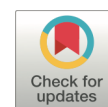


ORIGINAL ARTICLE



Management of perforations, leaks and fistulas of the gastrointestinal tract with clip on scope. Experience of a Latin American cancer center

Manejo de perforaciones, fugas y fístulas del tracto gastrointestinal con clip sobre el endoscopio. Experiencia de un centro oncológico Latinoamericano

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Abstract

Introduction. Fistula of the digestive tract derived from neoplastic diseases as well as leaks following surgical procedures are not uncommon and usually cause significant morbidity when are managed surgically. Diagnostic and therapeutic endoscopic procedures may present perforations during their performance; if they are managed non-operatively, an adequate recovery is obtained. The purpose of this study was to describe the clinical characteristics and the short and long-term outcomes of patients with perforations, fistulas and leaks of the gastrointestinal tract managed endoscopically with over the scope clip (OTSC).

Methods. Descriptive, retrospective study of patients brought to digestive endoscopy with OTSC placement with diagnosis of postoperative perforation, leak or fistula at the National Cancer Institute in Bogota, Colombia, between January 2016 and April 2020.

Results. Twenty-one patients were taken for OTSC application for the management of perforations, leaks and fistulas of the gastrointestinal tract, 52.4% of them were women. The median age was 66 years. The median diameter of

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the defect was 9 mm. Technical success was achieved in 95%. Early clinical success was described in 85.7% of the cases; 76.1% of patients remained symptom-free at 3-month follow-up.

Conclusions. Management of perforations, leaks and fistulas with OTSC appears to be feasible and safe. In most of these patients, clip release and endoscopic identification of closure was achieved immediately after management; however, in the case of fistulas, late clinical success was not achieved in all cases.

Keywords: intestinal perforation; intestinal fistula; anastomotic leak; digestive system endoscopy; gastrointestinal endoscopy; OVESCO.

Resumen

Introducción. Las fístulas derivadas de enfermedades neoplásicas del tracto digestivo, así como las fugas posteriores a procedimientos quirúrgicos, no son infrecuentes y ocasionan una morbilidad importante cuando se manejan de forma quirúrgica. También durante los procedimientos endoscópicos se pueden presentar perforaciones y, si se logra un manejo no operatorio, se alcanza una adecuada recuperación. El objetivo de este estudio fue describir las características clínicas y los resultados de los pacientes con perforaciones, fístulas y fugas del tracto gastrointestinal, manejadas endoscópicamente con clip sobre el endoscopio.

Métodos. Estudio descriptivo, retrospectivo, de pacientes con perforación, fuga o fístula postoperatoria, llevados a endoscopia digestiva con colocación de clip sobre el endoscopio, en el Instituto Nacional de Cancerología en Bogotá, Colombia, entre enero de 2016 y abril de 2020.

Resultados. Se incluyeron 21 pacientes, 52,4 % de ellos mujeres. La mediana de edad fue de 66 años y del diámetro del defecto fue de 9 mm. En el 95 % se logró éxito técnico. Hubo éxito clínico temprano en el 85,7 % de los casos. El 76,1 % de los pacientes permanecieron sin síntomas a los 3 meses de seguimiento.

Conclusiones. El manejo de perforaciones, fugas y fístulas con clip sobre el endoscopio parece ser factible y seguro. En la mayoría de estos pacientes se logró la liberación del clip y la identificación endoscópica del cierre inmediatamente después del procedimiento, sin embargo, en el caso de las fístulas, no se alcanzó el éxito clínico tardío en todos los casos.

Palabras clave: perforación intestinal; fístula intestinal; fuga anastomótica; endoscopia del sistema digestivo; endoscopia gastrointestinal; OVESCO.

Introduction

With endoscopic or surgical procedures on the gastrointestinal tract, several complications can occur, such as acute perforations and postoperative leaks or fistulas. The increase in endoscopic procedures, such as screening procedures, dilations, mucosal resections, endoscopic ultrasonography biopsies, endoscopic retrograde cholangiopancreatography, among others, may increase the frequency of accidental perforations¹. The incidence of perforation in diagnostic procedures has been reported between 0.01 and 0.6% and in the case of the-

rapeutic endoscopies, up to 5.5%. Although the frequency of this complication is low, it has a high morbidity and mortality².

These three clinical conditions have traditionally been managed with surgical interventions, adding disability and risk to the lives of patients, with the consequent increase in care costs.

In recent years, various options have been reported using endoscopic techniques for the management of these complications¹⁻³. The OTSC®, from English Over The Scope Clip (Ovesco endoscopy AG, Tübingen, Germany), is a system

consisting of a cup fitted over the endoscope and a device for releasing a nitinol clip, which has a high degree of elasticity and it provides the possibility of handling defects smaller than 2 cm, due to its ability to include the entire thickness of the tissue given its compression force^{4,5}; the affected tissue is captured with forceps, inserted into the cup, and then the clip is released¹. It is described that defects larger than 2 cm could be approached with endoscopic suture devices⁶.

The objective of this study was to evaluate the results of management by means of OTSC of patients with perforations, leaks or fistulas.

Methods

The database of the National Institute of Cancerology, Bogotá, D.C., Colombia, was reviewed, selecting adult patients treated with OTSC between January 2016 and April 2020, for the management of gastrointestinal tract perforations, leaks, and fistulas with minimal follow-up of 30 days.

Perforation was defined as a full-thickness defect, produced accidentally or intentionally, during a diagnostic endoscopy or one aimed at resection of a lesion; leak as that where there is a communication between the intestinal lumen and the surgical bed, usually after an anastomosis⁷, and fistula as an abnormal communication covered by epithelium between the lumen of the digestive tract and another space⁸, secondary to underlying disease or chronic leak.

The data found in the medical records of each of the patients selected in the collection instrument (RedCap 7.1.2[®] capture form) were recorded. Using the statistical program SPSS V17, the analysis of the different variables was performed.

Endoscopic procedure

All procedures were carried out under sedation in the endoscopy service. Initially, the solution of continuity in the digestive tract was identified and, prior to the use of suction or traction forceps to include the tissue in the cup, the assembly of the OTSC device was continued for its release.

A technically successful procedure was considered when clip release was achieved with endoscopic evidence of defect closure (9); early clinical success, when there was no clinical or imaging evidence of a persistent discontinuity, and late clinical success, when the patient did not present symptoms, signs, or images suggestive of persistent perforation, leak, or fistula in the digestive tract for the 3 months of follow-up.

Statistic analysis

All statistical analyzes were performed in the R – Project v4.0.3 software (R Core Team, 2020). In the first instance, it was determined whether the quantitative variables came from a population with a normal distribution (Shapiro-Wilk test: $p > 0.05$). Quantitative variables with normal distribution were expressed as mean along with their standard deviation, and those that did not present normal distribution were expressed as median and interquartile ranges, along with the minimum value and maximum value, which expressed the variable as complementary descriptive measures. Qualitative variables were characterized by absolute and relative frequencies (counts and percentages).

Results

At the National Institute of Cancerology, Bogotá, D.C., 21 patients underwent OTSC application between January 1, 2016 and April 30, 2020. The median age was 66 years (IQR=11), with values between 31 and 81 years (Table 1).

Clinical features

The indications for the procedure were perforation in seven patients (33.3%), suture leakage in three (14.2%), and fistula in 11 (52.3%). The cancer most frequently related to the indication for the procedure was stomach cancer (n=6), followed by head and neck cancer (n=4), and colorectal cancer (n=3). Only in two patients was the indication not related to progression of the neoplasia or its treatment. The most frequent medical history was cardiovascular disease.

Table 1. Clinical characteristics of patients undergoing clip-on-endoscope management.

Characteristics	Median (IQR)	Frequency (%)
Age, years	66 (11)	
Sex		
Female		11 (52.4)
Male		10 (47.6)
BMI, kg/m ²	22.7 (5.1)	
Defect diameter, mm	9 (5)	
Location of perforation, leak or fistula		
Esophagus		4 (19)
Stomach		10 (47.6)
Jejunum		1 (4.8)
Ileum		1 (4.8)
Colon		3 (14.3)
Rectum		2 (9.5)
Type and etiology of the clinical situation		
Perforations		7 (33.3)
Without intention		5
Intentional by resection		2
Leaks		3 (14.2)
Esophagojejunal anastomosis		1
Colocoloanastomosis		1
Gastrorrhaphy		1
Fistulas		11 (52.3)
Endoscopic gastrostomy		4
Previous surgery		5
Tumor compromise		2

Source: Own authors.

Etiology and description of cases

Seven acute perforations were handled and two of them were intentional, as part of the resection plan in the case of gastric neuroendocrine tumors with suspected infiltration of the submucosa, achieving a negative microscopic margin, which was considered sufficient for their treatment (10). The remaining five occurred accidentally, three in therapeutic procedures, and another two in diagnostic procedures (Figure 1).

Three leaks associated with surgical sutures were managed, one of them after a partial gastric resection, another after a colonic anastomosis,

and another due to a dehiscence of an esophagojejunal anastomosis, which could not be initially resolved with the placement of a stent. Technical and clinical success was achieved in all of them (Figure 2).

In the fistula group, the most frequent cause was the persistence of gastro-cutaneous communication after removal of the gastrostomy tube. There were two fistulas associated with tumor growth, in which clinical success could not be documented. Another five fistulas had a history of surgical management for stomach, prostate, colon, and rectal cancer (Figure 3).

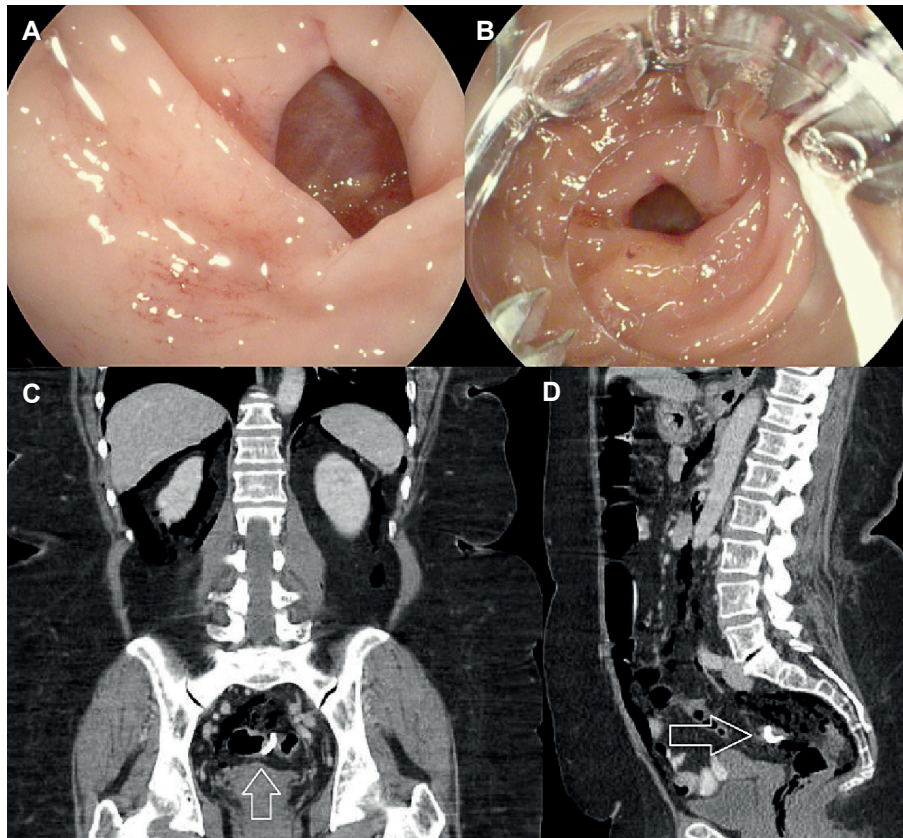


Figure 1. A. Perforation at the level of the rectosigmoid junction during diagnostic colonoscopy. B. Vision prior to OVESCO placement. C. Coronal image showing residual retroperitoneum with clip in proper position (arrow). D. Sagittal image confirming early clinical success, ruling out contrast medium extravasation with clip in proper position (arrow). Source: Own authors.

Outcomes

The clip could not be released in only one case due to the impossibility of facing the perforation. In two cases, radiological control showed persistent leakage, one due to an esophageal lesion during pulmonary lobectomy and another due to a sinus tumor with mediastinal compromise. In two more patients the signs of fistula reappeared during follow-up, one esophagomediastinal fistula due to esophageal cancer and another rectovesical case associated with colostomy closure (Table 2).

Of three patients who required stenting as an additional management to OTSC, late success was only obtained in one patient, as well as in half of the six patients who required surgical or percutaneous drainage.

There were no complications related to the placement of the device. In three cases the procedure was performed with the traction forceps and in most cases (90.5%) only one clip was required for closure.

Of the six patients (28.5%) who died during follow-up, in 3 OTSC treatment failure was documented, secondary to esophagopleural tracts: one with breast cancer, another of the esophagus, and another of the esophagogastric junction. The other three patients who died presented pulmonary thromboembolism, locoregional and distant progression, two due to gastric cancer and another due to tonsil cancer; however, the situation indicated by the OTSC was resolved.

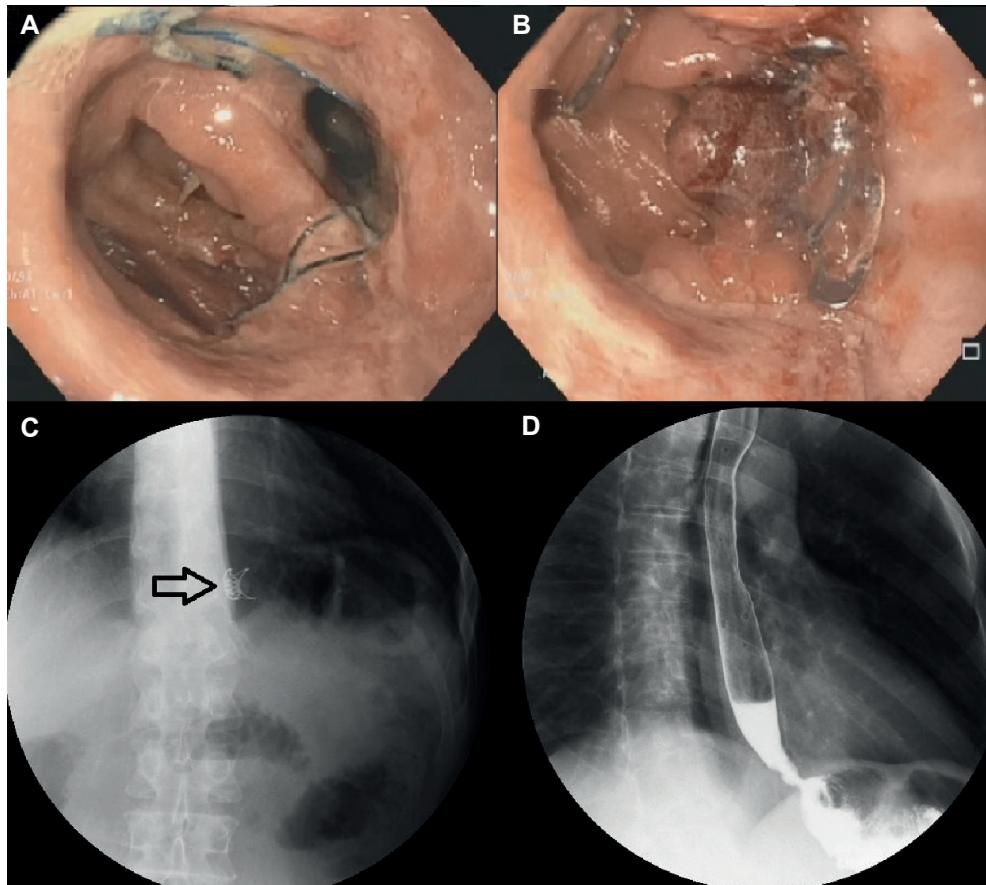


Figure 2. A. Esophagojejunoanastomosis leak endoscopic view. B. Ovesco properly released. C. Radiological control showing evidence of a clip (arrow). D. Absence of contrast medium leakage in x-ray of the digestive tract confirming (Early clinical success). Source: Own authors.

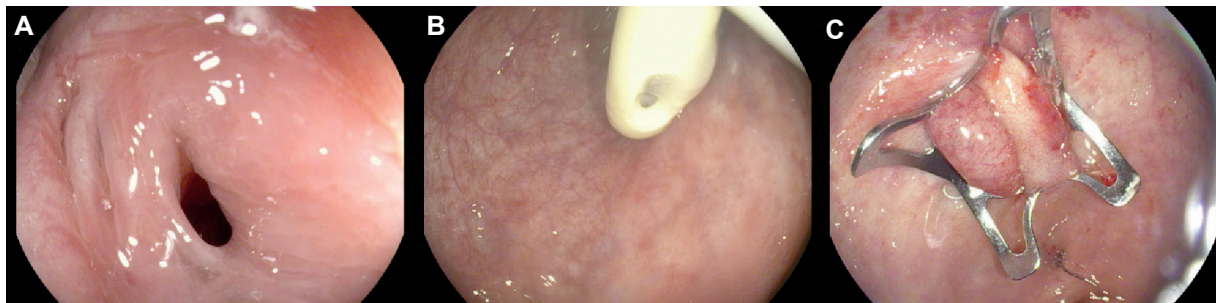


Figure 3. A. Rectovesical fistula. B. Identification of bladder catheter through fistula. C. Clip released with adequate fistula closure (Technical success). Source: Own authors.

Table 2. Result of clip-on-endoscope treatment (OTSC).

Result	Frequency (%)
Technical success*	
Yes	20 (95.2)
No	1 (4.8)
Early clinical success**	
Yes	18 (85.7)
No	2 (9.5)
Late clinical success***	
Yes	16 (76.1)
No	2 (9.5)

*Technical success: clip release was achieved with endoscopic evidence of defect closure. **Early clinical success: there was no clinical or imaging evidence of a persistent break in continuity. ***Late clinical success: absence of symptoms, signs or images suggestive of persistence during the 3-month follow-up. Source: Own authors.

Discussion

The incidence of perforations due to digestive endoscopic procedures depends on whether their intent is diagnostic or therapeutic; in the case of diagnostic endoscopy it ranges from 0.01 to 0.06%². In upper digestive procedures, the esophagus is most frequently affected, followed by the duodenum¹¹, while in the case of diagnostic colonoscopies, the main perforation site is the sigmoid colon, followed by the rectosigmoid junction.

In the Latin American literature, the causes for the use of this endoscopic device are variable, also describing its use in benign disease^{4,13}. For our group of patients, 90% of the cases were related to cancer or clinical situations derived from its treatment, results that are expected when coming from patients treated in an institution specialized in the management of cancer patients. Additionally, the indications are related to the morbidity associated with the management of cancer patients^{1,3}.

In this series, overall technical success was achieved in 95.2% of the patients, a value higher than the 93.8% reported in other series, without distinguishing the indication for OTSC¹⁴. The main causes of failure of this device are the inability to

endoscopically address the defect due to anatomical conditions, the rigidity of the surrounding tissue, and a diameter of the defect greater than the closing capacity of the device, situations that occur more frequently in fistulas².

In our study, the median of the defect was 9 mm, slightly higher than other studies that report medians of 7 mm¹⁴. A size greater than 20 mm has been described as a predictor of failure in treatment with OTSC¹⁵.

The overall clinical success of our series was 85.7%, higher than the 78% reported by Kobara et al.¹⁶ in a multicenter study that evaluated 1517 patients over 7 years. When specific clinical success for perforations was analysed, it reached 85.7%, similar to the 86% reported by Honegger et al.¹⁷. For patients with fistulas, clinical success was obtained in 81.8%, a value that is highly variable in the different publications (25-100%)^{15,18}. In the multivariate analysis performed by Haito-Chavez et al.¹⁴, patients who underwent OTSC placement due to perforations and leaks had significantly greater long-term success than those with fistulas (OR 51.4 and 8.36, respectively), a situation comparable to that observed in our series, where of the five cases that did not present late success, four had a fistula as an indication for the use of OTSC.

Intestinal anastomosis leakage after esophagectomy and gastrectomy for cancer management occurs in up to 8% of cases and has a mortality rate greater than 50%³. In the treatment of colorectal cancer, anastomotic leakage has been reported in 11% of patients, with a mortality of 12%¹, while in this series three leaks are described, all of them managed with clinical success, although the values reported in the literature for this group of patients are between 33 and 100%^{19,20}. In three of the five cases in which late clinical success was not achieved, the defects were located in the middle esophagus, a situation previously reported by Piyachaturawat et al. as a factor associated with treatment failure². Fistula cases after gastrostomy were fully resolved, similar to what has been reported in other studies²¹.

The complications associated with the use of this endoscopic system include the inclusion of

another structure at the time of device release and lumen stenosis in 1.7% of cases. In order to avoid these complications, the traction clamp was used in those cases where the location offered a risk. In this series, no complications of this type were observed during follow-up.

Our study has several limitations, including its retrospective nature, with a limited number of patients, which does not allow us to suggest possible factors associated with late clinical failure, especially in the case of patients with fistulas, where the heterogeneity of causes and associated conditions could explain these outcomes. However, this report is a contribution to the evidence under construction, it offers relevant information for the surgeon on endoscopic management with a system available in our environment in patients with leaks, fistulas, and perforations of the gastrointestinal tract, with or without an underlying oncological pathology.

Conclusions

The access and availability of this intervention is increasing in our environment, therefore, the knowledge of the usefulness, limitations and outcomes allows us to expand the therapeutic possibilities of our patients. Management of perforations, leaks, and fistulas with OTSC appears to be feasible and safe. In most cases, clip release and endoscopic identification of closure were achieved immediately after handling; however, studies aimed at determining factors associated with long-term failure of this intervention are necessary in our setting.

Compliance with ethical standards

Informed consent: This clinical research work adheres, both in its design and in its execution, following the principles established in the Good Clinical Practice guidelines of the International Committee for Harmonization and the ethical principles of the Declaration of Helsinki. Following the CIOMS guidelines and Resolution 008430 of October 4, 1993 of the Ministry of Health of the Republic of Colombia. The Research Ethics Committee of the National Institute of Cancerology, based on Resolution No. 008430 of 1993 of the Ministry of Health, which establishes technical and administrative scientific standards for health research,

established that this research corresponds to A risk-free study, therefore, informed consent is not required and, verifying compliance with the requested requirements, approved the research study through resolution N°-CEI-00921-20.

Conflict of interest: none declared by the authors.

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Author's contributions

- Conception and design of the study: Raúl Pinilla-Morales, Juliana Restrepo-López, Erika Benito-Flórez.
- Acquisition of data: Erika Benito-Flórez, Helena Facundo, Jorge Vélez, María Eugenia Manrique, Clara Briceño-Morales, Juliana Rendón.
- Data analysis and interpretation: Raúl Pinilla-Morales, Ricardo Oliveros, Juliana Restrepo-López, María Eugenia Manrique, Juliana Rendón, Clara Briceño-Morales.
- Drafting the manuscript: Raúl Pinilla-Morales, Silvia Guerrero-Macías, Jorge Vélez, Juliana Restrepo-López.
- Critical review: Ricardo Oliveros, Helena Facundo, Silvia Guerrero-Macías.

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