# Endoscopic sutured gastroplasty with endomina in diabetic, obese patients * prospective interventional study

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The primary objective of this study is to evaluate the efficacy of endoscopic sutured gastroplasty (ESG) with the endomina device (EndoTools Therapeutics S.A.) in combination with optimal lifestyle measures on glycemic control, in obese patients...

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| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Diabetic complications |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON51445

**Source**
ToetsingOnline

**Brief title**
GATE-study

### Condition

- Diabetic complications
- Gastrointestinal therapeutic procedures

**Synonym**
Diabetes

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Endotool Therapeutics,Endotools

Therapeutics

## Intervention

**Keyword:** Bariatrics, Diabetes, Endoscopy, Obesity

## Outcome measures

### Primary outcome

The primary endpoint is a reduction of HbA1C of at least 0.7% one year after ESG.

### Secondary outcome

Safety:

1. Rate of Serious Adverse Events (SAE) and Serious Adverse Device Effects (SADE) during and post procedure

2. Adverse events up to 1-month follow-up for subjects undergoing the procedure under procedural sedation with propofol

3. Cardiovascular events (stroke/TIA, myocardial infarction, admission for heart failure) and all-cause mortality

DM2:

4. Reduction of HbA1C at 14 days, 1 month, 3, 6, and 9 months after ESG

5. Reduction in fasting plasma glucose levels at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

6. Proportion of subjects with reduced number and/or reduced dose(s) of diabetes medication at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

Weight Loss:

7. Proportion of subjects with mean % excess weight loss (EWL) of more than 25% at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

8. Proportion of subjects with mean % total body weight loss (TBWL) of more than 5% at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

Comorbidity:

9. Decrease in blood pressure expressed in mmHg at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

Quality of Life:

10. EQ-5D-5L at 14 days, 1 month, 3, 6 and 12 months after ESG

11. Diabetes Treatment Satisfaction Questionnaire at 14 days, 1 month, 3, 6, 9 and 12 months after ESG

12. Quality adjusted life years (QALYs)

Costs:

13. Costs and cost-effectiveness. Costs including health care recourses used (including intervention including endomina device and TAPES, hospital admissions, visits to specialists and GP, emergency room visits, medications used), costs for insulin therapy (including medication, administration, glycemia measurement material)

# Study description

**Background summary**

Diabetes mellitus is a chronic disease often associated with long-term macrovascular and microvascular complications (e.g., heart disease, stroke and renal failure) and decreased life expectancy. (2) Approximately 70% of patients with type 2 diabetes mellitus (DM2) are overweight or obese. (3) Findings from a national cohort of US adults showed that the risk for DM2 increases with 4.5%, for every kilogram increase in weight. (4) Besides DM2, obesity is associated with among others impaired quality of life, cardiovascular diseases, arthrosis, cancer and reduced life expectancy. (5)

Weight loss benefits several aspects of DM2, such as improved glycemic control, increased insulin sensitivity and reduced fasting insulin. This results in a reduction in glycated hemoglobin. In addition, coexisting disorders such as hypertension and dyslipidemia improve as well. (2)
Interventions for weight loss in patients with DM2 include diet, exercise, but also pharmacotherapy and bariatric surgery. Current standard pharmacotherapeutic treatment for patients with DM2 in the Netherlands starts with metformin, followed by insulin. However, in patients with DM2 and obesity (BMI > 30 kg/m²), it is recommended to add a glucagon-like peptide 1 (GLP1) agonist (6). These incretin hormones interact with the GLP1 receptor in the pancreas to stimulate insulin production, delay gastric emptying and decrease hunger feelings in the nucleus arcuate of the hypothalamus. (7, 8)
Bariatric surgery is indicated at a BMI > 35 kg/m², in combination with other comorbidities such as DM2, hypertension, sleep apnea. (6) It is associated with better glycemic control and more weight reduction, compared to intensive medical treatment alone, with more than 90% of patients in the surgical group having glycemic control without using insulin. (9) However, bariatric surgery is associated with perioperative and long-term complications, (10) and 6% of patients require revision surgery. (11)

For patients with not adequately controlled DM2, with a BMI of < 35 kg/m², the therapeutic gap could be filled by one of the currently available endoscopic therapies. These therapies have a much less-invasive feature, without the significant risks associated with surgery.
Endoscopic therapies can be categorized in three different techniques: 1) insert a (temporarily) space-occupying device (balloon) in the stomach aiming to reduce the stomach*s capacity, 2) redirect calories away from the stomach by aspiration therapy or 3) decrease the stomach size by endoscopic suturing. (12, 13) This last technique can be performed with the endomina device (EndoTools Therapeutics S.A.).

**Study objective**

The primary objective of this study is to evaluate the efficacy of endoscopic sutured gastroplasty (ESG) with the endomina device (EndoTools Therapeutics S.A.) in combination with optimal lifestyle measures on glycemic control, in obese patients with DM2 under insulin therapy.

Secondary objectives are:
- To evaluate the effect of ESG on reduction in diabetes medication at 14 days, 1 month, and 3, 6, 9 and 12 months after ESG
- To evaluate the efficacy of ESG on weight loss at 14 days, 1 month, and 3, 6, 9 and 12 months after ESG
- To evaluate the safety of ESG with the endomina device under procedural sedation, based on rate of (Serious) Adverse Events ((S)AE) and (Serious) Adverse Device Effects ((S)ADE) during, and post-procedure.
- To evaluate the effect of ESG on blood pressure post procedure, at 14 days, 1

month, and 3, 6, 9 and 12 months after ESG, in patients with hypertension at inclusion
- To evaluate quality of life at inclusion, at 14 days, 1 month, and 3, 6, 9 and 12 months after ESG, with the quality-of-life questionnaires EQ-5D-5L and Diabetes Treatment Satisfaction Questionnaire as well as Quality adjusted life years.

**Study design**

Type of study
This study is designed as a prospective interventional study.

Summary of study design
Patients will be screened for eligibility in 2 centers (Radboudumc Nijmegen, Rijnstate Arnhem). All inclusions and interventions will be performed in Rijnstate.
Patients from the outpatient population of the Internal medicine department in Rijnstate and Radboudumc, known with DM2 will be screened for eligibility. Patients diagnosed with DM2 developed less than 10 years ago, with a BMI between 30 and 40 kg/m² and treated with insulin are eligible for inclusion. During an regular outpatient visit at the endocrinologist, the study will shortly be explained by their attending physician and an information letter will be handed. If the patient is interested, the attending physician will inform one of the members of the study team about the possible study participant. The coordinating investigator will call the patient to five an extensive explanation of the study. Patients will receive 7 days to consider participation. Furthermore, patients will undergo an identical screening, conform standard of care of patients receiving a surgical gastric sleeve.
A subject will be considered *enrolled* if he/she has passed all screening criteria, signed the informed consent form and has undergone the procedure.

Subjects will be admitted to the Rijnstate on the day before the procedure. Baseline demographics and measures, including EQ-5D-5L, Diabetes Treatment Satisfaction Questionnaire, time since DM II diagnosis, blood pressure, weight, HbA1c, fasting glucose levels, anti-diabetic medication will be measured before the procedure. After the procedure, subjects are kept on a liquid diet for 3 days and mashed food for the next 7 days.

Follow-up
Afterwards, clinical follow-up visits at the outpatient department of the internal medicine in Rijnstate will be scheduled at 14 days, 1 month, and at 3, 6, 9 and 12 months after the index procedure for assessment of the primary and secondary endpoints and safety analysis. The EQ-5D-5L, Diabetes Treatment Satisfaction Questionnaire, blood pressure, weight, HbA1c, anti-diabetic medication and fasting glucose levels will be measured again, as well as potential vitamin deficiencies will be evaluated. Also, safety endpoints will be checked with subjects, as well as in medical records.

Time schedule
The study will start during the 4th quartile of 2022, and will take approximately 30 months in total. The first 24 months will consist of inclusion and follow-up of subjects. The last 6 months will consist of finalizing follow-up and analysis of the data.

## Intervention

The endomina (sponsor EndoTools Therapeutics, Gosselies, Belgium) is a device that can be attached to an endoscope and allows remote actuation of the device during a peroral intervention. It offers the possibilities of making transoral full thickness tissue apposition and may allow performing, via a transoral route, large plications with tight serosa to serosa apposition.
It starts with an upper GI endoscopy, followed by introducing two guidewires into the duodenum. The endomina system can be introduced over these guidewires into the stomach. Then 2 plicatures will be made on opposite sites of the stomach wall. This procedure will be repeated from antrum to fundus, along the great curvature.
Suturing will be performed with TAPES, a single use suture.
In addition to the endomina device any other required endoscopic accessories can be used during the procedure.

## Study burden and risks

A case report published in 2018 showed 2 patients that underwent an endoscopic suture gastroplasty with the endomina. Both patients had a BMI > 35 kg/m². After 3 months, both patients had relevant weight loss of 7kg and 14kg respectively. No long-term follow-up is available. (18)
Another safety and feasibility study showed a mean percentage of excess weight loss of 9% after 1 month, and 41% after 6 months and no adverse events were observed. (1)
A multicenter prospective trial in 45 obese patients showed a 29% excess weight loss, and 7% total weight loss after an endoscopic suture gastroplasty with the endomina. No adverse events occurred during follow-up. (14)
A randomised trial presented the short-term safeness and effectiveness of the endomina system on weight loss in 71 patients with a BMI of 30-40 kg/m². This study showed a 25% better excess weight loss after 6 months in patients that underwent a combination of lifestyle modification and endoscopic suture gastroplasty with the endomina, compared with lifestyle modification alone. This also led to a substantial improvement in quality of life. No procedure-related or device-related severe adverse events were seen. (19)

Previous studies have shown small periprocedural adverse events, consisting of small self-contained bleedings, which all stopped when the knot was tightened. For suturing, a needle is attached to a suture and a pre-tied knot. First, the needle is pushed through 2 layers of the gastric wall and the suture and

pre-tied knot are released. Then a second plicature is made on the other side of the stomach. Afterwards, the pre-tied knot is tightened. The small bleedings occurred only within these 2 steps. (14)
Adverse events shortly after the procedure were transient abdominal cramps (79.4%), transient nausea (66.2%), or vomiting (66.2%). In 71 patients, 1 aspiration pneumonia occurred at extubation, which did not require longer hospitalization or antibiotic treatment. (19)
No severe adverse events were observed, no surgical intervention or readmission were needed, and no mortality occurred. (1, 19)

Procedural sedation has a low risk of adverse events. In a prospective observational study, almost 12.000 patients were included who received procedural sedation in the Netherlands. Minimal adverse events (e.g., vomiting, muscle rigidity, or agitation) were seen in 1517 (12.8%), minor adverse events (e.g., oxygen desaturation 75-90% for less than 60s, airway obstruction, or hypotension) in 113 (1.0%), and major adverse events (e.g., oxygen desaturation <75% or 75-90% for more than 60s, aspiration, or cardiac arrest) in 80 patients (0.7%). Five unfavourable patient relevant outcomes (0.07%) occurred within this study. This included admission to ICU, cardiac arrest and asystole secondary to pneumodilation of the oesophagus. (20) Another retrospective cohort included 2937 procedures, in which no catastrophic events and a low rate of severe events (1.09%) occurred. The most common severe events were severe desaturation (0.6%) and hypertension (0.2%). Moreover, the most common events with potential adverse health consequences were significant desaturation (1.6%) and significant hypotension (8.8%). Nonetheless, no patient suffered lasting health consequences. (21)

# Contacts

**Public**
Selecteer

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**Scientific**
Selecteer

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

- Age between 18-65 years;
- Diagnosed with DM2
o since at least 1 year
o but diagnosed no longer than 10 years ago
o currently under stable dose of insulin for at least 6 months
- HbA1c level of 7.0-11.0% (53-75 mmol/mol)
- BMI of 30-40 kg/m² with or without hypertension

## Exclusion criteria

- Achalasia and any other esophageal motility disorders
- Severe esophagitis (grade C or D)
- Gastro-duodenal ulcer
- GI stenosis or obstruction
- Any history of esophageal or gastric surgery
- Heart diseases: unstable angina, myocardial infarction within the past year, or heart disease classified within the New York Heart Association*s Class III or IV functional capacity
- Uncontrolled hypertension (systolic blood pressure >180 mm Hg and/or diastolic blood pressure >100 mm Hg under medication) during last 3 months;
- Severe renal, hepatic, pulmonary disease or cancer (cancer in the past 5 years, except basal cell carcinoma
- Pregnancy, breast feeding or desire for pregnancy in the coming 12 months
- Any previous bariatric surgery, or endoscopic obesity-related intervention (including POSE, OverStitch, etc.). Intragastric balloon removed within the last 6 months
- Planned gastric surgery 60 days post intervention
- Anticoagulant therapy that cannot be temporarily stopped at the time of the

procedure.

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 40 |
| Type: | Anticipated |

# Ethics review

Not approved

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|---|---|
| Date: | 19-12-2022 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL82297.091.22 |