NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

Endo-SPONGE for treating low rectal anastomotic leakage

The National Institute for Health and Care Excellence (NICE) is producing guidance on using Endo-SPONGE for treating low rectal anastomotic leakage in the NHS in England. The medical technologies advisory committee has considered the evidence submitted by the company and the views of expert advisers.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the public. This document should be read along with the evidence (see the committee papers).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and resource savings reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?

Note that this document is not NICE's final guidance on Endo-SPONGE for treating low rectal anastomotic leakage. The recommendations in section 1 may change after consultation.

After consultation the committee will meet again to consider the evidence, this document and comments from the public consultation. After considering the comments, the committee will prepare its final recommendations which will be the basis for NICE's guidance on the use of the technology in the NHS in England. For further details, see the medical technologies evaluation programme process and methods guides.

The key dates for this guidance topic are:

Closing date for comments: 6 August 2020

Second committee meeting: 18 September 2020

Details of the advisory committee are given in section 5.

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice.

If the case for adopting the technology is supported, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. If the technology is recommended for use in research, the recommendations are not intended to preclude the use of the technology in the NHS but to identify further evidence which, after evaluation, could support a recommendation for wider adoption.

1 Recommendations

1.1 Endo-SPONGE shows promise for treating anastomotic leakage in the low rectal area. However, there is not enough good-quality evidence to support the case for routine adoption in the NHS.

1.2 Research is recommended to address uncertainties about the benefits of Endo-SPONGE. This research should:

- identify the selection criteria for people who could have Endo-SPONGE
- assess the comparative rate of stoma reversal and bowel function recovery using Endo-SPONGE compared with other treatments
- include patient-reported outcome measures such as health-related quality of life
- determine the relative cost of Endo-SPONGE compared with other treatments for anastomotic leakage.

Why the committee made these recommendations

Anastomotic leakage is a serious complication after colorectal surgery.

Endo-SPONGE is designed to treat leaks after a low rectal anastomosis.

There is no good-quality evidence assessing the clinical effectiveness of Endo-SPONGE compared with other non-surgical or surgical treatments in the NHS. Evidence from observational studies suggests that Endo-SPONGE may reduce anastomotic leakage and the chance of a permanent stoma, but this evidence is limited. Based on the published evidence and expert advice, it is uncertain how patients would be selected for Endo-SPONGE treatment.

There are uncertainties about the cost modelling because of the weak clinical evidence. Endo-SPONGE may be cost saving in the long term (over 10 years) compared with a percutaneous drain. But, this is not certain because there is no clinical consensus about the care pathway for people who have leakage after a low rectal anastomosis.

Further research on Endo-SPONGE is recommended to resolve the clinical and cost uncertainties.

2 The technology

Technology

2.1 Endo-SPONGE is a minimally invasive surgical treatment for anastomotic leakage in the low rectal area. It consists of an open pore sponge with a drain tube, a sponge pusher, silicon overtube guides and a drainage set and system. The system is designed to improve the clearance of leaking discharge in the anastomotic leakage cavity and to promote granulation tissue formation and healing. Risks associated with Endo-SPONGE include residual sponge particles left in the cavity, erosion of structures next to the sponge, injury to the intestinal wall and bleeding.

The sponge needs to be replaced every 2 to 3 days. The replacement sponge is cut to the size of the leakage cavity as it gets smaller and the drainage tube exits the body through the anus. The first insertion procedure is usually done in an operating theatre under general anaesthesia. The replacement procedures can be done in a day-case theatre or endoscopy suite under light sedation.

Innovative aspects

2.2 Endo-SPONGE is a vacuum therapy. The sponge is inserted into the leakage cavity using a flexible endoscope or open access through the anus. A drainage tube is connected to the sponge at one end with a drainage bottle at the other end. The bottle has a low-vacuum drainage container that uses suction to put continuous negative pressure on the sponge.

Intended use

2.3 Endo-SPONGE is intended for people with extraperitoneal rectal anastomotic leakage. It is inserted by colorectal surgeons, endoscopists and gastroenterologists in a hospital setting. The Endo-SPONGE system is not suitable when the following conditions are present: malignant tumour wound; necrotic tissue or gangrene; untreated osteomyelitis; anastomotic leakage directly adjacent to vessels; bladder or small bowels obstruction, non-drainable septic focus, systemic sepsis and clotting disorders.

Relevant pathway

2.4 NICE has not published guidelines on rectal anastomotic leakage and the clinical experts noted that there is no standard care pathway for treatment. Guidance from the Association of Surgeons of Great Britain and Ireland on Prevention, Diagnosis and Management of Colorectal Anastomotic Leakage (March 2016) states that people with anastomotic leakage who are clinically stable may be treated conservatively using fluids, antibiotics and oxygen, with close clinical observation. However, for people showing signs of sepsis, steps must be taken to remove the source of the leak within 3 to 18 hours, depending on the underlying condition and severity of infection. In less severe cases of sepsis associated with extraperitoneal rectal anastomotic leakage, proximal defunctioning of the anastomosis with trans-anal or trans-peritoneal drainage may be considered. If there is radiological evidence that the anastomotic cavity is separate from the

bowel, or if there are multiple sites of anastomotic leakage, surgical intervention is needed.

Costs

2.5 The Endo-SPONGE kit costs £250.20 (excluding VAT) for a single sponge. The company estimates that complete treatment with Endo-SPONGE needs about 7 or 8 sponges. The drain bottle is bought separately, costing £20.90 per bottle (excluding VAT). Any glycerol-based hydrogel can be used and costs between £1 and £1.50 per tube.

For more details, see the website for Endo-SPONGE.

3 Evidence

Clinical evidence

Relevant evidence comes from 20 observational studies, including 2 comparative studies

3.1 There were 20 studies relevant to the decision problem in the scope:

- 2 comparative studies (Schiffmann et al. 2019, Wasmann et al. 2019)
- 4 prospective studies (Jiménez Rodríguez et al. 2018, Milito et al. 2017, Rottoli et al. 2018, Strangio et al. 2015)
- 14 retrospective studies (Arezzo et al. 2015, Boschetti et al. 2018, Huisman et al. 2019, Katz et al. 2018, Keskin et al. 2015, Kuehn et al. 2016, Manta et al. 2016, Mussetto et al. 2017, Nerup et al. 2013, Riss et al. 2010, Riss et al. 2009, Srinivasamurthy et al. 2013, van Koperen et al. 2009, Weidenhagen et al. 2008).

There were also 3 abstracts of non-comparative studies included (DiMitri et al. 2010, Martel et al. 2013, and McAuley et al. 2013). There were 3 studies done in the UK.

The evidence is limited because of a heterogenous population and inconsistent reported outcomes

3.2 The external assessment centre (EAC) considered the quality of the evidence for Endo-SPONGE very low. It found a high risk of bias because of the retrospective study design and small sample sizes (ranging from 3 to 34). It noted the clinical heterogeneity related to population characteristics and the definition of surgical site infections and success. It also found inconsistencies for how long Endo-SPONGE was in place and how many times it was changed, the length and frequency of follow up and concurrent or additional treatments. This might reflect the clinical uncertainty and variation in practice when treating people with anastomotic leakage. The clinical experts suggested that there is no clearly defined care pathway, and treatment is based on a number of factors. These include the patient's overall condition, the anastomotic defect size and location, the indication for primary resection and the presence of a proximal stoma.

The limited evidence suggests that Endo-SPONGE could be an option to treat anastomotic leakage

3.3 The limited evidence suggests that Endo-SPONGE could be considered as a treatment option for anastomotic leakage. The success rate of cavity closure for Endo-SPONGE was about 85% and ranged from 40% to 100%, but the definition of success varied across studies. The stoma reversal rate after successful Endo-SPONGE treatment was about 77%, ranging from 38.5% to 92.3%. One study reported that 6 out of 8 patients would be willing to have Endo-SPONGE treatment again if needed.

Cost evidence

The company estimates that using Endo-SPONGE saves £2,419.50 per person in the first year

3.4 The company presented a de novo cost analysis with an Endo-SPONGE decision tree and a comparator decision tree. Each decision tree had 4 branches for different grades of anastomotic leak that may result in non-

surgical or surgical treatment. The results from the company model estimated that Endo-SPONGE was cost saving by £2,419.50 per person in the first year.

There are 3 possible scenarios proposed by the EAC to reflect clinical practice in the NHS

3.5 The EAC noted that there was no standard treatment pathway for anastomotic leakage management. The procedure cost varied by care setting (inpatient or outpatient), types of sedation (general or local anaesthetic) and whether or not it was combined with other interventions. The EAC proposed 3 scenarios based on available evidence and expert advice to explore the cost impact in clinical practice.

The EAC has revised key clinical parameters based on published data but also uses clinical parameters from the company submission

3.6 The EAC considered the company model structure, a 1-year cycle and a 10-year time horizon to be appropriate. It changed the clinical and cost parameters based on published studies and expert advice. However, there was uncertainty about the most appropriate inputs to the model because there was no clearly defined care pathway. The EAC applied the clinical parameters submitted by the company with its revised parameters to the cost model.

The cost impact of Endo-SPONGE varies depending on the scenarios and clinical parameters considered

3.7 The EAC noted that the cost impact of Endo-SPONGE compared with percutaneous drainage varied depending on the scenarios and clinical parameters considered. One scenario expected Endo-SPONGE insertion to be done in theatre under general anaesthesia with subsequent sponge changes in an outpatient setting such as an endoscopy suite. Using the company's clinical parameters in the model, this scenario estimated that Endo-SPONGE would save £726 per person compared with percutaneous drainage in the first year. Using the EAC alternative clinical inputs in the model, Endo-SPONGE was estimated to have an additional

cost of £1,141 per person compared with percutaneous drainage. If both the insertion and replacement procedures were done in an operating theatre under general anaesthesia, then Endo-SPONGE was cost incurring in the first year. If a percutaneous drain was used as well as Endo-SPONGE, then the modelling estimated that the treatment was cost incurring in the first year.

Endo-SPONGE may be cost saving in the long term (10 years after the insertion procedure)

3.8 The EAC model estimated that Endo-SPONGE was cost saving over a 10-year time horizon. This was when the insertion procedure was done in an operating theatre and sponge changes were done in an endoscopy suite or day-case theatre under light sedation. Using the company's or EAC's clinical parameters, this would result in cost savings of £2,829.30 and £68.20 per person at 10 years, respectively, compared with percutaneous drainage.

4 Committee discussion

Clinical-effectiveness overview

Endo-SPONGE could treat anastomotic leakage in a relatively small number of carefully selected patients

4.1 The clinical experts advised that Endo-SPONGE was only suitable for treating a small selection of people. They explained that there were several key factors that informed decision making for treatment options for anastomotic leakage. These included the anatomy of anastomosis, the location and accessibility of the leakage, and the patients' general clinical conditions (specifically sepsis severity and their general health status).The clinical experts explained that, in their clinical experience, Endo-SPONGE would be considered if:

- the anastomotic leakage was in the low colorectal area
- the leakage cavity was accessible through the anus

- the leak remained localised with no abdomen or peritoneum contamination
- the patient was clinically stable enough to have the procedure.

The committee agreed that Endo-SPONGE was indeed a 'niche' technology that could be considered for a relatively small number of patients. There was no evidence that define the criteria for patient selection. It concluded that a clearer understanding of the patient population who could benefit from Endo-SPONGE was important. This should be included in future research objectives.

The benefits of Endo-SPONGE are not consistently defined and reported in the included studies

4.2 The definition of treatment success after Endo-SPONGE varied between studies. It was most frequently defined as closure of the leakage cavity to less than 1 cm, or complete granulation and resolution of the cavity. Also, the reported stoma reversal rates varied widely between studies. The committee agreed that there was some evidence that Endo-SPONGE may improve anastomotic leakage cavity healing and stoma reversal. However, the evidence was low quality with considerable variation in important clinical end points between studies. Also, a recently published systematic review was not included in the evidence review and its reported stoma reversal rate was considerably lower than the external assessment centre (EAC) pooled rate (Mahendran et al, 2020). The committee concluded that, while Endo-SPONGE showed promise, the evidence base was not robust enough to support the claimed clinical benefits.

More evidence is needed to assess how acceptable Endo-SPONGE is to patients

4.3 The clinical experts advised that Endo-SPONGE was likely to improve patients' quality of life. This was because it offers the possibility of stoma reversal and restoration of bowel function. However, only 2 studies reported patient outcomes that included patient acceptability (Riss et al. 2009) and functional bowel recovery (Huismann et al. 2019). In the clinical

experts' experience, pain and discomfort were the 2 most reported adverse symptoms. Also, treatment with Endo-SPONGE was only stopped because of pain in a small number of their patients. The committee concluded that, while Endo-SPONGE may be poorly tolerated by some patients, there was uncertainty about how tolerable the treatment was. More real-world evidence is needed to understand the effect of Endo-SPONGE on health-related quality of life and residual bowel function.

National databases could improve the evidence for Endo-SPONGE

4.4 The committee concluded that the overall quality of the current evidence was low with a high risk of bias. This was because of the retrospective study design, limited comparators and small sample sizes. The clinical experts explained that the patient groups for whom Endo-SPONGE might be suitable would be small and carefully selected. So, it is unlikely that it would be practical to do a randomised controlled trial. However, they suggested that using a national database or clinical registry could help evaluate the clinical benefits of Endo-SPONGE and define the most appropriate patient population. The committee agreed that further research with observational and real-world data would strengthen the evidence.

NHS considerations overview

Managing anastomotic leakage is challenging without a clearly defined care pathway

4.5 The clinical experts noted that the rate of anastomotic leak after colorectal surgery in the UK is relatively low. One clinical expert estimated that the rate of anastomotic leak after colorectal surgery was approximately 6%. Around 10% to 15% of this would be leakage in the low rectal areas, for which Endo SPONGE can be used. The clinical experts recognised that there have been improvements in techniques for colorectal surgery such as stapling and robotics. This could help reduce the incidence of anastomotic leakage. However, it remains a serious complication after

colorectal surgery in some patients. The clinical experts explained that the treatment care pathway for patients with anastomotic leakage varied across the NHS. It depends on local clinician experience as well as the facilities and resources available. The committee concluded that managing anastomotic leakage could be challenging without a clearly defined care pathway.

Training

The Endo-SPONGE procedure is easy to learn but specific training is needed

4.6 The clinical experts advised that specific training is needed for the Endo-SPONGE procedure but the procedure is easy to learn. The company provides free on-site training. The main challenge of getting clinical experience for this technology is the relative lack of patients for whom it can be used. A clinical expert explained that, in their organisation, Endo-SPONGE may only be suitable for about 4 to 5 patients per year. Support from the company providing access to training such as simulation training may help to resolve this issue. The committee concluded that the Endo-SPONGE procedure is easy to learn but specific training is needed.

Cost modelling overview

Comparing Endo-SPONGE and percutaneous drainage may not be appropriate because they are likely to be used in different clinical scenarios

4.7 Both the company and the EAC did an indirect cost comparison of Endo-SPONGE with percutaneous drainage for treating anastomotic leakage. However, the clinical experts advised that this comparison may not be appropriate. Alternative comparators such as the placement of a trans-rectal or trans-anal drain may be used for leaks after a low rectal anastomosis. Patients who can have treatment with either Endo-SPONGE, a trans-anal drain or a percutaneous drain may have different clinical and anatomical characteristics. The committee understood that trans-rectal and trans-anal drains are surgical alternatives for treating anastomotic leakage and that the decision problem covered all

surgical techniques. The committee concluded that Endo SPONGE and percutaneous drainage are likely to be used in different clinical scenarios. A like-for-like comparison between Endo SPONGE and trans-anal and trans-rectal in people with similar clinical and anatomical characteristics is needed.

The cost consequences of Endo-SPONGE are uncertain

4.8 There were 3 clinical scenarios modelled by the EAC. Of these, the clinical experts agreed on a scenario that most reflected clinical practice. This was the one in which the first assessment and Endo-SPONGE insertion was done in an operating theatre under general anaesthesia, with sponge changes done in an outpatient setting under local anaesthesia or light sedation. The clinical experts also added that, in their experience, endoscopy is not needed to insert Endo-SPONGE, because of how close the leakage cavities are to the anal verge. The committee noted that in the cost modelling, the main cost drivers were reoperation rates and rates of avoiding costs associated with a permanent stoma. However, a wide range of values for these important clinical parameters were reported in the studies. The committee concluded there were significant uncertainties related to the cost consequences of using Endo-SPONGE.

Further research

Endo-SPONGE shows promise and further research is needed

4.9 Endo-SPONGE shows promise for treating anastomotic leakage, but further research is needed to help define the clinical and cost benefits. This research should address the uncertainties around patient selection. It should also evaluate the effect of avoiding further surgery and the rates of stoma reversal and bowel function restoration for Endo-SPONGE and other treatments. This research should include patient-reported outcome measures to explore patient experience and the acceptability of this technology.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technology advisory committee which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technology advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more technical analysts (who act as technical leads for the topic), a technical adviser and a project manager.

YingYing Wang
Health technology analyst

Bernice Dillon
Health technology adviser

Victoria Fitton
Project manager

ISBN: [to be added at publication]

