Obesity and metabolic disorders: role of therapeutic endoscopy

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European Endoscopy Training Centre - Rome

Institut de Chirurgie Guidée par l’Image de Strasbourg

Centre for Endoscopic Research Therapeutics and Training
Treatments for obesity

1-2% patients receive surgery

SOARD 2013, 9: 159-91

Courtesy of B.K. Abu Dayyeh
Treatments for obesity

1-2% patients receive surgery
SOARD 2013, 9: 159-91

Courtesy of B.K. Abu Dayyeh
Obesity Continuum

- Life-style
- Medications
- Endoscopic Procedures
- Surgical Procedures

Risk

Efficacy

Courtesy of B.K. Abu Dayyeh
Satiation, Satiety, and the Gut-Brain Axis
Gastric EBTs

Balloons

Endomina

ESG

Others
Small Bowel EBTs

- Duodenal Sleeves
- Gastroduodenojejunal Sleeves
- Duodenal Mucosal Resurfacing
Other EBTs

Aspiration Therapy

Full Sense Device

Self-assembling Magnets for Endoscopy
AspireAssist® System

Two modes: Drain & Lavage

Connector attaches to Skin-Port to initiate aspiration

Lanyard

Water reservoir for infusion

Stomach contents drain into lavatory

A-Tube

Skin-Port
Aspiration Therapy

✓ Indications: BMI 35 - 55 kg/m²

✓ Partial gastric content removal (30%) through a specific percutaneous gastrostomy

✓ Aspiration gastric contents 20 -30 minutes after meals

✓ Together with lifestyle modification it helps in weight loss and its long term managing.
US Clinical Study: Weight Loss Results

**Total Body Weight Loss**

![Graph showing total body weight loss for AspireAssist and Control groups.]

- AspireAssist: 14.2%
- Control: 4.9%

**Excess Weight Loss**

![Graph showing excess weight loss for AspireAssist and Control groups.]

- AspireAssist: 37.2%
- Control: 13.0%

REVITA Duodenal mucosal resurfacing
DMR Safety and Tolerability

- Total ~100 cases in early First-in-Human ("FIH") and ongoing multicenter Revita-1 study
- Post-procedure: favorable tolerability profile with minimal GI symptoms
- Three duodenal stenoses in early FIH experience → each successfully treated with single non-emergent balloon dilation and no later sequelae
- One small bowel perforation SAE in recent use
- No other device/procedure related SAEs No apparent hypoglycemic risk
- No evidence of malabsorption
- No late adverse events observed (60+ patients >12 months)
Revita-1 Trial Key Finding: Durable Lowering of HOMA-IR

- Durable reductions in insulin resistance (HOMA-IR) - highlights our mechanism of action
- Reductions seen in both glucose levels and insulin levels
- Weight loss independent of metabolic improvement
- No lifestyle intervention in the study
- Consistent with observations from duodenal bypass surgery
- 27 patients at study entry & 23 patients at 12 month follow up
Revita-1 Trial: Blood Glucose

- 12 month data shows durable improvements in blood sugar
- Baseline pancreatic function at baseline can be used to identify those patients most likely to respond, as seen with bariatric surgery²-⁴

DATA ON FILE; FRACTYL LABS

Revita-1 Trail: Lowering of Microalbuminuria and Hepatic Transaminase

- Reduction in abnormal microalbuminuria – a marker of heart attack and stroke risk¹
- Normalization of ALT - a marker of NAFLD-NASHr²
- Both valuable surrogate markers of insulin resistance and broader cardiometabolic risk

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¹ Diab Med Volume 20, Issue 4 April 2003 Pages 277–282
REVITA-2 Multi-Center Study

Two-Phased Multi-Center Study in Europe
- Phase 1: Non-randomized (completed)
- Phase 2: Double blind, sham control (completed)

Inclusion Criteria
- T2DM<10 years
- 28-75 years old
- BMI 24-40
- HbA1c 7.5 -10%
- At least one oral glucose lowering medication for at least 3 months
- No injectable medication

Endpoints
- Procedural safety
- HbA1c improvement at 6 months
- Long term follow up for safety
Endoscopic Sleeve Gastroplasty (ESG)
Surgical Gastric Sleeve
80% stomach removed to leave ‘sleeve’

Endoscopic Sleeve Gastroplasty (ESG)
Stomach left intact, stitched to form ‘sleeve’
Indications

- BMI > 40 kg/m²
- BMI > 35 kg/m² with diabetes not controlled by medical therapy
- BMI > 30 kg/m² with comorbidities

Wentworth JM et al. Lancet Diabetes Endocrinol 2014
Multidisciplinary approach
Apollo Overstitch (Apollo Endosurgery)

Endomina (Endotools)

Pose (USGI Medical) (?)
Endoscopic Sleeve Gastroplasty with Apollo Overstitch
Endoscopic sleeve gastroplasty
Endoscopic sleeve gastroplasty
Real life
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients N</th>
<th>Mean BMI</th>
<th>6 Mo TWL</th>
<th>12 Mo TWL</th>
<th>24 Mo TWL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharaiha RZ, 2015</td>
<td>25</td>
<td>38.5 ± 4.6</td>
<td>NA</td>
<td>18.7 ± 10.7</td>
<td>NA</td>
</tr>
<tr>
<td>Kumar N, 2015</td>
<td>126</td>
<td>36.2</td>
<td>NA</td>
<td>20 ± 3.8</td>
<td>NA</td>
</tr>
<tr>
<td>Lopez-Nava G, 2016</td>
<td>25</td>
<td>35.5</td>
<td>17.8 ± 7.5</td>
<td>18.7 ± 10.7</td>
<td>NA</td>
</tr>
<tr>
<td>Abu Dayyeh BK, 2017</td>
<td>10</td>
<td>45.2</td>
<td>33</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lopez-Nava G, 2017</td>
<td>248</td>
<td>37.8 ± 5.6</td>
<td>15.2</td>
<td>NA</td>
<td>18.6</td>
</tr>
<tr>
<td>Sartoretto A, 2018</td>
<td>112</td>
<td>37.9 ± 6.7</td>
<td>16.4 ± 10.7</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Reported complications 2%
Short-term outcomes of endoscopic sleeve gastroplasty in 1000 consecutive patients

Aayed Alqahtani¹*, MD, FRCSC, FACS; Abdullah Al-Darwish¹; Ahmed Elsayed Mahmoud¹, MD; Yara A. Alqahtani¹, MD; Mohamed Elahmedi¹, MBBS

¹Obesity Chair, Department of Surgery, College of Medicine, King Saud University, Riyadh, Saudi Arabia.

Gastrointest Endosc. 2018

Single-Surgeon Registry

N=1,000
BMI=33.3 ± 4.5kg/m²
Age=34.4 ± 9.5 years
% Excess Weight Loss after ESG

- 3 Months: 49.3%
- 6 Months: 64.3%
- 12 Months
- 18 Months

Change in Co-morbidities after ESG

- n=4
- n=14
- n=13
- n=18
- n=28

Readmissions after ESG

- Readmitted: 24 patients (2.4%)

- Perigastric collection: 4 (0.4%)
- Severe abdominal pain / nausea: 8 (0.8%)
- Fever: 5 (0.5%)
- Blood loss: 7 (0.7%)
- Conservative management: 5 (0.5%)
- Reversal of ESG: 3 (0.3%)
Endoscopic Sleeve Gastroplasty with ENDOMINA
Devices are designed to be compatible with most endoscopes and surgical tools

- Single use
- Assembled within the stomach to avoid orifices size limitation
- Adds triangulation to endoscope
- Universal (i.e. can be used with any endoscope and endoscopy tools), limiting upfront costs
- Easy to use (3h initial training, learning curve 5-7 patients)
- Deeper suture than any other device on the market (key for long lasting tissue apposition)
Restrictive surgery on the stomach

- Reduces size of the stomach
- Limits distensibility of the stomach
- 5-10 tissue approximations

Target impact (under clinical trial):

- Long lasting tissue approximation
- Volume restriction lower than surgery
- Improved quality of life vs surgery
- Highly reduced rate of complications
Real life
Clinical results confirm endoscopic techniques positioning between temporary treatment and surgery (>180 patients; 2 papers published)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Follow-up</th>
<th>Excess weight loss</th>
<th>SAE rate</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon</td>
<td>6 months</td>
<td>28 %</td>
<td>N/A</td>
<td>[1]</td>
</tr>
<tr>
<td>Gastric band</td>
<td>1 year</td>
<td>34 %</td>
<td>8 %</td>
<td>[2, 3]</td>
</tr>
<tr>
<td>Endoscopic Treatment (with endomina)</td>
<td>1 year</td>
<td>ASGE guideline is 25%</td>
<td>0 %</td>
<td>No serious adverse event so far (N&gt;180)</td>
</tr>
<tr>
<td>Sleeve gastrectomy</td>
<td>1 year</td>
<td>51 %</td>
<td>9 %</td>
<td>[2, 3]</td>
</tr>
<tr>
<td>Gastric bypass</td>
<td>1 year</td>
<td>63 %</td>
<td>12 %</td>
<td>[2, 3]</td>
</tr>
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Endoscopic gastric reduction with an endoluminal suturing device: a multicenter prospective trial with 1-year follow-up.

Huberty V, Machytka E, Boškoski I, Barea M, Costamagna G, Deviere J.

Abstract

BACKGROUND: Obesity is the pandemic disease of this century. Surgery is the only effective treatment but cannot be offered to every patient. Endoscopic sutured gastroplasty is a minimally invasive technique that may potentially fill the gap between surgery and behavioral therapy. In this study, we prospectively investigated the efficacy and safety of a novel suturing device.

METHODS: After a pre-bariatric multidisciplinary work-up, class 1 and 2 obese patients were included. Using a simple triangulation platform, transmural sutures with serosa-to-serosa apposition were performed in the gastric cavity. Patients were followed according to the same routines as those performed for bariatric procedures.

RESULTS: Between November 2015 and December 2016, 51 patients were included across three European Centers. Mean body mass index at baseline was 35.1kg/m² (SD 3.0). Excess weight loss and total body weight loss at 1 year were 29% (SD 28) and 7.4% (SD 7), respectively, for the whole cohort (45 patients). At follow-up gastroscopy, 88% of sutures were still in place (30 patients). No severe adverse events were observed.

CONCLUSIONS: Endoscopic sutured gastroplasty using this novel device is safe and achieved weight loss results in line with criteria expected for these endoluminal techniques. Further prospective studies vs. placebo or nutritional support are needed.

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PMID: 29906810 DOI: 10.1055/a-0630-1224
Up to date trials – Endomina v2 for Endoscopic Sutured Gastroplasty (ESG)

<table>
<thead>
<tr>
<th>T1 – Feasibility study</th>
<th>T2 – Multicentric efficacy study</th>
<th>T3 – Randomized Control Trial</th>
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<tr>
<td>▪ 12 patients between April and July 2015</td>
<td>▪ 51 patients in Brussels / Rome / Ostrava between February and December 2016</td>
<td>▪ 70 patients planned, starting September 2017, ongoing</td>
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<td>▪ BMI 33.5 kg/m² SD 2.6</td>
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<td>▪ 1 patient excluded</td>
<td>▪ 0 patient excluded</td>
<td>▪ 0 patient excluded so far</td>
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<tr>
<td>▪ 8 women / 4 men</td>
<td>▪ 24 women / 2 men</td>
<td>▪ Procedure versus diet</td>
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<td>▪ Light follow-up, similar to routine balloon follow-up</td>
<td>▪ Same follow-up</td>
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<tr>
<td>▪ GE visit : 1, 3, 6, 9 and 12 months</td>
<td></td>
<td>▪ 23 patients in control arm</td>
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<tr>
<td>▪ Dietician visit : 1, 3, 6, 9 and 12 months</td>
<td></td>
<td>▪ Control arm = diet for 6 months then crossover</td>
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- ClinicalTrials.gov NCT02534662
- ClinicalTrials.gov NCT02582229
- ClinicalTrials.gov NCT03255005
Endoscopic Sleeve Gastroplasty with POSE
POSE Procedure

A. 

B. 

C.
Mechanisms of action of POSE procedure

1. Invaginate the Fundus Completely
   - No reservoir for food – decreases functional capacity for meal
   - Speeds food to antral mill: physiologic fullness rapidly

2. Plical Antral Inlet
   - Dysmotility delays total gastric emptying time
   - Prolongs fullness, delays onset of hunger
New pattern for POSE procedure

Endoscopic Gastroplasty
Mechanisms of Action

2 mechanisms of action:

- Gastric volume reduction
- Delayed Gastric Emptying
(A) Changes in gastric emptying of solids before and 3 months after ESG.

(B) Percent gastric retention of a solid meal at 240 minutes before and 3 months after ESG.

(C) Gastric scintigraphy image at 240 minutes after a solid meal ingestion depicting retained solid meal in a small gastric fundus cap after ESG.

(D) Upper gastrointestinal series with a radiopaque contrast demonstrating a sleeve effect with a small fundus cap.
The future is bright!
Robotic Endoscopists

MASTER (Singapore)

ISIS/Stras (Strasbourg)

ENDOSAMURAI (Tokyo)
## Results and Follow-up (54 pts)

<table>
<thead>
<tr>
<th></th>
<th>WL (Kg)</th>
<th>%EWL</th>
<th>%TBWL</th>
<th>BAROS</th>
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<tbody>
<tr>
<td><strong>Follow-up 1 mo</strong></td>
<td>9.2 (range -6 – 17)</td>
<td>17.9 (range -9 – 30.4)</td>
<td>8.1 (range -5 – 12.8)</td>
<td>2.6 (range -2 – 5.25)</td>
</tr>
<tr>
<td><strong>Follow-up 3 mo</strong></td>
<td>15.9 (range 5 – 27)</td>
<td>30.1 (range 7.5 – 49.1)</td>
<td>13.7 (range 3.8 – 21.4)</td>
<td>3.9 (range 0.5 – 6.5)</td>
</tr>
<tr>
<td><strong>Follow-up 6 mo</strong></td>
<td>18.4 (range -5 – 37)</td>
<td>33.8 (range -7 – 83.7)</td>
<td>15.5 (range -4 – 32.5)</td>
<td>3.9 (range -2 – 9)</td>
</tr>
</tbody>
</table>

From January 2018: 71 ESG
Multidisciplinary approach
40 pts (2017 pre-MA) vs. 54 pts (2018 post-MA)

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<tr>
<td></td>
<td>pre-MA</td>
<td>post-MA</td>
<td>pre-MA</td>
<td>post-MA</td>
</tr>
<tr>
<td>1 month follow-up</td>
<td>5.7</td>
<td>10.7</td>
<td>11.5</td>
<td>20.5</td>
</tr>
<tr>
<td>3 months follow-up</td>
<td>12.1</td>
<td>18.1</td>
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<td>33.9</td>
</tr>
<tr>
<td>6 months follow-up</td>
<td>14.1</td>
<td>28</td>
<td>26.5</td>
<td>47.5</td>
</tr>
</tbody>
</table>

WL = Weight Loss; EWL = Excess Weight Loss (%EWL); TBWL = Total Body Weight Loss; na = non available
BAROS = Bariatric Analysis and Reporting Outcome System.
Bariatric Endoscopy

intervention

Follow-up

MA

Family

Endoscopy

Surgeon

Psychiatrist

Dietitian

Family

Patient

Endocrinologist

Gastroenterologist
Maintainence

Graph showing weight over time with markers at T0, 6mo, 12mo, 1y, and 2y.
 Maintainence

Weight

T0  6mo  12mo  1y  2y

---

62
D.R. F, 54 yrs

- In 2016 had ESG with Apollo Overstich (BMI 39) with hypertension

- All follow-up visits OK, lost 35 Kg, is following diet and physical activity, patient is HAPPY

- November 2018 M.C. has epigastric pain and «burning», no other symptoms, OK with PPIs, still EGD is planned
So ????

- ESG was successful!
- Patient changed his lifestyle!
Conclusions

- Endoscopy plays a pivotal role in the multidisciplinary management of morbid obesity

- New bariatric endoscopic technologies and techniques mimicking surgery are expected

- Combination of techniques and “hybrid” approaches will be developed
Obesity Continuum

1

Risk

Life-style

Medications

Endoscopic Procedures

Surgical Procedures

Courtesy of B.K. Abu Dayyeh
Revita-1 Trial Key Finding: 
Durable Lowering of HOMA-IR

- Durable reductions in insulin resistance (HOMA-IR) - highlights our mechanism of action
- Reductions seen in both glucose levels and insulin levels
- Weight loss independent of metabolic improvement
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- Two-Phased Multi-Center Study in Europe
  - Phase 1: Non-randomized (completed)
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- Inclusion Criteria
  - T2DM<10 years
  - 28-75 years old
  - BMI 24-40
  - HbA1c 7.5 -10%
  - At least one oral glucose lowering medication for at least 3 months
  - No injectable medication

- Endpoints
  - Procedural safety
  - HbA1c improvement at 6 months
  - Long term follow up for safety

Phase 2 Patient Flow

1. Recruitment
2. 4 week run-in
3. Sham
4. Revita DMR
5. Unblinding & Sham Cross-Over
6. 6 month follow up
7. 3 year follow up
8. Long term follow up
Multidisciplinary approach
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- 12 patients between April and July 2015
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intervention

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ENDOLIVE ROMA

SAVE THE DATE
8-9-10 MAY 2019

INTERNATIONAL CONFERENCE ON:
Live demonstration workshop on GI ENDOSCOPY