

Laparoscopy and Intra-Abdominal Sepsis

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Received: April 6, 2015; Revised: May 25, 2015; Accepted: May 27, 2015

Context: Intra-abdominal sepsis has significant morbidity and mortality. In the developed world, there are many common causes originating from the lower gastrointestinal tract including diverticular disease, appendicitis, perforated cancers, and inflammatory bowel disease. It has a high cost and is associated with high levels of significant morbidity and mortality. Management options include radiologic drainage and surgical options include resection for more widespread sepsis. Laparoscopic surgery has increased and has been useful in elective setting. Its use in the emergency setting is less evaluated.

Evidence Acquisition: Evidence was acquired by searching online medical databases including Pubmed, Medline and Embase.

Results: Laparoscopic surgery has been shown to have a role in the acute setting. Studies show it has become the gold standard in the appendicitis. High quality Randomized controlled trials are in short supply but observational and cohort studies have shown equivalence and with increasing experience complication rates are reduced. Evidence is also increasing in the management of diverticular disease, crohn's and ulcerative colitis as well as post-operative complication management and acute presentations of colorectal cancer.

Conclusions: Laparoscopic surgery is feasible in the management of intra-abdominal sepsis. It has become the new accepted standard in the management of appendicitis, and is safe, feasible and increasing in the management of complex diverticular disease, acute IBD and colorectal cancer in the emergency and post-operative setting.

Keywords: Diverticulitis; Appendicitis; Laparoscopy; Crohn's Disease; Colorectal Cancer; Ulcerative Colitis

1. Context

Pelvic sepsis is a common problem. There are multitudes of causes leading to this presentation. Common causes include perforated viscus (appendix, diverticular disease, and tumors), gynecological diseases (pelvic inflammatory disease [PID]), and rare causes such as opportunistic infections (tuberculosis and actinomyces) (Table 1). The detected causative agents depend on the site and cause, but include gastrointestinal (GI) organism such as *Escherichia coli* and bacteroides. Management of sepsis includes source control; thus, identification of source is crucial to subsequent management. Diverticular disease is one of the leading causes of intra-abdominal sepsis in the developed world, but little evidence and consensus about its management exists. We examined the evidence behind presentation and treatment strategies.

2. Evidence Acquisition

A search of Medline, Embase and Pubmed was undertaken. All relevant studies were sourced and reviewed to help undertake this review.

3. Results

3.1. Diverticular Disease

Diverticular disease is a common pathology, is often asymptomatic, and may be detected incidentally on investigation for other pathology. There is also an overlap between irritable bowel syndrome (IBS) and diverticular disease. The term diverticulitis should only be used for proven inflammation to avoid miscommunication and overtreatment. Indeed, subsequent resection can lead to continuing symptoms in up to 25% of this patient population (1).

Table 1. Causes of Intra-Abdominal Sepsis

Cause	Level	Coexisting Pathologies Often Found
Ascites	Primary or secondary	Liver failure: alcohol, viral hepatitis (hepatitis B and C), and peritoneal dialysis
Gastrointestinal pathology	Lower	Acute inflammation: appendicitis, diverticulitis, tumors, and inflammatory bowel disease
Trauma	Any abdominal organ	Usually penetrating wounds, infected hematoma, eg, conservatively managed blunt trauma such as splenic injury
Gynecological	Pelvic inflammatory disease	tuboovarian abscess, rarely tumors

Most symptomatic patients present as an emergency. Diverticular disease can present with abscess formation, free perforation, bleeding, fistula, or stricture and large bowel obstruction.

Common classifications such as the Hinchey system (Table 2) help assess the degree of complication and stratify treatment of diverticular disease in the United Kingdom (2, 3).

Definitive imaging options include ultrasonography (USG), water-soluble contrast study, and computed tomography (CT); however, CT remains the gold standard method of diagnosis (4). CT helps to exclude obstruction and detect malignancy. Following an acute attack, performing luminal endoscopy with a view to exclude a cancer/polyp is recommended. This can be technically challenging; however, CT colonography (CTC) has been proposed as a viable alternative. Both the SIGGAR (Specialist Interest Group in Gastrointestinal and Abdominal Radiology) trial and other studies have shown it to be comparable to endoscopy and barium enema (5, 6).

3.1.1. Emergency Presentation

Treatment of acute diverticulitis involves the resuscitation, adequate analgesia, and use of broad-spectrum antibiotics. Definite management falls into four categories:

3.1.1.1. Conservative management

For patients with localized signs or those who are systemically well, a thorough trial of conservative management is appropriate. Initial imaging may show Hinchey 0/1 diverticulitis. CT is still useful as a diagnostic test and in case of subsequent deterioration. Most abscesses < 5 cm will resolve with conservative management (7). The use of antibiotics in treatment has also come under scrutiny in recent years. A recent Cochrane review (8), however, found limited evidence in support of the use of antibiotics for uncomplicated diverticulitis. They did not stop progression to complicated disease or reduce the need for intervention. Nonetheless, no meta-analysis was possible and further studies are required before antibiotics are no longer used or required in the management of diverticular disease.

3.1.1.2. Radiological Drainage

Percutaneous drainage remains an option for confirmed collections around a diverticular phlegmon. It should be remembered that small collections (less than 5

cm) usually resolve with conservative management and rarely require intervention (9). Drainage can be done as a bridge to elective surgery and is feasible and safe, if a safe passage to the collection is seen on imaging studies (9). This is a particularly appealing therapeutic option in patients with high predicted mortality from surgery or general anesthesia, such as those with severe cardio-respiratory co-morbidities, but remain stable with a definitive collection (10).

3.1.1.3. Laparoscopic Drainage

Since 2008 (11), laparoscopic washout and drainage is feasible as a viable emergency option for perforated diverticulitis (Hinchey 2/3). Whilst this had been shown to be possible in selected small case series, it was not accepted as a mainstay of treatment (12, 13). In some centers, laparoscopic drainage has replaced radiologic drainage and can lead to lower morbidity and mortality (14). The LADIES trial and the DILALA trials are currently looking at the role of laparoscopic lavage further in both Europe and Scandinavia (15, 16). The initial and pretrial results from the Dutch Diverticular Disease Study Group suggest that laparoscopic lavage is feasible, but state overt sigmoid perforation (with significant contamination or large defect in the colonic wall) and patient selection is crucial (17). Some authors advocate the use of on-table sigmoidoscopy (rigid or flexible) to insufflate to assess the perforation site if it is not readily visible. However, this runs the risk of conversion of a localized sealed perforation into an open one necessitating resection. It is also possible to suture a small (less than 1cm) defect laparoscopically or use an omental patch to cover the defect.

The main advantage of lavage however is the ability to turn the emergency resection into an elective procedure where conversion rates are lower, with reduction in morbidity (18, 19).

3.1.1.4. Definitive Surgery

In those with Hinchey 4 perforated diverticulitis or those in whom a large perforation or systemic signs are present, definitive therapy is surgery. The options are open drainage +/- diversion (colostomy) and resection +/- anastomosis (+/- defunctioning ileostomy). Anastomosis is preferable for patients and avoids the need for a second major procedure to re-anastomose. However, in the presence of sepsis and an acutely unwell patient, a leak can prove fatal.

Table 2. Modified Hinchey Classification of Diverticulitis

Level	Symptoms
0	Diverticulitis
1	A: Confined pericolic inflammation B: Pericolic abscess
2	Pelvic, distant intra-abdominal or retroperitoneal abscess
3	Generalized purulent Peritonitis
4	Fecal Peritonitis

A Hartmann's procedure remains a safe emergency procedure. There remains morbidity associated with the formation of a stoma-retraction (especially in the obese patient), separation, obstruction—as well as the potential for pelvic sepsis related to blowout from the rectal stump suture/staple line. Most colorectal surgeons would divide the rectal stump using a stapler (and then over sew it to re-enforce the staple line) at a convenient site, usually close to the pelvic brim (it can be marked with long non-absorbable sutures) allowing reversal in the future.

There is evidence that primary resection and anastomosis leads to lower mortality (7.4% vs. 15.6% for Hartmann's procedure) (14). However, these trials are both heterogeneous and no difference existed at levels Hinchey 2 and above. Further work is still required. The decision to anastomosis remains a personal one with experience and status of the patient, considering pre-morbid and disease-related status. Improvements in postoperative care, nutrition and perioperative management with intensive care means that the decision to anastomosis can be made in those undergoing resection. Where Hinchey 4 peritonitis, i.e. an unstable or frail patient is present, a Hartmann's procedure remains the best option. Both of these options in experience hands can be performed laparoscopically when possible; however, conversion to open procedure is often required. The SIGMA trial showed that in the elective setting laparoscopy is feasible (20), and advocates have advanced this to the emergency setting as well.

The issue of providing a covering ileostomy when anastomosing again remains a personal choice. The anastomosis is usually high and the proximal colon is unprepped. If an ileostomy is proposed, it may be prudent to lavage the proximal colon, either using the appendix or caecum or milking from the distal end.

3.1.2. Appendicitis

Appendicitis is one of the most common general surgery emergencies. It has a lifetime incidence of 7 to 12% in the United States and Europe (21-23), and is commoner in males whilst a higher appendectomy rate is noted in females (often undergoing surgery with other identified pathologies) (21). The highest incidence is noted between 19 to 30 years old (21-23).

Appendicitis is triggered by bacterial infection due to obstruction of the appendix orifice in the caecum. Commonly, this is caused by a fecalith, but can be triggered by other pathology such as parasite infections (helminths), tumors (carcinoid), lymphoid aggregates, and post-pneumocolon in colonoscopy. The disease progresses and full-thickness inflammatory responses are seen. This can lead to ulceration, necrosis, and secondary perforation. In turn, it can lead to peritonitis or localized abscess formation.

Classically, appendicitis presents with migratory midgut (central) to right iliac-fossa pain over 12 to 24 hours. Associated symptoms include anorexia, nausea,

and fevers. The location of the appendix varies and pelvic appendicitis can be associated with urinary or GI disturbance. In the presence of abscess formation, a mass may be palpable.

The use of laparoscopy as a diagnostic test has changed management of suspected appendicitis. Blood tests including increased white cell count (leukocytosis), elevated inflammatory markers (CRP), and liver function test such as bilirubin have been shown to have a role, particularly in perforated appendicitis (24, 25). Procalcitonin, a newer blood test, has been shown to be useful in detecting those with complicated appendicitis, but is not used widely (26).

The diagnosis of appendicitis mainly remains a clinical or radiologic one, but two scoring system exist to help clinicians. The Alvarado score gives a score on a ten-point scale (Table 3). Scores < 5 strongly suggests another diagnosis whilst a score of ≥ 7 is a strong predictor (27, 28). A lesser-known system, incorporating the use of USG, is the Tzanakis system (Table 4). This gives a score on a 15-score scale, with more than 96% predictive value (29).

Table 3. The Alvarado Scoring System for Acute Appendicitis ^a

Sign/Symptom	Score, points
Migratory pain	1
Anorexia	1
Nausea or vomiting	1
RIF tenderness	2
Rebound tenderness	1
Fever more than 37.3°C	1
Leukocytosis > 10000 cells/μL	2
Neutrophilia/shift to the left	1
Total	10

^a Abbreviation: RIF, Right Iliac Fossa.

Table 4. Tzanakis Scoring System for Acute Appendicitis ^a

Sign/Symptom	Score, points
RIF pain	4
Rebound tenderness	3
white cells > 12000 cells/μL	2
+ve USS	6
Total	15

^a Abbreviations: RIF, Right Iliac Fossa; and +ve USS, positive ultrasound.

The use of imaging for diagnosis of acute appendicitis has increased. The USG is cheap, simple, and easily accessible in most hospitals. It is used not only to diagnose appendicitis but also to detect other pathology including gynecological pathologies in females. The USG for GI pathology in the United Kingdom relies predominantly on GI sonographers or consultants with a dedicated interest. However, it can have a sensitivity of 44 to 99% and specificity of 47 to 100%. CT has a higher diagnostic rate with sensitivity of 92.5% and specificity of 89% (30, 31). Concerns exist over the use of ionizing radiation and increased future cancer risk with CT. There has been an increasing move to utilize magnetic resonance imaging (MRI). The OPTIMAP study group showed MRI to be comparable to USG with conditional CT use in diagnosis. However, both sets of imaging could under-stage complicated appendicitis as simple appendicitis, which can affect subsequent treatment (32). The greatest population who benefit in UK practice are pregnant females or children. Its use has been validated with high negative predictive value, but variable sensitivity (33).

3.1.3. Emergency Presentation

Treatment of appendicitis involves the use of analgesia, fluid resuscitation, and antibiotics. There are a number of definitive management strategies.

3.1.3.1. Conservative Management

Until recently, conservative management was reserved for those deemed unfit for surgical intervention, where a trial of antibiotics alone would be used. In recent years, a shift to nonoperative management is seen and a number of trials has demonstrated its efficacy in the management of uncomplicated appendicitis. A recent Cochrane review (34) demonstrated that whilst some studies found positively in favor of antibiotics, the overall results are inconclusive. A recent meta-analysis (35) demonstrated that antibiotics had a 63% success rate and a 20% recurrent appendicitis rate of which 20% had complicated appendicitis. However, one of the major problems with this strategy remains the correct identification of complex appendicitis versus simple appendicitis in imaging studies.

3.1.3.2. Laparoscopic Versus Open Appendectomy

Laparoscopic appendectomy has become the gold standard and mainstay of surgical treatment of appendicitis. Its main advantages include the ability to identify the appendix as the primary pathology, recognizing other pathologies, especially pelvic pathology in females, and excellent obtainable views of the whole abdomen. The laparoscopic view also enables through washout of the whole abdomen. There are a number of trials and meta-analyses demonstrating shorter length of stay, reduced wound infections, reduced postoperative bowel obstruction (36-40), and less pain, but a slightly higher rate of

intra-abdominal abscesses. There is also evidence that show fewer patients are re-admitted postoperatively (41). An updated Cochrane review in 2010 recommends laparoscopy as first-line operation (42).

In the early 1990s, initial results were treated with skepticism and indeed high rates of complications including abscess were recorded. Recent studies (43) have shown reduction in these rates. Whilst complication rates are noted, these are lower than previously thought. Earlier studies had small numbers and short follow-up period, and were indeed heterogeneous and underpowered to look at postoperative septic complications. The upsurge in laparoscopy has undoubtedly raised standards and training programs have accentuated this. Rates of intra-abdominal abscesses remain high in studies ($\times 3$), but it may be over-represented by trial powering. The benefits in females of childbearing age and obese patients are increased (42).

Apart from intra-abdominal abscess, the other main concern with laparoscopic appendectomy was stump appendicitis. As technique has improved this has been found to be an extremely rare phenomena. Recent studies and reviews show similar rates in laparoscopic and open appendectomies (43-45). If this occurs, the diagnosis is often clouded by a history of prior appendectomy and CT is often indicated. Treatment can be with either laparoscopic or open appendectomy, but prevention and proper ligation are the keys (45).

Appendectomies are increasingly performed using further minimally invasive techniques including single port incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (NOTES) (46, 47). A recent meta-analysis of SILS surgery found better cosmetic satisfaction, with similar results for complications and length of stay. However, conversion rates and operating times were longer, reflecting the complexities and possibly the learning curve of newer techniques (46).

3.1.3.3. Appendix Abscess: Radiological Treatment, Conservative Management, and Surgery

Appendix abscess is the result of the natural walling-off of the inflammatory change around the appendix. Options for management include surgery (open or laparoscopic) and percutaneous drainage. CT-guided drainage is a safe and effective treatment modality (48). It can allow the inflammatory component to settle with an entirely conservative approach or for interval appendectomy to be performed in patients with on-going or recurrent symptoms. Depending on the age, comorbidity, initial imaging, and length of history, clinicians will be guided to decide whether an operative or drainage approach is required; abscess size is often helpful. A drainage route often treats abscesses with diameter of > 4 cm in stable patients. A large meta-analysis demonstrated that drainage failure rates are around 7% and immediate surgery is associated with higher morbidity

than nonsurgical treatments. Malignant disease was identified in 1.2% of such cases (49).

3.2. Tumors

Colorectal Cancer is common in the developed world. It is the fourth most common cause of cancer death on a global scale (50). Unfortunately, despite access to health-care, emergency presentation is common and is linked to poorer patients' outcome (51). There are excess cancer-related and inter-current deaths related to those presenting as an emergency (51).

There has been an increasing change in elective practice to minimally invasive surgery including laparoscopic, SILS, and robotic surgery. Studies have found no inferiority of oncological outcome and improvements in length of stay, less postoperative pain, reduced blood loss, and earlier return to function (52-54). Initial concerns regarding lymph node yield addressed port-site recurrence. Initial experience showed that T4 tumors (including perforations) were a contraindication to laparoscopy, but as experience has increased, surgeons are successfully able to tackle emergency cases successfully. However, Evidence is scant at present, but some observational level studies have shown no inferiority and a shorter length of stay. Long-term data is currently unavailable (55). As with other forms of surgery, progress is not abated. There are cases reports of emergency robotic colectomies for hemorrhage (56) and over the next 10 to 20 years, this field is likely to expand. Perforated tumors are by definition T4 in origin and a source of pelvic and abdominal sepsis. Laparoscopic management is possible.

3.3. Inflammatory Bowel Disease

Crohn's disease (CD) and ulcerative colitis (UC) are common diseases throughout Europe. Surgery is an important management option, especially in the emergency presentation. The incidence of UC and CD are 10.4 per 100000 and 5.6 per 100000 persons, respectively (57).

For UC, guidelines for the management in its acute phase are available (58). For those failing medical therapy or those with perforation, mega colon/obstruction surgery has the main role. A number of papers (59-61) compare laparoscopic with open resection and management. Overall, while operating times are longer, complication rates are similar. The main advantage of laparoscopic surgery is in the further operations that may be required, such as the completion proctectomy and formation of an ileo-anal pouch.

The CD is a transmural inflammatory condition that can affect anywhere in the GI tract. Laparoscopy in the elective setting has become the mainstay of resectional treatment. It is also feasible in the emergency setting. The most thorough meta-analysis concluded that laparoscopy for ileocolic CD is associated with a faster recovery and shorter length of stay with equivalent morbidity and mortality (62, 63) as well as reduction in reoperation and

hernias (63). Laparoscopy has also been shown to be safe in reoperation for CD (64, 65).

Acute inflammatory bowel disease (IBD) flares can often be due to superimposed infections such as acute gastroenteritis (*Campylobacter*, *E coli*, *Salmonella*) and viral infections such as cytomegalovirus (CMV) as well as *Clostridium difficile*. Stool cultures should be taken in all patients with acute colitis prior to surgery unless the clinical situation dictates otherwise (e.g. perforation). In patients for whom stool or biopsies confirm superimposed infection, treatment is usually medical.

IBD (both UC and especially CD) can present with intra-abdominal perforation and abscess formation. CD may also present with enterocutaneous fistula. Laparoscopy has been shown to hold advantages of benign internal fistula compared with open surgery in carefully selected patients, and it is certainly not a contraindication as once thought. Rates of conversion are higher in those with vaginal or duodenal involvement suggesting more complex disease (66). The advantages would seem more obvious in CD where multiple surgeries within a patient's lifetime are often encountered, especially with fistulating disease. Enteric fistula management is possible in CD (67); however, further studies are required for this area.

3.4. Pelvic Inflammatory Disease

Laparoscopy remains the gold standard tool for diagnosis and management of complex PID. It allows both diagnosis and treatment of pelvic conditions in chronic and acute pelvic pain. Samples can be taken for culture and management of tuboovarian abscess is possible using similar techniques to laparoscopic appendectomy and lavage in diverticulitis. Young females presenting as an emergency with lower abdominal pain should have considered it as a possible diagnosis if a history with risk factors such as unprotected sex is present. High vagina swabs for candida and bacterial vaginitis and endocervical swabs for gonorrhea and chlamydia (using polymerase chain reaction [PCR]) are often used; however, urine PCR can be used for chlamydia.

Laparoscopic treatment for PID can utilize a number of treatment modalities. Irrigation of infected and purulent fluid can act as treatment and allow targeted antimicrobial management. The results of vaginal and abdominal swabs are often different and isolated organisms vary (68); thus, laparoscopy has a diagnostic role. However, laparoscopy also has a therapeutic role. treatment options include adhesiolysis, drainage of pyosalpinx, drainage of tuboovarian abscesses, and extirpation of disease (69).

3.5. Rare Infections

In endemic areas, infections such as tuberculosis and actinomyces can present with abdominal abscesses or infections. These can be detected prior to or during surgery with subsequent infection picked up on culture. In non-

endemic areas, the key to diagnosis remains a high index of suspicion. Patients at higher risk such as those with a relevant travel or exposure history or immunosuppression should lower the diagnostic threshold and swabs and cultures should be sent from any abscess drained.

3.6. Complications

Anastomotic leak is a dreaded complication of colorectal surgery. Rates of anastomotic dehiscence varied from 2.4 to 19% with higher rates for low pelvic anastomosis and irradiated rectum (70). Gross contamination and an unstable patient often preclude a laparoscopic approach, but in selected patients, lavage, laparoscopic repair, drainage, and de-functioning can have a role. Vennix et al. highlighted this in 38 patients (71). However, further studies are required. Early results have been promising with higher long-term stoma closure rates, reduced complications and mortality, and reduced infection (72).

3.7. The Future

3.7.1. Single Incision Laparoscopic Surgery

SILS surgery uses a transumbilically-placed incision (around 5 cm). Then a specially designed port is placed. The same technique has been used in both ileocecal resection and total colectomy procedures. It is increasingly used for appendectomy and has the advantage of facilitating a learning curve for more complex procedures. However, results have been mixed with some studies demonstrating no difference (73). A recent meta-analysis showed better cosmetic results without short-term complications (46), but results on outcomes including post-operative herniation rates are awaited. Similar improved cosmetic results have been shown for colectomies without increasing complication rates and equivalent oncologic results, but a large multicenter randomized clinical trial has not been conducted yet (74, 75). It has been shown to be of use particularly in young patients with IBD (76).

3.7.2. Natural Orifice Transluminal Endoscopic Surgery

NOTES utilizes natural orifices (vagina or stomach) to extract the specimen and endoscopic instruments to perform the procedure. Hybrid approaches are possible using a combination of standard laparoscopic and NOTES approaches. It has been shown to be feasible in colon resection (77). There are current case series, but no randomized clinical trial has demonstrated advantages; however, its application is increasing. A recent article in the British Journal of Surgery (78) showed its increasing use and acceptance.

4. Conclusions

Intra-abdominal sepsis is common. It can be devastating and lower GI sources are commonplace. Laparoscopy

is increasingly used in the management of diverticulitis, appendicitis, and acute presentation of IBD and cancer and its use is developing and growing. In many centers, it has become the gold standard and mainstay of treatment. Longer follow-up results are required, but the evolution of surgery is already pushing the boundaries of what is possible. Reduced surgical trauma and minimally invasive techniques are being refined to shift the paradigm of surgical management to limit and restrict further trauma rather than to add to it—laparoscopy is one such modality.

Authors' Contributions

Study Concept and design: Peter Edward Coyne and Reza Kalbassi; Acquisition of data: Peter Edward Coyne; Analysis and interpretation of data: Peter Edward Coyne; Drafting manuscript: Peter Edward Coyne; Critical revision of the manuscript for important intellectual content: Peter Edward Coyne and Reza Kalbassi; Statistical analysis: N/A; Administrative, technical, and material support: N/A; Study supervision: Reza Kalbassi.

References

- Munson KD, Hensien MA, Jacob LN, Robinson AM, Liston WA. Diverticulitis. A comprehensive follow-up. *Dis Colon Rectum*. 1996;**39**(3):318-22.
- Hinchey EJ, Schaal PG, Richards GK. Treatment of perforated diverticular disease of the colon. *Adv Surg*. 1978;**12**:85-109.
- Wasvary H, Turfah F, Kadro O, Beauregard W. Same hospitalization resection for acute diverticulitis. *Am Surg*. 1999;**65**(7):632-5.
- Fozard JB, Armitage NC, Schofield JB, Jones OM. ACPGBI position statement on elective resection for diverticulitis. *Colorectal Dis*. 2011;**13** Suppl 3:1-11.
- Atkin W, Dadswell E, Wooldrage K, Kralj-Hans I, Edwards R, von Wagner, et al. Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial. *Lancet*. 2013;**381**(9873):1194-202.
- Chabok A, Smedh K, Nilsson S, Stenson M, Pahlman L. CT-colonography in the follow-up of acute diverticulitis: patient acceptance and diagnostic accuracy. *Scand J Gastroenterol*. 2013;**48**(8):979-86.
- Ambrosetti P. Diverticulitis of the left colon. *Recent advances in surgery*. 1997;**20**:145-60.
- Shabanzadeh D, Wille-Jorgensen P, Shabanzadeh DM. Antibiotics for uncomplicated diverticulitis. *Cochrane Database Syst Rev*. 2012;**9**(11):CD009092.
- Singh B, May K, Coltart I, Moore NR, Cunningham C. The long-term results of percutaneous drainage of diverticular abscess. *Ann R Coll Surg Engl*. 2008;**90**(4):297-301.
- Gaertner WB, Willis DJ, Madoff RD, Rothenberger DA, Kwaan MR, Belzer GE, et al. Percutaneous drainage of colonic diverticular abscess: is colon resection necessary? *Dis Colon Rectum*. 2013;**56**(5):622-6.
- Myers E, Hurley M, O'Sullivan GC, Kavanagh D, Wilson I, Winter DC. Laparoscopic peritoneal lavage for generalized peritonitis due to perforated diverticulitis. *Br J Surg*. 2008;**95**(1):97-101.
- O'Sullivan GC, Murphy D, O'Brien MG, Ireland A. Laparoscopic management of generalized peritonitis due to perforated colonic diverticula. *Am J Surg*. 1996;**171**(4):432-4.
- Mutter D, Bouras G, Forgione A, Vix M, Leroy J, Marescaux J. Two-stage totally minimally invasive approach for acute complicated diverticulitis. *Colorectal Dis*. 2006;**8**(6):501-5.
- Constantinides VA, Tekkis PP, Athanasiou T, Aziz O, Purkayastha S, Remzi FH, et al. Primary resection with anastomosis vs. Hartmann's procedure in nonelective surgery for acute colonic diverticulitis: a systematic review. *Dis Colon Rectum*. 2006;**49**(7):966-81.
- Thornell A, Angenete E, Gonzales E, Heath J, Jess P, Lackberg Z, et

- al. Treatment of acute diverticulitis laparoscopic lavage vs. resection (DILALA): study protocol for a randomised controlled trial. *Trials*. 2011;**12**(1):186.
16. Swank HA, Vermeulen J, Lange JF, Mulder IM, van der Hoeven JA, Stassen LP, et al. The ladies trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with primary anastomosis for purulent or faecal peritonitis in perforated diverticulitis (NTR2037). *BMC Surg*. 2010;**10**:29.
 17. Swank HA, Mulder IM, Hoofwijk AG, Nienhuijs SW, Lange JF, Bemelman WA, et al. Early experience with laparoscopic lavage for perforated diverticulitis. *Br J Surg*. 2013;**100**(5):704-10.
 18. Reissfelder C, Buhr HJ, Ritz JP. Can laparoscopically assisted sigmoid resection provide uncomplicated management even in cases of complicated diverticulitis? *Surg Endosc*. 2006;**20**(7):1055-9.
 19. Zingg U, Pasternak I, Guertler L, Dietrich M, Wohlwend KA, Metzger U. Early vs. delayed elective laparoscopic-assisted colectomy in sigmoid diverticulitis: timing of surgery in relation to the acute attack. *Dis Colon Rectum*. 2007;**50**(11):1911-7.
 20. Klarenbeek BR, Veenhof AA, Bergamaschi R, van der Peet DL, van den Broek WT, de Lange ES, et al. Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial: short-term results of the Sigma Trial. *Ann Surg*. 2009;**249**(1):39-44.
 21. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol*. 1990;**132**(5):910-25.
 22. Barrett ML, Hines AL, Andrews RM. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD): 2006. Trends in Rates of Perforated Appendix, 2001-2010: Statistical Brief #159.
 23. Benjamin IS, Patel AG. Managing acute appendicitis. *BMJ*. 2002;**325**(7363):505-6.
 24. Nomura S, Watanabe M, Komine O, Shioya T, Toyoda T, Bou H, et al. Serum total bilirubin elevation is a predictor of the clinicopathological severity of acute appendicitis. *Surg Today*. 2014;**44**(6):1104-8.
 25. Farooqui W, Pommergaard HC, Burcharth J, Eriksen JR. The diagnostic value of a panel of serological markers in acute appendicitis. *Scand J Surg*. 2015;**104**(2):72-8.
 26. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg*. 2013;**100**(3):322-9.
 27. Owen TD, Williams H, Stiff G, Jenkinson LR, Rees BI. Evaluation of the Alvarado score in acute appendicitis. *J R Soc Med*. 1992;**85**(2):87-8.
 28. Kalan M, Talbot D, Cunliffe WJ, Rich AJ. Evaluation of the modified Alvarado score in the diagnosis of acute appendicitis: a prospective study. *Ann R Coll Surg Engl*. 1994;**76**(6):418-9.
 29. Tzanakis NE, Efstathiou SP, Danulidis K, Rallis GE, Tsioulos DI, Chatzivasilioni A, et al. A new approach to accurate diagnosis of acute appendicitis. *World J Surg*. 2005;**29**(9):1151-6.
 30. Karabulut N, Kiroglu Y, Herek D, Kocak TB, Erdur B. Feasibility of low-dose unenhanced multi-detector CT in patients with suspected acute appendicitis: comparison with sonography. *Clin Imaging*. 2014;**38**(3):296-301.
 31. Pinto F, Pinto A, Russo A, Coppolino F, Bracale R, Fonio P, et al. Accuracy of ultrasonography in the diagnosis of acute appendicitis in adult patients: review of the literature. *Crit Ultrasound J*. 2013;**5** Suppl 1:S2.
 32. Leeuwenburgh MM, Wiezer MJ, Wiarda BM, Bouma WH, Phoa SS, Stockmann HB, et al. Accuracy of MRI compared with ultrasound imaging and selective use of CT to discriminate simple from perforated appendicitis. *Br J Surg*. 2014;**101**(1):e147-55.
 33. Vu L, Ambrose D, Vos P, Tiwari P, Rosengarten M, Wiseman S. Evaluation of MRI for the diagnosis of appendicitis during pregnancy when ultrasound is inconclusive. *J Surg Res*. 2009;**156**(1):145-9.
 34. Wilms IMHA, de Hoog DENM, de Visser DC, Janzing HMJ. Appendectomy versus antibiotic treatment for acute appendicitis. *Cochrane Database Syst Rev*. 2011;**9**(11):CD008359.
 35. Varadhan KK, Neal KR, Lobo DN. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. *BMJ*. 2012;**344**:e2156.
 36. Attwood SE, Hill AD, Murphy PG, Thornton J, Stephens RB. A prospective randomized trial of laparoscopic versus open appendectomy. *Surgery*. 1992;**112**(3):497-501.
 37. Frazee RC, Roberts JW, Symmonds RE, Snyder SK, Hendricks JC, Smith RW, et al. A prospective randomized trial comparing open versus laparoscopic appendectomy. *Ann Surg*. 1994;**219**(6):725-8.
 38. Markar SR, Penna M, Harris A. Laparoscopic Approach to Appendectomy Reduces the Incidence of Short- and Long-Term Postoperative Bowel Obstruction: Systematic Review and Pooled Analysis. *J Gastrointestinal Surg*. 2014;**18**(9):1683-92.
 39. Sauerland S, Lefering R, Holthausen U, Neugebauer E. A Meta-Analysis of Studies Comparing Laparoscopic with Conventional Appendectomy. In: Krahenbuhl L, Frei E, Klaiber CH, Buchler MW editors. *Acute appendicitis: standard treatment or laparoscopic surgery?* Karger; 1998. pp. 109-14.
 40. Golub R, Siddiqui F, Pohl D. Laparoscopic Versus Open Appendectomy: A Metaanalysis. *J Am College Surg*. 1998;**186**(5):545-53.
 41. Wang CC, Tu CC, Wang PC, Lin HC, Wei PL. Outcome comparison between laparoscopic and open appendectomy: evidence from a nationwide population-based study. *PLoS One*. 2013;**8**(7):e68662.
 42. Sauerland S, Jaschinski T, Neugebauer EAM, Sauerland S. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database Syst Rev*. 2010;**6**(10):CD001546.
 43. Kathkouda N, Mason RJ, Towfigh S, Gevorgyan A, Essani R. Laparoscopic versus open appendectomy: a prospective randomized double-blind study. *Ann Surg*. 2005;**242**(3):439-48.
 44. Leff DR, Sait MR, Hanief M, Salakianath S, Darzi AW, Vashisht R. Inflammation of the residual appendix stump: a systematic review. *Colorectal Dis*. 2012;**14**(3):282-93.
 45. Subramanian A, Liang MK. A 60-year literature review of stump appendicitis: the need for a critical view. *Am J Surg*. 2012;**203**(4):503-7.
 46. Cai YL, Xiong XZ, Wu SJ, Cheng Y, Lu J, Zhang J, et al. Single-incision laparoscopic appendectomy vs conventional laparoscopic appendectomy: systematic review and meta-analysis. *World J Gastroenterol*. 2013;**19**(31):5165-73.
 47. Horgan S, Cullen JP, Talamini MA, Mintz Y, Ferreres A, Jacobsen GR, et al. Natural orifice surgery: initial clinical experience. *Surg Endosc*. 2009;**23**(7):1512-8.
 48. Marin D, Ho LM, Barnhart H, Neville AM, White RR, Paulson EK. Percutaneous abscess drainage in patients with perforated acute appendicitis: effectiveness, safety, and prediction of outcome. *AJR Am J Roentgenol*. 2010;**194**(2):422-9.
 49. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg*. 2007;**246**(5):741-8.
 50. American Institute for Cancer Research, World Cancer Research Fund. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. Washington, DC.: American Institute for Cancer Research; 2007.
 51. McArdle CS, Hole DJ. Emergency presentation of colorectal cancer is associated with poor 5-year survival. *Br J Surg*. 2004;**91**(5):605-9.
 52. Clinical Outcomes of Surgical Therapy Study G. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med*. 2004;**350**(20):2050-9.
 53. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AMH, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLAS-ICC trial): multicentre, randomised controlled trial. *Lancet*. 2005;**365**(9472):1718-26.
 54. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol*. 2005;**6**(7):477-84.
 55. Odermatt M, Miskovic D, Siddiqi N, Khan J, Parvaiz A. Short- and long-term outcomes after laparoscopic versus open emergency resection for colon cancer: an observational propensity score-matched study. *World J Surg*. 2013;**37**(10):2458-67.

56. Felli E, Brunetti F, Disabato M, Salloum C, Azoulay D, De'angelis N. Robotic right colectomy for hemorrhagic right colon cancer: a case report and review of the literature of minimally invasive urgent colectomy. *World J Emerg Surg.* 2014;**9**:32.
57. Shivananda S, Lennard-Jones J, Logan R, Fear N, Price A, Carpenter L, et al. Incidence of inflammatory bowel disease across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD). *Gut.* 1996;**39**(5):690-7.
58. Brown SR, Haboubi N, Hampton J, George B, Travis SP, Acpgbi. The management of acute severe colitis: ACPGBI position statement. *Colorectal Dis.* 2008;**10** Suppl 3:8-29.
59. Bell RL, Seymour NE. Laparoscopic treatment of fulminant ulcerative colitis. *Surg Endoscopy.* 2002;**16**(12):1778-82.
60. Dunker MS, Bemelman WA, Slors JF, van Hogezaand RA, Ringers J, Gouma DJ. Laparoscopic-assisted vs open colectomy for severe acute colitis in patients with inflammatory bowel disease (IBD): a retrospective study in 42 patients. *Surg Endosc.* 2000;**14**(10):911-4.
61. Marcello PW, Milsom JW, Wong SK, Brady K, Goormastic M, Fazio VW. Laparoscopic total colectomy for acute colitis. *Dis Colon & Rectum.* 2001;**44**(10):1441-5.
62. Rosman AS, Melis M, Fichera A. Metaanalysis of trials comparing laparoscopic and open surgery for Crohn's disease. *Surg Endosc.* 2005;**19**(12):1549-55.
63. Eshuis EJ, Polle SW, Slors JF, Hommes DW, Sprangers MA, Gouma DJ, et al. Long-term surgical recurrence, morbidity, quality of life, and body image of laparoscopic-assisted vs. open ileocolic resection for Crohn's disease: a comparative study. *Dis Colon Rectum.* 2008;**51**(6):858-67.
64. Wu JS, Birnbaum EH, Kodner IJ, Fry RD, Read TE, Fleshman JW. Laparoscopic-assisted ileocolic resections in patients with Crohn's disease: Are abscesses, phlegmons, or recurrent disease contraindications? *Surg.* 1997;**122**(4):682-9.
65. Hasegawa H, Watanabe M, Nishibori H, Okabayashi K, Hibi T, Kitajima M. Laparoscopic surgery for recurrent Crohn's disease. *Br J Surg.* 2003;**90**(8):970-3.
66. Pokala N, Delaney CP, Brady KM, Senagore AJ. Elective laparoscopic surgery for benign internal enteric fistulas: a review of 43 cases. *Surg Endosc.* 2005;**19**(2):222-5.
67. Regan JP, Salky BA. Laparoscopic treatment of enteric fistulas. *Surg Endosc.* 2004;**18**(2):252-4.
68. Schindlbeck C, Dziura D, Mylonas I. Diagnosis of pelvic inflammatory disease (PID): intra-operative findings and comparison of vaginal and intra-abdominal cultures. *Arch Gynecol Obstet.* 2014;**289**(6):1263-9.
69. Molander P, Cacciatore B, Sjoberg J, Paavonen J. Laparoscopic management of suspected acute pelvic inflammatory disease. *J Am Association Gynecologic Laparoscopists.* 2000;**7**(1):107-10.
70. Kingham TP, Pachter HL. Colonic anastomotic leak: risk factors, diagnosis, and treatment. *J Am Coll Surg.* 2009;**208**(2):269-78.
71. Vennix S, Abegg R, Bakker OJ, van den Boezem PB, Brokelman WJ, Sietes C, et al. Surgical re-interventions following colorectal surgery: open versus laparoscopic management of anastomotic leakage. *J Laparoendosc Adv Surg Tech A.* 2013;**23**(9):739-44.
72. Lee CM, Huh JW, Yun SH, Kim HC, Lee WY, Park YA, et al. Laparoscopic versus open reintervention for anastomotic leakage following minimally invasive colorectal surgery. *Surg Endosc.* 2015;**29**(4):931-6.
73. Carter JT, Kaplan JA, Nguyen JN, Lin MY, Rogers SJ, Harris HW. A prospective, randomized controlled trial of single-incision laparoscopic vs conventional 3-port laparoscopic appendectomy for treatment of acute appendicitis. *J Am Coll Surg.* 2014;**218**(5):950-9.
74. Velthuis S, van den Boezem PB, Lips DJ, Prins HA, Cuesta MA, Sietes C. Comparison of short-term surgical outcomes after single-incision laparoscopic versus multiport laparoscopic right colectomy: a two-center, prospective case-controlled study of 100 patients. *Dig Surg.* 2012;**29**(6):477-83.
75. Kwag SJ, Kim JG, Oh ST, Kang WK. Single incision vs conventional laparoscopic anterior resection for sigmoid colon cancer: a case-matched study. *Am J Surg.* 2013;**206**(3):320-5.
76. Gardenbroek TJ, Tanis PJ, Buskens CJ, Bemelman WA. Surgery for Crohn's disease: new developments. *Dig Surg.* 2012;**29**(4):275-80.
77. D'Hondt M, Devriendt D, Van Rooy F, Vansteenkiste F, Dozois E. Transvaginal pure NOTES sigmoid resection using a single port device. *Tech Coloproctol.* 2014;**18**(1):77-80.
78. Bingener J, Ibrahim-zada I. Natural orifice transluminal endoscopic surgery for intra-abdominal emergency conditions. *Br J Surg.* 2014;**101**(1):e80-9.