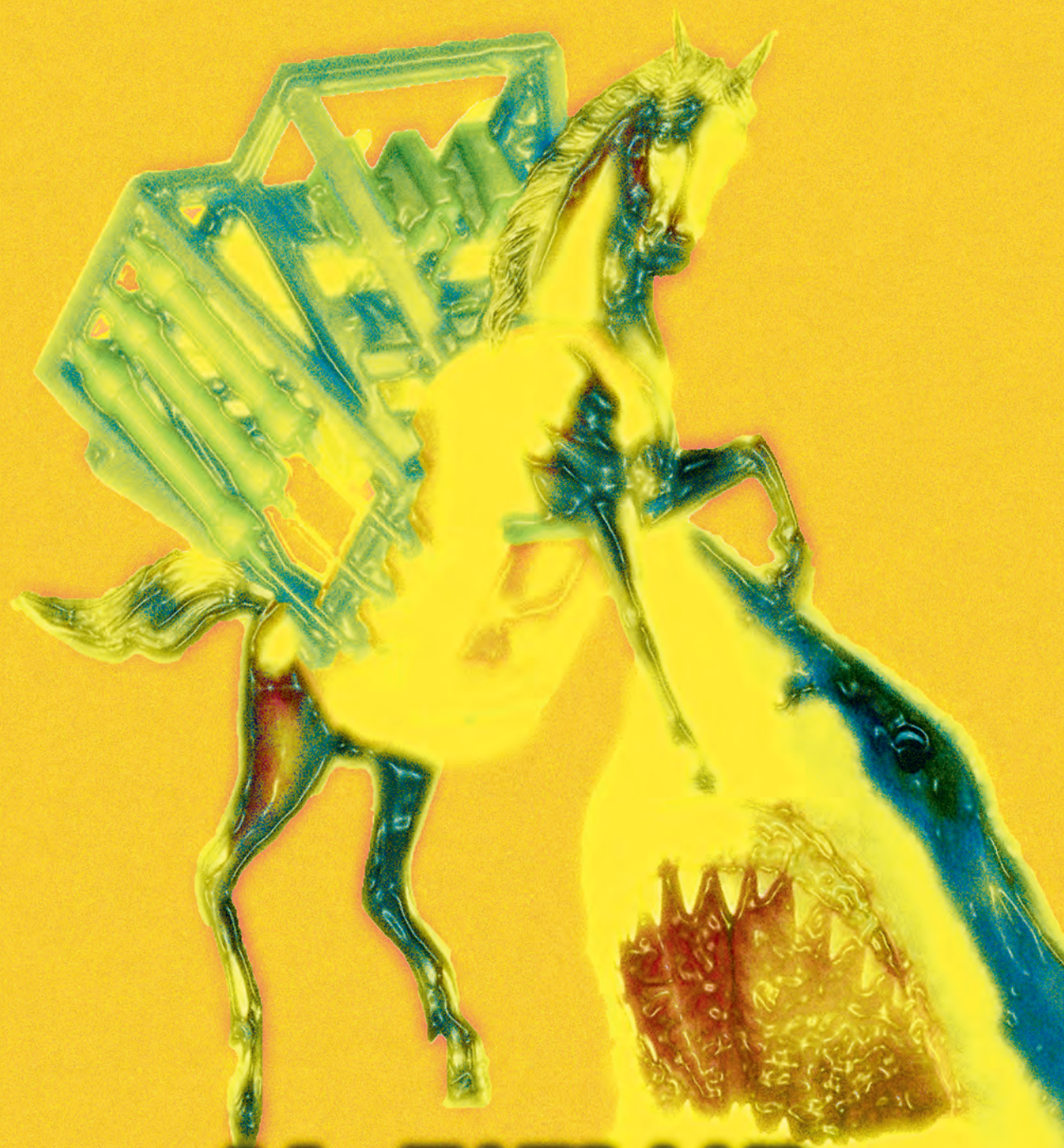
ABOUT BITES AND STEPS



J.J. HARLAAR

About Bites and Steps

Aetiology and prevention of incisional hernia

Joris J. Harlaar

Colofon

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General introduction

Chapter 2

Small bites with small suture distances increase laparotomy closure strength

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American Journal of Surgery (2009) 198, 392–395

Abstract

Background

There is no conclusive evidence which size of suture stitches and suture distance should be used to prevent burst abdomen and incisional hernia.

Methods

Thirty-eight porcine abdominal walls were removed immediately after death and divided into 2 groups: A and B (N=19 each). Two suturing methods using double-loop polydioxanone were tested in 14-cm midline incisions: group A consisted of large stitches (1 cm) with a large suture distance (1 cm), and group B consisted of small stitches (0.5 cm) with a small suture distance (0.5 cm).

Results

The geometric mean tensile force in group B was significantly higher than in group A (N=787 vs N=534; P=0.006).

Conclusions

Small stitches with small suture distances achieve higher tensile forces than large stitches with large suture distances. Therefore, small stitches may be useful to prevent the development of a burst abdomen or an incisional hernia after midline incisions.

Introduction

Suture techniques for midline incisions have been subject of investigation for a long period of time. Incidences of incisional hernia and burst abdomen after laparotomy are 2-20% and 1-3%, respectively. Although much is known about patient related risk factors, technical risk factors such as suture techniques have not been investigated thoroughly.[1-4] Especially in high-risk patients in whom incidences of incisional hernia are reported up to 35%, surgeons should take care to use optimal suture technique to avoid short and long-term complications.[5] The optimal suture technique should be easy to perform, quick, reliable and give high long-lasting breaking strengths to improve wound healing.

For prevention of incisional hernia, many clinical trials and meta-analyses have shown that a mass closure technique with simple running sutures is the best option to close a midline incision.[6-11] Such a technique is also more easily to perform and quicker than layered techniques with interrupted sutures.
Furthermore, the use of long lasting absorbable suture material compared with non-absorbable suture material decreases postoperative pain and wound infection.[9-12]

Israelsson has argued that a suture length to wound length ratio (SL:WL) of four or more must be achieved, since a lower ratio is associated with a threefold increase in the rate of incisional hernia.[13-15] It is often recommended to place continuous stitches more than 10 mm from the wound edge in combination with a long stitch length.[16-22] A long stitch is the result of a large bite with the largest portion of fascia possible, aiming to increase tensile strength and decreasing the risk of facial dehiscence. However, long stitches have been associated with high rates of both wound infection and incisional hernia.[13, 23, 24]

Israelsson and his group preformed experimental and clinical studies on suture technique in benefit of the small bites.[13-15, 25-28] Small stitches are placed 4–6 mm from the wound edge and cut only through the aponeurosis and not through the rectus abdominis muscle. Because the small stitch is placed in the aponeurosis only, it is also possible to place more stitches in one incision.

In daily practice, most surgeons use the large bite technique with large suture distances. With large bites, SL:WL ratio depends on the thickness of the abdominal wall including the muscles and the number of stitches. With small stitches, SL:WL ratio is mostly dependent on the number of stitches. There is no proof of principle which technique is the best option to close the abdominal wall to prevent incisional hernia and fascial dehiscence.

The aim of this study was to compare the large and small bites techniques on tensile strength and type of dehiscence in a controlled lab setting with use of porcine abdominal walls.

Materials and methods

Thirty-eight porcine abdominal walls (Yorkshire pigs, 40-60 kg) were removed immediately after sacrifice and were freezed at -20°C for at least 4 days (mean time 7 days).[29] After a defrosting period of 16 hours, fat and skin were removed, and a midline incision was made through the aponeurosis.

Two suturing methods using double loop polydioxanone (PDS II 1.0 Ethicon 240 cm) were tested in 14-cm-midline incisions: A) large bites (1 cm) with large suture distance (1 cm) with a total of 14 continuous stitches and B) small bites (0.5 cm) with small suture distance (0.5 cm) with a total of 28 continuous stitches. The techniques were used in alternate order and by two circulating investigators to avoid selection bias. To standardise the suture technique, the place of the stitch was measured with a ruler and marked with a needle (Braun sterican 0,5x16 mm), consequently the stitch were made. SL:WL ratios were calculated for all specimens.

Subsequently, abdominal walls were fixed on a tensile testing machine (Testometric® , Rochdale, England) (figure 1).[30] Tensile force was increased at a constant rate of 10 mm/min. Each test was filmed (Sony Cybershot DSC-S700, Japan) and type of dehiscence (e.g. aponeurosis, lateral of sutures, site of fixation or no dehiscence at maximum force) was recorded.

The test setting is shown in Figure 1.

Figure 1 Photograph of the test setting used. The sutured abdominal wall is fixed in the tensile testing machine and is pulled apart at a constant rate of 10 mm/min.

The force at the moment of the first drop resulting into dehiscence through the aponeurosis was considered the primary outcome. For experiments in which other types of dehiscence occurred it can be concluded that the true force to result in dehiscence through the aponeurosis will be greater than the recorded force (right-censored observation). To take account of such censored observations, STATA software was used (procedure CNREG). Forces were logarithmically transformed in this analysis to get approximate normal distributions. The same method was used to evaluate the relation between the SL:WL ratio and the primary outcome. P-values **<** 0.05 were considered significant. Power calculations based on pilot data had led to two groups of 19 abdominal walls each.

Results

In group A (large bites; n=19) and group B (small bites, n=19) there were respectively 14 and 7 experiments which resulted in dehiscence through the aponeurosis (P=0.049; Fisher's exact test). In group A there were 5 experiments not resulting in dehiscence through the aponeurosis (3 on the fixation device, 2 lateral to the incision). In group B there were 12 experiments not resulting in dehiscence through the aponeurosis (8 on the fixation device, 3 lateral to the incision).

Analyzing the resulting forces of all 38 experiments, the tensile forces in group B were significantly higher than in group A with geometric mean tensile force able to create dehiscence through the aponeurosis of 534 N in group A and 787 N in group B (P=0.006). This corresponds to a 47% increase. Following the law of Laplace and assuming a mean abdominal diameter of 30 cm, a tensile force of 360 N represents the force created by Valsalva's maneuver.

Mean SL:WL ratios were 4.1 (range 2.8 - 5.1) in group A and 6.9 (5.0 - 8.6) in group B. In group A, an increase in SL:WL ratio was significantly associated with an increase in tensile strength (P<0.001), with each 1 point higher SL:WL ratio resulting in a 61% increase in tensile strength (Figure 2). No significant relation was found in group B (P=0.102). In none of the tests knots had slipped or sutures had broken.

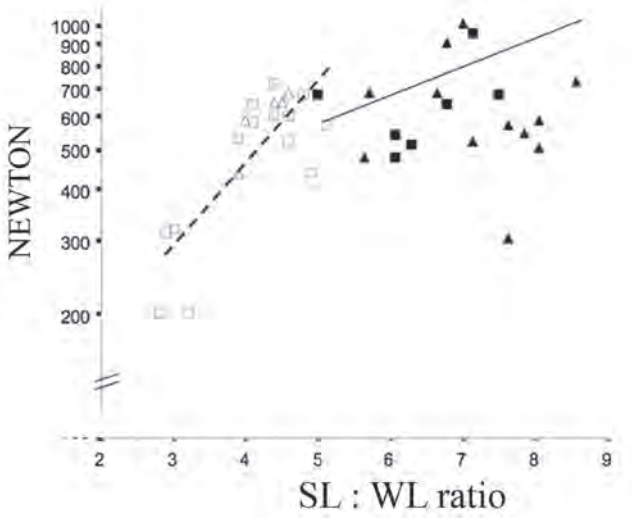
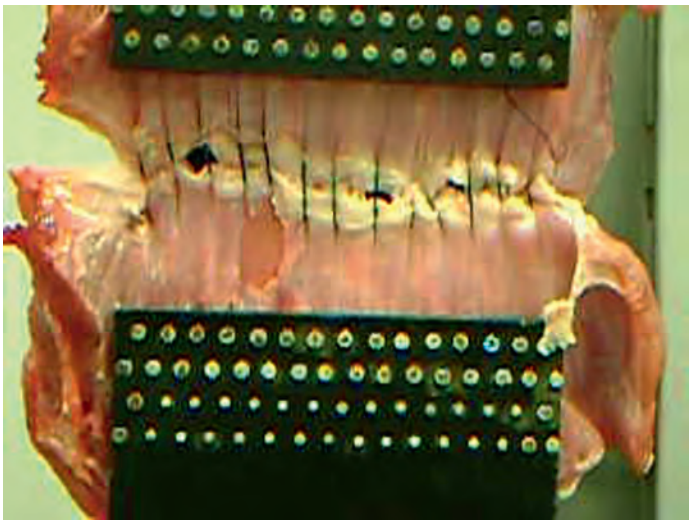
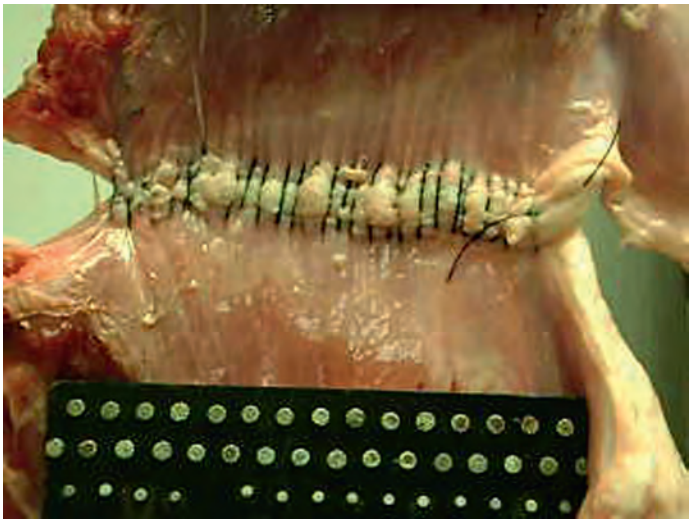


Figure 2 Scatter plot of tensile force versus the SL:WL ratio, with regression lines. Open and closed symbols represent tensile forces for group A (large stitches) and group B (small stitches), respectively. Triangles within each group represent forces that did not result in dehiscence through the aponeurosis (censored observations



A



B

Figure 3 (A) Large-stitch group: slacking effect. Example of the slacking effect in the large-stitch group. Sutures first cut through the relatively weak tissue lateral to the aponeurosis, causing wound edges to separate. (B) Small-stitch group. In the small-stitch group, separation of wound edges was not observed. This possibly is owing to a better distribution of tensile forces, resulting in dehiscence far lateral from the aponeurosis.

Type of dehiscence was very characteristic for group A compared with group B. During the experiments, large bites were slacking through the muscle and the most tensile force was generated when the sutures were hanging on the aponeurosis whilst the wound edges were separated. This effect has been described before.[27] When bites were placed in the aponeurosis and the slacking effect was not observed.

Discussion

This is the first experimental study comparing large versus small tissue bites with documented SL:WL ratios on breaking strength in a model anatomically comparable to humans. A number of rat studies has been performed on wound healing and bursting pressure in the past, but forces in small animals are hardly comparable to human physiology.

In the small bites group, more stitches resulted into a better division of tension over the abdominal wall. Furthermore, due to the achievement of high SL:WL ratios, tension was divided over a longer suture thread. In the large bites group, high SL:WL ratios were needed to create acceptable tensile strength and although standardized bites of one cm were used, half of all SL:WL ratios were below four. In the large bites group, the ratio is dependent on bite size, the thickness of the abdominal wall and the extent of force used to haul the suture.

This suture length wound length ratio of four, as described by Jenkins, was based on a mathematical approach.[31] No specifications concerning the desired bite size or anatomical location were described. Surgeons expect to always achieve ratio 4:1 by taking two cm-bites of the abdominal wall with a continuous suture, and are reluctant to place stitches in the aponeurosis. Not only do surgeons fear that the aponeurosis is not strong enough to withstand tensile forces of the abdomen, the placement of many stitches in the aponeurosis is also assumed to inflict local necrosis. This study shows that the aponeurosis is strong enough to hold sutures. Furthermore, Cengiz et al. have described the benefits of small bites in several studies: better wound healing, no separation of wound edges and less trauma of abdominal muscles.[26-28] These effects could not be established in this study due to the use of devitalized abdominal walls. However, no good alternatives are

available to analyze and measure tensile forces and types of dehiscence in the clinical situation.

Our experiments show that the use of the small stitch technique might have clinical advantages. Experience of the individual surgeon with this technique will influence the eventual result. In patients with midline laparotomy, using small bites with small suture distances may prove the best strategy. Randomized clinical trials should be performed to provide convincing data to support a change of technique.

Conclusion

Small bites with small suture distances achieve higher tensile forces than large bites with large suture distances in our porcine in-vitro model. Large bites should only be used when high SL:WL ratios are achieved in order to achieve acceptable tensile strengths. Small bites with small suture distances are recommended to easily achieve high SL:WL ratios and higher tensile strengths. Therefore, small bites may be useful to prevent development of burst abdomen and incisional hernia after midline incisions in patients.

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Chapter 3

A multicenter randomized controlled trial evaluating the effect of small stitches on the incidence of incisional hernia in midline incisions (STITCH trial, NCT01132209)

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BMC Surg 2011;11:20.

Abstract

Background

The median laparotomy is frequently used by abdominal surgeons to gain rapid and wide access to the abdominal cavity with minimal damage to nerves, vascular structures and muscles of the abdominal wall. However, incisional hernia remains the most common complication after median laparotomy, with reported incidences varying between 2-20%. Recent clinical and experimental data showed a continuous suture technique with many small tissue bites in the aponeurosis only, is possibly more effective in the prevention of incisional hernia when compared to the common used large bite technique or mass closure.

Design

The STITCH trial is a double-blinded multicenter randomized controlled trial designed to compare a standardized large bite technique with a standardized small bites technique. The main objective is to compare both suture techniques for incidence of incisional hernia after one year. Secondary outcomes will include postoperative complications, direct costs, indirect costs and quality of life.

Methods

A total of 576 patients will be randomized between a standardized small bites or large bites technique. At least 10 departments of general surgery and two departments of oncological gynaecology will participate in this trial. Both techniques have a standardized amount of stitches per cm wound length and suture length wound length ratio's are calculated in each patient. Follow up will be at 1 month for wound infection and 1 year for incisional hernia. Ultrasound examinations will be performed at both time points to measure the distance between the rectus muscles (at 3 points) and to objectify presence or absence of incisional hernia. Patients, investigators and radiologists will be blinded during follow up, although the surgeon can not be blinded during the surgical procedure.

Conclusion

The STITCH trial will provide level 1b evidence to support the preference for either a continuous suture technique with many small tissue bites in the aponeurosis only or for the commonly used large bites technique.

Trial registration: Clinicaltrials.gov NCT01132209

Background

The median laparotomy is frequently used by abdominal surgeons to gain rapid and wide access to the abdominal cavity with minimal damage to nerves, vascular structures and muscles of the abdominal wall. However, incisional hernia remains the most common complication after median laparotomy, with reported incidences varying between 2-20%.[1-5] Even higher incidences up to 30-35% have been reported in obese and aortic aneurysm patients(6-10). Incisional hernia can cause discomfort, impair quality of life or result in serious life-threatening conditions, such as incarceration or strangulation of the bowel.[5] Median laparotomies and incisional hernias have been subject of investigation for a long period of time already. Although a lot is known about patient related risk factors and suture materials, technical risk factors such as suture techniques have not been investigated thoroughly.[5, 11, 12]

For prevention of incisional hernia, many clinical trials and meta-analyses have demonstrated that a mass closure technique with a simple running suture is the best option to close a midline incision. A mass closure technique with a running suture is also easier and quicker to perform than layered techniques with interrupted sutures.[5, 12-14] Furthermore, the use of slowly resorbable suture material compared with non-resorbable suture material decreases the incidence of incisional hernia, and it also lowers the incidence and intensity of postoperative pain and wound infection.[12, 15, 16]

Suture length to wound length ratio and small bites

Several authors have stated that a suture length to wound length ratio (SL:WL) of four or more must be achieved, since a lower ratio is associated with an increased rate of incisional hernia.[7, 17-20] It has often been recommended to place continuous stitches more than 10 mm from the wound edge in combination with a long stitch length.[19, 21-28] A long stitch is the result of a large bite with the largest portion of fascia possible, aiming to increase tensile strength and to decrease the risk of fascial dehiscence. However, long stitches have been associated with high rates of both wound infection and incisional hernia.[17, 29, 30] A long stitch length may be associated with higher risks of wound infection due to an increase in the amount of necrotic tissue within the wound. In experimental studies, the long stitch length has been found to compress or cut through soft tissue included in the stitch.[31, 32]

The risk of incisional hernia may be higher because the stitch tends to slacken, which allows wound edges to separate.

Small stitches, placed 4–6 mm from the wound edge, only cut through the aponeurosis and not through the rectus abdominis muscle. Recent experimental data show that the small bites technique results in stronger wounds and faster healing than the routine large bite technique.[33] Our experiments in a porcine model showed a 47% increase in breaking strength when small bites were used compared to the routine technique.[32] A recent randomized of randomised clinical study by Millbourn et al. reported a decrease of incidence of incisional hernia of 70% 18% to 5.6%, p<0.001) and a decrease of 50%, (10.2% to 5.2%, p=0.020) of wound infection.[34,35] These results are very promising with regard to the prevention of incisional hernia and wound infection. The benefits of this technique need to be confirmed in a multicenter double-blinded randomized controlled trial.

In daily practice, most surgeons in the Netherlands use the large bite technique with large suture distances. With large bites, SL:WL ratio depends on the thickness of the abdominal wall including the muscles, the bite size, the number of stitches and the traction on the sutures during suturing. With large bites, an unanswered question remains with regard to how the SL:WL ratio of 4 should be reached. With a low traction force, fewer stitches are needed, but the slacking effect during the postoperative period may influence results.

With small stitches, SL:WL ratio is mostly dependent on the number of stitches. There is no sufficient evidence to prefer one suture closure technique over the other in order to prevent incisional hernia and fascia dehiscence.

Objective

The objective of the STITCH trial (Suture Techniques to reduce the Incidence of The inCisional Hernia) is to compare the small bites technique decribed by Millbourn et al. with a standardized large bites technique.

The overall objective of the study is reduction of the incidence of the most frequent complication of abdominal surgery, i.e., incisional hernia. We hypothesize that the small bites technique will result in a significant reduction of the incidence of incisional hernia, which may lead to a reduced morbidity and a better quality of life for patients and a significant reduction of costs.

Primary endpoint will be incisional hernia occurrence within one year after surgery, either clinically and/or ultrasonographically detected. Secondary endpoints include postoperative complications, in particular surgical site infection, burst abdomen and wound pain in the first postoperative month.

Methods

Trial Design

The STITCH trial has been designed as a prospective, multicenter, double-blind, randomized controlled trial, in which the large bites technique will be compared with the small bites technique.

Participants

Patients scheduled for an elective abdominal operation through a midline incision will be asked for informed consent at the outpatient clinic or in hospital on the day preceding the day of surgery. Also, emergency laparotomies can be included in this trial if the patient is able to sign the informed consent. We intend to investigate the efficacy of the small bites technique in all risk groups. This also includes oncological gynaecological patients in centers with at least 50 median laparotomies a year.

Inclusion criteria:

- Signed informed consent
- Laparotomy through a midline incision
- Age 18 years or older

Exclusion criteria:

- Previous incisional hernia or fascial dehiscence with secondary healing after a midline incision

- Abdominal surgery through a midline incision within the last three months
- Pregnancy

Since the STITCH trial is an intervention study, it is not considered desirable to combine this trial with other intervention studies. In case of non-intervention (registration) studies, it will be judged on individual basis whether it is suitable and ethically correct to include a patient in both the STITCH trial and in another study. Patients will be included in the STITCH trial in combination with one other trial (registration trials only), provided that it is possible to organize the informed consent and the follow up in a proper way for the individual patient for both trials.

Registration procedure

Included patient are registrated before surgery in an online data base (designed and managed by HOVON data center, Rotterdam, the Netherlands,) after signed informed consent via the Internet via TOP (Trial Online Process; see www.stitchtrial.nl). The patient namecode, date of birth, name of caller, name of responsible physician, sex and eligible criteria will be registered. Every participating institution has its own login code.

Randomisation procedure

The randomization process is started only 15 minutes before closure to prevent consequences due to the trial during the operation with the online TOP randomisation.

Patients will be randomized between closure with the large tissue bites technique or with the small tissue bites technique. Randomisation is stratified by center, and between surgeon or resident with a minimization procedure, ensuring balance within each stratum and overall balance. The randomization result will be given immediately by TOP. A confirmation email without randomization result will be send to the investigator.

Patients will be kept unaware of the type of closure until the endpoint of the trial. Surgeons or residents blinded for the procedure will perform out patient clinic controls. Postoperative ultrasonography will be performed by radiologists blinded

for type of closure. The randomisation procedure, blinding and objectification of incisional hernia by ultrasound will provide the best possible data to support preference for the large bites technique or the small bites technique over the other for closure of the abdominal wall.

Interventions

In this trial the large bites technique will be compared with the small tissue bites technique as developed in Sundsvall Hospital, Sweden(18). In the first group, the conventional large bites technique will be applied with bite widths of 1 cm and intersuture spacing of 1 cm with the use of one PDS plus II loop with a 48 mm needle. In the second group, the small bites technique will be applied with bite widths of 0,5 cm and intersuture spacing of 0,5 cm with the use of PDS plus II 2-0 with a 31 mm needle. In the small bites technique, twice as many stitches will be placed per sutured cm, with a smaller needle and thinner suture material. In the Swedish hospital where the small bites techniques has been in use for many years, this combination proved the easiest and safest method to perform the small bites technique.[18, 34]

In both groups wound length is measured before closing of the fascia. After measument of the woundlength, the number of stitches is calculated. In the large bites technique at least one suture per cm wound length must be placed. In the small bites technique at least two sutures per cm wound length must be placed. The number of stitches is counted by the assistant during closure.

In both arms, suturing is initiated at both ends of the incision towards the middle where an overlap will be created of at least 2 cm. The remaining sutures will be measured and the suture length used for closure of the fascia and the SL:WL ratio will be calculated by the scrub nurse. In both arms, suture length to wound length ratios (SL:WL) of 4:1 are aimed at.

Implementation

In every hospital the OR nurses the surgeons or gynecologists and residents are instructed before the start of the trial in the individual institution during presentations and demonstration movies. During at least the first five inclusions the study coordinator will be present in the OR before randomization to assist randomization and control the correct applying of the standardized techniques.

For every included patient a form with the detailed closing protocol in added to the clinical chart. Only when the surgeon is familiar with both the techniques, the nurses with the counting and measuring of the stitches and suture material and the study, centers are allowed to run the trial. Also for every included patient a form with the detailed closing protocol in added to the clinical chart. During the study unplanned audits are performed to control quality.

Outcome parameters

Primary outcome

- Primary outcome will be incisional hernia occurrence within one year after surgery, either clinically and/or ultrasonographically detected.

Secondary outcome

- Postoperative complications
- Pain
- Quality of life
- Cost effectiveness

We use the definition of the incisional hernia by the European Hernia Society: 'any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging'. The classification made by the European Hernia Society is used.[35] The classification of incisional hernias: Incisional hernias will be classified according to their localization, size, reducibility and symptoms.

Discharge dates and complications will be registered. Patients who fail to keep their annual clinic appointment will be given the option of a further appointment at a more suitable date or a visit to their home if they cannot make it to the outpatient clinic. The following data will be gathered at different points in time:

Preoperative data

- Date of birth
- Length and weight
- Current smoker (Yes or No).

- Medical history (including chronic obstructive pulmonary disease (COPD), diabetes mellitus, cardiac disease, prior laparotomies)
- Preoperative radiotherapy or chemotherapy
- Preoperative or perioperative corticosteroids
- Previous abdominal operations
- Other abdominal wall hernias
- American Society of Anaesthesiologists (ASA) classification
- Width of linea alba (if preoperative Computed Tomography Imaging is available)

Operation data

- Type of operation
- Suture length : wound length ratio
- Number of stitches
- Length of incision
- Closure time
- Blood loss
- Operation time
- Antibiotic prophylaxis
- Drains and location
- Thrombosis prophylaxis
- Pain medication
- Peroperative complications (intestinal lesions, bleeding, other)
- Epidural catheter

Postoperative data

- Blood transfusion
- Postoperative ventilation and duration
- Postoperative corticosteroids
- Postoperative radiation therapy
- Postoperative pain medication
- Postoperative ileus and duration
- Postoperative complications:
  - o Centers for Disease Control criteria for Surgical Site Infection, according to the guidelines proposed by Mangram in 1999.[36]
  - o Wound haematoma: accumulation of blood in the wound area,

which warrants surgical exploration and intervention.
    - Pulmonary infections
    - Ventilation problems
    - Re-admission and indication
    - VAS pain score until day 6 post operative

At 1 and 12 months, ultrasound imaging will be performed to examine the midline for any asymptomatic clinically not detectable incisional hernias. Size and location of any incisional hernias will be registered.

Outpatient clinic follow up

- Outpatient clinic visit at 1 and 12 months
    - Incisional hernia
    - Wound infection
    - Seroma formation
    - Other wound problems
    - Other abdominal wall hernia
- Ultrasound at 1 and 12 months
- VAS pain scores and Quality of Life forms preoperatively (day of operation or the day before) and at 1,3, 6 and 12 months

Ultrasound examinations

During the 1 month and 1 year follow up an ultra sound examination will be performed to measure the distance between the rectus muscles at 3 point in the incision and control for incisional hernia. A specific score is used for the ultrasound examination. At ten points, which include 4 measurements of the distance between the rectus muscle, the quality of the scar in the abdominal wall is objectified. With this method the conclusion if there is an incisional hernia can also be made on the score list. In this list is controlled for:

- An intact linea alba?
- Bulging without Valsalva manouvre?
- Bulging with Valsalva manouvre?
- Distance between rectus muscles in scar on 1/3 cranial part in cm?
- Distance between rectus muscles in scar on 1/3 caudal part in cm?
- Maximum distance between rectus muscles in scar in cm?
- Maximum distance between rectus muscles at place of bulging or

defect in cm?
- Is there a defect? If yes, the size of the defect and location
- Is there fatty tissue in the defect?
- Is there a bowel loop in the defect?

The radiologist is asked to make prints of every measurement and finding.

Quality of life will be assessed based on standardized Quality of Life forms including the EuroQol-5D and Short Form-36 before and at 1 month, 3 months, 6 months, and 12 months after surgery.

Economic evaluation

We will perform an ex-post economic evaluation in which a new suture technique using small bites is compared with the traditionally applied large bites technique, from a societal perspective. The economic evaluation will be performed in accordance with Dutch guidelines (Oostenbrink, 2004).

To measure the economic impact of the new suture technique using small bites the cost-effectiveness will be assessed by calculating the incremental cost-effectiveness ratio, defined here as the difference in average costs between both suture techniques divided by the difference in average effects. The primary outcome measure will be the costs per reduced incisional hernia within 1 year. Secondary, a cost-utility analysis will be performed using costs per quality adjusted life year (QALY) as outcome measure, using the EQ-5D.

Costs for all separate actions and time used by all individual health care professionals, and all other materials will be measured from a societal perspective for both bites techniques, which means that both direct medical costs (e.g. intervention costs, intramural and extramural medical costs) and indirect costs (absence from work, patient costs) will be included in the analysis.

For the most important cost items, unit prices will be determined by following the micro-costing method (Gold et al, 1996), which is based on a detailed inventory and measurement of all resources used. Resource costs arise within the hospital and consist of outpatient visits, inpatient days, use of the operation room, radiology examinations, blood tests, etc. Real medical costs will be calculated by

multiplying the volumes of health care use with the corresponding unit prices. For instance, the calculation of the costs of both suture techniques will consist of detailed measurement of investments in manpower, equipment, materials, housing and overhead. The salary schemes of hospitals and other health care suppliers will be used to estimate costs per hour for each health care professional. Taxes, social securities and vacations will be included.

Data on effects (reduction of incisional hernia), costs (time costs of new suture technique and material and development costs) and savings (reduced health care use of patients without incisional hernia) will all be collected in this study. Data on treatment (hospitalisation) and follow-up consultations will be collected retrospectively from (electronic) patient charts and hospital administration. This data will be collected by health care professionals using a data-collection form. Information will collected on:

- length of hospital stay
- length of stay in ICU
- reinterventions

Data on extramural care, work absence and other patient costs will be gathered via questionnaires at each follow-up (1 and 12 months).

For a description of the calculation of the effect measures see paragraph 'outcome parameters'. Discounting of future costs and effects is not relevant because of the limited time horizon of 1 year. When costs of a treatment are similar across subgroups, the absolute benefit determines the cost-effectiveness of a treatment for a specific subgroup. Randomized controlled trials are designed to evaluate the effects of treatment at the group level, and cost-effectiveness is usually calculated for this group as a whole. There could however be substantial and relevant between subgroup variability. It is therefore common to consider subgroup specific effects of interventions. The subgroup specific cost-effectiveness will be estimated by first deriving a prognostic index, based on the predefined predictors of incisional hernia: abdominal aneurysm aorta (AAA), obesity, diabetes, COPD, corticosteroid usage, radiotherapy, cardiovascular disease, smoking, age, cancer, other abdominal wall hernias and collagen disorders.

Sample size calculation

Millbourn et al. found a decrease in the incidence of incisional hernia from 18% to 5,6% in a randomized controlled trial. [34] In this trial, follow-up consisted of clinical instead of radiological examination for incisional hernia occurrence. In this trial, ultrasound examination will be used in order to be able to diagnose incisional hernia with higher sensitivity. It is expected that a relative decrease of the incidence incisional hernia after one year of 50% is reasonable. The mean reported one year incidence of incisional hernia in literature is 15%(1-5). In order to reduce the mean incidence of incisional hernia from 15 to 7.5%, power calculations showed that two groups of 259 evaluable patients each are needed (power=0.80, alfa=0.05). Loss to follow-up is estimated at 10% of included patients. A total of 576 patients (2 x 288) will be included in the study to correct for loss to follow-up. Overall effects will be calculated adjusted for predictive baseline characteristics, which will lead to a higher statistical power.

Statistical analysis

Descriptive statistics will include median and interquartile range for continuous variables, and absolute numbers (with %) for categorical variables. Randomized groups will be compared for imbalance without formal statistical testing. Analysis will be by intention-to-treat. Differences between randomized groups will be tested with appropriate statistical methods, including t-tests or Mann-Whitney tests for continuous variables (considering whether the normality assumption is rejected by the Kolmogorov-Smirnov test with Lilliefors correction test), and chi-square tests for categorical variables. The primary outcome (incisional hernia) will be analyzed with Kaplan–Meier analysis and a Cox regression analysis, to adjust for any loss to follow up between 30 days and 1 year after surgery. The primary analysis is a covariate adjusted Cox model, which includes the following predefined, well-establihed predictors of incisional hernia: abdominal aneurysm aorta (AAA), obesity, diabetes, corticosteroid usage, radiotherapy, COPD, smoking, age, cancer, inguinal hernia, cardiovascular disease and collagen disorders.

Subgroup effects will be assessed by tests of interaction to prevent overinterpretation of apparent differences in effectiveness. Quality of life data will be analyzed by paired T-tests, comparing baseline with follow-up measurements, and repeated measures analysis. A two-sided $p<0.05$ will be taken to indicate statistical significance.

Monitoring

The Erasmus University Medical center is the sponsor of this trial. Adverse events are defined as any undesirable experience occurring to a subject during a clinical trial, whether or not considered related to the investigational intervention. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded. A serious adverse event (SAE) is any untoward medical occurrence or effect that at any dose results in death; is life threatening (at the time of the event); requires hospitalization or prolongation of existing inpatients' hospitalization; results in persistent or significant disability or incapacity; is a new event of the trial likely to affect the safety of the subjects, such as an unexpected outcome of an adverse reaction, major safety finding from a newly completed animal study, etc. All SAEs will be reported to the accredited Medical Ethical Committee (MEC) that approved the protocol, according to the requirements of that MEC. Serious Adverse events are death and burst abdomen. Adverse Events are readmission and reoperations.

An independent data and safety monitoring committee will evaluate the progress of the trial and will examine safety parameters every 3 months. The committee can unblind the data whenever deemed necessary based on reported adverse events. All involved physicians will repetitively be asked to report any potential adverse events caused by the study protocol. These adverse events will be listed and discussed with the monitoring committee. The monitoring committee can ask for a full report in order to discuss a specific adverse event. A copy of this report will be sent to the central ethics board and to the involved physicians. All deceased patients will be evaluated by the safety committee for cause of death and possible trial related serious adverse effects. Every death will be reported to the central ethics board and the local ethics board. The Data Safety Monitoring Board will consist of an epidemiologist/statistician and two independent surgeons.

Ethics

This study will be conducted in accordance with the principles of the Declaration of Helsinki and 'good clinical practice' guidelines. The Medical Ethical Committee of the Erasmus University Medical Center Rotterdam has approved the protocol. The Ethical Committees of the participating centers are applied for local feasibility. Prior to randomization, written informed consent will be obtained from all patients.

Discussion

A major issue in all suture studies is standardisation of technique. In a multicenter trial it is difficult to achieve standardisation because many surgeons and residents will contribute in this trial. The benefit of a large group of participants is that the results will be representable for daily practice.

In this trial two major parameters have been standardized: the difference between small and large bites and the amount of stitches per running cm of wound resulting in an appropriate SL:WL ratio.

In daily practice, most surgeons use the large bite technique with large suture distances. With large bites, SL:WL ratio depends on the thickness of the abdominal wall including the muscles, the bite size, the number of stitches and the traction on the sutures during suturing. With large bites there is an unanswered question under which conditions an optimal SL:WL ratio of 4 should be reachable. With low traction on the suture fewer stitches are needed, but the slacking effect during the postoperative period will influence the results. For this reason in a RCT on suture techniques it is necessary to standardize the amount of stitches per centimetre of wound length.

Conclusion

The STITCH trial is a multicenter randomized trial (trialregister: http://clinicaltrials.gov/ct2/show/NCT01132209) comparing the costs and effectiveness of a standardized small tissue bites suture technique with a standardized large tissue bites technique in midline incisions. This trial will provide the surgical society the evidence needed to optimize a surgical technique used to prevent common surgical complications.

Competing interests

The authors declare that they have no competing interests. The Erasmus MC "Doelmatigheids Onderzoek grant 2008" and Johnson and Johnson Medical BV, the Netherlands, Investigator Initiated Clinical Research Funding Grant (09-107) have financially supported this trial.

Appendix 1

Criteria for defining a Surgical Site Infection (SSI)

Superficial Incisional SSI

Infection occurs within 30 days after the operation and infection involves only skin or subcutaneous tissue of the incision and at least one of the following:

1. *Purulent drainage, with or without laboratory confirmation, from the superficial incision.*
2. *Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.*
3. *At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative.*
4. *Diagnosis of superficial incisional SSI by the surgeon or attending physician.*

Do not report the following conditions as SSI:

1. *Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration).*
2. *Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI).*

Deep Incisional SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissue (e.g., fascial and muscle tissue) of the incision and at least one of the following:

1. *Purulent drainage from the deep incision but not from the organ / space component of the surgical site.*
2. *A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness, unless site is culture negative.*
3. *An abscess or other evidence of infection involving the deep incision is found on direct examination, during re-operation, or by histopathological or radiological examination.*
4. *Diagnosis of a deep incisional SSI by a surgeon or attending physician.*

Notes:

1. *Report infection that involves both superficial and deep incision sites as deep incisional SSI.*
2. *Report an organ/space SSI that drains through the incision as a deep incisional SSI.*

Organ/Space SSI

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

1. *Purulent drainage from drain that is placed through a stab wound into the organ / space.*
2. *Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ space.*
3. *An abscess or other evidence of infection involving the organ / space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.*
4. *Diagnosis of a deep organ / space SSI by a surgeon or attending physician.*

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Chapter 4

Small bites versus large bites for closure of abdominal midline incisions: results of a double blinded multicenter randomized trial (STITCH-trial)

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Abstract

Background

Incisional hernia is a frequent complication of midline laparotomy and is associated with high morbidity, decreased quality of life, and high costs. We aimed to compare the large bites suture technique with the small bites technique for fascial closure of midline laparotomy incisions.

Methods

We did this prospective, multicentre, double-blind, randomised controlled trial at surgical and gynaecological departments in ten hospitals in the Netherlands. Patients aged 18 years or older who were scheduled to undergo elective abdominal surgery with midline laparotomy were randomly assigned (1:1), via a computer-generated randomisation sequence, to receive small tissue bites of 5 mm every 5 mm or large bites of 1 cm every 1 cm. Randomisation was stratified by centre and between surgeons and residents with a minimisation procedure to ensure balanced allocation. Patients and study investigators were masked to group allocation. The primary outcome was the occurrence of incisional hernia; we postulated a reduced incidence in the small bites group. We analysed patients by intention to treat. This trial is registered at Clinicaltrials.gov, number NCT01132209 and with the Nederlands Trial Register, number NTR2052.

Findings

Between Oct 20, 2009, and March 12, 2012, we randomly assigned 560 patients to the large bites group (n=284) or the small bites group (n=276). Follow-up ended on Aug 30, 2013; 545 (97%) patients completed follow-up and were included in the primary outcome analysis. Patients in the small bites group had fascial closures sutured with more stitches than those in the large bites group (mean number of stitches 45 [SD 12] *vs* 25 [10]; p<0.0001), a higher ratio of suture length to wound length (5.0 [1.5] *vs* 4.3 [1.4]; p<0.0001) and a longer closure time (14 [6] *vs* 10 [4] min; p<0.0001). At 1 year follow-up, 57 (21%) of 277 patients in the large bites group and 35 (13%) of 268 patients in the small bites group had incisional hernia (p=0.0220, covariate adjusted odds ratio 0.52, 95% CI 0.31–0.87; p=0.0131). Rates of adverse events did not differ significantly between groups.

Interpretation

Our findings show that the small bites suture technique is more effective than the traditional large bites technique for prevention of incisional hernia in midline incisions and is not associated with a higher rate of adverse events. The small bites technique should become the standard closure technique for midline incisions.

Introduction

Incisional hernia is a frequent complication of abdominal operations with an incidence of 10–23%, which can increase to 38% in specific risk groups.[1-4] In the USA 4 million to 5 million laparotomies are done annually, suggesting that at least 400 000–500 000 incisional hernias can be expected to occur every year. Incisional hernia is associated with pain and discomfort, resulting in a decreased quality of life.[5] Moreover, incarceration and strangulation of abdominal contents can take place, for which emergency surgery is indicated, with associated morbidity and mortality.[6] About 348 000 operations for incisional hernia are done every year in the USA with US$3.2 billion in annual associated costs.[7] Prevention of incisional hernia is therefore of paramount importance. Several suturing techniques for abdominal closure after a midline abdominal incision have been studied in the past few decades. Findings from meta-analyses have shown that a running technique with long-lasting monofilament suture material reduces the incidence of incisional hernia compared with interrupted suture techniques.[3,8] Nowadays, most surgeons, urologists, and gynaecologists use the running closure technique with large tissue bites to close midline incisions.[9] In 2009, a study from Sweden[10] showed that a running suture technique with small tissue bites, developed by Israelsson, decreased the incidence of incisional hernia compared with a running suture technique with large tissue bites. In this study, small tissue bites were defined as placement of a stitch every 5–8 mm from the wound edge. This promising technique is contradictory to old surgical principles and needs to be thoroughly investigated before it can be widely implemented.[11, 12] We did the STITCH study to compare the common conventional large bites suture technique with the small bites technique for fascial closure of midline laparotomy incisions.

Methods

Study design

We did this prospective, multicentre, double-blind, randomised controlled trial at surgical and gynaecological departments in ten hospitals in the Netherlands. The trial protocol has been previously published.[13] Patients aged 18 years or older and scheduled to undergo elective abdominal surgery through a midline incision were asked to participate in the trial at the outpatient clinic or in hospital on the day

before surgery. We excluded patients with a history of incisional hernia or fascial dehiscence after midline laparotomy, those who had undergone abdominal surgery through a midline incision within the past 3 months, those who were pregnant, or those who had participated in another intervention trial. The study protocol was approved by the institutional review board of Erasmus University Medical Center, Rotterdam, and by the review boards of each study centre before start of inclusion. All participants gave written informed consent. An independent data and safety monitoring board was constituted before the start of the trial. This board consisted of two independent surgeons and one biomedical statistician. All serious adverse events, defined as death and burst abdomen that happened during the study, were reported to the institutional review board of Erasmus University Medical Center. The progress of the trial and all adverse events were reported every 3 months to the data and safety monitoring board and the safety of the trial was examined.

Randomisation and masking

After provision of consent, patients were registered in an online database in which they were assigned a unique trial code. During surgery, about 15 min before closure, patients were randomly assigned (1:1), via a computer-generated randomisation sequence, to receive small tissue bites of 5 mm every 5 mm, or large bites of 1 cm every 1 cm (control group), for fascial closure. Randomisation was stratified by centre and between surgeons and residents with a minimisation procedure to ensure balance within each group and overall. Patients and study investigators were masked to group allocation. The data and safety monitoring board had access to unmasked data whenever deemed necessary.

Procedures

The principle of the small bites technique constituted placement of at least twice as many stitches as the incision length in cm with USP 2-0 PDS Plus II (Ethicon, Somerville, NJ, USA) with a 31 mm needle.[10, 13-15] The suture technique was applied with tissue bites of 5 mm and intersuture spacing of 5 mm. In all cases the stitch incorporated the aponeurosis only and incorporation of fat or muscle tissue was avoided. The conventional large tissue bites or mass closure technique was applied with tissue bites of at least 1 cm and intersuture spacing of 1 cm with USP 1 double loop PDS Plus II (Ethicon) with a 48 mm needle. In both groups, suturing was started at both ends of the incision towards the centre where an

overlap of at least 2 cm of both the cranial and caudal sutures was created and both sutures were separately knotted. An additional knot from both the cranial and caudal sutures was allowed. The number of stitches was counted, wound length and length of the remaining suture measured, and ratio of suture length to wound length calculated by dividing the length of the suture used to close the fascia by the wound length. For both suture techniques, we aimed for a suture length to wound length ratio of 4:1 or higher.[14] Patients were invited for follow-up at the outpatient clinic 1 month and 1 year after surgery. The 1 year follow-up visit was defined as a follow-up visit up to month 15 after surgery. During these visits patients underwent physical examination by a medical doctor and abdominal ultrasonography by a radiologist, both of whom were masked to group allocation. Any abdominal CT done after surgery was also used to identify the presence or absence of incisional hernia. Physical examination and assessment of CT of all patients was done by two medical doctors (EBD and JJH) specially trained for this trial. Patients who did not attend the outpatient clinic received a repeated invitation or were offered a home visit. In case of conflicting observations, the observation by radiological imaging was decisive. Patients were regarded as censored observations if they underwent re-laparotomy through midline incision, were deceased, or ended follow-up. Patients remained unaware of the type of closure until completion of follow-up. All participants were asked to fill out quality of life questionnaires preoperatively and at 1, 3, 6, and 12 months postoperatively. We assessed quality of life with the Short Form-36 (SF-36) and the EuroQoL-5D (EQ-5D) questionnaires.[16,17] EQ-5D includes a visual analogue scale to rate overall health status on a scale of 0 (worst imaginable health state) to 100 (best imaginable state). Additionally, in the first postoperative week, patients scored their pain on a visual analogue scale once a day.

Outcomes

The primary outcome was the occurrence of incisional hernia during follow-up. We used the definition of incisional hernia from the European Hernia Society (EHS): "any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging".[18] Secondary outcomes were short-term postoperative complications (eg, surgical site infection [scored as superficial, deep, or involving organ or space, as specified in the protocol(13)]), burst abdomen (fascia dehiscence), cardiac events, length of hospital stay, and health-related quality of life. Main endpoints regarding quality

of life were differences between patients assigned to the small bites technique and those assigned to the large bites technique, and between patients with and without development of incisional hernia during follow-up.

Statistical analysis

We postulated a reduced incidence of incisional hernia in the small bites group. On the basis of the results of the Swedish trial,[10] we calculated that 259 patients would be needed in each group to provide 80% power to detect a reduction of 50% (15% *vs* 7.5%) in the incidence of incisional hernia at a two-sided α level 0.05. We aimed for a total of 576 patients (n=288 per group) to correct for an estimated 10% loss to follow-up.[10,13] We analysed differences between groups with *t* tests for continuous variables and χ^2tests for categorical variables. For continuous variables, we tested equality of variance with Levene's test. Normal distribution of data was tested and confirmed by limited skewness and kurtosis. We analysed the primary outcome with cross-tables with χ^2testing and logistic regression to adjust for baseline covariates.[19] We estimated final treatment effects with stratum of randomisation as a random effect in a generalised linear mixed model. We used a binomial error and logit link function in the glmer function of the lme4 package in R statistical sofware (version 3.1.0.).

Considered baseline covariates were predefined potential predictors of incisional hernia: abdominal aneurysm aorta, body-mass index, diabetes mellitus, corticosteroid usage, preoperative chemotherapy, preoperative radiotherapy, chronic obstructive pulmonary disease (COPD), smoking, age, collagen disorders, non-incisional hernias (including inguinal hernia), and cardiovascular disease.[13] For patients with missing covariate data for BMI, we imputed the mean BMI value. We assessed subgroup effects by tests of interaction to prevent over-interpretation of apparent differences in effectiveness for all baseline characteristics. We chose not to do Cox-regression analysis as specified in the protocol. Because most patients had available two-time measurements (1 month and 1 year postoperatively), we defined incisional hernia as a binary endpoint if it took place up to 15 months after randomisation, with cross-table and logistic regression as the natural analyses, rather than Kaplan-Meier and Cox-regression analyses. Statistical comparison of quality of life between patient groups (small *vs* large bites technique and with or without incisional hernia during follow-up) was done by multilevel analysis (linear mixed-effects model with random effect

for each patient). Time, randomisation (small *vs* large bites), and the interaction between time and randomisation were main effects, with adjustment for age and sex. Analysis was by intention to treat. We did statistical analysis with SPSS (version 20.0) and R statistical software (version 3.1.0,).

This trial is registered with Clinicaltrials.gov, number NCT01132209, and Nederlands Trial Register, number NTR2052.

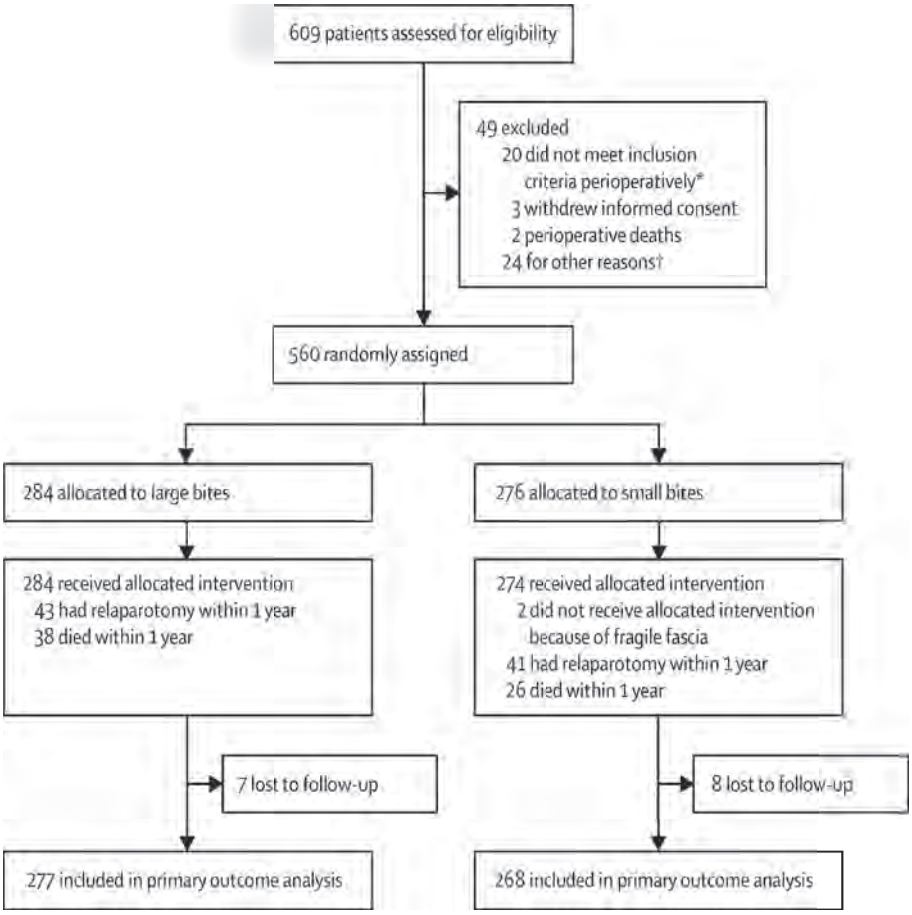
Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The figure shows the trial profile. Between Oct 20, 2009, and March 12, 2012, we randomly assigned 560 patients to the large bites group (n=248) or the small bites group (n=276). Follow-up ended on Aug 30, 2013; 545 (97%) completed follow-up and were included in the primary outcome analysis (figure). Baseline characteristics were similar between groups, except that slightly more patients with COPD were included in the small bites group (table 1). Most surgical procedures were for gastrointestinal oncological diseases and consisted of opening or partial resection of the gastrointestinal tract (table 1).

Figure 1. CONSORT flow-chart of study enrollment.(20)



*Not operated through midline incision, need to (partly) resect the abdominal wall or incisional hernia detected during incision. †Logistical reasons, computer randomisation issues, or surgeon was unfamiliar with this study.

Table 1: Baseline characteristics

	Large bites group (n=284)	Small bites group (n=276)
Sex		
- Male - n (%)	139 (48%)	137 (50%)
- Female - n (%)	145 (51%)	139 (50%)
Age - years (median, IQR)	63 (54-71)	62 (53-72)
BMI - kg/m^2* (median, IQR)	24 (22-27)	24 (22-27)
Smoking - n (%)	65 (23%)	77 (28%)
Diabetes Mellitus - n (%)	39 (14%)	29 (11%)
COPD - n (%)	27 (10%)	44 (16%)
Cardiovascular disease - n (%)	116 (41%)	101 (37%)
Corticosteroid usage - n (%)	18 (6%)	28 (10%)
Non incisional hernias† - n (%)	34 (12%)	37 (13%)
Aneurysma abdominal aorta - n (%)	12 (4%)	13 (5%)
Previous laparotomy - n (%)	43 (15%)	49 (18%)
ASA classification - n (%)		
• 1	58 (20%)	61 (22%)
• 2	183 (64%)	162 (59%)
• 3 or higher	43 (15%)	53 (19%)
Preoperative chemotherapy - n (%)	75 (26%)	62 (22%)
Preoperative radiotherapy - n (%)	55 (19%)	59 (21%)
Type of surgery - n (%)		
• Gynecological	41 (14%)	41 (15%)
• Upper gastrointestinal	89 (31%)	74 (27%)
• Lower gastrointestinal	133 (47%)	140 (51%)
• Vascular	21 (7%)	21 (8%)

BMI=Body Mass Index. COPD=Chronic Obstructive Pulmonary Disease. ASA=American Society of Anesthesiologists. *Data for BMI were missing for 12 patients.†Eg, inguinal, umbilical, and epigastric hernias in history.

Peri-operative complications (gastrointestinal perforation, haemorrhage, or cardiopulmonary event) arose in 64 (11%) patients and were equally distributed between groups. The amount of blood loss and numbers of inserted drains were also equally distributed (data not shown). Approximation of subcutaneous tissue and method of skin closure did not differ between both groups (data not shown). Table 2 shows details of the suture techniques.

Table 2: Details of suture techniques

	Large bites group(n=284)	Small bites group(n=276)	p value
Number of stitches (mean; SD)	25 (10)	45 (12)	<0.0001
Total length of used sutures (cm) (mean; SD)	95 (34)	110 (39)	<0.0001
Wound length (cm) (mean; SD)	22 (5)	22 (5)	0.982
Rati of suture length to wound length (SL:WL) (mean; SD)	4.3 (1.4)	5.0 (1.5)	<0.0001
Time of fascial closure (minutes) (mean; SD)	10 (4)	14 (6)	<0.0001

Of 545 patients, follow-up assessments were done by clinical and radiological examination in 338 (62%) patients, by radiological examination in 76 (14%), and by physical examination in 131 (24%) patients. Follow-up methods were similar between groups. 1 year postoperatively, 57 (21%) of 277 patients had incisional hernia in the large bites group and 35 (13%) of 268 patients had incisional hernia in the small bites group (p=0.0220; adjusted odds ratio [OR] 0.52, 95% CI 0.31–0.87; p=0.0131). No subgroup effects were identified; all p values for interaction tests were greater than 0.20. In patients followed-up by both physical and radiological examination, incisional hernia was identified in 43 (49%) of 87 patients by both physical and radiological examination, in 41 (47%) of 87 solely by radiological examination, and in 3 (3%) of 87 solely by physical examination. In patients with incisional hernia, the mean fascial defect was 3.4 cm (SD 4.4). The size of the hernia defects did not differ significantly between groups (data not shown). Incisional hernias diagnosed by radiological examination alone were not significantly smaller than those diagnosed by both physical and radiological examination (mean 2.4 cm [SD 4.0] *vs* 4.2 cm [0.5]; p=0.0650.

Almost half of patients had postoperative complications, the incidence of which did not differ significantly between groups (table 3). Readmission rates and adverse events did not differ significantly between groups (table 3). Pain scores on the visual analogue scale did not differ significantly between groups in the first postoperative week (data not shown). 452 (94%) of 483 patients completed the SF-36 questionnaire and the EQ-5D questionnaire 12 months post-operatively. None of the SF-36 subdomains, the mental component summary (MCS) score, the physical component summary (PCS), or EQ-5D dimensions differed significantly between groups at 12 months (data not shown). Patients who developed incisional hernia during follow-up had lower general health SF-36 scores than did those without incisional hernia 12 months post-operatively (mean 60.16 [SD 18.27] *vs* 64.84 [48.70]; p=0.0326) and reported more problems in EQ-5D dimension of mobility (1.46 [1.06] *vs* 1.36 [0.46]; p=0.0318). We noted no significant differences for the other SF-36 domains, the MCS, the PCS, EQ-5D dimensions, or overall health status on VAS (data not shown).

Table 3: Secondary outcome parameters

	Large bites group (n=284)	Small bites group (n=276)	p value
Patients with postoperative complications - n (%)	129 (45%)	125 (45%)	1.000
Ileus - n (%)	33 (12%)	28 (10%)	0.590
Pneumonia - n (%)	40 (14%)	35 (1%)	0.710
Cardiac event - n (%)	30 (11%)	25 (9%)	0.573
Surgical Site Infection (SSI) - n (%)	68 (24%)	58 (21%)	0.419
• Superficial Incisional SSI*	33 (12%)	23 (8%)	0.207
• Deep incisional SSI*	12 (4%)	8 (3%)	0.496
• Organ/space SSI*	23 (8%)	27 (10%)	0.554
Burst abdomen - n (%)	2 (1%)	4 (1%)	0.444
Length of hospital stay (days) – mean (SE)	14 (24)	15 (35)	0.585

*detailed criteria for SSIs can be found in the published study protocol(13).

Discussion

Our findings show that suturing of the fascia after abdominal midline incision with a continuous small bites technique reduces the incidence of incisional hernia compared with suturing with the conventional large bites technique. The small bites technique with a single suture USP 2-0 is a safe technique in view of the low incidence of burst abdomen, and is easily learnt and performed with the small needle.[15] With a mean additional closure time of 4 min, the small bites technique is not very time consuming; additionally, the technique is not associated with a difference in postoperative pain. Our results are generalisable to the general surgical population in view of the participation of residents and specialists of vascular, general, gastrointestinal and gynaecological surgical specialties.

Although the Swedish trial[10] was the first prospective trial comparing large and small bites, this study had methodological limitations. Patients were quasi-randomised (alternated per calendar week) and radiological examination of the abdominal wall was not done. As a diagnostic technique for the presence of incisional hernia, ultrasonography has a reported sensitivity of 70–98%; physical examination has a reported sensitivity of 58–74% in diagnosis of incisional hernia.[21,22] Furthermore, in 16–28% of patients with complaints of discomfort at their scar, but without a palpable defect during physical examination, an incisional hernia was diagnosed by ultrasonography.[21,22] Because almost half of incisional hernias in the present

trial were diagnosed solely during radiological examination, our results attest that radiological imaging is essential to assess the presence of incisional hernia. Guidelines on the closure of abdominal wall incisions from the European Hernia Society strongly recommend that prospective studies with incisional hernias as a primary outcome should integrate medical imaging in the follow-up.[2,9,18,21] In our trial, roughly three-quarters of patients received radiological imaging during follow-up. Some patients had such an obvious clinical incisional hernia that imaging would have added no extra information. In some patients, radiological imaging was not done, either because patients were visited at home or because of local logistical difficulties. We considered achievement of standardisation to be important. Two major parameters were standardised: the technique of small and large bites and the target number of stitches per running cm of wound length, resulting in an appropriate ratio of suture length to wound length.

Our study has some limitations. Our primary analysis was done after 1 year of follow-up. Previous studies[2,4] have shown that incidence of incisional hernia increases during longer follow-up. Our follow-up of both clinical and radiological examination resulted in an incidence of 21% in the large bites group. These results are similar to those of other groups with longer follow-up.[2,4] Because radiological examination was done for the diagnosis of incisional hernia, small incisional hernias could have been diagnosed that would not have been detected by physical examination. We feel that the diagnosis of these smaller hernias explains the fairly high incidence in both groups at 1 year and might translate into a smaller increase in new hernias during longer follow-up. We do not expect that the effectiveness of the small bites will be affected with longer follow-up.

Another limitation might be that our results do not differentiate between an effect of the smaller bites or the use of different suture material. In this trial, we investigated the small bites technique described by Israelsson.[14] For the small bites technique the UPS 2-0 PDS Plus II (Ethicon) single suture thread with a 31 mm needle was used, whereas the large bites procedure was done with a thicker PDS 1 loop with a 48 mm needle. Therefore, analysis of whether the small bites or the thinner needle and suture material reduces the incisional hernias in the small bites group needs further research.

We included only patients undergoing elective surgery. Evidence about the best closure technique in emergency laparotomy incisions is scarce, even in the EHS guidelines no recommendation is given.[9] Whether results obtained by studies for elective laparotomies can be extrapolated to emergency laparotomies remains a topic of discussion.

We hypothesise that the small bite suture technique in our trial, with twice the amount of stitches including the aponeurosis only, provides close to ideal conditions for fascia healing because of avoidance of necrosis of the rectus abdominis muscles and of optimum distribution of forces leading to a reduced incidence of incisional hernia. Experimental studies show that a suture technique with an equal distribution of forces on the fascia is necessary to achieve an optimum ratio of collagen type 1 to type 3. Too high tensile force per suture will result in more scar tissue.[23,24] The holding force of a suture depends on the collagen that deposits in the suture, which is best achieved by suturing of the aponeurosis without muscle or fat tissue.[25] Experimental data show that the small bites technique is stronger than the large bites technique, which is consistent with the results of this clinical study.[26]

In this era of minimally invasive and robotic surgery, many patients with high-risk profiles or undergoing major abdominal surgical procedures will still have to have open surgical procedures with midline incision. Compared with previous trials, we examined a relatively high-risk group, which is relevant and consistent with present surgical practice. Challenging patient and surgical characteristics could be an explanation of the overall complication rate and the fairly high incidence of surgical site infection in both groups. The higher incidence of surgical site infection in our trial than in the Swedish trial might be explained by the difference in patient condition (eg, previous midline incision, more patients with diabetes, perioperative chemoradiation, and malnutrition), more major surgical procedures, and use of a strict standardised wound scoring method in this trial.[10, 27] Although surgical site infection was not the primary endpoint of our trial, our results emphasise that wound infection remains a frequent complication in this surgical population and should be monitored carefully.

We also reported health-related quality of life and pain of patients who received the small bites suture technique. Postoperative quality of life or pain did not

differ between the two groups. Patients with incisional hernia in both groups had significantly lower scores on the general health dimension and had more mobility problems. Furthermore, most of our patients had malignant disease, which is associated with a reduced quality of life in general.[5,28,29]

In conclusion, the small bites suture technique is more effective than the traditional large bites suture closure technique for prevention of incisional hernia in midline incisions. The small bites technique is not associated with more pain or adverse events and should be considered the standard closure technique for midline incisions.

Contributors

JJH did the literature search, designed the study; collected, analysed, and interpreted data; and wrote the report. EBD designed the figures; collected, analysed, and interpreted data; and wrote the report. EWS designed the figures; designed the study; analysed and interpreted data; and wrote the report. HEL, HCvD, JH, BPLW, WRS, HAC, HBACS, FJB, FPHLJD, and RSD collected, analysed, and interpreted data. APJ analysed data and wrote the report. GHvR designed the study; collected, analysed, and interpreted data; and wrote the report. G-JK interpreted data and wrote the report. JJ designed the study, interpreted data, and wrote the report. JFL designed the study, collected and interpreted data, and wrote the report.

Declaration of interests

We declare no competing interests.

Acknowledgments

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Chapter 5

Development of incisional herniation after midline laparotomy

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Abstract

Background:
Incisional herniation is a common complication after abdominal surgery associated with considerable morbidity. The aim of this study was to see if incisional hernia is an early complication to better understand the aetiology of incisional hernia formation.

Methods:
This study involved the secondary analysis of a subset of patients included in a large randomized controlled trial comparing small and large tissue bites (5 mm every 5 mm or 1 cm every 1 cm) in patients scheduled to undergo elective abdominal surgery by midline laparotomy. The distance between the rectus abdominal muscles was measured by a standardized ultrasound one month and one year after surgery. The relationship between one-year incidence of incisional hernia and the distance between the rectus abdominal muscles after one month, was investigated.

Results:
Some 219 patients were investigated. One month after surgery the distance between the rectus abdominal muscles was smaller in the small bite group (mean 1.90 cm; sd 1.18) compared to the large bite group (mean 2.39 cm; sd 1.34) (p=0.005). Incisional hernia patients (mean 2.43 cm; sd 1.48) had a wider distance between the rectus abdominal muscles at one month compared to patients without an incisional hernia (mean 2.03 cm; sd 1.19) at one year follow up (RR 1.14; 95%CI 1.03-1.26; p=0.015).

Conclusion:
A larger distance (>2 cm) between the rectus abdominal muscles one month after midline laparotomy is associated with incisional hernia. Closure with small bites results in a smaller rectus abdominis muscle distance.

Trial registration: Clinicaltrials.gov NCT01132209; Nederlands Trial Register NTR2052.

Introduction

Despite many decades of research there is little information about the aetiology of incisional hernia formation. Several hypotheses have been proposed to explain the development of these hernias.[1] Surgical technique seems important and two clinical trials have suggested that an increased distance between the rectus abdominis muscles one month after surgery predicts later incisional hernia formation.[2,3]

A recent randomized controlled trial demonstrated that a running suture technique with small tissue bites, developed decreased the incidence of incisional hernia compared to a running suture technique with large tissue bites.[4] In this study small tissue bites were defined as placement of a suture every 5 mm from wound edge at 5 mm intervals, based on preclinical studies that suggested the small bites technique induced wound healing, collagen type l formation and higher bursting strength.[5,6] The question of whether incisional herniation is an early complication and how the small bite technique may reduce its formation, is still unanswered.

The aim of our study was to see if the distance between the rectus abdominis muscles one month after surgery predicted incisional hernia formation and was this distance related to the small bites technique.

Methods

Study design

This study represents an explanatory secondary analysis of a randomized controlled trial (STITCH trial, trialnumber: Clinicaltrials.gov NCT01132209). The STITCH (**S**uture **T**echniques to reduce the **I**ncidence of **T**he in**C**isional **H**ernia) trial was a prospective, multicentre, double-blind, randomized controlled trial of patients scheduled for elective abdominal operation through a midline incision. The trial protocol and the primary endpoint results have been previously published.[4,7] Patients aged 18 years or older and were asked to participate in the trial at the outpatient clinic or in hospital on the day before surgery. Patients with a history of incisional hernia or fascial dehiscence after midline laparotomy,

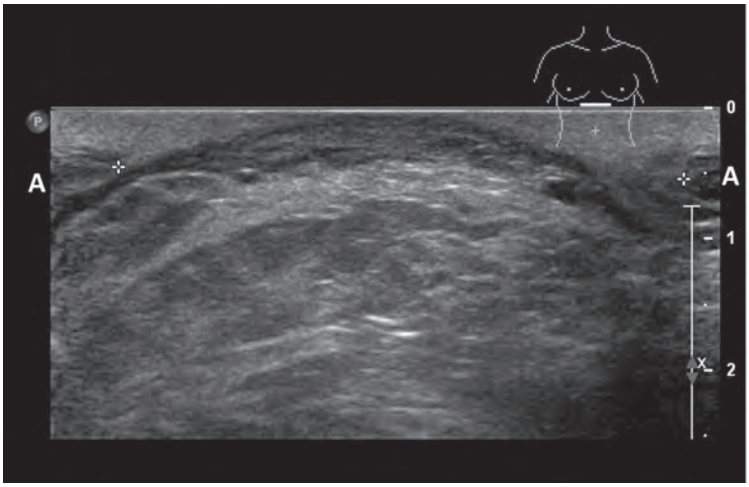
abdominal surgery through a midline incision within the previous last three months, current pregnancy or participation in another intervention trial were excluded.

Patients were randomly assigned between closure with the large tissue bites technique or with the small tissue bites technique. In the intervention group the principle of the small tissue bites technique consisted of placing at least twice as many stitches as the incision length in centimeters with USP 2-0 PDS Plus II™ (Ethicon Inc.) with a 31 mm needle.[7-10] The suture technique was applied with tissue bites of 5 mm and intersuture spacing of 5 mm. In the control group the conventional large tissue bites or mass closure technique was applied with tissue bites of at least 1 cm and intersuture spacing of 1 cm with USP 1 double loop PDS Plus II™ (Ethicon Inc.) with a 48 mm needle.

Outcome parameters

The primary outcome was the occurrence of incisional hernia and distance between the rectus abdominis in the laparotomy scar at one month and one year after surgery measured by a standardized ultra sound examination. All patients that completed a standardized ultra sound examination one month and one year postoperative were included in this study. Patients who underwent a relaparotomy within one year were excluded from analysis, to prevent the effect of several closure techniques in the outcome analysis.

Patients were invited for follow-up at the outpatient clinic one month and one year after surgery. During these follow-up visits patients underwent physical examination by a medical doctor blinded for the intervention group as well abdominal ultrasonography by a radiologist blinded for the intervention group. The ultrasound examinations were performed in a standardized fashion with focus on the distance between the rectus abdominis muscles (RAM) and occurrence of incisional hernia at one month and one year after surgery in the laparotomy scar. (fig 1)



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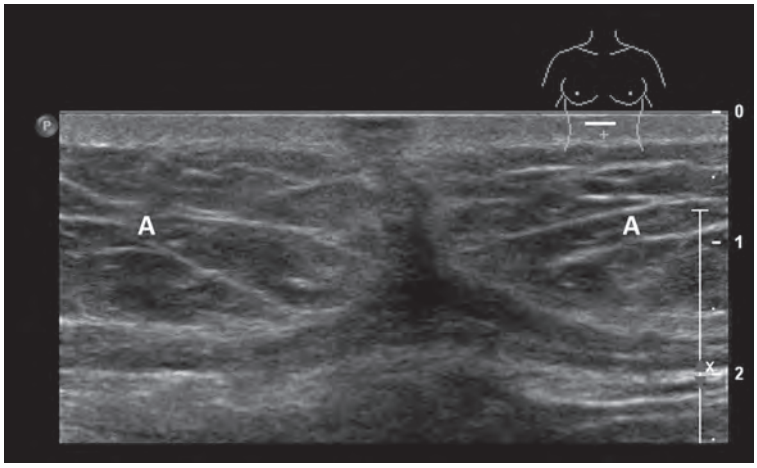

B

Figure 1 Ultrasound of a male patient, 63 years, with median laparotomy scar from Xiphoid to umbilicus.

A) Ultrasound image at upper 1/3 level of the laparotomy scar demonstrates bulging of intra-abdominal fatty tissue through a large distance of 4,3 cm between the medial borders (indicated by "+" markers) of the abdominal rectus muscles. The patient developed an incisional hernia during follow up.

B) Ultrasound image at the 2/3 level of the laparotomy scar demonstrates a tight junction between the medial borders of the abdominal rectus muscles in the mid-line.

The body mark (upper left) indicates de level and position (axial oriented) of the ultrasound probe (10-12 MHz, lineair array transducer). A: rectus abdominal muscle.

After ultrasonographic examination of the entire scar, RAM distance was measured at three levels: the cranial upper one third of the entire incision, the caudal lower one third and the maximum RAM distance. For further analysis, the maximum distance was used. The definition of incisional hernia by the European Hernia Society (EHS) was used: 'any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging'.[11]

Statistical analysis

Differences between randomized groups were tested with t-tests for continuous variables and chi-square tests for categorical variables. The one-year incidence of incisional hernia and the relationship with the distance between the rectus abdominal muscles after one month evaluated. The primary outcome was analyzed using logistic regression analysis. Multivariable logistic regression analysis was used to adjust for confounders.[12] A covariate variable was deemed a confounding variable in case it showed a significant univariable relationship with both the distance between rectus abdominal muscled after one month and with the presence of incisional hernia, using univariable regression analysis. Relative risk and 95% confidence intervals of the adjusted and unadjusted analysis are reported.[13] Relationships between suture characteristics and distance between the rectus abdominal muscles after one month were calculated using Pearson correlations.

The considered baseline covariates were the following predefined, potential confounders for incisional hernia development: abdominal aortic aneurysm, Body Mass Index (BMI), diabetes mellitus, corticosteroid use, preoperative chemotherapy, preoperative radiotherapy, chronic obstructive pulmonary disease (COPD), smoking, age, collagen disorders, non incisional hernias (including inguinal hernia), and cardiovascular disease.[7] Statistical analysis was performed with SPSS software, version 20.0 (IBM Corp. 2011, Armonk, NY).

Ethical considerations and monitoring

The study protocol was approved by the institutional review board (IRB) of Erasmus University Medical Center (Erasmus MC), Rotterdam (MEC-2009-026) and by the IRBs of each study center before start of inclusion. All participants gave written informed consent. An independent data and safety monitoring board

(DSMB) was constituted before the start of the trial. This DSMB consisted of two independent surgeons and one biomedical statistician. All serious adverse events (SAEs), defined as death and burst abdomen, which occurred during the study, were reported to the IRB of Erasmus MC. The progress of the trial and all adverse events were reported every three months to the DSMB and the safety of the trial was examined. The DSMB had access to unblinded data whenever deemed necessary. The trial was registered at Clinicaltrials.gov and Netherlands Trial Register before enrollment began and assigned number NCT01132209 and Netherlands Trial Register NTR2052.

Results

Study population

Between October 2009 and March 2012, 219 patients (113 small bites, 106 large bites) from a total of 560 patients completed a standardized ultrasound examination one-month and one-year post-operatively. Patients with a relaparotomy within a year were excluded from analysis. Follow-up ended August 2013. (see CONSORT flowchart, Figure 1).

Baseline characteristics were similar for the two groups except that more patients with COPD, smoking and prednisolone usage were included in the small bites group (Table 1). Most operations were resections undertaken for gastrointestinal neoplasms. Table 2 shows details of the suture techniques. Incisional herniation was identified in 38 (36%) of 106 patients in the large bites group and 22 (20%) of 112 patients in the small bites group (RR: 1.56; 95%CI: 1.09-2.23; p=0.007). Almost 40% of patients had postoperative complications, the incidence of which did not differ significantly between groups (table 3).

Figure 1: CONSORT flow-chart of study enrollment.[19]

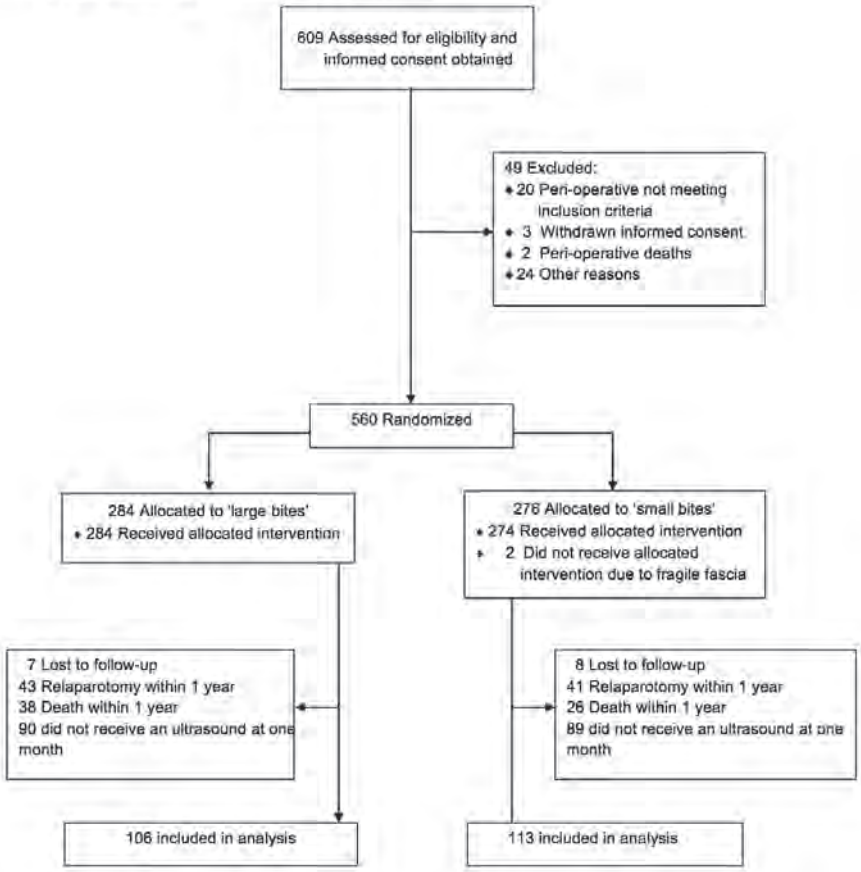

Table 1: Baseline characteristics

	Large bites (n=106)	Small bites (n=113)	P-value
Male sex - n (%)	55 (52%)	49 (43%)	p=0.21
Age - years (mean, sd)	62.4 (12.6)	61.8 (14.3)	p=0.72
BMI* - kg/m^2 (mean, sd)	25.5 (4.5)	25.4 (4.4)	p=0.86
Smoking - n (%)	17 (16%)	33 (29%)	p=0.02
Diabetes Mellitus - n (%)	11 (10%)	9 (8%)	p=0.54
COPD* - n (%)	9 (9%)	20 (18%)	p=0.047
Cardiovascular disease - n (%)	40 (38%)	43 (38%)	p=0.96
Corticosteroid usage - n (%)	1 (1%)	10 (9%)	p<0.001
Non-incisional hernias* - n (%)	12 (11%)	16 (14%)	p=0.53
AAA* - n (%)	3 (3%)	5 (4%)	p=0.53
Previous laparotomy - n (%)	19 (18%)	21 (19%)	p=0.90
ASA* classification - n (%)			p=0.88
• 1	2 (23%)	26 (23%)	
• 2	64 (60%)	65 (57%)	
• 3 or higher	18 (17%)	22 (20%)	
Preoperative chemotherapy - n (%)	20 (19%)	22 (20%)	p=0.91
Preoperative radiotherapy - n (%)	16 (15%)	26 (23%)	p=0.14
Type of surgery - n (%)			p=0.72
• Gynecological	12(11%)	18 (16%)	
• Upper gastrointestinal	22 (21%)	19 (17%)	
• Lower gastrointestinal	61 (58%)	65 (57%)	
• Vascular	11 (10%)	11 (10%)	

*BMI = Body Mass Index, COPD = Chronic Obstructive Pulmonary Disease, non-incisional hernias e.g. inguinal, umbilical and epigastric hernias in history, AAA = Aneurysm Abdominal Aorta and ASA = American Society of Anesthesiologists.

Table 2: Details of suture techniques

	Large bites (n=106)	Small bites (n=113)	p-value
Number of stitches (mean; SE)	24.3 (0.65)	43.4 (1.14)	<0.001
Total length of used sutures (cm) (mean; SE)	94.4 (3.73)	107.3 (3.74)	0.016
Wound length (cm) (mean; SE)	21.6 (0.49)	21.7 (0.48)	0.85
Suture length to wound length ratio (SL:WL) (mean; SE)	4.4 (0.15)	4.9 (0.12)	0.011
Time of fascial closure (minutes) (mean; SE)	9.8 (0.33)	13.8 (0.51)	<0.001
Number of sutures to wound length ratio (NoS:WL) (mean; SE)	1.1 (0.03)	2.0 (0.04)	<0.001
Suture length to number of stitches ratio (SL;NoS) (mean; SE)	4.6 (0.54)	3.3 (6.60)	0.11

Table 3: incisional hernia and post operative complications

	Large bites (n=106)	Small bites (n=113)	p value
Incisional hernia - n (%)	38 (36%)	22 (20%)	0.007
Patients with postoperative complications - n (%)	37 (35%)	43 (38%)	0.629
Ileus - n (%)	7 (7%)	13 (12%)	0.208
Pneumonia - n (%)	10 (9%)	8 (7%)	0.526
Cardiac event - n (%)	9 (9%)	4 (4%)	0.121
Surgical Site Infection (SSI) - n (%)*	23 (22%)	17 (15%)	0.203

*detailed criteria for SSIs can be found in the published study protocol[13]

At one month after surgery, the distance between the rectus abdominal muscles was smaller in the small bites group (mean 1.90 cm; sd 1.18, range 0.10-9.10) compared to the large-bites group (mean 2.39 cm; sd 1.34, range 0.20-7.00) (p=0.005). After one year, there was an increase in distance between the rectus abdominal muscles in both groups but the RAM distance remained smaller in the small bites group (mean 2.76 cm; sd 1.41, range 0.10-9.00) compared to the large-bites group (mean 3.32 cm; sd 2.06, range 0.10-6.00) (p=0.031).

Incisional hernia patients (mean 2.43 cm; sd 1.48) had a greater RAM at one month compared to those without an incisional hernia (mean 2.03 cm; sd 1.19) after one year follow up. There was a linear correlation between an enlarged RAM distance at one month and the likelihood of incisional hernia at one year of 14% per centimeter widening ($RR_{unadjusted}$ 1.14; 95%CI 1.03-1.26; p= 0.015). A distance of 2 cm or more at one month after surgery increased the risk of developing an incisional hernia by 32 percent ($RR_{unadjusted}$ 1.32; 95CI% 0.94-1.86; p =0.090). Age of the patient, Body Mass Index, and the presence of cardiovascular disease were shown to confound the relationship between rectus abdominis muscle distance at one month and the risk of incisional hernia at one year. Adjustment of the relationship for these confounders marginally lowered the incremental risk to 12% ($RR_{adjusted}$ 1.12; 95%CI 0.99 – 1.27; p=0.085) per centimetre widening, and the increment of risk of 31% for a distance of 2 cm or more at one month after surgery ($RR_{adjusted}$ 1.31; 95%CI 0.84 – 2.05; p=0.230).

The Pearson correlation test showed a significant correlation between distance between the rectus abdominal muscles and closure time (correlation *r* =-0.06 p=0.030).

Discussion

This study confirms that incisional hernia develops as an early complication after abdominal surgery. Compared to the large bites the small bites suture technique resulted in a smaller distance between the rectus abdominis muscle which was associated with a lower incidence of incisional hernia. This finding confirms the hypothesis that the small bites suture technique results in less separation of the fascial edges.

A linear correlation existed between an enlarged rectus abdominis muscle distance at one month and and the likelihood of incisional herniation being present at one year of 14% per centimeter widening .In the present study, a RAM distance above 20 mm seemed to be the cut off point, although earlier studies have suggested that 12 mm and 15 mm separation of the fascia edges or RAM distance, represent cut off points for risk of incisional hernia formation.[2,3] These differences may be caused by differences in methodology of radiological examination, although it should be noted that there are studies showing that a RAM distance of 20 mm at the level of the umbilicus is normal in a non-operated population.[14]

Ultrasound offers the advantages of real-time imaging, no ionizing radiation, but is investigator depended. Risk of bias in the present study was minimized by blinding the radiologist, using standardized outcomes and objective measurements. Earlier studies used CT or metal clips and x-ray examination, but it was felt for the present study that exposing patients to unnecessary radiation was no longer acceptable.

Preclinical studies have shown that small tissue bites prevent separation of the fascial edges in the early postoperative phase.[5,15] The present study identified a comparable phenomenon. It appears that this provides better conditions for fascial healing perhaps due to avoidance of necrosis of the rectus abdominis muscles and a better distribution of forces. There was a significant negative correlation between closure time and RAM distance one month post operatively, reflecting the longer time taken for closure with the small bites technique. This investment in time, however, did result in fewer incisional hernias.

This study has limitations. Despite 560 patients being randomized, it was difficult to schedule patients for the standardized ultrasound examination after one month. Patients who had a re-laparotomy, those who died within one year of follow-up and patients without an ultra sound examination at one month or one-year postoperatively could not be used for this study. This selection led to a high incidence of patients with incisional hernias. There were significantly more patients with COPD, steroid use and smoking in the small bites group. In the adjusted analyses age, BMI and presence of cardiovascular disease were confounders in the relationship between RAM distance at one month and the risk of incisional hernia at one year. These factors are know risk factors of incisional hernia formation and may have influenced the wound healing process.[16]

RAM distance increased with time, independent of the used suture technique. From earlier studies it is known that incidences of incisional hernia will increase during longer follow-up.[17] When suture repair was compared with mesh repair for incisional hernia repair, delayed incisional hernia recurrence was shown after 10 years follow up.[18] Experimental evidence, however, is supportive of the small bites technique. A suture technique with an equal distribution of forces on the fascia is necessary to achieve an optimal collagen I/III ratio. Too high tensile force per suture results in more scar tissue.[6,15] The holding force of a suture depends on the collagen that deposits in the suture, best achieved by suturing the aponeurosis without muscle or fat tissue.[19] Long term follow up studies will show whether the protective effect of small bites can be maintained

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Competing interests
We declare that we have no conflicts of interest.

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Chapter 6

Advanced glycosylation end products as a biomarker for incisional hernia

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Abstract

Background

Incisional hernia is one of the most frequent complications after abdominal surgery, with incidences up to 30%. A reliable biomarker for the prediction of this complication is lacking. Advanced glycosylation end products (AGEs), also known as non-enzymatic collagen crosslinks, are correlated with aging, smoking, hyperglycemia, hyperlipidemia and oxidative stress. In this study the accumulation of AGEs and the relation between AGEs and incisional hernia were investigated.

Materials and Methods

In an exploratory case-control study, twenty-three patients with incisional hernia after midline incision were compared with seventeen patients without clinical or radiological signs of incisional hernia after midline incision, AGEs were measured using a Skin Auto Fluorescence (SAF)-reader.

Results

Twenty-three patients with a clinically significant incisional hernia and 17 control patients were included. The study groups had significant differences in mean BMI. There was a significant difference between mean AGEs in patients with and without incisional hernia after midline incision (3.00±0.15 vs. 2.56±0.11, T-test p=0.03).

Conclusion

AGE accumulation measured in the skin indirectly with autofluorescence might be associated with incisional hernia. Prospective larger trials should confirm this finding.

Introduction

Incisional hernia is the most frequent complication of abdominal surgery requiring a reoperation. The reported incidence of incisional hernia following abdominal surgery ranges from 2-30%.[1-6] The cause of this frequent complication of abdominal surgery is unclear. Several factors may play a role, like suboptimal operative technique, postoperative complications such as wound infections, increased abdominal wall tension or disturbed metabolism in the extracellular matrix.[7]

A strong indication that the latter may play a role is the increased incidence of abdominal wall hernias in patients with aortic aneurysmatic disease. Other patient related factors like age, smoking, type 2 diabetes mellitus (DM), obesity, connective tissue diseases (i.e. Marfan's disease) and renal failure, are also known to affect both the metabolism in the extracellular matrix thereby promoting incisional hernia formation.[2,7-10]

In other connective tissue diseases like prolapse of the posterior vaginal wall, a significant higher level of Advanced Glycolysation Endproducts (AGEs) was found in tissue samples of the posterior vaginal wall.[11,12] AGEs are essential biomarkers of metabolic and glycemic stress. AGEs form cross-links with matrix proteins like collagen, laminin and elastin, undermining their flexibility. [13,14] AGEs have been implicated as causative factors in the progression of age-related diseases, such as atherosclerosis, diabetes and renal failure. AGEs accumulate in the human body with age.[15]

Due to the autofluorescent properties of AGEs, measurements can be carried out on the skin using auto-fluorescent readers (AF readers).[16] The levels of accumulated AGEs measured in the skin correlate with systemic AGE levels.[17]

This study aimed to explore the relationship between AGE levels, (measured with auto fluorescence) in incisional hernia patients in comparison to control patients with a history of abdominal surgery without an incisional hernia after surgery.

Materials and Methods

Study population

The local medical ethical committee approved the study protocol and signed informed consent was obtained from all participants. Forty patients with a history of open abdominal surgery through a midline incision were included. The patients were grouped in two categories. The first group (the cases) were patients with a clinically relevant incisional hernia or history of incisional hernia after a median laparotomy at least one year before the study. The second group consisted of a control group of patients, who had undergone a median laparotomy at least one year before the study, without development of an incisional hernia, neither on CT-scan nor during physical examination. Patients with a follow up shorter than 2 years have had a CT scan for diagnosis of "non-incisional" hernia. Patients with a parastomal hernia and patients with a darker skin tone were excluded, as the AGE-reader has not been validated in patients with this skin type.

AGE measurements

Skin AGE measurements were performed using a non-invasive AGE-reader (www.diagnoptics.com, DiagnOptics BV, Groningen, the Netherlands).[18] The AGE-reader illuminates skin surfaces of approximately 4 cm^2, with a wavelength between 300 and 420 nm (peak excitation 370 nm). Light reflections of the skin are measured with a spectrometer in the 300 to 600-nm range, using 200-µm glass fiber. Skin-auto fluorescence (SAF) is measured on the volar side of the lower arm, 10 to 15 cm below the elbow fold. Three consecutive measurements were performed on each patient. Hereafter, the mean SAF was calculated for each patient, to rule out local disruptions of auto fluorescence by imperfections of skin.

Statistics

Differences on baseline characteristics between cases and controls were tested using chi-square tests (categorical variables: indication for surgery, ASA, comorbidity, smoking, sex) or Student's t-test (continuous variables: age, BMI). If distributional assumption of normality was violated, Mann-Witney (MW) test was used. Mean SAF was calculated. The difference of mean SAF between cases and controls was tested using Student's t-test. The distribution between mean SAF and AGE was visualised in a graph. ROC curve analysis was performed to evaluate the diagnostic value of SAF for incisional hernia formation. Statistical analysis was conducted using SPSS 20.0 for MAC. A $p<0.05$ was considered to be statistically significant.

Results

Twenty-three patients with a clinically significant incisional hernia and 17 control patients were included. Twelve out of 17 (71%) controls have had a CT scan or ultrasound to confirm the non-incisional hernia. The other 5 patients had non incisional hernia diagnosed by clinical examination at least 2 years after operation. The study groups had significant differences in mean BMI. There was no difference between groups with regard to indication for operation, age, sex, American Society of Anesthesiologists score (ASA), cardiovascular disease, renal failure smoking and presence of COPD (Table 1).

Table 1. Basic characteristics

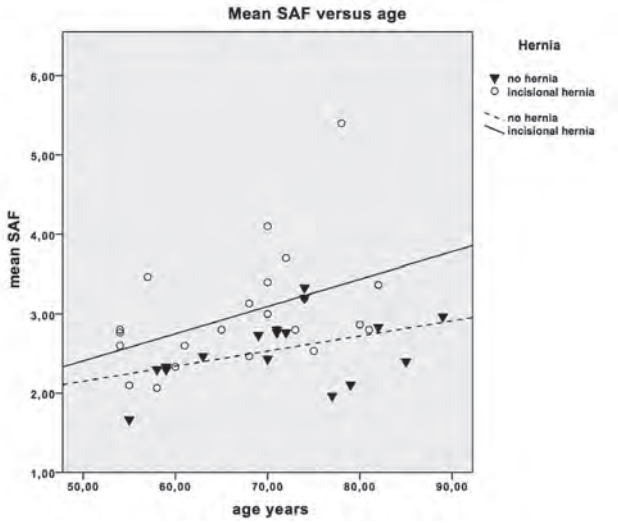
	Incisional hernia	No incisional hernia	p value
	n =23	n=17	
Indication			
Cancer	6	10	0,111*
AAA	3	1	NS*
other	14 ()	6 (35)	NS*
ASA -classification (%)			
ASA 1	4 (24)	5 (29)	0,458*
ASA 2	10 (40)	9 (53)	NS*
ASA 3	8 (32)	3 (18)	NS*
ASA 4	1 (4)	0	NS*
Comorbidity, *n* (%)			
COPD	9 (36)	2 (12)	0,057*
Diabetes mellitus 2	6 (24)	2 (12)	NS*
Renal failure	1 (4)	2 (12)	NS*
Cardiovascular	13 (52)	9 (53)	NS*
Smoking (%)	3 (12)	7 ()	NS*
Sex			
male	16 (64)	6(35)	0,53*
female	7 (36)	11 (65)	NS*
Age			
years	67 (54-82)	71 (55-89)	NS*
BMI			
Kg/m^2	30 (21-45)	25 (18-32)	0,005

* Chi-square
** t test

Skin auto fluorescence

There was a significant difference between mean SAF in patients with and without incisional hernia after midline incision (3.00±0.15 vs. 2.56±0.11, T-test p=0.03). Figure 1 shows the relation between SAF and age in years.

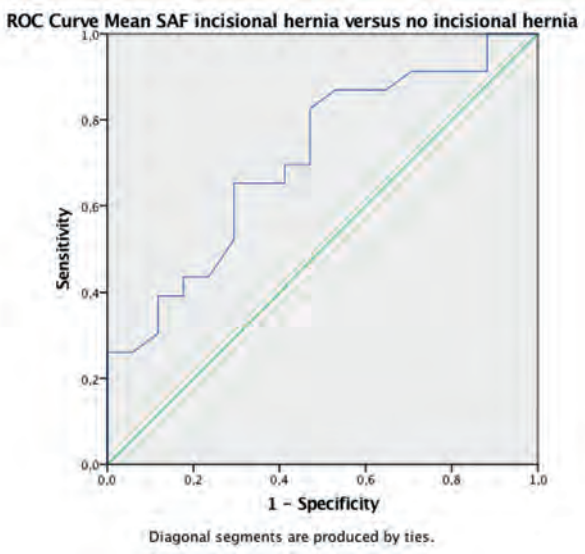
Figure 1: relation between age in years and mean SAF



ROC curve analysis

ROC curve analysis was performed to evaluate the diagnostic value of SAF for incisional hernia formation. (figure 2) The area under the curve (AUC) value for mean SAF was 0.71 (95% CI: 0.55–0.87) The mean SAF level, at cut off value of ≥2,5 or higher had 83% sensitivity and 53% specificity.

Figure 2: ROC curve Mean SAF incisional hernia versus no incisional hernia



Discussion

This is the first study investigating the relationship between AGEs and incisional hernia, the most frequent long-term complication in general surgery. The non-invasive measurement of SAF has a potential to select patients who are suitable for major surgical procedures. In this study we found a difference in SAF between patients with an incisional hernia and controls. In our study there were some younger incisional hernia patients with relatively higher levels of SAF and older patients without incisional hernia with relatively lower levels of SAF. The ROC curve showed a moderate sensitive diagnostic value of SAF for incisional hernia formation, but low specificity.

Age, smoking, type 2 diabetes mellitus (DM), obesity, aorta aneurism and renal failure are known individual risk factors for incisional hernia.(10) AGEs are elevated in DM, cardiovascular disease, smoking and renal failure patients especially in patients with a severe form and longer duration.(15) Measuring AGE accumulation with SAF may differentiate between high and lower risk groups within these known risk groups. For example an SAF level of above ≥2.70 is an independent risk factor for microvascular and macrovascular complications in DM and an independent predictor in 5-year mortality and cardiovascular events in patients with peripheral arterial disease.[19,20]

It is still unclear what the role of AGEs is in connective tissue metabolism and particularly in wound healing. Increased AGEs are correlated to inhibited expression of collagen type I and type III in human gingival fibroblasts.[21] Several studies have shown that patients with incisional hernia have a decreased collagen type I/III ratio in the scar of the abdominal wall and the skin and in the uninjured fascia laterally to the scar postoperatively.[8,22-24] A decreased collagen type I/III ratio has been associated with increased fibrotic tissue, resulting in an impaired strength of connective tissue. Also Matrix Metallo Proteinases (MMPs) 1, 2, 9 and 13 are up-regulated in incisional hernia patients. The balance between MMPs and their inhibitors, the tissue inhibitors of metalloproteinases (TIMPs), is one of the responsible factors for the remodeling of tissues.[23,25,26]

This study has several limitations. A limitation of this exploratory study is the small number of patients that was included. No previous studies have evaluated

the correlation between SAF and hernia disease, and therefore, no sample size calculation could be performed. For this pilot study we included clinical significant incisional hernia's which we compared with patients without clinical incisional hernia by the majority (71%) controlled by radiological examination. The majority of patients were examined several years after surgery. Unfortunately there is a small risk that later on incisional hernia might occur in the non-hernia groups. AGEs can also be elevated after a period of oxidative stress. A period of critical illness in the hospital or even intensive care may also influence SAF. The optimal set up for a future trial would be a large prospective (registry) trial with SAF measurements before surgery with standardized small bites closure technique and incisional hernia occurrence at least 3 years after surgery with both physical and radiological examination as a primary outcome.

A preoperative screening tool or biomarker for postoperative surgical complications may be helpful to select patients who are fit for surgery. This could lead to prevention of major complications like wound complications or anastomotic leakage. High-risk patients may need a prophylactic mesh or a protective ileostomy. Larger prospective studies are needed to investigate this preoperative screening marker.

Conclusion

AGE accumulation measured in the skin indirectly with autofluorescence might be associated with incisional hernia. Large prospective trials with a standardized closure technique and radiological outcome measurement should confirm this data and investigate other extracellular matrix components to select high-risk patients for a tailor made approach.

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Chapter 7

The anatomical limits of the posterior vaginal vault toward its use as route for intra-abdominal procedures

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A.J. Schneider

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Abstract

Background

The use of natural openings for abdominal surgery started at the beginning of the 21th century. A trans Douglas endoscopic device has been designed to perform most of the intra-abdominal operations in women through the pouch of Douglas. The posterior vaginal vault is limited in size and could be damaged by an oversized instrument. This study investigates the optimal dimensions of the instrument by measuring the limiting factor in the passage.

Methods

In ten female embalmed bodies the transversal and sagittal diameter of the fornix posterior vaginalis was measured by two observers. The pouch of Douglas was filled to its maximal capacity with mouldable latex through an open abdomen. By internal vaginal examination the connective tissue borders of the fornix posterior were palpated and the impression in the cast was measured. The mean value of these two diameters was evaluated in this study. The level of agreement between the observers was calculated.

Results

The mean fornix posterior diameter was 2.6 cm (standard deviation, SD 0.5 cm) with a range of 2.0–3.4 cm.The mean difference between the two observers of all measurements was 0.08 cm (not significant). Both observers had an acceptable intraobserver variation. The interobserver agreement was excellent.

Conclusion

Instruments with dimensions within the measured limits can be used safely for intra-abdominal operations via the natural orifice of the vagina.

The 19th century was the era of the laparotomy. Endoscopy was developed in the 20th century. The use of the natural openings for abdominal surgery started at the beginning of the 21th century. A Transdouglas Endoscopic Device (TED) has been designed in order to perform most of the intra-abdominal operations in women through the pouch of Douglas. In order to find what the optimal dimensions of this instrument should be, the limiting factor in the passage of this instrument through the vagina into the abdominal cavity, the fornix vaginalis, has to be measured. We report about these measurements in 10 female embalmed bodies.

Anatomy

The fornix vaginalis is formed anatomically by the vagina around the cervix uteri. It is most spacious dorsally where it is separated from the recto-uterine pouch of Douglas only by vaginal wall and peritoneum. The fornix to Douglas relation is not end-to-end. Douglas continues for a shorter or longer distance along the posterior vaginal wall.[1,2] In the embryological phase Douglas' pouch is deeper, reaching the perineum. It condensates later into the recto-vaginal septum as the cul de sac moves upward along the full length of the posterior vaginal wall. The recto-vaginal septum then extends from the caudal margin of the recto-uterine peritoneal pouch to the proximal border of the perineal body. It forms a fixation point for the perineal body and stiffens the anterior rectal wall during the defecation.[1]

Surgical techniques

The posterior fornix of the vagina has been used as an entrance and as an exit to the pelvic and abdominal cavity in several surgical developments in the last 100 years.[3,4]

In the first half of the twentieth century the fornix posterior was used as passage for the 1.2 cm diameter culdoscopes. In culdoscopy the pelvic organs were visualized without insufflation and with the patient in knee-elbow position. The technique was used to search for causes of pelvic pain, infertility and for diagnosing adnexal masses.[5]

Later it changed into transvaginal endoscopy with insufflation of the abdominal cavity with CO2 or fluid.[6] The fornix posterior here served as a gateway for a Veres needle-trocar system for insufflation as well as for access. The trocar had

a diameter of 3.9 mm and the patient was lying on her back. Complications of the transvaginal route in culdoscopy and transvaginal endoscopy were damage to the surrounding tissues, mostly bleeding of the entry site and puncture of the retroperitoneal rectum and were rarely of a serious nature.[7]

The posterior fornix can also serve as an exit for laparoscopically removed specimen like fibroids, gallbladder or fallopian tube that can not be removed through the abdominal wall without extension of the abdominal incision.

Materials and methods

In ten embalmed female human bodies, who had not undergone any previous pelvic surgery, the transversal and sagittal diameter of the fornix posterior was measured. In case of obesity the vulva was removed in order to get a better access.

The pouch of Douglas was filled to its maximal capacity with mouldable latex through the open abdomen (fig.1). Glycerin was used to reduce the adhesiveness of the cast. By internal vaginal examination the connective tissue borders of the fornix posterior were palpated and an impression was made in the cast (fig. 2).

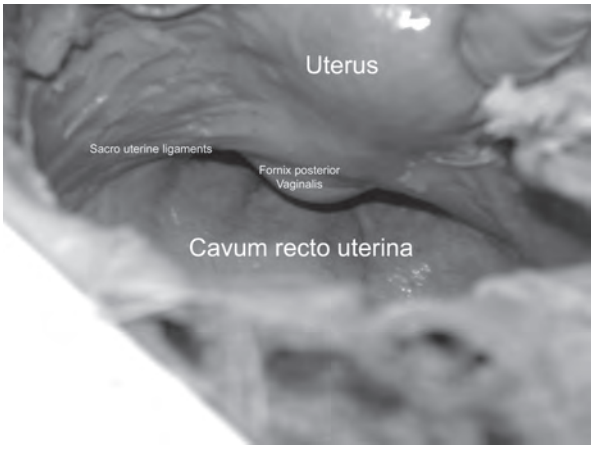

Fig 1 Posterior aspect of the uterus with protruding finger through the vagina into the posterior fornix in the pouch of Douglas.

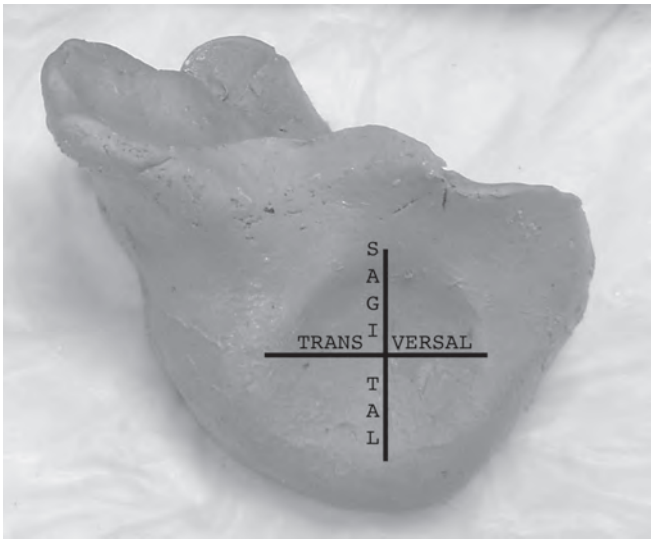

Fig 2 Impression of the fornix vaginalis in a Douglas pouch cast. The horizontal and vertical lines represent the transversal and sagital measurement diameter.

The imprint was measured in the transversal and sagittal direction with a marking gauge. Independently two observers conducted five separate measurements in each specimen. A coefficient of variation to assess the intra-observer variety was calculated. The mean values of the 5 measurements were used to calculate the intraclass correlation coefficient as measure of inter-observer agreement. A Bland and Altman plot, a statistical method to look for a systematic bias was used.

Results

The mean fornix posterior diameter in 10 embalmed specimen was 2,6 cm (+/- 0.5 cm) with a range of 2.0-3.4 cm.

Both observers had an acceptable intra-observer variety with a mean coefficient of variation of 8.0% and 6.9%. These did not differ significantly from each other (p=0.85, Wilcoxon). Comparing the two observers, the intraclass coefficient was 0.94 (fig. 3, left panel). An intraclass coefficient of more than 0.9 is generally considered to represent excellent agreement.

The mean difference between both observers in all measurements of 0.08 cm was not significant (p=0.15 paired T-test). The Bland and Altman plot showed an acceptable limit of agreement (fig 3, right panel).

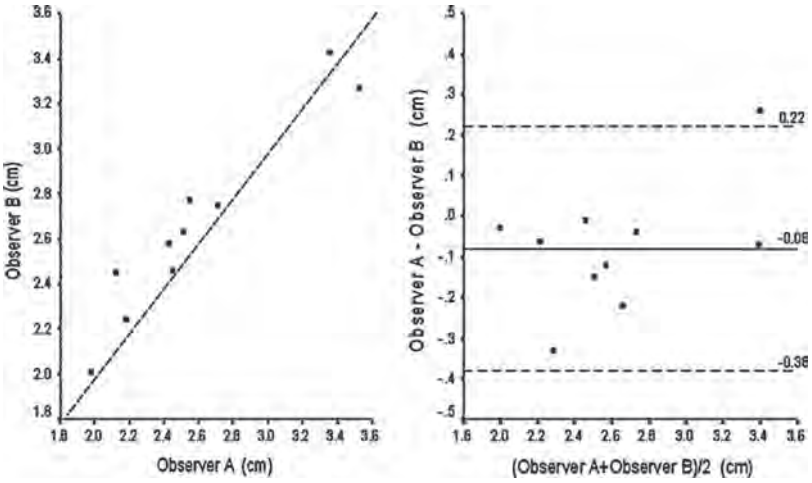

Fig. 3. Left panel: scatterplot of differences of both observers. The dotted line represents the line of identity. Right panel: Bland and Altman plot. The horizontal solid line represents the mean difference , and the two dotted lines represent the limits of agreement(mean +/- 2SD)

Discussion

The full surgical potential of the vagina will be realized in the “one entry, one instrument” principle of this kind of the natural orifice surgery.[8] The posterior fornix is the bottleneck of the entrée as the rest of the pouch of Douglas is wider. The diameter measured gives an idea to the potential diameter of the instrument. The diameters in embalmed human bodies can be seen as minimal diameters. The rigor mortis and the effect of the embalming have a significant influence upon these diameters. In vivo the anatomical limits should be wider. A further issue is the vicinity of the fixation point of the rectovaginal fascia. Depending on the chosen diameter of the instrument this point is in the direct vicinity or further away. The rectovaginal fascia has a considerable clinical significance. If damaged by an oversized instrument the anterior rectal wall may bulge during the straining of defecation, resulting in functional disturbances of bowel movement with possible chronic retention of faeces.

Conclusions

This study supports the feasibility of the posterior vaginal fornix as a safe natural orifice.

The mean anatomical diameter of the posterior vaginal fornix was found to be 2.6 cm (+/- 0.5 cm) with a range of 2.0-3.4 cm. Instruments with these dimensions can be used safely for intra-abdominal operations.

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Chapter 8

The new UX closure-technique for midline incisions: evaluation in an equine model

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J.F. Lange

Submitted

Chapter 9

The ‘AbdoMAN’: an artificial abdominal wall simulator for biomechanical studies on laparotomy closure techniques

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Hernia 2017

Chapter 10

General discussion and future perspectives

Summary

In **Chapter 1** the subject of this thesis is introduced presenting an outline of the thesis. Incisional hernia is a frequent complication of midline laparotomy and is associated with high morbidity, decreased quality of life, and high costs.
In this thesis, the following hypotheses will be investigated**:**

- Incisional hernia is an early complication due to failure of closure technique and can be prevented by using a small bite closure technique.
- Patient at risk for incisional hernia could be identified by collagen characteristics.
- With regard to prevention of incisional hernia natural orifice surgery may be a suitable option.
- For future hernia research alternative models are suitable to be used to avoid research on patients and animals.

In **Chapter 2** the small bite suture technique was investigated in an experimental model. The bursting strength of large and small bites in porcine abdominal walls was studied. The small bites had a higher bursting strength compared to the large bites suture technique. The result of this experimental study was the fundament of the STITCH trial.

In **Chapter 3** the protocol of the STITCH trial is disclosed. The STITCH trial is a multicenter randomized controlled clinical trial in surgical, gynelogical and urological departments in which the small bites suture technique was compared with the commonly used mass closure technique for incisional hernia development.

In **Chapter 4** the results of this large multicentre trial are described. Five hundred sixty patients who were scheduled to undergo elective abdominal surgery with midline laparotomy were randomly assigned to receive small tissue bites of 5 mm every 5 mm or large bites of 1 cm every 1 cm. At 1 year follow-up 21% of 277 patients in the large bites group and 13% of 268 patients in the small bites group had an incisional hernia. Rates of adverse events did not differ significantly between the groups. The findings show that the small bites suture technique is more effective than the large bites closure technique for prevention of incisional hernia in midline incisions. The small bites technique should become the standard closure technique for midline incisions.

In **Chapter 5** the aetiology of incisional hernia is investigated and determined if incisional hernia is an early complication of laparotomy closure. The rectus abdominus muscle distance was measured at one month and one year postoperatively and compared between small and large bites groups. A larger distance (>2 cm) between the rectus abdominal muscles one month after midline laparotomy was associated with later incisional hernia formation. Closure with small bites resulted in a smaller rectus abdominus muscle distance, which may induce a better fascia healing with lower risk of incisional hernia formation.
In **Chapter 6** the relation between advanced glycation endproducts (AGEs) and incisional hernia was investigated in order to select high risk patients on tissue characteristics. By skin measurements of autofluorescence of AGEs, the relation between non-enzymatic collagen crosslinks and incisional hernia formation was explored. In this small study incisional hernia patients had a higher level of AGEs compared to non-incisional hernia patients.

The unacceptable high incidence of incisional hernia despites recent developments advocates for novel study methods and approaches as addressed in the following Chapters:

In **Chapter 7** the anatomical limits of the posterior vaginal vault toward its use as a route for intra-abdominal procedures as natural orifice surgery concept was explored. Recent developments show that natural orifice surgery can avoid an incision in the abdominal wall and prevent incisional hernia formation.

In **Chapter 8** an experimental study is described investigating an inventive reinforced shoelace closure technique, the UX technique in an equine model. The UX technique was a very strong closure technique compared to the commonly used continuous technique and is already successfully used in living horses.

In **Chapter 9** the human abdominal wall is simulated in the 'AbdoMAN' project. This unique artificial abdominal wall is able to show what happens when the skin is closed providing a better understanding of the mechanical concepts of incisional hernia formation.

Nederlandse samenvatting

Hoofdstuk 1 is een algemene inleiding over littekenbreuken en een overzicht van de opbouw van dit proefschrift. Een littekenbreuk is een frequente complicatie van een mediane laparotomie en gaat gepaard met hoge morbiditeit, verminderde kwaliteit van leven en hoge kosten.
In dit proefschrift worden de volgende hypothesen onderzocht:

- Een littekenbreuk is een vroege complicatie en het gevolg van het falen van de sluitingstechniek. Deze kan worden voorkomen door de “kleine steken”-hechttechniek.
- Patiënten met een verhoogd risico op littekenbreuken zijn reeds in een vroeg stadium te identificeren door hun collageenkenmerken.
- Voor preventie van littekenbreuken is “natuurlijke opening”-chirurgie een goede optie.
- Voor toekomstig onderzoek worden alternatieve modellen onderzocht om te om studies in patiënten en proefdieren zoveel mogelijk te beperken.

In **Hoofdstuk 2** werd de “kleine steken”-hechttechniek voor het sluiten van de buikwand onderzocht. Eerst werd de sterkte van de grote en kleine steken hechttechniek in varkensbuikwanden onderzocht. De kleine steken hadden een grotere treksterkte vergeleken met de ‘’grote steken’’-hechttechniek. Het resultaat van deze experimentele studie was het fundament van de STITCH trial.

In **Hoofdstuk 3** is het protocol van de STITCH trial beschreven. In deze multicentrische gerandomiseerde gecontroleerde klinische studie werd de “kleine steken”-hechttechniek vergeleken met de gangbare “grote happen en stappen”-hechttechniek voor de preventie van littekenbreuken.

In **Hoofdstuk 4** worden de resultaten van de STITCH-trial beschreven. Vijfhonderdzestig patiënten, die gepland waren voor electieve abdominale chirurgie, ondergingen een mediane laparotomie en werden gerandomiseerd tussen de “kleine steken”-hechttechniek (5 mm per 5 mm) en de ”grote steken”-techniek (1 cm per 1 cm). Na een follow-up van 1 jaar had 21% van de 277 patiënten in de “grote steken”-groep een littekenbreuk en 13% van de 268 patiënten in de “kleine steken”-groep. Het aantal complicaties verschilde niet significant tussen de groepen. De bevindingen tonen aan dat de “kleine steken”-hechttechniek effectiever is dan de traditionele “grote steken”-hechttechniek voor de preventie

van littekenbreuken na mediane laparotomie is niet geassocieerd met een hoger percentage complicaties. De “kleine steken”-hechttechniek moet de standaard sluitingstechniek worden voor mediane incisies.

In **Hoofdstuk 5** wordt de etiologie van littekenbreuken onderzocht. Een maand en een jaar postoperatief werd de afstand tussen de rectus abdominus spieren gemeten en vergeleken tussen de grote en kleine steken-hechttechnieken. Er werd vastgesteld dat een littekenbreuk een vroege complicatie is na abdominale chirurgie.

In **Hoofdstuk 6** wordt de relatie tussen de advanced glycation end-products (AGEs) en een littekenbreuk onderzocht, met als doel om risicovolle patiënten op weefselkenmerken te identificeren. Door het meten van de autofluorescentie van AGEs in de huid werd de relatie met het risico op een littekenbreuk onderzocht. In deze kleine studie hadden littekenbreukpatiënten meer AGEs dan patiënten, die een operatie hadden ondergaan zonder het ontwikkelen van een littekenbreuk.

Ondanks de recente ontwikkelingen, is er nog steeds een onaanvaardbaar hoge incidentie van littekenbreuken. Hierdoor is essentieel dat nieuwe onderzoeksmethoden en benaderingen ontwikkeld worden, zoals in de volgende Hoofdstukken beschreven:

In **Hoofdstuk 7** werden de anatomische begrenzingen van de ruimte achter de vagina-achterwand bepaald met als doel om deze natuurlijke toegang als route voor intra-abdominale procedures te benutten. Recente ontwikkelingen laten zien dat “natuurlijke openingen”-chirurgie een wond in de buikwand kan vermijden.

In **Hoofdstuk 8** wordt een experimentele studie in een paardenmodel beschreven, waarbij een innovatieve sluitingstechniek, de UX-techniek, onderzocht werd. Deze techniek bleek een zeer relevante sluitingstechniek in vergelijking met de gangbare techniek te zijn en wordt inmiddels ook al met succes gebruikt bij levende paarden.

In **Hoofdstuk 9** wordt de buikwand van de mens gesimuleerd in het project ‘Abdoman’. Deze unieke artificiële buikwand is in staat om te laten zien wat er met de buikwand gebeurt, zodra de huid gesloten is. Dit model helpt de mechanica van de buikwand, nadat deze gesloten is, beter te begrijpen.

List of publications

1. **Harlaar JJ***, Deerenberg EB*, Dwarkasing RS, Kleinrensink GJ, Jeekel J, Lange JF * contributed equally
Development of incisional hernia. BJS open 2017
2. **Harlaar JJ**, Eker HH, Vakalopoulos KA, Castro Cabezas M, van der Ham AC, Vrijland, WW, Jeekel J, Lange JF
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PhD portfolio

Name PhD student: Drs. JJ Harlaar
Erasmus MC
Department: Surgery

PhD period: 2007 - 2017
Promotor(s): Prof. dr. J.F. Lange
Prof. dr. G.J. Kleinrensink
Co-promotor: Prof. dr. J. Jeekel

1. PhD training	Year	Workload (ECTS)
General courses		
- BROK (Basiscursus Regelgeving Klinisch Onderzoek)	2009	4.0
Specific courses (e.g. Research school, Medical Training)		
- Laboratory Animal Science Course	2008	4.0
- Workshop hernia surgery	2014	0.3
Presentations		
- Nederlandse Vereniging voor Heelkunde (4 presentations)	2008 - 2009 2010 - 2015	4.0
- European Hernia Society (4 presentations)	2008 - 2012 2014 - 2015	4.0
- American Hernia Society (2 presentations)	2011 - 2012	2.0
- European Surgical Association	2012	1.0
- Suvretta meeting (St. Moritz)	2008	1.0
- Rotterdam Interactive congress on Hernia	2007	1.0

2. Teaching	Year	Workload (ECTS)
Supervising practicals and excursions, tutoring		
- Erasmus MC Anatomy Research Project (EARP)	2007	6.0
- Project Advanced Products (TU Delft)	2008 - 2009	4.0
- Bachelor thesis Hogeschool Rotterdam	2009 - 2010	2.0
- Tutor pathology course Thanatopraxi	2011	0.5
Supervising Master thesis Erasmus MC		
- 2 Master Thesis	2009 - 2010	2.0
Other		
- President resident association VU Medical Center, Amsterdam	2013 - 2014	1.0
- President resident association West Fries Gasthuis, Hoorn	2015 - 2016	1.0
- Member of the Bloodgroup (research group on transfusion in colorectal cancer)	2015 - currently	3.0

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Curriculum vitae auctoris

Joris Jan Harlaar werd geboren op 4 mei 1984 in Amsterdam. In 2003 behaalde hij zijn gymnasium diploma aan scholengemeenschap “de Driemark” te Winterswijk. Na een week werktuigbouwkunde te hebben gestudeerd in Delft, startte hij in 2003 met Geneeskunde aan de Erasmus Universiteit te Rotterdam. In het tweede jaar kwam hij in aanraking met de chirurgische anatomie in de snijzaal van prof. dr. G.J. Kleinrensink. Hierna begon hij als student-onderzoeker bij de REPAIR groep (prof. dr. J.F. Lange, prof. dr. Jeekel en prof. dr. G.J. Kleinrensink) met een experimentele studie van twee verschillende hechttechnieken in varkensbuikwanden. Dit onderzoek heeft de basis gevormd van de STITCH trial. In 2008 behaalde hij het doctoraal examen en ging hij voor 1 jaar full time onderzoek doen. In dit jaar werden er twee subsidies voor de STITCH trial gehonoreerd en werd er de Abdoman ontwikkeld in samenwerking met de TU Delft. In december 2011 behaalde hij zijn artsexamen en in 2012 werkte hij als ANIOS chirurgie in het Sint Franciscus Gasthuis (opleider dr. G.H. Mannaerts). In 2013 startte hij de opleiding tot chirurg in regio 1 in het VU Medisch centrum Amsterdam (afdelingshoofd prof. dr. H.J. Bonjer en opleider Prof. Dr. D.L. van der Peet). In 2015 zette hij zijn opleiding voort in het West Fries Gasthuis in Hoorn (opleiders dr. D.J.A. Sonneveld en dr. J.W.D. de Waard) en in 2017 startte hij met de differentiatie Gastro Intestinale chirurgie. Tot december 2017 zal hij met zijn vriendin Leontien van Ravesteyn in een districtsziekenhuis in Zambia gaan werken (opleider prof. Dr. Bleichrodt) om hierna in het West Fries Gasthuis medio 2019 zijn opleiding af te ronden.