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BMJ Open

Prospective multicentre randomised trial comparing the efficacy and safety of single-anastomosis duodeno–ileal bypass with sleeve gastrectomy (SADI-S) versus Roux-en-Y gastric bypass (RYGB): SADISLEEVE study protocol

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ABSTRACT

Introduction Despite the non-negligible weight loss failure rate at midterm, Roux-en-Y gastric bypass (RYGB) remains the reference procedure in the treatment of morbid obesity with metabolic comorbidities. A recently emerged procedure, the single anastomosis duodeno–ileal bypass with sleeve gastrectomy (SADI-S), could be more effective on weight loss with similar morbidity and lower weight loss failure rate than RYGB. We propose the first randomised, open, multicentre superiority trial comparing the SADI-S to RYGB (SADISLEEVE).

Methods and analysis The main objective is to demonstrate the superiority at 2 years after surgery of the SADI-S compared with RYGB in term of excess weight loss percentage. The secondary objectives are the evaluation of nutritional status, metabolic outcomes, overall complication rates and quality of life, within 2 years after surgery. Key inclusion criteria are obese patients with body mass index (BMI) ≥40 kg/m^2 or ≥35 kg/m^2 with at least one comorbid condition and candidate to a first bariatric procedure or after failure of sleeve gastrectomy. Patients randomised by minimisation in two arms, based on centre, surgery as a revisional procedure, presence of type 2 diabetes and BMI >50 kg/m^2 will be included over 2 years. A sample size of 166 patients in each group will have a power of 90% to detect a probability of 0.603 that excess weight loss in the RYGB arm is less than excess weight loss in the SADI-S arm with a 5% two-sided significance level. With a drop-out rate of 10%, it will be necessary to include 183 patients per group.

Ethics and dissemination The study was approved by Institutional Review Board of Centre Hospitalier Universitaire Morvan (CPP1089-HPS1). Study was also approved by the French national agency for drug safety (2018061500148). Results will be reported in peer-reviewed scientific journals.

Strengths and limitations of this study

- This is a first randomised controlled trial single anastomosis duodeno–ileal bypass with sleeve gastrectomy comparing with Roux-en-Y gastric bypass.
- The multicentre design of the study including public and private hospitals of France increase the external validity of the results.
- Participants and treatment providers cannot be blinded due to the nature of the surgical procedures.
- Adherence of patients to follow-up is a real challenge.

Trial registration number NCT03610256.

INTRODUCTION

Obesity is a major public health problem worldwide. Since the early 2000s, bariatric surgery has proved to be the most effective treatment of morbid obesity in terms of weight loss and improvement of comorbidities during long-term follow-up.[1–3] Therefore, the number of bariatric procedures has increased exponentially, and bariatric surgery is now accepted as reference treatment of morbid obesity.[4] Since its first description in the early 1960s, the reference procedure in the treatment of morbid obesity remains the Roux-en-Ygastric bypass (RYGB)[5] (figure 1) for most bariatric teams. The RYGB has the advantage of affording a sustained weight loss with an average of 85% of excess weight loss (%EWL) at 2 years calculated as follows: ((initial weight – weight at 2-year visit)

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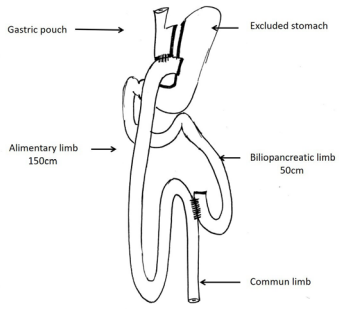


Figure 1 Roux-en-Y gastric bypass.

/ (initial weight –optimal weight)) × 100, and has a strong metabolic effect, particularly with regard to type 2 diabetes remission.[3 6–8] However, failures that is defined as insufficient weight loss at 18 months after surgery (%EWL <50) or as weight regain (+20% of nadir weight) are observed in the long term (up to 20%), particularly in super obese patients (body mass index (BMI) >50 kg/m²).[9 10] In this population, biliopancreatic diversion with duodenal switch (BPD-DS) is suggested due to its greater weight loss and metabolic effect[11 12] but is still little performed worldwide (<1%) because of its higher morbidity, surgical complexity and risk of malnutrition.[1 13]

A new procedure combining the physiological advantages of pylorus preservation and the technical benefits of single-loop reconstruction was introduced by Sánchez-Pernaute[13] in 2007, who described the single anastomosis duodeno–ileal bypass with sleeve gastrectomy (SADI-S) as an evolution of the BPD-DS: the SADI-S has the advantage of decreasing the complexity of the BPD-DS by avoiding one of the two intestinal anastomoses, making it technically easier and potentially less morbid (less internal hernia, anastomotic leaks and so on) (figure 2). With a 2.5 m common channel, the SADI-S seems to offer good results for the treatment of both morbid obesity and its metabolic complications, with an average %EWL up to 95% at 2 years (similar to BPD-DS) and may decrease the weight loss failure rate observed after the standard restrictive and malabsorptive procedure such as RYGB.[14–18] Moreover, when compared with BPD-DS, the SADI-S improves nutritional status probably through the increased common channel length (from 100 cm to 250 cm).[17–19] Another advantage of the SADI-S is that it is a 'one or two stage procedure', especially for super obese patients

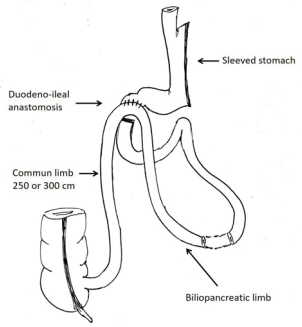


Figure 2 Single anastomosis duodeno–ileal bypass with sleeve gastrectomy.

in whom RYGB as a primary procedure is controversial due to its high operative risk and its high risk of failure.[17 20] Indeed, the SADI-S, as BPD-DS, can be a staged procedure by performing the sleeve gastrectomy (SG) first. For the second step, the SADI-S could also be an interesting alternative, as it is less morbid than the BPD-DS and seems more efficient than the RYGB. Finally, in case of SG failure, the SADI-S could be a new therapeutic option, superior to the RYGB, which has shown disappointing results in this situation.[17 20–22]

To date, there are only two non-randomised studies in progress comparing the SADI-S to BPD-DS: one from Spain (ClinicalTrials NCT01685177) and the other one from Canada (ClinicalTrials NCT02792166). Nevertheless, BPD-DS represents less than 1% of bariatric procedures and is only allowed in super obese patients in France. Thus, we only have preliminary data on SADI-S outcomes of poor scientific evidence. In the face of growing interest for this procedure, several reviews of the literature were recently published about SADI-S results.[16–18 20] These procedures also combine an SG and a single duodeno–ileal anastomosis or duodeno–jejunal enterostomy and aim to reduce the malnutrition risk observed after BPD-DS and to maintain similar weight loss and metabolic effect. Short-term literature data seem to demonstrate that SADI-S provides very good weight loss results and an improvement of the comorbidities, with good safety and reproducibility; even if larger series, long-term data and randomised control trials (RCTs) are needed to confirm these outcomes.[23]

Following the arguments set out above, we proposed a first RCT comparing the SADI-S with the RYGB.

Objectives

The main objective is to demonstrate the superiority of the SADI-S to the standard RYGB for weight loss outcomes, using the %EWL criteria at 2 years postsurgery.

The secondary objectives are to evaluate the SADI-S in comparison to RYGB with regard to:

1. Nutritional status.
2. Metabolic efficiency on glucose homeostasis and lipid profile.
3. Overall complication rates within 2 years after surgery.
4. Weight loss results.
5. Patient's quality of life.
6. Evolution of food choices and preferences within 2 years after surgery.

Trial design

Our trial protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (online supplementary appendix). This multicentre, open-label RCT of superiority was designed to test the efficacy and safety of laparoscopic SADI-S in comparison with laparoscopic RYGB. Recruitment began in October 2018 and is planned to last until October 2020 with a follow-up of 2 years after surgery. Trial Version V6 12 November 2019.

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METHODS AND ANALYSIS

Study setting

Bariatric teams involved as investigators of this RCT are composed of experts in the areas of bariatric and metabolic surgery, endocrinology, nutrition and malnutrition, epidemiology and biostatistics. Patients are recruited from 19 institutions specialised in bariatric and metabolic surgery in France. The list can be obtained on: https://clinicaltrials.gov/

Study endpoints

The primary endpoint will be assessed 2 years after surgery using %EWL. The use of %EWL is commonly accepted measure in the bariatric surgery field to evaluate the effectiveness on weight loss. The primary endpoint assessment is standardised between the centres and carried out under blind conditions.

Secondary endpoints will be assessed as follows: (1) nutritional status assessed by blood testing (malnutrition assessment, cholesterol, vitamin and ferric balances) and 24-hour steatorrhoea study; (2) metabolic efficiency on glucose homeostasis and lipid profile assessed by blood testing and evolution of antidiabetic, lipid-lowering and antihypertensive drugs and use of continuous positive airways pressure (CPAP) for obstructive sleep apnoea (OSA); (3) overall complication rate (medical and surgical complication rates within 24 months after surgery using the Dindo-Clavien classification), type and severity of early (within 30 days) and late complications for each procedure, length of stay, number of patients readmitted within 30 days after surgery[24]; (4) weight loss results according to absolute weight loss (in kg), BMI evolution and excess BMI loss percentage using 25 kg/m² as the optimal BMI ((initial BMI − BMI at each timepoint) / (initial BMI − optimal BMI)) ×100; (5) patient's quality of life evaluated by Gastrointestinal Quality of Life Index, Short Form 36 and Sigstad score questionnaires; and (6) evolution of food choices and preferences evaluated by Leeds Food Preference Questionnaire (only performed in the coordinating centre). Indeed, tastes are often modified after bariatric surgery, and it seems interesting to analyse if these modifications are increased with one or the other bariatric procedure. The preservation of pylorus in the SADI-S technique, which seems more physiological, could lead to less taste modifications and potentially less nutritional consequences.

Participant timeline

All enrolled patients will be reviewed at 1, 3, 6, 12, 18 and 24 months after surgery to collect data (figure 3). The schedule of all data collected is detailed in the protocol that can be found in ClinicalTrials.gov.

Eligibility criteria

To be eligible for the study, the patient must meet all the inclusion criteria and must not have any of the exclusion criteria.

Inclusion criteria

- Patients aged between 18 and 65 years old and suffering from morbid obesity with BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one comorbidity that is likely be improved by surgery (high blood pressure, type 2 diabetes mellitus, OSA, dyslipidaemia and arthrosis).
- Patient who had an upper GI endoscopy with biopsies to looking for *Helicobacter pylori*, within 12 months before surgery.
- Patient who had pluridisciplinary evaluation, with a favourable opinion for SADI-S or RYGB as a primary surgery or after failure of SG.
- Patient who understands and accepts the need for a long-term follow-up.
- Patient who agrees to be included in the study and who signs the informed consent form (ICF).

Exclusion criteria

- Patients with a history of previous bariatric surgery, other than an SG.
- Presence of a severe and evolutive life threatening pathology, unrelated to obesity.
- History of type 1 diabetes.
- History of chronic inflammatory bowel disease.
- Pregnancy or desire to be pregnant during the study.
- Presence of *H. pylori* resistant to medical treatment.
- Presence of an unhealed gastro-duodenal ulcer or diagnosed less than 2 months previously.
- Mentally unbalanced patients, under supervision or guardianship.
- Patient who does not understand French/is unable to give consent.
- Patient not affiliated to a French or European healthcare insurance.
- Patient who has already been included in a trial that has a conflict of interests with the present study.

Study arms and sample size

Enrolled patients are randomised between two arms: the experimental arm that underwent SADI-S versus the control group that underwent RYGB procedure. Both procedures are performed as a primary procedure or after failure of SG and are standardised between investigational centres. In the failure of SG arm,[25] %EWL will be calculated using the BMI after sleeve, just before the revisional procedure.

Assuming a mean %EWL of 72% 2 years after RYGB and about 82% EWL 2 years after SADI-S, with an SD of 27%, the probability that an observation in the RYGB arm is lower than an observation in the SADI-S arm is 0.603.

A sample size of 166 patients in each group will have a power of 90% to detect a probability of 0.603 that an observation in the RYGB arm is less than an observation in the SADI-S arm using a Wilcoxon (Mann-Whitney) rank-sum test with a 5% two-sided significance level.

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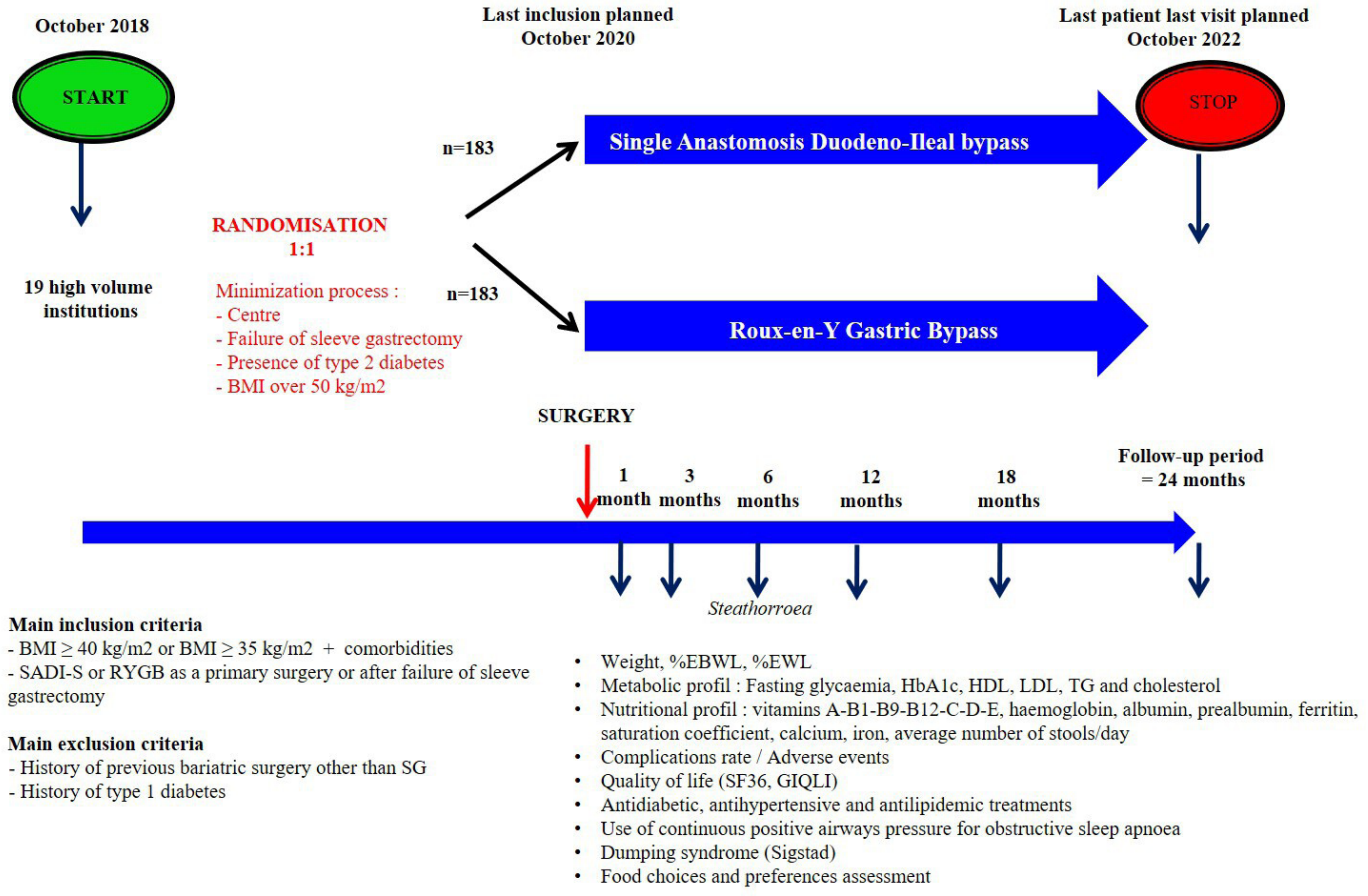


Figure 3 Participant timeline diagram. BMI, body mass index; %EBWL, excess body weight loss percentage; %EWL, excess weight loss percentage; HbA1c, glycated haemoglobin; HDL, high-density lipoproteins; LDL, low-density lipoproteins; GIQLI, Gastrointestinal Quality of Life Index; RYGB, Roux-en-Y gastric bypass; SADI-S, single anastomosis duodeno–ileal bypass with sleeve gastrectomy; SF, short form; SG, sleeve gastrectomy; TG, triglycerides.

With a drop-out rate of 10%, it will be necessary to include 183 patients per group, bringing to 366 the total number of enrolments.

Surgical procedures

Experimental group

Surgical technique of the SADI-S as a primary procedure:

First, an SG is performed: after release of the large gastric curvature, the antrum is preserved, and gastric section starts at 6 cm from the pylorus using a linear stapler. Gastric tube calibration is performed using a 48 French bougie.

Second, an omega loop common channel of 250 cm (if BMI >50 kg/m²) or 300 cm (if BMI ≤50) is measured from the ileocaecal valve and is ascended into an antecolic position up to the first duodenum. The first duodenum is sectioned at 3 cm from the pylorus using a linear stapler.

After an anterior duodenotomy and ileotomy, a manual end-to-side anastomosis is performed using running sutures. Anastomotic sealing is systematically verified using a methylene blue test.

Technical variant of SADI-S after a previous SG

The surgical technique is identical, except that the first step of SG will have been performed previously.

Surgical training: prerequisite

Participating centres have to be trained in SADI-S prior to the beginning of the project.

Most of the participating centres are already performing SADI-S, which involve duodenal section and manual duodeno-enteric anastomosis.

Other investigators routinely perform the BPD/DS procedure, which is the princeps technique, that is more complex, adding a Roux limb reconstruction to the duodenal switch.

Centres who do not yet perform SADI-S procedures will be asked to participate in SADI-S workshops either in French or foreign expert centres. The visual experience gained will be put into practice in their original centres with the assistance of an expert surgeon for the first five patients in order to validate the learning curve before beginning the inclusions.

Control group

Surgical technique of the RYGB as a primary procedure

A small gastric pouch (30 cc) is created using a linear stapler. The alimentary limb is moved up into an antecolic position after an epiploic transection so as to perform the gastro-jujenal anastomosis. The gastro-jejunostomy is

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performed manually or using a linear or circular stapler. Anastomotic sealing is verified using a methylene blue test. An alimentary limb of 150 cm and a biliary limb of 50 cm is measured in order to perform the latero-lateral jejuno-jejunal anastomosis using a linear stapler. All mesenteric defects (Petersen's space and mesenteric defect) are closed with a non-absorbable running suture.

Technical variant of RYGB after a previous SG

The surgical technique is identical, except that the first step will consist of creating the 30 cc gastric pouch by horizontally stapling the previous sleeve.

Surgical training

All the participating centres are already routinely performing this standard bariatric procedure.

Patient and public involvement

The patients and the public were not involved in the design or planning of the study.

Randomisation and allocation concealment mechanism

Patients are assigned randomly to the SADI-S arm or the RYGB arm. A minimisation process is employed to achieve balance between centre, failure of SG, presence of type 2 diabetes and BMI >50 kg/m^2.[26] The allocation of treatment groups uses the stratified randomisation method by minimisation that consists in seeking the treatment least used taking into account the stratification criteria of the patient being randomised (surgical centre and 'failure of sleeve gastrectomy or not'). The total number of patients per arm on each stratum concerned is calculated, and the least represented arm is selected for the patient to be randomised. If the number of patients in the arms is equal, the arm is allocated randomly. The algorithm used is that of POCOCK and SIMON.[26 27] This algorithm favours marginal equilibrium over strict equilibrium within each stratum. A random factor is added to decrease the predictability of arm allocation so that the allocation of an arm is 80% determined by the algorithm and 20% haphazardly. Eligible patients are sequentially randomised online using a specific module in the electronic case report fElectronic Case Report Form (e-CRF) in a 1:1 ratio and assigned to SADI-S group or RYGB group.

The study physician performs the randomisation online using a specific module in the e-CRF during the preoperative patient visit after having checked all eligibility criteria and after the informed consent signature has been obtained.

Blinding of participants was considered difficult in terms of patient acceptability and would probably have had a negative impact on recruitment. In addition, in case of complication (leak and haemorrhage), the surgical team must be aware of the type of surgery performed to be able to undertake the right decisions (revisional surgery, endoscopic treatment and so on). SADI-S and RYGB procedures have important conceptual differences and the management of their complications is not similar. Therefore, we chose to conduct an open label trial.

Data management

The clinical research unit of coordinating centre has developed an e-CRF (Ennov Clinical – Clinsight) to collect and computerise data for the study.

All information required by the protocol should be recorded prospectively during the patient's follow-up by investigators in the eCRF installed in each participating centre allowing the study coordination centre to rapidly access data. Quality control of the data will be performed by the data manager and/or the statistician.

Monitoring of the data by the clinical research associates will be performed in accordance with the monitoring plan previously prepared. Requests for clarification may be asked to the investigator. All modifications of the data must be justified and will be recorded in an audit trail. Once the data have been monitored, they will then be signed by the investigator. Once the last requests for clarification have been treated, the database may be frozen by the data manager after the agreement of the principal investigator, the project leader and the statistician. No modifications can be made without a justified unfreezing of the database.

Safety management

All adverse events (AEs), regardless of seriousness or relationship to the research, that occurred after the informed consent up to end of the study are to be recorded in the AE section of the eCRF. An AE is any untoward medical occurrence in a patient or clinical investigation patient that does not necessarily have a causal relationship with the research.

The investigator shall notify the sponsor, without delay and no later than 24 hours from the day of its knowledge, of all serious adverse events (SAEs) and serious incidents in the trial, with the exception of those identified in the protocol as not requiring notification without delay. SAE are defined as all untoward medical occurrence that:

- Results in death.
- Is life-threatening to the participant.
- Requires in-patient hospitalisation or prolongation of a hospitalisation.
- Results in persistent or significant disability or incapacity.
- Results in a congenital anomaly or birth defect.

To reinforce safety, we asked an independent Data and Safety Monitoring Board (DSMB) to examine all the problems that may appear in the trial, in particular scientific, ethical and tolerance, which may modify the benefit/risk ratio. Following this review, it shall transmit its recommendations in writing to the sponsor. These recommendations may concern in particular the continuation, modification or termination of the trial.

The DSMB meets regularly, before the first inclusion, after the inclusion of 20 patients, then 50 patients and every 100 patients included. The DSMB is composed of

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three experts: one bariatric surgeon, one nutritionist and one clinical research methodologist.

ETHICS, DISSEMINATION AND PERSPECTIVES OF THE TRIAL

Ethic and dissemination

Institutional Review Board approval (Comité de Protection des Personnes Ouest VI – Centre Hospitalier Universitaire Morvan – Batiment 1 RDC – 2 Avenue Foch – 29 609 BREST Cedex) was obtained prior to the beginning of the study (approval number: CPP Ouest6 – CPP1089-HPS1 on 30 July 2018). Study was also approved by the French national agency for drug safety (Agence Nationale de Sécurité du Médicament (number: 2018061500148 on 18 June 2018). This RCT was registered the 10 July 2018 on clinical trials.gov website.

Prior to enrolment in the RCT, the investigator in charge of the patient provides a letter with relevant information relating to the study objectives, potential benefits and possible AEs. In addition, the written ICF is signed, name filled in and personally dated by the subject by the person who conducted the informed consent discussion. A copy of the signed and dated written ICF is provided to the patient. Another copy is held in a patient's hospital file.

Access to the data is restricted to the people participating in the study only. Authentication is made using passwords, which is regularly changed.

The investigators and clinical research technicians of an investigational centre only have access to the data for their patients and enter the data directly into the eCRF using a secured site on the internet.

This study falls within the framework of the 'Reference Methodology' (RM-001) under the provisions of article 54, paragraph 5 of modified law no. 78–17 from 6 January 1978, related to information technology, files and liberties. The Hospices Civils de Lyon Institution, sponsor of the study, has signed a commitment of compliance to this 'Reference Methodology'.

Scientific communications and reports related to this study will be carried out under the responsibility of the study's principal investigator with the agreement of the associated investigators. The coauthors of the report and the publications will be the investigators and doctors involved, in proportion to their contribution to the study, as well as the methodologist, the biostatistician and the associated researchers. The publications rules will follow international recommendations.[28]

Patients enrolment

From the beginning, enrolment of patients in the SADISLEEVE trial was considered an important challenge. Currently, there are no guidelines issued from the French Society of Obesity Surgery and Metabolic Disorders regarding SADI-S procedure in the treatment of morbid obesity neither as primary nor as revisional surgery. The French high authority for health (Haute Autorité de Santé (HAS)) has not validated yet the procedure, and

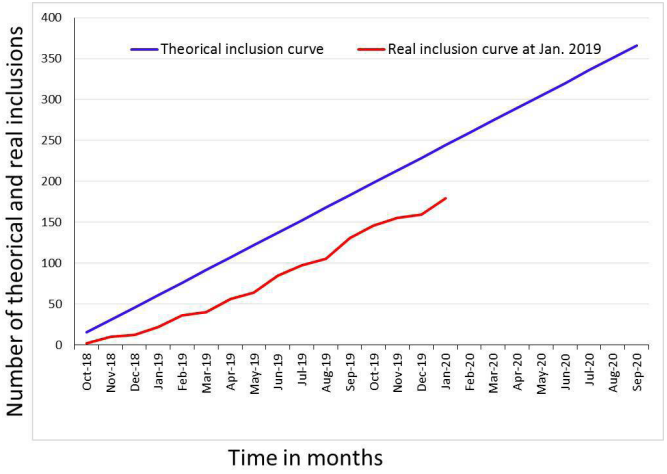


Figure 4 Theorical and real inclusions curves. The blue curve shows the rate of expected hypothetical inclusions needed to complete recruitment on time (n=366). The red curve shows the real number of inclusions between October 2018 and January 2020 (n=178).

reimbursement of the procedure by the public healthcare insurance system is accepted only in case of patient's participation to the SADISLEEVE national trial. In addition, the SADI-S is considered as a 'mini BPD-DS' and not so widely performed in France: there was therefore a natural fear of nutritional complications from many bariatric teams. Nevertheless, facing the very good outcomes published in the recent literature regarding SADI-S procedure,[29 30] many specialised bariatric centres are accepted to participate to SADISLEEVE trial. Meetings involving patients who already underwent and those waiting for surgery have also played an important role allowing to share their experience (regardless of the randomisation arm) and to know about the protocol. The actual inclusion curve closely follows the hypothetical curve of recruitment (figure 4). The estimated enrolment period was spread over 24 months. We believe that in maintaining the current enrolment dynamics, it is possible to reach the planned number of patients without increasing the inclusion period.

Surgical challenge

All investigators participating to the SADISLEEVE RCT routinely perform RYGB, and the majority of them had a large experience of duodeno-ileal anastomosis performed as part of the biliopancreatic diversion with duodenal switch.

To avoid the bias of the learning curve, centres who do not yet perform SADI-S procedures were asked to participate in SADI-S workshops either in French or foreign expert centres. The visual experience gained was put into practice in their original centres with the assistance of an expert surgeon for the first five patients in order to validate the learning curve before beginning the inclusions.

Additionally, a video of a SADI-S procedure was provided to the different teams before starting the study in order to standardise the practice among the different

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teams involved in the project, and if needed, the coordinator also visited each centre. We did not observe major surgical complications in the SADI-S arm among the first 178 patients included.

Patients' follow-up and data collection

Follow-up is a challenge in bariatric surgery. Secondary outcomes data collection such as nutritional blood test results (albumin, prealbumin, haemoglobin, calcium, ferritin, iron, % of transferrin saturation, vitamins A, B1, B9, B12, C D and E, prothrombin rate and 24 hours steatorrhoea at 6 months) and metabolic efficiency on glucose homeostasis and lipid profile (assessed by dosage of glycated haemoglobin (HbA1c) level, fasting glycaemia, high-density lipoproteins, low-density lipoproteins, cholesterol and triglycerides) and analysis of evolution of antidiabetic, antilipidaemic and antihypertensive drugs, use of CPAP are sometimes difficult to obtain due to omission by some patients of blood or stool testing. For this reason, we decided to perform the blood exam directly during medical appointments and to organise a day hospitalisation in the department of nutrition to complete the missing exams at each time point. To improve data collection, we also sensitised patients through phone calls by clinical research technician to remind the dates of appointments. The collection of these data is essential and has a double importance: first, it will allow to obtain reliable data to compare late complications such as malnutrition (vitamin and trace element deficiencies) or severe functional and digestive disorders (diarrhoea, steatorrhoea, gastro-oesophageal reflux and dumping syndrome) and second, it will allow to compare the improvement of comorbidities and changes in patient treatment.

Safety

To guarantee the safety, the independent data and safety monitoring committee reviewed the AEs and complications of the first 20 and 50 patients included in the trial: no unplanned SAEs were observed, and the decision to continue the clinical trial has been validated. Currently, it is well established that bariatric procedures with one anastomosis could be responsible of malnutrition and severe diarrhoea and/or steatorrhoea.[8] The insufficient length of the common channel has often been incriminated.,[8 31] Therefore, the length of the common channel in our patients who undergo SADI-S with BMI ≤50 kg/m^2 has been increased to 300 cm. At 1 year, a higher incidence of diarrhoea was observed in our patients who underwent a SADI-S procedure without being able to determine if there is a significant difference between patients with 300 cm versus 250 cm length of common channel yet. However, special attention for the monitoring of the number of stools was recommended by the independent DSMB in November 2019.

Pregnancy during the study is another issue. It is already established that weight loss improves fertility, but in counterpart, bariatric surgery could have a negative impact on the development of the fetus during the first year after surgery, and it is recommended that pregnancy should be avoided. Patients with desire for pregnancy are a real challenge especially because some of them wish to have bariatric surgery because of fertility problems related to polycystic ovary syndrome and advanced age. Even if contraception is recommended during the trial and if the patients agree to differ their pregnancy, some pregnancies still occur: in case of pregnancy, the investigator should monitor the patient until the end of the pregnancy or its interruption and notify the outcome. We did not encounter this problem during the first year, but from the experience of our previous RCT (YOMEGA study), it is likely to happen during the second year of follow-up.[8] A special warning is given to the female patients routinely.

The SADI-S is a recent procedure and is not yet validated into the armamentarium of the bariatric/metabolic surgery in France. The aim of our study is to assess the SADI-S compared with the RYGB in two situations: its efficacy as a primary and as a revisional procedure. However, the inclusion of patients with sleeve failure could induce a selection bias. To avoid this bias, the design of this study implies a randomisation by minimisation based on 'failure of sleeve gastrectomy or not' thus allowing a subgroup analysis to be carried out. The subgroup analysis will be specified in the detailed statistical analyses plan.

A set of arguments make us think that SADI-S is superior to RYGB on weight loss and metabolic results either as a first procedure or as a revisional one and that is a quite safe procedure. If all these advantages are confirmed, SADI-S could be of real benefit to obese patients who apply for bariatric surgery. This RCT was constructed in order to have the maximum of objective data that could legitimise this procedure and propose it as an alternative to the RYGB for patients undergoing primary or revisional surgery in case of failure of an SG.

Patient's recruitment and adherence to follow-up are the main difficulties of this RCT. To obtain reliable data, a logistical effort must be provided to accompany patients in the follow-up.

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Contributors MR and TP contributed equally to the report and share first authorship. MR, TP, SBD, SI, DM-B and DD conceived and designed the study. MR, TP, EP, AS and LKK performed the surgical procedures. ED, CB and SC performed nutritional follow-up. DD and SBD were responsible for data acquisition. DMB was responsible for analysis. MR, ED, SBD, DD, and DMB have access to the data. MR, TP, SC, ED and DM-B interpreted the data. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

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