

Wrapping colonic anastomoses: Omentoplasty versus a carrier-bound fibrin sealant

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Introduction: A leak from an intestinal anastomosis is the complication most feared by the colorectal surgeon. The role of omentoplasty in securing colorectal anastomoses shows some controversy: being recommended by some authors, being of equivocal value to others and to be recommend against by a third group of authors. Collagen-bound fibrin sealant sheets have recently been used in many aspects of surgery; for example: Hernia, GI, ophthalmic, gynecologic & obstetric, renal, vascular and cardiac surgeries; and many experimental animal studies proved its efficacy in securing GI anastomoses. The safety and feasibility of using collagen-bound fibrin sealant has been proven. Its application for sealing colonic anastomosis is a new field of its application and needs to be evaluated.

Aim: To evaluate and compare the efficacy of both omentoplasty and a newly introduced fibrin sealant; TachoSil[®]; in decreasing the rate of anastomotic leakage in colorectal anastomoses.

Results: 97 patients were included; 48 in omentoplasty group and 49 in TachoSil[®] group. The rate of clinical leakage in omentoplasty group was 8.3% and in TachoSil[®] group was 2%. Three out of four leakages in the omentoplasty group were sever (>500 cc/day) and the only case in TachoSil[®] group was less sever (<500 cc/day). The average hospital stay in omentoplasty group was 9.3 days and in TachoSil[®] group was 7.2 days ($P < 0.05$).

Conclusion: Omentoplasty proved no beneficial effect in sealing colonic anastomoses. There is a trend proving that TachoSil[®] is more effective than omentoplasty in preventing anastomotic leakage. The use of the collagen-bound fibrin sealant TachoSil[®] appears to be beneficial, being better than omentoplasty regarding the length of hospital stay and the severity of leakage, if leakage is inevitable.

Introduction:

A leak from an intestinal anastomosis is the complication most feared by the colorectal surgeon. Reported colonic anastomosis leak rates range from 1.5% up to 16% with mortality rates typically quoted between 10% and 20%.¹

Many factors were proven to affect the rate of anastomosis leakage; preoperative, intra-operative and postoperative. For example: age, sex, general fitness of the

patient, anastomotic tension, resection in an emergency setting, tumour stage, distal site, the need for postoperative blood transfusion, fecal contamination, increased blood loss during surgery, low preoperative serum albumin level, steroid use and increased duration of surgery.²⁻⁶

In order to decrease the rate and the severity of anastomotic leakage and infective complications, several methods have been proposed such as antibiotic prophylaxis,

colonic preparation with antiseptic enemas, fecal diversion for protecting high-risk anastomoses, biofragmentable anastomosis ring and pelvic irrigation.⁷ External coating of anastomoses with various materials has been proposed as a means to reduce the leakage rate.⁸

The omentum has long been used in gastrointestinal, cardiothoracic, neurological, gynaecological, orthopaedic, vascular, urological, plastic and reconstructive surgeries.⁹

The role of omentoplasty in securing anastomoses after oesophageal resections is well-established.¹⁰ Its role in securing colorectal anastomoses shows some controversy: being recommended by some authors,¹¹⁻¹³ to be of equivocal value to others⁷ and to recommend against by a third group of authors.¹⁴

Performing an omentoplasty is not without risks. Although uncommon, complications such as haemorrhage, necrosis of omentum and attribution to an internal herniation have been described.¹⁴

Even though technical modifications have decreased the rate of leakage in colonic anastomosis, the high mortality and severe morbidity in patients suffering from anastomotic leakage justify the necessity for evaluation of additional methods for decreasing the rate of anastomotic failure in these operations.¹⁵

Collagen-bound fibrin sealant sheets have recently been used in many aspects of surgery; for example: Hernia,¹⁶ Gastro-intestinal,^{17,18} ophthalmic,¹⁹ gynecologic & obstetric,²⁰ renal,²¹ vascular²² and cardiac^{23,24} surgeries; and many experimental animal studies proved its efficacy in securing GI anastomoses.²⁵⁻²⁷

In 2010, Huh et al. performed a prospective study involving 223 patients with rectal cancer who underwent laparoscopic resection. One group underwent surgery followed by application of fibrin sealant over the stapled anastomosis, while the other group underwent surgery alone. The clinical leakage rate was 5.8% for the fibrin group and 10.9 % for the other group.²⁸

De Stefano et al in 2011 conducted a study

on 63 open resective colorectal surgeries and concluded: "Our initial experience with TachoSil[®] has confirmed the safety of this patch and we can therefore suggest a possible positive effect on anastomotic healing".²⁹

In 2012, Parker et al¹⁷ concluded that the application of TachoSil[®] to reinforce the anastomotic line in colorectal resections appears to be feasible and well tolerated in most circumstances.

Aim of the work: In this study we are evaluating and comparing the efficacy of both omentoplasty and a newly introduced fibrin sealant; TachoSil[®]; in decreasing the rate of anastomotic leakage in colorectal anastomoses.

Patients and methods:

The study is carried out between May 2010 and April 2013 in 3 hospitals; namely: Menoufiya University hospital, Shibin Alkom, Egypt, King Saud hospital, Unayzah, KSA and Al-Hayat Private hospital, Jeddah, KSA. The study is prospective and patients' choice will be on consecutive basis; being alternating between both using omentoplasty and TachoSil[®] patch to externally wrap the completed anastomosis. The study is approved by the appropriate authority in each hospital. The colon will be chemically and mechanically prepared, thus patients undergoing emergency surgery will not be included. Patients with known allergy to any of the components of collagen-bound fibrin sealants will be excluded from the study.

Surgical technique: The surgical technique for resection anastomosis will be standardized according to the ASCRS Manual of Colon and Rectal Surgery.³⁰ Drainage of the abdominal cavity will be left to the choice of each surgeon.

In this study we will include only the clinically evident anastomotic leakage, thus the investigation for leakage will start on clinical basis i.e. if the patient is suffering abdominal pain, tenderness, fever, and/or leucocytosis. The occurrence of anastomotic leakage will be evidenced by the presence of fecal discharge through the pelvic drain left intra-operatively or inserted after radiological

evidences of leakage. Gastrograffin enema for detection of preclinical leakage will not be performed on routine basis.

All operations will be carried out by 3 surgeons using either hand sewn or a stapled technique without a protective stoma. After completing the anastomosis, and testing for air tightness,³¹ the patient will be assigned to either covering the anastomosis with an omentoplasty or with a TachoSil® patch.

Omentoplasty is defined as “A surgical procedure in which a portion of the greater omentum is used to cover or fill a defect, augment arterial or portal venous circulation, absorb effusions, or increase lymphatic drainage”.³²

We will follow the standard surgical techniques while performing omentoplasty, making sure that the vascular pedicle is intact, taking in consideration the valuable notes by Topor et al.¹²

TachoSil® is a registered trademark of Nycomed Pharma AS. It is a sterile, ready to-use, absorbable surgical patch consisting of an equine collagen sponge coated with human fibrinogen and human thrombin measuring 9.5 x 4.8 x 0.5 cm. This new carrier bound fibrin sealant was approved by the FDA,³³ the Scottish Medicines Consortium,³⁴ and the European Medicines Agency - Committee for Medicinal Products for Human Use.³⁵

While using TachoSil® patch, it will be pressed gently over the anastomotic line for 1-3 minutes, making sure that the sheet covered and adhered to at least one cm on each side of the anastomosis.

In each patient, we will record the following data (among others)³⁶: Age, gender, American society of anesthesiologists score (ASA) score, body mass index (BMI), smoking, alcoholism, steroids, neo-adjuvant therapy, site of anastomosis, intra-operative blood loss, post-operative blood transfusion, duration of surgery, use of drain, clinical leakage, severity of leakage, hospital stay, postoperative complication, postoperative mortality, anastomosis done manual or mechanical and time of evidence of GIT movement.

Each of these factors will be compared

between both groups with two intents: testing for homogeneity of the demographic data between the two groups, as well as comparing the outcomes. Patients will be followed up for 45 days postoperatively for evidences of leakage and other surgery-related complications. The average cost of TachoSil® patch per patient will be calculated.

Statistical analysis: The data collected were tabulated and analyzed using SPSS statistical package version 12 on IBM compatible computer. Groups were compared using the Chi square test for categorical variables and Student's t-test for continuous variables. Qualitative data were expressed as number and percentage (No and %) and analyzed by applying Chi-square test (X² test). All these tests were used as tests of significance at P < 0.05.

Results:

97 patients were included in this study, with an average of 11 patients per year for each hospital during the study period (3 years). We excluded one patient from the study who was found to have an atrophied omentum. We encountered no patients with allergy to any of the components of the collagen-bound fibrin sealant used in this study.

When the omentum was mobilized, it was most often based on the left gastroepiploic artery and it was wrapped loosely around the suture line, and fixed to the colonic segments proximally and distally by separate sutures. The average cost of TachoSil® patches per patient was 210 US Dollars. The mean postoperative stay in TachoSil® group was 7.2 days, and in omentoplasty group was 9.3 days (P < 0.05).

Table (1) represents the results of the study. A comparison between the two groups was done, taking the significance level to be at or less than 0.05%.

Discussion:

The uncomplicated healing of an intestinal anastomosis even after attentive technical performance from an experienced surgeon is still a challenge because the healing process is dependent on multiple physiological,

Table 1: the results of the study and a comparison between the two groups.

Item		Omentoplasty N= 48 patients	TachoSil® N= 49 patients	P value
Age (years)		48.87±6.43	51.51±9.68	0.11
Gender	Male	30/48	27/49	0.45
	Female	18/48	22/49	
ASA Score	I	5/48	6/49	0.74
	II	20/48	25/49	
	III	18/48	14/49	
	IV	5/48	4/49	
BMI	30 and above	3/48	4/49	0.71
	Loss of >5kg in 6 months	11/48	14/49	0.52
Smoking	yes	22/48	17/49	0.26
	No	26/48	32/49	
Alcoholism	yes	3/48	2/49	0.62
	no	45/48	47/49	
Steroids	yes	1/48	1/49	0.98
	no	47/48	48/49	
Neo-adjuvant Therapy	Radiotherapy	1/48	0/49	0.29
	Chemo- radiation	10/48	6/49	
	No	37/48	43/49	
Site of anastomosis	Right colon	9/48	9/49	0.84
	Left colon	11/48	9/49	
	rectum	28/48	31/49	
Intra-operative blood loss	Less than 500	8/48	5/49	0.46
	500-1000	22/48	28/49	
	More than 1000	18/48	16/49	
Post-operative blood transfusion	yes	11/48	6/49	0.16
	no	37/48	43/49	
Duration of surgery (minutes)	Less than 2 h	9/48	7/49	0.75
	2-4 hours	28/48	32/49	
	More than 4 h	11/48	10/49	
Use of drain	yes	22	17	0.26
	No	26	32	
Clinical leakage	yes	4/48	1/49	0.16
	No	44/48	48/49	
Severity of leakage	Less than 500	1/4	1/1	0.17
	More than 500	3/4	0/4	
Hospital stay (days)		9.3±2.1	7.2±1.9	<0.05

Item		Omentoplasty N= 48 patients	TachoSil® N= 49 patients	P value
Post-operative Complication	Wound complication	6/48	7/49	0.79
	Chest & UTI infections	13/48	14/49	0.87
	DVT	3/48	7/49	0.19
Postoperative mortality		1/48	0/49	0.31
Anastomosis done...	Manual	14/48	20/49	0.22
	Mechanical	34/48	29/49	
Time of evidence of GIT movement		6.5±1.52 days	4.8±1.15 days	< 0.05

biochemical, and morphological factors.³⁷

Anastomotic leaks are detected anywhere from 3 to 45 days postoperatively, and the diagnosis is mostly made between days 6 and 9. However, it stands to a reason that the processes which lead to the failure start much earlier, probably in the immediate postoperative period when the wound strength is believed to be low.²⁷

In our study, omentoplasty proved to be simple to perform and not time consuming, as evidenced by comparing the operative time between the two groups, where no statistically proven difference was noticed between the two groups ($P > 0.05$). No complication was noted due to the use of omentoplasty in our study during the follow up period. One limitation for the use of omentoplasty is atrophy of the omentum which may be congenital or acquired.³⁸

Anastomotic leakage after colectomy is one of the most serious complications in colorectal surgery. Best defined as “leak of luminal contents from a surgical join between 2 hollow viscera,” its incidence ranges from 2% to 4% with proximal anastomosis, to 6% to 12% with distal extraperitoneal anastomosis, and is associated with mortality rates of 10-30%.³

When comparing the two groups regarding the demographic data and other factors **Table (1)**; there was no statistically significant difference between both groups ($p > 0.05$), except in the length of hospital stay and the time of evidence of GIT movement (where $p < 0.05$).

The overall incidence of anastomotic leakage in this study is 5.15% (5/97), which is towards the lowest rate reported in other studies;¹ this may be attributed to the patient selection, as we excluded from this study all emergency colectomies. Emergency colectomy is well-documented to be associated with higher incidence of anastomotic leakage.³⁷

We excluded the emergency colectomies from this study due to a previous work by Chmelnik et al.³⁹ Their experimental study in rats showed severe pre-anastomotic dilatation in additionally sealed small-diameter anastomoses when using a fibrin-coated collagen patch. They attributed this finding to increased inflammation as a result of bacterial contamination and a disproportion between bowel wall and patch thickness. They reported: “As a result of our findings, the application of TachoSil® in small-diameter intestinal anastomoses cannot be recommended. Whether TachoSil® generally can be safely used in bacterially contaminated tissues needs to be investigated in future studies”. Thus, we excluded emergency colectomies to avoid applying TachoSil® in a heavily contaminated tissue.

Most of the recently published studies^{40,41} suggest that mechanical bowel preparation is of no value regarding the anastomotic integrity; a point that is in favour of omentoplasty and against TachoSil®. As already mentioned, it is better to avoid using TachoSil® in the presence of heavy bacterial contamination,³⁹ while such recommendation

is not applicable with omentoplasty. Colon preparation with antibiotics has recently been proved beneficial.⁴²

The rate of leakage in the TachoSil® group was 2% (1/49); while in the omentoplasty group it was 8.3% (4/48), which implies no beneficial effect of omentoplasty in preventing anastomotic leakage. This is in accordance with the most recent publication in this field.⁴³

When comparing the 2 groups, we found no statistically significant difference between the incidences of leakage after omentoplasty compared to the application of collagen-bound fibrin sealant ($P > 0.05$). However, the study showed that there is a trend of the collagen-bound fibrin sealant to be more effective than omentoplasty, because the rate was 4 cases in the omentoplasty group and one case in the TachoSil® group. Failure to demonstrate a statistically significant difference may be due to the relatively small number of the cases included in this study.

Another finding in our study is that: if leakage is going to occur, it tends to be less severe in the TachoSil® group compared to the omentoplasty group. Three out of four leakages in the omentoplasty group were severe leakages (> 500 cc per day), while the single case of leakage in TachoSil® group was less severe (< 500 cc day). This can be attributed to the difference in the mechanism of action between omentoplasty and TachoSil® in sealing the anastomosis.

Omentoplasty works to protect the anastomosis in many ways:

When placed in contact with an anastomotic gap, an entirely viable omentum forms an effective bridge over anastomotic defects and responds with an outgrowth of richly vascular tissue, which acts as the major vascular source to the wound. Omentoplasty provides an adherent sleeve that plugs or locally contains early anastomotic leakages during the dangerous period before revascularization occurs. The stimulated neo-angiogenesis and the richly vascularised tissue also could act as protective factors, lowering the incidence of anastomotic stricture.¹³

The mechanism of action of TachoSil®

follows the principles of physiological fibrin clot formation. Upon contact with a bleeding or leaking wound surface, or triggered by the presence of physiological saline, the coating of the collagen sponge dissolves and the subsequent thrombin-fibrinogen reaction initiates the last step of the coagulation cascade: Fibrinogen is converted by the action of thrombin into fibrin monomers which spontaneously polymerise to a fibrin clot. Thrombin can also activate endogenous factor XIII which covalently cross-links the fibrin to create a firm and stable fibrin network.³⁵

This stable fibrin clot leads to sealing of the anastomosis in many ways: the physical barrier created by the fibrin clot, the facilitation of tissue approximation, the promotion of tissue healing by the components, and the creation of adhesion with surrounding tissues.²⁸

These mechanisms of action of TachoSil® are reflected in our study: both the rate and the severity of leakage are lower in the TachoSil® group than the omentoplasty group.

In the postoperative period, the bowel anastomosis should be able to withstand forces in different directions. The bursting pressure, which reflects the capacity of the anastomosis to resist intra-luminal forces, is a good marker to test anastomotic strength.⁴⁴ Many researchers examined the effect of fibrin sealant on the bursting pressure following anastomoses and proved a beneficial effect.^{45,46}

It is known that colonic anastomoses are most fragile on days 3 and 4 because of low collagen content mediated by high activity of colonic collagenase induced by injury to the bowel wall during the healing phase of the anastomosis and on day 7 after anastomosis, collagenolytic activity reverts to normal values.¹⁵

We should stress that collagen-bound fibrin sealants are different from the earlier fibrin glues. Early studies on using fibrin glues to seal colon anastomoses were disappointing, with evidence that the glue inhibited wound healing and decreased anastomotic strength, burst strength, and collagen deposition at

treated wound sites. Fibrin glues may also inhibit macrophage migration and neutrophil function.^{25,27}

In our study, when we compared both groups regarding the timing of regaining gastrointestinal movement, we found a statistically significant result proving that omentoplasty, in some way; delays the recovery of gastrointestinal movement. This result was reported in a previous study.¹⁴ In this aforementioned study, the authors explained that the mechanisms involved, are the presence of a pedicled omentum in the abdominal cavity causing a relative mechanical obstruction and the devascularization of the greater curvature of the stomach, thus delaying gastric functioning.

The safety of TachoSil[®] in sealing of gastrointestinal anastomoses with a collagen patch coated with fibrin components has been proven before in a study by Nordentoft et al.²⁶ Their study revealed equal healing strength, and complication rate after sealing with a collagen patch coated with fibrin glue components compared with unsealed anastomoses. Furthermore, they found no difference in stenoses of the anastomoses. Another reported value of Fibrin sealants is decreasing intra-abdominal adhesions.⁴⁷ Furthermore, one study proved TachoSil[®] has no negative physiological or histological side effects.²⁶ Also, the feasibility of the application of TachoSil[®] for sealing colorectal anastomosis was proven.¹⁷

A shorter mean postoperative stay of 7.2 days was observed for patients where TachoSil[®] was applied compared to 9.3 days for patients of no- TachoSil[®]. This difference was mainly related to anastomotic insufficiencies recorded in the no- TachoSil[®] group. This was in accordance with a recent study from Italy.²⁹

Another point against TachoSil[®] is the possibility of transmission of blood-borne diseases. There is a potential risk of transmission of micro-organisms from the blood samples that are used to produce TachoSil[®], even if, according to the manufacturer, blood comes only from selected donors and all the active measures

against enveloped viruses are used.⁴⁸

In a comprehensive review of External coating of colonic anastomoses, Pommergaard et al⁸ concluded that the only beneficial effect of all the fibrin sealants was that of using TachoSil[®].

In our study, the average cost per patient in the TachoSil[®] group was 210 USD, which could be an argument against its use. This extra-cost could be compensated for, at least in part, by the shorter hospital stay. In our study, the TachoSil[®] group patients stayed for a shorter time in hospital and the difference from the omentoplasty group is statistically significant ($P < 0.05$). This finding was reported before.⁴⁹

One more argument against TachoSil[®] is its being a source of fibrin, thus it may lead to increase in the incidence of thrombotic complications postoperatively. In our study, there is a slight increase in the incidence of DVT in the TachoSil[®] group compared to the omentoplasty group, but it was not statistically significant ($P < 0.05$). The main effect of TachoSil[®] is the local activation of the coagulation cascade leading to the local deposition of stable fibrin network.³⁵ Whether or not this activation of the coagulation cascade can reach the systemic circulation needs further study.

Conclusion :

Within the limitation of the patient number included in this study, we conclude that omentoplasty proved no beneficial effect in sealing colonic anastomoses. There is a trend proving that TachoSil[®] is more effective than omentoplasty in preventing anastomotic leakage. The use of the collagen-bound fibrin sealant TachoSil[®] appears to be beneficial, being better than omentoplasty regarding the length of hospital stay, the timing of GIT movement and the severity of leakage, if leakage is inevitable. We agree with Konstantinos et al⁴² who reported: “the field of tissue adhesives is gaining ground in GI surgery. Despite years of research, the ideal tissue adhesive is yet to be found; however, the benefits of using adhesives are becoming more apparent”.

Conflict of interests:

The authors declare that they have no conflict of interests.

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