Improvement in Hepatic Transaminases Over 12 Months After Single Procedure Duodenal Mucosal Resurfacing in Type 2 Diabetes Patients

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Background

Type 2 diabetes (T2D) and fatty liver disease are often overlapping metabolic disorders, and insulin resistance is thought to be a common pathogenic driver. Moreover, simultaneous improvement of both conditions has been observed with insulin sensitizing interventions.[1] Duodenal Mucosal Resurfacing (DMR), a minimally invasive endoscopic procedure, has shown efficacy in improving metabolic indices in T2D likely via insulin sensitizing mechanism.[2]

Objective

To assess the 12 months efficacy data of a single DMR procedure in patients with uncontrolled T2D.

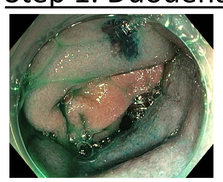
Methods

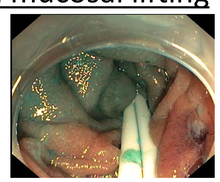
Revita-1 study Single arm, open label, multicentre study (NCT02879383).

Subjects Aged 25-75 years with T2D, HbA1c 7.5-10.0%, on oral glucose-lowering medication, treated in the first part of the study (Revita-1A) with dual catheter.

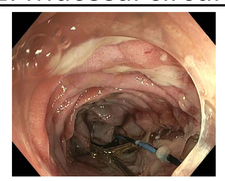
Duodenal Mucosal Resurfacing

Step 1. Duodenal mucosal lifting





Step 2. Mucosal circumferential ablation 9cm

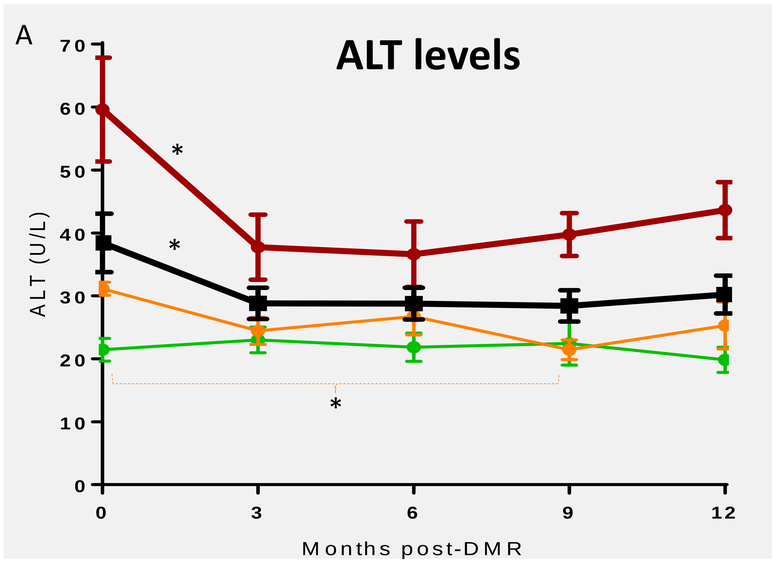


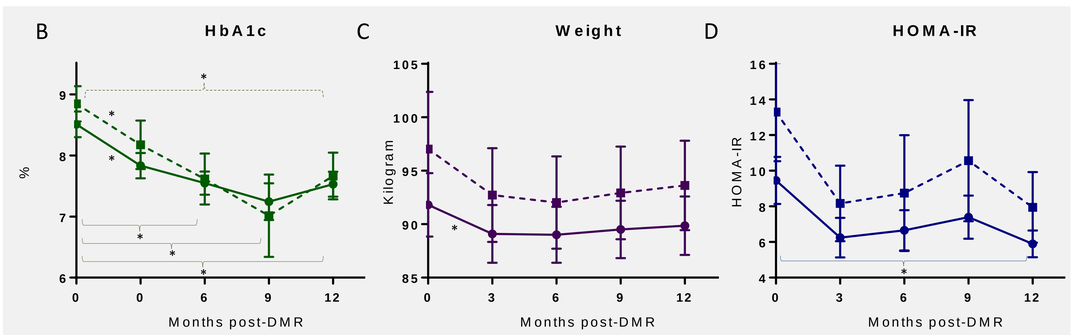
Glucoregulatory medication Sulfonylureas were discontinued 4 weeks before DMR. Other glucose lowering medication was kept stable for ≥6 months post DMR with subsequent medication modifications following local/international guidelines.

Postprocedural diet Gradually normalized diet for 2 weeks post DMR.

Efficacy analysis We stratified patients with ≥1 ablation (3cm) into baseline alanine aminotransferase (ALT) level tertiles: lowest <28 U/L, middle 28-37 U/L, and highest ≥37 U/L. Change from baseline in ALT, aspartate aminotransferase (AST), body weight, homeostasis model assessment index (HOMA-IR) and HbA1c were analyzed using repeated measures ANOVA with Bonferroni correction.

Results





Full cohort (n=27) demographics: Age 55±9 y; BMI 32.5±4.2 kg/m^2; ALT 37±21 U/L; HbA1c 8.7±1.0%; length DMR 8.1±0.4 cm (mean±SD)

High ALT tertile (n=9) demographics: Age 50±11 y; BMI 33.6±2.4 kg/m2; ALT 59±22 U/L; HbA1c 8.9±0,8%; length DMR 8.0±0.7 cm (mean±SD)

Although not displayed, qualitatively similar pattern of responses were observed with AST.

Graphs A-D. *ALT (A), HbA1c (B), Weight(C), and HOMA-IR (D) at 0 and at 3, 6, 9, and 12 months post DMR (mean±SEM).*

**p ≤ 0.05 between indicated time points (repeated measures ANOVA, Bonferroni correction).*

Graphs B-D. *Continuous line = full cohort; Dotted line = High ALT tertile subgroup.*

Conclusion

A single DMR procedure in T2D patients produced significant reductions in HbA1c and hepatic transaminases for 12 months. In the high baseline ALT subgroup, decrease in ALT levels was more pronounced, patients appeared to be more obese and insulin resistant (BMI and HOMA-IR) and experienced the same improvement in glycemia (HbA1c) observed in the full cohort. Further studies are planned to quantify the efficacy, safety and durability of the hepatic and glycemic effects associated with DMR.

[1]Ferrannini, E. et al. Diabetes Care 2009
[2]Rajagopalan, H. et al. Diabetes care 2016