

Application of collagen matrix in the prevention of anastomotic leaks following D2 gastrectomy with Roux-en-Y anastomosis

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ABSTRACT: Esophagoenteral anastomotic leaks are one of the most serious complications of gastric cancer surgeries. Leaking anastomosis has a negative impact on patient's prognosis as it translates into increased reoperation rates, direct and indirect mortality, as well as increased risk of cancer recurrence. Literature contains reports on the use of additional measures aimed at preventing anastomotic leaks. Collagen matrices with tissue adhesives used to prevent anastomotic leaks following D2 gastrectomy with Roux-en-Y anastomosis have not been described well in Polish literature. However, international reports on such use of these materials are available. Collagen matrices have been successfully applied in selected patients undergoing total or subtotal gastrectomy at the Department of General, Minimally Invasive, and Gastroenterological Surgery. We hereby present our experience in a group of 6 patients presenting with anastomotic leak risk factors.

KEYWORDS: anastomosis, collagen matrix with tissue glue, gastrectomy, leakage

ABBREVIATIONS

BMI – Body Mass Index
CT – computed tomography
ERAS – Enhanced Recovery After Surgery
HGB – hemoglobin
HTC – hematocrit
RBC – red blood cells

Gastric cancer ranks among the top ten of the most prevalent cancers in Poland. According to estimates, the incidence rate continues to exceed 5,000 cases per year [1]. Total gastrectomy with D2 lymphadenectomy is a standard of treatment for advanced gastric cancer in Poland and worldwide. The treatment involves extensive abdominal surgery with formation of esophagoenteral anastomosis to restore the continuity of gastrointestinal tract after the removal of the stomach [2]. Due to its extent, the surgery is associated with a number of possible complications. These include bleeding, anastomotic leaks, and intraabdominal infections. One of the most serious complications which may result in treatment failure is the esophagoenteral anastomotic leak. Various studies estimate the risk of this complication at 1–11% of cases [3]. Although the rates of complications are gradually reduced with the progress along the learning curve, and despite the use of modern medical instrumentation, including mechanical staplers [4], an additional post-operative risk consists in malnutrition of cancer patients which remains a major challenge in the era of advanced procedural techniques. With the development of endoscopic techniques, the possibilities for the treatment of these complications were expanded, with coated prosthetic grafting techniques [5] and other techniques such as endoVAC [6] being applicable. Despite the availability of various modalities for the management of complications, they continue to be responsible for prolonged hospitalization, the need for resurgery, or increased mortality rates of up to 50% [7]. Therefore, it is important to look for solutions that would reduce the risk of anastomotic dehiscence following enteric and gastric resection procedures. One of such solutions with the potential for the reduction in the incidence of anastomotic

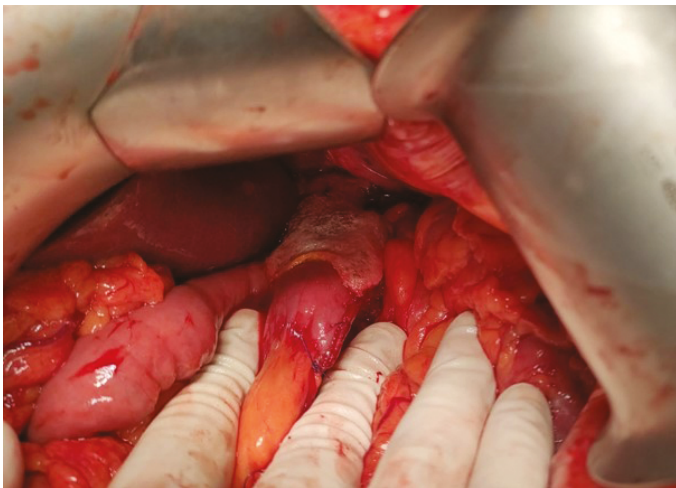
leak-related complications in the future, consists in TachoSil medicinal product consisting of fibrinogen and thrombin-coated collagen matrix, being applied at the site. To date, TachoSil was used in general surgery as a local hemostatic agent to stop bleeding from mesenchymal organs, its effectiveness being confirmed in a repeatable fashion. Fibrinogen and thrombin-coated collagen matrices were also used to stop bleeding from the liver [8] and spleen [9], as well as bleeding following tonsillectomy procedures [10]. The matrix presents with significant adhesive properties providing additional support and hemostasis at application site. In 2014, results of experimental studies were published showing a significant reduction in the rates of colonic anastomotic leaks in an animal model [11]. In recent years, a growing number of publications suggested that this use of coated collagen matrices can provide an effective way to reduce the risk of anastomotic leaks in human medicine [12–15]. In a further animal model study carried out by al-Saeedi in 2018, the adhesion of collagen matrix with tissue glue was shown to be highest among all the assessed materials, amounting to 90 mm Hg when used for sealing bile leakage [16]. The sealing properties of TachoSil were also confirmed by Ebel et al. The results of their in vitro study published in 2021 were demonstrative of the high adhesion strength of 74.17 ± 12.64 cm H₂O in a dura mater sealing model [17].

Marano et al. published the results of their study confirming the efficacy of collagen matrix with tissue glue in upper gastrointestinal cancer surgeries. In a group of 62 patients, the researchers demonstrated that the use of collagen matrix at the anastomosis staple line is useful to reduce the overall incidence of postoperative complications in the collagen matrix group, with a significant difference in anastomotic leak rates amounting to 0% in the collagen matrix group compared to 11.7% in the control group, $P < 0.001$ [18].

A male patient, aged 85, was admitted at the Department for gastric adenocarcinoma surgery. The tumor was diagnosed in gastroscopic examination performed due to significant loss of appetite and body weight. Examination revealed a circumferential tumor infiltrate at the body and antrum region. Signs of gastric lumen

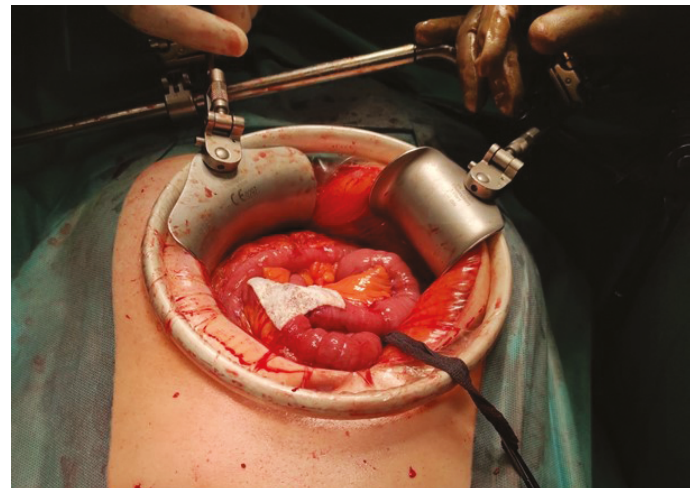
Tab. I. Anastomotic leak risk factors within the study group.

RISK FACTORS	PATIENT 1.	PATIENT 2.	PATIENT 3.	PATIENT 4.	PATIENT 5.
Male gender	X		X		X
Diabetes	X			X	X
Smoking		X		X	
Albumin level $n < 3.5$ mg/dL					X
Operation time > 150 – 180 min	X	X	X		
Age > 70 years					X

**Fig. 1.** Application of fibrinogen and thrombin-coated collagen matrix onto the enteroesophageal anastomosis.

narrowing were observed. Signs of necrosis and past bleeding were observed within the reported lesion. No liver metastases or enlarged lymph nodes were observed in CT scans acquired as part of in-depth diagnostics. Stomach walls thickening of up to 18 mm was observed at the site of infiltration, along with blurred presentation of the surrounding fat tissue. After a case conference, the patient was qualified for the primary surgical procedure. The body mass index (BMI) at admission was 27.4. Anemia was found in laboratory investigations performed on the day of admission: RBC 4.54 M/ μ L; HGB 10.9 g/dL, HTC 34.8%. A reduction in total proteins (5.69 g/dL) was observed with no signs of hypoalbuminemia. No other significant deviations were observed. Additional medical burden consisted of long history of diabetes (30 years) requiring insulin therapy, and hypertension. Echocardiographic examination was performed prior to the surgery, revealing no abnormalities. The surgery was preceded by nutritional support being provided to the patient for 5 days. After this period, the patient was subjected to gastrectomy D2 lymphadenectomy (the duration of the surgery was 145 minutes).

In light of the chronic comorbidity burden and the patient's age, the TachoSil collagen matrix was used when establishing the stapled esophagoenteral anastomosis during the gastrectomy. The matrix was placed around the staple line prior to the final cut and the removal of the stapler from the gastrointestinal tract lumen. After gentle pressure had been applied for approximately 5 minutes, the humidified matrix was well pressed against the surface of the newly formed esophagoenteral anastomosis. Postoperative management included full parenteral nutrition and an insulin pump to control blood glucose levels. Anastomotic leak test was performed 5 days

**Fig. 2.** Application of fibrinogen and thrombin-coated collagen matrix onto the enteral anastomosis.

after the procedure, followed by the removal of peritoneal drains. No evidence of contrast leaking beyond the gastrointestinal tract lumen was observed. Transient hypoalbuminemia was detected in additional postoperative investigations. The C-reactive protein level reached its peak at 53.6 mg/L. No transfusion of blood products was required. After oral nutrition had been resumed in adherence to dietitian's recommendations, the patient was discharged home in good overall condition.

The above procedure was subsequently repeated in 5 consecutive patients with no leak-related complications being observed in either case. All patients had presented with 2–4 risk factors for anastomotic leak. All the risk factors within the patient group are summarized in Tab. I.

Being fully aware that our study group is not statistically representative in any way, we believe that stepping up the research in this area would be advisable.

Extensive abdominal surgeries have always been associated with the risk of perioperative complications. In the case of total gastrectomy due to gastric cancer, this risk is further increased by additional factors such as carcinogenesis and progressive cachexia, comorbidities, or patient's age [19]. An important aspect of the surgical treatment being provided to cancer patients consists in the search for methods which reduce the risk of adverse events, with anastomotic leak being undoubtedly such an event. When preparing the patient for the procedure, it is worthwhile to introduce pre-rehabilitation principles which would facilitate faster recovery and reduce the risk of complications, particularly pulmonary



Fig. 3. Preparation of fibrinogen and thrombin-coated collagen matrix prior to application.

and cardiovascular complications. Nutritional support appears particularly important to avoid or reduce the degree of malnutrition caused by cancer. These principles will also facilitate broader application of ERAS protocols, thus reducing the burden exerted on the healthcare system by excessively long hospital stays. On the other hand, the development of instrumentation and operating techniques contributes to increased patient safety in the operating room. One such innovation includes the use of fibrinogen and thrombin-coated collagen matrices for protection of enteral and gastrointestinal anastomoses. All reports indicate that the technique may result in better anastomotic healing and reduced number of complications. This has also been confirmed by an Expert Panel statement as published in 2017 [19].

Complications associated with anastomotic leaks following cancer surgeries delay the subsequent treatment stages, thus reducing the patient's chances for being cured. They also lead to incalculable increase in the costs of treatment and social care for the patient. When preparing for the surgery, it may be advisable to evaluate the patient for the risk factors of anastomotic leak [19, 20]. The cost of collagen matrix being used in the high risk group appears to be significantly lower than the cost of prolonged hospitalization and, above all, potential resurgery due to anastomotic failure. However, the efficacy of the method cannot in any way be determined until appropriate studies are performed in broader populations.

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