TITLE

Prophylactic Mesh Placement Reduces the Incidence of Incisional Hernia in HBP Surgery.

CICAT STUDY

PREVENTION OF INCISIONAL HERNIA WITH PROPHYLACTIC MESH VERSUS PRIMARY SUTURE AFTER RIGHT SUBCOSTAL LAPAROTOMY. A DOUBLE-BLIND, RANDOMIZED, MULTICENTER CONTROLLED STUDY.

GENERAL INFORMATION

PROMOTER

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PARTICIPATING CENTERS

1. Virgen Macarena University Hospital, Seville.

STUDY RESEARCHERS

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EXPECTED DURATION

24 months

INTRODUCTION

In middle laparotomies, and despite the principles of correct closure of the abdominal wall (4:1 rule, small stitches and monofilament suture in a single aponeurotic plane) the incidence of incisional hernia occurs around 12.8% during the first two years. In patients with risk factors and with longer follow-up, the incidence rate increases. (1)

To avoid the appearance of incisional hernia, especially in patients at risk, the use of prophylactic meshes has been used in the closure of the middle laparotomies. One of the initial resistances to the widespread use of this procedure is the fear of infection and the possible complications derived from the use of them.

In an overall analysis of 1759 patients in whom a prophylactic mesh has been used in mean laparotomies, the overall wound infection rate was 12% and the mesh infection rate was 0.6%. The evidence analyzed indicates that the procedure may be safe in clean and clean contaminated surgery. There is no evidence regarding the use of them in dirty or contaminated surgery. (2)

In most published studies, the meshes used are permanent synthetic meshes and in some cases absorbable biological or synthetic mesh.

Regarding the position of the mesh, supraaponeurotic placement seems to be as safe as retromuscular placement, in terms of prophylaxis of incisional hernia in medium laparotomies.

Although the results regarding the decrease in the incidence of incisional hernia seem to justify the use of prophylactic meshes in the closure of mean laparotomies, more studies are needed to identify the risk factors of patients in which to do so with a high level of evidence. (3)

Subcostal incisions continue to be one of the most widely used ways of approaching the abdominal cavity, especially in the esophagogastric and hepatobiliopancreatic units, and despite the implementation of minimally invasive surgery.

The incidence of IH (Incisional Hernia) in subcostal laparotomies reported in the literature is estimated to be around 4.8%-31.3% according to the different published series. Although this incidence is lower than that reported in the case of medium laparotomies, their treatment is more complex for two reasons:

1. The rectus muscle is divided into two parts, whose ends are separated to a greater or lesser extent depending on the size of the hernia defect, making it difficult to repair completely and reposition it in its original position.
2. Because of their proximity to the rib bone ridge. (4)

The repair of subcostal IH has a recurrence rate of 25% and they are included in the group of the so-called complex eventrations, due to the characteristics described above. (3)

Currently, following the recommendations of the EHS regarding the prophylactic use of meshes in the closure of mean laparotomies, it seems that it can be an effective procedure to reduce the incidence of IH, especially in patients at high risk of developing it, although a greater number of studies are needed.

In relation to subcostal laparotomies, there is no indication with a level of evidence in this guideline. (3)

Only in a study published in ***Surgery 2016***, in bilateral subcostal incisions, does the use of prophylactic mesh appear to be safe and effective and reduces the incidence of IH in such laparotomies. (6)

Faced with this problem, the scarcity of literature on the subject, and following the trend of eventration prophylaxis with the use of midline meshes, the hypothesis of this working group in right unilateral subcostal laparotomies arises.

HYPOTHESIS

The use of a prophylactic mesh in a subaponeurotic position in the closure of a right unilateral subcostal laparotomy reduces the incidence of incisional hernia without increasing the incidence of complications.

OBJECTIVES

MAIN OBJECTIVE

To study the incidence of incisional hernia during the first two postoperative years in patients operated on with a right unilateral subcostal laparotomy, in both groups, with and without prophylactic mesh.

SECONDARY OBJECTIVES

1. Evaluation of surgical wound complications
    1. To evaluate and compare the incidence of superficial and deep surgical site infection in patients who underwent surgery.
    2. To evaluate and compare the incidence of Seromas in operated patients.
    3. To assess and compare the incidence of bruising in patients undergoing surgery
    4. To evaluate the incidence of evisceration in operated patients.
2. Study scar pain one month and three months after surgery.

SOURCE OF INFORMATION

The information will be obtained in all cases from the medical records of patients who have given their consent for the use of their data, and from interviews between them and the researchers. In no case will any procedure be performed outside of routine clinical practice, in order to obtain any data requested within the scope of this study.

STUDY DESIGN

Prospective, multicenter, randomized study. The assignment will be randomized into two groups:

1. Group 1: Prophylactic mesh. (Dynamesh Cicat®).
2. Group 2: Primary closure

SAMPLE SIZE

100 patients (100 each Group)

RANDOMIZATION AND MASKING

1. The assignment of each patient to each of the two study groups will be carried out by randomization generated by computer program.
2. The follow-up and assessment of complications will be carried out by an investigator other than the surgeon performing the intervention.

STUDY POPULATION

INCLUSION CRITERIA

1. Patients over 18 years of age.
2. Patients who are going to be operated on by means of a unilateral right or right extended subcostal laparotomy.
3. Patients who have given written informed consent.
4. Patients with 2 or more risk factors for incisional hernia:
   - Age > 60 years
   - BMI (body mass index) > 27
   - Diabetes
   - Chronic bronchopathy
   - Heart disease
   - Smoker
   - Neoplasia
   - Kidney failure
   - Liver disease
   - Immunosuppression

EXCLUSION CRITERIA

1. Emergency surgery.
2. Laparotomies in liver transplantation.
3. Prior eventration.
4. Previous laparotomy with a localized scar on the area to be made.
5. Presence of peritoneal carcinomatosis or advanced tumors with an estimated survival of less than 12 months.
6. Hemodynamic instability during surgery
7. Concurrent participation in another study that interferes with the intervention and/or outcomes.
8. Iron allergy.
9. Withdrawal or lack of written consent.
10. Patients with sufficient cognitive impairment to prevent understanding of the patient information sheet and informed consent.

WITHDRAWAL CRITERIA

1. The subject will be considered included in the study when, meeting the selection criteria, they give consent and the data corresponding to the baseline visit are recorded in a database. The participant may revoke his/her consent to participate in the study or to the use of his/her data in the analysis at any time, without justifying his/her decision, and without any liability or damage being derived for him/her.
2. Any patient who has to be reoperated within the first 30 postoperative days with removal of the implanted mesh and does not have a new mesh reimplanted.

OBSERVATION PERIOD

In addition to the assessment of postoperative complications during admission, the patient will be monitored at one month, 3 months, 6 months, 12 months, 18 months and 24 months after surgery in scheduled visits in the outpatient clinics of the respective services participantes.

METHODS OF CLOSING THE ABDOMINAL WALL

1. Before closing the abdominal wall, gloves will be changed and sterile material will be used for this purpose.
2. The closure of the abdominal wall will be performed with continuous suture of long-lasting synthetic monofilament nº 0 with a ratio of 4:1 in 2 planes and with the stitches separated at distances between 0.5 and 1 cm and taking 5 mm of tissue on each side.
3. The first layer will include the internal oblique muscle, transverse muscle and the posterior sheath of the rectum. The second layer will include the external oblique muscle, its aponeurosis, and the anterior sheath of the rectum.
4. In the case of random assignment to the "mesh" group, a medium/low-density, wide-pore polyvinylidene fluoride (PVDF) mesh (Dynamesh Cicat®) will be implanted in a retromuscular position, fixing the edges with intersecting dots of 2/0 resorbable monofilament 3/0 separated from each other by 3 cm. The mesh will be trimmed in length to fit the dissected space and the length of the incision, so that it exceeds the lateral and longitudinal edges of the incision by 3 cm.
5. The subcutaneous cellular tissue will be approached with 2/0 polyglycolic acid points, taking mesh to reduce dead spaces. The skin will approach with staples

FOLLOW-UP

Postoperative hospital stay.

Any readmission in the first two years after the procedure.

Follow-up in consultations at one month and then at 3, 6, 12, 18 and 24 months.

VARIABLES TO BE ANALYZED

1. Preoperative variables:
   1. Age.
   2. Sex.
   3. BMI

4. Diabetes mellitus.
5. Chronic treatment with corticosteroids.
6. Malnutrition (plasma albumin < 3.5 mg/dl).
7. COPD (Chronic obstructed pulmonary disease)
8. Smoking.
9. Connective tissue diseases (presence of aortic aneurysm).
10. Liver disease
11. Immunosuppression
12. Coagulopathy
13. Neoplasia
14. Diagnosis

2. Intraoperative variables:

1. Day of the intervention
2. Surgeon
3. Surgical intervention performed.
4. Incision length
5. Mesh Size Placed: Length x Width
6. Type of surgery (clean, clean-contaminated, contaminated, dirty).
7. Benign vs malignant pathology
8. Operating time (minutes).
9. Intraoperative complications.
10. Perioperative blood transfusion.

3. Postoperative variables:

1. Local complications:
    1. Surgical wound infection: superficial, deep or organ-space (based on Magram guidelines).
    2. Seroma
    3. Evisceration
    4. Hematoma
2. Systemic complications:
    1. Respiratory complications
    2. Cardiac
    3. Renal
    4. Septic shock
    5. ITU (urinary infection)
    6. Catheter
    7. Paralytic ileus
    8. Fistula/dehiscence
    9. Reoperation
3. Postoperative stay.
4. VAS (Visual analogical scale) at discharge, at one month and at 3 months.
5. Re-entry rate.
6. Mortality.

1. Incidence of eventration after surgery (clinical or radiological diagnosis) and time of onset (3, 6, 12, 16 or 18 months). CT (computed scan) of the abdomen at 12 months, abdominal wall assessment
2. MRI (magnetic resonance) abdomen at 6 months to see length and width of the mesh placed. And assessment of abdominal wall
3. If there is loss of follow-up, the cause will be collected.
4. Revisions:
    1. Eventration.
    2. Seroma.
    3. Chronic mesh infection.

STATISTICAL ANALYSIS

An intention-to-treat test will be performed. There will be an analysis of the mean and standard deviation for variables with continuous measures, while we will report frequencies and percentages for categorical variables. For the comparison of categorical variables, the Chi-square test or the Fisher test will be used when necessary. For the comparison of continuous variables, the Student's "t" test will be used. To identify variables related to the different objectives, Cox's linear, logistic or proportional multivariate analyses will be used. The occurrence of IH during follow-up will be analyzed using the Kaplan-Meier method. All analyses will be performed with hypothesis testing of 2 tails and a significance level of 5%. Statistical calculations will be performed with SPSS (SPSS Inc., Chicago, Illinois).

SAFETY

The safety of using a prophylactic mesh in the closure of laparotomies has been extensively demonstrated in different cohort studies and published clinical trials.
The mesh is approved for the use of parietal reinforcement and for the prevention of incisional hernia.

All adverse events that, in the opinion of the investigator, are relevant and/or related to randomized treatments will be collected.
An adverse event is any undesirable sign, symptom, or clinical condition that occurs after the start of the study (or therapy), even if it is considered unrelated to the study treatment. A serious adverse event is defined as an adverse event that results in death, threatens life, produces permanent disability or results in hospitalization or prolongation of hospitalization; in addition, congenital anomalies and malignant processes are also included.
Serious adverse events that are related or possibly related to the treatments will be reported to the Spanish Medicines Agency, to the competent bodies of the Autonomous Community of Madrid.

ETHICAL ASPECTS

This study should be conducted in accordance with the protocol and the standards of Good Clinical Practice (GCP), as described in Directive 91/507/EECC and the Declaration of Helsinki concerning medical research involving human subjects ("Recommendations for physicians involved in biomedical research involving human subjects").
Los investigadores acceden a seguir las instrucciones y procedimientos descritos en el mismo y por lo tanto cumplirá los principios de Buena Práctica Clínica en los cuales se basa.

Informed consent

The investigator must explain to each patient (or legally authorized representative) the nature of the study, its purposes, procedures, expected duration, and the potential risks and benefits related to participation in the study, as well as any inconveniences that the study may entail. Each participant should be advised that their participation in the study is voluntary and that they may leave the study at any time, without affecting their subsequent medical treatment or their relationship with the treating physician. Informed consent will be provided in the form of a standard written document, in language that is easily understandable to the participant. The patient must write his/her name and that of the informing physician in his/her own handwriting and date and sign the informed consent, as well as receive a copy of the signed document.

If the subject is unable to read or sign the documents, an oral presentation may be made or the signature of the subject's authorized legal representative may be obtained, provided that it is witnessed by a witness not involved in the study and is mentioned in the same document and/or medical history.

No patient may be included in the study without prior informed consent.

CONFIDENTIALITY

A temporary database will be created that will be hosted both on the website of the European Registry of Abdominal Wall Hernias (www.eurahs.eu) and in a database through the cardiolink website (www.cardiolink.es). Patients will be identified by an order number and by the medical record number. Only study researchers will have access to this database. In any case, these data will be handled in accordance with the Organic Law on the Protection of Personal Data 15/1999, of 13 December.