

**UNIVERSITY OF MEDICINE, PHARMACY, SCIENCES AND TECHNOLOGY OF
TARGU MURES**

PhD THESIS SUMMARY

**CLINICAL, IMMUNOHISTOCHEMICAL AND EXPERIMENTAL
EVALUATION OF ANASTOMOTIC LEAKAGE IN COLORECTAL
SURGERY**

PhD. Dr. GABRIEL ALEXANDRU POPESCU

Scientific Coordinator, Prof. Dr. LEONARD AZAMFIREI

Introduction

Despite the continuous developement of modern surgical techniques over the past decades, anastomotic leakage (**AL**) remains one of the most important and dreaded complications of colorectal surgery. Not only is it associated with high morbidity and mortality rates, but there is also a frequent need for hospital readmission, surgical reintervention, and prolonged hospitalization time, therefore the patients' quality of life is significantly impaired. Prediction and early recognition of AL is a challenging task, due to the multitude of clinical presentations, which are often indistinguishable from symptoms caused by postoperative physiological inflammatory response.

Aim

The purpose of this study is to determine the AL incidence and mortality rates after colorectal resection followed by "per primam" anastomoses for malignancies, for both emergency and elective surgery. In addition to this, we tried to assess the impact of two types of termino-terminal colon anastomosis on colonic mucosal healing on one hand, and the risk of anastomotic fistula based on increased levels of fatty acid binding proteins (I-FABP) in rats, on the other.

Clinical study

Anastomotic leakage is defined as a continuity defect, localized at the anastomosis site, hence creating a communication between intraluminal and extraluminal compartments. Numerous studies have investigated the causes of anastomotic leaks, in order to prevent and efficiently treat this perioperative complication. We included in our study clinical and surgical data from 431 patients that were operated in Second General Surgery Department, Clinical County Emergency Hospital Targu Mures, between January 2010 and December 2014. They were diagnosed with colorectal cancer, for which resection with restoration of digestive tube continuity through anastomosis was performed.

Experimental study

In this study, we attempted to determine whether the type of termino-terminal anastomosis affects the healing process of the intestinal mucosa and if the severity of the anastomotic leakage can be predicted based on the circulating level of intestinal-fatty acid binding protein. I-FABP is considered a marker of mucosal injury and ischemia, therefore serum I-FABP level is used as a tissue damage indicator. For our experiment, we used 18 healthy rats, on which we performed two types of segmental resection of the colon, followed by anastomosis; postoperatively we determined serum I-FABP, IHC expression of I-FABP in intestinal mucosa and peri-anastomotic tissue and analysed the histological features.

Discussions

Although AL is a major complication of colorectal surgery, no particular risk factors have been identified, so that the occurrence of fistula might be prevented. Tumor localization, as well as the type of resection and anastomosis, may influence the rates of anastomotic fistulas, though our study showed no statistically significant correlation. Usually, anastomotic leakage is diagnosed between day 5 and day 8 postoperatively. Early diagnosis of this complication, prior to the onset of generalized peritonitis, is essential when it comes to improving vital prognosis.

Our study confirms that the risk of fistula can be predicted by the increase in serum I-FABP levels, and the I-FABP serum level reached postoperatively, depends on the length of the ischemic mucosa, which is itself dependent on the time of intestinal ischemia. In case of anastomotic fistula, I-FABP levels remain 4 times higher than normal 5 days postoperatively, and 30 times higher at 7 days after surgery. Histological findings demonstrate a reduction in ischemic intestinal cells or absence of I-FABP expression, leading to easier identification of the ischemic areas. It was also proven that vessel harvesting increases mucosal ischemia and that epithelial cells do not express I-FABP, independently from the serum level of this marker. In cases with anastomosis performed without vascular damage, the I-FABP loss in the epithelium is correlated with significant increase of I-FABP in serum at 3-5 days after surgery, but its tissue level decreases at 7 days, in parallel with the regenerative processes.

Conclusions

Anastomotic leakage is a major complication of colorectal surgery, leading to generalized peritonitis, septic shock, and multiple organ failure, thus associating significant mortality. In spite of all technical and technological advancement, anastomotic leaks are still relatively frequent after this type of interventions. Prevention and early diagnosis of AL is essential for improving both short- and longterm morbidity and mortality. Identification of risk factors, the use of scoring systems, imaging techniques and biomarkers (I-FABP), can help surgeons establish an accurate and timely diagnosis of fistula after colorectal surgery. The risk of AL does not depend on the anastomotic method, although ischemia levels are higher in anastomoses that involve vascular damage.