

# Comparative study of intraperitoneal adhesions associated with the use of meshes of polypropylene and polypropylene coated with omega-3 fatty acid

## *Estudo comparativo de aderências intraperitoneais associadas ao uso das telas de polipropileno e de malha leve de polipropileno revestida com ácido graxo ômega-3*

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### A B S T R A C T

**Objective:** To compare intraperitoneal adhesion formation with placement of polypropylene mesh and use of lightweight polypropylene mesh coated with omega-3 fatty in rats. **Methods:** Twenty-seven Wistar rats were randomized into three groups. In group 0 no mesh was placed; in group 1 we implanted a polypropylene mesh; and in group 2 there was implantation of a polypropylene mesh coated with omega-3 fatty acid. We evaluated adhesions presence and degree, breaking strength, percentage of area covered and retraction of the implanted meshes. **Results:** Group 0 had no adhesion. Groups 1 and 2 showed adhesions on the surface of the mesh, omentum, liver and intestinal loops. There were grades 1 and 2 adhesions in 100% of the polypropylene coated group and in 60% of the polypropylene group. The remaining were grade 3 adhesions, and differed significantly between groups ( $p < 0.001$ ). The breaking strength of adhesions on the polypropylene coated group was significantly higher than with the polypropylene alone ( $p = 0.016$ ). There was no difference in mesh retraction or area covered by the mesh. The analysis of the mesh coated with omega-3 fatty acid distribution showed adhesions preferentially located at the edges when compared to polypropylene, predominantly in the center. **Conclusion:** The type of adhesions, percentage of surface affected and retraction were not significantly different between meshes. The fatty acids coated mesh had a lower degree of adhesions and these required a greater force to rupture, possibly by their occurrence at the edges of the mesh.

**Key words:** Adhesion tissue. Surgical mesh. Polypropylenes. Omega-3 fatty acids. Hernia.

### INTRODUCTION

Adhesions are formed as inflammatory response to an offending agent<sup>1</sup>. Among the main causes of adhesions, trauma, foreign body, ischemia and infection are the more frequent<sup>2</sup>. Risk factors for them are pelvic operation, intra-abdominal ischemia, gloves' powder, non-absorbable sutures, foreign bodies and infection<sup>3</sup>. Trauma, infections and tumors can also be responsible for abdominal wall defects that are difficult to be corrected without the use of prosthetic material<sup>4</sup>.

The incidence of hernias after surgery range from 3% to 40%. In cases where there is primary closure of the incision without the use of a mesh, their recurrence ranges from 25% to 52%<sup>5-6</sup>. Intestinal obstruction and enterocutaneous fistulas need to be prevented from

adhesions formation, since adhesions are responsible for 41% to 44% of cases of intestinal obstruction and overall mortality of 11,4%<sup>7,8</sup>. The prosthesis is meant to reinforce the abdominal wall without resistance to its mobility<sup>9,10</sup>. Among those used in the repair of incisional hernias through laparotomy, the most common is the polypropylene mesh. It is easily handled, stimulates cell growth of surrounding tissue, has good flexibility, satisfactory inflammatory response and low cost. However, it also induces the formation of adhesions when in contact with intra-abdominal contents<sup>2</sup>.

A study using rats has shown that inflammatory processes involving the polypropylene mesh can become chronic, slowing the proliferation phase of wound healing. The inflammatory infiltrate with macrophages and lymphocytes prolongs inflammatory states. The

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formation of collagen reaches its maximum level at 21 days postoperatively, with greater quantities of type III collagen at the beginning and, subsequently, collagen type I<sup>10</sup>.

Lightweight polypropylene mesh coated with bioabsorbable omega 3 fatty acid (C-Qur®) for repair of inguinal or ventral hernia has not been fully investigated. Preliminary results of this new mesh with bioabsorbable adhesion barrier showed that it is safe and effective in the short term when compared with the performance of other prostheses currently available<sup>11</sup>.

The aim of this study was to compare the formation of intraperitoneal adhesions between the polypropylene mesh and the lightweight polypropylene mesh coated with bioabsorbable omega 3 fatty acid.

## METHODS

This study was conducted in the Lutheran University of Brazil (ULBRA), Rio Grande do Sul State, Brazil. It was approved by the Ethics and Research Committee of the institution and was registered under the protocol number 2009-006.

For sample size calculation, we used "Sample size determination in health studies".

We used 27 Wistar rats (*Rattus norvegicus*) randomized into three groups: group 0 (group SHAM) consisting of six animals undergoing laparotomy and primary closure of the abdominal wall without mesh placement; group 1, or PP, composed of ten animals undergoing laparotomy with fixation of intraperitoneal polypropylene mesh in size 2x2 cm; group 3, or PR, composed of 11 animals with median laparotomy and intraperitoneal fixation of the lightweight polypropylene mesh coated with omega 3 fatty acid, 2x2 cm in size, after previous hydration of the mesh with saline for one minute.

All animals were anesthetized with an intramuscular injection of xylazine (0.1 ml of 2% solution diluted in 0.2 ml of 0.9% saline) at a dose 5 mg / kg and an intramuscular injection of ketamine (0.35 50 ml of mg / ml) at a dose of 50 mg / kg. After adequate anesthesia, trichotomy of the surgical field and abdominal antisepsis with alcohol solution and 2% chlorhexidine were carried out.

In the six animals of group 0 a midline incision measuring 3x4 cm was performed, with dissection of the subcutaneous tissue and opening of the peritoneal cavity through the linea alba. In this group there was no mesh use, only the closure of the abdominal wall using 3-0 polypropylene sutures.

In the ten animals of group 2 (PP) the same midline incision measuring 3x4 cm was done. After exposure of the cavity we implanted a polypropylene mesh measuring 2x2 cm. To fix the mesh to the abdominal wall we used 4-

0 polypropylene transfixing sutures in four quadrants. Closure of the abdominal wall was done in the same way.

In the 11 animals of group PR the surgical procedure was the same as in group 1, however in this case placing the mesh coated with fatty acid mega 3 measuring 2x2 cm after its hydration for one minute in saline solution. Fixation to the abdominal wall was made with 4-0 polypropylene transfixing sutures in four quadrants of the mesh taking care not to damage the layer of fatty acid that covers it. Closure of the abdominal wall was done in the same way.

All animals were hydrated by subcutaneous injection of 0.5 ml 0.9% saline and placed separately to recover in a warm environment. When fully awake, they were transferred to their cages and offered standard food and water *ad libitum*. After these procedures, the animals received dipirone orally, diluted in water (90mg/ml) for three days and were kept in the same preoperative conditions.

### Post-operative evaluation

All animals were killed in a closed chamber with carbon dioxide at the 21<sup>st</sup> day after surgery. After trichotomy, abdominal incision in U-shape along the abdominal wall was done. The defect was folded on both sides and we assessed the adhesions, the viscera involved in adhesions, the percentage of the mesh affected by adhesions and their tensile strength. The tensile strength was performed using a millimeter ruler with a 5N dynamometer. The dynamometer was pulled carefully and the strength required to the rupture was estimated at the break point. The grading of adhesions is in accordance with Figure 1.

### Statistical analysis

Data were analyzed after preparation of a database in SPSS v.17.0. The Fisher's exact test was used to test the association between categorical variables. To test the association between quantitative variables we used the Mann-Whitney test. The significance level was 0.05 ( $p = 0.05$ ).

## RESULTS

The group 0 or Sham had one death during anesthesia, before surgery. As a consequence, five animals belonged to this group, with no adhesions (Figure 2). Only one animal presented with the greater omentum sutured to the abdominal wall.

As for adhesion incidence by mesh type, PP displayed 100% adherence, 100% involving the omentum, 70% the liver and round ligament and 30% the intestine, especially the small one. The C-Qur® mesh also showed 100% of adherence, 100% being in the omentum, liver in 90.9%, 27.3% in the small intestine and no involvement of the colon (Figures 2 and 3).

**Table 1** - Description of the types of adhesions.

Adhesions type		Definition
0	NO	no adhesion
1	LIGHT	thin and easy release adherence
2	MODERATE	blunt dissection for release the adhesions
3	INTENSE	dense adhesions with application of greater force occurring injury or partial injury of the viscera involved

**Figure 1** - Description of the types of adhesions.**Figure 2** - Abdominal wall without adhesion on the Sham group.

Comparatively, there was no statistical difference between the two meshes in relation to adhesions (Table 1).

When adhesion grading was measured, we observed that the PR group showed 100% adhesions grades 2 or 3, while the PP had grades 1 and 2 in 60% and grade 3 in 40%. Fisher's exact test ( $p=0.001$ ) showed significant association between the mesh type and the degree of adherence (Table 2).

**Table 2** - Comparison of adhesions in involved viscera.

	Presence of adhesion		* p
	Polypropylene	C-Qur ®	
Omentum	10 (100%)	11 (100%)	!
Liver (including round ligament )	7 (70%)	10 (90.9%)	0.311
Intestine (small intestine + colon)	3 (30%)	3 (27.3%)	1.000

\* p value for Fisher's exact test



**Figure 3** - Adhesions in a polypropylene mesh.

Upon analysis of the average rupture strength of the adhesions (Mann-Whitney test), the mean strength for PR was 1.48 N +/-0.45, and for PP, 0.96 N +/- 0.39,  $p=0.016$ .

Regarding retraction, the polypropylene had 0.16 cm, and C-Qur®, 0.41 cm, with no statistical difference between the two meshes (Mann-Whitney).

The percentage of mesh area involved in the adhesion was 60% in the PP group. In the PR group, five animals (45.5%) had less than 50% commitment, and six (54.5%) more than 50% of the surface of the mesh. By the Fisher's exact test ( $p=0.670$ ), there was no association between the type of the mesh and the percentage affected.

## DISCUSSION

The need for development of a prosthesis that can be used in laparoscopy, with satisfactory tissue integration, biologically inert and without intraperitoneal adhesion is in constant research<sup>12-14</sup>. In this study we used a midline incision and continuous suture closing using polypropylene as control for the formation of intra-peritoneal adhesions<sup>15,16</sup>. When it comes to ventral hernias, Cassar and Munro, after extensive literature review, reported recurrence rates by suture repair only, open repair with prosthesis placement and laparoscopic repair of 49%, 10% and up to 9%, respectively<sup>7</sup>.

No statistical difference was demonstrated between the two groups of meshes. Schreinemacher *et al.*<sup>17</sup> conducted an experimental study in rats in 2009 comparing the formation of adhesions in six meshes available, including the two used in this study, which showed adhesions in almost all rats, mainly affecting the omentum<sup>17</sup>.

Mild to moderate adhesions predominated in the PR group, with statistically significant difference when compared to the findings of the PP group. The presence of the omega-3 fatty acid coating may be responsible for it.

The polypropylene and C-Qur® showed no significant difference in the percentage of surface area affected by adhesions, as well as no retraction in three weeks. However, the model used to adjust the mesh to the size of the animal may have influenced the results. The manufacturer of the prosthesis itself does not indicate this practice.

The C-Qur® reduces the formation of intraperitoneal adhesions in the short term (seven days), but the protective effect decreases over time<sup>12</sup>. Phagocytosis of the absorbent coating of the mesh may contribute to the formation of adhesions<sup>17</sup>.

Adhesion formation is a dynamic process, influenced not only by the chemical properties of a mesh, but also by their mechanical properties. Regardless of the mesh type, the fixation sutures and the edges of the mesh were the preferred sites for adhesion formation. Presumably, in the case of coated ones, the inner coating material is directly exposed to the abdominal wall, but not the peritoneal

**Table 3** – Grading of the adhesions.

Variables	Mesh				p-value (*)
	Marlex		C-QUR		
	n	%	n	%	
Degree of adhesion					<0.001
No adhesion (0)	0	0.0	0	0.0	
Mild (1)	1	10.0	10	90.9	
Moderate (2)	5	50.0	1	9.1	
Intense (3)	4	40.0	0	0.0	

surface. Thus, cuts in edges of the meshes should be avoided<sup>18,19</sup>.

Other works are needed to assess the consequences in long-term contact of the mesh with the intraperitoneal environment.

In conclusion, the type of adhesions, percentage of surface affected and retraction were not significantly different between the meshes. The one of low weight and coated with omega-3 fatty acids had lower grades of adhesions and greater rupture strength.

## R E S U M O

**Objetivo:** Comparar as aderências entre dois grupos de ratos Wistar submetidas à colocação intraperitoneal da tela de polipropileno e malha leve de polipropileno revestida com ácido graxo ômega-3. **Métodos:** Foram utilizadas 27 ratos Wistar randomizadas em três grupos. No grupo 0 não houve colocação de prótese, no grupo 1 houve implantação da prótese de polipropileno e no grupo 2, implantação de prótese de polipropileno revestida com ácido graxo ômega-3. Foi avaliadas a presença de aderências, grau, força de ruptura, percentual de área recoberta e retração das telas aferidas. **Resultados:** O grupo 0 não apresentou aderência. Os grupos 1 e 2 apresentaram aderência na superfície da prótese, omento, fígado e alça intestinal. Foram encontradas aderências grau 1 e 2 em 100% do grupo polipropileno revestida com ácido graxo ômega-3 e em 60% do grupo polipropileno. As demais eram aderências grau 3, e diferiram significativamente entre os grupos ( $p < 0,001$ ). A força de ruptura da aderência na tela polipropileno revestida com ácido graxo ômega-3 foi significativamente maior do que na tela de polipropileno ( $p = 0,016$ ). Não houve diferença na retração das telas ou superfície acometida pelas telas. A análise da tela revestida com ácido graxo ômega-3 demonstrou distribuição preferencialmente nas bordas em relação ao polipropileno, com predomínio no centro. **Conclusão:** O tipo de aderência, percentual de superfície acometida e retração não foram significativamente diferentes entre as telas. A tela de baixo peso apresentou menor grau de aderências, e, estas, necessitaram força maior para ruptura, possivelmente pelo predomínio de sua ocorrência nas bordas da tela.

**Descritores:** Aderências teciduais. Telas cirúrgicas. Polipropilenos. Ácidos graxos ômega-3. Hérnia.

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