



OTSC System – Update on clinical data

October 2012

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1 General remarks

2 Indication hemostasis

3 Indication closure of acute lesions/perforations

4 Indication closure of chronic lesions/fistulas

5 Comparison to endoclip studies

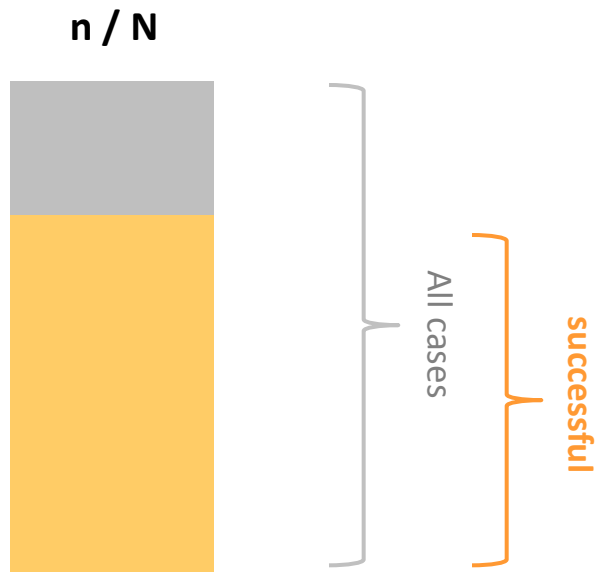
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Definitions / Glossary

- Technical success: successful application of clip at the desired location
Not specified in all publications
- Clinical success:
Permanent closure of defect/lesion as clinically intended
- Success rate:
Percentage of successful treatment of lesion/all lesions (n/N).



Technical success not specified in all studies!

Definitionen / Glossar

➤ Weighted **mean** success rate:

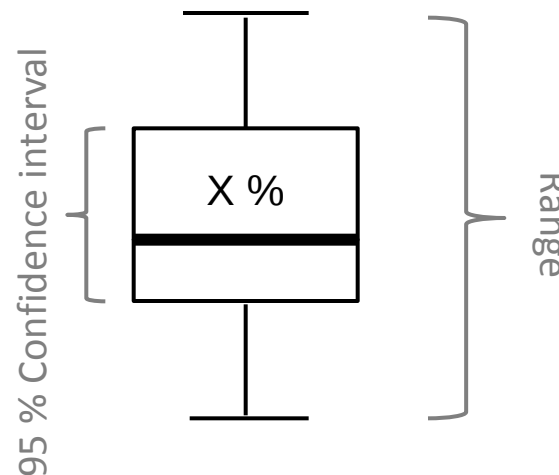
Average success rate of all studies: each study is being weighted according to reciprocal variance
=> the larger a study, the more precise the individual effect is to be assumed, the more weight it is attributed

➤ Confidence interval:

The true value can be assumed to be within this area with a 95% probability

➤ Range:

Describing the lowest and highest of all values



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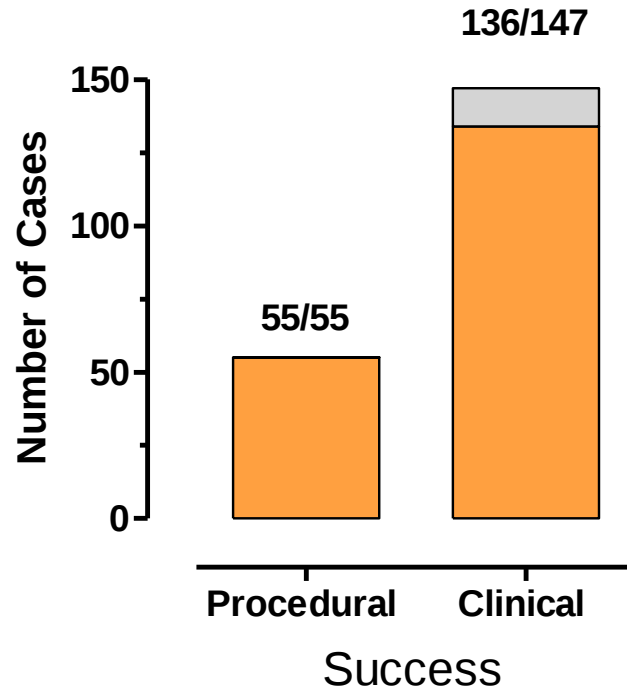


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Clinical data of hemostasis with OTSC® are very positive

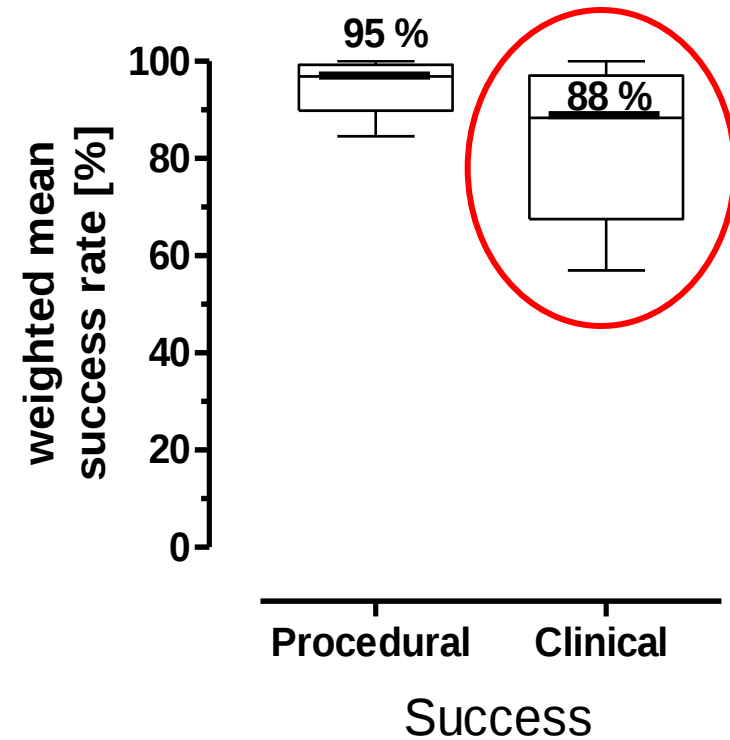
Author	Year	Lesions	Indication	Technical success	Clinical success
Albert <i>et al.</i>	2011	7	GI hemorrhage	100 % (7/7)	57 % (4/7)
Baron <i>et al.</i>	2012	7	GI hemorrhage	100 % (7/7)	100 % (7/7)
Kirschniak <i>et al.</i>	2007	7	GI hemorrhage	100 % (7/7)	100 % (7/7)
Kirschniak <i>et al.</i>	2011	27	GI hemorrhage	100 % (27/27)	100 % (27/27)
Kratt <i>et al.</i>	2012	69	GI hemorrhage	NA	94 % (65/69)
Repici <i>et al.</i>	2009	7	GI hemorrhage	100 % (7/7)	100 % (7/7)
Wedi <i>et al.</i>	2012	23	GI hemorrhage	NA	83 % (19/23)

NB: only clinical reports with $n \geq 4$ patients were included. Many reported cases were relapse bleedings after conventional endoscopic treatment or had an indication for surgery. Thus, they can be considered as severe bleedings.



Cases specified
 Clin. successful cases

Cases from published studies



Mean statistical success rate

Clinical data of gastro-intestinal hemorrhage from duodenal ulcer

Author	Year	Lesions	Indication	Technical success	Clinical success
Peters <i>et al.</i>	2012	1	Bleeding duodenal ulcer	√	√
Strain <i>et al.</i>	2012	1	Bleeding duodenal ulcer	√	√

NB: Clinical series/cases reports < 4 patients

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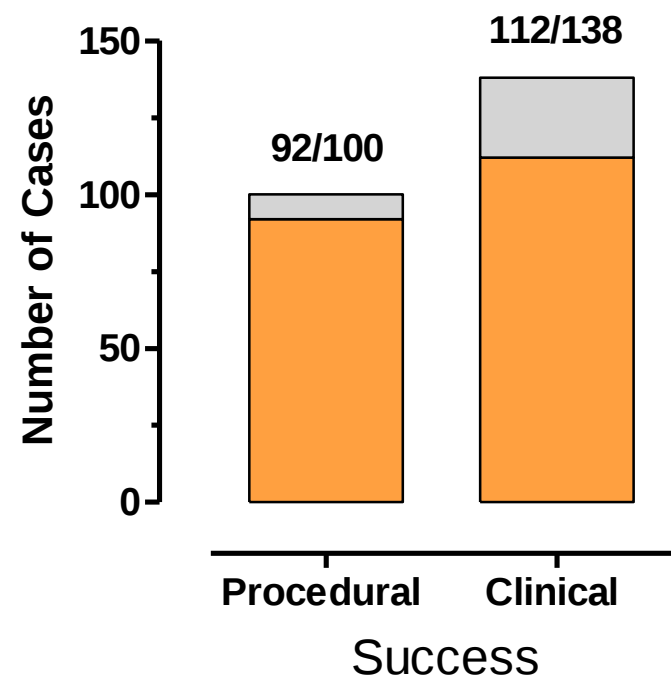
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The treatment of acute lesions is facing a shift towards endoscopy

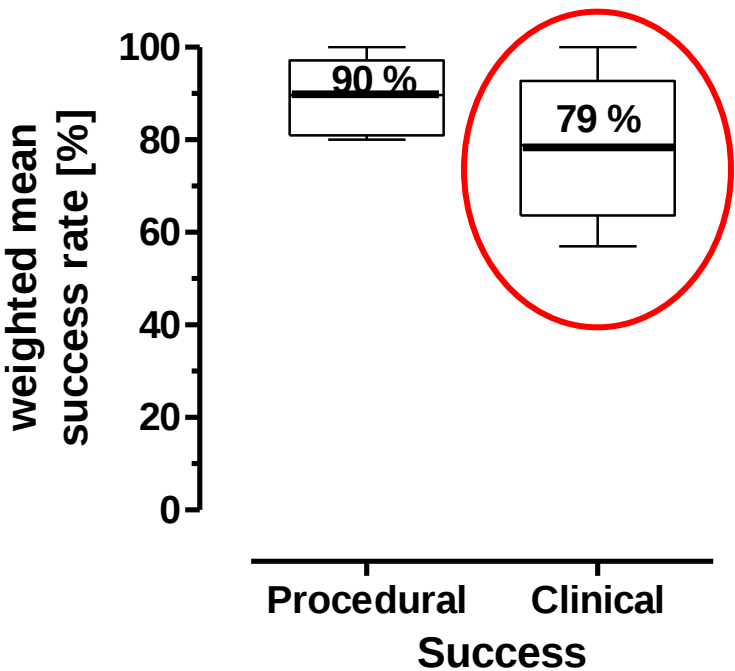
Author	Year	Lesions	Indication	Technical success	Clinical success
Albert <i>et al.</i>	2011	5	Leaks in GI tract	80 % (4/5)	80 % (4/5)
Arezzo <i>et al.</i>	2012	8	Acute colo-rectal leaks	87 % (7/8)	87 % (7/8)
Baron <i>et al.</i>	2012	8	Iatrogenic perforations in GI tract	NA	62 % (5/8)
Disibeyaz <i>et al.</i>	2012	6	Perforations and anastomotic leaks	NA	66% (4/6)
Gubler <i>et al.</i>	2012	14	Iatrogenic perforations in GI tract	93 % (13/14)	78 % (11/14)
Hagel <i>et al.</i>	2012	17	Iatrogenic perforations in GI tract	NA	65 % (11/17)
Kirschniak <i>et al.</i>	2007	4	Iatrogenic perforations and lesions in Colon	100 % (4/4)	100 % (4/4)
Kirschniak <i>et al.</i>	2011	11	Perforations in upper/lower GI tract	100 % (11/11)	100 % (11/11)
Manta <i>et al.</i>	2010	5	Anastomotic leaks	100 % (5/5)	80 % (4/5)
Parodi <i>et al.</i>	2010	6	Iatrogenic perforation/peptic ulcer	83 % (5/6)	83 % (5/6)
Sandmann <i>et al.</i>	2012	7	Perforations and anastomotic leaks in GI tract	NA	86 % (6/7)
Schlag <i>et al.</i>	2011	4	Gastric perforation	100 % (4/4)	100 % (4/4)
Seebach <i>et al.</i>	2010	7	Perforations and anastomotic leaks	85 % (6/7)	57 % (4/7)
Voermans <i>et al.</i>	2012	36	Iatrogenic perforations	92 % (33/36)	89 % (32/36)

NB: Clinical studies with n ≥ 4 patients, including anastomotic leakages

Closure of acute wall lesions/perforation incl. anastomotic leakage



Cases from published studies



Mean statistical success rate

Case reports supporting larger series/studies

Author	Year	Lesions	Indication	Technical success	Clinical success
Buffoli <i>et al.</i>	2012	1	ERCP-caused jejunal perforation	√	√
Coriat <i>et al.</i>	2011	1	Colon perforation after ESD	√	√
Fähndrich <i>et al.</i>	2011	1	Perforation to retroperitoneum after papillotomy	√	√
Kirschniak <i>et al.</i>	2007	1	Gastric perforation after necrotizing pancreatitis	√	√
Mori <i>et al.</i>	2012	1	Rectal perforation with abscess formation	√	√
Pohl <i>et al.</i>	2010	2	Post-surgery esophageal leakage	√ / √	√ / -
Repici <i>et al.</i>	2009	2	Lesion in colon / rectum	√ / √	√ / √
Swahn <i>et al.</i>	2011	1	Perforated peptic ulcer	√	√
Wedi <i>et al.</i>	2012	3	Iatrogenic perforations	√ / √ / √	√ / √ / √
Wedi <i>et al.</i>	2010	1	Perforated duodenal diverticula	√	√

NB: Clinical reports with n < 4 patients were included

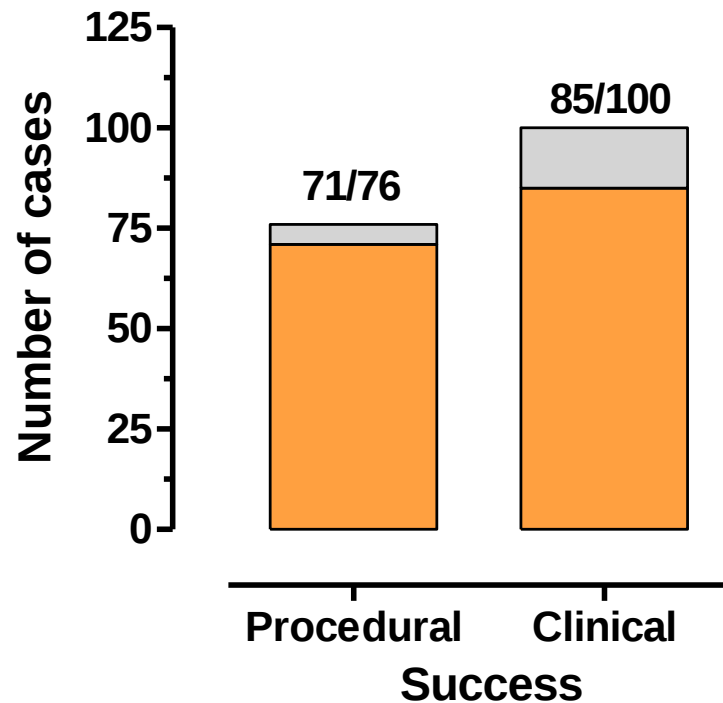
The treatment of acute perforations alone renders even better results than in the combined evaluation of perforations and acute anastomotic leaks.

Author	Year	Lesions	Indication	Technical success	Clinical success
Gubler <i>et al.</i>	2012	14	Iatrogenic perforations in GI tract	93 % (13/14)	78 % (11/14)
Hagel <i>et al.</i>	2012	17	Iatrogenic perforations in GI tract	NA	65 % (11/17)
Kirschniak <i>et al.</i>	2007	4	Iatrogenic perforations and lesions in Colon	100 % (4/4)	100 % (4/4)
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Sandmann <i>et al.</i>	2012	7	Perforations and anastomotic leaks in GI tract	NA	86 % (6/7)
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Seebach <i>et al.</i>	2010	7	Perforations and anastomotic leaks	85 % (6/7)	57 % (4/7)
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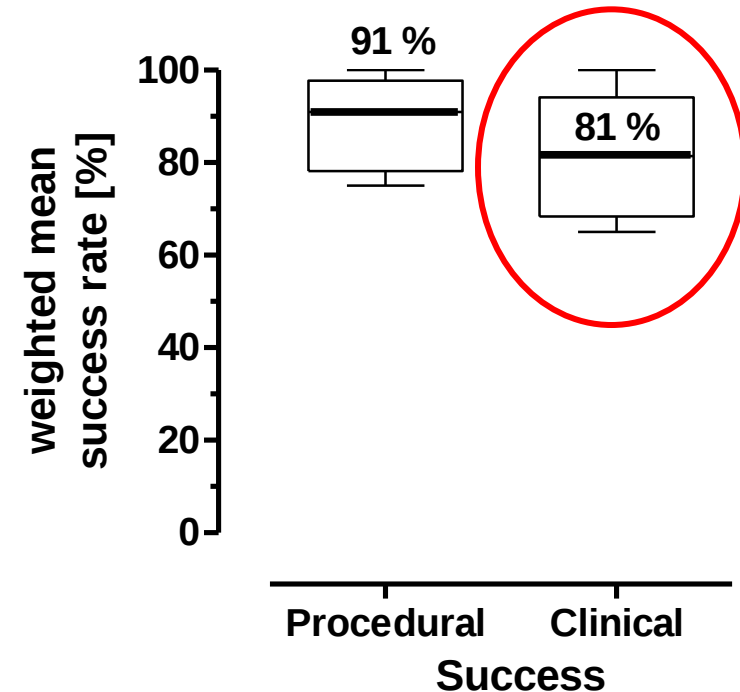
NB: Clinical reports with $n \geq 4$ patients, without anastomotic leaks

Closure of acute wall lesions/perforations **without** anastomotic leakage

The treatment of acute perforations alone renders even better results than in the combined evaluation of perforations and acute anastomotic leaks.



Cases from published studies



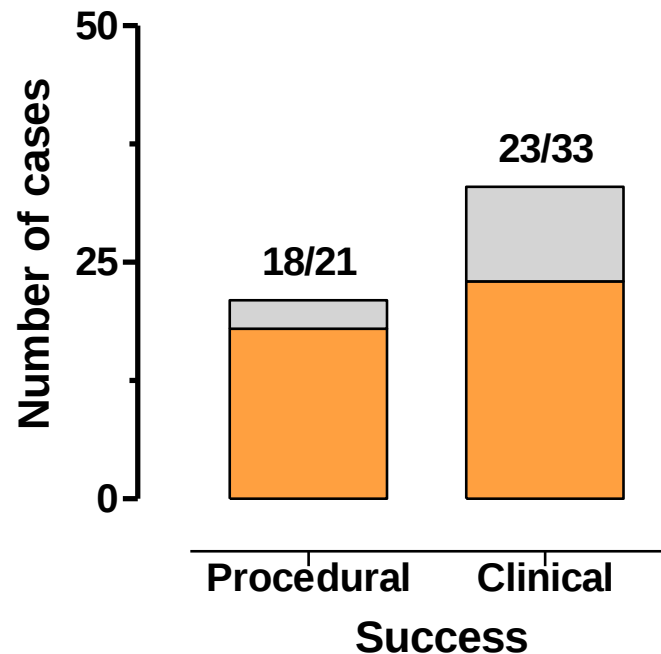
Mean statistical success rate

OTSC® is even suitable for the repair of anastomotic dehiscences

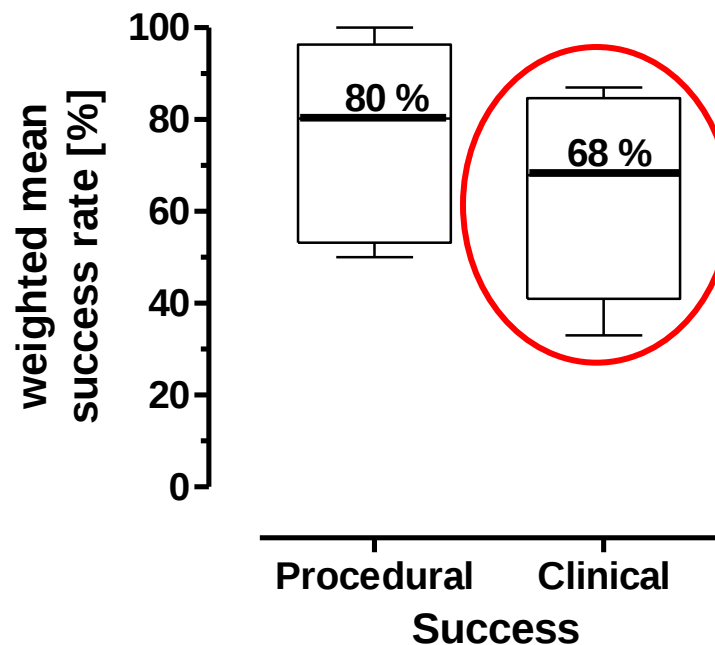
Author	Year	Lesions	Indication	Technical success	Clinical success
Albert <i>et al.</i>	2011	2	Postoperative leakages and dehiscence in GI tract	50 % (1/2)	50 % (1/2)
Arezzo <i>et al.</i>	2012	8	Post surgical acute anastomotic leakage in the colorectum	87 % (7/8)	87 % (7/8)
Baron <i>et al.</i>	2012	3	Anastomotic leakage after esophagectomy	n.s.	33 % (1/3)
Disibeyaz <i>et al.</i>	2012	5	Post surgical anastomotic leakage	n.s.	66 % (3/5)
Manta <i>et al.</i>	2010	5	Post surgical dehiscence	100 % (5/5)	80 % (4/5)
Parodi <i>et al.</i>	2010	3	Anastomotic dehiscence	66 % (2/3)	66 % (2/3)
Sandmann <i>et al.</i>	2012	4	Perforations and closure failure in the GI tract	n.s.	75 % (3/4)
Seebach <i>et al.</i>	2010	3	Anastomotic dehiscence	100 % (3/3)	66 % (2/3)

NB: anastomotic leakage is a rather frequent and serious complication in surgery with an incidence of up to 20% and a high morbidity and mortality. Surgical measures are rather invasive and accompanied by further complications, discomfort for the patient and high costs

OTSC® is suitable for the endoscopic repair of anastomotic leaks, as reported in the literature



Cases from published studies



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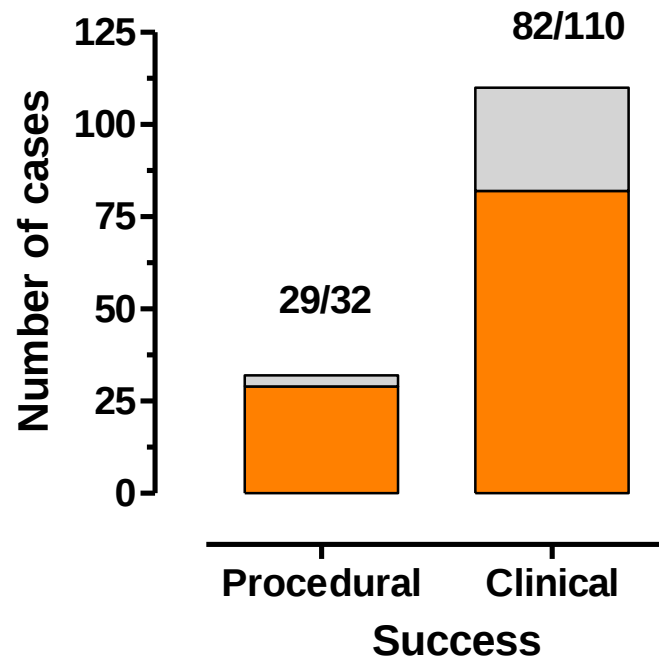
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OTSC® in the treatment of GI fistula with varying results in earlier papers.

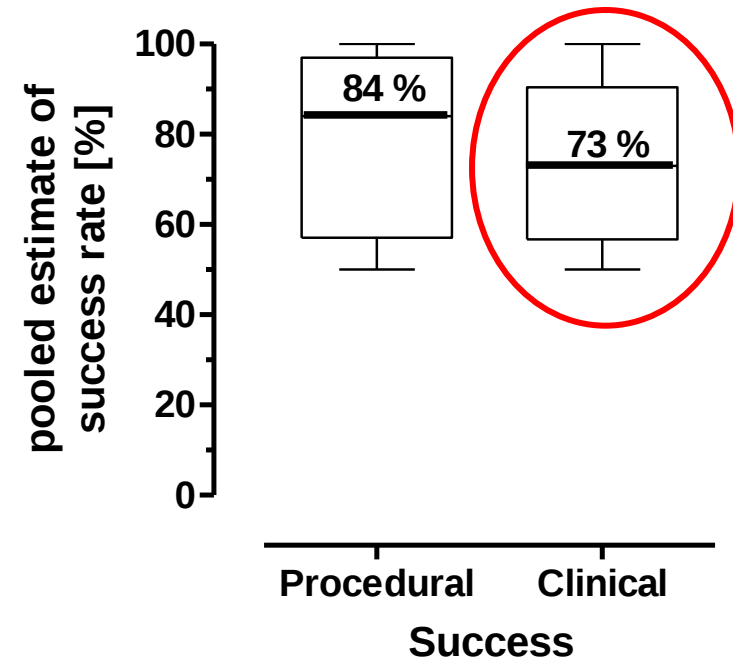
Author	Year	Lesions	Indication	Technical success	Clinical success
Albert <i>et al.</i>	2011	7	Fistulae GI tract	100 % (7/7)	71 % (5/7)
Arezzo <i>et al.</i>	2012	6	Chronic leakage in colo-rectum	83 % (5/6)	83 % (5/6)
Baron <i>et al.</i>	2012	28	Chronic fistulae in GI tract	NA	71 % (20/28)
Kirschniak <i>et al.</i>	2011	8	Chronic fistulae in GI tract	100 % (8/8)	38 % (3/8)
Manta <i>et al.</i>	2010	9	Postoperative fistulae	88 % (8/9)	88 % (8/9)
Parodi <i>et al.</i>	2010	4	Fistulae GI tract	100 % (4/4)	100 % (4/4)
Sandmann <i>et al.</i>	2012	6	Fistulae GI tract	NA	83 % (5/6)
Surace <i>et al.</i>	2011	19	Fistulae GI tract	NA	74 % (14/19)
von Renteln <i>et al.</i>	2010	4	Fistulae GI tract	50 % (2/4)	50 % (2/4)

NB: Clinical studies with $n \geq 4$ patients

The mean statistical success rates underline OTSC® as a solid therapeutic option in this difficult patient population.



Cases from published studies



Mean statistical success rate

Legend:
 Grey box: Cases specified
 Orange box: Clin. successful cases

Also small series show a broad range of fistula types treatable with OTSC®.

Author	Year	Lesions	Indication	Technical success	Clinical success
Bini <i>et al.</i>	2011	1	Gastro-intestinal fistula	√	√
Cavina <i>et al.</i>	2010	1	Recto-vesical fistula	√	√
Conio <i>et al.</i>	2010	1	Gastro-cutaneous fistula	√	√
Disibeyaz <i>et al.</i>	2012	3	Fistula in GI tract	NA	√ / - / -
Gallego-Perez <i>et al.</i>	2012	1	Gastro-cutaneous fistula	√	√
Grossmann <i>et al.</i>	2011	1	Colo-cutaneous fistula	√	√
Gubler <i>et al.</i>	2012	1	Esophago-pericardial fistula	√	√
Iacopini <i>et al.</i>	2010	2	Chronic fistula	√ / √	√ / √
Kothari <i>et al.</i>	2012	1	Gastro-cutaneous fistula	√	√

NB: Clinical series/case reports with n < 4 patients

Also small series show a broad range of fistula types treatable with OTSC®.

Author	Year	Lesions	Indication	Technical success	Clinical success
Kouklakis <i>et al.</i>	2011	1	Gastro-cutaneous fistula	√	√
Mangiavillano <i>et al.</i>	2010	1	Recto-vesical fistula	√	-
Mori <i>et al.</i>	2012	2	Rectal fistula	√ / √	√ / √
Murino <i>et al.</i>	2012	1	Gastro-colic fistula	√	√
Neumann <i>et al.</i>	2011	1	Choledocho-duodenal fistula	√	√
Prosst <i>et al.</i>	2012	1	Ano-rectal fistula	√	√
Rebelo <i>et al.</i>	2011	1	Broncho-esophageal fistula	√	√
Traina <i>et al.</i>	2010	1	Tracheo-esophageal fistula	√	√
Turner <i>et al.</i>	2010	1	Gastro-cutaneous fistula	√	-

NB: Clinical series/case reports with n < 4 patients

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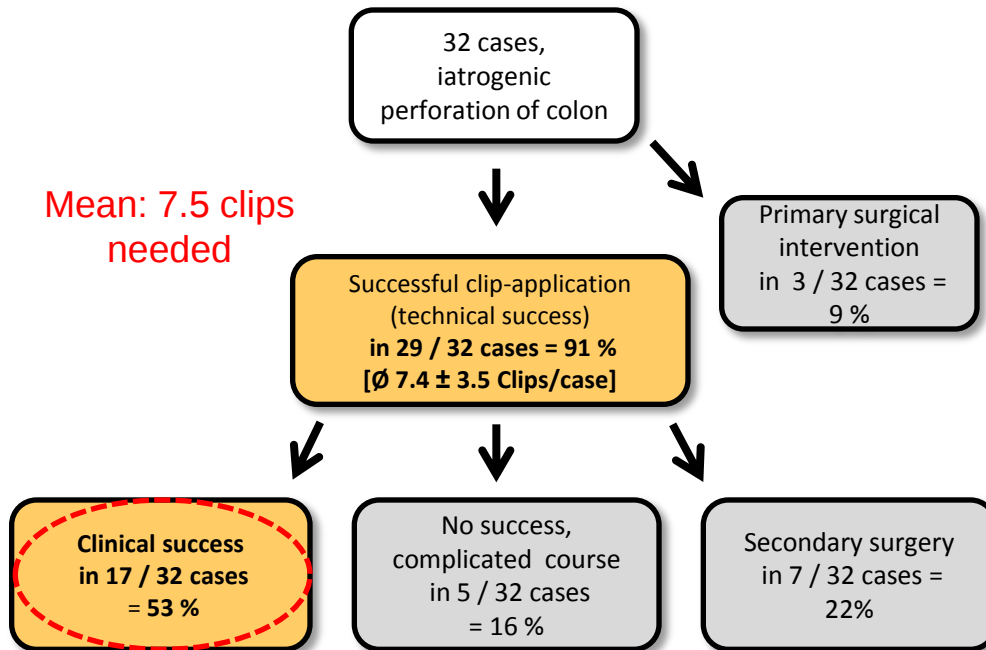


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OTSC® System vs. conventional endoclip study in the closure of iatrogenic perforations.

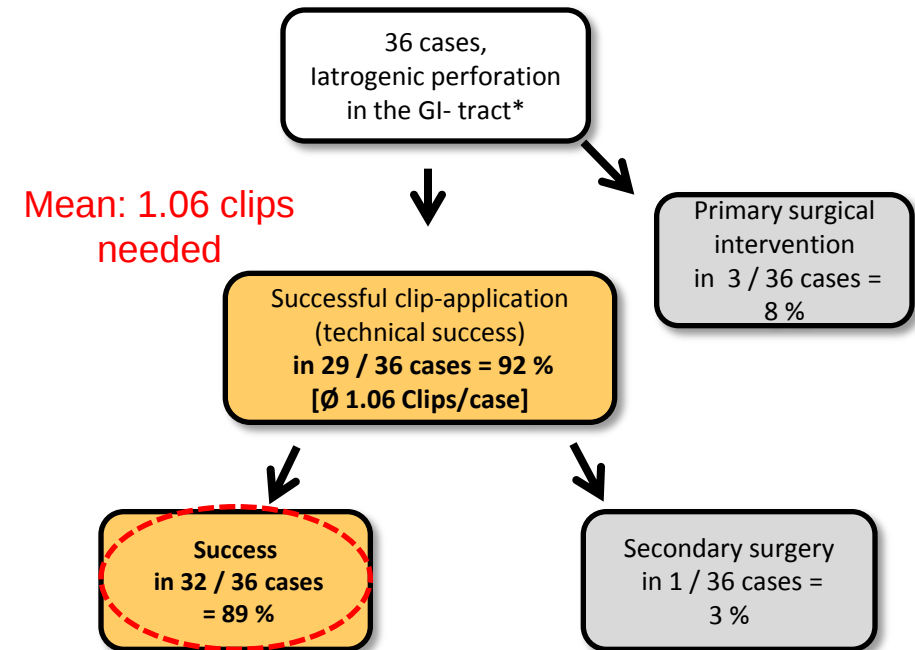
Conventional endoclips – Cho SB *et al.*, Surg Endosc 2012

Retrospective multi-center study on feasibility/safety of conventional endoclips for the closure of iatrogenic perforations of the colon (Intention-to-treat basis)



OTSC® System – Voermans RP *et al.*, CGH 2012

Prospective multi-center study on safety and efficacy of OTSC® for the closure of iatrogenic perforations in the GI-tract (Intention-to-treat basis)



*Location: colon (n=13), duodenum (n=12), stomach (6), esophagus (n=5),

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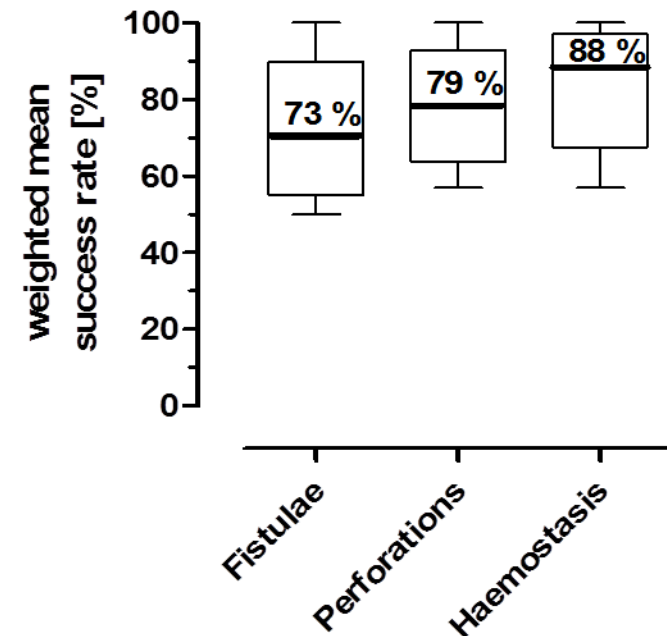
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Clinical data: success rates for hemostasis, perforation and fistula closure are 88%, 79% and 73 %, respectively.

- Over 40 peer reviewed clinical publications in “Pubmed”
- From case reports to retro- and prospective studies in all indications:

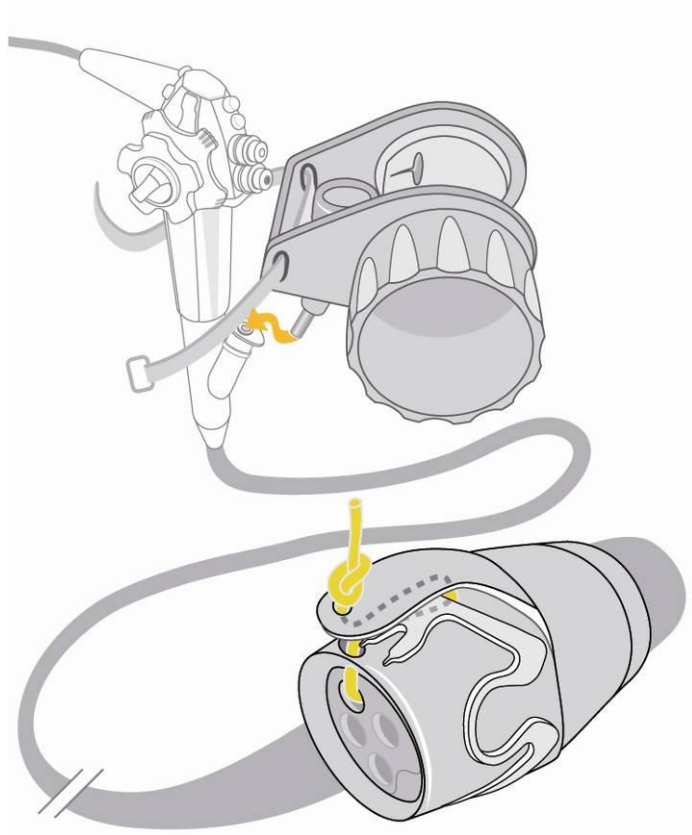
- Hemostasis
- Closure of iatrogenic perforations
- Closure of fistulas

Success rates between approx. 75 to 90 %.



- The OTSC® system compares to the effectiveness of a surgical intervention or offers a new therapeutic option in situations where surgery is not feasible.

Please contact us in case of any questions.



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