Minimally invasive strategies for the surgical treatment of colonic peritonitis
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General discussion and future perspectives
GENERAL DISCUSSION AND FUTURE PERSPECTIVES

Grading the severity of peritonitis – mind the gap

Treatment options for peritonitis largely depend on the severity and cause of the peritonitis. Back in the days, the clinical diagnosis of an “acute abdomen” did not require grading as the treatment would be explorative laparotomy regardless of severity and cause. Nowadays, we can choose between a variety of medical, radiological and surgical treatment options and must rely on clinical parameters and radiological examination to determine the best option for intervention. This means that the classic Hinchey classification\(^1\) is no longer suitable as it is an intra-operative grading system for perforated diverticulitis. Several others tried to translate these operative findings into a radiological grading system but failed to clearly link the grade to an therapeutic plan.\(^2\)\(^-\)\(^6\) Not all abscesses require percutaneous drainage and not all patients with intra-peritoneal air or fluid require surgical therapy, but none of these classifications provide sufficient guidance. Two even acknowledge that they cannot provide sufficient accuracy to distinguish faecal from purulent peritonitis.\(^2\)^\(^^4\)

A new clinical and radiological grading system is needed to determine the need for surgery. When surgery is required, the need for lavage or resectional surgery can be determined during diagnostic laparoscopy, supported by the radiological imaging. A proposal for such classification system is shown in figure 1, grade 1 as uncomplicated diverticulitis, grade 2 complicated with abscess (2A < 5cm, 2B > 5cm), grade 3 perforation with local air or fluid (covered perforation) and grade 4 with distant air or fluid (4A air without distant fluid or contrast leakage, 4B with distant fluid or contrast leakage). However, such a revised Hinchey classification does require clinical validation before it can be implemented and suggested definitions might need to be adjusted. Those patients classified as grade 4 require further differentiation using diagnostic laparoscopy before definitive surgical therapy.
Figure 1. Revised Hinchey classification
For anastomotic leakage following colorectal surgery, no such detailed classification exist either. At best, it is classified according to applied therapy. The International study group of rectal cancer graded leakage as A: leakage without change in postoperative management, B: leakage requiring medical or radiological intervention, and C: leakage requiring re-laparotomy. This is useful for quality registry and study outcomes, but does not help to choose the appropriate treatment. Similar to the suggested grading for perforated diverticulitis in figure 1, grading for the severity of colorectal anastomotic leakage should be applied. This is of importance as not all leakages require surgical management and not all that do, will require end-colostomy. The main difficulty diagnosing anastomotic leakage on CT is the presence of free air and fluid following laparoscopic colorectal surgery. Some remaining air and fluid following the initial laparotomy or laparoscopy should be considered normal in the early postoperative period, but the normal quantity is unknown. A suggestion for grading the severity of colorectal anastomotic leakage is shown in figure 2.

In both suspected colorectal anastomotic leakage and perforated diverticulitis, rectal contrast enhanced CT scan can be helpful to show leakage of bowel content and can therefore distinguish intraluminal from extra luminal air. Water soluble contrast should be used as barium contrast is toxic for the peritoneum. However the use of rectal contrast for acute abdominal CT scans is not routine practise and barely discussed in current guidelines.
When surgery is indicated for perforated diverticulitis, diagnostic laparoscopy can be used to further examine the severity of peritonitis and determine the need of sigmoidectomy and colostomy. Following the introduction of laparoscopic lavage, the surgeon can determine whether the peritonitis is caused by bacterial translocation, a properly covered perforation, or an overt perforation with (potential) faecal contamination. The latter is likely to be the case when extra-luminal contrast has been observed on CT-scan. As the phlegmon is often located at the pelvic entrance, occluding the view on Douglas pouch, faecal contamination of the pelvis can easily be missed. However, complete mobilisation of the phlegmon would expose a properly covered perforation and increase the need for sigmoidectomy instead of lavage only. Therefore it remains difficult to tell whether it is best to fully expose or not, and it might be an option to rely on the CT findings when deciding to expose the pelvic cavity. 
The rate of undiagnosed direct perforations must be estimated at 37%, as this is the rate of perforations found in the pathological specimens of both the sigmoidectomy group of the LOLA-arm and a previous study.15

Like perforated diverticulitis, diagnostic laparoscopy in suspected anastomotic leakage can be useful to confirm the diagnosis and determine the required therapy. Depending on the severity of anastomotic dehiscence, lavage and deviation with loop ileostomy, repair of the anastomosis, redo of the anastomosis or take down with end colostomy should be performed.8,9,16

**Conservative management of perforation and leakage**

According to the revised Hinchey classification as suggested in figure 1, almost all patients except those with large quantities of free air, generalised fluid or contrast leak, can be managed without surgical therapy. This is well known for Hinchey I and II, but a newer approach for those patients with limited signs of Hinchey III perforated disease.14 Successful treatment with laparoscopic lavage might therefore be overtreatment of those graded as Hinchey III but eligible for non-surgical management. Dharmarajan and colleagues17 scored the extent of free air and fluid on a CT-scan of patients with perforated diverticulitis. Of the 27 patients with distant free air collections without generalised free fluid, 25 (93%) were successfully managed non-operatively. Another study of 39 patients described a success rate of 92% for non-surgical management of perforated diverticulitis with free air and without rectal contrast extravasation on CT-scan.18 A third study reported a 62% success rate in 29 patients with distant intraperitoneal air and a 99% success rate in 82 patients with pericolic air only.19 Therefore non-surgical management might be suitable for those patients with perforated diverticulitis and the following criteria (1) distant free air without free fluid (2) distant free air without rectal contrast extravasation (3) pericolic free air only as used in figure 1. As the evidence is limited to three case series, further research is required to establish the definitive role of non-surgical management in these patients.
In contrast to the non-surgical management of diverticulitis, the option of non-surgical management in colorectal anastomosis highly relies on the presence of a deviating ostomy and sufficient drainage of the leak. Non-surgical management however largely requires adequate imaging as relaparotomy no longer can be the gold standard for the diagnosis. Some studies have shown water soluble enema was superior to CT scanning without intraluminal contrast.\textsuperscript{20} However, combining both might provide the best results as both contrast extravasation and the extent of intraperitoneal air and fluid can be assessed and evaluated. Combining non enhanced CT with rectal contrast CT directly afterwards helps to eliminate discussion about the origin of dense material outside the bowel wall as it might be contrast from previous series or operative material.

When CT shows a leakage in a contained space, as for instance can occur following low anterior resections in the presacral space, the leak can be drained instead of surgically treated in a non-septic patient. Drainage can either be percutaneously, transvaginally or transrectal directly via the anastomosis. Soeters et al.\textsuperscript{9} considered conservative management with antibiotics of small anastomotic abscesses with only mild clinical symptoms to be a safe treatment. Small leaks with larger abscesses should be treated with transrectal or radiological drainage, and larger leaks needed surgical treatment with resection of the anastomosis. Only in the case of failure of less than 50% of the circumference and the absence of generalised peritonitis, the anastomosis expected to heal spontaneously if a diverting enterostomy was present and abscesses were adequately drained.\textsuperscript{9}

To determine the possibility of non-surgical treatment of leakage, the grading in figure 2 can be used, however the clinical condition should be most important. In case of systemic sepsis, surgical treatment should not be proponed.\textsuperscript{21}

Safety of laparoscopy in peritonitis and other abdominal emergencies
Although questioned by many, there is no evidence that laparoscopy is more harmful than laparotomy in case of peritonitis. It is obvious that any new treatment modality is established first on the straightforward elective cases first, and that safety is the main focus of the first research.

Experimental studies have raised concern regarding a the risk of increased bacteraemia and hypercapnia due to the pressure of the pneumoperitoneum.\textsuperscript{22,23} This theory has never been proven nor disproven, but the gained experience with laparoscopic treatment in abdominal sepsis of various causes, such as appendicitis, cholecystitis, perforated peptic ulcer and diverticulitis does not support this hypothesis.\textsuperscript{21}

Many surgeons still regard general peritonitis and especially faecal peritonitis as a contraindication for a laparoscopic approach. This is based on mechanical concerns, with the risk of damage to the distended and vulnerable small bowel by the laparoscopic instrumentation and lack of sufficient overview. A systematic review reported a 64% success rate of laparoscopic treatment in 2005 patients with small bowel obstruction. Only
about 10% of the conversions were due to iatrogenic injury.\textsuperscript{24} Even a small bowel diameter greater than four centimetres was not considered to be an absolute contraindication for laparoscopy.\textsuperscript{25}

Although sufficiency of overview is difficult to measure, multiple studies have shown a low conversion rate due to inadequate exposure. Only 8% of the conversions were due to inadequate exposure, and less patients required additional surgery after relaparoscopy compared to relaparotomy, indicating adequate diagnosis and treatment.\textsuperscript{16,24} In our cohort of patients treated by laparoscopic sigmoidectomy in perforated diverticulitis, only 2 out of 44 needed conversion (5%), and a similar rate was observed in completing laparoscopic lavage in the Ladies trial.\textsuperscript{26}

In addition, many fear the establishment of a primary anastomosis in general peritonitis. Especially in perforated diverticulitis, up to now no study has shown an anastomotic leakage rate higher than a reasonable 5%.\textsuperscript{27,28} This is a similar rate compared to the leak rate following reversal of the alternative of Hartmann’s procedure. The results of the remaining DIVA arm of the Ladies trial are expected to support this result.\textsuperscript{29}

An obvious benefit of laparoscopic surgery is the integrity of the abdominal wall, reducing the rate of acute fascial dehiscence in high risk patients with peritonitis. The dehiscence rate was lower following laparoscopic treatment of anastomotic leakage with 3% compared to 22% in open surgery, a similar difference was observed in perforated diverticulitis wit 0% and 7%.\textsuperscript{16,26}

\textbf{Lavage, reinforcement, revising or resection of the diverticular segment or leak}

The old standard for anastomotic leakage or colon perforation is resection of the failing segment with end colostomy (Hartmann’s). In case of a right hemicolecction, this would be an end ileostomy. Even in patients with postoperative sepsis and a negative relaparotomy, the anastomosis is sometimes taken down “just in case” or “to prevent worse”. This is an invalidating choice as over 60% of the patients with end colostomy after leakage will never get reversal.\textsuperscript{16,30} This rigorous treatment is obviously driven by the anticipated high mortality rate following leakage, however this does not mean it is the best option. Pera et al.\textsuperscript{31} described successful salvage surgery with lavage and a diverting ileostomy in 6 out of 7 patients, including four laparoscopic procedures. Fracalvieri et al.\textsuperscript{32} described 39 patients with a salvage procedure and 54 with resection of the anastomosis, with less mortality (15% versus 37%) and better chances for reversal in the salvage group (91% versus 38%). In our own study, salvage occurred in 60% of patients following relaparoscopy and 33% of patients with relapartomy.\textsuperscript{16} Despite the higher salvage rate, less patients required additional surgical reinterventions.

Besides redo of the complete anastomosis, salvage of the anastomosis can be achieved by repair of the defect by either suture, tissue adhesives or in combination with omentoplasty. All of these options are similar to those applied in reinforcement of the anastomosis
to prevent leakage.\textsuperscript{33} In patients with a low rectal anastomosis, repair might even be performed transanally.\textsuperscript{34} Another new option which is currently under investigation is the use of an endosponge vacuum system in a presacral sinus followed by transanal closure of the defect.\textsuperscript{35} In the upper gastrointestinal tract, covered stents are successfully used to treat perforations and anastomotic leaks of the esophagus. Although stent migration is a troublesome complication, this technique can successfully applied with a clinical success rate of 81\%.\textsuperscript{36} Although metallic stents have been successfully used for colonic strictures, no such reports are available for colorectal anastomotic leakage. Only one animal study demonstrated successful application of a covered stent in the colonic anastomosis in pigs and reducing the abscess rate.\textsuperscript{37}

The role of extensive peritoneal lavage in addition or as sole treatment of purulent peritonitis remains unclear. In laparotomy, it is easy to rinse the abdominal cavity with large quantities of saline or other antibacterial solutions. In laparoscopy, flushing the same amount of fluid takes more time and effort. Therefore smaller quantities are often used. Although rising is appealing to the eye, it does not only wash away debris and bacteria, it also allows bacteria to spread throughout the abdominal cavity.\textsuperscript{38}

Laparoscopic lavage as a surgical treatment for perforated diverticulitis with purulent peritonitis was studied in the LOLA arm of our Ladies trial and three other randomised trials.\textsuperscript{29,39-41} All trials included a similar patient population, although inclusion criteria differed the baseline characteristics between trials did not. Previous series suggested improved morbidity and mortality outcomes following peritoneal lavage compared to historical data on Hartmann’s procedure. Ours and two others have presented the short term outcomes recently, but none can confirm any improvement in morbidity and mortality for laparoscopic lavage.\textsuperscript{26,42,43} The Scandiv trial group reported a 90-day severe morbidity rate (Clavien-Dindo ≥ 3B) of 31\% following lavage and 26\% following sigmoidectomy.\textsuperscript{43} The Danish DILALA group reported 21\% and 17\% for lavage and Hartmann’s procedure respectively at 6-12 weeks postoperatively. The LOLA trial reported a higher rate of 44\% and 24\% respectively but included 5 (11\%) elective sigmoidectomies just before the first 90 days. Although these results are much worse than reported in the case series, postoperative/30-day mortality was equally low in all trials regardless of treatment (0-7\%). Our results show that the long term outcomes are generally worse in the sigmoidectomy group due to Hartmann’s reversal. This results in similar morbidity outcomes for both groups at 12 months, but has to be confirmed by the long term results of the other trials. Troublesome is the rate of wrongfully included patients with perforated colon carcinoma, accounting for approximately 4-10\% of the patients. When resection is performed, this would be not affect the further treatment of the cancer, but in case of lavage, diagnosis and resection are delayed until follow up colonoscopy. This might result in an increased risk of (peritoneal) metastases and decreased survival.
On the positive side, the majority of patients in the lavage group avoided laparotomy and stoma formation and about half avoided sigmoidectomy within the first year. Whether or not the last is of benefit must still be shown in longer term results, but a decreased risk of fascial dehiscence is already seen (11% vs 17% in lavage and resection respectively in intention-to-treat population). All hernia in the lavage group occurred in patients following relaparotomy or conversion.

Future perspectives
Taking into account the observations in this thesis and those discussed above, the treatment of colonic peritonitis is likely to become less invasive in the next decades. Laparoscopic surgery will become the standard for both elective and emergency surgery, and the surgical therapy itself will become less extensive. The role of non-surgical management with antibiotics or percutaneous drainage will further increase, increasing the demand for more detailed clinical and radiological diagnosis and classification. If surgery cannot be avoided, lavage and salvage of the affected sigmoid or anastomosis will be preferred over Hartmann’s procedure in most patients. If resection of the affected segment is unavoidable, primary or redo anastomosis can be performed. Use of a loop ileostomy as a preventive measure will be reduced, but loop ileostomy will be used as part of a salvage procedure for early diagnosed anastomotic leakage instead.
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