



MICRO LABS LIMITED

Diabetes Update

Vol. 1 | Issue 13 | 2020

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Renal and Cardiovascular Outcomes After Weight Loss From Gastric Bypass Surgery in Type 2 Diabetes
- Effects of Novel Dual GIP and GLP-1 Receptor Agonist Tirzepatide on Biomarkers of NASH in Patients With Type 2 Diabetes
- Different effects of SGLT2 inhibitors according to the presence and types of heart failure in T2DM

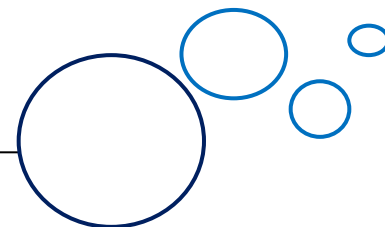
Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited





Renal and Cardiovascular Outcomes After Weight Loss From Gastric Bypass Surgery in Type 2 Diabetes

Obesity and type 2 diabetes mellitus (T2DM) are two of the most serious and accelerating public health burden worldwide. Cardiovascular disease (CVD) and renal disease have been strongly linked to both of them. This study examined detailed renal and cardiovascular (CV) outcomes after gastric bypass (GBP) surgery in people with obesity and type 2 diabetes mellitus (T2DM), across several renal function categories, in a nationwide cohort study.

Data was linked from the National Diabetes Register and the Scandinavian Obesity Surgery Register with four national databases holding information on socioeconomic variables, medications, hospitalizations, and causes of death and matched 5,321 individuals with T2DM who had undergone GBP with 5,321 who had not (age 18–65 years, mean BMI >40 kg/m², mean follow-up >4.5 years).

The risks of postoperative outcomes were assessed with Cox regression models.

During the first years post surgery, there were small reductions in creatinine and albuminuria and stable estimated glomerular filtration rate (eGFR) in the GBP group. The incidence rates of most outcomes relating to renal function, CV disease, and mortality were lower after GBP, being particularly marked for heart failure (hazard ratio [HR] 0.33 [95% CI 0.24, 0.46]) and CV mortality (HR 0.36 [(95% CI 0.22, 0.58)]). The risk of a composite of severe renal disease or halved eGFR was 0.56 (95% CI 0.44, 0.71), whereas nonfatal CV risk was lowered less (HR 0.82 [95% CI 0.70, 0.97]) after GBP. Risks for key outcomes were generally lower after GBP in all eGFR strata, including in individuals with eGFR <30 mL/min/1.73 m².

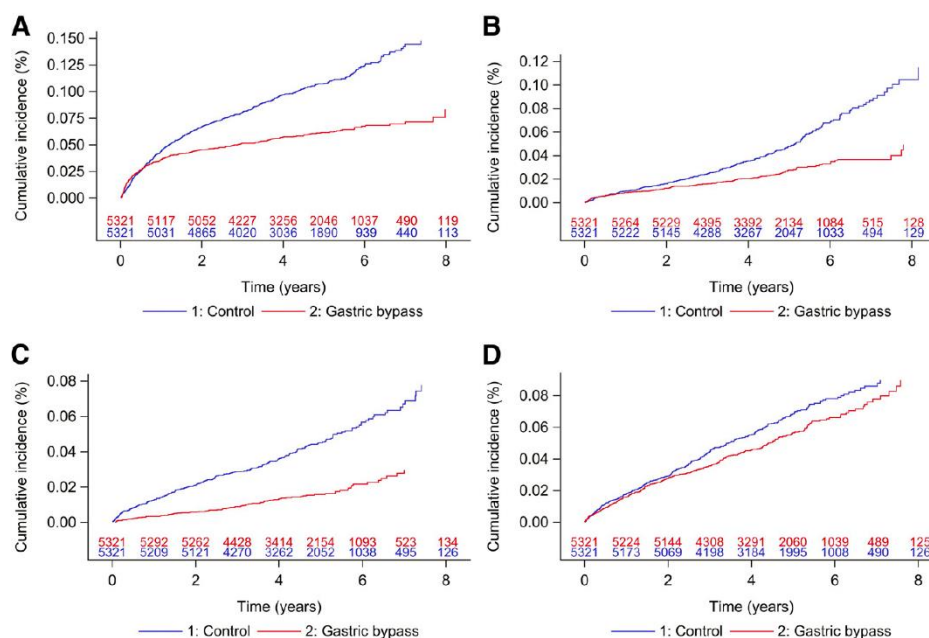


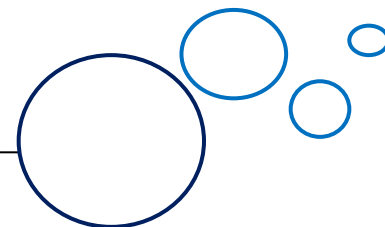
Figure 1—Cumulative incidence rates during the 9 years of follow-up. A: Macroalbuminuria. B: Severe renal disease or halved eGFR. C: Congestive heart failure. D: Nonfatal CVD.

The data suggest robust benefits for renal outcomes, heart failure, and CV mortality after GBP in individuals with obesity and T2DM. These results suggest that marked weight loss yields important benefits, particularly on the cardio renal axis (including slowing progression to end-stage renal disease), whatever the baseline renal function status.

In summary, on the basis of this nationwide observational study, we suggest that weight loss achieved by GBP contributes to lower risks of several diagnoses of renal disease and CVD and mortality in patients

with obesity and T2DM and, importantly, does so across the full spectrum of baseline renal function, an important observation given that some patients with advanced renal disease could have their march toward dialysis substantially slowed. The pattern of results also adds support for the importance of obesity on the cardiorenal axis in particular. While the effects of bariatric surgery on renal function in obesity and T2DM remain to be confirmed in prospective trials, our findings add strong support for intentional weight loss as a legitimate intervention to prevent or delay renal dysfunction and related

The data suggest robust benefits for renal outcomes, heart failure, and CV mortality after GBP in individuals with obesity and T2DM.



cardiac outcomes. Given the advent of newer drugs that can lower weight by 10 kg, it would be important to see how such therapies

affect relevant outcomes in the future.

Source: Liakopoulos V et al. Diabetes Care 2020;43:1276–1284 |

<https://doi.org/10.2337/dc19-1703>

Effects of Novel Dual GIP and GLP-1 Receptor Agonist Tirzepatide on Biomarkers of NASH in Patients With Type 2 Diabetes

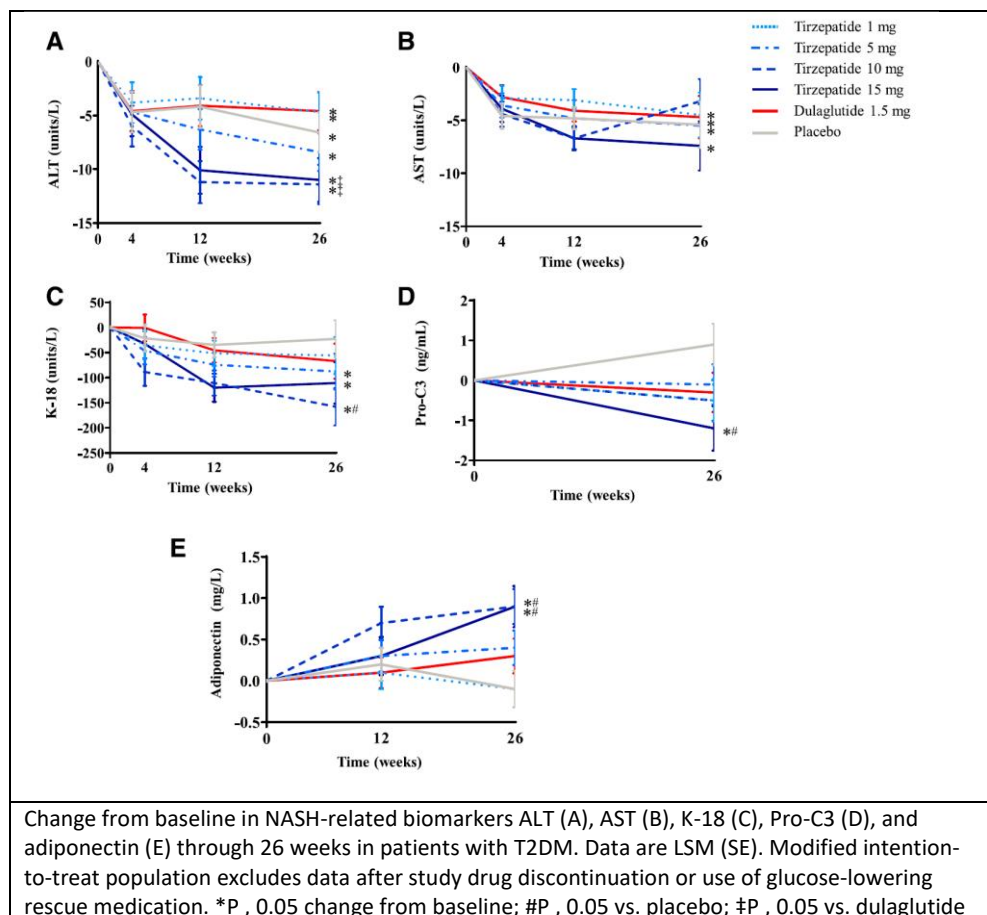
The prevalence of nonalcoholic fatty liver disease (NAFLD) is 25% globally and 60–75% in patients with type 2 diabetes mellitus (T2DM). The study was conducted to determine the effect of tirzepatide, a dual agonist of glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptors, on biomarkers of nonalcoholic steatohepatitis (NASH) and fibrosis in patients with type 2 diabetes mellitus (T2DM).

Patients from a phase 2 trial (N = 316) were included in these post hoc analyses. Patients with T2DM (HbA1c 7.0–10.5%, inclusive; with or without stable metformin therapy) were randomized (1:1:1:1:1) to receive once-weekly subcutaneous tirzepatide (1, 5, 10, or 15 mg),

dulaglutide (1.5 mg), or placebo for 26 weeks

Patients with T2DM received either once weekly tirzepatide (1, 5, 10, or 15 mg), dulaglutide (1.5 mg), or placebo for 26 weeks. Changes from baseline in alanine aminotransferase (ALT), aspartate aminotransferase (AST), keratin-18 (K-18), procollagen III (Pro-C3), and adiponectin were analyzed in a modified intention-to-treat population. Significant ($P < 0.05$) reductions from baseline in ALT (all groups), AST (all groups except tirzepatide 10 mg), K-18 (tirzepatide 5, 10, 15 mg), and Pro-C3 (tirzepatide 15 mg) were observed at 26 weeks. Decreases with tirzepatide were significant compared with placebo for K-18 (10

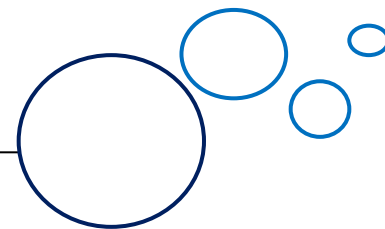
mg) and Pro-C3 (15 mg) and with In post hoc analyses, higher
dulaglutide for ALT (10, 15 mg). tirzepatide doses significantly
Adiponectin significantly increased decreased NASH-related biomarkers
from baseline with tirzepatide and increased adiponectin in
compared with placebo (10, 15 mg). patients with T2DM.



Higher doses of the dual GIP and GLP-1 RA tirzepatide significantly improved NASH-related biomarkers in a T2DM

In conclusion, higher doses of the dual GIP and GLP-1 RA tirzepatide significantly improved NASH-related biomarkers in a T2DM population. Because of the limitations of this study, these results should not be interpreted as providing evidence of efficacy for tirzepatide in patients with NASH. Nonetheless, these NASH biomarker data, along with the weight loss findings, support further evaluation of tirzepatide in patients with NASH.

Source: Hartman ML et al. Diabetes Care 2020;43:1352–1355 | <https://doi.org/10.2337/dc19-1892>



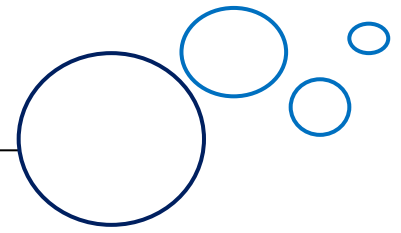
Different effects of SGLT2 inhibitors according to the presence and types of heart failure in T2DM

Despite the well-established clinical benefits of SGLT2i, only limited studies on the changes in cardiac function by SGLT2i have been made so far. Furthermore, it is unclear whether the cardiovascular benefits of SGLT2i would be similar between the diabetic patients with versus without HF, and between those with HFrEF versus HFpEF. The study aimed to compare the SGLT2i-induced changes in cardiac function and geometry assessed by echocardiography in type 2 diabetic patients according to the presence and types of HF, using a retrospective cohort.

Hwang et al. retrospectively identified 202 diabetic patients who underwent echocardiography before, and 6 to 24 months after the initiation of SGLT2i. After propensity score matching with diabetic patients without SGLT2i, the study population (n = 304) were categorized into group 1 (without HF nor SGLT2i; n = 76), group 2

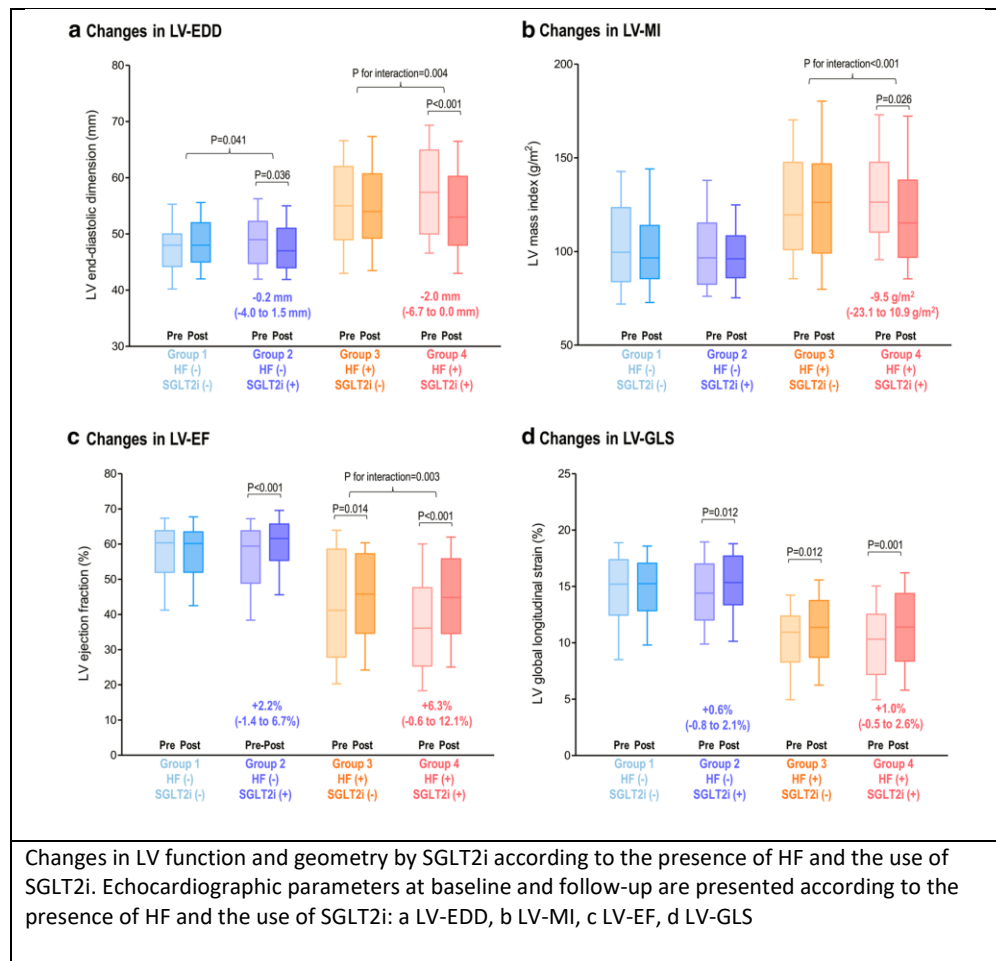
(without HF and received SGLT2i; n = 78), group 3 (with HF but without SGLT2i; n = 76), and group 4 (with HF and received SGLT2i; n = 74). Changes in echocardiographic parameters were compared between these 4 groups, and between HF patients with reduced versus preserved ejection fraction (EF).

After a median 13 months of follow-up, HF patients with SGLT2i showed a significant decrease in left ventricular end-diastolic dimension (LV-EDD; from 57.4 mm [50.0–64.9] to 53.0 mm [48.0–60.0]; $p < 0.001$) and improvement in LV-EF (from 36.1% [25.6–47.5] to 45.0% [34.8–56.3]; $p < 0.001$). LV mass index and diastolic parameters also showed improvements in HF patients with SGLT2i. The SGLT2i-induced improvements in cardiac function were more prominent in HF patients than those without HF, and in HFrEF patients than HFpEF patients.



In this retrospective cohort study, those with HFrEF patients compared the use of SGLT2i improved LV to those with HFpEF or those systolic and diastolic function, as without HF. These effects of SGLT2i well as LV geometry, in diabetic patients may contribute to the reduction in patients regardless of the presence HF morbidity and mortality in of HF. The improvement in LV diabetic patients. function was more prominent in

Use of SGLT2i improved cardiac function in diabetic patients, regardless of the presence of HF



Source: Hwang et al. Cardiovasc Diabetol 2020. 19:69. <https://doi.org/10.1186/s12933-020-01042-3>



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