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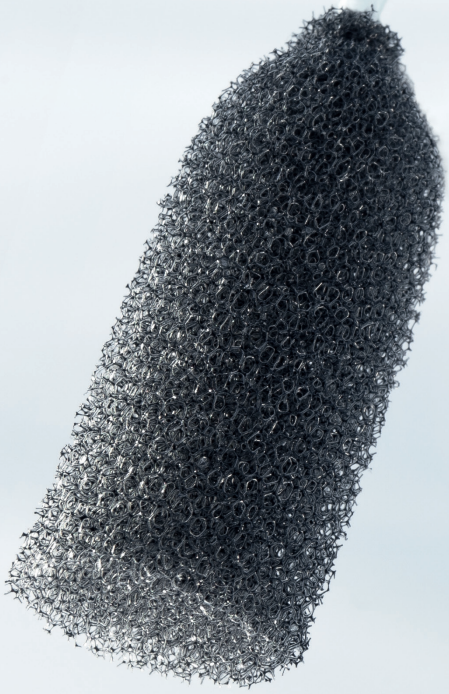

CLINICAL EVIDENCE FOLDER ENDO-SPONGE™

Endoluminal vacuum therapy for the treatment of rectal anastomotic leakage

RATIONALE

Anastomotic leakage is a major complication with an incidence of 10-13 % after anterior rectal resection[1]. The frequency depends on various patient characteristics, the height of the anastomosis and the prior treatment in the case of a carcinoma. A rectal anastomotic leakage has the potential to lead to a high patient morbidity and mortality up to 22 %[2], because contents from the intestine can enter the minor pelvis via the anastomotic leakage and form an infected cavity. If the secretion continues to rise, generalized peritonitis can result, with severe septic progression involving multiple organ failure and potentially culminating in the death of the patient. In former times this complication has been treated conservative by transrectal rinsing if the patient shows no signs of a peritonitis, but this treatment method is associated with a very long postoperative period and healing time up to one year or more for the anastomotic leak. In addition, in some cases the creation of a permanent stoma is also necessary or the infection can not be controlled, leading to a reoperation of the patient with the necessity of a second stoma.

The vacuum drainage developed for wound therapy, represent an alternative treatment for anterior rectal anastomotic leaks. The principle of this method is the application of negative pressure on the wound surface with the help of a sponge connected to a pump. The physiological mechanism of this improvement in wound healing is the effective removal of fluid, tissue edema and bacteria, with subsequently improved local blood circulation, which in turn stimulates wound healing (increased growth of granulation tissue).
The endoluminal vacuum therapy as a minimally invasive method for the treatment of an anastomotic leakage after a low anterior rectum resection has been developed by the B. Braun together with Dr. Rolf Weidenhagen from the University hospital, Munic-Großhadern, Germany. The product “Endo-SPONGE” was introduced on the market in May 2006.

Using the Endo-SPONGE treatment it is possible to achieve a continuous drainage of the secretion of the leakage cavity with simultaneous debridement, granulation of the surface and reduction of the size of the cavity. Endo-SPONGE consists of an open-pored sponge connected to a drainage tube. After endoscopic insertion of the sponge into the leakage cavity the drainage tube is routed out through the anus and connected to a vacuum system. The application of the vacuum leads to a continuous drainage of the fluid and the sponge in the cavity promotes the cleaning of the surface. To achieve an effective treatment the size of the sponge is cut to fit the cavity. Depending on the size of the leakage cavity it can be necessary to place more than one sponge into the cavity. The sponge system is changed very 24-72 hours. To change the sponge the vacuum is disconnected. Removal of the sponge is easier with prior irrigation with 0.9 % saline solution to remove the granulated tissue from the surface of the sponge. The sponge is removed through the anus and size of the new sponge is adapted to the size of the leakage cavity. Endo-SPONGE treatment is stopped as far as the cavity reaches a size of 1 x 0.5 cm, because no further reduction of the sponge size is technically possible.

Figure 1: Endo-SPONGE treatment

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ENDOLUMINAL VACUUM THERAPY FOR THE TREATMENT OF RECTAL ANASTOMOTIC LEAKAGE

COHORT STUDIES

The endoluminal vacuum therapy (EVT) for rectal anastomotic leakage treatment was firstly described by Weidenhagen in 2008[3]. Since then various retrospective and prospective cohort studies have been published using Endo-SPONGE to treat lower Gastrointestinal (GI) defects. Up to present 40 publications including posters are available in Pubmed and EMBASE for Endo-SPONGE EVT and the outcome of these scientific investigations is summarized in the present clinical evidence folder.

Kuehn et al. performed in 2016 a retrospective patient series to analyse the result of EVT for lower GI defects[4].

In total 41 patients were included between 2007 and 2015. Twenty patients were treated due to an anastomotic leakage after rectal resection, in 12 cases a Hartmann stump insufficiency was diagnosed, a rectal perforation was observed in 3 patients and in further 6 patients the EVT was applied due to other indications. In total 20 of 32 patients, whose suffered either of a rectal anastomotic leakage or a rectal stump insufficiency received preoperatively a radiotherapy- or a radio-chemotherapy. A protective enterostoma was created in 19 of 20 patients with a diagnosed rectal anastomotic leakage.

The enterostoma could be closed in 15 of 19 patients (79 %). EVT was performed without using sedation or anesthesia. In all cases a vacuum of 125 mm Hg was applied and the sponges were changed very 3 days and adapted to the size of the cavity.

In total 426 sponges were applied during 360 endoscopic procedures. The median number of sponge insertions was 6 [1-37]. The median length of treatment duration was 23 days for anastomotic leakage, 12 days for rectal stump insufficiencies and 20 days for other GI defects. Depending on the gastrointestinal defect the success rate varied from 75 % to 90 %. In total 34/41 patients were successfully treated using Endo-SPONGE EVT. Mortality rate was 2.4 %.

The current cohort study is the largest patient series which has been published so far. The results showed that EVT is highly effective to treat various lower gastrointestinal defects. EVT has become the standard treatment within the University of Rostock, Department of General Thoracic, Vascular and Transplantation Surgery for anastomotic leakage after rectal resection.

Strangio et al. aimed to assess the efficacy and safety of Endo-SPONGE treatment in a large cohort and they also performed a review of the literature[5].

Consecutive patients (N = 25) with an anastomotic leakage after a colorectal surgery with or without the need of a protective stoma were included in this retrospective cohort study. A protective stoma was performed in 13 patients (52 %). The size of the circumference leading to an anastomotic leakage ranged from 70 to 270 degrees. The detection of the anastomotic leakage took place after a median of 17 days after surgery. The Endo-SPONGE treatment started after a median of 16 days after detection. The sponges were changed every 48-72 hours. A median number of 9 sponges were applied per patient [min. 1 – max. 39]. The treatment was stopped when the cavity was less than 1 cm in diameter. Healing of the cavity was observed after a median duration of 28 days [min. 7 – max. 128 days]. Success rate of Endo-SPONGE treatment was 88 % (22/25 patients). In total 3 patients developed a major complication (ureteric fistula, ileal fistula, pararectal abscess).

Ureteric fistula was surgical treated with the placement of an uteric J stent and antibiotic therapy. The ileal fistula was managed with a second laparotomy with bowel segmental resection and anastomotic leak repair. The patient with the pararectal abscess received a CT guided transgluteal drainage, antibiotic therapy and hyperbaric oxygen therapy but only a partial improvement could be observed. Mortality rate was 12 % (3/25 patients). The patients died due to tumor progression, but in none of these cases a possible relationship with Endo-SPONGE was recorded. Closure of the stoma could be performed in 11 of 13 patients (84.6 %).

During their literature research the authors could identify 12 publication using Endo-SPONGE for colorectal anastomotic leakage. In total 174 patients were recorded ranging from 1 to 29 patient per cohort study. Subanalysis of the 7 largest case series including in total 149 patients showed a complete healing rate of the cavity in 94.3 %, over a treatment duration of 34 days with a median application of 11 sponges and a closure rate of the stoma from 55-92 %. A complication rate of 20 % was reported mainly including abscess recurrence, fistula and anastomosis stenosis.

Authors confirm the safety and efficacy of Endo-SPONGE treatment for colorectal anastomotic leakage with a low complication rate.

Gardenbroek et al. evaluated the effectiveness and direct costs of Endo-SPONGE to treat anastomotic leakage after ileal pouch-anal anastomosis (IPAA) construction in comparison to conventional treatment[6].

The current study was prospectively performed. In 15 patients Endo-SPONGE was early applied to manage the anastomotic leakage in a short term course, thereafter the defect was closed surgically. As a retrospective control group 29 patients were used, whose were treated conventionally. The conventional treatment consists of the creation of a diverted ileostomy and depending on the size of the cavity, in addition a transanal or percutaneous drainage of the abscess was performed. After confirmation of the healing of the cavity stoma was closed. The main outcome of this cohort study was the percentage of secondary healed anastomosis until 6 months, without the presence of an anastomotic defect or abscess. Costs were calculated for both treatments including the costs from the diagnosis of the anastomotic leakages until the closure of the stoma or until 2 years if a stoma closure could not yet be performed.

In total 14 of 15 patients received a protective stoma in the Endo-SPONGE treated group. The VAC therapy was started after a median of 2 days after diagnosis of the anastomotic leakage.

Patients were treated for a median duration of 12 days with 3 sponge changes. The surgically closure treatment of the anastomotic defect was performed after a median of 15 days. In 2 patients the surgical closure was not successful therefore, a second round of VAC treatment was initiated. The following surgically closure lead to success. Anastomotic healing rate was 100 % in the Endo-SPONGE group and 52 % in the conventional treatment group; $p = 0.003$. Healing was achieved in the Endo-SPONGE group after 48 days, whereas 70 days were necessary in the conventional treated group; $p = 0.013$. At the end of the follow-up a functional pouch was observed in 24 of 28 conventional treated patients and in 14 of 15 patients receiving Endo-SPONGE therapy. Costs for the Endo-SPONGE treatment were calculated at 27.627 € per patient and 33.441 € for a conventionally treated patient; $p = 0.529$.

In conclusion, this study demonstrated that Endo-SPONGE treatment is a highly effective method to treat anastomotic leakages after IPAA by avoiding permanent stoma without an increase of direct med-

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ical costs. Aim of the retrospective study performed by **Nerup et al.** was to evaluate the VAC therapy for anastomotic leaks after low anterior resection of rectal cancer[7].

Endoscopic vacuum therapy using Endo-SPONGE was applied in 13 patients receiving a protective temporary ileostomy for 3 months. Sponges were changed every 2-3 days and the sponges were trimmed to the size of the cavity. The endoscopic vacuum treatment was stopped as far as the cavity was covered by granulated tissue and possessed a width of 3 cm. A median hospital stay of 25 days [7-39 days] was reported. All abscess cavities could successfully treated. Per patient a median number of 8 sponges were applied. A median duration of 18 days was recorded for Endo-SPONGE treatment and no patient deceased. Only one complication was recorded. In one patient a stenosis occurred which was managed by a reoperation and a permanent colostomy. No recurrent abscess was observed in the study population. Closure rate of the protective stoma was 92 % (12/13 patients).

The endoscopic vacuum therapy using Endo-SPONGE is safe to treat lower GIT defects. Endoscopic VAC therapy shortens the duration of the treatment period in comparison to conservative irrigation.

Srinivasamurthy et al. reported their initial experience using minimal invasive Endo-SPONGE treatment in patients with low pelvic anastomotic leakage[8].

Eight patients were included in this case series suffering from leaks after low anterior resection for rectal cancer. All patients had a protective ileostomy at the initial surgery. Radical radiotherapy was performed previously in 7 patients due to a carcinoma of the bladder and 6 patients underwent preoperatively a short course of radiotherapy due to the rectal cancer. Endo-SPONGE treatment was performed according to the instruction of use. The anastomotic leaks were detected postoperatively after a median time of 29 days. In most of the cases 4 sponges were needed for endoscopic VAC therapy during a median treatment duration of 26 days. The presacral abscess completely healed or was reduced in 6 of 8 patients. A stoma closure rate of 62.5 % was reported. Two patients were managed with a permanent stoma and in one case an abdominoperineal excision of the rectum was done due to persisting perineal sepsis. Authors summarized that the minimal invasive endoscopic vacuum therapy using Endo-SPONGE is a highly effective and a well tolerated approach to treat and to close presacral cavities after pelvic anastomotic leakage. Furthermore, this treatment reduces the risk for a permanent stoma and results in an acceptable bowel function.

Riss et al. designed a multicentric study to analyse the long term efficacy of Endo-SPONGE treatment for lower GIT defects[9].

In six centers 20 consecutive patients were enrolled whose underwent rectal cancer surgery. Endo-SPONGE treatment was performed in 17 of 20 patients due to an anastomosis leakage and in 3 patients because an insufficiency of the Hartmann stump was diagnosed. The median time from the primary surgery until the diagnosis of the anastomotic leakages was 12.5 days. One patient received neoadjuvant short-term radiotherapy, in 5 patients a long term chemo/radiotherapy was indicated before rectal surgery. Patients were followed up for 17 months [1.5 – 29.8 months]. Five patients died, four due to tumor progression and one patient because of a liver failure. Median duration for Endo-SPONGE treatment was 21 days [7-106 days]. During Endo-SPONGE treatment 9 patients had a protective ileostomy and 8 patients a colostomy.

In 13 patients (76.5 %) the stoma was closed after successful Endo-SPONGE treatment. The overall success rate of Endo-SPONGE treatment was 75 % (15/20 patients). In five patients a recurrent abscess was observed. Median time between last Endo-SPONGE treatment and occurrence of the abscess was 255 days [21-733 days].

Authors showed that after primary successful Endo-SPONGE treatment, 25 % of the patients developed a recurrent abscess. Therefore, patients should be monitored very closely within the first 2 years, because abscess recurrence might be occurred.

Van Koperen et al. aimed to evaluate the effectiveness of Endo-SPONGE treatment for anastomotic leakage after colorectal cancer surgery[10]. After reviewing the patient's charts between July 2006 and April 2008, in total 16 patients could be identified whose were eligible for this retrospective cohort analysis. Thirteen patients were operated due to a rectal cancer and 3 patients underwent ulcerative colitis. In 9 of 13 patients scheduled for a colorectal resection a radiotherapy was preoperatively performed and in 2 patients a chemoradiotherapy was done. A protective stoma was created in 8 patients. The anastomotic leakage was observed after a median duration after surgery of 11 days [3-150 days]. Half of the patients were treated with Endo-SPONGE within 6 weeks after surgery and the sponges were placed after a median time of 24 days [13-39 days]. Treatment of the remaining patients started at a median period of 74 days [43-1.602 days]. In 16 patients a median number of 13 [8-17] sponge changes were reported. Median healing time of the cavity was 40 days [28-90 days]. Closure of the abscess cavity was seen in 56 % (9/16 patients).

Authors conclude that Endo-SPONGE is a promising device and could potentially be helpful in the treatment of anastomotic leakage after colorectal surgery and may prevent the development of a chronic presacral sinus. Early treatment with Endo-SPONGE is probably more effective than the late treatment of the abscess cavity.

The first assessment of the safety and efficacy of Endo-SPONGE was performed by **Weidenhagen et al.** in 2008[3].

In this cohort study endoscopic vacuum therapy using Endo-SPONGE was applied in 29 patients to manage anastomotic leakages followed by anterior rectum resections. Primary surgery was performed due to rectal carcinoma (N = 22), rectosigmoidal cancer (N = 3), a large rectal adenoma (N = 2), a diverticultis (N = 1) and a rectal infiltration of endometrial cancer (N = 1). In total 9 of 29 patients received a radiochemotherapy preoperatively. A protective stoma was created in 25 patients. The anastomotic leakage was diagnosed 8.2±3.6 days postoperatively. Patients were treated for a median duration of 34 days [4-79 days] using a median number of 11 [1-27] sponges. Granulation of the tissue was seen after initial treatment in all cases. Healing rate of the abscess cavity was 96.5 % (28/29 patients). Protective stoma could be closed in 22 of 25 patients. Postoperative stay varied between 10 and 69 days.

Weidenhagen et al. summarized that the endoscopic vacuum treatment is a safe and efficient minimal invasive option to drain an abscess occurring after anterior rectal resections. Further studies are needed to demonstrate that this treatment have the potential to reduce the high mortality rate of patients suffering from this disease and to preserve at the same time the spincter function.

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Table 1: Publications using Endo-SPONGE for rectal anastomotic leakage treatment

Author	Year	Number of patients	Age of the patients (years) [min. – max.]	Number of sponges [min. – max.]	Median treatment duration (days) [min. – max.]	Success rate	Stoma closure	Mortality rate
Kuehn et al.[4]	2016	N = 41	70 [29-91]	6 [1-37]	20 days [2-131]	34/41 82.3 %	15/19 78.9 %	1/41 2.4 %
Strangio et al.[5]	2015	N = 25	67 [37-89]	9 [1-39]	28 days [7-128]	22/25 88 %	11/13 84.6 %	3/25 12 %
Gardenbroek et al.[6]	2015	N = 15	37 [25-56]	3 [2-4]	12 [7-15]	15/15 100 %	14/15 93.3 %	0/15 0 %
Nerup et al.[7]	2013	N = 13	64 [36-71]	8 [1-18]	18 [3-40]	13/13 100 %	12/13 92.3 %	0/13 0 %
Srinivasamurthy et al.[8]	2013	N = 8	66 [45-79]	4 [1-7]	26 [7-49]	6/8 75 %	5/8 62.5 %	0/8 0 %
Verlaan et al.[11]	2011	N = 6	52 [29-68]	3 [1-6]	14 [5-28]	6/6 100 %	5/6 83.3 %	0/8 0 %
Arezzo et al.[12]	2010	N = 3	69 [62-73]	2 [1-4]	21 [NA]	1/3 33.3 %	2/3 75 %	0/3 0 %
Riss et al.[9]	2010	N = 20	66 [55-91]	NA	21 [7-106]	15/20 75 %	13/17 76.5 %	5/20 25 %
Riss et al.[13]	2010	N = 9	63.5 [50-71]	NA	21 [14-56]	6/9 66.6 %	NA	1/9 11.1 %
Heeney et al.[16]	2010	N = 2	68.5 [58-79]	NA	21 [NA]	2/2 100 %	NA	0 0 %
van Koperen et al.[10]	2009	N = 16	64 [19-78]	13 [8-17]	40 [28-90]	9/16 56 %	5/8 62.5 %	0/16 0 %
Weidenhagen et al.[3]	2008	N = 29	66.7 [42-79]	11 [1-27]	34 [4-79]	28/29 97 %	22/25 88 %	0/29 0 %
Richterich et al.[14]	2008	N = 1	60	NA	9	1/1 100 %	NA	0 0 %
van Koperen et al.[15]	2008	N = 2	29 [18-40]	NA	45.5 [35-56]	2/2 100 %	NA	0 0 %

Legend: NA: Not applied

CONCLUSION

Since its introduction into the market in 2006, numerous clinical investigations including over 290 patients have been performed using Endo-SPONGE to treat anastomotic leakages occurring after anterior rectal cancer resection. The authors assessed the endoscopic vacuum treatment using Endo-SPONGE as a safe minimal invasive option. This approach is well tolerated by the patient and associated with a low complication rate. The Endo-VAC treatment reduces the high mortality rate of the patients, prevents the development of a chronic presacral sinus and minimises the risk of a permanent stoma. After diagnosis of the anastomotic leak the endoscopic vacuum treatment should be started immediately because early treatment is more effective as late treatment of the abscess cavity. Chemo-radiotherapy delays the closure of the abscess. In comparison to conservative irrigation, Endo-SPONGE treatment shortens the treatment period and patients return quicker to normal life and work. The endoscopic vacuum therapy using Endo-SPONGE reduces the costs for the patient medical treatment. A success rate between 56 % and 100 % has been reported in the literature for this minimal approach.

KEY MESSAGES

- Endo-SPONGE treatment is a safe approach to treat anastomotic leaks occurring after anterior rectal cancer resection[3-7,10].
- Endo-SPONGE is well tolerated by the patient[8,13,14].
- The Endo-VAC treatment may reduce the risk of a permanent stoma[3].
- Endo VAC treatment using Endo-SPONGE shortens the treatment period in comparison to conservative irrigation[7,10].
- Endo-SPONGE treatment leads to a quicker return to normal life and work[3].
- The use of Endo-SPONGE may reduce the costs for patient's medical treatment [3]. Endo-VAC treatment may help avoid complicated, time- and cost consuming open surgical reoperations. Also the total cost of treatment can be reduced in endoscopically treated patients by reducing the time of total parental nutrition, systemic antibiotics and intensive care.
- Success rate of Endo-SPONGE treatment ranges between 56-100% (table 1).
- The earlier the Endo VAC treatment is initiated after leak diagnosis the better the outcome[10].

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