

Title:

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Authors:

David Villaescusa Arenas , Enrique Rodríguez de Santiago, Miguel Ángel Rodríguez Gandía, Sofía Parejo Carbonell, Beatriz Peñas García, Antonio Guerrero García, José Ramón Foruny Olcina, Ana García García de Paredes, Juan Ángel González Martín, Enrique Vázquez-Sequeiros, Agustín Albillos

DOI: 10.17235/reed.2022.8722/2022

Link: [PubMed \(Epub ahead of print\)](#)

Please cite this article as:

Villaescusa Arenas David, Rodríguez de Santiago Enrique, Rodríguez Gandía Miguel Ángel, Parejo Carbonell Sofía, Peñas García Beatriz, Guerrero García Antonio, Foruny Olcina José Ramón, García García de Paredes Ana, González Martín Juan Ángel, Vázquez-Sequeiros Enrique, Albillos Agustín. Over the scope clip (OTSC) as a rescue treatment for gastrointestinal bleeding secondary to peptic ulcer disease. Rev Esp Enferm Dig 2022. doi: 10.17235/reed.2022.8722/2022.

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Over-the-scope-clip (OTSC®) as a rescue treatment for gastrointestinal bleeding secondary to peptic ulcer disease

David Villaescusa Arenas, Enrique Rodríguez de Santiago, Miguel Ángel Rodríguez Gandía, Sofía Parejo Carbonell, Beatriz Peñas García, Antonio Guerrero García, José Ramón Foruny Olcina, Ana García García de Paredes, Juan Ángel González Martín, Enrique Vázquez Sequeiros and Agustín Albillos Martínez

Gastroenterology and Hepatology Department. Hospital Universitario Ramón y Cajal. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS). Centro de Investigación Biomédica en Red (CIBEREHD). Universidad de Alcalá. Madrid, Spain

Received: 18/02/2022

Accepted: 02/04/2022

Correspondence: Enrique Rodríguez de Santiago. Gastroenterology and Hepatology Department. Hospital Universitario Ramón y Cajal. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS). Centro de Investigación Biomédica en Red (CIBEREHD). Universidad de Alcalá. Madrid, Spain
e-mail: e_rodriguez_de_santiago@hotmail.com

Conflict of interest: Enrique Rodríguez de Santiago has participated in teaching and lecturing activities with Olympus. The rest of authors declare no conflict of interest.

ABSTRACT

Background and aims: over-the-scope-clips (OTSC®) have been proposed as a rescue treatment for bleeding peptic ulcers. However, their effectiveness has not been evaluated in Spain.

Methods: this retrospective and single-center study (January 2018-December 2021) assessed the technical success, clinical success and safety of the device within 30 days. All patients with upper gastrointestinal bleeding due to a peptic ulcer and treated with

the OTSC® clip (OVESCO) as a rescue therapy were included in the study.

Results: a total of eleven patients were included in the study, nine due to rebleeding and two due to persistent bleeding. Technical success was 81.9 % (9/11, confidence interval [CI] 95 %: 52-95 %). The per-protocol and intention-to-treat clinical success were 88.9 % (8/9, CI 95 %: 57-98 %) and 72.7 % (8/11, CI 95 %: 43-90 %), respectively. No device-related adverse effects were recorded.

Conclusion: the OTSC® clip was an effective and safe rescue therapy for bleeding peptic ulcers.

Keywords: Gastrointestinal hemorrhage. Peptic ulcer. Peptic ulcer hemorrhage. Over-the-scope-clip. Rebleeding.

INTRODUCTION

Non-variceal upper gastrointestinal bleeding (UGIB) due to peptic ulcer continues to be one of the main reasons for admission to gastroenterology departments (1). Currently, first-line endoscopic therapy includes the use of through-the-scope-clip (TTSC), thermal therapy and sclerotherapy, with a success rate of nearly 90 % (2,3). However, there is a percentage of patients in whom primary hemostasis is not achieved (5-10 %) or there is a rebleed (10-15 %) (4). This clinical scenario represents a therapeutic challenge and is associated with high morbidity and mortality and consumption of healthcare resources.

OTSC® (over-the-scope-clip) clips have become popular for the treatment of fistulas and perforations. In comparison with TTSC clips, OTSC® clips are able to grasp a larger surface area and have a higher closing force, which allows them to reach deeper tissue layers (5). These properties explain the growing interest in evaluating this system as a hemostatic treatment for gastrointestinal bleeding. In fact, new European and American clinical practice guidelines (6,7) propose their use as the treatment of choice for rebleeding and persistent bleeding in peptic ulcers. However, the effectiveness of this therapeutic modality has not been explored in Spain.

The aim of this study was to evaluate the effectiveness and safety of the OTSC® clip as a rescue treatment for UGIB secondary to a peptic ulcer.

METHODS

Design

All patients in whom the OTSC® clip (Ovesco Endoscopy AG, Tübingen, Germany) was used as rescue treatment (persistent bleeding or rebleeding) for UGIB due to peptic ulcer were included in this retrospective study. No exclusion criteria were established. Persistent bleeding was considered as bleeding that remained active after conventional first-line endoscopic therapy (sclerotherapy, thermal therapy or TTSC clips). Rebleeding was defined using international recommendations: a) melena or hematic aspirate in the nasogastric tube six hours after endoscopy; b) appearance of melena or hematochezia after normalization of stool color; c) decrease of more than 2 g/dl of the hemoglobin value after two stable hemoglobin readings (less than 0.5 g/dl variation) separated by at least three hours; d) occurrence of hemodynamic instability in the absence of an alternative explanation; or e) endoscopically by the presence of active bleeding on a second endoscopy or by an interventional radiological (embolization) or rescue surgical procedure (8).

The study period was from January 2018, when the first OTSC® clip was placed in UGIB, until December 2021. The information was collected from medical records, of both in-hospital and Primary Care. The study was performed in accordance with the Declaration of Helsinki and was approved by the Investigation Ethics Committee of our center (Code 296/21).

Outcomes

The primary outcomes were technical and clinical success. Technical success was defined as the application of the OTSC® clip over the peptic ulcer. Clinical success was defined as intraprocedural hemostasis (explicitly documented in the endoscopy report) and the absence of rebleeding within 30 days after device placement. Adverse events associated with the application of the OTSC® clip (stenosis, perforation, acute pancreatitis or unintended release) and 30-day mortality were secondary outcomes.

Endoscopy technique

The suction technique was used in all cases. The vessel of interest was placed in the center of the visual field and continuous suction was applied until OTSC® clip deployment (Fig. 1), similar to endoscopic band ligation therapy. No clamp/harpoon was used in any case for OTSC® placement. All endoscopists (n = 3) had experience with OTSC® clip placement in an indication other than UGIB.

Statistical analysis

The primary analysis of the study was the intention-to-treat analysis, which included all patients in whom OTSC® clip placement was attempted. Only technically successful patients were included in the per-protocol analysis. The 95 % confidence interval (CI) of the binary variables was calculated by the Wilson's method using the Stata/IC 14.1 program (StataCorp, Texas, USA).

RESULTS

A total of 260 UGIB of peptic origin were recorded during the study period. Endoscopic conventional treatment failed in 22 patients (8.46 %) (Fig. 2). A total of eleven patients treated with the OTSC® clip were included, nine due to rebleeding (81.9 %) and two due to persistent bleeding. The most frequent location of the ulcers was the anterior (n = 4) and posterior (n = 4) wall of the duodenal bulb. Most patients (n = 5) had received initial treatment with combination therapy. Patient characteristics are detailed in tables 1 and 2.

The technical success rate was 81.9 % (9/11, 95 % CI: 52-95 %). The OTSC® clip was not placed in one patient due to lack of visibility in the context of a massive hemorrhage, which required urgent surgical treatment. The other technical failure was secondary to the presence of severe fibrosis that prevented an adequate suction and release of the OTSC® clip.

Per protocol and intention-to-treat clinical success rates were 88.9 % (8/9, 95 % CI: 57-98 %) and 72.7 % (8/11, 95 % CI: 43-90 %), respectively. There was only one rebleed. This patient presented hematemesis the day after OTSC® clip placement and required embolization by interventional radiology. No device-related adverse events were recorded. The mortality rate at 30 days was 9.1 % (1/11); the cause of death was

unrelated to OTSC® placement (ischemic stroke complicated by bilateral polymicrobial pneumonia).

DISCUSSION

Conventional endoscopic treatment offers suboptimal results in refractory peptic ulcer UGIB. The classic risk factors for rebleeding or persistent bleeding are the presence of fibrotic ulcers, size > 2 cm and location in the lesser curvature or posterior duodenal wall (9,10). Our initial experience in the context of UGIB suggests that the OTSC® clip is an effective treatment, and supports its use as a rescue treatment.

The technical success rate in our series (81.9 %) is below the technical success rate estimated by a recent meta-analysis (97.7 %) (11). This may be because our cohort represents the initial experience in the indication of UGIB and the small sample size, where a single technical failure leads to a significant change in the success rate. The presence of massive bleeding and severe fibrosis, as occurred in our study, are the most frequent causes of technical failure (11). Suction technique is the most common in the literature and was used in all patients (12). The use of the OTSC® Anchor clip could help with non-aspirable fibrotic ulcers, although there are no studies that support its usefulness.

The use of the OTSC® clip in our center has made it possible to avoid surgical or endovascular treatments, with a high rate of control of severe UGIB. The per-protocol clinical success was similar to that reported in the literature, where the success rate ranges between 80 % and 100 % (11). This should be viewed as a high success rate considering that these ulcers are refractory to first-line endoscopic treatment. The most representative clinical trial in the context of rebleeding was published in 2018 and reported a success rate for conventional treatment (TTSC clips or thermal therapy) of 42.4 %, compared to 84.8 % with the OTSC® clip ($p = 0.001$) (13). The last cohort published in Spain that evaluated a rescue treatment in UGIB was published in 2019. This multicenter project evaluated the effectiveness of Hemospray®, whose success rate (62.4 %) was lower than that found in our study (14). The OTSC® clip has demonstrated a similar effectiveness to interventional radiology, but allows immediate application during endoscopy and has been associated with a shorter Intensive Care

Unit stay and in-hospital mortality (15). Surgery should always be reserved as the last resource due to its high morbidity and mortality (6).

The favorable results of OTSC® in the setting of refractory UGIB have prompted its evaluation as a first-line treatment. A recent clinical trial (16) and several observational studies (17,18) suggest that its use as an initial therapy in high-risk peptic ulcers could be cost-effective. In fact, the latest clinical practice guideline of the European Society of Gastrointestinal Endoscopy (6) makes a weak recommendation in favor of its use as a first-line treatment for ulcers > 2 cm, with a large vessel size (> 2 mm), fibrotic or excavated ulcers or in those located in high-risk areas (areas irrigated by the gastroduodenal artery or left gastric arteries). However, the available evidence in this scenario is still limited and the decision must be individualized according to the availability of the device, the clinical situation of the patient and the experience of the endoscopist.

OTSC® clip placement is a safe procedure, as reflected by the absence of adverse effects in our series. A review of more than 1,500 patients found an adverse event rate of less than 2 %, 0.59 % of them severe (5). The main limitations of the study are its retrospective design and the absence of a control group. Due to the small sample size, the inclusion of a comparative arm was not considered as appropriate.

In conclusion, the OTSC® system is an effective and safe rescue treatment in UGIB secondary to peptic ulcer. Our preliminary results support its use as the treatment of choice in this setting.

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Table 1. Patient characteristics (n = 11)

Age (years), median (range)	58 (40-92)
Male sex	7 (63.6 %)
Anticoagulation and/or antiplatelet medication	
No	7 (63.6 %)
Dual antiplatelet therapy	1 (9.1 %)
Anticoagulation	3 (27.3 %)
Enoxaparin 40 mg/24 h	1
Enoxaparin 100 mg/24 h	1
Apixaban 5 mg/24 h	1
Risk scores (median, range)	
Rockall	8 (7-9)
Glasgow-Blatchford	14 (11-17)
Blood units transfused	
≤ 3	4 (36.4 %)
4-7	4 (36.4 %)
≥ 8	3 (27.3 %)
Prior endoscopic therapy	
Sclerotherapy + TTSC	5 (45.5 %)
Sclerotherapy (adrenaline + etoxiesclerol)	3 (27.3 %)
Others	3 (27.3 %)
Endotracheal intubation	5 (45.5 %)
Deep sedation	6 (54.5 %)
Location of ulcer	
Stomach	2 (18.2 %)
Duodenal bulb-anterior wall	4 (36.4 %)
Duodenal bulb-posterior wall	4 (36.4 %)
Second duodenal portion	1 (9.1 %)
Pre-OTSC® endoscopies	
0	1 (9.1 %)
1	8 (72.7 %)

2	1 (9.1 %)
3 o more	1 (9.1 %)
Ulcer size	
≤ 1 cm	2 (18.2 %)
1-2 cm	6 (54.5 %)
≥ 2 cm	1 (9.1 %)
Missing	2 (18.2 %)
Forrest classification at the time of OTSC® placement	
Ia	1 (9.1 %)
Ib	4 (36.4 %)
IIa	5 (45.5 %)
III	1 (9.1 %)

TTSC: through-the-scope clip; OTSC®: over-the-scope-clip.

Table 2. Patient characteristics

<i>Patient</i>	<i>Age</i>	<i>Comorbidities</i>	<i>Antithrombotics</i>	<i>Rebleeding or persistent bleeding</i>	<i>Technical success</i>	<i>Clinical success</i>	<i>Size</i>	<i>Location</i>	<i>Forrest</i>
1	53	HT, liver cirrhosis, CKD	Clexane 100 mg/24 h	Rebleeding	Yes	No	10 mm	Duodenal bulb- anterior wall	IIA
2	53	HT, DM	No	Rebleeding	No	No	15 mm	Duodenal bulb- posterior wall	IIA
3	92	CKD	No	Persistent bleeding	Yes	Yes	-	Duodenal bulb- anterior wall	IB
4	84	No	Clexane 40 mg/24 h	Rebleeding	Yes	Yes	7 mm	Duodenal bulb- anterior wall	IB
5	66	DVT	Apixaban 5 mg/24 h	Rebleeding	Yes	Yes	17 mm	Duodenal bulb- anterior wall	IB
6	91	No	No	Persistent bleeding	Yes	Yes	15 mm	Gastric body	IA
7	58	HT	No	Rebleeding	Yes	Yes	15 mm	Gastric antrum	IB
8	40	VHL	No	Rebleeding	Yes	Yes	15 mm	Duodenal bulb- posterior wall	IIA
9	70	HT, ischemic heart disease	AAS 100 mg/24 h	Rebleeding	No	No	20 mm	Duodenal bulb- posterior wall	III

HT:

hypertension; DVT: deep venous thrombosis; VHL: Von Hippel-Lindau; DM: diabetes mellitus; HIV: human immunodeficiency virus; COPD: chronic obstructive pulmonary disease; AAS: acetylsalicylic acid; CKD: chronic kidney disease.



Fig. 1. Placement of the OTSC® device on bleeding peptic ulcer. A. Peptic ulcer with adherent clot and bleeding in oozing, 48 hours after sclerotherapy and through-the-scope-clip clip placement. B. Placement of the vessel in the center of the visual field and aspiration inside the OTSC® clip cap. C. OTSC® system released over the bleeding ulcer, achieving intraprocedural hemostasis.

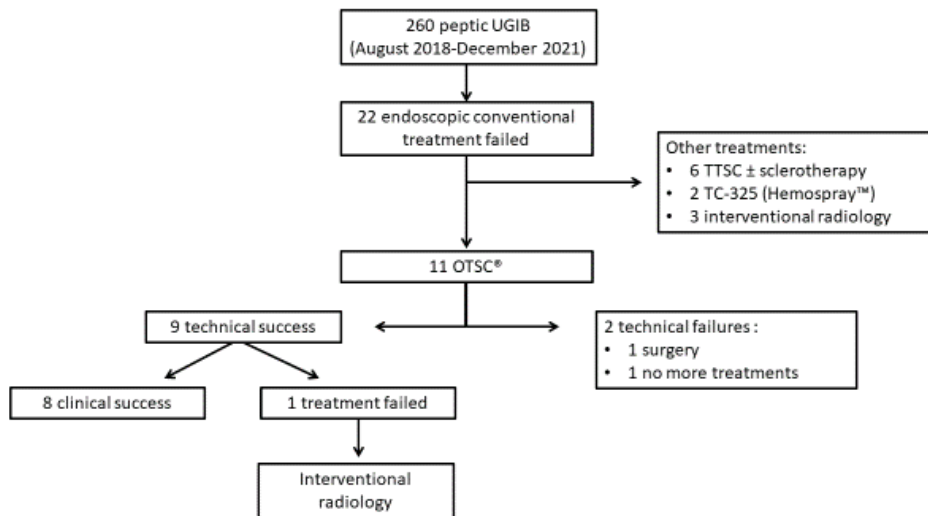


Fig. 2. Study diagram. UGIB: upper gastrointestinal bleeding; TTSC: through the scope clip; OTSC®: over the scope clip.