

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](https://clinicaltrials.gov), number NCT01132209 and with the Netherlands 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 Sweden¹⁰ 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^2 tests 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^2 testing 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 software (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.

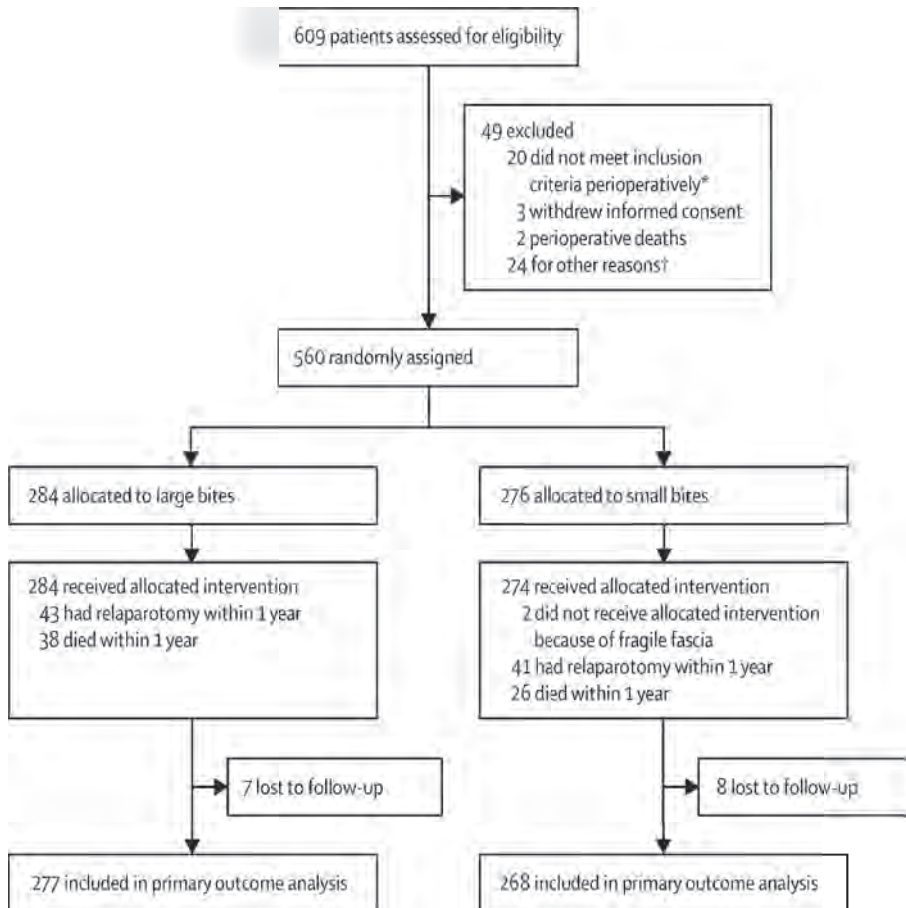
Role of the funding source

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 trial¹⁰ 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.

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References

1. Bevis PM, Windhaber RA, Lear PA, Poskitt KR, Earnshaw JJ, Mitchell DC. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. *The British journal of surgery*. 2010;97(10):1497-502.
2. Bloemen A, van Dooren P, Huizinga BF, Hoofwijk AG. Randomized clinical trial comparing polypropylene or polydioxanone for midline abdominal wall closure. *The British journal of surgery*. 2011;98(5):633-9.
3. Diener MK, Voss S, Jensen K, Buchler MW, Seiler CM. Elective midline laparotomy closure: the INLINE systematic review and meta-analysis. *Annals of surgery*. 2010;251(5):843-56.
4. Fink C, Baumann P, Wenthe MN, Knebel P, Bruckner T, Ulrich A, et al. Incisional hernia rate 3 years after midline laparotomy. *The British journal of surgery*. 2014;101(2):51-4.
5. van Ramshorst GH, Eker HH, Hop WC, Jeekel J, Lange JF. Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. *American journal of surgery*. 2012;204(2):144-50.
6. Nieuwenhuizen J, van Ramshorst GH, ten Brinke JG, de Wit T, van der Harst E, Hop WC, et al. The use of mesh in acute hernia: frequency and outcome in 99 cases. *Hernia : the journal of hernias and abdominal wall surgery*. 2011;15(3):297-300.
7. Poulouse BK, Shelton J, Phillips S, Moore D, Nealon W, Penson D, et al. Epidemiology and cost of ventral hernia repair: making the case for hernia research. *Hernia : the journal of hernias and abdominal wall surgery*. 2012;16(2):179-83.
8. van 't Riet M, Steyerberg EW, Nellensteyn J, Bonjer HJ, Jeekel J. Meta-analysis of techniques for closure of midline abdominal incisions. *Br J Surg*. 2002;89(11):1350-6.
9. Muysoms FE. European Hernia Society Guidelines on the closure of abdominal wall incisions. . *Hernia*, in press. 2015.
10. Millbourn D, Cengiz Y, Israelsson LA. Effect of stitch length on wound complications after closure of midline incisions: a randomized controlled trial. *Arch Surg*. 2009;144(11):1056-9.
11. Jenkins TP. The burst abdominal wound: a mechanical approach. *The British journal of surgery*. 1976;63(11):873-6.
12. DesCoteaux JG, Temple WJ, Huchcroft SA, Frank CB, Shrive NG. Linea alba closure: determination of ideal distance between sutures. *J Invest Surg*. 1993;6(2):201-9.
13. Harlaar JJ, Deerenberg EB, van Ramshorst GH, Lont HE, van der Borst EC, Schouten WR, et al. A multicenter randomized controlled trial evaluating the effect of small stitches on the incidence of incisional hernia in midline incisions. *BMC surgery*. 2011;11:20.
14. Israelsson LA, Millbourn D. Prevention of incisional hernias: how to close a midline incision. *The Surgical clinics of North America*. 2013;93(5):1027-40.
15. van Ramshorst GH, Klop B, Hop WC, Israelsson LA, Lange JF. Closure of Midline Laparotomies by Means of Small Stitches: Practical Aspects of a New Technique. *Surgical technology international*. 2013;XXIII:34-8.
16. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Annals of medicine*. 2001;33(5):337-43.
17. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical care*. 1992;30(6):473-83.
18. Muysoms FE, Miserez M, Berrevoet F, Campanelli G, Champault GG, Chelala E, et al. Classification of primary and incisional abdominal wall hernias. *Hernia : the journal of hernias and abdominal wall surgery*. 2009;13(4):407-14.
19. Hernandez AV, Steyerberg EW, Habbema JD. Covariate adjustment in randomized controlled trials with dichotomous outcomes increases statistical power and reduces sample size requirements. *J Clin Epidemiol*. 2004;57(5):454-60.
20. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Annals of internal medicine*. 2010;152(11):726-32.

21. Bloemen A, van Dooren P, Huizinga BF, Hoofwijk AG. Comparison of ultrasonography and physical examination in the diagnosis of incisional hernia in a prospective study. *Hernia : the journal of hernias and abdominal wall surgery*. 2012;16(1):53-7.
22. Schreinemacher MH, Vijgen GH, Dagnelie PC, Bloemen JG, Huizinga BF, Bouvy ND. Incisional hernias in temporary stoma wounds: a cohort study. *Arch Surg*. 2011;146(1):94-9.
23. Cengiz Y, Gislason H, Svanes K, Israelsson LA. Mass closure technique: an experimental study on separation of wound edge. *Eur J Surg*. 2001;167(1):60-3.
24. Hoer JJ, Junge K, Schachtrupp A, Klinge U, Schumpelick V. Influence of laparotomy closure technique on collagen synthesis in the incisional region. *Hernia : the journal of hernias and abdominal wall surgery*. 2002;6(3):93-8.
25. Klink CD, Binnebosel M, Alizai HP, Lambertz A, Vontrotha KT, Junker E, et al. Tension of knotted surgical sutures shows tissue specific rapid loss in a rodent model. *BMC surgery*. 2011;11:36.
26. Harlaar JJ, van Ramshorst GH, Nieuwenhuizen J, Ten Brinke JG, Hop WC, Kleinrensink GJ, et al. Small stitches with small suture distances increase laparotomy closure strength. *American journal of surgery*. 2009;198(3):392-5.
27. van Ramshorst GH, Vos MC, den Hartog D, Hop WC, Jeekel J, Hovius SE, et al. A comparative assessment of surgeons' tracking methods for surgical site infections. *Surgical infections*. 2013;14(2):181-7.
28. Arndt V, Merx H, Stegmaier C, Ziegler H, Brenner H. Quality of life in patients with colorectal cancer 1 year after diagnosis compared with the general population: a population-based study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2004;22(23):4829-36.
29. Lee JA, Kim SY, Kim Y, Oh J, Kim HJ, Jo DY, et al. Comparison of health-related quality of life between cancer survivors treated in designated cancer centers and the general public in Korea. *Japanese journal of clinical oncology*. 2014;44(2):141-52.

