

Endoscopic duodenal mucosal resurfacing (DMR) improves metabolic measures including hepatic transaminase levels in patients with type 2 diabetes (T2D): Data from a first-in-human study

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BACKGROUND

- Bariatric surgeries that prevent nutrient contact with the duodenum improve measures of metabolism in type 2 diabetes (T2D), including indicators of fatty liver disease
- Duodenal mucosal resurfacing (DMR), a minimally invasive investigational endoscopic procedure involving thermal ablation of the duodenal mucosa, may offer similar metabolic benefit

AIM

- To evaluate the effect of DMR on metabolic parameters and assess procedural safety in patients with suboptimally controlled T2D (HbA1c > 7.5% on ≥ 1 anti-diabetic agent)

METHODS

- Using novel balloon catheters (Revita™ DMR System, Fractyl Laboratories, Waltham, MA, USA), we performed thermal ablation on varying lengths of duodenum in anesthetized patients with suboptimally controlled T2D
- Procedures were performed by trained endoscopists at a single medical center (Santiago, Chile)
- Procedural steps: Duodenal sizing → Lifting of mucosa using saline → Circumferential hydrothermal ablation of superficial mucosa to stimulate regeneration
- 2-week, low calorie, graduated diet for all patients post-procedure (liquids → soft → puree)
- No specific recommendation on post-procedure management of anti-diabetic medication

- 44 consecutive patients enrolled, 39 treated (Mean age: 53.3 y; mean BMI: 30.9 ± 3.5 kg/m²)
 - 28 received long-segment DMR (LS ablation length 9.3 cm); 11 received short segment DMR (SS: ablation length 3.4 cm)
- Excluded patients: 4 did not receive DMR (2 failed screening endoscopy, 1 tortuous anatomy, 1 had procedure stopped prior to ablation to prevent prolonged anesthesia), 1 excluded for anti-GAD+, indicative of type 1 diabetes, after index procedure

Efficacy

- More potent glycemic effect observed among LS cohort
 - No correlation between weight loss and glycemic improvement
- Robust reduction in hepatic transaminase levels also observed (Fig. 1-3)
- Changes in LS cohort metabolic parameters summarized in Table 1.

Safety & Tolerability

- Procedure well tolerated with minimal GI symptoms
- 3 duodenal stenoses resolved with endoscopic balloon dilation
- No GI bleeds, perforation, pancreatitis, malabsorption, or severe hypoglycemia
- Follow up endoscopy indicated full mucosal healing at 1 month

Table 1. Changes (mean ± SD) in metabolic parameters in long segment DMR cohort

	Screening	1 Month	3 Month	6 Month	Normal Range*
HbA1c - %	9.6 ± 1.4	7.9 ± 1.1	7.1 ± 0.9	8.2 ± 1.6	4.0 – 6.0
Weight - kg	86 ± 11	82 ± 11	83 ± 12	85 ± 11	--
ALT - IU/L	40 ± 23	32 ± 17	27 ± 14	27 ± 12	≤ 38
AST - IU/L	32 ± 17	27 ± 11	23 ± 8	22 ± 6	≤ 40

Abbreviations: HbA1c=glycated hemoglobin; ALT=alanine transaminase; AST=aspartate transaminase.

*Normal range based on ranges reported by the laboratory that processed the samples.

RESULTS

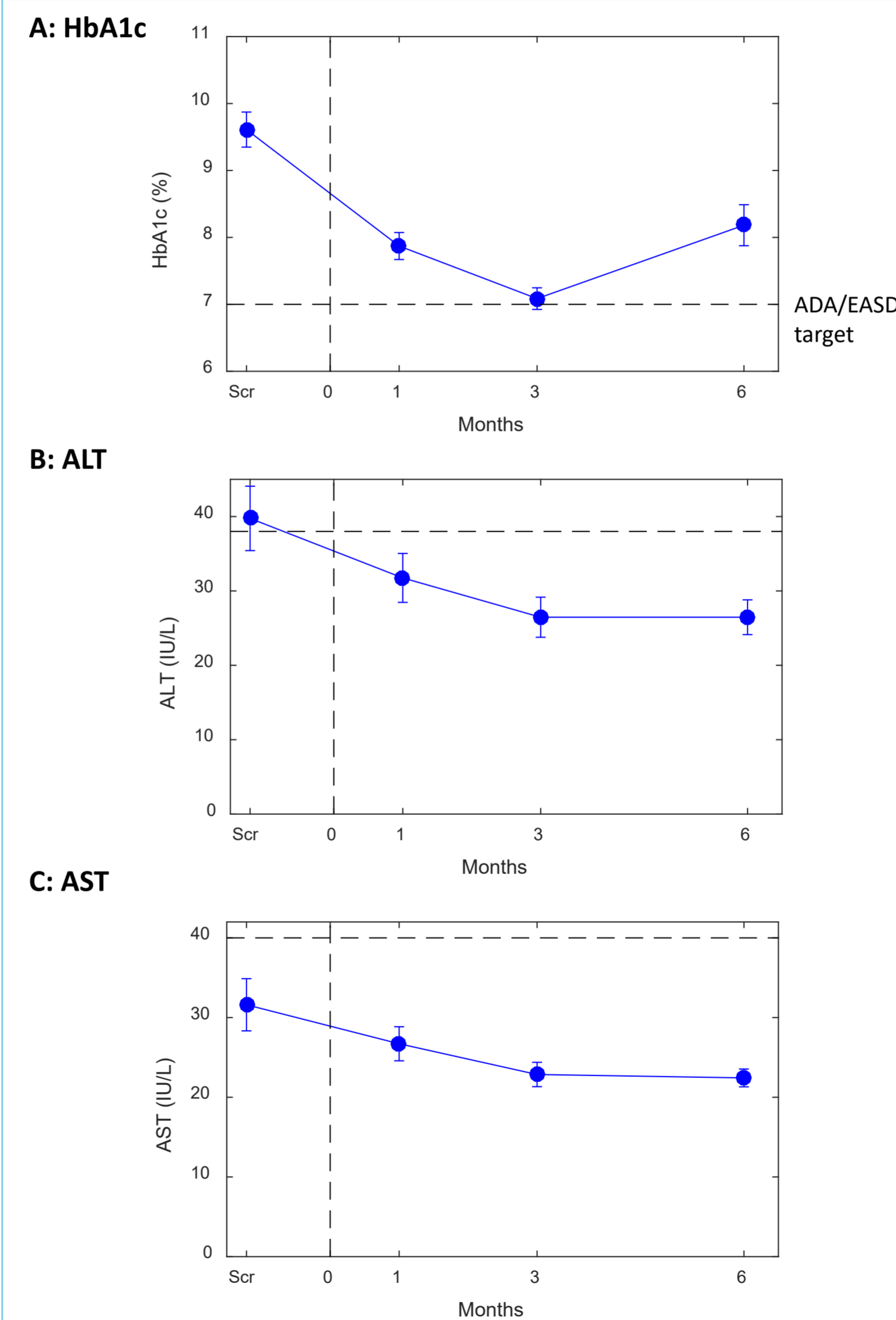


Figure 1. Glycemic improvement and reduction in hepatic transaminase levels after DMR. Average change in HbA1c (A), alanine transaminase (ALT) (B) and aspartate transaminase (AST) (C) in the long segment DMR cohort (N=28) is shown (mean ± SEM).

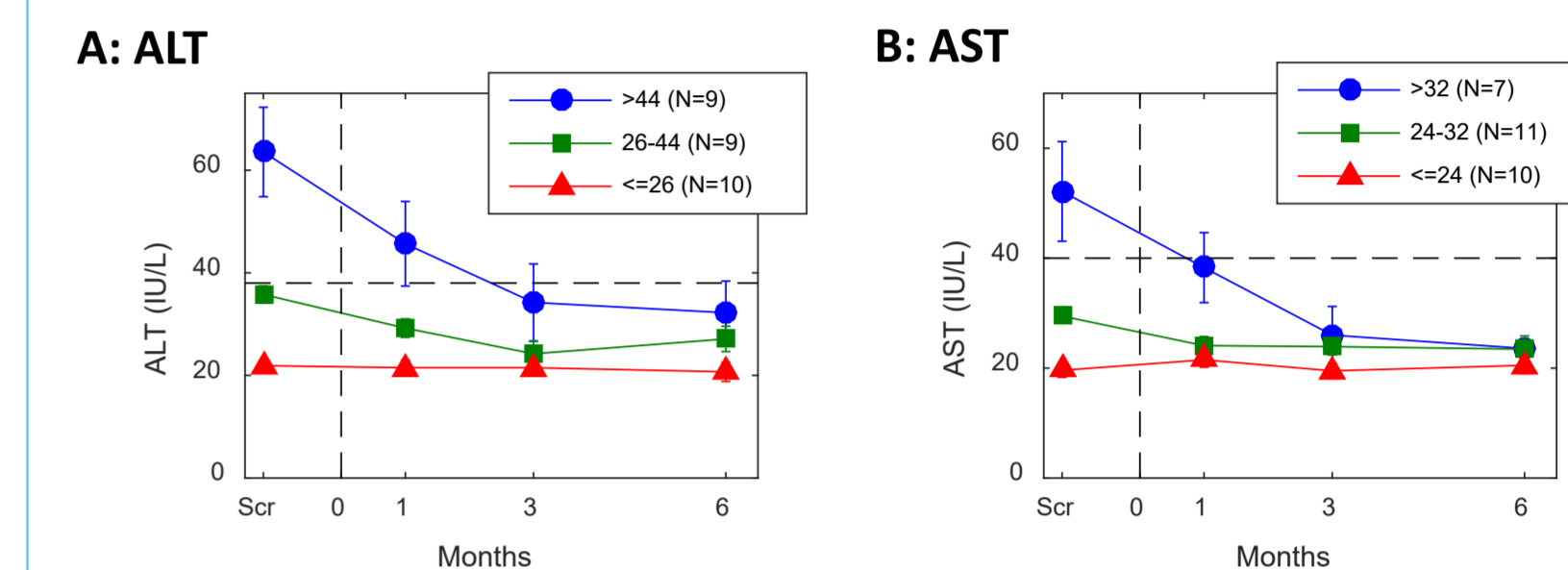


Figure 2. Tertiles for ALT (A) and AST (B) in long segment DMR cohort.

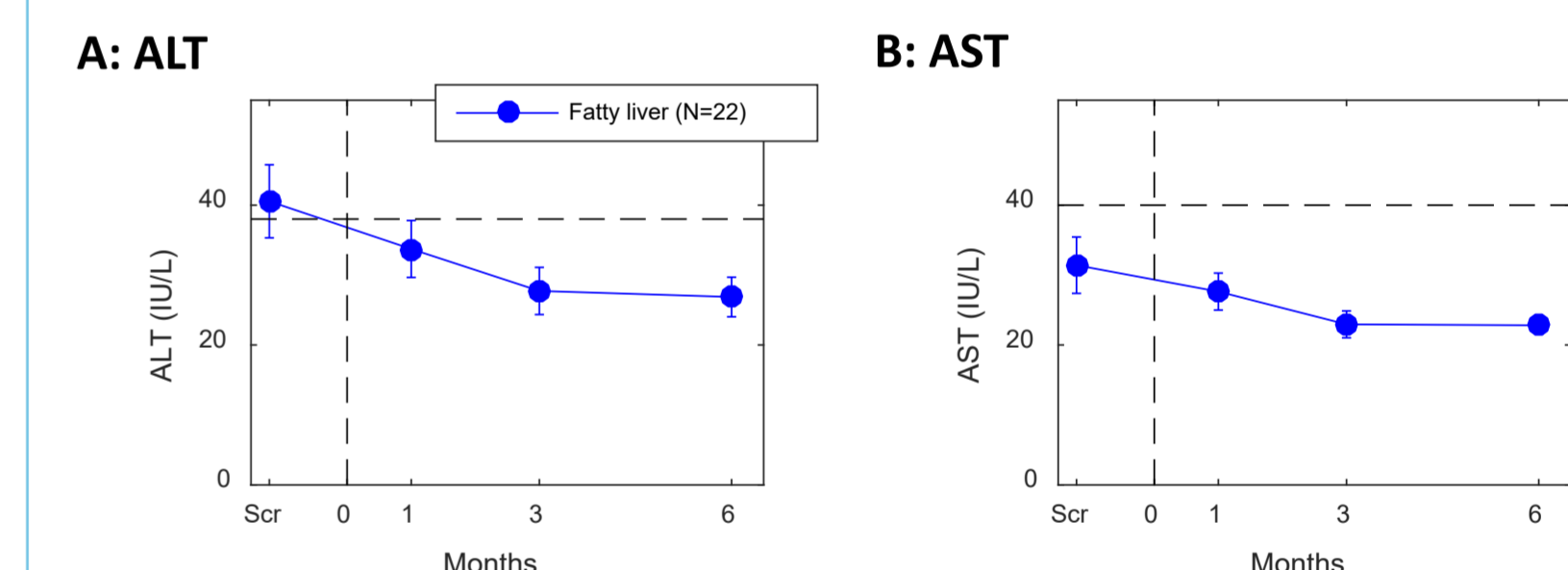


Figure 3. Changes in ALT (A) and AST (B) among long segment DMR patients with incidental finding of fatty liver on ultrasound.

CONCLUSIONS

- DMR improves metabolic control in T2D patients, including a robust and sustained lowering of hepatic transaminase levels, suggesting favorable end-organ hepatic effect
- DMR offers the potential for a single-point intervention that improves both glycemia and fatty liver
- Further study in patients with fatty liver disease is warranted

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