


BMJ Open Nissen-Sleeve procedure versus laparoscopic Roux-en-Y gastric bypass in patients with morbid obesity and gastro-oesophageal reflux disease: protocol for a non-inferiority randomised trial (GINSBY)

Judith W H 't Hart ^{1,2}, Bo J Noordman,¹ Laser U Biter,¹ Ivonne Leeuwenburgh,³ Martin Dunkelgrun,¹ Jan A Apers¹

To cite: 't Hart JWH, Noordman BJ, Biter LU, *et al*. Nissen-Sleeve procedure versus laparoscopic Roux-en-Y gastric bypass in patients with morbid obesity and gastro-oesophageal reflux disease: protocol for a non-inferiority randomised trial (GINSBY). *BMJ Open* 2022;**12**:e061499. doi:10.1136/bmjopen-2022-061499

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-061499>).

Received 27 January 2022
Accepted 24 May 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Surgery, Franciscus Gasthuis en Vlietland, Rotterdam, The Netherlands

²Surgery, Erasmus MC, Rotterdam, The Netherlands

³Gastroenterology, Franciscus Gasthuis en Vlietland, Rotterdam, The Netherlands

Correspondence to

Judith W H 't Hart;
j.hart@franciscus.nl

ABSTRACT

Introduction Laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) are the most frequently performed procedures in bariatric surgery. In patients with morbid obesity and gastro-oesophageal reflux disease (GORD), LRYGB is the most accepted procedure. For patients with a contraindication for LRYGB or a strong preference for LSG, the Nissen-Sleeve procedure may be a viable new option. The aim of this study is to compare effectiveness of Nissen-Sleeve with LRYGB.

Method and analysis This is a single-centre, phase III, parallel-group randomised controlled trial in a high-volume bariatric centre in the Netherlands. A total of 88 patients with morbid obesity and GORD will be randomised to evaluate non-inferiority of Nissen-Sleeve versus LRYGB (non-inferiority margin 15%, power 80%, one-sided α 0.025, 9% drop out). Patients with morbid obesity aged 18 years and older with GORD according to the Montreal definition will be included after obtaining informed consent. Exclusion criteria are achalasia, neoplastic abnormalities diagnosed during endoscopy, super obesity (body mass index ≥ 50 kg/m²), Crohn's disease and medical history of major abdominal surgery. After randomisation, all patients will undergo an upper gastrointestinal endoscopy. Patients in the Nissen-Sleeve arm will undergo a timed barium oesophagram to exclude oesophageal motility disorders. Patients will complete six questionnaires at baseline and every year until 5 years of follow-up. At day 1 postoperative, patients in the Nissen-Sleeve arm will undergo a swallow X-ray to confirm passage. At 1 year, all patients will undergo another endoscopy. The primary outcome is GORD status. Absence of GORD is defined as < 8 points on the GORD questionnaire. Secondary outcome measures are long-term GORD improvement; failure rate of procedure; health-related quality of life; weight loss; proton pump inhibitor use; postoperative complications < 30 days and > 30 days; length of hospital stay; duration of primary surgery; effect on comorbidities; presence and grade of oesophagitis (grade A–D) and/or presence of Barrett's oesophagus and cost-effectiveness.

Ethics and dissemination The protocol was approved by the Medical Research Ethics Committees United (MEC-U),

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Patients in the intervention arm might have a direct benefit since both morbid obesity and gastro-oesophageal reflux disease (GORD) will be treated.
- ⇒ Long-term follow-up of 5 years will provide information on GORD status and quality of life of Nissen-Sleeve compared with laparoscopic Roux-en-Y gastric bypass.
- ⇒ Patients undergo an extra upper gastrointestinal endoscopy 1 year postoperatively to monitor oesophagitis or Barrett's oesophagus.
- ⇒ Patients and the surgical team will not be blinded for safety reasons as both procedures have different aftercare.
- ⇒ The non-invasive and globally well-accepted Montreal consensus will be used for inclusion to define GORD instead of a manometry.

Nieuwegein, on 15 September 2021. Written informed consent will be obtained for all participants in the study. The study results will be disseminated through peer-reviewed publications and conference presentations.

Trial registration number NL9789; The Netherlands Trial Registry.

INTRODUCTION

The incidence of morbid obesity is increasing rapidly and herewith the incidence of bariatric surgery.¹ Laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) are the most frequently performed procedures in bariatric surgery.² Unfortunately, LSG can worsen pre-existing gastro-oesophageal reflux disease (GORD) or can cause new onset GORD.^{3–6} GORD has negative impact on the health-related quality of life (HrQoL) and often leads to proton pump inhibitor (PPI) dependency.⁷

Moreover, GORD can cause Barrett's oesophagus, which is a risk factor for oesophageal adenocarcinoma.⁸

LRYGB is the most accepted procedure for patients with morbid obesity and GORD. In addition to inducing weight loss, LRYGB can improve GORD by bypassing corpus and fundus, which contain most acid-producing parietal cells.⁹ Nevertheless, 11% of all patients undergoing LRYGB develop GORD.⁴ Furthermore, LRYGB is contraindicated in a small portion of patients. Contraindications for LRYGB include inflammatory bowel disease, intestinal adhesions due to previous surgery or other abnormalities of the abdomen (such as a large ventral hernia of the abdominal wall). In addition, some patients do not want to undergo LRYGB because of the changes in anatomy and risk of long-term complications, such as internal herniation, vitamin deficiencies or chronic abdominal pain and diarrhoea.^{10 11}

The Nissen-Sleeve (N-Sleeve) is a novel surgical technique first described by Nocca *et al* for patients with morbid obesity and GORD.¹² The N-sleeve is a combination of an antireflux procedure (Nissen fundoplication) and LSG. So far, the N-Sleeve has only been studied in small pilot studies. Results of 25 patients with morbid obesity and GORD who underwent N-Sleeve suggest that N-sleeve is effective with 88% of patients no longer experiencing GORD, and an excess weight loss (EWL) of 58% after 1 year. These results also suggested that N-sleeve is safe with a complication rate of only 4%.¹² In another cohort study, 70 patients who underwent N-Sleeve showed a 91% recovery rate of GORD, an EWL of 69% and a complication rate of only 10%.¹³ These results suggest that GORD improvement, weight loss after N-Sleeve is similar to LRYGB, complication rates after N-sleeve are comparable to LSG (8%) and LRYGB (17%).^{14 15} However, there are no randomised controlled trials and no long follow-up (FU) to validate these results. The aim of the current randomised controlled trial is to compare GORD status in patients with morbid obesity and GORD status after N-Sleeve versus LRYGB.

Methods and analysis

This is a single centre, phase III, parallel-group randomised controlled non-inferiority trial in a high-volume bariatric centre in the Netherlands. We will compare outcomes of N-Sleeve versus LRYGB in patients with morbid obesity and GORD. Patients will be randomised with an allocation ratio of 1:1. A summary of the trial registration information is found in [table 1](#).

Eligibility and exclusion criteria

Patients will be asked to participate in this study if they have GORD according to the Montreal definition, are ≥ 18 years and found suitable for bariatric surgery according to the national and international guidelines ([table 2](#)).^{16–18} To be eligible subjects must meet the following inclusion criteria: primary bariatric procedure, good knowledge of Dutch or English and written informed consent. Potential subjects will be excluded from participation

Table 1 Trial registration information

Data category	Information
Primary registry and trial Identifying number	Netherlands Trial Register: NL9789
Date of registration in primary registry	5 October 2021
Secondary identifying numbers	Medical Research Ethics Committee united: R21.040; The Central Committee on Research Involving Human Subjects: NL77783.100.21; Franciscus Gasthuis & Vlietland (CastorSMS): 2021–102
Sources of monetary and material support	Monetary support: Stichting BOF (Foundation for the promotion of research Franciscus).
Primary sponsor	Franciscus Gasthuis & Vlietland
Secondary sponsor(s)	NA
Contact for public queries	J.W.H. 't Hart, MD, j.hart@franciscus.nl
Contact for scientific queries	J.W.H. 't Hart, MD, j.hart@franciscus.nl
Public title	N-Sleeve vs Roux-en-Y gastric bypass in patients with morbid obesity and gastroesophageal reflux disease
Scientific title	Nissen-sleeve procedure vs laparoscopic Roux-en-Y gastric bypass in patients with morbid obesity and gastroesophageal reflux disease: protocol for a non-inferiority randomised trial (GINSBY)
Countries of recruitment	The Netherlands
Health condition(s) or problem(s) studied	Morbid obesity and GORD
Intervention(s)	N-Sleeve
Inclusion and exclusion criteria	<p>Patients with morbid obesity and GORD</p> <p>Inclusion criteria: ≥ 18 years, primary bariatric surgery, GORD diagnosed by the Montreal definition</p> <p>Exclusion criteria: Pregnancy, body mass index (BMI) ≥ 50 kg/m², achalasia, Crohn's disease, malignancy or other abnormalities (such as low- and high-grade dysplasia) at endoscopy, and a medical history of major abdominal surgery.</p>
Study type	<p>Interventional</p> <p>Allocation: randomised, parallel assignment, two arms, open label</p> <p>Primary purpose: to cure</p> <p>Phase III</p>

Continued

Table 1 Continued

Data category	Information
Date of first enrolment	September 2022
Sample size	88, 44 per arm
Recruitment status	Planning to recruit
Primary outcomes	GORD status after N-Sleeve vs LRYGB, improvement defined as <8 points on the GORD-Q questionnaire
Secondary outcomes	Long-term GORD improvement, technical failure rate; Health related quality of life; weight loss; PPI use; complications rates <30 days and >30 days; length of hospital stay; duration of primary surgery; comorbidity; presence and grade of oesophagitis and/ or Barrett's oesophagus, cost-effectiveness
Ethics review	Approved by the Medical Research Ethics Committee (in Dutch: Medisch Ethische Toetsingscommissie (METC)) Medical Research Ethics Committees United (MEC-U), Nieuwegein, the Netherlands
GORD, gastro-oesophageal reflux disease; GORD-Q, gastro-oesophageal reflux disease questionnaire; LRYGB, laparoscopic Roux-en-Y gastric bypass; NA, not applicable; N-Sleeve, Nissen-Sleeve; PPI, proton pump inhibitor.	

when meeting any of the following criteria: pregnancy, body mass index $\geq 50 \text{ kg/m}^2$, achalasia, Crohn's disease, malignancy or other abnormalities at endoscopy making bariatric surgery inadvisable (such as low-grade and high-grade dysplasia) and a medical history of major abdominal surgery such as laparotomy.

Recruitment

In the Franciscus Gasthuis & Vlietland hospital, roughly 1000 bariatric procedures are performed annually. Approximately, 30% of these patients have GORD at time of diagnosis and are eligible for inclusion. An inclusion rate of one out of three patients and a drop out of 9% are expected. Therefore, we estimate to include 88

patients within 12–24 months (see Sample size section). All eligible patients will receive written information attached with the invitation letter for the appointment at the outpatient clinic. The coordinating researcher will inform the patient about the study. Patients who are willing to participate will be asked to provide written informed consent (see online supplemental appendix 1). Patients will have 1 week to consider their decision. We plan to start recruitment in September 2022 and close recruitment in September 2024.

Treatment allocation and blinding

After obtaining informed consent at the outpatient clinic, patients will be randomised using computer Variable Block Randomisation software by Ciwit B.V. (Castor EDC). Patients will either undergo N-Sleeve or LRYGB (figure 1). The surgical team cannot be blinded. Patients cannot be blinded either, as different multivitamin supplements are necessary after the procedures and both procedures are associated with different postoperative complications.

Interventions

Patients will complete the GORD questionnaire (GORD-Q), Research and Development-36 questionnaire (RAND-36), Bariatric Analysis and Reporting Outcome System (BAROS), EuroQol 5 Dimensions (EQ-5D), iMTA Medical Consumption Questionnaire and iMTA Productivity Cost Questionnaire at baseline and at 1, 2, 3, 4 and 5 years FU.^{19–24} According to international guidelines, an upper gastrointestinal (GI) endoscopy will be performed preoperatively, to diagnose oesophagitis (grade A–D), Barrett's oesophagus or other abnormalities.²⁵ Additionally, patients in the N-sleeve arm will undergo a preoperative timed barium oesophagram to exclude important oesophageal motility disorders. Patients who smoke will be strongly encouraged to quit smoking.

Two dedicated surgeons will perform the procedures. The intervention group will undergo the N-Sleeve procedure as described by Nocca *et al* (figure 2). Patient positioning, anaesthesia and trocar placement are similar to LSG surgery, as previously described.²⁶ If present, a hiatal hernia will be dissected and reduced. An extension of

Table 2 Montreal definition

GORD was defined as a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications.			
Oesophageal syndromes		Extra-oesophageal syndromes	
Symptomatic syndromes	Syndromes with oesophageal injury	Established associations	Proposed associations
1. Typical reflux syndrome 2. Reflux chest pain syndrome	1. Reflux esophagitis 2. Reflux stricture 3. Barrett's oesophagus 4. Oesophageal Adenocarcinoma	1. Reflux esophagitis 2. Reflux stricture 3. Barrett's oesophagus 4. Oesophageal Adenocarcinoma	1. Pharyngitis 2. Sinusitis 3. Idiopathic pulmonary fibrosis 4. Recurrent Otitis Media
GORD, gastro-oesophageal reflux disease.			

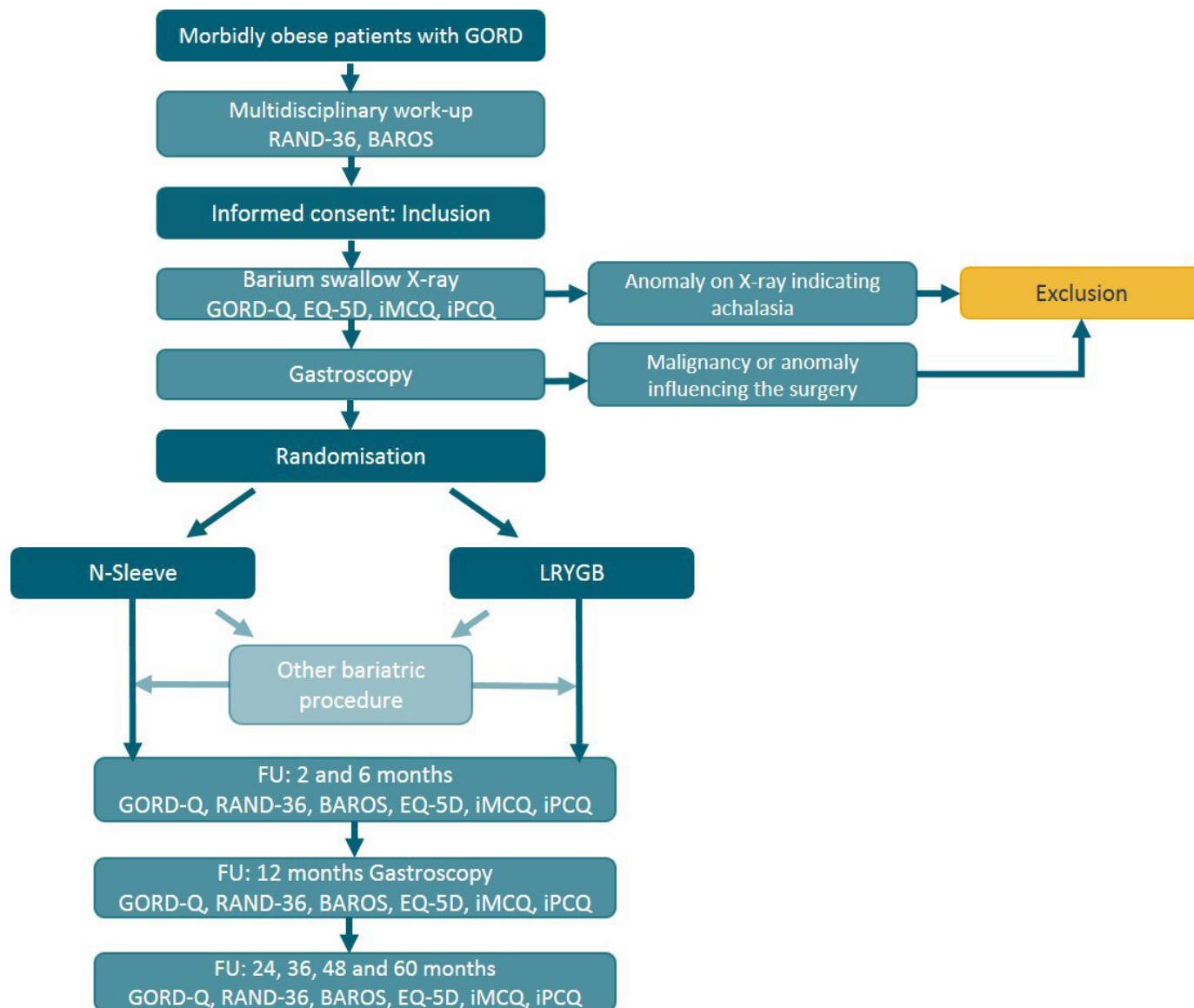


Figure 1 Flowchart: inclusion, exclusion, randomisation and follow-up. BAROS, Bariatric Analysis and Reporting Outcome System; EQ-5D: EuroQol 5 Dimensions; GORD-Q, Gastro-oesophageal Reflux Disease Questionnaire; GORD, gastro-oesophageal reflux disease; FU, follow-up; iMCQ, iMTA Medical Consumption Questionnaire; iPCQ, iMTA Productivity Cost Questionnaire; N-Sleeve, Nissen-Sleeve; LRYGB, laparoscopic Roux-en-Y gastric bypass; RAND-36, Research and Development-36 Questionnaire.

at least 3–5 cm of abdominal oesophagus is aimed to be achieved, after which the hiatal space will be closed. The greater curvature of the stomach is then dissected from the short gastric vessels and gastrocolic ligament to 4 cm proximal to the pylorus. At the level of the gastric fundus, a careful dissection will be performed, which will be used to create the fundoplication. A 34F calibration tube will be introduced to the stomach. A Nissen fundoplication of 3 cm will be created. Dissection of the rest of the greater curvature will continue until 6 cm from the pylorus. A 60 mm endoscopic linear stapler will be used to divide the stomach parallel to the calibration tube along the lesser curvature, leaving just enough space for a gastric boogie to pass, with extra attention to the lateral side of the fundoplication, avoiding stapling double layers. At day 1

postoperative, a swallow X-ray will be made to confirm the passage.²⁷

The control group will undergo a LRYGB procedure as described earlier, with the exception of the enteroenterostomy, which is made at 100 cm distally from the gastroenterostomy with a 100 cm biliopancreatic limb.²⁸

If, perioperatively, N-Sleeve is deemed technically impossible to perform, LRYGB will be performed as a first option. If that is also impossible, another bariatric procedure (LSG or one-anastomosis gastric bypass (OAGB)) will be performed. Similarly, if LRYGB is deemed technically impossible, N-Sleeve will be performed as first option. If that is also impossible, another bariatric procedure (LSG or OAGB) will be performed.



Figure 2 Technical aspects of the N-Sleeve. N-Sleeve, Nissen-Sleeve.

Outcomes

The primary outcome measure is GORD status. Absence of GORD is defined as <8 points on the GORD-Q¹⁹. Secondary outcome measures are long-term GORD improvement, technical failure rate of procedure, HrQoL, weight loss, PPI use, complication rate within 30 days postoperatively, long-term complication rate, length of hospital stay, duration of primary surgery, effects of the surgery on comorbidity; presence and grade of oesophagitis (grade A–D) and/or Barrett’s oesophagus and cost-effectiveness (table 3).

Data management

Identification of participants will be protected by using study numbers non-traceable to patients’ identity. Only members of the research team will have access to the databases. Data will be kept for 15 years. The data will be monitored by a committee that is appointed by the hospital’s research department.

Safety and stopping rules

The N-sleeve procedure should neither lead to a significant increase in GORD and weight, nor should it lead to more severe complications. Furthermore, both surgery techniques should be reasonably feasible. Therefore, the following parameters are closely monitored after 10, 20 and 30 patients are included in the N-Sleeve arm (table 4):

- ▶ Severe complications (Clavien-Dindo grade ≥ 3).
- ▶ Conversion of N-Sleeve to LRYGB due to technical difficulties.

If outcomes of one or both stop rules are reached, the sponsor will be notified immediately and further inclusion will be stopped. Patients in the intervention arm who

have already been included will be informed and offered the other treatment arm (LRYGB) if not yet been operated. An independent data safety and monitoring board (DSMB) was installed prior to the first inclusion. Monitoring will take place according to the NFU guideline Quality Assurance Human Research 2020.²⁹ The DSMB has been established in accordance with the European Medicines Agency (EMA) guideline and will perform an interim assessment of the stopping rules after inclusion of the first 10 patients in the N-Sleeve arm.³⁰ Serious adverse events will be reported to the medical ethical committee.

Withdrawal of patients

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons, such as mentioned in the exclusion criteria. Patients who withdraw consent after randomisation, but before surgery, will be replaced. Patients who withdraw consent after surgery will not be replaced. The data of the latter group will remain in the analysis and every effort will be made to acquire FU data with the patient’s consent, unless the patient explicitly prefers otherwise. Based on previous randomised trials performed by our research group, we have accounted for an expected (voluntary) withdrawal of approximately 9% of included patients in the power calculation (see Sample size section).

Sample size

The power analysis for a non-inferiority trial (power=80%, $\alpha=2.5\%$ one-sided) calculated a required sample size of $2 \times 40 = 80$ patients. Non-inferiority was defined as a 1-year GORD recovery rate that is no more than 15 percentage points below the expected 75% GORD recovery rate among patients in de LRYGB arm. To allow 9% drop out, a total of 88 patients are required for randomisation.

Statistical methods

Data will be analysed following intention-to-treat (primary analysis) and as-treated principles (secondary analysis). Efforts will be made to prevent missing data by contacting subjects that did not attend their FU visit. GORD status and long-term GORD status will be analysed using a generalised linear model (model type: binary response; link: binary logistic). Dependent variable is GORD-Q score $\leq / \geq 8$, covariables are allocated group (N-Sleeve/LRYGB), time and interaction effect of allocated group X time. This analysis will be supported by a repeated measurements analysis (linear mixed model). Results will be evaluated at a significance threshold of $p < 0.025$ (one sided).

Total weight loss in percentage between the groups will be evaluated a using repeated measurements analysis. Univariable comparisons between groups over time will be tested using the Bonferroni-Sidak adjustment for multiple testing. HRQoL will be analysed using the RAND-36, the EQ5D5L and BAROS, and according

Table 3 Schedule: assessment, study procedures and follow-up

	0	5–8 d	Prior to inter-vention 10–60 d	Surgery 3 mo	After surgery 3 mo +2 D	12 5 mo mo	36 24 mo mo	48 mo	60 mo
Enrolment									
Consult surgeon/ diagnosis	X								
Patient folder	X								
Consult anaesthesiologist		X							
Obtaining Informed consent		X							
(Timed) Barium swallow			X		X				
Endoscopy: presence of oesophagitis (grade A–D)/ Barrett’s oesophagus/malignancy			X			X			
Randomisation			X						
Surgery									
N-Sleeve/LRYGB				X					
Primary outcome									
GORD-Q			X			X	X	X	X
Secondary outcome									
EQ-5D			X			X	X	X	X
RAND-36			X			X	X	X	X
BAROS			X			X	X	X	X
iMCQ			X			X	X	X	X
iPCQ			X			X	X	X	X
Weight	X					X	X	X	X
PPI use	X					X	X	X	X
Complication registration				X	X	X			
Duration procedure				X					
Length of hospital stay					X				
Hypertension (BP)	X					X	X	X	X
Diabetes mellitus (blood test)	X					X	X	X	X
Dyslipidaemia (blood test)	X					X	X	X	X
FU surgeon						X			
FU internist						X	X	X	X
X	=	Standard care							
X	=	Study procedure							

BAROS, Bariatric Analysis and Reporting Outcome System; BP, blood pressure; d, days; EQ-5D, EuroQol 5 Dimensions; FU, follow-up; GORD-Q, Gastro-oesophageal Reflux Disease Questionnaire; iMCQ, iMTA Medical Consumption Questionnaire; iPCQ, iMTA Productivity Cost Questionnaire; LRYGB, laparoscopic Roux-en-Y gastric bypass; mo, months; N-Sleeve, Nissen-Sleeve; PPI, proton pump inhibitor; RAND-36, Research and Development-36 questionnaire.

to the manual instructions of the questionnaire.^{20 21 31} Repeated measurements analysis (linear mixed model) will be used to evaluate between group differences. Technical failure rate and presence/grade of oesophagitis (grade A–D) and Barrett’s oesophagus between both groups will be analysed using the χ^2 test, similar as PPI use, complication rates and the effects on comorbidity, for which also a Kaplan-Meier analysis will be performed. The length of hospital stay (days) between the groups will be analysed using the Mann-Whitney U test or the

χ^2 test, as appropriate. Duration of procedure between the groups will be tested using the unpaired Student’s t test. Results will be evaluated at a significance threshold of $p < 0.05$ (two sided). Cost-effectiveness analyses will also be performed. Incremental cost-effectiveness (model type: cost-utility analysis will be studied from the perspective of a ‘cost-effectiveness analysis alongside the clinical trial’ and in line with the Dutch and international guidelines).³² Utility will be measured with the EQ5D5L (Dutch

Table 4 Stop rules

Stop rules	After 10 included patients in the N-Sleeve arm	After 20 included patients in the N-Sleeve arm	After 30 included patients in the N-Sleeve arm
1. Severe complications Clavien-Dindo grade \geq III*	>40%	>35%	>30%
2. Conversion of N-Sleeve to LRYGB, due to anatomical difficulties. (feasibility)†	>30%	>20%	>16,7%

*Percentages are based on the upper limit of the 95% CI of 17% (30-day postoperative or in-hospital mortality).¹⁴
†Percentages are based on the upper limit of the 95% CI of 6% (conversion, based on Sleeve bypass trial).²⁸
.LRYGB, laparoscopic Roux-en-Y gastric bypass; N-Sleeve, Nissen-Sleeve.

tariffs).³¹ Costs will be studied from a societal perspective, distinguishing healthcare costs inside and outside hospital, patient-related costs and other non-healthcare costs.

Patient and public involvement

Patients were not invited to comment on the study design and will not be consulted to develop patient-relevant outcomes or interpret the results. Patients will not be invited to contribute to the writing or editing of this document for readability or accuracy. The results of this study will be communicated to the patient association, who may disseminate the results among their members.

Ethical and dissemination

This study has been approved by the Medical Research Ethics Committees United (MEC-U), Nieuwegein (R21.040) and has been registered in the Netherlands Trial Register (NTR 9789). The study will be conducted according to the standards of Good Clinical Practice principles, in agreement with the Declaration of Helsinki, with Dutch law in general, and with the Medical Research Involving Human Subjects Act in particular. The principal investigator (JAA) will be responsible for recruitment, data collection, FU, completion of case report forms, and adherence to the study protocol. This will be performed according to the local guidelines for data management of the Franciscus Gasthuis & Vlietland hospital. The supervising doctor or any other doctor of the surgical team will point out the ongoing study to the subjects. Patients will be informed by the investigator about both treatment arms and asked for their consent using a standard patient information letter and an informed consent form.

If protocol revisions are made, the new protocol must be approved by MEC-U before implementation. Case record

forms including data validation checks and change confirmations are created by Ciwit B.V., Amsterdam, V.8.51 (Castor EDC) prior to the start of the study. Randomisation and allocation of individual trial numbers will also be performed via Variable Block Randomisation software by Ciwit B.V. (Castor EDC). Results will be communicated via national and international conferences and via publications in peer-reviewed journals.

DISCUSSION

In this trial, we investigate the effect of N-Sleeve versus LRYGB in patients with morbid obesity and GORD. Patients with obesity are 2–2.5 times more at risk of developing GORD.³³ Earlier studies have shown an incidence of GORD of 10%–30% after LSG. However, more recent data after LSG suggest a higher incidence of GORD as well as a higher risk of development of Barrett's oesophagus.⁵ For patients with GORD who cannot or do not want to undergo LRYGB, the N-Sleeve may be a more suitable alternative compared with LSG. Since Barrett's oesophagus generally does not develop until 3 years after LSG,³³ patients will be followed for 5 years.

Other antireflux surgery technics such as anterior fundoplication or Rossetti fundoplication in combinations with LSG have been described.^{34–36} However, these studies included a limited number of patients, with short FU and insufficient data on postoperative complications. As most experience and data are available for the N-Sleeve technique, this is currently considered the most appropriate technique for combination with the LSG procedure.²⁷

This study has some limitations. The golden standard to diagnose GORD is 24-hour oesophageal (impedance) pH monitoring or manometry. However, these are intensive and invasive procedures that would reduce patient willingness to participate in the study and consequently lead to low inclusion rates. In addition, the 24-hour oesophageal (impedance) pH monitoring also has its limitations. In 12.7% of all patients, the 24-hour pH monitoring was positive although they did not have GORD.³⁷ Therefore, the Montreal definition is used for inclusion, as it is a non-invasive and globally well-accepted consensus to define GORD.^{12 13 34 36 38} To objectify and quantify GORD, we will use the validated GORD-Q questionnaire and endoscopy at baseline and during FU.^{19 39} The FU upper GI endoscopy is an additional invasive procedure, which will be discussed with the patient in the outpatient clinic. The risk of this study procedure is low and the extra information is very useful for patient treatment and can be used as comparison material to the upper GI endoscopy preoperatively.⁴⁰ Another limitation is that patients and the surgical team will not be blinded. Blinding the surgical team is impossible since they have to perform the procedure. In addition, it is considered unsafe to blind the patients because of different aftercare. Patients need different multivitamins after both procedures to address potential deficiencies. Moreover, there are other possible

complications after both procedures. Patients should know what symptoms to be alert for. The current study does not investigate sleeve gastrectomy or OAGB. There are numerous studies comparing ‘normal’ sleeve gastrectomy to LRYGB. It is known that there is a higher risk of (de novo) GORD after LSG.⁴ As this study will investigate an antireflux procedure, sleeve gastrectomy has not been considered as additional study arm. After OAGB reflux can occur, which is defined as biliary reflux. Biliary reflux increases the risk of oesophagitis and Barrett oesophagus, which might bias the outcome of the study.⁴¹ Therefore, no LSG- nor OAGB-arm was added to this study.

Protocol version V.2.0, 15 September 2021

Contributors JWHtH drafted the first version of this manuscript. BJN, LUB, MD, IL and JAA participated in the study design and critically revised the manuscript. JWHtH, BJN, LUB, MD, IL and JAA drafted the original study protocol. JWHtH, BJN, LUB, MD, IL and JAA acquired funding for the trial. JAA initiated the trial and is the principal investigator. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Funding This work was supported by, Stichting BOF (Foundation for the promotion of research Franciscus). This funding source had no role in the design of this study and they will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The identified individual clinical trial participant-level data, protocols and the statistical analysis plan will be available upon reasonable request at publication. These data will be available for researchers who provide a methodologically sound proposal to achieve the aims in the approved proposal. Proposals should be directed to j.apers@franciscus.nl, and to obtain access, data requestors will need a data access agreement. This data sharing plan was updated in the trial registry (NTR (trialregister.nl)) on 29 April 2022.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Judith W H 't Hart <http://orcid.org/0000-0002-2239-8449>

REFERENCES

- Kelly T, Yang W, Chen C-S, et al. Global burden of obesity in 2005 and projections to 2030. *Int J Obes* 2008;32:1431–7.
- Angrisani L, Santonicola A, Iovino P, et al. Bariatric surgery and endoluminal procedures: IFSO worldwide survey 2014. *Obes Surg* 2017;27:2279–89.
- Burgerhart JS, Schotborgh CAI, Schoon EJ, et al. Effect of sleeve gastrectomy on gastroesophageal reflux. *Obes Surg* 2014;24:1436–41.
- Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. *JAMA* 2018;319:255–65.
- Qumseya BJ, Qumsiyeh Y, Ponniah SA, et al. Barrett's esophagus after sleeve gastrectomy: a systematic review and meta-analysis. *Gastrointest Endosc* 2021;93:343–52.
- Yeung KTD, Penney N, Ashrafian L, et al. Does sleeve gastrectomy expose the distal esophagus to severe reflux?: a systematic review and meta-analysis. *Ann Surg* 2020;271:257–65.
- Krstić M, Damjanov D, Ngorni A. [Observational study in primary health care: symptoms control of gastroesophageal reflux disease and influence on the quality of life]. *Srp Arh Celok Lek* 2013;141:54–60.
- Drahoš J, Li L, Jick SS, et al. Metabolic syndrome in relation to Barrett's esophagus and esophageal adenocarcinoma: results from a large population-based case-control study in the clinical practice research Datalink. *Cancer Epidemiol* 2016;42:9–14.
- Smith CD, Herkes SB, Behrns KE, et al. Gastric acid secretion and vitamin B12 absorption after vertical Roux-en-Y gastric bypass for morbid obesity. *Ann Surg* 1993;218:91–6.
- Quezada N, León F, Jones A, et al. High frequency of internal hernias after Roux-en-Y gastric bypass. *Obes Surg* 2015;25:615–21.
- Shoar S, Nguyen T, Ona MA, et al. Roux-en-Y gastric bypass reversal: a systematic review. *Surg Obes Relat Dis* 2016;12:1366–72.
- Nocca D, Skalli EM, Boulay E, et al. Nissen sleeve (N-Sleeve) operation: preliminary results of a pilot study. *Surg Obes Relat Dis* 2016;12:1832–7.
- Amor IB, Casanova V, Vanbiervliet G, et al. The Nissen-Sleeve (N-Sleeve): results of a cohort study. *Obes Surg* 2020;30:3267–72.
- Peterli R, Borbély Y, Kern B, et al. Early results of the Swiss multicentre bypass or sleeve study (SM-BOSS): a prospective randomized trial comparing laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass. *Ann Surg* 2013;258:690–4.
- Wang F-G, Yan W-M, Yan M, et al. Outcomes of mini vs Roux-en-Y gastric bypass: a meta-analysis and systematic review. *Int J Surg* 2018;56:7–14.
- NvV H. Algemene indicatiestelling bij chirurgische behandeling van obesitas: Kennisinstituut van de Federatie van Medisch Specialisten, 2020. Available: [https://richtlijnendatabase.nl/richtlijn/chirurgische_behandeling_van_obesitas/indicatiestelling_bij_chirurgische_behandeling_van_obesitas.html](https://richtlijnendatabase.nl/richtlijn/chirurgische_behandeling_van_obesitas/indicatiestelling_bij_chirurgische_behandeling_van_obesitas/algemene_indicatiestelling_bij_chirurgische_behandeling_van_obesitas.html)
- Di Lorenzo N, Antoniou SA, Batterham RL, et al. Clinical practice guidelines of the European association of endoscopic surgery (EAES) on bariatric surgery: update 2020 endorsed by IFSO-EC, EASO and ESPCOP. *Surg Endosc* 2020;34:2332–58.
- Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006;101:1900–20.
- Jonasson C, Wernersson B, Hoff DAL, et al. Validation of the GerdQ questionnaire for the diagnosis of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2013;37:564–72.
- Hays RD, Sherbourne CD, Mazel RM. The Rand 36-Item health survey 1.0. *Health Econ* 1993;2:217–27.
- Oria HE, Moorehead MK. Updated bariatric analysis and reporting outcome system (BAROS). *Surg Obes Relat Dis* 2009;5:60–6.
- Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.
- Group PHR. *Medical consumption questionnaire Vragenlijst*, 2018.
- Group PHR. *Productivity costs questionnaire Vragenlijst*, 2018.
- Anderson MA, Gan SI, et al. ASGE STANDARDS OF PRACTICE COMMITTEE. Role of endoscopy in the bariatric surgery patient. *Gastrointest Endosc* 2008;68:1–10.
- Gadiot RPM, Biter LU, Zengerink HJF, et al. Laparoscopic sleeve gastrectomy with an extensive posterior mobilization: technique and preliminary results. *Obes Surg* 2012;22:320–9.
- Nocca D, Nedelcu M, Loureiro M, et al. The Nissen sleeve gastrectomy: technical considerations. *J Laparoendosc Adv Surg Tech A* 2020;30:1231–6.
- Biter LU, Gadiot RPM, Grotenhuis BA, et al. The sleeve bypass trial: a multicentre randomized controlled trial comparing the long term outcome of laparoscopic sleeve gastrectomy and gastric bypass for morbid obesity in terms of excess BMI loss percentage and quality of life. *BMC Obes* 2015;2:30.

- 29 Margriet Schneider M. *Guideline quality assurance of research involving human subjects*. Netherlands federation of university medical centres, 2020.
- 30 DAMOCLES Study Group, NHS Health Technology Assessment Programme. A proposed charter for clinical trial data monitoring committees: helping them to do their job well. *Lancet* 2005;365:711–22.
- 31 M Versteegh M, M Vermeulen K, M A A Evers S, *et al*. Dutch tariff for the five-level version of EQ-5D. *Value Health* 2016;19:343–52.
- 32 Nederland Z. Richtlijn voor Het uitvoeren van economische evaluaties in de gezondheidszorg, 2016. Available: <https://www.zorginstituutnederland.nl/over-ons/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-gezondheidszorg>
- 33 Qumseya B, Gendy S, Wallace A, *et al*. Prevalence of Barrett's esophagus in obese patients undergoing pre-bariatric surgery evaluation: a systematic review and meta-analysis. *Endoscopy* 2020;52:537–47.
- 34 Del Genio G, Tolone S, Gambardella C, *et al*. Sleeve gastrectomy and anterior fundoplication (D-SLEEVE) prevents gastroesophageal reflux in symptomatic GERD. *Obes Surg* 2020;30:1642–52.
- 35 Moon RC, Teixeira AF, Jawad MA. Safety and effectiveness of anterior fundoplication sleeve gastrectomy in patients with severe reflux. *Surg Obes Relat Dis* 2017;13:547–52.
- 36 Olmi S, Uccelli M, Cesana GC, *et al*. Modified laparoscopic sleeve gastrectomy with Rossetti antireflux fundoplication: results after 220 procedures with 24-month follow-up. *Surg Obes Relat Dis* 2020;16:1202–11.
- 37 Franzén T, Grahn LT. Reliability of 24-hour oesophageal pH monitoring under standardized conditions. *Scand J Gastroenterol* 2002;37:6–8.
- 38 Aiolfi A, Micheletto G, Marin J, *et al*. Laparoscopic Sleeve-Fundoplication for morbidly obese patients with gastroesophageal reflux: systematic review and meta-analysis. *Obes Surg* 2021;31:1714–21.
- 39 Jones R, Junghard O, Dent J, *et al*. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. *Aliment Pharmacol Ther* 2009;30:1030–8.
- 40 Guilford WG. Upper gastrointestinal endoscopy. *Vet Clin North Am Small Anim Pract* 1990;20:1209–27.
- 41 Szymański M, Marek I, Wilczyński M, *et al*. Evaluation of esophageal pathology in a group of patients 2 years after one-anastomosis gastric bypass (OAGB) - Cohort study. *Obes Res Clin Pract* 2022;16:82–6.