Clinical study protocol reference number: EC number REK Vest 421917.

Sleeve Pex

A clinical intervention study exploring gastropexy as a measure to reduce gastro-oesophageal reflux disease after laparoscopic sleeve gastrectomy.

Person responsible for research at responsible institution: John Roger Andersen

Entity responsible for research: Helseforsking Sogn og Fjordane, Helse Førde, Norway

Revision history

Version number	Date
1	06.01.2022
2	15.11.2022
3	16.12.2022
4	21.08.2023

Villy Våge

_____ _____

Project Leader Signature **Date**

John Roger Andersen

_____ _____

Representative for the research responsible institution **Date**

Signature

This document contains confidential and proprietary information and may not be copied or reproduced in whole or part without the written permission of Villy Våge.

Følsomhet Intern (gul)

CLINICAL STUDY AGREEMENT SIGNATURE LOG

I, the undersigned, have read and understand the specific research protocol, and agree with the contents.

I agree to conduct in person or to supervise the study.

I agree to ensure that all who assist me in the conduct of the study have access to the research protocol plus any amendments and are aware of their obligations.

Researcher:

_____	_____	_____
Name	Signature	Date

_____

Institution

Project Leader
Name: Villy Våge
Professional position: MD, PhD
Address: Leitet 4a, 5018 Bergen
E-mail address: villy.vage@helse-bergen.no
Phone number: 47 90863744

Contact information of other study sites in which the clinical study will be conducted.
Name: Magnus Sundbom
Professional position: MD, Professor
Address: Uppsala University Hospital
E-mail address: magnus.sundbom@akademiska.se
Phone number: 46 705432989

Følsomhet Intern (gul)

CLINICAL STUDY SUMMARY

Title:	Sleeve-pex.
Study objectives:	Reduce gastro-oesophageal reflux disease (GORD) after laparoscopic sleeve gastrectomy (LSG).
Clinical study design:	Interventional. A randomized clinical control trial where patients planned for LSG are randomized to LSG *with* or *without* gastropexy.
Inclusion / exclusion criteria:	Inclusion criteria: Patients planned for bariatric surgery with primary LSG. Exclusion criteria: Age below 18 years. Use of acid-reducing medication (ARM) for other reasons than reflux. Previous antireflux surgery. Inability to comprehend and respond to patient related outcome (PRO) questionnaire. LSG planned as the first step of Biliopancreatic Diversion with Duodenal Switch (BPDDS).
Primary performance endpoints:	Continuous use of acid-reducing medication (ARM) due to reflux symptoms at two years after surgery, or reoperation due to GORD within two years postoperatively.
Secondary performance endpoints:	Patient reported outcome (HRQL and GerdQ). Endoscopic findings (visible oesophagitis, hiatal hernia), pH-metry and impedance in a subgroup of patients.
Safety endpoints:	Complications graded as Clavien Dindo grade 3b or worse.
Duration of study:	Eight years.
Follow-up:	Six weeks: Focusing on 30 day complications. One, two, and five years: Clinical, biochemical and PRO-data. At two years also endoscopy, pH-metry and impedance measurements.

TABLE OF CONTENTS

Følsomhet Intern (gul)

Følsomhet Intern (gul)

Følsomhet Intern (gul)

Følsomhet Intern (gul)

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Explanation
AE (Adverse Event)	An unfavorable change in the health of a participant that happens during a clinical. This change may or may not be caused by the intervention being studied.
ARM	Acid-reducing medication
ASMBS	American Society for Metabolic and Bariatric Surgery
BPDDS	Biliopancreatic Diversion with Duodenal Switch
CRF	Case Report Form (electronic or paper)
Clinical study	A research study using human subjects to evaluate biomedical or health-related outcomes. Two types of clinical studies are Interventional studies (or clinical trials) and Observational studies
Completed	The clinical study has ended normally, and participants are no longer being examined or treated (that is, the "last subject, last visit" has occurred).
Controlled trial	A type of clinical trial in which observations made during the trial are compared to a standard, called the control. The control may be observations of a group of participants in the same trial or observations from outside the trial (for example, from an earlier trial, which is called a historical control).
DMC	Data Monitoring Committee
EC	Ethics Committee, synonymous to Institutional Review Board (IRB) and Independent Ethics Committee (IEC) and Regional Ethics Committee (REC)
Eligibility Criteria	The key standards that people who want to participate in a clinical study must meet or the characteristics they must have. Eligibility Criteria include both inclusion criteria and exclusion criteria. For example, a study might only accept participants who are above or below certain ages.
Enrollment	The number of participants in a clinical study. The "estimated enrollment" is the number of participants that the researchers need for the study.
Exclusion criteria	The factors, or reasons, that prevents a person from participating in a clinical study.
GerdQ	Gastro-oesophageal reflux disease questionnaire
GOJ	Gastro-oesophageal junction
GORD	Gastro-oesophageal reflux disease. In this document defined as either daily use of ARM for at least one month due to reflux symptoms, or based on findings on endoscopy, pH-metry or impedance.

Følsomhet Intern (gul)

HRQL	Health related quality of life
IFSO	International Federation for Surgery of Obesity
Inclusion criteria	The factors, or reasons, that allows a person to participate in a clinical study.
Intervention Model (Design)	The general design of the strategy for assigning interventions to participants in a clinical study.
Interventional study (or clinical trial)	A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the research protocol. Participants may receive diagnostic, therapeutic, or other types of interventions
ITT	Intention to treat analysis.
LOS	Lower Oesophageal Sphincter
LSG	Laparoscopic sleeve gastrectomy
LSGG	Laparoscopic sleeve gastrectomy with gastropexy. Gastropexy in this document means suturing the staple-line of the gastric remnant to the gastrocolic ligament including the gastroepiploic arterial arcade.
Primary Outcome Measure	The planned Outcome Measure in the protocol that is the most important for evaluating the effect of an intervention. Most clinical studies have one Primary Outcome Measure, but some may have more than one.
Primary Purpose	The main reason for the clinical trial. The types of Primary Purposes are Treatment, Prevention, Diagnostic, Supportive Care, Screening, Health Services Research, Basic Science, and Other.
Principal Investigator	Statistician working in SOReg-Norway
PRO	Patient Reported Outcome
Protocol	The written description of a clinical study. It includes the study's objectives, design, and methods. It may also include relevant scientific background and statistical information.
Secondary Outcome Measure	A planned Outcome Measure in the protocol that is not as important as the Primary Outcome Measure but is still of interest in evaluating the effect of an intervention. Most clinical studies have more than one Secondary Outcome Measure.
Serious Adverse Event (SAE)	An adverse event that results in death, is life-threatening, requires inpatient hospitalization or extends a current hospital stay, results in an ongoing or significant incapacity or interferes substantially with normal life functions. Medical events that do not result

Følsomhet Intern (gul)

	in death, are not life-threatening, or do not require hospitalization may be considered serious adverse events if they put the participant in danger or require medical or surgical intervention to prevent one of the results listed above. By definition, any complication classified as Clavien Dindo grade 3b or more is a serious adverse event.
SOReg	Scandinavian Obesity Surgery Register. Consists of SOReg Sweden (SOReg-S) and SOReg Norway (SOReg-N).
Study completion date	The date on which the final data for a clinical study were collected because the last study participant made the final visit to the study location (that is, "last subject, last visit"). The "estimated study completion date" is the date that the researchers assume will be the completion date for the study.
Study start date	The date on which the enrollment of participants for a clinical study began
TSC	Trial Steering Committee

Følsomhet Intern (gul)

1 INTRODUCTION

LSG has become the most commonly performed bariatric procedure worldwide.[1] The operation consists of a longitudinal resection of the stomach leaving the intestines intact, thereby lowering the risk for side-effects due to rerouting of the small bowel.

Although such side-effects mostly are avoided, GORD has been reported to increase after LSG. Increased intragastric pressure, loss of distensibility, kinks/torsion of the gastric remnant, development of a neo-fundus, dysfunction of the LOS, and intrathoracic migration of the upper part of the remaining stomach have all been postulated as potential mechanisms of the increased incidence of GORD after LSG.[2-4]

The LOS has a crucial role in preventing reflux, and the two most important factors for its function are: a) an intra-abdominal position, and b) proximity to the crural diaphragm. Based on this, *Våge* et al sutured the gastric remnant to the gastrocolic ligament (gastropexy) in an attempt to prevent kinks, torsion and intrathoracic migration, and found less use of ARM two years postoperatively in the LSGG-group than in the LSG group.[5]

The proposed study is a multi-centre, randomized, clinical intervention study designed to examine the outcome of LSGG. Since gastropexy is not routinely performed in most centers, the technique represents a challenge to current practice.

900 patients will be enrolled in this study, please see calculation of sample size (chapter 7.2).

2 STUDY DESCRIPTION

2.1 Background

GORD is an obesity-related disease, and in the SOReg-N we find that ≈ 17 % of all patients undergoing bariatric surgery are using acid-reducing medication (ARM) preoperatively. In addition, patients might have asymptomatic reflux. This can be detected by gastroscopy and/or 24hr pH-measuring.

After LSG, many centers report an increase in the use of ARM. In the study by Våge et al, the use of ARM increased from 10% preoperatively to 30% after two years in the group without gastropexy.[5] In a recent review article including 10 718 patients, the authors found an increase of 19% from preoperative until two years or more after the operation, and de novo reflux (i.e. new reflux) of 20% but with large variations between institutions.[6]

2.2 Study Rationale

The intention is to refine the LSG in order to prevent/reduce an increase in the prevalence of GORD after this operation.

Symptoms of reflux can be anything from mild dyspepsia to severe, nightly reflux/regurgitation affecting sleep. Reflux can also be asymptomatic. Independent of whether it is symptomatic or not, it can induce oesophagitis and possibly Barret's. Because of this, both the ASMBS and IFSO recommends pre- and postoperative gastroscopy for sleeve-operated patients as surveillance.[7, 8] Although many patients will experience reduced symptoms when starting ARM, symptom control is not achieved in all. Also, oesophagitis might not heal even when using high doses of ARM. In such cases revisional surgery might be necessary to alleviate the reflux.

For the individual, avoiding GORD will improve HRQL and reduce the need for ARM and revisional surgery due to reflux issues.

Følsomhet Intern (gul)

The cost of adding gastropexy to the LSG is considered minimal as it requires almost no equipment costs, and only requires a longer operation time in the range of 10 - 15 minutes.

For the society and public health service, avoiding reflux will reduce healthcare expenditure due to reduced need for medical consultations, ARM, revisional surgery and surveillance. Considering the high number of LSG being performed worldwide, the potential for reduced costs is large.

Academically, this study might give new insight into the mechanism(s) for reflux after LSG.

3 OBJECTIVES AND HYPOTHESIS

3.1 Clinical study - objectives

3.1.1 Primary objective:

Reduce GORD after LSG as evaluated by the use of ARM and reoperations due to GORD.

3.1.2 Secondary objectives:

a) Evaluate PRO using the GerdQ and questions on HRQL.

b) Prevent ascend of the GOJ as evaluated by endoscopy.

c) Reduce GORD as evaluated by endoscopy and pH-metry.

3.1.3 Other study objectives

None as planned per today.

3.2 Hypothesis

Kinks and torsion of the gastric remnant may obstruct the passage of food and fluid through the gastric remnant thereby predisposing to reflux. It has also been found that the GOJ ascends following LSG, thereby leading to the formation of a gastric pouch (hiatal hernia) above the diaphragm.[4] There is a clear association between hiatal hernia and reflux, and an ascend of the gastric remnant could therefore be the main reason for development of reflux after LSG.[9, 10]

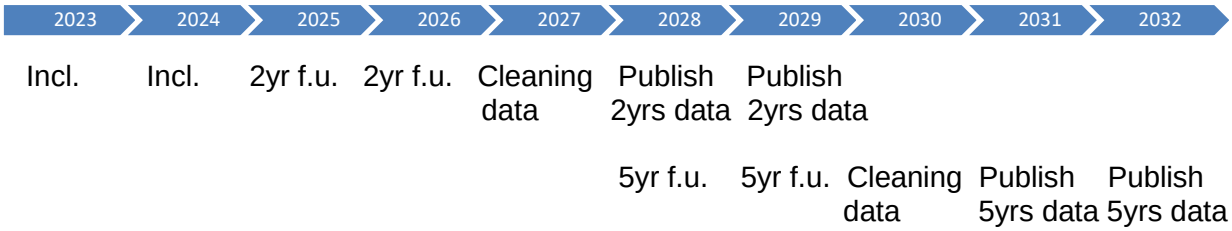
The hypothesis is that suturing the gastrocolic ligament (including the gastroepiploic artery) to the remnant stomach will prevent kinks, torsion and intrathoracic migration of the gastric remnant and hence reduce the incidence of GORD.

3.3 Any results expected during the project period

Safety will be monitored continuously. The inclusion period is estimated to approximately two years, and the follow-up for primary and secondary objectives will be two and five years postoperatively. Adding 6-12 months to collect and clean the data gives a project period of eight years. It is expected that both primary and secondary objectives for the two year outcome will be achieved 6-7 years after commencement of the study.

Følsomhet Intern (gul)

Figure 1. Time-schedule of the project.



3.4 Risks and anticipated adverse events that are to be assessed

Leaks from the stomach remnant and bleeding from the stomach or gastrocolic ligament are well-known adverse events following LSG that will be assessed. However, none of these have been found to increase after LSGG in previous studies. Unintentional kinking / torsion / stricture of the gastric remnant could be potential adverse events of the gastropexy, but our hypothesis is that these will be reduced or prevented by this technique.

Prolonged operation time is foreseeable and could possibly lead to unanticipated adverse events. If so, this should become evident in the 30 day morbidity report and presented to the DMC.

4 PROJECT METHODOLOGY

Hospitals performing more than 10 LSG annually will be invited to participate. A maximum of 200 patients will be accepted from any hospital. The start of the study is the date at which the first patient is operated. The inclusion of new patients will stop when 900 patients have been included (i.e. randomized), estimated to be reached after approximately two years. The number of included patients will be monitored continuously.

Evaluation of outcome will be based on data at two and five years postoperatively. Given an inclusion period of maximum two years, follow-up after two and five years, and another year for delayed follow-up and data processing, the project period will be for a maximum of eight years.

This study is an international, multicentre, randomized, triple-blind (blinded to patients, caregivers and researchers) prospective clinical intervention trial. For primary and secondary endpoints, analysis will be performed according to ITT. All patients will thus be analysed within the allocated group.

5 STUDY DESIGN

5.1 General

5.1.1 Description

This study is a multicentre, randomized, triple-blind, prospective clinical intervention study comparing LSG to LSGG.

5.1.2 Primary and secondary endpoints

The primary endpoint is continuous **use of ARM for GORD symptoms, or reoperation due to GORD within two years.** This is easily measured and registered in most bariatric surgical

Følsomhet Intern (gul)

registries including SOReg. Daily use of ARM due to dyspepsia during the last month (as defined in SOReg) / reoperation due to GORD will be defined as “yes”, otherwise “no”.

Secondary endpoints are:

a) **PRO** using the GerdQ and questionnaires for HRQL. GerdQ is a six item, easy to use questionnaire developed as a diagnostic tool for GORD.[11] It uses a four graded Likert scale (0-3), giving a total GerdQ score range of 0-18. Besides GerdQ, the questionnaires used for evaluating HRQL will be those that are already incorporated in the hospitals that will participate in the study. In Sweden this will be the SF-36, while in Norway only the initial question from SF-36 will be used together with PROSURG.[12]

b) **GORD** as evaluated by endoscopy, pH-metry and impedance.

Endoscopy: Thirty patients will be submitted to a gastroscopy prior to, and two years after LSG/LSGG. A standard formula for evaluating and describing findings at gastroscopy will be used (appendix 1).

Reflux oesophagitis will be defined according to the Los Angeles classification (LA grade A-D), where grade C and D entails high-grade oesophagitis.[13] LA grade C and D, Barret`s oesophagus and a peptic stricture will be considered confirmatory evidence of GORD.

pH-metry: GORD will be defined according to the oesophageal acid exposure time and the number of reflux episodes per 24 hrs.[14] pH-metry will only be performed in the subgroup of 30 patients before and two years after surgery using the Bravo-capsule. Patients having reflux symptoms responding to PPI but without acid reflux as evaluated by the Bravo capsule will be offered pH-impedance measurement.

c) **Presence of a hiatal hernia** as evaluated by endoscopy. The distance between the teeth and diaphragm, secondly the teeth and the GOJ will be measured and the difference calculated. If a part of the remaining stomach ascends into the thorax this will predispose to reflux as it is well known that a hiatal hernia (defined as ≥2 cm difference) is a predictor of reflux.[15]

5.1.3 Equipment

Only hospitals that already performs bariatric surgery will be invited to participate in the study, therefore most of the equipment, infrastructure and resources will already be at site.

Written informed consent must be obtained from each patient and stored in a secure place.

A local register operating in accordance with the local EC/IRB must be used for data capturing. In Norway and Sweden, hospitals will be using the SOReg. If answers to the PRO-questionnaires (HRQL and GerdQ) cannot be captured electronically in the register, paper version of these questionnaires will be distributed and collected, and the answers entered manually into the local register.

pH-metry will be performed before and two years after surgery in a subgroup of patients using the Bravo-capsule.[16] The capsule is attached to the mucosa of the distal oesophagus during gastroscopy.

The capsule dislodges by itself after 4-6 days and does not have to be removed. The capsule transmits data wirelessly to a receiver outside the body. It causes little or no discomfort to the patient, and allows continuous pH-measurement during a period of 48-72 hrs.

Følsomhet Intern (gul)

Patients having reflux symptoms responding to PPI, but with non-acidic reflux (as evaluated by the Bravo capsule) will be offered pH-impedance measurements in order to characterize the reflux further.

5.1.4 Methodology

Data will be collected prior to the operation and at six weeks, one year, two years and five years after the operation. Clinical data, and answers to the PRO questionnaires will be collected and entered into the local register at these points except at six weeks where only data on complications will be entered. Data completeness at each time point will be assessed continuously at each hospital. Interim analysis will be performed every six month for 30 day complications, and every 12 months for primary endpoints.

5.1.5 Measures to minimise bias

The study is a multicentre study with participating hospitals from at least two countries (Norway and Sweden). Patients will be allocated by randomization, and patients, health care workers and investigators will be blinded. The surgeons operation note will state that "randomization was performed according to protocol" and will not contain information on whether gastropexy was performed or not. The study coordinator at each hospital will be responsible for keeping an updated list of patients participating in the study including who has received a pexy or not. This information must be stored at a safe place and in such a way that it can be made available for caregivers if deemed necessary. An updated list should be sent to SOReg-N on the first day of every month (see also 6.6.2).

All details regarding surgical technique except whether a pexy was performed or not must be registered in SOReg. To adjust for possible surgeon-related influence on outcome, a code number must be registered in SOReg for the individual main operating surgeon. A code number will be administered from SOReg-N to qualified surgeons whom will receive an envelope containing five numbers, and each participating surgeon within that hospital must draw one number after having been certified either by the study administrator or by a locally qualified surgeon. In Sweden the prefix for each number will be "S" and in Norway "N". The individual surgeon must use the same code number during the whole study period.

Patients will be informed about the importance of follow-up both for clinical and investigational reasons. For PRO, one reminder will be send to non-responders.

5.1.6 Including more subjects to compensate for drop-outs

If the recruitment of patients are lower than expected in Norway and Sweden, hospitals in other countries (primarily Netherland) will be invited to participate.

In order to reduce drop-outs, patients will be randomized in the operating room after being anesthetized and after the surgeon has decided to proceed with a LSG, but before surgery starts. Randomization will be performed by the use of sealed envelopes containing information on group allocation. Any patient who has signed for participation but are withdrawn before randomization will be replaced by one new subject. A list of patient(s) who withdraw after inclusion must be kept at the participating hospital and the reason for withdrawal must be stated. This list should be presented to SOReg-N on the first day of every month (see also 6.6.2).

Patients who withdraw or are withdrawn from the study after randomization cannot be replaced.

Følsomhet Intern (gul)

5.2 **Study treatment**

5.2.1 Description

The surgical technique of LSGG is described in detail in appendix 2. Furthermore, a video of the technique will be made avaliable.

5.2.2 Justification comparator

The comparator will be LSG performed in the same way without gastropexy.

5.2.3 Concomitant therapy

Crural repair for all patients with a Hill grade IV, and for Hill grade III if judged necessary by the operating surgeon and in accordance with the first international consensus conference on reflux and LSG.[17] The repair should be performed to such an extent that the diaphragmatic crura comes close to the oesophageal wall. Crural repair is shown in the illustrating video.

6 RISKS AND BENEFITS

Complications that might appear are assumed to be similar to what is already known for the LSG.

6.1 **Anticipated clinical benefits**

The anticipated benefit will be reduced incidence of GORD. If so, for the individual patient this should have the potential to improve HRQL and reduce the need for ARM and reoperation due to GORD. On a societal level this could reduce costs for ARM and possibly reduce the necessity for postoperative surveillance.

6.2 **Anticipated adverse events**

Leaks, excess bleeding, and unintentional kinking/torsion/stricture of the gastric remnant could be potential adverse events. However, no increase in such events have been found in the few studies published on this technique.

6.3 **Possible interactions with concomitant treatments**

A crural repair is recommended in conjunction with LSG if the hiatus is enlarged.[17] Although this is recommended by experts through consensus statements, it is per as today not always performed. In this study it will be standard to perform crural repair if indicated (see 5.2.3), independent of what group the patients is allocated to. A crural repair by itself might influence GORD, but since it will be performed on the same indications in both groups, the specific influence of gastropexy can be studied independently of whether crural repair have been done or not.

6.4 Steps to be taken to control or mitigate risks

A video illustrating the surgical technique of gastropexy and crural repair will be available. Surgical teams who wish to participate in the study must record a video illustrating the performance of the LSGG. This video will be presented to the TSC who will evaluate the performance and decide whether to allow entrance to the study or not.

Følsomhet Intern (gul)

6.5 Subjects

6.5.1 Inclusion criteria

Inclusion criteria will be based on guidelines for bariatric surgery as stated by IFSO/ASMBS:[18]

- BMI ≥ 35

6.5.2 Exclusion criteria

The following must not be present at the time of enrolment:

- Age below 18 years
- Previous bariatric surgery
- Previous antireflux surgery
- Use of acid-reducing medication (ARM) for other reasons than reflux
- Inability to comprehend and respond to the PRO questionnaire
- LSG planned as the first step of a Biliopancreatic Diversion with Duodenal Switch (BPDDS).

6.5.3 Criteria for withdrawal or discontinuation

Subjects can withdraw from the clinical study at any time without any rationale, and without compromising their future medical care. Patients may withdraw from the PRO-part, but still be included in the rest of the study procedures. Patients who are withdrawn from the study will be followed according to standard care.

6.5.4 Enrolment

Patients with obesity who qualifies for bariatric surgery (see 6.5.1) and are being planned for LSG are candidates for enrolment in this clinical study. Following review of the inclusion and exclusion criteria, eligible subjects will be invited to participate in this clinical study. Information on the study, the fact that it involves research, the purpose of the clinical study, potential risks/benefits and the necessity of including individual information on height, weight, diseases, use of medication, smoking and findings at gastroscopy will be given to the subject.

All subjects must give written informed consent prior to participation. Once the subject has given written informed consent, they can be enrolled into the clinical study.

Hospitals might differ in regard to selection criteria for offering LSG, and also how the LSG is performed. This study is not intended to influence on the individual hospital selection criteria, but when a patient is included in this study, the protocol should be followed.

The subject's participation in this clinical study is completely voluntary. If the subject decides not to participate in the clinical study, their decision will have no impact on any services or treatment the subject are currently receiving, and will also not affect their relationship with their caregivers. Subjects are allowed to withdraw their participation at any time during the course of the study without sacrificing their rights as a patient or compromising their quality of medical care.

6.5.5 Duration of the clinical study

The duration of the study will partly be dependent on the number of participating hospitals, partly on the number of LSG`s performed within these hospitals, and partly on the patients willingness to participate. The date of operation for the first included patient represent the

Følsomhet Intern (gul)

study start date, and the final follow-up is five years after the day of operation of the last patient. We estimate an inclusion period of two years, hence the maximum time from inclusion to last patient visit will ideally be four years for the two-year data, and seven years for the five-year data. Allowing six months for delayed follow-ups, and six months for data processing/cleaning, the total duration for the clinical study will be eight years. See figure 1 (chapter 3.3) for time-schedule of the project.

6.5.6 Expected subject duration

The treatment period for the individual patient will be five years.

6.5.7 Number of subjects

A total of 900 patients will be randomized, see chapter 7.2.

6.5.8 Time to select all subjects

The study will remain open for enrolment until the planned number of subjects is randomized (n=900), estimated to approximately two years.

6.6 **Procedures**

6.6.1 Clinical study procedures

At the screening visit the following tests and examination will be carried out to screen eligible subjects and provide baseline information for those patients that meet the study criteria:

- History and physical examination including height, weight and blood pressure.
- Laboratory tests.
- Gastroscopy, pH-metry and impedance measurements in a subgroup of patients (n=30).

All tests must be completed not more than six months prior to undergoing the LSG unless otherwise stated.

PRO-questionaires and the GerdQ will be answered by the patients preoperatively and at one, two and five years.

Follow-up: The time point for follow-up will be six weeks, and one, two and five years after the operation. The six-week follow-up will focus on complications. At the one, two and five year follow-up, clinical, biochemical and PRO-data including GerdQ will be collected. Gastroscopy and pH-metry will be performed two years after the operation, and the findings will be reported using the same standardized form as the preoperative gastroscopy (appendix 1).

6.6.2 Activities performed by representatives for research responsible institution and participating hospitals

The research responsible institution will have the main responsibility for the study. This includes writing and revising the research protocol, EC application with attachments, site documentation (video documentation) from each hospital before entry to the study, distributing envelopes with codes for participating surgeons, distributing sealed envelopes for randomization, receiving and storing the data in a secure database, data management and statistics. Surveillance and management of adverse events will be performed in cooperation with the TSC.

Følsomhet Intern (gul)

One representative for each participating country will be responsible for writing an EC application applicable for his or her country.

Each participating hospital will point out one person to coordinate the study within that hospital. This includes patient recruitment, obtaining written informed consent, local data management, correspondence with the national coordinator and with the Project Leader / institution responsible for this study. All included patients will be given a unique patient ID number. This number is the ID that is generated automatically by SOReg. All included patients in Sweden will thus have a six digits code number and all included patients in Norway will have a five digits code number. An updated list of included patients with overview of group allocation must be kept in a safe place within the hospital. A copy of this list containing the patient ID (no name or other identifiable data) shall be sent to SOReg-N on the first day of every month (see also 5.1.5 and 5.1.6 and appendix 17.6). Hospitals participating in the Bravo-arm of the study must balance the number of patients themselves so that an equal number of patients are allocated to the pexy and no-pexy group, respectively.

6.6.3 Factors that may compromise the outcome of the clinical study / interpretation of the results

This study is a randomized trial where the patients will be randomized into two groups. Potential differences between the groups like age, preoperative use of ARM and smoking will be accounted for by statistical methods.

Potential differences in performance between surgeons will be explored and adjusted for by statistical methods if found.

Missing values at two years will be accounted for by multiple imputation as necessary. Missing value at baseline will exclude the patient from the study.

Potential differences in culture and tradition between hospitals and countries for prescribing ARM, and similarly potential differences among patients demand for having ARM will be sought overcome by standardizing the information: ARM used in conjunction with the operation should be stopped at the latest by four weeks postoperatively. Patients using ARM after this period should actively be asked about this at the first follow-up (usually six weeks), and if no obvious reason exists it should be stopped. Similarly, if a patient is using ARM at the one-, two- or five year follow-up, the reason for this should be addressed.

Indications for reoperations due to GORD should be similar between institutions participating in this study. In general, patients having severe reflux symptoms despite high-dose ARM, and patients having endoscopically visible oesophagitis despite high-dose ARM could be considered for reoperation. Reoperations due to GORD are expected to be low during the first two years after the primary operation but possibly higher after five years.

6.6.4 Follow-up

The time point for follow-up will be six weeks and one, two and five years after the operation. This is an established pattern for follow-up after bariatric surgery, and patients in this study will not deviate from this. Primary outcome is continuous use of ARM due to reflux symptoms at two years after surgery, or reoperation due to GORD within two years postoperatively. This should be a sufficient period of time to represent a realistic test of the performance of the study treatment, and allow any risks associated with potentially adverse effects over that period to be identified and assessed. One-year data will not be published separately. This is partly because it is generally not recommended to publish data for outcome with less than two-year follow after bariatric surgery, and partly because according to the literature there is an increase in the use of ARM after LSG also between one and two years postoperatively.

Følsomhet Intern (gul)

The follow-up visit at one, two and five years will include collection of the same data as for baseline, but gastroscopy and pH-metry will only be performed at the two-year follow-up. PRO-data at follow-up will be collected internet-based if possible.

6.6.5 Follow-up medical care

All patients having participated in the study will receive medical care and follow-up as all other patients according to national and/or hospital routine.

7 STATISTICAL CONSIDERATIONS

7.1 Statistical design

Patients will be allocated in a 1:1 fashion between LSG and LSGG. Participating hospitals will administer this by block randomization with 10 patients (i.e. 5 LSG, 5 LSGG) in each block. Group allocation will be determined by opening of sealed envelopes. The envelopes will be distributed to participating hospitals from SOReg-N.

All patients will be given a unique patient number, and SOReg-N will be informed regularly about group allocation.

Analysis for outcome will be performed according to ITT. All patients will thus be analysed within the allocated group. Missing data at two and five years will be handled by multiple imputation. The main analysis for outcome will be based on logistic mixed effect models with odds ratio between groups corrected for age, smoking and surgeon. A sensitivity analysis including hospitals will also be performed.

Information on group allocation will be blinded to patients and researchers.

7.2 Sample size

LSGG are presently being performed in a small minority of hospitals in Norway, but the technique used differs between hospitals and surgeons making the results difficult to interpret. However, in order to avoid a potential influence from these hospitals on the power calculations, these hospitals have been excluded from this sample size evaluation.

The sample size calculation is based on stipulated changes in the use of ARM since we gather this as the most relevant known clinical variable reflecting patients symptoms.

According to recent, unpublished data from SOReg-S and SOReg-N, we find a three-fold increase in the use of ARM from preoperatively until two years after LSG for both countries. The prevalence of ARM-use before LSG however differs between the countries: In Norway, approximately 7% of the patients are using ARM on a daily basis while the corresponding figure in Sweden is approximately 5%.

In Norway, the use of ARM increase from 7 % to approximately 20 % as a mean observed at the two-year follow-up, while in Sweden the corresponding numbers are 5 % increasing to approximately 13%.

Since the population and number of hospitals performing bariatric surgery in Sweden is about twice that of Norway, we estimate a 2:1 composition of participants. Hence, the composite figures will be ≈ 6 % at baseline, increasing to ≈ 16 % at two years.

In order to account for a potential improvement in the LSG-group because of participation in a study (the Hawthorn-effect), the estimated rate for ARM-use in the LSG-group at two years will be set at 14 %.

Følsomhet Intern (gul)

According to the clinical experience encountered by Våge et al, adding gastropexy to the LSG reduced a rise in the use of PPI from preoperatively until two years. Stipulating a change from 6 to 14% in the LSG group, and from 6 to 7% in the LSGG-group, this will require a total of 686 patients using power 1 – beta = 85 %.

7.3 The level of significance and power of the clinical study

We have used the significance level of alpha = 5 % and power 1 - beta = 85 %.

7.4 Expected drop out rates

Based on clinical experience we estimate a drop out rate of ≈ 20% at two years. Adding this to the equation will make it necessary to randomize 858 patients. To be on the conservative side we plan to randomize 900 patients.

7.5 Pass/fail criteria

Using ARM or having been reoperated due to GORD will be classified as a failure for the main outcome.

7.6 Provision for interim analyses

Interim analysis will be performed for complications by the DMC. Complications will be evaluated and compared between the two groups based on 30 day morbidity rates by data extraction and analysis every sixth month.

7.7 Criteria for stopping the clinical study

Major complications possibly related to the surgical technique will be looked into and evaluated in detail.

Significantly more complications in one of the groups will be discussed in the TSC and if needed, necessary actions will be taken if needed.

7.8 Specification of subgroups

Gastroscopy and pH-metry of the distal oesophagus will be performed in a subgroup of 30 patients in hospitals where the Bravo capsule is available. Patients suspected of having non-acid reflux will be recommended pH- impedance measurements.

Patients having been reoperated due to reflux will be classified as failures and analyzed together with the ARM-group in their original cohort (LSG or LSGG), according to the ITT-principle.

Patients having been reoperated for other reasons (rare) will also be included in the ITT analysis.

7.9 Procedures to take into account all subject data

Patients reoperated due to reflux will be grouped together with patients in the same group as those using ARM, thereby making ITT analysis possible for both main outcomes.

7.10 Treatment of missing, unused, spurious data

Missing data for outcome will be handled by multiple imputation. For main outcome and PRO at two years this will be based on baseline and one-year data, while for the secondary outcome of endoscopic (and pH metry) findings this will be based mainly on baseline data.

Følsomhet Intern (gul)

Similarly, missing data for five years will be handled by multiple imputation including two-year data.

Continuous variables will also be analysed by mixed effect models that can handle missing values.

Patients with missing baseline data will be excluded from the study.

Since every patient will be assigned a unique identifying number it will be possible to double-check any spurious data against the patients medical record. Spurious data discovered within a participating hospital will be double-checked against the patients medical record before transferring to the common study database in Norway. For spurious data discovered after transfer to the common database, the project leader will contact the national coordinator or the participating hospital querying the data.

7.11 Exclusion of data from hypothesis testing

Patients will be excluded for main outcome (hypothesis testing) if baseline data is missing.

7.12 Min/max number of subjects per centre (multi-centre study)

The minimum number will be 10, and the maximum 200 subjects per center.

7.13 Special reasoning

Beside what is mentioned above, we do not see any special statistical reasoning pertaining to this study as per today.

8 DATA MANAGEMENT

8.1 Procedures for data review, database cleaning, and issuing and resolving queries

Each participating country will have a national coordinator who will review the captured data and query individual hospitals for odd values. Only reviewed and cleaned data will be transferred to the central database in Norway.

This study will have a TSC consisting of five members: Two from Norway (including the project leader) and three from Sweden. If more countries are included, one representative from each other country will be included. The TSC will carry the main responsibility for the study. Potential queries not intended for the DMC will be solved in the TSC.

8.2 Procedures for verification, validation and securing electronic data systems

Data will be entered manually into an approved register. In Norway and Sweden this will be SOReg. Each patient will be deidentified and given a unique number before transferring data to the central database for the project (i.e. in Norway).

8.3 Procedures for data retention

All data will be transferred to, and retained in a secure database at Helse Førde, Norway. Only the project leader and approved researcher(s) will have access to the database.

8.4 Specified retention period

The main focus will be on data from the two-year follow-up, however data from five year follow-up will also be published. The inclusion-period will be 2023 – 2024, and collecting five-year data will extend into 2030. It is stipulated that publications based on five-years data will extend through 2032.

Følsomhet Intern (gul)

Documentation for the clinical study will be retained for a period decided by the EC/REC, usually **five years** after the final study report/publication (Norway). Since we stipulate the last publication to be in 2032 the data will be deleted before 2038.

9 AMENDMENTS TO THE RESEARCH PROTOCOL

The Research Protocol may require to be amended during the conduct of the study. Any amendment to the Research Protocol will be agreed upon in the TSC. The amendments will be approved by the ethics committee (EC/REC).

10 DEVIATIONS FROM THE RESEARCH PROTOCOL

10.1 Statement that investigator is not allowed to deviate from the research protocol

The study will be performed in accordance with this research protocol.

10.2 Procedures for recording, reporting and analyzing protocol deviations

All research protocol deviations will be reviewed by the representative for the research responsible institution for impact on subject's participation in the clinical study. The representative for the research responsible institution will notify the project leader of deviations. All deviations will be reported to the appropriate regulatory bodies as required.

11 STATEMENTS OF COMPLIANCE

11.1 Statement of compliance with ethics principles

The study will be performed in accordance with the ethical requirements defined in the Declaration of Helsinki.[19]

11.2 Statement regarding ethical approval

The clinical study shall not commence until written approval/favourable opinion is given from the REC. Such approval will be obtained for each participating country separately.

11.3 Additional requirement from ethics committee

The clinical study performance will include any additional requirements requested/mandated by the EC/REC.

11.4 Statement of insurance cover

In Norway, patients are covered by "Norsk Pasientskadeerstatning". In Sweden, patients are covered by "Patientförsäkringen" (Patient Insurance)

12 INFORMED CONSENT PROCESS

12.1 General informed consent

Informed consent shall be obtained in writing from the subject prior to inclusion in the study.

The process must adhere to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the clinical study, the investigator will have EC/REC approval / favourable opinion of the written informed consent form and any other information intended to be provided to the subjects.

Følsomhet Intern (gul)

Authorised personnel will conduct the informed consent process of explaining the clinical study to the subject as well as providing the subject with a copy of the subject information sheet. The consent information will include all aspects of the clinical study that are relevant to the subject's decision to participate in the language in which the subject is most proficient. The language will be non-technical and easily understood.

The informant will avoid coercion, will not appear to waive the subject's legal rights in any way, will allow sufficient time for the subject to inquire about the details of the clinical study, ask any questions and make the decision to participate or not in the clinical study.

Should the subject decide to participate in the clinical study, the informed consent form will be signed and personally dated by the subject and by the authorised person who conducted the informed consent discussion. A copy of the consent form will be given to the subject. Any significant and relevant new information that arises during the course of the clinical study will be provided to the subject and their consent to continue will be sought.

12.2 **Informed consent, where subject is unable to give informed consent (incapacity/emergency)**

This study will not include such subjects.

13 ADVERSE EVENTS

13.1 **Definition of adverse event (AE)**

An adverse event (AE) is defined as any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs in subjects, users or other persons, whether or not related to the study treatment.

This includes:

- Events related to the study treatment or the comparator
- Events related to procedures involved (any procedure in the research protocol)

13.2 **Definition of serious adverse event (SAE)**

Serious adverse event (SAE) is any event (whether or not associated with the study treatment) that:

1. Results in death
2. Lead to serious deterioration in the health of the subject that either resulted in
   a) life threatening illness or injury, or
   b) a permanent impairment of a body structure or a body function, or
   c) in-patient or prolonged hospitalization, or
   d) need of medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or body function.

NOTE: This includes events that might have led to a serious adverse event if

a) suitable action had not been taken or,

b) intervention had not been made or,

c) the circumstances had been less fortunate.

Følsomhet Intern (gul)

These are handled under the SAE reporting system.

NOTE: Planned hospitalisation for a pre-existing condition, or a procedure required by the research protocol, without serious deterioration in health, is not considered a serious adverse event.

13.3 **Reporting adverse events**

Adverse events occurring during the study will be captured in the register and categorized according to the Clavien Dindo score. Patients will be followed according to the protocol, but with additional support as needed.

All adverse events shall be reported according to juridical guidelines for the actual hospital or nation.

13.4 **List of foreseeable adverse events, anticipated adverse treatment/intervention effects.**

Leaks, excess bleeding, and unintentional torsion of the gastric remnant could be potential adverse events. However, no increase in such events have been found in the very few studies published on this technique.

13.5 **Emergency contact details for reporting SAEs**

All adverse events will be entered into the register by the bariatric surgical team. In addition, unexpected serious adverse events shall be reported to the national coordinator by telephone at an early stage. The national coordinator will forward the report to the Principal Investigator (= the trial statistician, which is the statistician working in SOReg-N), and a decision will be made as to whether inform the DMC immediately or at the regular DMC-meeting that will occur every six months.

13.6 **Data monitoring committee (DMC)**

Members and terms of reference:

The DMC will have three members: Two experts (one surgeon and one medical gastroenterologist) with a special knowledge of LSG and reflux, and one statistician. The DMC shall:

1. Monitor the data from the trial and make recommendations to the TSC (following each DMC meeting) on whether there are any ethical or safety reasons why the trial should not continue.

2. Ensure that the safety, rights and well-being of the trial participants is given highest priority.

3. Determine if additional interim analysis of trial data should be undertaken.

4. Consider the data from interim analyses, unblinded if considered appropriate, plus any additional safety issues for the trial and relevant information from other sources.

5. Consider any requests for release of interim trial data and to recommend to the TSC on the advisability of this.

6. The DMC may be asked by the TSC to consider data emerging from other related studies.

Følsomhet Intern (gul)

DMC meetings:

The DMC shall meet every six months, or more often if deemed necessary. Meetings will be called for and organized by the Principal Investigator of the trial in association with the Chairperson of the DMC. Dates for DMC meetings should be agreed in advance, and only altered with agreement of all members. All significant communications between the Principal Investigator and the DMC shall be in writing, or if they have to be verbal, they should be backed up by written records.

The role of the DMC is to look at the (unblinded) data from an ethical standpoint, the safety rights and wellbeing of the participants being paramount. The DMC is the only body involved in the trial that has access to the unblinded comparative data.

DMC Processes

The Principal Investigator should prepare a comprehensive report for the DMC. This should be prepared and circulated well in advance of the meeting to allow DMC members time to study the data. The content of the report should be agreed in advance with the DMC Chairperson. The trial statistician may be invited by the Chairperson to attend part of the meeting to present the data; otherwise, no one involved with the trial or TSC should be present to see the unblinded data.

A full confidential report should be made in writing by the Chairperson of the DMC providing advice to the TSC on whether the trial should continue or not. It is the responsibility of the TSC to decide whether or not to act on the information received from the DMC.

Information provided by the DMC is likely to fall into the following categories:

- Information that might lead to the TSC stopping the trial prematurely in the event of a clear outcome if this is deemed to be appropriate in light of the accumulating data from the study or on the basis of information available from other sources.

- Information that might lead to the TSC modifying the design of the trial if this is deemed to be appropriate in the light of the accumulating data from the study or on the basis of information available from other sources.

Følsomhet Intern (gul)

14 SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL STUDY

14.1 Criteria for suspension of the whole clinical study or in one or more sites

Potentially clinical relevant deviation in the number of serious events between the two groups (LSG – LSGG) will be discussed in the bi-annual meetings in the DMC. Similarly, interim-analysis will be performed on one-year follow-up data, and if differences in main outcome is found this will be addressed by the DMC. If the deviation is at one or a few sites only, these hospitals will be suspended until an explanation has been found. The steering committee will then decide whether or not to allow re-entry of this/these hospitals.

The study may be terminated by the representative for the research responsible institution or the investigator at any time. However, scheduled follow-up, as described in paragraph 6.6.4 and 6.6.5 should be continued for all subjects who were treated prior to termination of the study.

14.2 Criteria for un-blinding

Un-blinding on a subject level can be performed at any time if deemed necessary by the clinicians taking care of the patient. Un-blinding the clinical study as a whole requires major differences in the main outcome either at the interim-analysis on one-year data, or in the final results. Un-blinding the clinical study also requires agreement in the TSC to do this.

14.3 Requirements for subject follow-up

The project leader will be the person in charge from the research responsible institution. Subject follow-up will be surveilled by the local representative for the study in each participating hospital. In general, patient follow-up will be the same independently of whether a patient is included in the study or not. If necessary, the local representative will contact the national coordinator or the project leader if any queries concerning follow-up of a particular patient.

15 PUBLICATION POLICY

The study will be registered at ClinicalTrials.gov before starting.

Upon study completion, the results of this study will be submitted for publication in peer-reviewed journals.

A summary of the study findings will be submitted to the Ethics Committee according to national regulations in Norway.

All personnel who have contributed significantly with the planning and performance of the study (Vancouver convention 1988) may be included in the list of authors.

16 BIBLIOGRAPHY

List of some bibliographic references pertaining to the clinical study:

1. Brown W, Kow L, Shikora S, et al. 6th IFSO Global Registry Report 2021. 2021.
2. Altieri MS, Pryor AD. Gastroesophageal reflux disease after bariatric procedures. *Surg Clin North Am* 2015; 95(3):579-91.
3. Saber AA, Shoar S, Khoursheed M. Intra-thoracic Sleeve Migration (ITSM): an Underreported Phenomenon After Laparoscopic Sleeve Gastrectomy. *Obes Surg* 2017; 27(8):1917-1923.

Følsomhet Intern (gul)

4. Genco A, Soricelli E, Casella G, et al. Gastroesophageal reflux disease and Barrett's esophagus after laparoscopic sleeve gastrectomy: a possible, underestimated long-term complication. *Surg Obes Relat Dis* 2017; 13(4):568-574.
5. Vage V, Behme J, Jossart G, et al. Gastropexy predicts lower use of acid-reducing medication after laparoscopic sleeve gastrectomy. A prospective cohort study. *Int J Surg* 2020; 74:113-117.
6. 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(2):257-265.
7. Campos GM, Mazzini GS, Altieri MS, et al. ASMBS position statement on the rationale for performance of upper gastrointestinal endoscopy before and after metabolic and bariatric surgery. *Surg Obes Relat Dis* 2021; 17(5):837-847.
8. Brown WA, Johari Halim Shah Y, Balalis G, et al. IFSO Position Statement on the Role of Esophago-Gastro-Duodenal Endoscopy Prior to and after Bariatric and Metabolic Surgery Procedures. *Obes Surg* 2020; 30(8):3135-3153.
9. Berstad A, Weberg R, Froyshov Larsen I, et al. Relationship of hiatus hernia to reflux oesophagitis. A prospective study of coincidence, using endoscopy. *Scand J Gastroenterol* 1986; 21(1):55-8.
10. Stene-Larsen G, Weberg R, Froyshov Larsen I, et al. Relationship of overweight to hiatus hernia and reflux oesophagitis. *Scand J Gastroenterol* 1988; 23(4):427-32.
11. 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(10):1030-8.
12. Aasprang A, Vage V, Flolo TN, et al. Patient-reported quality of life with obesity - development of a new measurement scale. *Tidsskr Nor Laegeforen* 2019; 139(11).
13. Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999; 45(2):172-80.
14. Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. *Gut* 2018; 67(7):1351-1362.
15. Kahrilas PJ, Kim HC, Pandolfino JE. Approaches to the diagnosis and grading of hiatal hernia. *Best Pract Res Clin Gastroenterol* 2008; 22(4):601-16.
16. Hasak S, Yadlapati R, Altayar O, et al. Prolonged Wireless pH Monitoring in Patients With Persistent Reflux Symptoms Despite Proton Pump Inhibitor Therapy. *Clin Gastroenterol Hepatol* 2020; 18(13):2912-2919.
17. Assalia A, Gagner M, Nedelcu M, et al. Gastroesophageal Reflux and Laparoscopic Sleeve Gastrectomy: Results of the First International Consensus Conference. *Obes Surg* 2020; 30(10):3695-3705.
18. Eisenberg D, Shikora SA, Aarts E, et al. 2022 American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. *Obes Surg* 2022.
19. World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310(20):2191-4.

17 APPENDICES

17.1 Surgical technique

Laparoscopic sleeve gastrectomy with gastropexy (supplementary to the video).

The greater curvature has been mobilized from the pylorus to the left crus. The hiatus is briefly explored and in this patient the hiatal opening does not seem enlarged. If enlarged[1], a crural

Følsomhet Intern (gul)

repair should be done if possible, leaving the diaphragmatic opening about the size of the oesophagus.

A 32 french tube is passed into the stomach and down to the pylorus. Torsion of the stomach while stapling is avoided.

The resection is started 1-2 cm from the pylorus. This surgeon prefers to use a black cartridge on the antrum to avoid cracks in the serosa. The resection at this part is performed loosely along the 32 french tube.

Above the incisura angularis the stapler is closer to the 32 fr tube.

The resection continues in a straight line along the tube, and ends one cm lateral to the gastro-oesophageal junction. Whether to staple through the fat pad like here, or remove parts of the fat pad in order to better visualize the gastro-oesophageal junction can be decided by the operating surgeon.

The gastric tube is removed.

Whether the upper end of the staple line is oversewn, inverted or reinforced by other means is decided by the operating surgeon. In this case no suturing or reinforcement is used.

It is important that the gastropexy starts at the upper end of the staple line. A 2-0 non-absorbable suture like Etibond is used.

The gastro-splenic ligament is approached and sutured to the upper end of the staple line. It is important to catch a good bite of the gastro-splenic ligament, preferentially larger than shown here, in order to creat a cushion attempting to prevent the cardia from intrathoracic migration.

The second stitch is placed in a similar manner including a good bite of the gastro-splenic ligament. To avoid using a thinner and weaker part of the gastro-splenic ligament, and to avoid too much traction between the tissues, the surgeon here decides to go lateral to the resection-line on the gastrosplenic ligament.

If there is a dimple or kink in the staple line on the stomach, this can be lifted by the suture as shown here.

On the one hand the sutures should include good bites of the fatty ligament, while on the other hand a suture must not become too tight when approximating the tissues in order to avoid a pull-through of the fat or staple line. When pulling a suture in order to approximate tissues, the angle of traction must always be greater than 90 degrees on the staple line in order to avoid a possible cutting effect.

Further down, the gastroepiploic artery or arcade becomes visible, and the surgeon outlines the gastroepiploic arcade for us. This arcade should be included in the suture line in order to increase the support for the suture, reduce the risk of a pull-through and strengthen the force of downward traction on the gastric remnant.

Performing gastropexy on the antrum of the stomach might be somewhat more difficult because of the angulation for suturing if the “French position” is used, and some of you might want to suture backhand here. Standing on the patients right side could make this part of the suturing easier. The gastropexy is continued to well below the incisura angularis. Performing gastropexy on the last 3-4 centimetres of the staple line does probably not contribute to traction on the upper part of the gastric remnant and is therefore not a part of the study. It might however be performed based on the surgeons preference since it compresses the staple line and thereby potentially could reduce bleeding.

Følsomhet Intern (gul)

The end result of the gastropexy should be a gastric remnant without kinks and torsion, and with a continous traction from the gastrosplenic and gastrocolic ligament in order to keep the gastro-oesophageal junction below the diaphragm.

If possible, crural repair should be performed if a hiatal hernia, a Hill grade IV and possibly also if a Hill grade III has been found either on the preoperative gastroscopy or during the operation, in accordance with the 1st international consensus conference on sleeve and reflux. The cardia is mobilized and a full hiatal dissection is performed. The gastro-oesophageal junction is brought into the abdomen. A posterior crural repair is performed with non-absorbable material using double sutures. In this case also an anterior crural suture is used in order to approximate the crura to the empty oesophagus.

1. Enlarged = Hill grad IV, and possibly Hill grade III (decided by the operating surgeon).

17.2 Gastroskopi

Standard gastroskopi for Sleeve pex studien.

Under nedføring av skopet, sjå etter øsofagitt eller anna patologi i øsofagus. Dersom synleg øsofagitt; klassifiser etter Los Angeles klassifikasjonen (grad A, B, C eller D).

Skopet førast til duodenum. På veg tilbake tek ein slimhinneprøver frå antrum og corpus for analyse på Helikobakter pylori (HP). Dersom pasienten brukar PPI tek ein ikkje slimhinneprøve men i staden feces-prøve (tilrådd), alternativt blodprøve eller pusteprøve.

I øvre del av magesekken retroflekterer ein skopet og vurderer diafragmaåpninga nedanfrå. Grader diafragmaåpninga etter Hill's gradering (grad I, II, III, IV). Preoperativt er dette uproblematisk, postoperativt etter sleeve er dette oftast umogeleg.

Mål avstanden tannrekka-diafragma, deretter avstanden tannrekka GØ-overgangen på veg ut.

Dersom eit funn er mistenkeleg på Barret's; estimer lengste utstrekning i breidde- og lengderetning i cm (Prague Circumferential and Maximal extent (CM) kriteria). Berre slimhinnetunger som er ≥ 1 cm over GØ-overgangen og inneheld intestinal metaplasia blir definert som Barret's.

Ved postoperative skopiar, noter konfigurasjonen på rest-magesekken: Pen form? Striktur? Vridning? Andre spesielle forhold? (Førast under «Andre funn» i gastroskopi-skjemaet til SOReg).

Dokumenter gjerne funn med foto eller video. Ta eventuelle biopsiar til slutt.

Referansar:

1. Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999; 45(2):172-80.

2. Hill LD, Kozarek RA. The gastroesophageal flap valve. J Clin Gastroenterol 1999; 28(3):194-7.

3. Sharma P, Dent J, Armstrong D, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology 2006; 131(5):1392-9.

Følsomhet Intern (gul)

4. Weusten B, Bisschops R, Coron E, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy 2017; 49(2):191-198.

Sjå gastroskopi-skjemaet på SOReg si heimeside: Gastroskopi-skjema 2020.pdf (helse-bergen.no)

English text:

Standard gastroscopy for the Sleeve Pex study.

When starting, look for oesophagitis or other pathology in the oesophagus. If oesophagitis is observed; classify according to the Los Angeles classification (grade A, B, C, D).

Pass the endoscope to the duodenum. When retracting the scope, take mucosal-samples from the antrum and body of the stomach in order to check for Helicobacter Pylori (HP). Do not take samples if the patient is using PPI; then use fecal test (advised), blood-test or breathing test.

Retroflect the scope in the upper part of the stomach and evaluate the diaphragmatic opening from below. Grade the opening according to Hill`s grade (grad I, II, III, IV). Preoperatively this is easily performed, postoperatively this is often not possible after a sleeve gastrectomy.

Measure the distance from the teeth to the diaphragm, secondly the distance from the teeth to the GO-junction.

If an area is suspicious of Barret`s; estimate the longest and broadest area in cm (Prague Circumferential and Maximal extent (CM) criteria). Only mucosal tongues that extends ≥ 1 cm up from the GO-junction and have intestinal metaplasia are defined as Barret`s.

For postoperative endoscopies: Note the configuration of the gastric remnant. Smooth form? Stricture? Torsion? Other findings? (Findings can be noted under “other findings” in the gastroscopy-modul in SOReg).

Findings should be documented by a photo or video. If biopsies are taken, these should be taken at the end of the procedure.

17.3 Kontroll av operasjonsteknikk

Video for kontroll av operasjonsteknikk før inklusjon i Sleeve pex studien.

Før ein inkluderer pasientar til deltaking i studien må ein verifisere at det kirurgiske teamet utfører operasjonen i samsvar med protokoll. Dette gjer ein ved å utføre operasjonen med video-opptak av dei sentrale delane av operasjonen: Ventrikkelreseksjon og gastropexi.

For å kunne gjere video-opptak må pasienten vere informert om studien, om at det vert gjort opptak av operasjonen, og at videoen vil bli vurdert av styremedlemmer frå styrekomiteen for studien. Det må dokumenteras i pasienten sin journal at pasienten har fått slik informasjon.

Videoen skal vere anonym, dvs den skal ikkje innehalde bilete, tekst eller liknande som kan bidra til å identifisere pasienten. Den skal berre innehalde bilete frå innsida av abdomen. Den må vise ventrikkelreseksjonen og gastropexien uredigert. Formatet må vere slik at den kan avspelast på eit framvisingsprogram som er godkjent for bruk i helsevesenet.

Video sendast på kryptert minnepenn som brevpost til: Helse Bergen, SOReg-N v/Villy Våge, Postboks 1400, 5021 Bergen. Videoen blir vurdert av medlemmer av styringskomiteen. Det kirurgiske teamet får tilbakemelding og minnepennen vert returnert.

Følsomhet Intern (gul)

English text:

Video to verify correct operation technique before including patients:

Before enrolling patients into the study, the surgical team at the individual hospital must verify that the operation is being performed according to the protocol. This is done by recording the most important parts of the operation: The gastric resection and the gastropexy.

Before recording, the patient must be informed about the study and the recording, and that the video will be evaluated by representatives for the steering committee of the study. It must be documented in the patient chart that the patient has received such information.

The video shall not contain pictures, text or other elements that can identify the patient. Only recordings from inside the abdomen must be used. The video must show the full gastric resection and gastropexy, and the format be must such that it can be shared in a safe way.

17.4 Bruk av syreblokkerande medisin

Retningslinjer for bruk av syreblokkerande medisin.

For pasientar som ikkje brukar syreblokkerande medisin før operasjon: Kan starte lågdose PPI (t.d. Somac 20 mgx1) like etter operasjon og bruke dette i inntil fire veker etter operasjon. Samstundes viktig å informere pasienten om at dersom problem med oppstøyt etter fire veker kan fastlege skrive ut ny resept.

For pasientar som brukar syreblokkerande medisin før operasjon: Kontinuer fram til operasjon. Start lågdose PPI etter operasjon og kontinuer i inntil fire veker. Samstundes viktig å informere pasienten om at dersom vedvarande problem med oppstøyt etter fire veker så kan fastlege skrive ut ny resept.

Alle tablettar (inkl PPI) som pasienten tek dei to første vekene etter operasjon må vere mindre enn ei ert for å unngå potensiell skade på stifterekka i magesekken. Tablettar som er større og som pasienten treng må delast eller knusast.

Ved kontrollar (6-vekers, eit år, to år, fem år): Dersom pasienten fortsatt brukar PPI eller anna syreblokkerande medisin, spør om dette. Vurder kvifor pasienten brukar PPI, om det er behov for å bruke PPI eller om pasienten kan trappe ned og slutte.

English text:

Guidelines for the use of acid-reducing medication (ARM):

For patients not using ARM before the operation: Patients may start a low dose PPI (like 20 mg pantoprazole once daily) just after the operation and use this for four weeks. The patient must be informed that if reflux symptoms persists after four weeks the doctor can write a new prescription.

For patients using ARM before the operation: Continue the use of ARM until the operation. After the operation the patient should use a low dose PPI for four weeks as above. The patient must be informed that if reflux symptoms persists after four weeks, the doctor can write a new prescription.

All tablets that a patient must use during the first two weeks after the operation (including PPI) must be smaller than a pea in order to avoid potential damage to the staple line. Tablets that are larger must be split into parts that are smaller than a pea.

Følsomhet Intern (gul)

At follow up (six weeks, one year, two years, five years): If the patient still uses PPI or other ARM, ask the patient about this. Evaluate why the patient is using ARM and whether this can be stopped.

17.5. Reoperasjon grunna refluks.

Retningslinjer om indikasjon for reoperasjon grunna refluks.

Reoperasjon kan vere aktuelt for pasientar med:

- Uttalte refluks-symptom trass høgdose PPI (t.d. nattleg regurgitasjon).
- Endoskopisk synleg øsofagitt trass høgdose PPI.

English text:

Guidelines on the indication for a reoperation due to reflux.
A reoperation might be performed for patients with:

- Severe reflux symptoms despite using a high dose PPI (like nightly regurgitations).
- Endoscopic visible oesophagitis despite using a high dose PPI.

17.6 Månadsvis oversikt over inkluderte pasientar ved eit sjukehus.

Sjukehus:	
År:	**Månad:**
Pasientar randomisert (n):	
Pexi (SOReg-PID):	
Ikkje pexi (SOReg-PID):	
Pasient trekt frå studien etter inklusjon (SOReg-PID og årsak):	

English text:
Monthly overview of included patients from a hospital.

Hospital:	
Year:	**Month:**
Patients randomised (n):	
Pexy (SOReg-PID):	
No pexy (SOReg-PID):	
Patients removed from the study (SOReg-PID and the reason for removal):	

Følsomhet Intern (gul)