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## Original Article

# Evaluation of tensile strength of tissue adhesives made of fibrin and cyanoacrylate used as reinforcement of colon suture in “ex vivo” swine



Alexandre Venâncio de Sousa<sup>a</sup>, Marcus Vinicius Henrique de Carvalho<sup>b</sup>, Roberto Anania de Paula<sup>a</sup>, Evaldo Marchi<sup>b</sup>, Juliana Querino Teixeira<sup>c,\*</sup>, Caroline Von Abel de Sousa<sup>c</sup>, Daniel Perez<sup>c</sup>

<sup>a</sup> Colégio Brasileiro de Cirurgiões, Rio de Janeiro, RJ, Brazil

<sup>b</sup> Faculdade de Medicina de Jundiaí (FMJ), Departamento de Cirurgia, Jundiaí, SP, Brazil

<sup>c</sup> Faculdade de Medicina de Jundiaí (FMJ), Jundiaí, SP, Brazil

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## ABSTRACT

**Aim:** To evaluate rupture pressures of tissue adhesives of cyanoacrylate (Omnex<sup>®</sup>) and fibrin (Evicel<sup>®</sup>), used as reinforcement in colonic suture from “ex vivo” swine.

**Methods:** Surgical procedures were performed in the Surgical Technique Laboratory. From a division in segments of 10 cm of descending colon and sigmoid colon from three “ex vivo” female swine, Landrace breed, which were resected in less than six hours after the slaughter time, 30 segments were selected, 10 of each animal. They were stored in saline solution 0.9% at 36°C, being randomly allocated in three groups (Control, Evicel and Omnex), each one containing 10 segments.

**Results:** The lower and higher pressure values found in the groups Control, Evicel and Omnex were 36 mmHg and 41 mmHg, 70 mmHg and 90 mmHg, 90 mmHg and 120 mmHg, respectively. Containing statistical significance ( $p$ -value <0.0001) concerning the 2 to 2 comparisons (Control, Evicel and Omnex) with 95% trusting rate based on the application of the Turkey Method.

**Conclusion:** One concludes that the use of tissue adhesives in anastomoses colonic in an experimental animal model of “ex vivo” swine increased the anastomoses rupture pressures. Among the tested adhesives, cyanoacrylate presented higher rupture pressure in relation to fibrin adhesive.

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\* Corresponding author.

E-mail: [julianaqteixeira@hotmail.com](mailto:julianaqteixeira@hotmail.com) (J.Q. Teixeira).

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## Avaliação da força tênsil de adesivos teciduais de Fibrina e Cianoacrilato usados como reforço de sutura de colo de suínos “ex vivos”

### R E S U M O

**Palavras-chave:**  
Adesivos teciduais  
Suturas  
Ruptura  
Fibrina

**Objetivo:** Avaliar as pressões de ruptura dos adesivos teciduais de Cianoacrilato (Omnex®) e de Fibrina (Evicel®), usados como reforço em suturas colônicas de suínos “ex-vivo”.

**Métodos:** Os procedimentos cirúrgicos realizados foram realizados no Laboratório de Técnica Cirúrgica. A partir da divisão em segmentos de 10 cm do colo descendente e colo sigmoide de três suínas fêmeas ex-vivo, da raça Landrace, ressecados em tempo inferior a seis horas em relação ao momento do abate, foram selecionados 30 segmentos, 10 de cada animal. Foram armazenados em soro fisiológico 0,9% a 36 °C, alocando-se aleatoriamente esses segmentos em três grupos (Controle, Evicel e Omnex) com 10 segmentos cada.

**Resultados:** Os menores e maiores valores pressóricos encontrados nos grupos Controle, Evicel e Omnex foram 36 mmHg e 41 mmHg, 70 mmHg e 90 mmHg, 90 mmHg e 120 mmHg, respectivamente. Com significância estatística (Valor-p < 0,0001) para as comparações 2 a 2 (Sutura, Evicel e Omnex) com um intervalo de confiança de 95% construído a partir da aplicação do método de Turkey.

**Conclusão:** A partir desse estudo conclui-se que o uso de adesivos teciduais em anastomoses colônicas, em modelo experimental animal de suíno ex-vivo, aumentou as pressões de ruptura das anastomoses. Dentre os adesivos testados, o adesivo de Cianoacrilato apresentou maiores pressões de ruptura em relação ao adesivo de Fibrina.

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## Introduction

Although the incidence of anastomotic dehiscence has decreased in recent years,<sup>1</sup> this complication remains a great concern among surgeons,<sup>1-3</sup> since its occurrence culminates in increased morbimortality. Adherences, fistulas and stenosis also consist in complications from entero-anastomoses that increase morbimortality when present.<sup>1,2</sup>

Experimental studies with rats showed that intestinal anastomoses presented high resistance during the immediate postoperative period, however, they suffered an abrupt drop in resistance in the first postoperative days, followed by a gradual elevation.<sup>4,5</sup>

Hogstrom in an experimental study with rats noted that the reduction of anastomoses resistance found in the first postoperative days may consist in an important risk factor for dehiscence and, meanwhile, the integrity of intestinal anastomoses is completely dependent on suture.<sup>5</sup>

The search for a complication-free anastomosis promoted not only the improvement of techniques and materials used, but also the development of supporting products in the conservation of tensile strength of the sutures.<sup>1-3,6,7</sup>

In this scenario, tissue adhesives have played an important role in recent years.<sup>1-3,6,7</sup>

## Objectives

To assess the rupture pressures of the tissue adhesives of cyanoacrylate (Omnex®) and Fibrin (Evicel®) used as reinforcement in “ex vivo” swine colonic sutures.

## Material and method

This research was approved by the Ethics and Research Commission of the Medical School of Jundiaí, under the protocol number of CEUA 133/2013.

Surgical procedures were performed at the Laboratory of Surgical Technique of the Medical School of Jundiaí.

### Sample

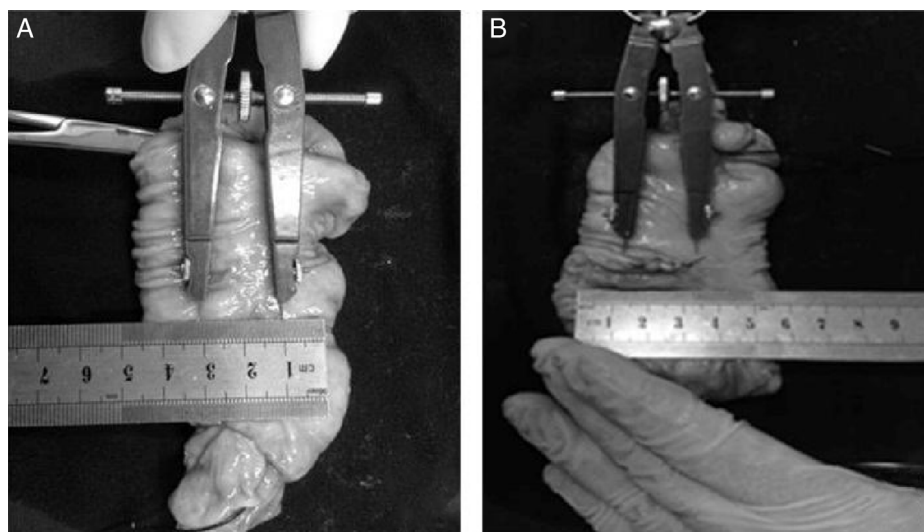
From a division in segments of 10 cm of descending colon and sigmoid colon from three “ex vivo” female swine, Landrace breed, which were resected in less than six hours after the slaughter time, 30 segments were selected, 10 of each animal. They were stored in saline solution 0.9% at an approximate temperature of 36 °C, being randomly allocated in three groups (Control, Evicel and Omnex), each one containing 10 segments.

The colonic segments were acquired at a slaughterhouse located in the city of Cosmópolis, State of São Paulo.

### Suture of segments of colon

The procedure was performed in the Control, Evicel and Omnex groups.

A two-centimeter cross-sectional incision was performed on the antimesenteric border, followed by single-point sutures, in a singular plane contemplating mucosa, submucosa, muscularis mucosa and serosa, with 3-0 polyglactin 910 (Vicryl®) wire. Five points at each incision were performed (Fig. 1).



**Fig. 1 – Incision and suture of colon segments. (A) Demarcation of the incision; (B) sutured incision. All surgical procedures were performed by the same team.**

#### *Application of the adhesive on the suture line*

The following procedures were performed in the Evicel and Omnex groups.

Concerning the Evicel group, the implemented adhesive was the fibrin adhesive, whereas in the Omnex group the adhesive used was the cyanoacrylate one.

A thin layer (approximately 1 mm) of adhesive was applied on the suture and, according to the orientation of the adhesive manufacturers, the drying time of the products was respected with the absence of manipulation of the tissues near the application area, in order to carry on with the procedure.

Prior to the application of the adhesives, the suture line was dried with a gauze.

#### *Rupture pressure test*

The test consisted of determining the intra-luminal pressure required to tear the suture line performed on the examined colon segment.

##### *Setting the assessment system of the “Rupture Pressure”*

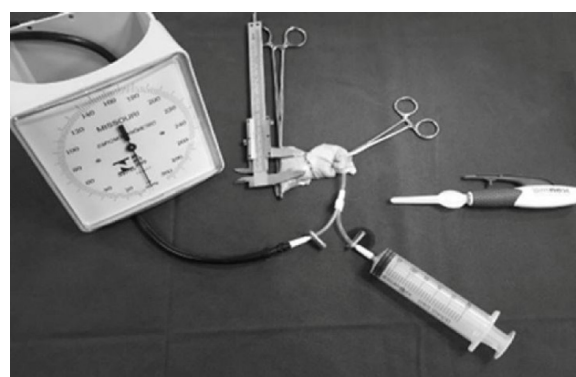
The assessment system consisted of a two-path catheter that connects a manometer to an infusion device (20 mL syringe) and a colon segment of one of the evaluated groups.

In order to accomplish the test, the proximal and distal ends of the colon segments were occluded. In the lumen at the proximal extremity, one of the catheter paths was fixed by means of ligature with 2-0 cotton thread. This ligature, in addition to the fixation of a pathway of the catheter, occluded the proximal end of the colonic segment.

The occlusion of the distal end of the colon segments was performed by clamping the whole circumference of the colonic segment with a Kocher's forceps (Fig. 2).

##### *Establishment of the “Rupture Pressure”*

Through the assembled assessment system, based on the infusion of a solution to the lumen of the colon segment



**Fig. 2 – Assessment system of the “Rupture Pressure”.**

under continuous pressure, the intra-luminal pressure was raised. The pressure value presented at the manometer at the moment of the extravasation of the solution through the suture line was defined as “Rupture Pressure”.

The solution used in this study contained 1 mL of Methylene Blue mixed with 500 mL of Voluven®. The use of Methylene Blue favored the observation of extravasation of the solution through the suture line.

#### *Statistical analysis*

Statistical analysis for rupture pressure data was performed through Analysis of Variance (ANOVA), and the averages were compared by the Tukey Test, at the level of 5% ( $p < 0.05$ ) of probability through the Program SAS version 9.2.

#### *Results*

The results of the rupture pressure analyses of the Control, Omnex and Evicel groups can be visualized in Table 1.

**Table 1 – Rupture pressure values in groups (mmHg).**

| Piece | Control (mmHg) | Evicel (mmHg) | Omnex (mmHg) |
|-------|----------------|---------------|--------------|
| 1     | 38             | 75            | 90           |
| 2     | 40             | 80            | 100          |
| 3     | 38             | 75            | 110          |
| 4     | 36             | 90            | 120          |
| 5     | 41             | 70            | 105          |
| 6     | 39             | 70            | 99           |
| 7     | 40             | 75            | 100          |
| 8     | 37             | 80            | 110          |
| 9     | 38             | 78            | 120          |
| 10    | 40             | 77            | 100          |

**Table 2 – Rupture pressure analysis of each group.**

| Group   | Average | Standard deviation | Median | Minimum value | Maximum value |
|---------|---------|--------------------|--------|---------------|---------------|
| Control | 38.7    | 1.6                | 38.5   | 36.0          | 41.0          |
| Evicel  | 77.0    | 5.8                | 76.0   | 70.0          | 90.0          |
| Omnex   | 105.4   | 9.6                | 102.5  | 90.0          | 120.0         |

**Table 3 – ANOVA test.**

| 2 to 2 comparisons | p-value |
|--------------------|---------|
| Evicel × Control   | <0.0001 |
| Omnex × Control    | <0.0001 |
| Omnex × Evicel     | <0.0001 |

The lowest pressure value found in the Control group was 36 mmHg and the highest one was 41 mmHg. In the Evicel group, the lowest rupture pressure value was found to be 70 mmHg and the highest one was 90 mmHg. The lowest and highest rupture pressure values found in the Omnex group were, respectively, 90 mmHg and 120 mmHg.

The median of the rupture pressure values verified in the Control, Omnex and Evicel groups were 38.5 mmHg, 102.5 mmHg and 76 mmHg, respectively.

The average of the pressure values of rupture found in the Control, Omnex and Evicel groups were 38.7 mmHg (standard deviation of 1.6), 77 mmHg (standard deviation of 9.6) and 105.4 mmHg (standard deviation of 5.8) (Table 2).

In order to evaluate whether the rupture pressure values found in the different groups were statistically significant, the Analysis of Variance (ANOVA) was applied with a confidence rate of 95% constructed from the application of the Turkey Method (Table 3).

The sutures which were reinforced with the tissue adhesives showed higher rupture pressures in relation to the sutures to which the tissue adhesive was not applied.

## Discussion

Tissue adhesives are substances that, when solidified, are able to establish a connection between their molecular structure and that of the tissue to which they are applied.<sup>6,8</sup> Ideally after its application, the solidification on the applied tissue must be fast and capable of generating a stable and impermeable tissue union,<sup>6,7,9</sup> without altering the tissue configuration,

nor implying toxic, carcinogenic or allergenic effects.<sup>6,9</sup> Such adhesives can be classified, according to their composition, in synthetic or natural.<sup>3,6,9,10</sup>

The objective of this study consisted of evaluating the rupture pressures of intestinal anastomoses after their reinforcement with tissue adhesives of cyanoacrylate (Omnex®) and Fibrin (Evicel®) in “ex vivo” colon segments. The choice of pigs as animal experimentation model is justified since, among the domestic mammals, swine have more similar intestines in relation to the human being. Another important feature is the facility of obtaining homogeneous groups of animals within the species.<sup>11</sup>

The choice of the tissue “ex vivo” by the researchers aimed at excluding deleterious effects, especially concerning the production of collagenases derived from the cicatrization process, since studies have shown that the tensile strength of intestinal anastomosis depends on the amount and quality of collagen presented in the tissues.<sup>4,5,12</sup>

Although there are several experimental studies that associate tissue adhesives to the healing process, the methodological multiplicity employed,<sup>6</sup> along with a great variety of compounds within the same type of adhesive, hamper the evaluation of these products.

On the other hand, from the bibliographical survey carried out by the researchers it was noticed that the tissue adhesives have been studied and tested in different tissues, as well as in different models of animal experimentation. Researches performed on swine, dogs, rabbits and rats as an experimental model, concerning the effectiveness of adhesives in digestive anastomoses as an alternative to maintaining border coaptation, have been showing promising results regarding some controversies.<sup>2</sup>

The most commonly mentioned adhesive is the Fibrin glue,<sup>7</sup> which is currently the only adhesive authorized by the Food Drug Administration (FDA) for clinical use as a hemostatic agent, sealant and tissue adhesive<sup>8,10</sup> although it contains hemoderived products in its formulation.<sup>3,6-10,12</sup>

Regarding the use of cyanoacrylate, studies are divergent in its applicability.<sup>8,13</sup> Since its first formulations, in order to reduce the toxic effects that this substance used to cause to the tissues where it was applied, there were plenty of modifications in its original composition.<sup>3,9,10,12</sup> In intestinal anastomosis, the results are controversial,<sup>8,13</sup> inasmuch as it is believed that the biochemical reactions that occur in the intraperitoneal cavity, due to the application of the adhesive, differ from the reactions of other tissues since they cause an intense inflammatory process which may even evolve to foreign body reactions, granulomas, and tissue necrosis.<sup>8</sup>

In our study, when analyzing rupture pressures among the groups, a significant difference was verified concerning all the comparisons, obtaining higher rupture pressure values in the Evicel group in relation to the Control group, as well as higher rupture pressure values in the Omnex group in relation to both the Control and the Evicel groups. In these comparisons, the increased resistance to rupture in the intestinal segments that were covered by tissue sealants (Evicel and Omnex) was evident, with better results in the Omnex group. This fact corroborates with the revisions made by Silva et al.<sup>9</sup> and Carvalho et al.<sup>10</sup>

## Conclusion

From this study one concludes that the use of tissue adhesives in colonic anastomoses in an experimental animal model of "ex vivo" swine increased the rupture pressures of the anastomoses.

Among the tested adhesives, the cyanoacrylate adhesive had higher rupture pressures than the fibrin adhesive.

## Conflicts of interest

The authors declare no conflicts of interest.

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