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# Differences in Tissue Damage-Related Markers Between *Large-Stitch* Versus *Small-Stitch* Surgical Closure Techniques

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## Abstract

**Background and aims:** This study assessed the differences on hemogram and some tissue damage-related markers between large stitches versus small stitches surgical closure techniques in general surgeries.

**Patients and methods:** A hundred of patients (50% female, 62.0 ± 15.1 years, body mass index = 27.6 ± 5.1 kg/m$^2$) were randomised into large stitches (n=50) or small stitches (n=50) surgical closure groups. Large stitches closure is considered the standard suture while Small stitches closure can be defined as a smaller suture. Surgeries performed included exploratory laparotomy, intestinal and colon resections, and hepatobiliary, pancreatic, gastric and oesophagi interventions.

**Results and conclusion:** There were baseline differences regarding the closure technique employed for each type of surgery, which greater hepatobiliary, pancreatic, gastric and oesophagi interventions with large stitches closures and greater colon and intestinal interventions with small stitches closures (p<0.001). After adjusting for baseline values and type of surgery, patients sutured with the large stitches closure increased Creatine kinase concentrations in 141.6 mg/dL in the post-surgery compared to the pre-surgery, whereas patients sutured with the small stitches closure increased it by only 18.5 mg/dL (between-group differences: 123 mg/dL; 95% confidence interval: 16.9 to 239.6; p<0.001). Borderline significant, but probably clinically meaningful, large stitches closure resulted in 78% greater leukocytes (1.8 million more) and 177% greater lactate dehydrogenase concentrations (172.7 UI/L more) compared to the small stitches closure (both, p<0.130).

These analyses suggest that small stitches closure induces lower tissue damage, which reinforces the recommendation of employing this technique rather than traditional large stitches closure when possible.

**Keywords:** Monoblock surgical closure; Israelson surgical closure; Creatine kinase; Inflammation; Hernia; Surgical infection; Hemogram.

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## Introduction

There is an ongoing debate about which suturing techniques are best for achieving a definitive wound closure while minimising the risk of short- and long-term complications [1,2]. To date, there are different closure techniques that are widely employed sometimes indistinctly in the general surgery clinical practice [1,2]. This is the case of the *large-stitch* (Monoblock) versus *small-stitch* (Israelsson) [3] surgical closures [1].

On the one hand, the *large-stitch* technique could be considered the classical and traditionally employed closure [2]. It consists on using a one-loop multifilament and rapid absorbable with a 48 mm needle. It starts with a normal knot making full-wall stitches (fascia, muscle and peritoneum) separated by one centimeter and taking one centimeter of tissue [1]. On the other hand, Israelsson et al. [3] recommend to begin by making an autolock knot to maintain tension throughout the entire suture using a 2/0 monofilament and a slowly absorbable suture with a 26 mm needle involving only the fascia. In this case, the distance between the points should be from 4 to 5 mm, and between 5 and 8 mm to fascia [3].

Some studies have been conducted trying to determine which is the best closure technique to reduce complications, mainly evisceration, hernia and infection of the surgical wound. The conclusions obtained by comparing factors such as the type of material (monofilament vs. multifilament or absorbable vs. non-absorbable materials), length of the suture, continuous suture or intermittent stitches, is that there is not enough clinical evidence [1]. Uniquely, monofilament (the one employed in *small-stitch* closures) has been shown to have a lower risk of abdominal hernia [2,4].

Notwithstanding, the effects of different types of surgical closures on tissue damage-related markers have not been explored enough. Indeed, as far as we know, no prior study has explored the influence of both types of surgical closures on the postoperative hemogram and tissue damage-related biochemical markers.

In the general clinical practice, the most widely employed biochemical markers in order to determine the existence of an inflammatory process have been C-reactive protein and pro-calcitonin. Similarly, the assessment of lactate dehydrogenase (LDH), creatine kinase (CK), fibrinogen and transaminases is common to assess tissue damage [5-7]. Therefore, it would be of clinical and public health interest to explore whether the employment of the *small-stitch* closure induces clinical advantages compared with the *large-stitch* traditional closure in the above-mentioned objectively assessed tissue damage-related markers. If contrasted, the employment of *small* rather than *large-stitch* closure technique could reduce health system costs (from both, the pharmaceutical and assistance point of view) via improvements in postoperative tissue damage and pain.

Consequently, the aim of this study was to assess the differences in the hemogram and some tissue damage-related markers between *large* versus *small-stitch* surgical closure techniques in general surgeries.

## Methods

**Subjects:** Briefly, inclusion criteria for the current interventional study were: (1) aged 18–80 years old; (2) patients submitted to a laparotomy; (3) planned or emergent surgery; (4) ASA I, II or III; (5) body mass index (BMI) lower than 40 kg/m$^2$; (6) no previous laparotomy or abdominal incision, or pre-existing hernia. Exclusion criteria were: (1) acute or terminal illness; (2) to have suffered a major cardiovascular event in the past 6 months; (3) unable to ambulate; (4) unstable cardiovascular disease or other medical conditions; (5) fracture; (6) unwillingness to complete the study requirements.

In this pseudo-randomised controlled trial, a total sample of 100 patients awaiting a surgery (50% women, age range 18-80 years old, mean age 62.0 ± 15.1 years) from Granada (Southeast Spain) were included. All patients signed an informed consent to take part in the present study. Patients were randomized to wound closure with small or large stitches. Randomization was achieved by using one closure technique or the other on alternating weeks.

### Procedures

The same group of researchers assessed clinical characteristics as well as body composition on a single day and in this order. Hemogram and biochemical parameters were taken at baseline (within one week before the intervention) and within the twenty-four hours after surgery. The presence of surgical wound infection, dehiscence, oedema and/or hematoma was also registered, as well as every negative phenomenon reported by the patients.

The study was reviewed and approved by the Ethics Committee of the "San Cecilio" University Hospital (code: CDT2016).

### Surgical closure techniques

#### Large-stitch closure

For this closure, a first surgical stitch is made at the distal end of the incision with a one-loop polyglactin (Vicryl™) with a 48 mm needle passing through the loop of the thread. Points are done by taking 1 centimetre of the entire thickness of the wall from the fascia, including muscle and peritoneum, with a separation of one centimetre. A first thread is used until the umbilicus is over, where a normal knot is made. Finally, the procedure continues with a new strand making the same steps to the caudal end of the incision.

#### Small-stitch closure

This closure technique starts with a 2/0 (1.5 meters) 4-polyhydroxybutyrate (Monomax™) suture making an autolock knot. We proceed to suture with small stitches taking only the abdominal fascia (5-8 mm) with a 4-5 mm distance between points. Then, a single strand is used until completing the incision closure maintaining the same tension along the closure.

### Outcomes

#### Pharmaceutical and clinical registry

The pharmaceutical and clinical registry of each patient was obtained through the medical history from the DIRAYA system, used by the Andalusian Health Service ("Diraya - Servicio Andaluz de Salud," n.d.).

#### Anthropometry and body composition

A portable eight-polar tactile-electrode impedanciometer (In-

Body R20, Biospace, Seoul, Korea) was used to measure body weight. Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). We calculated BMI as weight (kg) divided by height (m) squared.

**Hemogram and serum tissue damage-related markers**

Venous blood samples were collected in fasting conditions. A hemogram was performed to all blood samples to account red and white cells as well as haemoglobin concentration (Siemens Advia2 2120). Serum CK, LDH, C-reactive protein, total proteins, glutamic-pyruvic transaminase, glutamic oxaloacetic transaminase, gamma-glutamyltransferase transaminase and fibrinogen concentrations were determined through an autoanalyser (AU 5800 Bfkman-Koulta).

### Statistical analysis

Descriptive statistics (mean (standard deviation, SD) for quantitative variables and number of patients (%) for categorical variables) were employed to describe and compare baseline characteristics of the study sample by surgical closure groups (Table 1). Students't tests were employed to explore differences in continuous variables. Differences in categorical variables (type of surgery and sex) were explored by using the Chi-squared test.

The effects of the closures on the studied outcomes were assessed with linear regression analyses (Table 2). We included the changes (post−pre surgery) in each hemogram and biochemical outcome as dependent variables in separate models and the closure group (*Large stitches*=0 and *Small stitches*=1) as an independent variable. The baseline value was a potential cofounder for all variables. We also adjusted the models for age, sex, medication and type of surgery.

The statistical analysis was conducted with the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). The statistical significance was set at $p<0.05$.

### Results

Of the 100 patients that were randomised into *Large-stitch* (n=50) and *Small-stitch* (n=50) surgical closures, 50 percent were women. Baseline characteristics of the study participants by type of surgical closure are shown in Table 1. Mean age of the sample was 62.0 ± 15.1 years old, with a mean body mass index of 27.6 ± 5.1 kg/m$^2$ (overweight). Regarding the type of surgery performed, there were differences according to closure technique: more hepatobiliary, pancreatic, gastric and oesophagi interventions with *large-stitches* closures and more colon and intestinal interventions with *small-stitches* closures ($p<0.001$). We registered one wound dehiscence and five surgical site infections in the *large-stich* closure group and no wound dehiscence and three surgical site infections in the *small-stitch* closure group.

Changes after surgery in the hemogram and serum biochemical markers by type of closure employed, after adjusting for baseline values, age, sex and type of surgery performed, are shown in Table 2. The *large-stitch* closure group resulted in 123 mg/dL significantly higher CK concentrations compared with the *small-stitch* closure group ($p=0.004$). The *Large-stitch* closure group resulted in 78% higher leukocytes (1.8 million more) and 177% higher LDH concentrations (172.7 UI/L more) compared with the *small-stitch* closure (non-significant trend, $p=0.129$ and p=0.122 respectively).

**Table 1:** Baseline characteristics of the study participants by type of surgical closure employed.

| | ***"Large-stitch"*** **(Israelsson) closure (n=50)** | ***"Small-stitch"*** **(Monoblock) closure (n=50)** | |
|---|---|---|---|
| | mean (SD) | mean (SD) | P |
| Age (years) | 63.8 (13.5) | 60.1 (15.4) | 0.217 |
| Height (cm) | 164.9 (9.0) | 165.2 (9.0) | 0.903 |
| Weight (Kg) | 72.2 (12.7) | 69.3 (13.7) | 0.285 |
| Body mass index (Kg/m$^2$) | 28.2 (5.0) | 27.1 (5.3) | 0.288 |
| | n (%) | n (%) | |
| Woman (yes) | 22 (48.9) | 23 (51.1) | 0.841 |
| Type of surgery | | | |
| *Exploratory laparotomy* | 18 (36.0) | 12 (24.0) | <0.001 |
| *Intestinal resection* | 2 (6.0) | 7 (14.0) | |
| *Hepatobiliary and pancreatic* | 13 (26.0) | 2 (4.0) | |
| *Colon* | 7 (14.0) | 28 (56.0) | |
| *Gastric and oesophagi* | 9 (18.0) | 1 (2.0) | |

SD: Standard Deviation.

**Table 2:** Postoperative change differences in the hemogram and serum biochemical markers by type of surgical closure employed.

| **Marker** | ***"Large-stitch"*** **(Israelsson) closure (n=50)** | ***"Small-stitch"*** **(Monoblock) closure (n=50)** | **Between groups-difference (95% CI)** | **P*** |
|---|---|---|---|---|
| | **Differences from pre to post surgery (SEM)** | **Differences from pre to post surgery (SEM)** | | |
| Hemogram | | | | |
| *Erythrocytes (mill)* | -0.18 (0.10) | -0.21 (0.13) | 0.03 (-0.30 to 0.35) | 0.911 |
| *Haemoglobin (mg/dL)* | -0.68 (0.27) | -0.76 (0.25) | 0.08 (-0.70 to 0.80) | 0.508 |
| *Platelets (mill)* | 5.81 (22.8) | -10.7 (22.4) | 16.6 (-51.6 to 81.3) | 0.342 |
| *Leukocytes (mil)* | 4.12 (1.05) | 2.32 (0.80) | 1.80 (-0.59 to 4.31) | 0.129 |
| Serum tissue damage-related markers | | | | |
| *Creatine kinase (mg/dL)* | 141.6 (49.8) | 18.5 (25.1) | 123.1 (16.9 to 239.6) | 0.004 |

| | | | | |
|---|---|---|---|---|
| *C-reactive protein (mg/dL)* | 33.2 (16.6) | 19.5 (19.5) | 13.7 (-39.6 to 66.9) | 0.512 |
| *Lactate dehydrogenase (UI/L)* | 270.3 (172.8) | 97.6 (44.2) | 172.7 (-166.5 to 511.9) | 0.122 |
| *GOT (mg/dL)* | 166.1 (121.5) | 293.7 (135.7) | -127.6 (-472.8 to 243.0) | 0.181 |
| *GPT (mg/dL)* | 78.4 (44.3) | 63.0 (30.0) | 15.4 (-88.0 to 119.8) | 0.166 |
| *GGT (mg/dL)* | -76.0 (57.6) | 21.3 (12.7) | -97.3 (-212.4 to 9.50) | 0.179 |
| *Total proteins* | -0.76 (0.22) | -0.50 (0.24) | -0.26 (-0.92 to 0.35) | 0.211 |
| *Fibrinogen (mg/dL)* | -38.3 (0.29) | -40.6 (0.32) | 2.34 (-79.8 to 89.4) | 0.932 |

Mean results show the differences between post-pre intervention results for each variable; SEM: Standard Error Of The Mean; GPT: Glutamic-Pyruvic Transaminase; GOT: Glutamic Oxaloacetic Transaminase; GGT: Gamma-Glutamyltransferase Transaminase; *Model adjusted for baseline value of the variable and type of surgery.

## Discussion

Suturing techniques for midline abdominal wall incisions vary between surgeons. *Large-stitch* closure is currently considered the classical standard suture while *small-stitch* closure can be defined as a smaller advanced suture. The main findings of this trial indicate that patients sutured with the *small-stitch* closure showed 662% lower CK concentrations than those sutured with the *large-stitch* closure. Moreover, with a non-significant trend but clinically meaningful, *small-stitch* closure resulted in 78% lower leukocytes and 177% lower LDH concentrations. These results suggest that *small-stitch* closure induces lower tissue damage, which reinforces the recommendation of choosing this closure technique when possible.

To the best of our knowledge, there are no prior studies comparing haematological and biochemical markers of tissue damage between *large-* and *small-stich* closures (i.e. *monoblock* and *Israelson* closures, respectively). Nevertheless, numerous comparisons have been made trying to stablish a closure that minimizes complications such as hernia or wound infection [4,8,9]. Millbourn et al. [4] developed the first big intervention study contrasting *large-* and *small-stich* length closures in 737 randomized patients. They observed that surgical site infection occurred in 10% patients in the *large-stitch* group and in 5% in the *small stitch* group. Incisional hernia was present in 18% in the *large-stitch* group and in 6% in the *small-stitch* group, what also concurs with our rates. Therefore, the authors concluded that current recommendations of placing stitches at least 10 mm from the wound edge should be changed to avoid patient suffering and costly wound complications in midline incisions closed with a running suture and having a suture length to wound length ratio of at least 4 [4]. Recent studies have confirmed such findings regarding infection and the appearance of inguinal hernia. They concluded that in midline incisions closed with a single-layer running suture, the rate of wound complications is lower when a suture length to wound length ratio of at least 4 is accomplished with a short stitch length rather than with a long one (without increased pain or other side adverse effects) [1,10,11]. Finally, a recent biomechanical study [10] also additionally suggested that small separations should be combined with large bite depths [10]. Therefore, these findings support altogether that small separations are more effective than large separations to prevent hernias. Notwithstanding, Deerenberg et al. [1], in the guidelines of the European Hernia Society and the recent randomized STITCH (Suture Techniques to Reduce the Incidence of The inCisional Hernia) trial, affirmed that there is no high-quality evidence available concerning the best suture material or technique to reduce incisional hernia rate when closing a laparotomy. Nonetheless, they suggested that, when using a slowly absorbable suture and a continuous suturing technique with small tissue bites, the incisional hernia rate is significantly reduced compared with a large-bite technique. This advantage may also constitute a decrease in the hospital stay length and health expenditures [10].

The fact that we found lower CK concentrations and evidence of a significant association regarding lower LDH in the *small-stitch* closure compared with the *large-stitch* one also suggests that this technique could also induce less tissue necrosis. We hypothesize that the small-stitch closure could induce less tissue necrosis by different mechanisms: first, when using a needle of less size and a 2/0 monofilament, the trauma of the wall seems to be less; second, when maintaining the tension throughout the suture in a stable manner with the same distance between the stitches, no tears are produced from the wall, which might also reduce cell death [10]. Therefore, this greater tissue necrosis induced by the *large-stitch* closure could be the responsible of the increased release of the tissue damage-related markers studied in the present trial (i.e. serum CK and LDH, mainly).

*Small-stich* closure also showed evidence of a significant association with less serum leukocytes compared with *large stitches*. This finding reinforces those studies that found a decrease in the appearance of surgical site infection with this closure [4,12,13]. The mechanisms explaining this positive fact could be various. Although the cause of surgical site infection is multifactorial, some of their recognized risk factors, that could be potentially diminished through this closure, might be the degree of wound contamination or the degree of trauma of the wall [14,15]. In contrast, in a recent meta-analysis [13] the suture material or suture method for fascial closure did not seem to influence the rate of surgical site infection and burst abdomen. Previous meta-analyses have evaluated whether subcutaneous skin closure or skin closure with sutures or staples had an impact on surgical site infection [8,16], and there is no convincing evidence of the superiority of any method over the other [8,12,13,16].

Regarding the studied hemogram parameters, the absence of differences between closures could be due to the fact that we performed complex surgeries where there is a bleeding greater than half a litre and, consequently, the wall closure should not additionally influence the total blood loss. We consider the 13 mg/dL lower serum CRP observed in the surgical group submitted to *small stitches* in the same way, as these complex surgeries performed in both closures highly increase CRP, and thus, a difference of 13 mg/dL could not be considered clinically meaningful.

Finally, a relevant factor to be taken into account is postoperative pain, which can be also considered a surgical complication. In this sense, our group has recently confirmed that LDH concentrations were strongly associated with greater postoperative pain, and that LDH was able to discriminate between presence and absence of major postoperative pain [1].

Altogether, *small-stitches* closure seems to present a lower risk of hernia or evisceration as well as infection. Infection of the surgical wound is one of the most frequent socio-economic consequences since it increases hospital stay and health spending and worsens the emotional well-being and quality of life of patients. Its overall incidence is 5-10%, with a direct mortality of 0.6% (Gallo et al. 2009; Zúniga and Gómez-Márquez 2016). Surgical complications involve a longer stay (20.1 vs. 5.5 days) and costs (€11,670 vs. €3,354), with infectious diseases being the most frequent. The incidence of postoperative complications can reach up to 40% (Khan et al. 2006), even with an appropriate surgical indication and patient selection. Complications lead to an increase in stay (Khan et al. 2006) but also mortality and readmissions (Tevis et al. 2016; Gomez-Rosado, Salas-Turrens, and Olry-de-Labry-Lima 2018). In fact, there are different studies that estimate the increase in costs for complications up to 1.89 times (Vaughan-Sarrazin et al. 2011) assuming $37,917 per patient (Eappen et al. 2013; Gomez-Rosado, Salas-Turrens, and Olry-de-Labry-Lima 2018). In the present trial, taking into account the data in the literature, *large-stich* closure resulted in €17,236 increased cost due to the higher incidence of complications.

Hence, if we combine cost-effectiveness and the best response in the biochemical parameters studied with a lower risk of hernia and infection of the surgical site, *small-stitch* closure seems to be, by far, the most appropriate technique. More studies are required to confirm the present findings, and to establish the utility of this technique for the closure of any abdominal incision, not only laparotomies.

### Limitations and strengths

Firstly, patients included in this study belonged to general surgery, which hinder the extrapolation to other kind of surgeries (e.g. gynaecological). Secondly, this study lacks some serum hormonal analyses, such as cortisol, or some pro-inflammatory cytokines, such as Interleukin 1 and 6, which could have been of interest for a better interpretation of the present results. Third, there were baseline differences regarding the closure technique employed for each type of surgery due to the prevalence of different kind of surgeries and the own final surgeon's closure election, but we further adjusted the model for type of surgery. Finally, we did not assess pain, and we could not contrast if this lower tissue-damage promoted by the *small-stitch* closure resulted in less postoperative pain and thus, greater patient satisfaction and lower analgesic expenditure. On the other hand, the sample size was relatively representative, and the measurement tools employed were widely valid and reliable, and thus, the accuracy of the present results is warranted.

### Conclusion

Overall, the *small-stitch* closure showed lower postoperative tissue damage and inflammation than the *large-stitch* closure. Therefore, *small-stitch* closure should be considered the preferred surgical closure technique when the surgery circumstances make it possible. These results have no precedents and might be of potential importance for the Health Care Systems.

### Declarations

**Conflict of interest:** The authors declare that they have no competing interest.

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