UNIVERSITAT DE GIRONA
FACULTAT DE MEDICINA

THE PELOSI-TYPE VERSUS THE MODIFIED MISGAV-LADACH: A RANDOMIZED TRIAL OF TWO SURGICAL TECHNIQUES FOR CESAREAN SECTION

FINAL DEGREE PROJECT

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AUTHOR: António Soudo Ventura

TUTOR: Fernando Montero Muñoz

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1. SUMMARY

Cesarean section (CS) is now the most common major surgical procedure performed on women worldwide. A quarter of deliveries in Spain are performed by cesarean section. With the increasing rates of the operation, there is the need to use evidence-based techniques to optimize outcomes and minimize complications.

The goal of this study is to employ a well-designed randomized controlled trial to evaluate the intraoperative blood loss of two surgical techniques for cesarean section, the Pelosi-type and the modified Misgav-Ladach. The trial will take place in Hospital Universitari de Girona Dr. Josep Trueta. From 2014 to 2015, 512 pregnant women undergoing delivery by their first lower segment cesarean section in this center will be selected through a consecutive non-probability sampling. We will collect the main obstetrical characteristics, intraoperative outcomes, short-term outcomes for the baby and postoperative outcomes. We will evaluate the intraoperative blood loss by comparing the changes in hemoglobin levels, pre and postoperatively. Patients will be followed during the postoperative period and in a two-week postoperative appointment. We will analyze the continuous variables, such as the differences in hemoglobin levels, using an unpaired two-sided Student's t-test, while for the categorical variables Fischer's exact test will be used.

2. INTRODUCTION

2.1. Background

Cesarean section (CS) is the most commonly performed major surgery worldwide [1]. Rates vary widely between and within countries and have increased substantially, particularly in developed countries, during the last decades [2]. In 2011, 24,9% of Spanish women gave birth by cesarean section, increasing from 19,8% in 1997 [2, 3]. The increasing rates are likely due a number of factors, including advanced maternal age, multiple pregnancy, maternal obesity, induction of labor, women's preferences and obstetrician's characteristics and care practices around labor and birth, particularly in relation to vaginal birth after cesarean (VBAC) [4].

Cesarean section should be only performed when offers a clear benefit either to the mother or to the neonate, since women who undergo this procedure face substantially increased risks of maternal morbidity and mortality compared with women who deliver vaginally. The

risk is three to five times higher for maternal death, four times higher for hysterectomy, and twice as high for being admitted to intensive care unit and hospital stay more than seven days [5]. Cesarean section carries a risk of short-term complications, such as, pain, hemorrhage, need of blood transfusion, injury to the intra-abdominal organs (bowel, bladder or ureters), infection and thromboembolic disease [4, 6, 7]. Chronic maternal morbidities include chronic pelvic pain and surgical adhesions. As for the subsequent pregnancies and birth outcomes, there is increased risks of abnormal placentation and its associated consequences, uterine rupture, reduced fetal growth, preterm birth and possibly stillbirth [4, 6 - 8]. Cesarean section may also increase the risk of adverse reproductive effects, including decreased fertility, increased risk of spontaneous abortion and ectopic pregnancy [7]. However, the effect of cesarean section on these long-term outcomes have not been well assessed in randomized controlled trials to date. In addition, maternal complications impact not only on physical health but also on emotional wellbeing, influencing a woman's ability to care for her infant, as well as her perception of her childbirth experience [4].

Cesarean section is not done in a standardized way, and there are many variations in the surgical techniques used. Improving the techniques may contribute to reduce both short- and long-term morbidity associated with the operation and although differences may be relatively modest, the commonness of the operation means that even small differences in outcome may result in substantial improvements in health for thousands of women and considerable cost savings for health services [6].

These techniques have developed over the past century as the low segment cesarean section [9].

In 1900, Pfannenstiel proposed the use of a curved transverse supra-pubic incision in the abdominal skin (currently known as the "bikini cut") [8, 11]. It is made 2 to 3 cm above the symphysis pubis, with the midportion of the incision within the shaved area of the pubic hair [1]. The merits of the transverse incision include a better cosmetic outcome and less operative pain when compared to the midline incision [12]. The idea of incising the fascia transversely was also introduced by Pfannenstiel [11].

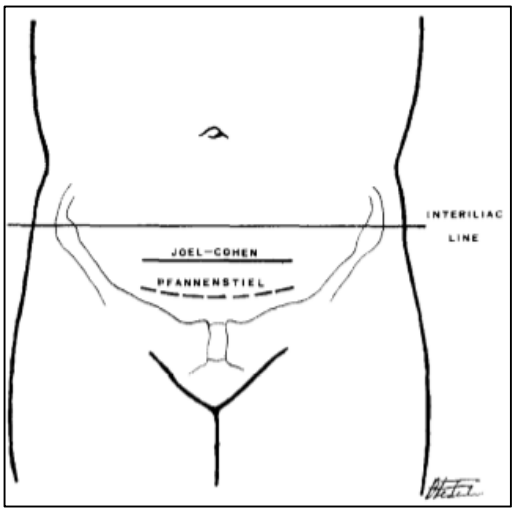

Figure 1 - Transverse abdominal incisions for cesarean section [16].

In 1926, Kerr introduced the transverse lower uterine segment incision as opposed to the upper classical variety. The advantages are less blood loss, reduced risk of adhesions and postoperative obstructions and decreased risk of uterine rupture during subsequent trials of vaginal delivery [8, 11]. These techniques gained wide acceptance in obstetric practice during the second half of the twentieth century, although many small variations were probably employed by different clinicians [13].

In 1972, Joel-Cohen suggested a new method for opening the abdominal wall, involving a straight transverse incision 3 cm below the level of the anterior superior iliac spines (slightly higher than the traditional Pfannenstiel incision) and blunt dissection of the abdominal wall [1, 8, 11]. Joel-Cohen–based cesarean section compared with Pfannenstiel cesarean section is associated with reduced blood loss, operating time, time to oral intake, fever, duration of postoperative pain, analgesic injections, and time from skin incision to birth of the baby [7, 14].

During the late 1980s and 1990s, one-layer suturing of the uterus and non-closure of the peritoneum were also advocated [13].

In an attempt to simplify the operation as well to achieve the least possible damage to the tissues through elimination of superfluous steps, in 1995, Stark and colleagues modified the Joel-Cohen method at Misgav-Ladach General Hospital in Jerusalem. This led to a unique improvement of the Misgav-Ladach method (MLM), in which manual manipulation rather than surgical instruments is recommended to achieve surgical minimalism [15-17]. The main features of the Misgav-Ladach method for cesarean section are documented to be the Joel-Cohen incision for opening the abdomen, suturing the hysterotomy in one layer and nonclosure of the visceral and parietal peritoneum [15-17]. Although reduction in operation time was not the purpose of this technique, it is the most evident and considerable consequence. This method also decreases the time of child delivery and the time of recovery [16].

While the simplicity and the advantages of the Misgav-Ladach method have been well demonstrated, the adoption of the Joel-Cohen incision limited its implementation, mainly because patients disfavor its aesthetic result. Many women dislike having the abdominal skin disfigured by a highly positioned scar. This aspect, together with emerging evidence in favor of alternative individual steps for the procedure, led to the proposal of a modified Misgav-Ladach method (MMLM) [13, 18-21].

Also in 1995, Pelosi and Pelosi introduced a simplified technique of cesarean section [22]. It was based on the premise that the lower abdominal transverse incision is located directly over the surgeon's designated target area, the lower uterine segment. The authors illustrated that in the gravid, hyperemic patient, the surgeon has no need for dissecting above or below the plane of the skin incision. Traditional dissection of the rectus muscles from the overlying fascia, which can be associated with bleeding, iatrogenic fascial defects, increased operative time and postoperative pain, are eliminated. The Pelosi technique also eliminates the formation of a bladder flap and makes the hysterotomy into the lower uterine segment through the upper aspect of the vesicouterine peritoneal fold. After delivery of the infant, the surgeon awaits spontaneous placental expulsion. The hysterotomy is closed in one layer [22]. Recently, in 2004, this technique was improved by adding a soft, self-retaining abdominal retractor, by extending the transverse uterine incision vertically and by identifying a subgroup in whom peritoneal closure is strongly recommended. Some advantages include short operative time, minimal instrumentation, less surgical dissection, reduced risk of blood loss, infection, wound complications and postoperative pain [23].

2.2. Justification

The need to develop this project lies on the fact that are no studies comparing the Pelosi-type cesarean section to other techniques [14, 24].

As mentioned before, given the fact that the operation is conducted so frequently, any attempt to reduce risks associated with it, even with relatively modest alterations in the surgical procedure for a particular outcome, is likely to yield significant benefits in terms of better health outcomes for women and cost savings for the national health system.

The technical capacity to carry out the study is optimal, since on average 352 cesarean deliveries are made each year at Hospital Universitari de Girona Dr. Josep Trueta.

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4. QUESTION

Is the Pelosi-type technique as effective as the modified Misgav-Ladach method in reducing intraoperative blood loss at cesarean section?

5. HYPOTHESIS

This trial will assess the following null hypotheses: in women undergoing delivery by cesarean section, no differences will be detected with respect to intraoperative blood loss when comparing the Pelosi-type and the modified Misgav-Ladach techniques.

6. OBJECTIVES

6.1 Primary objective

To compare the effectiveness of the Pelosi-type technique with the modified Misgav-Ladach method in reducing intraoperative blood loss at cesarean section.

6.1 Secondary objectives

- To evaluate the intraoperative outcomes of both techniques including duration of surgery, operative complications, need for blood transfusion and drop in hematocrit.
- To evaluate the short-term outcomes for the baby in both techniques such as time from skin incision to delivery, cord blood pH, APGAR score, birth trauma and admission to neonatal intensive care.
- To evaluate the postoperative outcomes of both techniques including length of hospital stay, doses of extra analgesia required, use of antibiotics, time to mobilization and bowel function restitution.
- To evaluate the postoperative complications of both techniques such as wound complications, endometritis and febrile morbidity.

7. METHODS

7.1 Study design

Prospective, randomized, controlled and triple blind trial.

7.2 Participants

The study population will be all pregnant women undergoing delivery at Hospital Universitari de Girona Dr. Josep Trueta, between 2014 and 2016.

7.2.1 Inclusion criteria

- Women undergoing delivery by their first lower segment cesarean section
- No clear indication for any particular surgical technique to be used
- Gestational age of 37 weeks or more
- Singleton pregnancy
- Women aged 18 years or over
- Women who are able to cooperate and have given informed written consent

7.2.2 Exclusion criteria

- Previous cesarean section
- Previous lower abdominal surgery
- Previous postpartum hemorrhage
- Antepartum hemorrhage
- Chorioamnionitis
- Moderate-severe anemia (hemoglobin [Hb] < 9,9 g/dl), preoperative blood transfusion or bleeding disorders
- Body mass index greater than 40 (extremely obese)
- Placenta previa, placental abruption and severe preeclampsia or HELLP syndrome
- Participation in another trial with interference of intervention and outcome of this study

7.3 Sample selection

A consecutive non-probability sampling will be taken. The sample recuitment will take part at Hospital Universitari de Girona Dr. Josep Trueta for 2 years. Women will be approached at their 34-36 week prenatal visit (corresponding to the 3rd trimester ultrasound scanning) regarding potential study participation. They will be given an information sheet describing the study (annex II). If a woman is interested, she will be contacted by a trial doctor who will obtain informed consent (annex III). In any case, women will be approached prior to the date of cesarean section to provide adequate time to review the study and ask questions.

7.4 Sample size

The sample size and power calculator GRANMO was used. Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 256 subjects in the first group and 256 in the second (512 in total) are necessary to recognize as statistically significant a difference greater than or equal to 0.25 g/dl. The common standard deviation is assumed to be 1. It has been anticipated a drop-out rate of 5%. The estimated reduction of intraoperative blood loss was based on a drop of 1,5 ± 1 g/dl between pre- and postoperative levels for serum hemoglobin in the modified Misgav-Ladach method [20]. It is estimated that at the Hospital Universitari de Girona Dr. Josep Trueta approximately 700 cesarean deliveries will be made during 2 years.

7.5 Interventions

7.5.1 Randomization methods

Consenting women will be randomized after the decision to deliver by cesarean section is made. Randomization will be performed in blocks to control for scheduled versus unscheduled cesarean deliveries using a random numbers generator. Assignments will be kept in sequentially number opaque envelopes.

7.5.2 Degree of blinding

This will be a triple blind trial since its participants, assessors (those collecting outcome data) and statistical consultant (data analyst) will remain unaware of the intervention assignments. Women will not be informed of their intervention group assignment until after discharge from the hospital. The operative team will be aware of group assignment. The ward medical team, who will do the postoperative data collection, will be different from the team who performed the operation in order to preserve the assessors' blinding which helps to reduce the differential assessment of outcomes.

7.5.3 Description of the surgical procedures

- Modified Misgav-Ladach method [13]: after a Pfannenstiel skin incision, the subcutaneous tissue is opened upward in the midline, to reach the rectus sheath above the insertion of the pyramidalis muscles. Lateral extension of the subcutaneous tissue, rectus sheath incision and separation of the two rectus muscles are performed digitally. If the rectus sheath was opened below the insertion of the pyramidalis muscles, a single cut with the scissors is performed in the midline to allow the separation of these two structures. Opening of the parietal peritoneum at the upper level of the intermuscular space is performed digitally. A transverse 2-3 cm lower uterine segment incision in the midline, using a scalpel and involving both peritoneum and myometrium is accomplished with subsequent dissection of the remaining uterine fibers and opening of the fetal membranes using a Kelly's clamp. After lateral digital extension of the uterine incision, the fetus is extracted and the placenta is removed by transabdominal uterine massage combine with light cord traction. Closure of the uterine incision is accomplished with one-layer continuous nº1 poliglactin 910 (Vicryl®, Ethicon) suture, using additional hemostatic stitches if required. After the inspection of the peritoneal cavity and removal of accessible blood and clots, the visceral and parietal peritoneum is left unsutured. The rectus muscles, subfascial space and subcutaneous tissue are inspected for hemostasis, and the rectus sheath is closed using a continuous suture of polyglactin 910 nº1 (Vicryl®, Ethicon). The subcutaneous tissue is sutured if its depth exceeds 2 cm. The skin is closed with metal staples.

- Pelosi-type technique [23]: after a Pfannenstiel skin incision, the subcutaneous tissue and the fascia are opened transversely with an electrocautery knife. Separation of the rectus muscles in the mideline by vertical blunt finger dissection. Opening of the parietal peritoneum, which is facilitated by upward traction and elevation of the superior edge of the abdominal incision, allowing easy digital perforation using the index or middle finger. Abdominal entry is completed by stretching the full thickness of the abdominal wall transversely to the full size of the skin incision using one or two fingers of each hand. To facilitate placement of the self-retaining abdominal retractor, upper traction is applied and the superior edge of the abdominal incision is elevated, squeezing the inner ring and inserting it into the abdominal cavity toward the patient's head. The outer ring is held and then rolled into the plastic sleeve until the ring is completely inverted. The process is repeated until the top ring is snug against the patient's skin. A transverse 2 cm uterine incision is made with a scalpel, approximately 1 cm above the vesicouterine peritoneal fold. After vertical digital extension of the uterine incision, the fetus is extracted and the placenta is removed only after it separates spontaneously. Manual placental delivery only if it has not separated spontaneously after 5 minutes. Closure of the uterine incision in situ using a single-layer closure with running suture of polyglycolic acid. After the uterine closure, individual figure-of-8 sutures are used to control areas of persistent bleeding. The visceral and parietal peritoneum are not closed, nor are the rectus muscles reapproximated, except in cases in which one or both rectus muscles have been transected to increase surgical exposure. Closure of the rectus fascia with a continuous nonlocking 0 suture after the rectus muscles fall into place. The subcutaneous tissue is sutured if its depth exceeds 2 cm by interrupted 3-0 absorbable synthetic sutures. The skin is closed with metal staples.
  The figures illustrating this technique can be reviewed in annex I.

Summary of both techniques:

Variable	**Modified Misgav-Ladach**	**Pelosi-type**
Skin incision	Pfannenstiel	Pfannenstiel
Subcutaneous layer opening	Incised and bluntly divided	Transversely opened with an electrocautery knife
Fascia opening	Transversely incised 3 cm, divided bluntly	Transversely opened with an electrocautery knife
Peritoneal opening	Bluntly opened in vertical direction	Bluntly opened in vertical direction
Self-retaining abdominal retractor	No	Yes
Uterine incision	Sharply opened in the superficial layers; deeper layers opened and extended bluntly	Sharply opened in the superficial layers; deeper layers opened and extended bluntly
Uterine incision extension	Laterally	Vertically
Placenta removal	Spontaneous	Spontaneous
Uterine closure	Single layer closed by continuous, unlocked sutures	Single layer closed by running sutures
Peritoneal closure	Not closed	Not closed (except in cases in which one or both rectus muscles have been transected)
Fascia closure	Closed by interrupted sutures	Closed by continuous non-locking 0 sutures
Subcutaneous layer closure	Not sutured (except in obese patients with at least 2 cm of thick subcutaneous tissue)	Not sutured (except in obese patients with at least 2 cm of thick subcutaneous tissue)
Skin closure	Closed by metal staples	Closed by metal staples

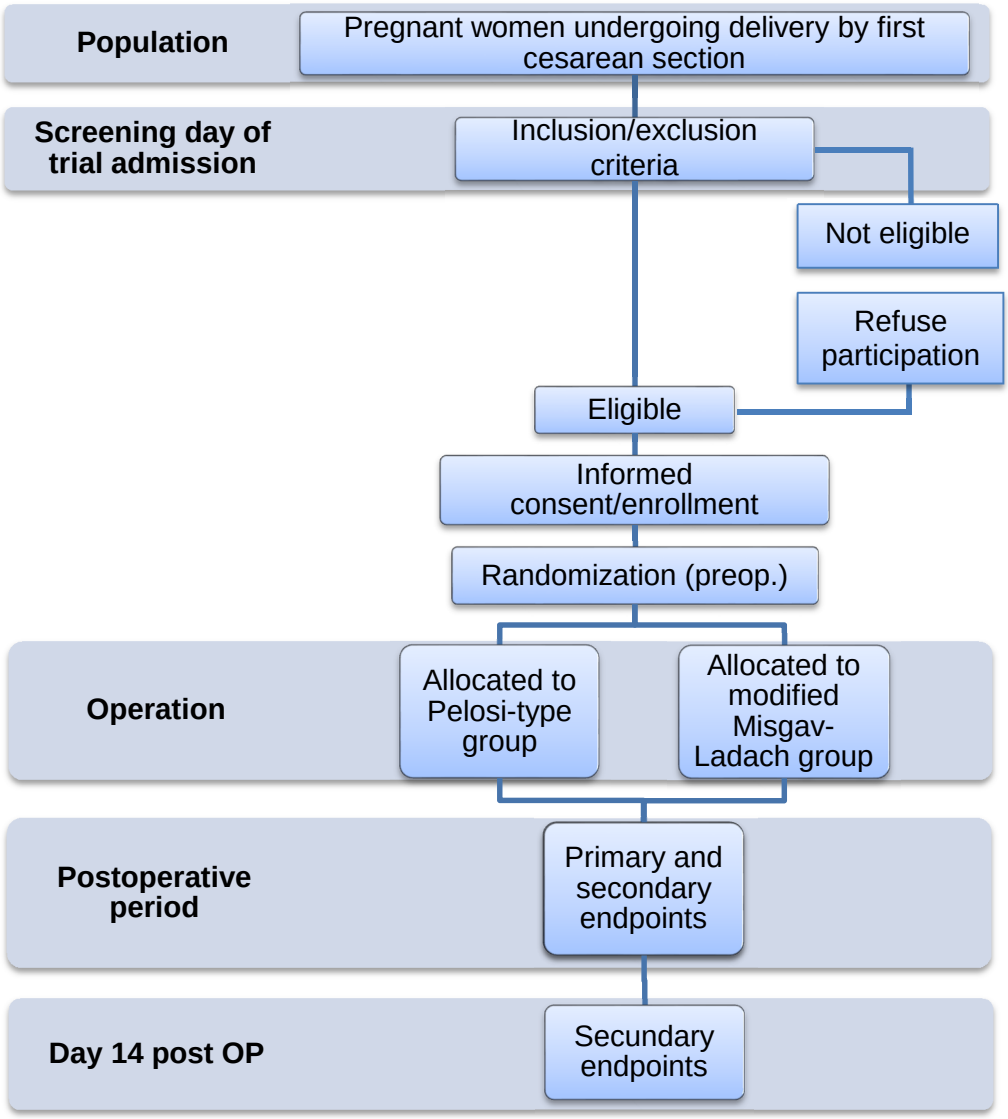


Figure 2 – The progress of subjects throughout the study.

7.6 Variables

7.6.1 Dependent variable

Intraoperative blood loss: it will be estimated by measuring the hemoglobin levels immediately after maternity unit admission and one hour postoperatively in recovery room.

7.6.2 Independent variable

Being allocated in the Pelosi-type technique group or in the modified Misgav-Ladach method group for cesarean section.

7.6.3 Covariables

- Main obstetrical characteristics**:** maternal age (years), gestational age at delivery (weeks), weight (kg), height (meters), body mass index (kg/m^2), type of cesarean section (scheduled or unscheduled), indication for cesarean section (unreassuring fetal state, failure to progress/cephalopelvic disproportion, multiple gestation, breech presentation, labor dystocia, maternal and fetal disorders contra-indicating vaginal delivery, macrosomia, others), anesthesia employed for cesarean section (general, spinal, epidural).

- Intraoperative outcomes: total operating time (from skin incision to closure of the skin; min), operative complications (hematomas, bladder or ureter injury, unintended extension of the uterine incision, additional hemostatic sutures), need for blood transfusion, drop in hematocrit (difference between pre- and postoperative levels).

- Short-term outcomes for the baby: time from skin incision to delivery (min), cord blood pH < 7.2, APGAR score < 7 at 5 minutes, birth trauma, admission to neonatal intensive care.

- Postoperative recovery: bowel function restitution by second postoperative day, length of postoperative hospital stay for the mother (hours), extra analgesia required (number of doses), postoperative antibiotics, time to mobilization (hours), need for blood transfusion.

- Postoperative complications: wound complications (seroma or hematoma, infection, dehiscence), endometritis (lower abdominal pain, uterine tenderness, foul-smelling lochia, leukocytosis and at least two separate episodes of temperature increases to or above 38ºC, 6 hours apart, after the first 24 hours postpartum period), febrile morbidity (at least two separate episodes of temperature increases to or above 38ºC, 6 hours apart, after the first 24 hours postpartum period or 38,7ºC at any time).

7.7 Measure instruments

The only measure instrument needed will be a dual height and weight station SECA (model 764), which is located in the maternity ward.

7.8 Methods of data collection

Most of the data will be collected from the electronic medical records of the participating women and will be reflected in the trial database. Homogeneity in data collection must be ensured. Moreover, information will be collected at following times:

- Trial entry and randomization
- At maternal unit admission
- During the operation
- During the postoperative period
- At two-week postoperative appointment

8. STATISTICAL ANLYSIS

For continuous variables with normal distribution, the mean and the standard deviation or number (percentage) will be estimated and differences will be evaluated using an unpaired two-sided Student's t-test. For categorical variables, Fischer's exact test will be used. Statistical analysis will be performed using SPSS for Windows®.

9. ETHICAL ASPECTS

This trial is designed in accordance with the medical ethics requirements defined on the World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (last revised in October 2013) and it has been approved by the Clinical Research Ethics Committee (CEIC) of the Hospital Universitari de Girona Dr. Josep Trueta.

As it is now recommended, the trial has also been registered with an International Standard Randomised Controlled Trial Number (http://www.controlled-trials.com) and has been submitted to ClinicalTrials.gov (http://clinicaltrials.gov).

The information will be confidential, guaranteeing the anonymity of the patients involved in the study under the Organic Law of Data Protection 15/1999. In addition, patients will be informed about the interventions (annex II) and they must sign an informed consent (annex III) before being included in the trial.

10. STUDY LIMITTIONS AND BIASES

The randomized prospective design of the trial lowers the risk of bias regarding background factors. One possible limitation could be the lost to follow-up, however in this trial the lost will be minimum since patients included will just be followed until the two week postoperative appointment. Another possible limitation of the study is that it only assesses short-term outcomes for both surgical techniques. A future study would be needed to detect long-term effects of these techniques.

11. WORK PLAN

Investigators: António Ventura (AV), Fernando Montero (FM).

Collaborators: Alexandra Bonmatí (AB), Anna Borrell (AB), Anna Florensa (AF), Anna Maria Heller (AH), Anna Taltavull (AT), Cristina Adrados (CA), Cristina Noguera (CN), Elena Alvarez (EA), Elisabeth Merino (EM), Eduard Sala (ES), Esther Vila (EV), Eva López (EL), José Ruiz (JR), Josep María Ramos (JR), Lorena Rozas (LR), Luis Miguel Alonso (LA), Montserrat Farré (MF), Sara Torrent (ST), Vigmar Iriarte (VI).

The trial has been designed in five phases:

1. **Coordination phase (1 month):** All investigators, collaborators and nursing staff. There will be an organization meeting with all the team at the beginning of the trial. The timeline of the study will be planned and the methods of data collection will be shared. In this period will also take place the training of collaborators to perform the surgical techniques as described in the trial protocol and the training of nursing staff.

2. **Field research (24 months):** All investigators, collaborators and nursing staff. 730 working days in 2 years are calculated and it is necessary to include approximately 5 patients per week to recruit the 512 participants needed. With each patient: A)

Approach at the 34-36 week prenatal visit (corresponding to the 3rd trimester ultrasound scanning). B) Interview: provision of information sheet, explanation of both purposes of the study and voluntary participation, signature of the consent form. C) At maternal unit admission, the nursing staff will extract a blood sample for complete blood count (pre-operative hemoglobin and hematocrit levels) and weight and height will be measured. D) During the operation, a scrub nurse will make note of the intraoperative outcomes and some of the short-term outcomes for the baby. E) At recovery room, one hour after the operation another blood sample will be extracted for complete blood count (postoperative hemoglobin and hematocrit levels). F) At the postpartum ward and at the two-week postoperative appointment, postoperative outcomes will be assessed. G) Communication of our gratitude to the women for their cooperation in the study.

3. **Data extraction and processing data base (28 months):** All investigators and collaborators. Data will be entered in the database simultaneously with the trial development. An analysis of data will be performed regularly to control its evolution.

4. **Data analysis (4 months):** Investigators (AV, FM) and statistical consultant. After processing the data base, all data collected will be analyzed using the appropriate statistical test.

5. **Interpretation of results, publication and dissemination of research findings (7 months):** Investigators (AV, FM). An interpretation of the outcomes will be performed and the corresponding articles will be written. The timeline is provided in annex IV.

12. DISSEMINATION PLAN

It is important that the findings of this research are widely disseminated. The dissemination strategy includes conference presentations, meetings, trainings sessions, journal articles, reports, among others.

13. AVAILABLE MEANS TO CARRY OUT THE PROJECT

The project will take place at Hospital Universitari de Girona Dr. Josep Trueta, where the center will provide all means for performing the cesarean deliveries. The hospital has all the necessary items, including the informatics equipment suitable for processing databases for the trial development without additional cost. However, the nursing staff, the statistical consultant, the lab service and the disposable items, such as Mobius® elastic abdominal retractors, blood collection tubes, syringes and latex gloves will be paid by the project.

14. BUDGET

	CATEGORY	QUANTITY	TIME	COST
PERSONNEL COSTS	Nursing staff	3	24 months	7200€
	Statistical consulting and analysis of study data	1	-	1200€

	ITEM	QUANTITY	DESCRIPTION	PRICE	COST
SERVICES AND DISPOSABLE ITEMS COSTS	Mobius® Elastic Abdominal Retractor	52	Box of 5	730€	37.960€
	Lab service (complete blood count)	1024	-	10€	10.240€
	Blood collection tubes (EDTA tubes)	21	Pack of 50	4€	84€
	Latex gloves	21	Box of 100	5€	105€
	Syringes	11	Box of 100	7,45€	81,95€

	ACTIVITY	COST
TRAVEL COSTS	Coordination meetings	400€
	Investigators meetings (SEGO national congress)	1200€

TOTAL AMOUNT OF AID CLAIMED	58.470,95€

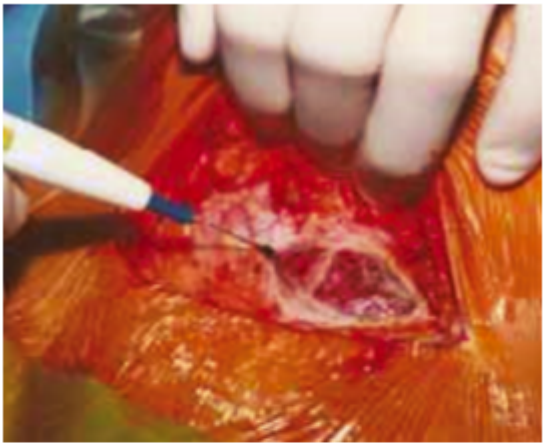
15. ANNEXES

15.1 Annex I: Pelosi-type technique

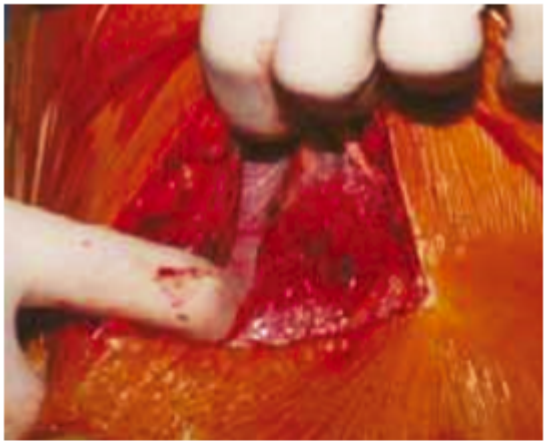
Figures taken from: Pelosi MA II, Pelosi MA III. Minimally invasive cesarean: improving an innovative technique. OBG Management. [Internet]. 2004 Jul;16(7).

FIGURE 1

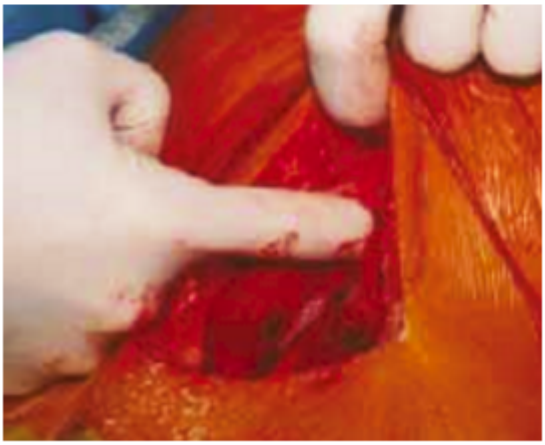
Create a modified abdominal incision



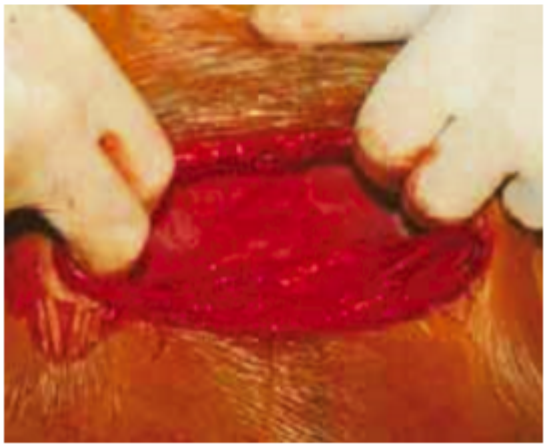
A. After making a straight low transverse incision with a scalpel, divide the subcutaneous tissue transversely with an electrocautery knife. Open the fascia transversely with the electrocautery knife to the same length as the skin incision.



B. Separate the rectus muscles in the midline by vertical blunt finger dissection.



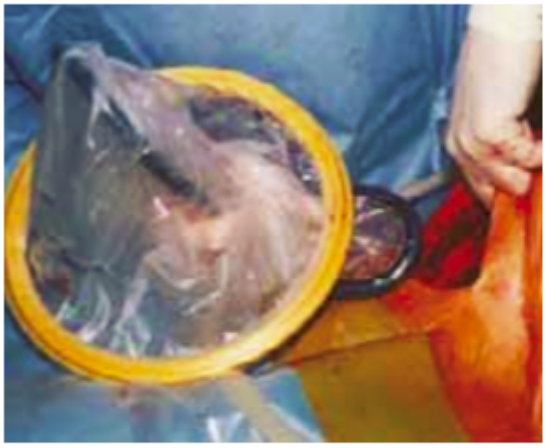
C. Open the peritoneum by finger perforation.



D. Stretch the full thickness of the abdominal wall to full size of the skin incision. Include the skin, subcutaneous tissue, fascia layer, rectus muscles, and peritoneum.

FIGURE 2

Place the abdominal retractor



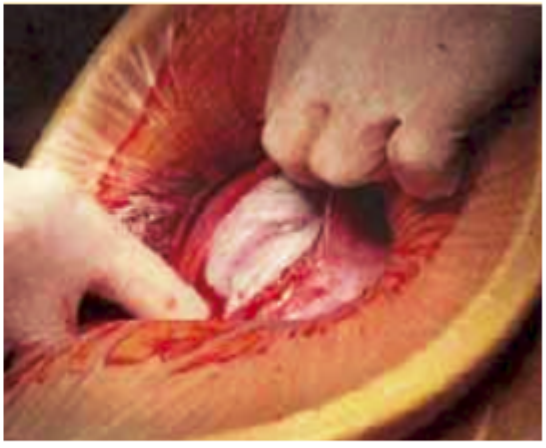
A. While applying upper traction and elevating the superior edge of the abdominal incision, squeeze the inner ring and insert it into the abdominal cavity toward the patient's head, allowing the device to spring open against the parietal peritoneum.

B. Hold up the outer ring, then roll it into the plastic sleeve until the ring completely inverts. Repeat until the top ring is snug against the patient's skin.

FIGURE 3

Use a standard hysterotomy in the lower uterine segment

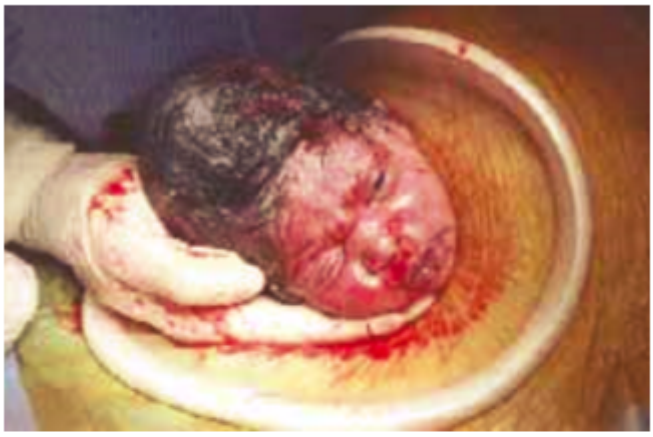
A. Make a transverse 2-cm uterine incision with a scalpel, approximately 1 cm above the vesicouterine peritoneal fold, omitting bladder-flap creation.



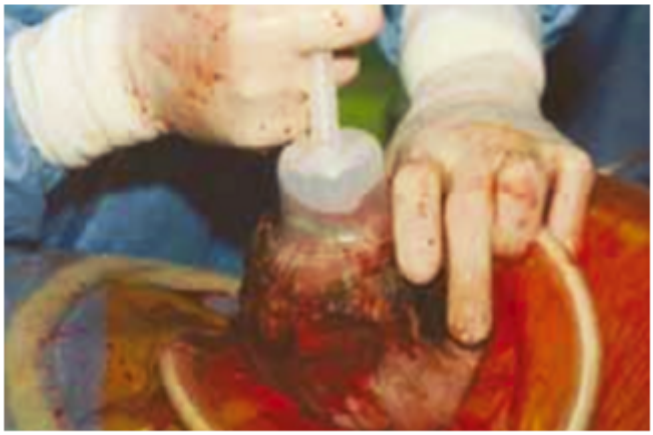
B. Digitally extend the incision vertically.

FIGURE 4

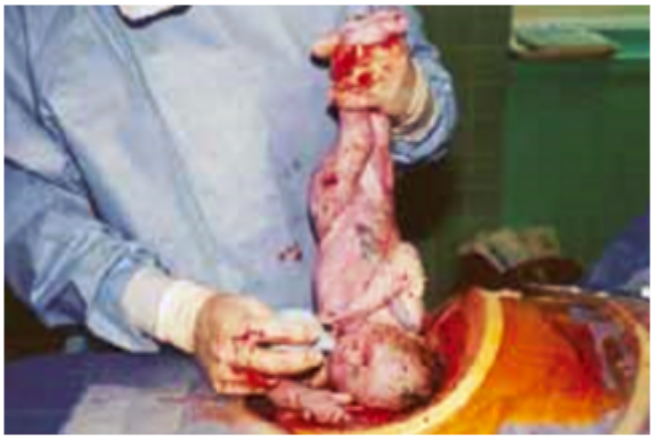
Deliver the fetal head



A. Deliver the fetal head in the standard fashion. The self-retaining retractor facilitates delivery of the fetal head by creating a rigid border around the abdominal incision.



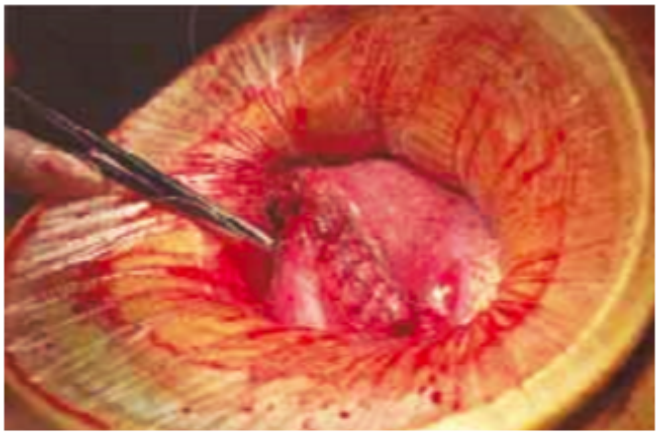
B. When head extraction proves difficult, a soft vacuum cup may be used.



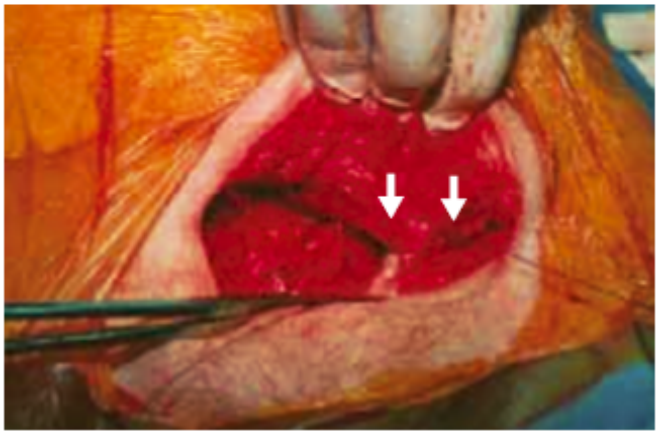
C. Breech extraction is performed using standard extraction maneuvers.

FIGURE 5

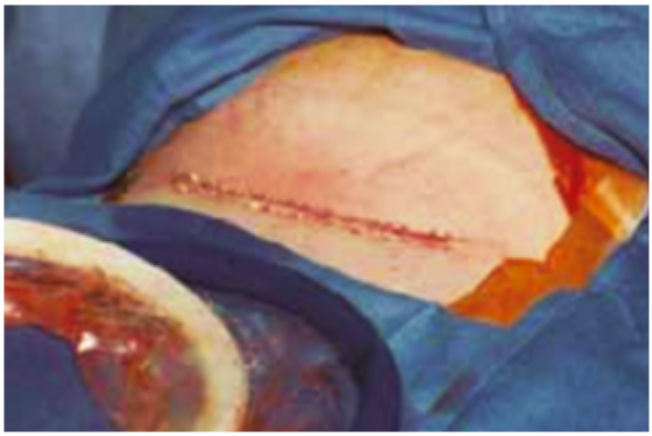
Close the incisions



A. Repair the hysterotomy in situ in a single layer, using figure-of-8 sutures as needed to control areas of persistent bleeding.



B. Close the rectus fascia in a continuous, nonlocking fashion with delayed-absorbable sutures placed at least 1 cm from the fascial wound edge (arrows). The visceral and parietal peritoneum are not closed, nor are the rectus muscles reapproximated.



C. Close the skin with metal staples (pictured) or subcuticular sutures.

15.2 Annex II: Information sheet for participants

Participant Information Sheet

Project title: "The Pelosi-type versus the modified Misgav-Ladach: a randomized trial of two surgical techniques for cesarean section"

Investigators: António Ventura, Fernando Montero

Collaborators: Alexandra Bonmatí, Anna Borrell, Anna Florensa, Anna Maria Heller, Anna Taltavull, Cristina Adrados, Cristina Noguera, Elena Alvarez, Elisabeth Merino, Eduard Sala, Esther Vila, Eva López, José Ruiz, Josep María Ramos, Lorena Rozas, Luis Miguel Alonso, Montserrat Farré, Sara Torrent, Vigmar Iriarte.

Location: Hospital Universitari de Girona Dr. Josep Trueta, Department of Obstetrics and Gynecology.

You are being invited to take part in a research study. Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

1. What is the purpose of this study?

Our study will compare the effectiveness of two surgical techniques for cesarean section in reducing the intraoperative blood loss. This operation is not done in standardized way and there are many variations in the surgical techniques used. Improving these techniques may contribute to reduce both short- and long-term complications associated with the operation. Given the fact that cesarean section is now the most common major surgical procedure performed worldwide, thousands of women could benefit in terms of better health outcomes and there also could be some cost-savings for the national health system.

2. Do I have to take part?

Participation in this study is voluntary. It is completely up to you whether or not you participate. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. A decision not to take part will not affect the standard of care you receive.

3. What will happen if I take part?

You will be participating in a randomized controlled research project. As said before, we do not know which is the most effective surgical technique for cesarean section. To find out we need to compare different surgical techniques. We put people into groups and give each group a different surgical technique. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). In addition, this research is also a triple blind study. This means that you, the study doctor who will collect the postoperative data and the data analyst will not know in which surgical technique group you are. After the hospital discharge, if you wish this information can be shared with you.

4. What do I have to do?

You will be asked to give two blood samples, one before the operation and another 1-hour after it, in order to analyze your hemoglobin and hematocrit levels. Weight and height measurements will be taken after maternal unit admission. Finally, a two-week postoperative appointment will be scheduled to examine the abdominal incision and to make sure everything is following a normal course.

5. Will my taking part be kept confidential?

Yes. The information that we collect for this research project will be kept confidential in accordance with the Organic Law of Data Protection (15/1999) and the data will be used exclusively for the purposes of this project. Any information about you will have a number on it instead of your name.

6. What if I change my mind about taking part?

If you decide to withdraw from the study, your standard of care will not be affected. You will still be asked to attend the routine follow-up clinics required by your doctor and hospital as part of your standard care. These follow up clinics will not be part of the study.
If you withdraw from the study, all samples and clinical information that we have obtained up to the point of you coming out of the study will continue to be used for the purpose of the study.

7. What if there is a problem?

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact Dr. António Ventura or Dr. Fernando Montero on 972 94 02 35.

8. How will the information I provide be used?

We plan to publish the results in a health journal so others can read about and learn from the results of the study.

9. Who has reviewed this study?

The hospital's Clinical Research Ethics Committee (CEIC) have reviewed the study and given it a favorable opinion.

10. Further Information

If you require more information about this study please call one of the telephone numbers provided to speak to a clinical member of the research team.

Thank you for reading this.

If you have any questions or would like any more information please contact

Dr. António Ventura or Dr. Fernando Montero by phone:

972 94 02 35

Please keep this information sheet for your records.
If you agree to enter the study, please sign the
attached consent form and we will return a copy to you.

15.3 Annex III: Informed consent for participants

CONSENT FORM

Project title: "The Pelosi-type versus the modified Misgav-Ladach: a randomized trial of two surgical techniques for cesarean section"

Investigators: António Ventura, Fernando Montero

Patient Identification Number for this trial:

Please initial all boxes

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by study doctors and nurses, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Doctor taking consent	Date	Signature

15.4 Annex IV: Timeline

ACTIVITY	PERSONNEL	JAN-FEV 2014	FEV-JUL 2014	AGO-JAN 2015	FEV-JUL 2015	AGO-JAN 2016	FEV-MAY 2016	JUN-SEP 2016	OCT-DEC 2016
Coordination phase	All the team								
Field research	Investigators and collaborators								
Data extraction and processing database	All the team								
Data analysis	Investigators and statistical consultant								
Interpretation of results, publication and dissemination of research findings.	Investigators								