mg reduced HbA_{1C} of renally impaired patients by -0.75% and weight by -2.20 kg after 104 weeks, which was not significantly different than the placebo group.
- Müller-Wieland et al. (2018) found that combination medication of dapagliflozin 10 mg and saxagliptin 5 mg lowered HbA_{1C} and bodyweight by 1.2% and 3.2 kg respectively, which is significantly more compared to the control of glimepiride ($p = 0.001$, $p < 0.001$).
- Ridderstråle et al. (2018) found that empagliflozin 25mg reduced HbA_{1C} by 0.29% and weight by 4.9 kg after 208 weeks, which were both significantly more than individuals taking glimepiride 1-4 mg ($p = 0.0129$, $p < 0.0001$, respectively).

Discussion

- RYGB resulted in significantly greater reductions in HbA_{1C} and bodyweight compared to medical therapy alone.
- Amount of weight loss following RYGB was not predictive of diabetes remission or relapse.
- Single studies showed semaglutide appeared to be superior to liraglutide and empagliflozin in reducing HbA_{1C}. However, it also tended to have the highest rate of discontinuation due to adverse effects.
- Semaglutide's superiority over other antidiabetic drugs that result in weight loss is not corroborated as there were no other studies directly comparing the medications discussed in this project. More long-term research directly comparing these medications should be done.
- Liraglutide did appear to lower HbA_{1C} and bodyweight significantly compared to a placebo, as did empagliflozin.
- Dapagliflozin was not shown to significantly lower HbA_{1C} and bodyweight compared to a placebo in renally impaired patients. When given as a combination drug with saxagliptin, dapagliflozin did significantly lower HbA_{1C} and bodyweight compared to a sulfonylurea medication in non-renally impaired patients.





These figures show the average changes in HbA_{1C} and body weight across the 16 studies used in the literature review this poster is based upon. It is not corrected for the different n-values and lengths of the studies, nor does it account for the standard deviation in each study. These figures are merely meant to aid in visualization of the information discussed.

Applicability to Clinical Practice

- This information allows clinicians to recommend RYGB as a long-term option to type II diabetics who are interested in improving blood glucose control and losing weight and meet the criteria for bariatric surgery.
- These findings also show available medication options, their efficacy, and some of their strengths and weakness. This information can help to guide medication selection for type II diabetics who are interested in improving blood glucose control and losing weight but are unable to get bariatric surgery for one reason or another.

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