Aus der Klinik für Geburtsmedizin

der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

The incidence of surgical site infection in Caesarean Sections with the use of a plastic sheath wound retractor compared to the traditional self-retaining metal retractor

zur Erlangung des akademischen Grades

Doctor medicinae (Dr. med.)

vorgelegt der Medizinischen Fakultät

Charité – Universitätsmedizin Berlin

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Datum der Promotion: 09 Dezember 2016

CONTENTS

Abbreviations

BMI   Body Mass Index

CDC   Centers for Disease Control and Prevention

CI   Confidence Interval

Fig   Figure

g   gram

HIV   Human Immune Deficiency Virus

IUGR Intrauterine Growth Restriction

min   minutes

mm   millimeter

n   number

NICE National Institute for Clinical Excellence

NNT Number Needed to Treat

No   Number

OP   Operation

Pic   Picture

RCOG Royal College of Obstetricians and Gynecologists

RR   Relative Risk

SSI   Surgical Site Infection

WHO World Health Organization

US   United States

USA   United States of America

Abstract

Background: There has been an unprecedented rise in worldwide Caesarean Section rates of up to 19.4%. Surgical Site Infection is an increasing problem with rates of up to 13.5%. Plastic-sheath wound retractors have been shown to reduce the rate of Surgical Site Infection in abdominal bowel surgery. However, there is limited evidence for the use of plastic sheath retractors in women having Caesarean Sections.

Methodology: In a single center, prospective, randomized controlled trial we evaluated the use of the Alexis® O C-Section Retractor in the prevention of surgical site infection. We randomized patients undergoing their first planned Caesarean Section to either the Alexis® O C-Section Retractor or the traditional Collins Self-Retaining Metal Retractor. The primary outcome was Surgical Site Infection within 30 days of operation as defined by the Centers for Disease Control and Prevention. The secondary outcomes included ease of application and removal of the retractor, intraoperative surgical parameters such as the use of electrical diathermy to control hemostasis, bowel handling, postoperative pain scores and the short and long-term satisfaction with wound healing.

Results: From October 2013 to December 2015, we enrolled a total of 214 patients. We excluded 16 patients from the analysis as 11 went into labor, one required an Emergency Caesarean, one required a laparotomy and 3 declined participation. We assigned 98 patients to the Alexis® O C-Section Retractor group and 100 to the traditional Collins Self-Retaining Metal Retractor. We show that in low risk women having their first planned Caesarean Section, there was a statistically significant reduction in the rate of Surgical Site Infections when the Alexis® O C-Section Retractor was used for wound retraction compared to the traditional Collins metal self-retaining wound retractor 1% vs 8% (RR 7.84, 95% CI (2.45-70.71) p=0.035). There was also a significant reduction in the need for diathermy heat treatment for bleeding subcutaneous vessels 35% vs 82% (RR 2.36, 95% CI (1.97-2.85), p=0.001) and bowel handling 3% vs 22% (RR 7.19, 95% CI (3.39-18.37) p=0.001).

Conclusions: Our study shows that the use of the Alexis® O C-Section Retractor compared to the traditional Collins self-retaining metal retractor in low risk women, having the first Caesarean Section is associated with a significantly reduced risk of Surgical Site Infection. There is also significant reduction in the use of electric cautery for subcutaneous bleeding, bowel handling and postoperative pain. Operator satisfaction is improved and postoperative pain is less.

Zusammenfassung

Hintergrund: Die Kaiserschnittrate ist weltweit drastisch gestiegen auf 19,4%. Zudem steigt die Inzidenz von Wundinfektionen auf eine Rate von bis zu 13,5%. In Studien konnte gezeigt werden, dass der Einsatz von ringförmigen Kunststoff-Wundretraktoren das Risiko für Wundinfektionen in der Abdominalchirurgie reduziert. Es gibt bislang unzureichende Evidenz für die Anwendung des Alexis® O C-Section Retraktor bei Frauen, die einen Kaiserschnitt erhalten.

Methodik: In einer prospektiv randomisierten kontrollierten Single-Center Studie untersuchten wir die Anwendung des Alexis® O C-Section Retraktors hinsichtlich der Prävention von Wundinfektionen. Patientinnen für einen ersten geplanten Kaiserschnitt wurden entweder für die Verwendung eines Alexis® O C-Section Retraktors oder einen traditionellen Metall- bauchdeckenspreizer (Metall Collins Retraktor) randomisiert. Der primäre Endpunkt war die Wundinfektion laut der Definition des "Centers for Disease Control and Prevention". Sekundäre Endpunkte waren unter anderem die subjektive Beurteilung der Einfachheit der Anwendung beider Wundspreizer, die Notwendigkeit zur Koagulation des Unterhautfettgewebes, die Häufigkeit, den Darm zur reponieren, der postoperative Wundschmerz und die Zufriedenheit der Patientinnen mit der Wundheilung.

Ergebnisse: Von Oktober 2013 bis Dezember 2015 wurden 214 Patientinnen rekrutiert. 16 Patientinnen wurden von der Untersuchung ausgeschlossen, 11 aufgrund vorzeitiger Wehen, eine Patientin wegen einer Notsectio, eine Patientin aufgrund einer Relaparotomie und drei Schwangere hatten ihre Teilnahme abgesagt. Es wurden 98 Patientinnen in die Alexis® O C-Section Retraktor Gruppe und 100 in der traditionellen Metall Collins Retraktor Gruppe randomisiert. Unsere Studie zeigte, dass die Anwendung des Alexis® O C-Section Retraktors zu einer signifikanten Reduktion der Inzidenz von Wundinfektionen führte (1% vs 8% (RR 7.84, 95% CI (2.45-70.71) p=0.035)). Zudem zeigte sich eine signifikante Reduktion der Notwendigkeit von Koagulation des Unterhautfettgewebes (35% vs 82% (RR 2.36, 95% CI (1.97-2.85), p=0.001)) und Darmmanipulation (3% vs 22% (RR 7.19, 95% CI (3.39-18.37) p=0.001)).

Schlussfolgerung: Unsere Studie zeigte, dass der Einsatz des Alexis® O C-Section Retraktors im Vergleich zum traditionellen Collins Metall-Wundretraktor die Rate von Wundinfektionen bei primären Kaiserschnitten signifikant senkt. Zudem zeigte sich ein reduzierter Bedarf elektrischer Koagulation im Unterhautfettgewebe. Ferne musste weniger Darm intraoperativ reponiert werden und es traten signifikant weniger postoperative Schmerzen auf. Auch die Zufriedenheit der Operateure bezüglich der technischen Anwendung zeigte deutliche Vorteile in der Gruppe des Alexis® O C-Section Retraktors.

1. INTRODUCTION

The Caesarean Section is the commonest operation performed on women of the reproductive age worldwide, with estimates of 1 in 5 births being by Caesarean Section. There continues to be an unprecedented rise in the Caesarean Section rate.[1] In a 2016 study, Betrán et al. showed in an analysis from 150 countries, a global rise in the rate of Caesarean Sections from 6.7% in 1990 to 19.4% in 2014. Caesarean Section rates across different countries and regions are variable with the highest rate in South America where Caesarean Sections are performed in 42.9% of all pregnancies.[2]

A study from Mylonas et al. in 2015 showed that in Germany, the rate of Caesarean Sections doubled from 15.3% in 1991 to 31.7% in 2012.[3] The ministry for statistics in Germany has reported the latest rate in 2014 to be at 31.8%.[4]

The wide variation in rates of Caesarean is multifactorial and based not only on clinical indications but also on the variable implementation of national guidelines on Caesarean Section and possibly on social and cultural factors. [1,5-9]

In Germany, the increase in Caesarean Sections has been partly explained by increasing clinical indications for Caesarean Section such as breech presentation, multiple pregnancy, fetal macrosomia, a history of previous Caesarean Section, increasing maternal medical indications such as preeclampsia, maternal cardiac conditions and the maternal request for elective Caesarean Section.[3]

Kolip et al. have recently published extensive data on the rise of Caesarean Section across Germany, which also highlights the variations in the Caesarean Section rates across the different regions of Germany from 17% in some regions and 51% in others. The highest rates are recorded in Bayern, Niedersachsen and Rheinland-Pfalz. While this may be explained by the variation in patient populations and the quality and availability of midwifery care, there appears to be a significant element of defensive medicine and perceived risk avoidance, influencing mode of delivery decisions. Nevertheless, the rate is rising and continues to rise and so with it the risks of complications.[10]

There are well-established complications, which occur intraoperative and include the risks of infection, bleeding, trauma, hysterectomy and anesthetic problems. [11-19]

There are also postoperative complications such as thrombosis, adhesion formation and postoperative pain.[20-25]

Risks and complications for future pregnancies also exist and include abnormal placenta implantation and the risk of placenta accreta, increta and percreta, uterine rupture, hysterectomy and reduced fertility. [26-35]

Introduction

More specifically, infection at the time of Caesarean Section can occur at the site of surgery, the so-called Surgical Site Infection (SSI) but also in other organ systems as well such as the urinary tract, the lungs and as a general systemic infection or sepsis.[17,36,37] In addition to the immediate risk and short-term problems of SSIs, there are also long-term complications that can occur. Readmission for repeated operations such as wound revisions for the treatment of abdominal wall abscess and hematomas as well as laparotomy for deep abdominal abscess pose prolonged risks. Subsequent intra-abdominal adhesion formation and chronic pelvic pain are significant long-term consequences.[21-24] Psychological trauma and negative feelings about the operation are also long-term issues after SSI.[38]

Prolonged intensive care hospitalization and treatment as well as the long-term effects after multi-organ infection following generalized sepsis including abnormal renal function, cardiac function, psychological stress and even death are also important to consider. [39,40]

Enquiry reports into maternal death have revealed that sepsis is an important cause in 10 percent of cases.[17] In England, the Maternal Mortality Enquiry has highlighted the increasing incidence of maternal sepsis and death.[41] In the United States of America sepsis is the second leading cause of maternal mortality.[42] The single most important risk factor identified in cases of maternal death from sepsis is the Caesarean Section.[43,44] Furthermore, the mortality rate associated with surgical site infection is 3% and 75% of SSI associated deaths are directly caused by SSI.[45]

The World Health Organization recognizes the worldwide increasing rates of infection post partum, the rate of maternal sepsis and death. These rates are highest in sub-Saharan Africa where access to obstetric care, sterile surgical conditions and antibiotic prophylaxis is limited. The WHO and other national and international steering groups have recommended strategies to reduce the rates of infection especially at the time of Caesarean section.[46-48]

The cost of dealing with infection after elective planned surgery can have a significant impact on health care provision.[49] Work by Plowman et al. in England has shown that the cost of readmission and treatment for infection after surgery carries a potential annual cost of up to 930 million pounds for health care providers.[50] Whereas in the United States of America, the financial burden of 6.5 Billion US dollars per annum has been estimated. A meta-analysis in 2016 from Arefian et al. has shown that strategies to reduce the incidence of hospital acquired infection can lead to significant cost savings for health care providers.[51]

Looking specifically at the rates of surgical site infection after Caesarean Section, this has been reported in the literature as being extremely variable where Dyrkorn et al have quoted a rate of as high as 17%.[52] Numerous studies have tried to evaluate the incidence of SSI and these studies all show a variation in rates. Wilson et al describe a rate of 9.8 % in England

across 44 different hospital sites. [53] Klingel and Patel describe the rate of SSI after Caesarean Section in the United States of America as 7.5%, this being the average between 2.4% and 13.6% as reported by the Centre for Disease Control (CDC) in 2004.[54,55]

The variation in the SSI rates may be secondary to the advent and use of preoperative antibiotics, possible variations in the techniques of the Caesarean, variations in the adherence to strict sterile operative field protocols, aseptic techniques and most importantly the detection and surveillance for infection postoperatively. [52]

For many years, Caesarean Sections were performed without the use of antibiotic prophylaxis. Preoperative antibiotics to reduce the risk of intraoperative and postoperative infections became recommendations 22 years ago.[56,57] The implementation of national recommendations remains variable, as is the timing of administration of antibiotic prophylaxis (preoperative vs. after umbilical cord clamping).[58-61]

In Germany, the current standard of practice is such that antibiotic prophylaxis preoperatively is a recommendation for good practice.[62] However, wound infection can still occur if the wound site is contaminated.[39]

The variation in Surgical Site Infections is not only influenced by the use of antibiotic prophylaxis but also importantly by specific obstetric risk factors.

Zerr et al. have shown that the risk of surgical site infection is increased in patients with medical conditions such as diabetes mellitus and obesity.[63]

There are increasing rates of diabetes worldwide with increasing rates of associated complications in pregnancy and for delivery. The rise in incidence has warranted guidelines on the management and treatment of diabetes in pregnancy. Strict adherence to glucose control is required to minimize the complications at delivery including Surgical Site Infection. [64-68]

Additionally, obesity is a recognized and well-established health risk factor and has an influence on wound healing and the risk of SSI. [68-72]

Intrapartum factors can also increase the risk of surgical site infection such as in Caesarean Sections that are performed in labor or as an emergency and also where there is suspected chorioamnionitis. [68,72]

Not only are the patient dependent risk factors significant and the timing of the Cesarean important but also the surgical specific factors that may play a role in the risk of surgical site infection.

The technique of the Caesarean Section has evolved over the years. The varying methods have developed with the goal of minimizing risks to the patient, especially the risk of infection. Adherence to sterile conditions, blunt dissection of tissues where possible,

minimization of tissue handling, avoidance of uterus exteriorization, avoiding suturing of the peritoneum, avoiding suturing of the rectus muscle, reducing the risk of subcutaneous hematoma formation with subcutaneous suturing if the subcutaneous layer is > 2cm, avoidance of skin closure with staples and avoidance of drainage have been shown to improve outcomes. [73-76]

There are also various techniques employed for performing a Caesarean Section.[77]

The modified Misgav Ladach technique is internationally well accepted and it is in the Charité University Hospital the standardized surgical approach.[78,79] Occasionally, the surgeon is allowed where necessary deviation from this approach when desired for clinical reasons.

Various surgical factors may play a role in the development of SSI. It has been shown that in the setting of a caesarean section, the amniotic fluid and meconium may no longer be sterile and can act as a transport medium for bacteria after ruptured membranes and may pose a risk to surgical site infection and may even act as irritants negatively affecting wound healing. [72]

The role of subcutaneous electric cautery to achieve hemostasis may also theoretically cause the formation of necrotic tissue through thermal damage and carbonization of tissue, which serve as a risk factor for wound breakdown and SSI. [80] A recent randomized study by Moreira et al has shown that patients who received electrodiathermy to achieve hemostasis upon closure have an increased incidence of wound healing problems 14 days after Caesarean with a relative risk of 1.5 when compared to those without electrodiathermy.[81]

There are evidence-based, surgical technique recommendations to reduce the incidence of SSI. These include showering with 4% chlorhexidine gluconate on the night before Cesarean, clipping rather than shaving of pubic hair preoperatively, avoidance of vaginal examinations, avoidance of unnecessary instrumentation, skin disinfection with chlorhexidine-alcohol skin preparation, intravenous preoperative antibiotic prophylaxis, avoidance of manual placenta removal, avoidance of skin closure with staples, the maintenance of strict glycemic control in patients with diabetes and early urinary catheter removal. [82-89]

On the other hand, several reviews have shown that some strategies have no impact on the rate of SSI, such as closure of the pelvic peritoneum, single versus double-layer uterine closure, exteriorization of the uterus, preoperative vaginal cleaning with iodine, administration of perioperative oxygen and saline wound irrigation. [90-94]

The rates of SSI are not only multifactorial but also highly dependent on the detection rates and the definition of what an SSI is.

Recent work by Wilson et al in 2013 has shown that the detection rates of SSI are not optimal and in most cases are not reported or picked up.[53] Ng et al have shown that a post discharge surveillance up to 6 weeks after the operation can improve the detection rates of SSI and

provide a true reflection of actual incidence rates and help in the enforcing and implementation of infection protocols and standards. [95,96]

1.1 Definition of Surgical Site Infection (SSI)

The definition of a surgical site infection has been standardized by the Center for Disease Control and Prevention (2014) and can be grouped in incision, deep and organ infections (see Table 1).

A surgical site infection must meet the following criteria:

Table 1. Surgical Site Infection

Surgical Site (Incisional) Infection
Infection occurs within 30 days after operative procedure (where day 1 = the procedure date), and
involves only skin and subcutaneous tissue of the incision and
patient has at least one of the following:
a. purulent drainage from the superficial incision.
b. organisms isolated from an aseptically-obtained culture of fluid or tissue from the superficial incision.
c. superficial incision that is deliberately opened by a surgeon, attending physician or other designee and is culture positive or not cultured and patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; redness; or heat. A culture negative finding does not meet this criterion.
d. diagnosis of a superficial incisional SSI by the surgeon or attending physician or other designee.
Surgical Site (Deep) Infection
Infection occurs within 30 or 90 days after the operative procedure (where day 1 = the procedure date) and
involves deep soft tissues of the incision (e.g. fascial and muscle layers) and
patient has at least one of the following:
a. purulent drainage from the deep incision.
b. a deep incision that spontaneously dehisces or is deliberately opened by a surgeon,

attending physician or other designee and is culture-positive or not cultured

and

patient has at least one of the following signs or symptoms: fever

(>38°C); localized pain or tenderness. A culture-negative finding

does not meet this criterion.

c. an abscess or other evidence of infection involving the deep incision that is detected on direct examination, during invasive procedure, or by histopathologic examination or imaging test.

Organ/Space Surgical Site Infection
Infection occurs within 30 after the operative procedure (where day 1 = the procedure date) and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and patient has at least one of the following: a. purulent drainage from a drain that is placed into the organ/space b. organisms isolated from an aseptically-obtained culture of fluid or tissue in the organ/space c. an abscess or other evidence of infection involving the organ/space that is detected on direct examination, during invasive procedure, or by histopathologic examination or imaging test.

1.1.1 The role of wound retraction

Whilst the definition of a surgical site infection (SSI) is important, the development is also dependent on the nature of the operation, the creation of the incision, wound retraction and method of the surgery. The first steps in the surgical performance of the Caesarean Section is the initial creation of the abdominal incision, gaining access to the abdominal cavity and then employing a method of wound retraction necessary to perform the delivery of the baby.

Abdominal wall retraction is traditionally performed with metal retractors. Variable metal retractors are available. Some are hand held retractors (e.g. Fritsch and Deaver Retractors) and others such as the Collins Retractor are self-retaining retractors (Pic 1).

Introduction

Self-retaining retractors were developed to provide more freedom of movement and visualization for the surgeon whilst enabling the assistant to perform other necessary tasks. [97,98]

The method of wound retraction is an important aspect of the operation and plays a role in the risk of SSI. Protection of the wound during the time of operating by maintaining a sterile field should lead to reduction in wound contamination and SSI development. Additionally, achieving maximum hemostasis of subcutaneous tissue reduces hematoma formation, wound breakdown and infection.

A newly developed abdominal wall retractor for Cesarean Section is the Alexis® O C-Section Retractor which is formed of 2 plastic rings and an interconnecting plastic polyurethane sheath where the flexible inner ring is placed into the abdomen and the rigid outer ring is rolled to create tension on the plastic sheath providing 360° circular abdominal wound retraction with a simultaneous tamponade effect and covering the abdominal wound during the Caesarean Section.

Extensive work has been done in the field of general abdominal surgery, which have shown reductions in the risk of SSI with the use of the Alexis® O Retractor. Cheng et al have looked at 72 patients having colorectal resections and showed a reduction from 20% in the control group to 0 % in the study group. Hariouchi and colleagues showed in 272 patients with gastrointestinal surgery a significant reduction in bacterial wound infection with the use of the Alexis® O Retractor. [99,100]

Mihaljevic et al published in 2015 a large systematic review of 16 randomized controlled trials studies including 3695 patients, where it was shown that the use of wound protectors significantly reduces SSI (relative risk 0.45; 95% CI, 0.24-0.82). [101]

To date no work has been done to compare the use of the new Alexis® O C-Section Retractor in comparison with the traditional Collins self-retaining metal wound retractor at the time of Caesarean Section in primary elective Caesarean Section in women without major comorbidities for wound infections and without a previous Caesarean Section.

Introduction

1.2 Null Hypothesis

The Null Hypothesis to be tested:

"The use of the Alexis® O C-Section Retractor in comparison to the traditional Collins self-retaining metal wound retractor does not affect surgical site infection rates in low risk women having a planned primary Caesarean Section"

1.3 Aims and Outcomes

1.3.1 Primary Outcome

The primary aim of the study is to investigate the incidence of surgical site infection (SSI) in low risk women having a first time planned Caesarean Section using the Alexis® O C-Section Retractor and the traditional Collins Self-Retaining Metal Retractor.

1.3.2 Secondary Outcomes

The secondary outcomes of the study were to investigate other aspects of the use of the retractor, which play an important role in the surgical performance of the operation and the patient satisfaction with the wound healing. These included an assessment of intraoperative surgical parameters, the surgical outcomes including the surgeon's subjective experience, ease of application and removal of the retractor, postoperative pain scores and the short and long term satisfaction with wound healing.

The specific secondary outcomes include:

• Subjective Assessment of the Ease of Application of Retractor Instrument

• Incision to Delivery Time

• Incision to Skin Suture Time

• Subjective Assessment of Visualized Operative Field

• Subjective Assessment of Freedom of Surgical Movement

• Interference from Descending Bowel or Adnexal Tissue

• Bowel and Bladder Trauma

• Need for Bowel Repositioning

Introduction

- Need for Paracolic Cleaning of Blood and Amniotic Fluid

- Need for Uterus Exteriorization Intraoperatively

- Rectus Sheath Trauma

- Muscle Trauma

- Muscle Suturing

- Coagulation of the Subcutaneous Tissue

- Subcutaneous Tissue Thickness

- Skin Lacerations

- Trauma to the Baby

- Estimated Blood Loss

- Ease of Retractor Removal

- Analgesia Requirements Post Operative

- Wound Healing Problems on Discharge and at 6 Weeks (Telephone Interview)

- Wound Infections (As defined by Centers for Disease Control)

- Time to Hospital Discharge

- 6-Week Scar Pain Scores (Telephone Interview)

- Patient Satisfaction with Wound Healing (Telephone Interview)

2. METHODOLOGY

2.1 Ethical approval

The Study was given ethical approval from the Charité Ethics Committee and has an Ethics Approval Number: EA1/091/13.

The Study is registered at ClinicalTrials.gov with the Identifier Number: NCT02685696

Patient selection for the study required the meeting of inclusion and exclusion criteria.

2.2 Sample size calculation

We estimated a sample size for the trial based on a rate of surgical site infection of 8%. The SSI rate in the control group was 8% and this is in keeping with the average reported rate by the Centers for Disease Control and Prevention (CDC). Recently, in a study published in the New England Journal of Medicine by Tuuli et al, the SSI rate of 8% was also used as a reference.[54,102]

We estimated that the study required 186 participants with 93 in each arm in order to have 80% power to detect a difference in the rates of surgical site infection. To accommodate possible loss to follow up we anticipated enrolling 200 patients.

2.3 Inclusion criteria

Only patients having their first planned Caesarean Section were to be included.

Patients would be randomized into two groups to receive either the Alexis® O C-section Retractor or the traditional Collins metal self-retaining retractor.

2.4 Exclusion criteria

Because of the influence of risk factors on the incidence of wound infection and wound breakdown, patients with particular risks factors were excluded. These patients were those with diabetes, chronic auto immune diseases such as Lupus, immune deficiency diseases such as HIV, known bleeding disorders, patients receiving full anti-coagulation therapy, patients with a history of wound healing problems, patients who had a previous Caesarean Section and patients who had previous major abdominal surgery such as a laparotomy. Furthermore,

patients in the active phase of labor and patients with suspected or confirmed chorioamnionitis were excluded.

2.5 Recruitment

All women attending the antenatal care unit at the Charité University Obstetric Department who required their first planned, primary Caesarean Section for delivery were invited to participate in the study. Patients were provided with detailed information on the study and given time to consider.

The study was described in lay terms within a Patient Information Form and given to each patient who was suitable for the study and as supplement material during the consenting process.

Once patients approved to be included into the study an individual consent form was signed.

Patients were then prospectively randomized using the method of block randomization into two groups. Group 1 received the Alexis® O C-section Retractor and Group 2 received the traditional Collins Metal self-retaining Retractor. Patients were not informed into which group they would be randomized.

Patients were free to decline recruitment into the study and also free to withdraw at a later date if so desired.

All surgical operators were thoroughly trained in the use and application of the Alexis® O C-section Retractor prior to the start of the study and supported by regular teaching demonstrations. The Obstetric Theatre Team was also informed and trained in use and application of the Alexis® O C-section Retractor within the Study Design.

On the day of the Caesarean Section the type of retractor was revealed to the operator.

2.6 Performance of the Operation

All patients were operated on according to the standardized method employed at the Charité University Hospital.

All patients received preoperative 'single shot' prophylactic antibiotic therapy in the form of cefuroxime 1,5 g or with clindamycin 900 mg (in patients with a penicillin allergy) given intravenously 30 minutes before the operation.

All patients in the study received a spinal anesthetic prior to operation. The operative field is cleaned with Softasept® N disinfection solution, in which the active ingredients are per 100g solution; 74.1g ethanol (100%) and 10g propan-2-ol. This is then allowed to dry.

Methodology

The patient is then draped with a sterile drape, which has an adherent plastic window to be placed over the operative field on the abdomen.

The modified Misgav Ladach technique of Caesarean Section is the technique of choice.

All abdominal incisions are made in the transverse fashion approximately 3-4 cm above the symphysis pubis. The subcutaneous fat is bluntly dissected. The rectus sheath is incised and also bluntly dissected laterally. The rectus muscle is left intact and entry into the abdomen is achieved using blunt digital dissection through the midline. All opened layers are then manually stretched to achieve operative access to the uterus.

The wound retractor is then placed and secured and the operation proceeds as per routine. The peritoneal bladder fold is then incised and the bladder dissected downwards. A transverse uterine incision is made in the lower uterine segment, initially sharp and then with blunt dissection laterally. On entry into the uterine cavity amniotic fluid and blood is suctioned away from the operative field. The baby is delivered as per routine and when desired the parents were allowed to view the birth of the baby as described by Armbrust et al and under sterile conditions the partner is allowed to cut the umbilical cord.[103] The baby is then handed to the attending midwife. The operation continues with the application of uterotonics in the form of an oxytocin (Syntocinon) bolus 3 I.U. followed by a continuous infusion of 9 I.U. diluted in 500ml over 4 hours. The delivery of the placenta is achieved with cord traction or manual removal and the uterine incision then closed with No. 1 Vicryl (CTX Plus ETHICON®) suture material. The technique of closure is variable and the preference of the surgeon. Occasionally, the uterus is delivered abdominally to perform uterine closure. This was recorded according to whether this was a surgeon preference or if the operator found it to be clinically indicated to ensure better suturing of the uterus. The techniques of uterine closure include; either in a single layer or a double layer with the initial layer either in a continuous or interlocking fashion. The second overlapping layer is closed in a continuous fashion. Occasionally, hemostatic figure of 8 sutures may be required to achieve hemostasis. The management of any unexpected postpartum hemorrhage followed standardized postpartum bleeding protocols.

The parietal and visceral peritoneum layers were not sutured and rectus muscle was sutured only if there was a muscle injury or because of surgical preference. If necessary, this was performed using No. 0 Vicryl (CT-1 ETHICON®) Suture.

The subcutaneous layer was usually closed or adapted where the estimated thickness was more than 2 cm and where bleeding was present, this was treated with electrical diathermy or hemostatic sutures.

The skin was then closed with subcuticular 3/0 Prolene (ETHICON®) which is then routinely removed on the 4th postoperative day.

Disinfection solution was then applied to the skin around the incision site and the incision covered with sterile strips or surgical plaster.

The patient was then transferred to the observation area for 2-4 hours and thereafter to the postnatal ward. All patients received a postoperative pain therapy protocol. In this protocol patients had regular pain medication with the option to have extra pain therapy according to the patient's desire.

2.7 The Alexis® O C-Section Retractor

Figure 1.

The Alexis® O C-Section Retractor (Applied Medical, Rancho Santa Margarita, California, USA) is comprised of 2 plastic rings separated by a cylindrical reinforced polyurethane sheath. The soft inner ring is flexible and is placed into the peritoneal cavity and the outer ring lies externally on the outside of the abdomen. The rigid external ring is then rolled towards the abdomen until the polyurethane sheath becomes taunt and circumferentially evenly retracts the abdominal wound. The ring diameters are such that abdominal incisions up to 14 cm can be accommodated. A larger retractor is also available for incisions up to 17 cm. The depth of the retractor sheath can be varied and has a depth of up to 32 cm. The retractors are disposable and cost 49 Euros each.

2.8 The traditional Collins Metal Self-retaining Retractor

Figure 2.

The Collins self-retaining retractor is made of polished stainless steel and utilizes a ratchet system to spread, lock and hold the lateral blades of the retractor apart. The abdominal wound edges are held apart within lateral tissue holding blades that swivel and come to rest against

the lateral corners of the transverse abdominal incision. The Collins retractor can be reused after sterilization and cost 150 Euros each. Costs may vary depending on the supplier.

2.9 Post Operative Pain assessment and Pain Therapy

The assessment of pain was made with the use of visual analogue scales with 0 being no pain and 10 maximum pain, as shown in the information gathering form. There is a standardized pain therapy protocol for all patients after Caesarean Section under spinal anesthesia. Patients requiring extra pain therapy medication were documented.

Table 2. Postoperative Analgesia Regimen

Pain Therapy after Caesarean	Medication
Baseline analgesia	Ibuprofen 600mg three times daily for 3 days then when desired
Pain Scale Scores between 4-7	Paracetamol 1g intravenously. Maximum 4 g in 24 hours
Further therapy despite baseline therapy	Morphine 10 mg . Maximum 50 mg in 24 hours

 The postnatal ward doctor reviewed patients every day and prior to discharge the status of the wound was inspected and documented.

2.10 Data Collection

On completion of the Caesarean Section operation the surgeon filled the information gathering form.

Prior to discharge the patient was reviewed and the information form was updated.

A following review was made for patients subsequently readmitted with wound healing problems or infections and all patients were contacted per telephone 6-8 weeks after the operation date for a review of symptoms and completion of the data collection.

All data and patient information was anonymised in keeping with the ethical standards of the study.

Data on satisfaction were scored using Linkert scales and visual pain analogue scales were used to assess subjective postoperative pain.

2.11 Data Collection Form

Information Sheet: Alexis O Study

Patient Code:_____

Indication for Caesarean _____

Surgeon _____

Date _____

OP Time :_____

Study Group: Alexis O C- Section Retractor ☐   Collins Metal Retractor ☐

Application of the retractor is simple?

1	2	3	4	5
I--------------I--------------I---------------I--------------I
strongly   agree   neutral   disagree   strongly
agree   disagree

Time between skin incision and delivery of baby   _____minutes

Time between skin incision and skin closure _____minutes

Satisfaction score with the visualization of the operative field

1	2	3	4	5
I--------------I--------------I---------------I--------------I
strongly   agree   neutral   disagree   strongly
agree   disagree

Satisfaction score with operative freedom of movement

1	2	3	4	5
I--------------I--------------I---------------I--------------I
strongly   agree   neutral   disagree   strongly
agree   disagree

Disturbance during operation from prolapsing bowel or adnexa: Yes ☐   No ☐

Bowel trauma: Yes ☐   No ☐

Bladder trauma: Yes ☐   No ☐

Need for bowel or adnexal replacement with swabs: Yes ☐   No ☐

Need for paracolic cleaning and suction of blood and amniotic fluid: Yes ☐   No ☐

Uterus exteriorization: Yes ☐   No ☐   Elective ☐

Rectus Sheath trauma :   Yes ☐   No ☐

Muscle trauma :   Yes ☐   No ☐

Muscle Suture: Yes ☐   No ☐   Elective ☐

Coagulation of Subcutaneous Fat: Yes ☐   No ☐

Estimated thickness of the Subcutaneous Fat_____ mm

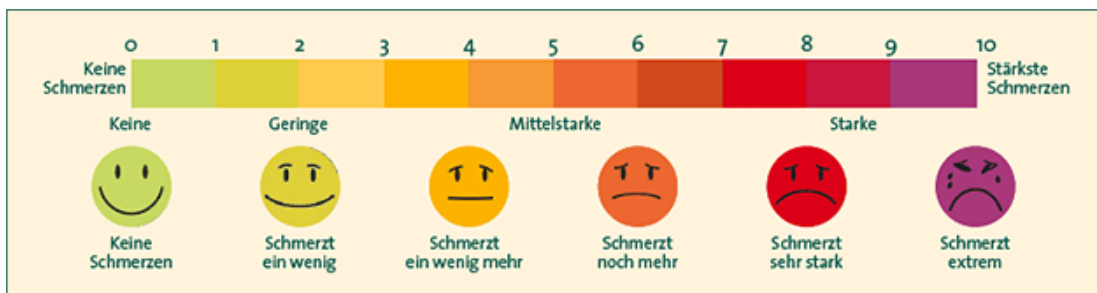Skin injury: Yes ☐   No ☐

Baby injury: Yes ☐   No ☐

Blood loss:_____ml

Removal of the retractor is simple?

```
1              2              3              4              5
I--------------I--------------I--------------I--------------I
strongly     agree        neutral      disagree     strongly
agree                                               disagree
```

Wound healing problem at discharge: Yes ☐   No ☐

Scar pain at discharge

Extra pain medication required :   Yes ☐   No ☐

Time to Discharge_____ Days

Scar pain 6 Weeks post op (Telephone interview): Yes ☐   No ☐

Problems with wound healing 6 weeks post op (Telephone Interview): Yes ☐   No ☐

Patient satisfaction with wound healing: Yes ☐   No ☐

Surgical Site Infection (CDC Definition):   Yes ☐   No ☐

3. STATISTICAL ANALYSIS

3.1 Data preparation

This analysis is based on data provided in "AlexisOring.xlsx". Apgar scores are only evaluated for singleton births. In addition to numeric scores, Apgar was reclassified into categories 1-7, 8, 9, 10. Blood loss was reclassified into categories <500, 500-1000, 1000-1500, >1500ml.

3.2 Statistical Analysis

All quantitative measures were classified as ordinal due to either their nature of assessment or distribution characteristics. Ordinal variables: Age, BMI, Gestational Age, Incision to Delivery Time, Incision to Skin Suture Time, Subcutaneous Tissue Thickness, Birthweight, Umbilical artery pH and Time to Hospital Discharge.

The following variables were classified as categorical or ordered categorical where appropriate: Gravida, Primary Indication for Caesarean Section, Ease of Application of Retractor Instrument, Visualized Operative Field, Freedom of Surgical Movement, Interference from Bowel/Adnexal Tissue, Bowel Trauma, Bladder Trauma, Bowel Repositioning, Paracolic Cleaning of Blood/Amniotic Fluid, Need for Uterus Exteriorization, Rectus Sheath Trauma, Muscle Trauma, Coagulation of Subcutaneous Tissue, Skin Lacerations, Trauma to the Baby, Ease of Retractor Removal, Wound Healing Problems on Discharge, Scar Pain at Discharge, Extra Analgesia Requirements Post Operative, 6-Week Scar Pain Scores, Wound Healing Problems at 6 Weeks, Patient Satisfaction with Wound Healing, Wound Infections, Blood Loss, APGAR scores at 1 minute, 5 minutes and 10 minutes.

Descriptive statistics for ordinal measures were median and 25th/75th percentiles. Group differences were tested by the Wilcoxon rank sum test. Categorical data are reported as absolute und relative frequencies, group differences are tested by the Fisher's exact test or generalized Cochran-Mantel-Haenszel test for ordered categories, taking their relative order into account.

Analyses were conducted with R(R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

4. RESULTS

4.1 Patient Allocation

Figure 3.
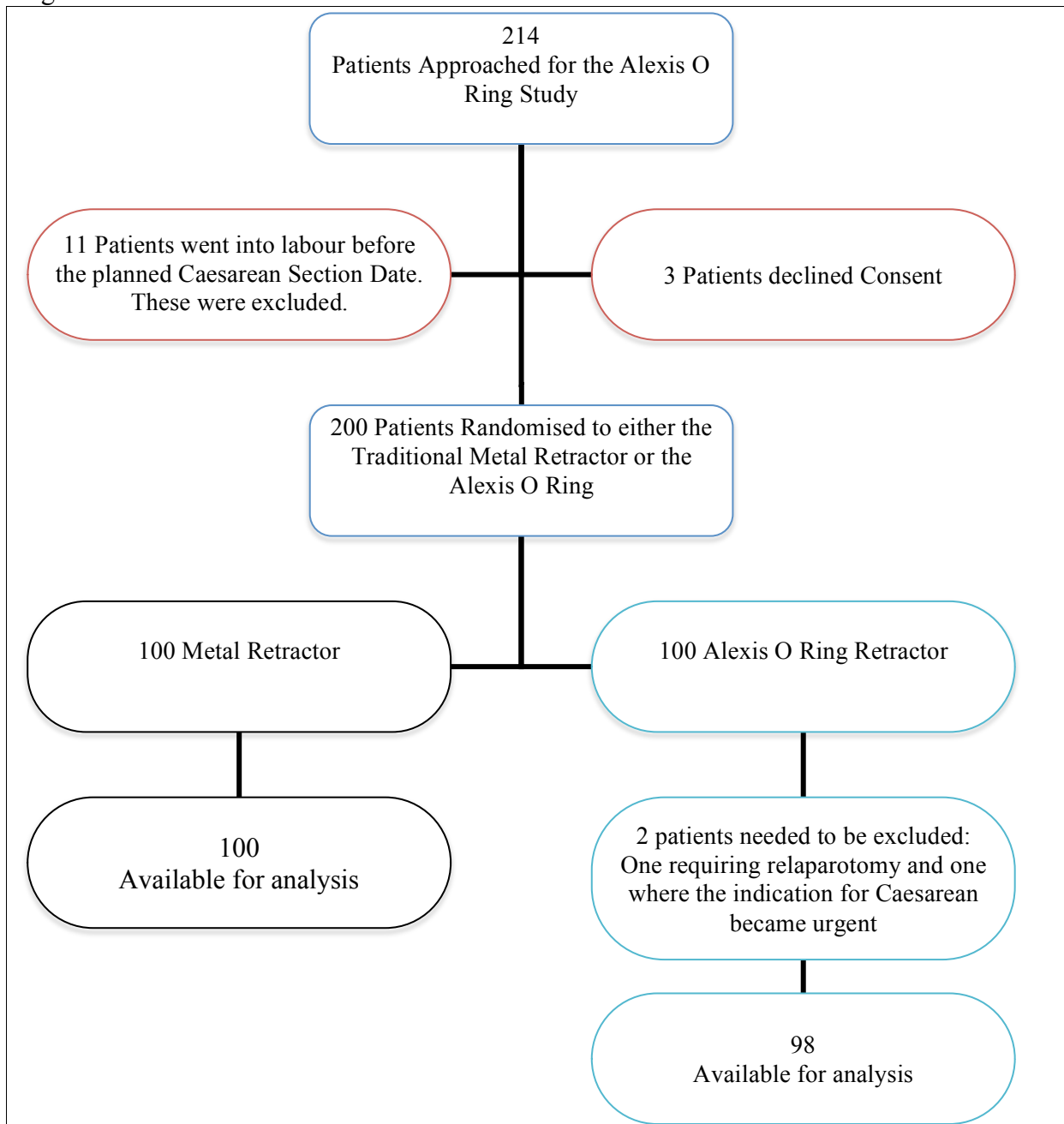
4.2 Descriptive Statistics

Table 3: Descriptive statistics, Median (25th,75th percentile)

Variable	Alexis	Metal	p	RR	CI
No. of patients (n)	98	100			
Age (years)	33 (27/36)	32 (28/35)	0.705		
Body Mass Index (BMI)	22.4 (20.5/24.5)	22.8 (20.3/25.8)	0.440		
Gestational Age (weeks)	38 (37/39)	38 (37/39)	0.932		
Incision to Delivery Time (mins)	5 (4/7)	5 (3/6)	0.231		
Incision to Skin Suture Time (mins)	39 (32/47)	39 (34/45)	0.502		
Subcutaneous Tissue Thickness (mm)	12 (10/20)	11 (10/20)	0.434		
Birthweight (gm)	3280 (2956/3578)	3308 (2880/3585)	0.811		
Umbilical artery pH	7.3 (7.2/7.3)	7.3 (7.2/7.3)	0.155		
Time to Hospital Discharge (days)	4 (3/4)	4 (3/4)	0.751		

Results

Table 3 continued: Descriptive statistics, frequency (%)

Variable	Alexis	Metal	p	RR	CI
Gravida					
1	69 (70%)	62 (62%)	0.250		
2	16 (16%)	20 (20%)			
3	5 (5%)	8 (8%)			
4	5 (5%)	6 (6%)			
5	2 (2%)	1 (1%)			
6	1 (1%)	2 (2%)			
7	0 (0%)	1 (1%)			
Primary Indication for Caesarean			0.877		
Breech Presentation	29 (30%)	27 (27%)			
Fetal Anomaly	3 (3%)	2 (2%)			
IUGR	2 (2%)	5 (5%)			
Macrosomia	4 (4%)	8 (8%)			
Maternal Indication	8 (8%)	6 (6%)			
Maternal Request	33 (34%)	33 (33%)			
Placenta Praevia	3 (3%)	5 (5%)			
Triplets	2 (2%)	1 (1%)			
Twins	13 (13%)	13 (13%)			
Vasa Praevia	1 (1%)	0 (0%)			
Ease of Application of Retractor					
Instrument	84 (86%)	18 (18%)	0.001		
strongly agree	13 (13%)	70 (70%)			
agree	1 (1%)	9 (9%)			
neutral	0 (0%)	3 (3%)			
disagree	0 (0%)	0 (0%)			
strongly disagree					

Results

Table 3 continued: Descriptive statistics, frequency (%)

Variable	Alexis	Metal	p	RR CI
Freedom of Surgical Movement				
strongly agree	82 (84%)	21 (21%)	0.001	
agree	12 (12%)	62 (62%)		
neutral	3 (3%)	13 (13%)		
disagree	1 (1%)	4 (4%)		
strongly disagree	0 (0%)	0 (0%)		
Interference from Bowel/Adnexal			0.001	5.07 (3.25 - 8.25)
Tissue	8 (8%)	41 (41%)		
yes	90 (92%)	58 (59%)		
no				
Bowel Trauma				
yes	0 (0%)	0 (0%)		
no	98 (100%)	99 (100%)		
Bladder Trauma				
yes	0 (0%)	0 (0%)		
no	98 (100%)	100 (100%)		
Bowel Repositioning			0.001	7.19 (3.39 - 18.37)
yes	3 (3%)	22 (22%)		
no	95 (97%)	78 (78%)		
Paracolic Cleaning of Blood/Amniotic			0.001	4.38 (3.12 - 6.24)
Fluid	15 (15%)	67 (67%)		
yes	83 (85%)	33 (33%)		
no				

Table 3 continued: Descriptive statistics, frequency (%)

Variable	Alexis	Metal	p	RR	CI
Need for Uterus Exteriorization			0.001		
no	75 (77%)	31 (31%)			
Clinical Indication	4 (4%)	26 (26%)			
Routine	19 (19%)	43 (43%)			
Rectus Sheath Trauma			0.369	3.92 (1.65 - 24.19)	
yes	1 (1%)	4 (4%)			
no	97 (99%)	96 (96%)			
Muscle Trauma			0.767	1.37 (1.19 - 1.64)	
yes	5 (5%)	7 (7%)			
no	93 (95%)	93 (93%)			
Coagulation of Subcutaneous Tissue			0.001	2.36 (1.97 - 2.85)	
yes	34 (35%)	82 (82%)			
no	64 (65%)	18 (18%)			
Skin Lacerations			0.121		
yes	0 (0%)	4 (4%)			
no	98 (100%)	96 (96%)			
Trauma to the Baby					
yes	0 (0%)	0 (0%)			
no	98 (100%)	100 (100%)			
Ease of Retractor Removal			0.001		
strongly agree	84 (86%)	18 (18%)			
agree	14 (14%)	70 (70%)			
neutral	0 (0%)	10 (10%)			
disagree	0 (0%)	2 (2%)			
strongly disagree	0 (0%)	0 (0%)			
Wound Healing Problems on Discharge			0.246		
yes	0 (0%)	3 (3%)			
no	98 (100%)	97 (97%)			
Scar Pain at Discharge			0.001		
0	43 (44%)	1 (1%)			
1	36 (37%)	3 (3%)			
2	15 (15%)	22 (22%)			
3	1 (1%)	30 (30%)			
4	2 (2%)	32 (32%)			
5	0 (0%)	10 (10%)			
6	1 (1%)	2 (2%)			
Extra Analgesia Requirements Post Operative			0.001	2.22 (1.85 - 2.69)	
yes	19 (19%)	43 (43%)			
no	79 (81%)	57 (57%)			

continued: Table 3 : Descriptive statistics, frequency (%)

Variable	Alexis	Metal	p	RR	CI
6-Week Scar Pain Scores			0.005	10.78	(3.02 - 110.47)
yes	1 (1%)	11 (11%)			
no	97 (99%)	89 (89%)			
Wound Healing Problems at 6 Weeks			0.014		
yes	0 (0%)	7 (7%)			
no	98 (100%)	92 (93%)			
Patient Satisfaction with Wound Healing					
strongly agree	95 (100%)	79 (79%)	0.001		
agree	0 (0%)	9 (9%)			
neutral	0 (0%)	0 (0%)			
disagree	0 (0%)	1 (1%)			
strongly disagree	0 (0%)	11 (11%)			
Wound Infections			0.035	7.84	(2.45 - 70.71)
yes	1 (1%)	8 (8%)			
no	97 (99%)	92 (92%)			
Blood Loss					
<500	19 (19%)	3 (3%)	0.006		
500..1000	76 (78%)	94 (94%)			
>1000..1500	2 (2%)	3 (3%)			
>1500	1 (1%)	0 (0%)			
Apgar at 1 min					
1..7	21 (26%)	23 (28%)	0.929		
8	12 (15%)	7 (9%)			
9	49 (60%)	52 (63%)			
10	0 (0%)	0 (0%)			
Apgar at 5 min					
1..7	58 (71%)	57 (70%)	0.710		
8	7 (9%)	5 (6%)			
9	17 (21%)	20 (24%)			
10	0 (0%)	0 (0%)			
Apgar at 10 min					
1..7	65 (79%)	67 (82%)	0.477		
8	0 (0%)	3 (4%)			
9	17 (21%)	12 (15%)			
10	0 (0%)	0 (0%)			

4.3 Primary Outcome Results

Surgical Site Infection
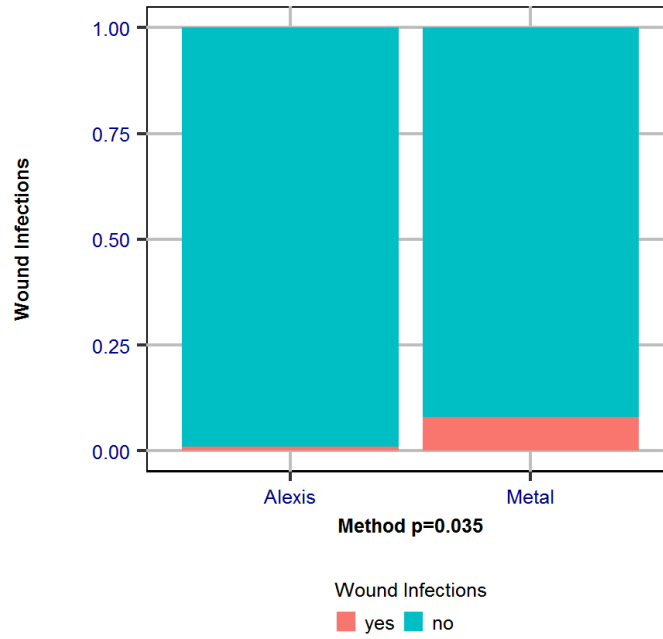
Figure 4.

There was a significant difference in the incidence of Surgical Site Infection (as defined by the Center for Disease Control and Prevention) with 8% in the Collins Metal group and 1% in the Alexis® O C-Section Retractor group, RR 7.84, CI (2.45-70.71) p=0.035.
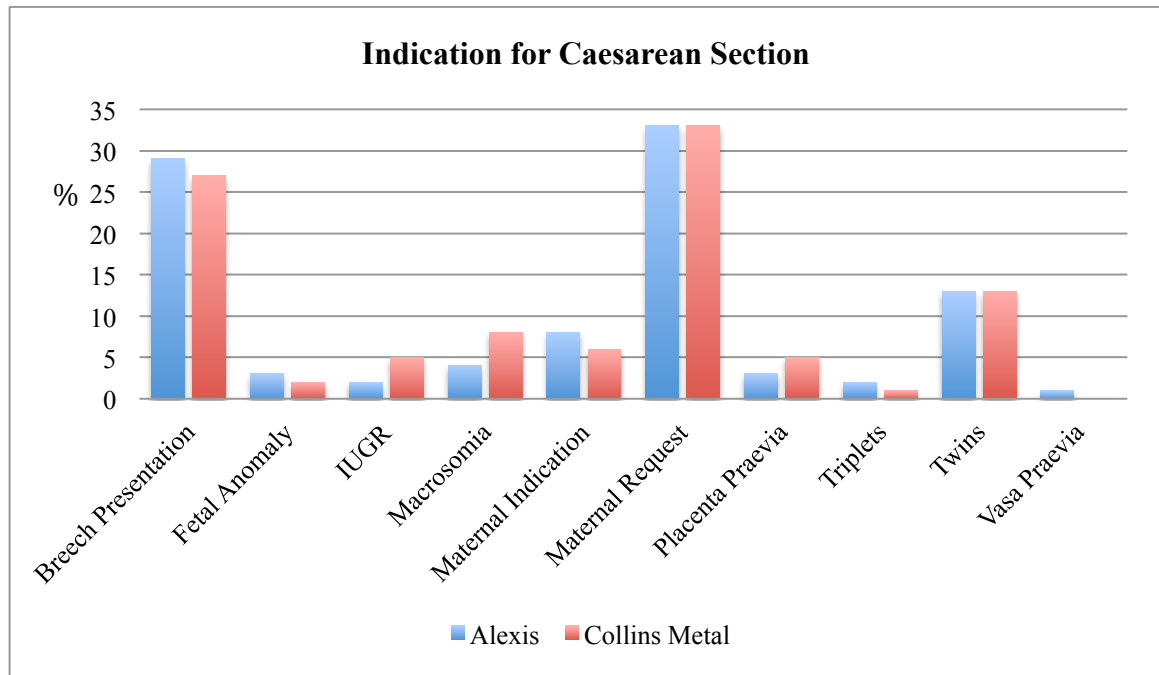
4.3.1 Indication for Caesarean Section

Figure 5.

There is no statistical difference between both groups in terms of the indications for Caesarean Section (p=0.877), (IUGR-Intrauterine Growth Restriction). Maternal Request and Breech Presentation were the most frequent indication in the study population.

4.3.2 Secondary Outcomes: Surgeons Perspective

6(a)

6(b)

6(c)

6(d)
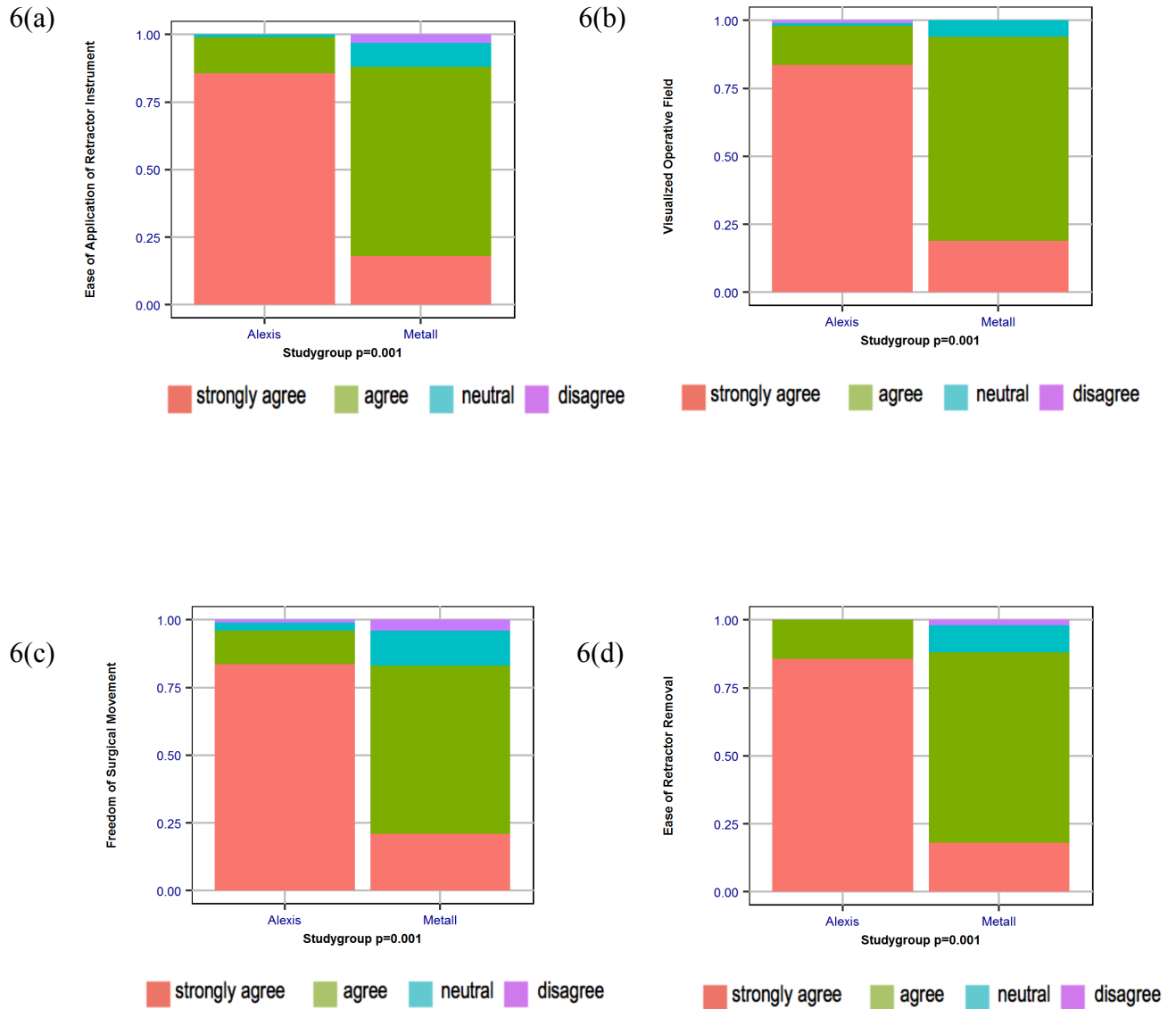
Figure 6 (a-d).

The surgeon had easier application (a) and removal (d) of the Alexis® O C-section Retractor as well as more visualization (b) and subjective freedom of movement (c) of the operative field in comparison to the Collins metal retractor (p=0.001).

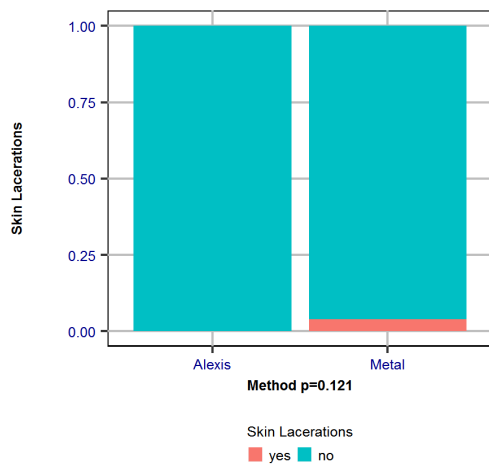**4.3.3 Secondary Outcomes: Intraoperative Findings**

7(a)
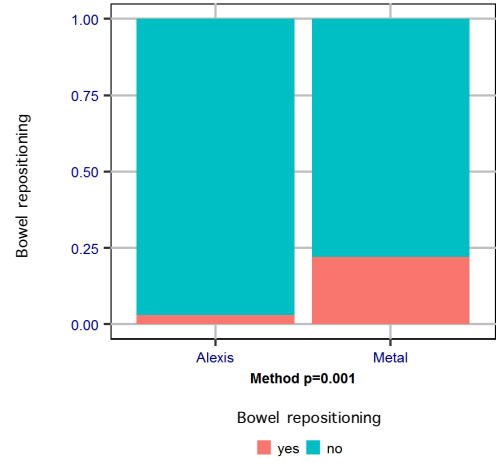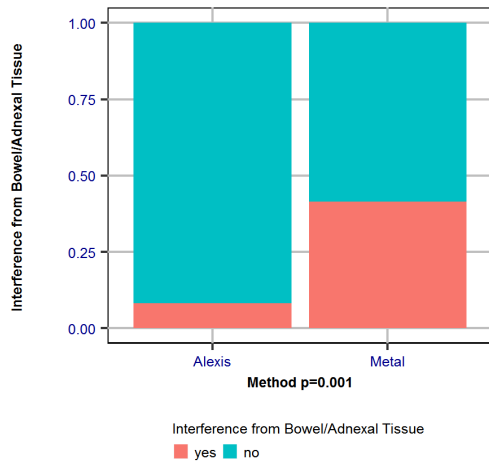
7(c)
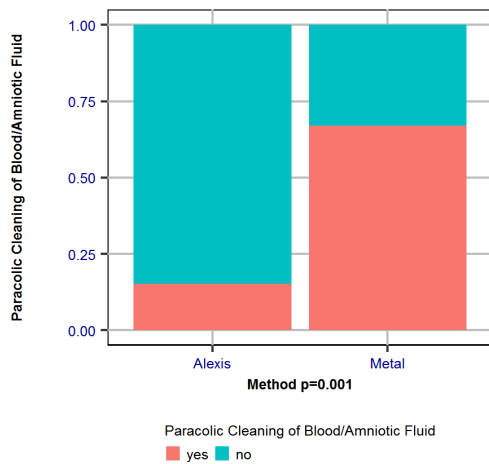
7(d)
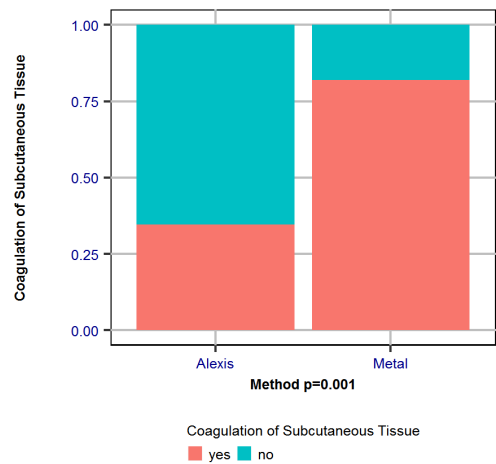
7(e)

7(f)
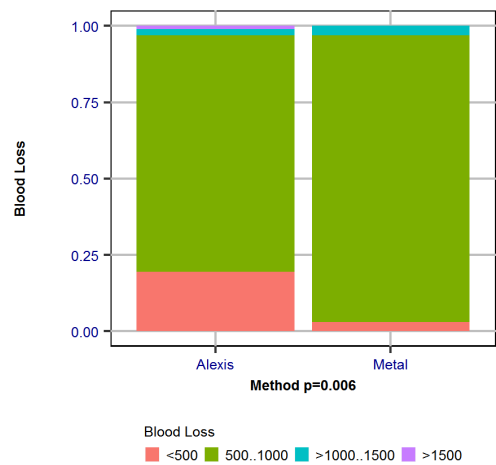
Figure 7(a-f): Significant differences between the Alexis® O C-Section Retractor group and the Collins metal group: more interference from (a) prolapsing bowel (p=0.001), (b) bowel repositioning (p=0.001), (c) paracolic gutter manipulation (p=0.001), (d) coagulation of the subcutaneous fat and (e) skin lacerations (p=0.046) in the Collins metal group compared to the Alexis® O C-section Retractor. There was significantly less (f) blood loss (<500ml) (p=0.006) in the Alexis® O C-section Retractor compared to the Collins metal group.

4.3.4 Secondary Outcomes: Postoperative Findings

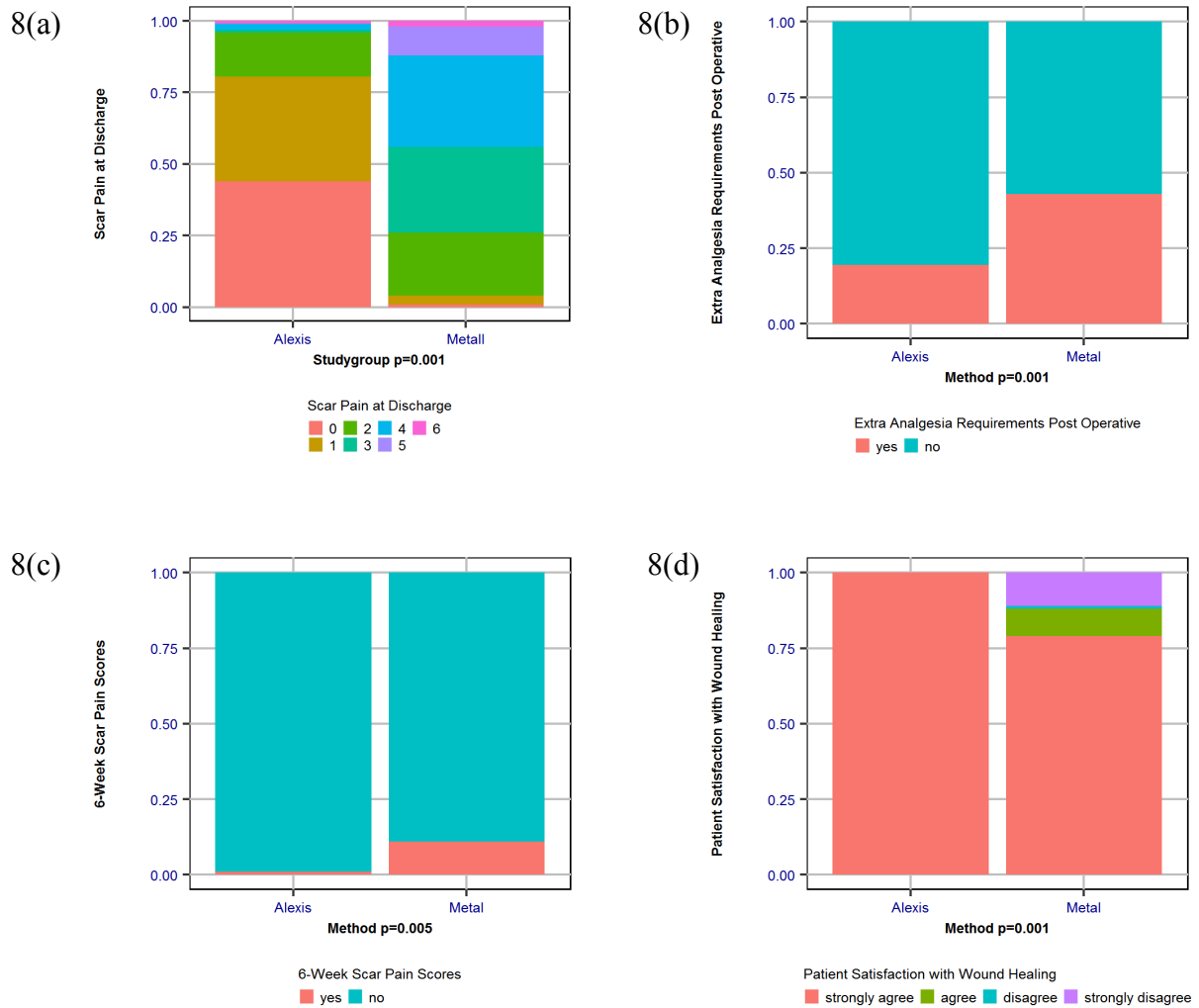Figure 8.

Postoperative patients had more scar pain on discharge (a) (p=0.001), required more pain relief postoperatively (b) (p=0.001), had more scar pain at 6 weeks post operatively (c) (p=0.005) and overall satisfaction with the wound (d) (p=0.001) was less in the Collins metal group compared to the Alexis® O C-Section Retractor group.

4.3.5 The Timing of Diagnosis and Characteristics of Surgical Site Infection (SSI)

Tabel 4. In the Collins Metal control group the incidence of SSI was 1% (n=1) prior to discharge and this rose to 8%, as the remaining 7 (87.5%) cases of SSI were detected during the postoperative surveillance period (6 Superficial/Deep and 1 Organ). In the Alexis® O C-Section Retractor group the 1 (1%) case of SSI was also detected during postoperative surveillance.

Alexis® O C-Section Retractor SSI Case	Collins Metal Retractor SSI Case
1. Incisional SSI after hospital discharge. Readmission with pain, dehiscence and wound discharge. One week antibiotic treatment and wound lavage.	1. Incisional SSI. Massive hematoma prior to hospital discharge. Pain. Wound discharge. Multiple reviews and antibiotic treatment.
	2. Incisional SSI after hospital discharge. Postoperative wound infection. Pain, antibiotics. Wound swab negative.
	3. Incisional SSI after hospital discharge. Wound dehiscence after discharge. Pain and wound discharge.
	4. Incisional SSI. After discharge wound infected. Antibiotic treatment. Chronic pain. Surgical revision.
	5. Incisional SSI after hospital discharge. Wound dehiscence with antibiotics and wound lavage treatment. Multiple reviews. Healing by secondary intention.
	6. Deep SSI after hospital discharge. Wound dehiscence and pain. Wound resutured and treated with antibiotics.
	7. Deep SSI after hospital discharge. Wound dehiscence after discharge. Resutured and antibiotic treatment. Wound swab negative.
	8. Organ SSI after hospital discharge. Organ SSI. Endometritis. Antibiotics and ambulant treatment.

4.3.6 Number of infections per Indication

Table 5. Number of infections per indication

Indication	No	Yes
Breech Presentation	53	3
Fetal Anomaly	5	0
IUGR	4	3
Macrosomia	11	1
Maternal Indication	13	1
Maternal Request	65	1
Placenta Praevia	8	0
Triplets	3	0
Twins	26	0
Vasa Praevia	1	0

4.3.7 Number needed to treat

The incidence rate (95% CI) for wound infections in the control group (Metal) was 8% (4% - 15%), for the Alexis® O C-Section Retractor group incidence rate was 1.02% (0% - 6%). Odds ratio is 8.4 (1.03 - 69), p for association of type of retractor with infection risk is 0.035. To prevent a single infection, 14 patients have to be operated using the Alexis® O C-Section Retractor rather than Metal device, NNT with 95% confidence interval is 14 (7 - 342).

4.3.8 Logistic regression analysis

Table 6a: Logistic regression for predicting risk of infection

Risk factor	p
Method	0.022
Primary Indication for Section	0.092
BMI	0.539

Table 6b: Logistic regression for predicting risk of infection

Risk factor	p
Method	0.214
Primary Indication for Section	0.142
BMI	0.607
Bowel Repositioning	0.015
Paracolic Cleaning of Blood/Amniotic Fluid	0.173
Need for Uterus Exteriorization	0.259
Coagulation of Subcutaneous Tissue	0.363

When testing indication, method, and BMI simultaneously as risk factors for infection, only method was significant with an odds ratio of 0.121 (0.006 - 0.76).

When adding Bowel Repositioning, Paracolic Cleaning of Blood/Amniotic Fluid, Need for Uterus Exteriorization, need for bowel repositioning became the sole significant risk factor with an odds ratio of 0.166 (0.0106 - 0.65).
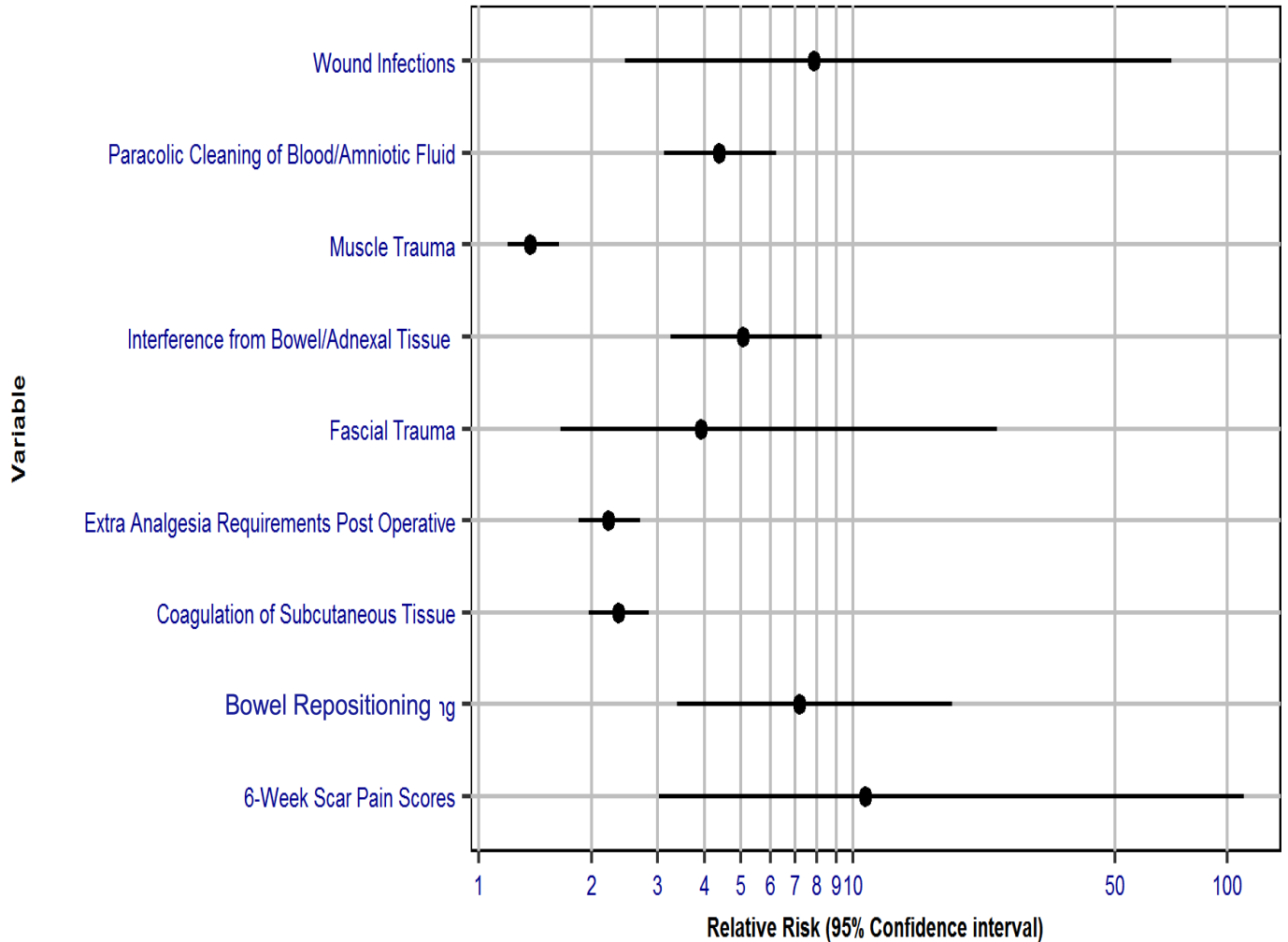
4.4 Relative Risk Ratios

Figure 11. The relative-risk ratios for significant variables when the Collins Metal Retractor was used compared to the Alexis® O C-Section Retractor. Our analysis showed in the metal group significant increased relative risk ratios for paracolic cleaning of blood and amniotic fluid (RR: 4.38), muscle trauma (RR: 1.37), interference from bowel and adnexal tissue (RR: 5.07), fascial trauma (RR: 3.92), extra analgesia requirements (RR: 2.22), coagulation of subcutaneous tissue (RR: 2.36), bowel repositioning (RR: 7.19) and 6 week scar pain scores (RR: 10.78).
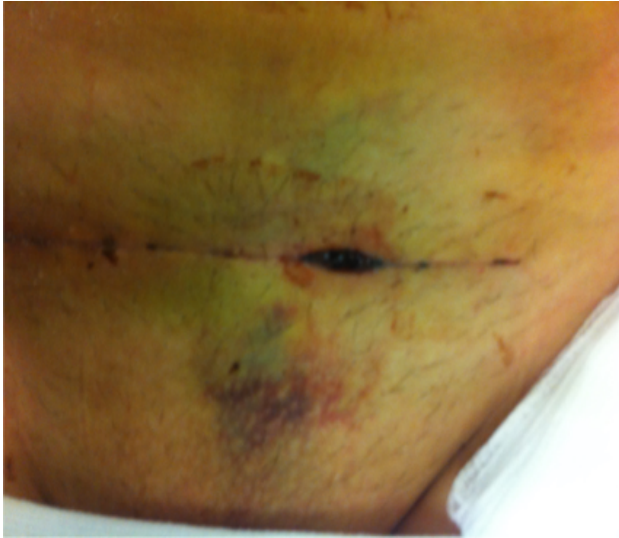
4.5 Photo Documentation

Fig. 12a- Wound dehiscence and discharge

Fig 12.b- Massive hematoma and subsequent infection

Fig. 12c- Resutured wound after dehiscence and discharge

Fig. 12a- Resutured wound after dehiscence and discharge

Fig. 12 (a-d): Photo documentation of Surgical Site Infection cases detected by postoperative surveillance in our study.
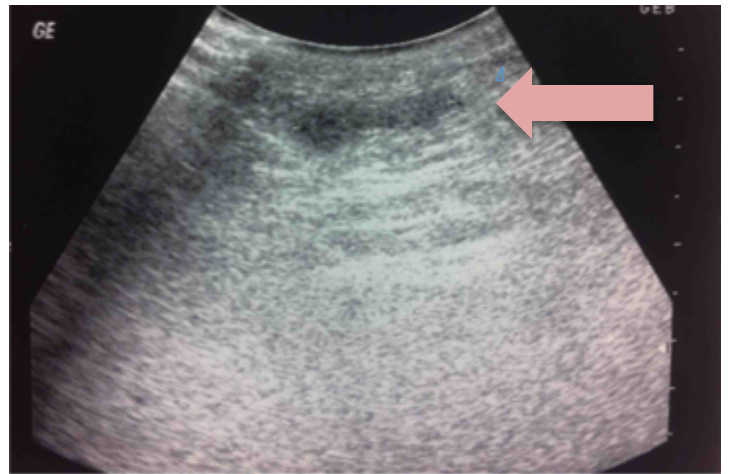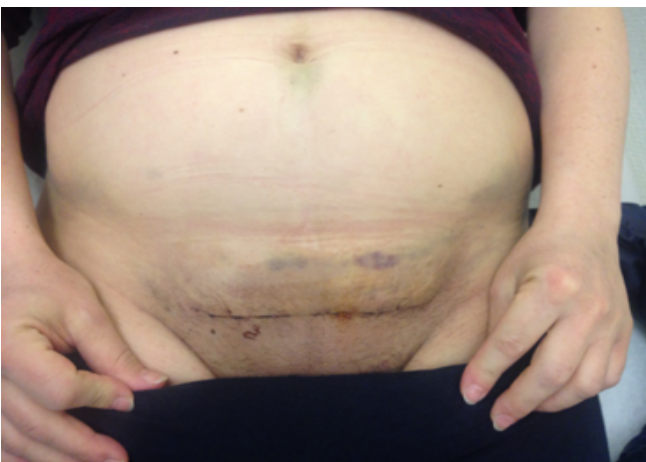
Results

Fig. a

Fig. d

Fig. b

Fig. c

Fig. 13: Management course of one case of infected painful wound hematoma with dehiscence and wound discharge requiring multiple ambulant clinical reviews and antibiotic treatment (a-c). Ultrasound confirmation was performed with the hematoma represented by the echo poor area as show by the arrow (d).

Fig. 14 a: On day of discharge Alexis® O C-Section Retractor group

Fig. 14 b: On day of discharge Alexis® O C-Section Retractor group

Fig. 14 c: On day of discharge Alexis® O C-Section Retractor group

Fig. 14 (a-c): Examples of patients on discharge after Caesarean Section with Alexis® O C-Section Retractor

Fig. 15: On day of discharge-Alexis® O C-Section Retractor group

Fig. 16: On day of discharge-Alexis® O C-Section Retractor group
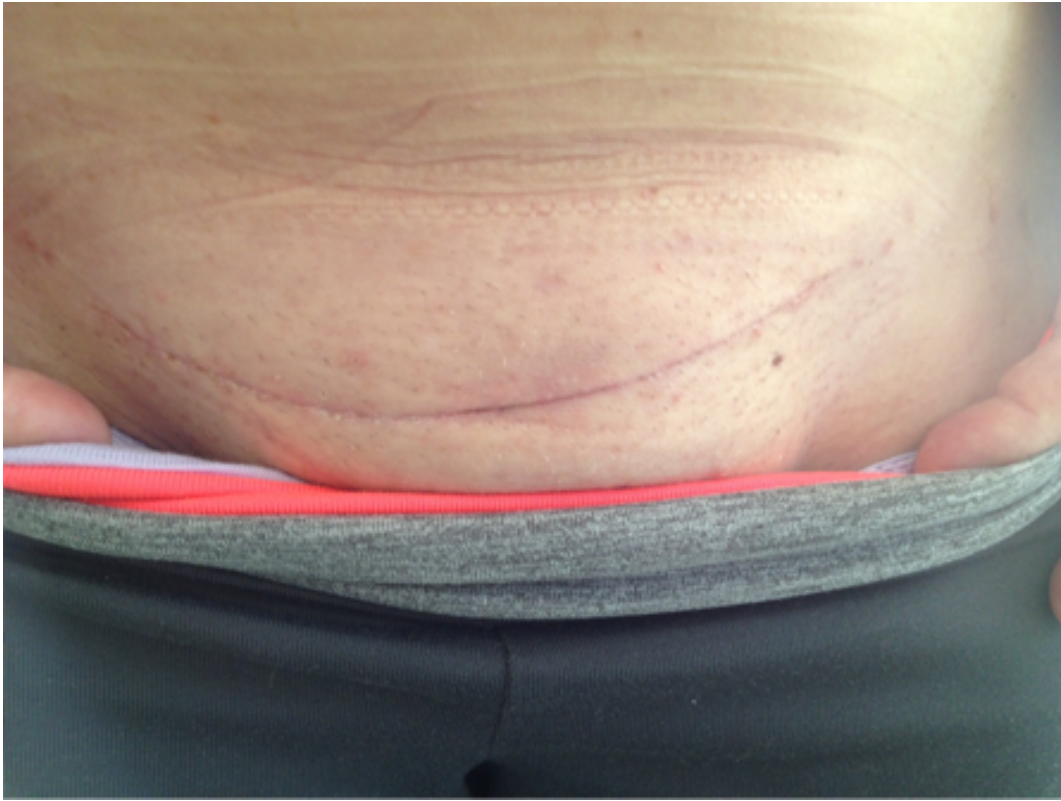
Fig. 17: On day of discharge-Alexis® O C-Section Retractor group

Fig. 18: 2 years postop in the following pregnancy-Alexis® O C-Section Retractor group

5. DISCUSSION

We have shown in our study, that in low risk women having their first planned Caesarean Section, there was a statistically significant reduction in the rate of surgical site infections when the Alexis® O C-Section Retractor was used for wound retraction compared to the traditional Collins metal self-retaining wound retractor (1% vs. 8%, RR 7.84, 95% CI (2.45-70.71) p=0.035)

Generally speaking, the clinically high rate of SSI after Caesarean Section is severely underestimated and poses an enormous burden on a patient's well-being and recovery, not only clinically but psychologically as well afterwards.[38,104] There is an urgent need therefore to address this situation, especially in light of the unprecedented rise in the rate of Caesarean Sections worldwide.[2] Importantly, the costs of readmission, antibiotic therapy and long-term treatment have financial implications for health care providers.[49] Thus, the reduction of the rate of SSI is an important goal and warrants not only urgent strategic health care policy implementation but also improved intraoperative surgical performance to achieve this.

Work by Dyrkorn et al has shown that the adherence to a strict hygiene protocol and aseptic technique regarding Caesarean section can reduce infection rates.[52]

The implementation of a comprehensive and proactive SSI surveillance system after Cesarean Section, with audit results and regular feedback to the corresponding obstetric units can also provide better actual rates of SSI and help improve results. In Germany, this approach has also been studied by Bärwolff et al, where they have shown that by using an intensive reporting system (KISS: Krankenhaus Infektions Surveillance System), this lead to a reduction in the rate of SSI by Caesarean Section from 2.4% to 1.9% over 3 years. One setback with this study though, was that the intensive surveillance occurred only in the inpatient setting and there was no proactive surveillance after the patient was discharged. This is therefore, a reasonable explanation for the lower overall SSI rates but nevertheless a reduction was realized with inpatients.[105] In a large Brazilian study by Couto et al they showed that the true rate of SSI with postnatal surveillance rose up to 9.6% when compared to only in-patient surveillance, which had a rate of 1.2%. Surveillance is important, while not only does it avoid underestimation of the genuine incidence rates but also feedback to health care providers can be helpful in guiding the implementation of SSI reduction strategies.[96]

Ng et al showed a reduction of SSI after Caesarean from 8.2% to 4.1 % over 5 years in a study which included 7,985 patients by employing an intensive postnatal surveillance with patients contacted after 6 weeks. This study highlighted the improvements to be gained by surveillance in itself and by fostering better feedback of information to the SSI monitoring team.[95] Specific patient obstetric-based risk factors for SSI are also important to identify

patients at risk and to target better surveillance, and this further ensures high standards of aseptic techniques and antibiotic prophylaxis in future practice. [106] We therefore elected to perform postnatal surveillance of SSI for up to 6-8 weeks after Caesarean Section in our study. All patients were contacted within this period to complete the standardized information gathering form.

In our study, in the control group the incidence of SSI was 1% (n=1) prior to discharge and this rose to 8%, as the remaining 7 (87.5%) cases of SSI were detected during the postoperative surveillance period. In the Alexis® O C-Section Retractor group the 1 (1%) case of SSI was also detected during postoperative surveillance.

Apart from the improvement in surveillance and better detection of SSI, surgical technique is an important area where improvements can also be made. Here, the development of polyurethane, sheathed ring wound retractors such as the Alexis® O C-section Retractor have been shown in the field of abdominal and bowel surgery to be effective in reducing the incidence of SSI. Cheng et al shown that in 64 patients undergoing colorectal surgery, there was a significant reduction in the incidence of SSI from 20% to 0% compared to controls with the use of the Alexis® O Retractor.[99]

Hariouchi et al also showed that in a randomized control trial of 221 patients there was a similar significant reduction from 16% to 8% in SSI compared to controls with the use of the Alexis® O Retractor in abdominal surgery.[107]

Mihaljevic et al performed a large systematic review of the literature and meta-analysis where 16 randomized studies were analyzed and showed that in 3695 patients there was a significant reduction in the rates of SSI with a relative risk reduction of 0.65 (95%CI (0.15-0.55) p=0.0007) when wound edge protectors are used.[101]

Contrary to this finding, Scolari et al showed that in a randomized study in obese patients, where 144 had a Caesarean Section with the Alexis® O C-Section Retractor compared to 157 controls, there was no significant difference in the rates of SSI.[108] This study had however, several critical flaws. The study did not restrict their study population and allowed a significant degree of selection-bias into the study group, as patients with significant risk factors for infection and wound-healing problems were not excluded or identified in the study population. This is a serious flaw and affected the interpretation of the results. A significant proportion of the study groups were patients already in active labor with additional risk factors for infection such as chorioamnionitis. Different types of abdominal incisions were used including the vertical abdominal incision in the study group. And in a significant proportion of patients, staples were used for skin closure, which is a well-established risk factor for wound infection.[89] Another error in the study is that there is no explanation of the

methods used for wound retraction in the control group and the type of retractors used. The authors also admit themselves, that the process of randomization may have been suboptimal. The heterogeneous nature of the patient population and selection bias make the interpretation of the findings in this study difficult and possibly inadequate.

Against this setting, our current study avoided these problems as from the outset we were interested in looking only at patients without additional risk factors for infection, having the first, planned Caesarean Section and excluded patients with previous major abdominal surgery and those with wound healing problems. This avoided the introduction of significant selection bias into the study population and revealed a better interpretation of the true impact on the influence of the use of the Alexis® O C-Section Retractor and the incidence of wound infection in a low risk population, which may serve as a reference for future studies. We also clearly defined the method of retraction in the control group where wound retraction was performed with the traditional Collins self-retaining metal retractor. All of our patients received preoperative antibiotics according to protocol. There were no cases where wound irrigation or wound drainage was performed. All incisions were transverse abdominal incisions in keeping with the modified Misgav Ladach technique.[79] Staples were not used in any cases for wound closure. None of our patients were in labor or had ruptured membranes or chorioamnionitis.

In testing our null hypothesis, that the Alexis® O C-Section Retractor in comparison to the traditional Collins Metal retractor made no difference to the rate of SSI, our results show that the null hypothesis is disproven and the use of the Alexis® O C-Section Retractor does indeed provide a statistically significant reduction from 8% to 1% (RR 7.84, 95% CI (2.45-70.71) p=0.035) in the rate of SSI when used in low risk Caesarean Sections.

The SSI rate in the control group was 8% and this is in keeping with the average reported rate by the Centers for Disease Control and Prevention (CDC). Recently, in a study published in the New England Journal of Medicine in 2016 by Tuuli et al, the SSI rate of 8% was also used as a reference.[54,102]

There are established evidenced based recommendations to reduce surgical site infection such as showering with 4% chlorhexidine gluconate preoperatively, clipping rather than shaving hair, avoidance of vaginal examinations, avoidance of unnecessary instrumentation, skin disinfection with chlorhexidine-alcohol skin preparation, preoperative antibiotic prophylaxis, avoidance of manual placenta removal, avoidance of skin closure with staples, the maintenance of strict glycemic control in patients with diabetes and early urinary catheter removal. [82-89,109,110] However, the additional benefit from a protective wound sheath can help reduce the risk of SSI even further.

Discussion

The Alexis® O C-section Retractor probably combats these predispositions to infection in a number of ways:

- Firstly, by shielding the wound intraoperatively and preventing contamination of the wound area. Protecting the tissue area from fetal tissues, liquor, meconium, blood and surgical manipulation, which have been shown by Pelle et al to increase infection.[72]

- Secondly, by reducing subcutaneous bleeding, providing better hemostasis and thereby reducing the need for electrocautery. The tamponade effect across the wound site acts circumferentially in 360° and reduces the incidence of bleeding. In our study, we show that in the Alexis® O C-Section Retractor Group there was a significant reduction in the need for diathermy heat treatment for bleeding subcutaneous vessels 35% vs. 82% (RR 2.36, 95% CI (1.97-2.85), p=0.001). This in turn reduces thermal injured tissue in the wound site. Less use of the diathermy probably leads to a reduction in necrosis tissue associated with poor healing, wound breakdown and wound infection.[80] Interestingly, a recent large study by Moreira et al showed that when diathermy was used to achieve hemostasis at the time of Caesarean Section, there was an increased risk of SSI of 23% compared to 16% in those without electrocautery.[81] The Royal College of Obstetricians and Gynecologists (RCOG) also recommends the avoidance of diathermy.[110] There are some studies however, which show no difference in wound infection rates.[111] But it must be highlighted that these studies were primarily concerned with the use of the diathermy to create the incision and not the treatment of bleeding on wound closure. Our study shows a strong association between reduced wound infections, reduced diathermy use and the use of the Alexis® O C-Section Retractor, which is probably explained by the tamponade effect and hemostatic effect of the 360-degree retraction of the wound edges. Our study did not intend to look at the use of diathermy and wound infection at the time of Caesarean Section, however this important finding highlights an area that warrants further research because of the association with SSI.

- Thirdly, by providing better visualization of the operative field and less tissue handling. It is generally considered that minimization of tissue trauma and gentle tissue handling reduces wound infections. [112-114] In our study there was significantly less uterus exteriorization in the Alexis® O C-Section Retractor group compared to the control group (4% vs. 26%, p=0.001). Exteriorization of the uterus is much debated and there is evidence from the CORONIS (Caesarean Section Techniques) study that it is not associated with infection. However, the recommendation from the NICE and RCOG Guidelines advocates that exteriorization not be performed, whilst it

is associated with more postoperative pain.[110,115] There was also statistically significant disturbance of the operative field with prolapsing bowel (41% vs. 8%, RR 5.07, 95% CI (3.25-8.25), p=0.001) in the Collins metal retractor group and increased need for bowel replacement and repositioning (22% vs. 3%, RR 7.19, 95% CI (3.39-18.37) p=0.001). Post hoc logistic regression analysis showed bowel handling to be a strongly associated risk factor for SSI with an odds ratio of 0.166 (0.01 - 0.65). This may also be associated with increased risk of intraabdominal adhesion formation and long-term postoperative pain. However, the study may have been underpowered to confirm this. The Collins metal retractor does cause asymmetric distension of the wound. This theoretically, also increases the risk of bowel injury and the increase in tissue manipulation and increased operative time.

There were in total 29 different surgeons involved in performing the Caesarean Sections. Intraoperative satisfaction scores were ascertained using Linkert scoring charts. We show in our study that the surgeons described more ease of application and removal of the Alexis® O C- Section Retractor in comparison to the traditional Collins metal retractor (p =0.001). This may be explained by the difficulty in applying the metal retractor in patients with an abdominal wall thickness greater than the accommodating width of the lateral holding blades and occasional mechanical difficulty with the moving parts of the retractor, for example dislodgement of the lateral blades.

Other significant findings included more satisfaction with the visualization of the operative field (p=0.001). This means more freedom of movement is possible (p=0.001). The surgical assistant also has more freedom to assist with suture holding, suture cutting and helping with the delivery of the baby. These findings supported an improvement in operative performance and surgeon satisfaction.

The increase need for suction and swabbing out of the paracolic gutters with the traditional metal retractors (p=0.001) can increase the risk of wound contamination and increase the risk of tissue damage and operating time. This may be explained by the observation that the Alexis® O C- Section Retractor appeared to form a seal between the anterior uterine wall and the abdominal wall during the operation. In our study however the patient population is not sufficient to confirm this and warrants further research.

The need for muscular suturing was more likely to be electively indicated. There was no statistically significant difference in the risk of either muscle trauma, rectus sheath trauma or skin lacerations between the two groups, even though the incidence was higher in the metal group. There were no reports of bladder or bowel injury.

Discussion

There was no difference in the time from skin incision to delivery of the baby or indeed a difference in the overall operating time between the 2 interventions. The estimated blood loss was less with the use of the Alexis® O C-Section Retractor, however the study may be under powered to look at this specifically.

Neonatal Outcomes

In both groups there were also no cases of trauma to the baby and there was no reported difficulty in the delivery of the babies. Outcomes for babies were similar across both groups.

Patients had higher pain scores upon discharge in the Collins metal retractor group (p=0.001) and there was more recourse to extra pain therapy 43% vs. 19% (RR 2.22, 95% CI (1.85-2.69), p=0.001) outside the normal pain therapy regimen although this may not be statistically powered to detect a true difference.

Patients were interviewed 6-8 weeks postoperatively and were more satisfied with the wound healing in the Alexis® O C-Section Retractor group than in the Collins metal retractor group (95% vs. 79%, p = 0.001) and also had less pain (1% vs. 11%, RR 10.78 95% CI (3.02-110.47), p = 0.005).

The cost to health care providers for the management of SSI in the USA is known to be approximately 6.5 billion US dollars per year and in England estimates of 930 million pounds per annum have been calculated. In England, SSI infection contributed to prolonged hospital stay with individual costs of between £814 and £6626 depending on the severity of infection. This represents a significant burden on healthcare systems.[49,50,110] The reduction of SSI will save money and is obviously financially beneficial.[51] The cost is not only clinical but also psychological and patients can suffer long-term psychological stress and depression.[38] Reducing the incidence of SSI will counteract this. From a number needed to treat calculation, our study shows that to prevent one case of SSI in a low risk patient having a first Caesarean Section, 14 cases with the Alexis® O C- Section Retractor would need to be performed. 14 Alexis® O C- Section Retractor at 49 Euros each would cost 686 Euros to prevent one Surgical Site Infection. This may represent significant cost savings when looking at the cost of treating a patient with SSI.[116]

This study is robust in that it is a prospective randomized study with a large sample population and well powered to detect a statistical difference between the two groups. The study looked to avoid co-morbidities, so that patients with risk factors for infection such as diabetes, auto immune diseases, previous operation (previous Caesarean), patients in labor, patients with chorioamnionitis and patients with risk factors for wound hematoma formation such as full anticoagulation therapy were excluded to minimize the effects of confounding variables. This allowed a better assessment of the effect of the Alexis® O C- Section

Retractor. The patient populations were well balanced and comparable as revealed in the descriptive statistics and this reflects well on the randomization process.

One drawback with the study is the lack of patient and operator blinding. Though patients were not informed as to which retractor would be used, complete patient blinding would however not have been possible to achieve as patients and their partners are allowed to visualize the delivery of the baby at the time of the Caesarean by lowering the cranial side of the operating drape, thereby making it difficult to ensure complete blinding. The operators obviously could not be blinded to which retractor was actually used.

5.1 Conclusion

In summary, our study shows that the use of the Alexis® O C-Section Retractor compared to the traditional Collins self-retaining metal retractor in low risk women, having the first Caesarean Section is associated with a significantly reduced risk of Surgical Site Infection. There is also significant reduction in the use of electric cautery for subcutaneous bleeding, bowel handling and postoperative pain. Operator satisfaction is improved and postoperative pain is less. We recommend the use of the Alexis® O C-section Retractor in low risk women undergoing their first elective Caesarean Section to reduce the risk of surgical site infection. We suggest further studies are warranted on the use of the Alexis® O C-section Retractor in women with significant comorbidities such as diabetes, obesity and those having repeated Caesarean Sections. And we also suggest that the use of electrocautery and bowel handling, as individual risk factors for surgical site infection be further evaluated in larger studies.

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Eidesstattliche Versicherung

„Ich, Larry Hinkson, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: "The incidence of surgical site infection in Caesarean Sections with the use of a plastic sheath wound retractor compared to the traditional self retaining metal retractor" selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)" des ICMJE -*www.icmje.org*) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Betreuer/in, angegeben sind. Sämtliche Publikationen, die aus dieser Dissertation hervorgegangen sind und bei denen ich Autor bin, entsprechen den URM (s.o) und werden von mir verantwortet.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst."

Datum   Unterschrift

Anteilserklärung an etwaigen erfolgten Publikationen

Larry Hinkson hatte folgenden Anteil an der folgenden Publikation:

Publikation (Referenz 103): Armbrust R, Hinkson L, von Weizsacker K, Henrich W. The Charite cesarean birth: a family orientated approach of cesarean section. J Matern Fetal Neonatal Med 2016;29:163-8

Beitrag im Einzelnen: Mitarbeit und Überarbeitung des Manuskripts hinsichtlich sprachlicher und inhaltlicher Korrektheit.

Unterschrift, Datum und Stempel des betreuenden Hochschullehrers

Unterschrift des Doktoranden

Curriculum vitae

(excluded for data protection reasons)

62

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R Armbrust , **L Hinkson**, KD Kalache, W Henrich
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C. Bamberg , V. Bujak , E. Rodekamp , M. Brauer , **L. Hinkson** , K. Kalache , W. Henrich

A Longitudinal transvaginal ultrasound evaluation of the Caesarean scar thickness after single or double layer uterotomy closure

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Johannes Gruenwald , Jens H. Stupin , Lars Hellmeyer , **Larry Hinkson**

Innovation, scientific Expertise and "Hands-on-Workshop" in a family Atmosphere

Geburtshilfe und Frauenheilkunde 01/2014; 74(11):989-991. DOI:10.1055/s-0034-1383264 . 0.94 Impact Factor

S Fazeli , C Bamberg , M Brauer , B Mayer , A Salama , D Hüsemann , **L Hinkson** , W Henrich

Perinatales Management bei fetaler Anämie durch irreguläre Antikörper: 2 Fälle schwerer fetaler Anämie bei Alloimmunisierung durch Anti-cellano- Antikörper und Anti-Rh 17-Antikörper

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A Weichert, KD Kalache, R Armbrust , A Thomas, W Henrich , **L Hinkson**

Einsatz des Fetal Pillow unter der Geburt vor einer Sectio casearea in der Austreibungsperiode

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The effects of booking body mass index on obstetric and neonatal outcomes in an inner city UK tertiary referral centre

Obstetric Medicine 12/2008; 1(2):88-91. DOI:10.1258/om.2008.080029

Unterschrift:

Danksagung

Ich möchte mich herzlich bei Herrn Prof. Dr. med. Wolfgang Henrich für die konstruktiven Diskussionen und Empfehlungen sowie den freundlichen Zuspruch während der Durchführung der Arbeit bedanken.

Grosser Dank gilt auch Herr Dr. med. Jan-Peter Siedentopf, der mir bei der Methodenentwicklung mit Rat zur Seite stand.

Weiterhin spreche ich allen Ärztinnen und Ärzten der Klinik für Geburtsmedizin der Charite im Campus Mitte und Virchow meinen Dank aus für ihre fortwährende Hilfe bei der Rekrutierung der Patientinnen für diese Studie.

Herrn Dr. Andreas Busjahn danke ich für die freundliche Unterstützung bei der statistischen Auswertung und Erstellung von Abbildungen.

Nicht zuletzt gilt mein besonderer, großer Dank meiner Familie und meinen Freunden, die mir stets mit Rat und Motivation zur Seite standen.