Danish national guidelines for treatment of diverticular disease

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These guidelines for the treatment of diverticular disease are elaborated by a working group under the auspices of the Danish Surgical Society in September 2010 – May 2011. This work was inspired by the fact that in several other countries attempts has been made to standardize the treatment of diverticular disease, as the area has been characterized by low evidence and surgeons personal preferences.

Evidence and recommendations

The guidelines are based on an updated review of the literature (updated may 2011) and recommendations are based on current scientific evidence, and if there is none, based on consensus reached in the working group. The classification system used by the Danish Colorectal Cancer Group (DCCG) was selected (www.dccg.dk).

Level of evidence:

Ia. Meta-analysis of randomized controlled trials
Ib. At least one randomized controlled trial
IIa. At least one good controlled not randomized study
IIb. At least one other type of good experimental not randomized study
III. Good descriptive studies (cohort, case control and case series)
IV. Expert committees, Esteemed Authorities, cases

Grade of recommendation:

A. At least one randomized controlled trial among several good studies, all of which are fundamental to the recommendation (Ia, Ib)
B. Requires good clinical studies as a basis for the recommendation (IIa, IIb or III)
C. Requires expert committee or authority, but says there are no good clinical studies as a basis

Etiology, pathogenesis, prevalence and incidence

A colonic diverticulum is a herniation of mucosa and submucosa, corresponding to a weak point where the vasa recti penetrate the tunica muscularis (1). In 1965 Painter et al. presented the hypothesis that diverticular disease was caused by excess pressure in the colon due to segmentation based on insufficient intake of dietary fibre (2). Diverticulosis was described primarily as a disease of the Western civilization, thus a relationship was postulated between low dietary fibre intake and increased colonic transit time, intraluminal pressure and development of diverticula. A substantial difference in colonic transit time and daily stool weight between individuals in industrialized and developing countries was documented (3,4).

In the Western world diverticulosis occurs primarily in the sigmoid - corresponding to the highest intraluminal pressure - but may be prevalent in varying degrees in the rest of the colon. Diverticula of the rectum are described only in a few case reports.

The relationship between a low intake of dietary fibre and diverticulosis is rendered probable partly by animal experimental studies and partly by a large prospective cohort study. In the rat experiment a significant inverse relationship was found between the fibre intake and the development of colonic diverticula (5). The cohort study included 43,881 male health professionals between 40 and 75 years. Dietary habits were assessed by a validated food questionnaire and endpoint was self-reported diverticular disease. The intake of fibre was inversely related to risk of diverticular disease (RR=0.63(0.44-0.91))(6). The same group (Aldoori et al) found a significant inverse relationship between physical activity and incidence of both diverticulitis and diverticular bleeding (7,8). Additionally, obesity (BMI≥30) and use of NSAIDs or acetaminophen was significantly associated with diverticular disease including diverticular bleeding (9,10). Smoking was not significantly associated with symptomatic diverticular disease (RR=1.36(0.94-1.97))(11). In a Swedish cohort study of women aged 40 – 75 years – with a questionnaire response rate of 70 % (39,227 women) – 1,6 % developed symptomatic diverticular disease at follow-up in 11 years, based on reporting to the Swedish Patient Register. Again smoking was not significantly associated with symptomatic diverticular disease (RR=1.23(0.99-1.52)), but smokers suffered a higher risk of complicated diverticular disease (RR=1.89(1.15-3.10))(12).

There is no evidence of a genetic predisposition (apart from an increased incidence of diverticulosis with rare connective tissue defects)(13).

The prevalence of colonic diverticulosis increases with age, i.e. 5 % of the population of 30-39 years and 60 % of those over 80 years have diverticulosis (14).

The standardized incidence rate of hospitalization for acute diverticulitis was found – by a sample consisting of 20% of the U.S.

population – rising from 59 per 100,000 per year to 71 per 100,000 per year from 1998 to 2005 (15).
Diverticulitis is inflammation of a diverticulum – presumed to occur as a result of impacted faecal matter at the diverticular neck – ultimately leading to perforation (1).
In cases of symptomatic diverticulosis of the sigmoid colon this part of the bowel wall is often thickened (16).
The incidence rate of perforated diverticulitis (Hinchey stage 1-4) is 3.5 to 4.0 per 100,000 per year (17,18). The incidence of lower gastrointestinal bleeding is 21 per 100,000 per year, one half due to diverticular bleeding (19).

Conclusion:
There is a relationship between low dietary fibre intake and the development of diverticulosis and diverticulitis (evidence IIb).
There is a relationship between low physical activity, obesity and the use of NSAIDs and the development of diverticulosis and diverticulitis (evidence III).
There is no clear correlation between smoking and the development of diverticular disease, but smoking status is associated a higher risk of complications in diverticulitis (evidence III).

Recommendation:
A high daily fibre intake is recommended to reduce the risk of diverticular disease (grade B).

Staging of diverticulitis
Diverticulosis is defined by the presence of one or more diverticula. The majority of individuals with diverticulosis are asymptomatic - only about one out of five has symptomatic diverticular disease.
Acute diverticulitis ranges in severity from uncomplicated phlegmonous diverticulitis to complicated diverticulitis with abscess or perforation. Rarely chronic diverticulitis is seen with late complications as stenosis or fistula to nearby organs (most often bladder) or the skin.

In 1978 *Hinchey* et al. described a staging of acute complicated diverticulitis, which since then has been prevalent (20):
Stage 1: Mesocolic / pericolic abscess
Stage 2: Pelvic abscess
Stage 3: Generalized peritonitis
Stage 4: Faecal peritonitis

In 1999 a more comprehensive staging of diverticular disease was proposed by *Hansen & Stock* (21,22):
Stage 0: Diverticulosis
Stage 1: Acute uncomplicated diverticulitis (endoscopy: inflammation, CT: wall thickening)
Stage 2: Complicated diverticulitis
Stage 2a: Peridiverticulitis / phlegmonous diverticulitis (CT: inflammatory reaction of pericolic fat)
Stage 2b: Diverticular abscess (sealed perforation)
Stage 2c: Free perforation (CT: free air or free liquid)
Stage 3: Chronic recurrent diverticulitis (stenosis or fistula)

In 2002 *Ambrosetti* et al. proposed a simplified staging of acute diverticulitis based on CT criteria and showed its prognostic significance in a prospective study (23,24):
Moderate diverticulitis defined by wall thickening of ≥ 5 mm and signs of inflammation of pericolic fat
Severe diverticulitis defined by wall thickening accompanied by abscess, extraluminal air or extraluminal contrast

Conclusion:
There are various classifications of diverticular disease. We propose a distinction between asymptomatic and symptomatic diverticulosis. Acute diverticulitis is divided into uncomplicated and complicated diverticulitis - for the last mentioned condition the Hinchey classification is most widely used in the literature.

Recommendation:
Acute diverticulitis is divided into uncomplicated and complicated diverticulitis. Complicated diverticulitis is stage divided by the Hinchey classification (grade C).

Diagnosis of diverticulitis
Clinical presentation:
The typical patient with acute sigmoid diverticulitis is presenting with acute pain and tenderness in the left lower quadrant, accompanied by fever and elevated infection parameters. However the clinical diagnosis of diverticulitis is uncertain. Thus positive and negative predictive values of 0.65 and 0.98 for clinically diagnosed acute diverticulitis were found in a prospective analysis of 802 consecutive patients with acute abdominal pain (25). Using logistic regression analysis, Lameris et al., developed a clinical decision rule for diagnosis of diverticulitis, consisting of 3 criteria: 1) direct tenderness in the left lower quadrant, 2) CRP> 50 mg/l and 3) absence of vomiting. If all three criteria were met 97 % had diverticulitis (29/30) and if less than the three were met 55 % had diverticulitis (51/96)(26). However, in practice, this decision rule is not used.

Imaging investigations
The radiological investigations which have been used for the diagnosis of acute diverticulitis is water-soluble contrast enema, ultrasound, CT and MRI.
The diagnostic criteria for diverticulitis that has been used in US and CT are: 1) at least one diverticulum, 2) signs of inflammation of periodic fat (dirty fat/stranding) and 3) thickened bowel wall > 4-5 mm (27).
In a prospective study of 542 patients suspected of acute left sided diverticulitis triple-contrast CT-scans (intravenous, oral and rectal) were compared to water-soluble contrast enema. CT scan had a significant higher diagnostic sensitivity of 0.98 versus 0.92 ($p<0.01$). Colonic contrast enema showed in only 29 % of cases with CT proven abscess indirect evidence of this (24).
In a *systematic review* of imaging accuracy in acute diverticulitis (28) only a few studies of good or acceptable methodological quality according to the CEBM criteria (29) were found: US (30,31,32), CT (30) and MRI (33). All diagnostic studies with Barium enema were of poor quality. In only 2 studies a comparison of the diagnostic accuracy of US and CT in diverticulitis has been made. Thus in a study by Pradel et al. from 1997 there were no significant differences in diagnostic sensitivity and specificity, positive or negative predictive values. There was a non-significant tendency for CT to demonstrate free air or abscess more frequently compared with US (30). In a recent study a diagnostic sensitivity of US and CT of respectively 1.00 and 0.98 and a diagnostic specificity of 1.00 for both investigative modalities were found (34).
In a *meta-analysis* of test accuracy in acute diverticulitis, in which graduated compression US and CT were compared, no significant differences were found: diagnostic sensitivity for US 0.92 (95 % CI:0.80-0.97) versus CT 0.94 (95 % CI:0.87-0.97) and diagnostic

specificity for US 0.90 (95 % CI:0.82-0.95) versus CT 0.99 (95 % CI:0.90-1.00)(27).
In a prospective evaluation of the value of MRI with intravenous Gadolinium in the diagnosis of acute diverticulitis comprising 55 patients, a diagnostic sensitivity and specificity of respectively 0.94 and 0.88 were found - similar to CT values (35).
According to the *American College of Radiology* CT with intravenous and possibly supplemented with oral and rectally administered contrast is the investigation of choice in suspicion of diverticulitis, except when it comes to women of childbearing age where graduated compression US is preferred (36). CT is useful in evaluation of severity and complications of diverticulitis, in detection of differential diagnoses and for treatment planning purposes (37). Using US avoids radiation exposure and intravenous contrast, but US is investigator dependent.
MRI can be used in expert hands, but carries the risk of nephrogenic systemic fibrosis using Gadolinium for renal patients and abscess drainage can not be guided by MRI.
According to the guidelines of the *Association of Coloproctology of Great Britain and Ireland* a diagnosis of diverticulitis should be verified during the acute hospitalization with imaging studies as US or CT, depending on the local expertise (38).

Colonoscopy
In practice, colonoscopy is rarely used for diagnostic purposes in the acute setting, but patients with confirmed or suspected diverticulitis should be recommended a colonoscopy in a quiet phase to exclude malignancy. Ambrosetti et al. found that 3 out of 402 patients with CT-proven diverticulitis undergoing later colonoscopy turned out to have a sigmoid cancer, equivalent to 0.7 % (24). Sakhnini et al. found 2 cases of sigmoid cancer by colonoscopy in 107 patients with CT-proven diverticulitis, corresponding to 1.9 % (39).
Colonoscopy is usually done after 6 weeks in order to avoid risk of converting a sealed to a free perforation (40). In a randomized study by Lahat et al. it was found that early colonoscopy can be done safely during index hospitalization provided absence of free or pericolic air on CT (40). However in a pilot study early colonoscopy provoked a case of free perforation in a patient with peridiverticular air on CT (39).
Strictures that can not be passed by scope pose a diagnostic problem. In a case series by King et al. from 1990 it was found that 6/15 patients with this problem turned out to have a cancer, the rest had diverticulitis (41). In a case series of acute large bowel obstruction the cause of the obstruction was found to be diverticulitis in 12 % of cases (35/300) (42). There are no comparative studies of sigmoidoscopy versus colonoscopy in follow up of CT-proven diverticulitis.

Investigation strategy on suspicion of colovesical fistula:
Oral intake of 250 g blue poppy seed followed by evaluation of urinary excretion the next 2 days were introduced in 2001 by Schwaibold et al. as an inexpensive and reliable test for vesicoenteric fistula (43). Kwon et al. found a diagnostic sensitivity of 1.00 (20/20), better than all other investigation modalities (44).
In a comparative study by Melchior et al. comprising 49 patients who underwent surgery for colovesical fistula, the poppy seed test were found to have the highest diagnostic sensitivity (94.6 %), exceeding CT, MRI, contrast enema, cystography, cystoscopy and colonoscopy (45).

Conclusion:
The clinical diagnosis of acute diverticulitis is not sufficiently precise (evidence III).
Diverticulitis should be verified with imaging studies that can provide guidance on the treatment plan in the acute phase. Both CT and US can be used (evidence IIa).
CT is less investigator dependent than US (evidence IV).
On follow up endoscopy less than 2 % of CT-diagnosed cases of diverticulitis turn out to be cancers instead (evidence III).
Colonoscopy can be carried out safely in the acute phase provided the absence of air outside the intestinal lumen on CT (evidence Ib).
The poppy seeds test is superior to other investigation modalities in diagnosing colovesical fistula (evidence III).

Recommendation:
CT with intravenous contrast is generally recommended for evaluation of patients suspected of diverticulitis (grade B).
In expert hands US can be used instead of CT in the examination of women of childbearing age (grade C).
After conservative treatment of diverticulitis endoscopy should be performed in a quiet phase (i.e. 6 weeks later) to exclude malignancy (grade B).
Urgent endoscopy is recommended where increased suspicion of malignancy is raised clinically or radiologically (grade B).
The choice of sigmoidoscopy or colonoscopy as a control measure may depend on whether the identified diverticulitis area can by inspected by the chosen modality (grade C).
The poppy seed test is recommended when colovesical fistula is suspected (grade B).

Treatment of acute uncomplicated diverticulitis
Approximately 70 % of acute diverticulitis cases are uncomplicated and can be treated conservatively (46). A British study has shown that a non-operative strategy is effective in 85 % of diverticulitis cases with a subsequent annual recurrence of 2 % (47). In a prospective study with a median follow-up of 9,5 years further complications were avoided in 68 % of non-operatively treated patients (48).
Treatment has traditionally been restricted oral intake and antibiotics, but evidence for this regime is poor or absent. Many studies concerning antibiotic treatment of diverticulitis simply compares different antibiotic regimens (49,50).
In order to clarify the need for antibiotics in uncomplicated diverticulitis a recent large Swedish prospective randomized multicentre study has been conducted. The study included 623 patients with CT-proven uncomplicated diverticulitis not blindly randomized to antibiotics or not. Patients with sepsis, affected general condition, pregnancy or in immunosuppressive therapy were excluded. No significant differences in subsequent frequency of abscess, perforation or need for surgery within 1 year were found. Thus this study indicates that antibiotics do not prevent complications in the short term (51). A slightly older study retrospective study gave the same result (52).
No studies have examined the value of dietary restriction or bed rest (38).

Conclusion:
There is no evidence of a beneficial effect of antibiotics in uncomplicated diverticulitis (evidence Ib).
Use of antibiotics in uncomplicated diverticulitis is justified by septicaemia, affected general condition, pregnancy or immunosuppression (evidence IV).
The value of dietary restriction or bed rest has not been studied.

Recommendation:
Antibiotics are not routinely recommended for the treatment of uncomplicated diverticulitis (grade A).
Until more solid evidence is available antibiotics should still be used for the treatment of uncomplicated diverticulitis by septicaemia, affected general condition, pregnancy or immunosuppression (grade C).
Dietary restriction and bed rest is unproven.

Treatment of abscesses (Hinchey stages 1 and 2)
Approximately 15 % of patients admitted with acute diverticulitis have an abscess on CT scan (53,54). Previously, surgery was the sole option, but improved imaging tools and effective antibiotics has expanded treatment spectrum. Abscess drainage in patients with acute diverticulitis is a field with low evidence as most of the published material consists of reviews, case reports and small retrospective series.
Ambrosetti et al. followed 73 patients who had CT-guided puncture of a mesocolic (59 %) or pelvic (41 %) abscess. 18 % of patients underwent surgery during the first hospitalization due to persistent abscess, peritonitis, bowel obstruction or fistula development. In addition 34 % were operated later (2 months to 9 years after). The need for surgery during first hospitalization was significantly higher if the abscess had a pelvic location, but at long term follow-up no difference were found. Thus, 41 % avoided surgery after CT-guided abscess drainage (54).
Siewert et al. assessed 30/181 patients with CT verified diverticulitis with an abscess (17 %) of which 22 cases (73 %) were classified as small (3 cm or less) and treated solely with antibiotics. Only 8/22 underwent resection later on. The 8 patients with abscesses larger than 3 cm were in 4 cases treated with antibiotics and in 4 cases with CT-guided drainage. 5/8 (62.5 %) underwent resection (55).
Bahadursingh et al. assessed 192 patients with diverticulitis, of which 67 % had a CT scan, in 16 % showing an abscess, half of which were drained either percutaneous or transrectally (53).
Durmishi et al. has published a series of 34 patients with Hinchey stage 2 diverticulitis treated with drainage. Abscess size varied between 3 and 18 cm (average 6 cm) and the drain was left for a median of 8 days (1-18 days). Drainage was successful in 23 cases (67 %). Of these 12 cases had an elective resection without mortality or need for a stoma. In the 11 cases where drainage failed due to sepsis, relapse or fistula formation, acute resection was necessary in 10 cases with a stoma rate of 80 % and a mortality of 33 %. The authors concluded that a conservative regimen is effective and may postpone surgery, thus reducing mortality risk and need for a stoma. No criteria were set for discontinuing of drains (56).
Kumar et al. retrospectively studied 114 patients with abdominal abscess occurring in connexion with appendicitis, diverticulitis or postoperatively. Approximately half the patients were treated by drainage after initial antibiotic treatment, the rest experienced improvement on antibiotics only. The drained group of patients had significant bigger abscesses and more often fever (57).
DeStigter et al. recommended contrast investigation through the drain before removal, to exclude intestinal fistula (37).

Conclusion:
15-20 % of diverticulitis cases develop abscess (Hinchey 1 and 2).
US- or CT-guided abscess drainage is well-established treatments avoiding hazardous acute surgery in at least 30 to 40 % of cases (evidence III).
Smaller abscesses (≤ 3 cm) can often be treated successfully with antibiotics alone, larger abscesses by combined drainage and antibiotics (evidence III).
It is unclear whether puncture and aspiration is as effective as drainage in the case of smaller abscesses.
There is no evidence concerning flushing regimen or criterias for discontinuation of drains.
All reported series of abscess drainage have used antibiotics.

Recommendation:
Abscesses suitable for drainage are recommended drained under US- or CT-guidance combined with antibiotics (grade C).
Abscesses not suitable for drainage are treated conservatively with antibiotics under clinical observation (grade C).
Drains are flushed several times daily and may be discontinued after a radiological control or when purulent production has ceased (grade C).
In cases of continuing purulent production or suspicion of faecal content in the drain a contrast investigation through the drain is recommended on suspicion of intestinal fistula (grade C).
Treatment failures are handled surgically (grade C).

Surgical treatment of perforated diverticulitis (Hinchey stages 3 and 4)
The three-stage operation originally described by Mayo in 1907 (58) remained for decades the mainstay in the early surgical treatment of perforated diverticulitis. An initial diverting colostomy with drainage was followed by delayed resection, and definitive closure of the stoma as the third stage. In 1942 a series of 52 patients treated with this concept and a mortality of 17 % was published (59).
Since the 1960s and 1970s the operative strategy gradually changed: a primary resection of the sigmoid combined with suture closure of the rectal stump and construction of a colostomy and subsequent colostomy reversal (Hartmann procedure) was introduced, assuming that prompt elimination of the infectious focus would reduce mortality (60 – 63). Eventually, the Hartman procedure replaced the three stage operation, albeit the evidence remained limited as only few randomized studies with inconsistent results were published: Kronborg et al. (64) randomized 62 patients with purulent or faecal peritonitis to either suture closure of the perforation with a diverting colostomy or Hartmann's operation. In patients with a purulent peritonitis (n=46) mortality was significantly lower when treated with suture closure and diverting colostomy as compared to the Hartmann procedure (0/21 vs. 6/25). In 16 patients with faecal peritonitis the mortality in the two groups did not differ significantly (6/10 vs. 2/6). Zeitoun et al. (65) concluded that primary resection was to be preferred, since re-operations and instances of generalized, postoperative peritonitis were less common in this group. On the other hand mortality rate was higher in the resection group (24% vs. 19%), although the difference was not statistically significant.
During the 1990s resection with primary anastomosis with or without relieving colostomy became an issue, despite the absence of randomized trials (66-74). In a review of 98 series (75) the mortality rate following resection with primary anastomosis (n=559) were found to be lower (10 %) when compared with Hartmann's procedure (19 %) (n=1051). In non-randomized series however, selection bias may be a significant factor, as a trend to do Hartmann´s procedure in the most severe cases is likely to be present. Accordingly, Constantinides et al. (76) reviewed studies where patients were matched for degree of peritonitis and found

no difference in mortality, when primary anastomosis was compared with Hartmann's procedure (14.1 % vs. 14.4 %).
Laparoscopic resection for perforated diverticulitis is technically possible, but the value remains unclear (77,78).
In 1996 O'Sullivan et al. (79) described a non-resection procedure involving laparoscopic inspection of the colon, peritoneal lavage and placement of intraperitoneal drains in Hinchey stage 3 disease. Several subsequent small series using this method reported good results with a low morbidity and a mortality of less than 5 % (80,81). Karoui et al. (82) in a comparative study found no differences in postoperative morbidity or mortality between patients treated with laparoscopy and peritoneal lavage (n=35) and patients treated with open primary resection with diverting colostomy (n=24 (historical controls matched for Hinchey stage)). Laparoscopy with peritoneal lavage, however, reduced hospital stay and avoided stoma construction. Myers et al. (83) reported a series of 100 consecutive patients with perforated diverticulitis. In 92 patients with Hinchey stage 3 disease treated with peritoneal lavage, drainage and antibiotics, the morbidity and mortality rates were 4% and 3 %. Only one patient needed a Hartmann's procedure and recurrence occurred in only 2 cases with a median follow-up of 36 months. 8 patients with Hinchey stage 4 disease had a Hartmann's procedure – mortality and morbidity in this group were not cited.
In summary, the evidence-based foundation for past and current treatment regimens is sparse and the absence of randomized, controlled studies is striking. The mortality and morbidity, however, seem considerable lower in series treated with laparoscopic peritoneal lavage when compared to resection strategies. In progress are currently several randomized studies using peritoneal lavage for Hinchey stage 3 disease, including a large Dutch multicenter study ("Ladies trial") randomizing both between peritoneal lavage and resection (LOLA arm), and Hartmann's procedure and primary anastomosis (DIVA arm) (84).

Conclusion:
There is evidence that the surgical treatment of acute perforated diverticulitis is laparoscopy with peritoneal lavage and drainage in case of Hinchey stage 3 (purulent peritonitis) (evidence III), and resection of the sigmoid by Hinchey stage 4 (faecal peritonitis) (evidence III). In case of resection, it is not evident, whether one should perform a Hartmann resection or make primary anastomosis.

Recommendation:
By radiological evidence of perforated diverticulitis diagnostic laparoscopy is recommended (grade B).
By Hinchey stage 3 disease (purulent peritonitis) laparoscopic lavage, drainage and antibiotics is recommended (grade B).
By Hinchey stage 4 disease (faecal peritonitis) resection is recommended (grade C).

Surgical principles by elective surgery
Elective surgery for diverticulitis can be performed either openly or laparoscopic. Two randomized trial fall in favour of laparoscopy: In the "Sigma Trial", a multicentre study which included 52 patients in each group, the inclusion criteria were ≥ 2 cases of diverticulitis, previously CT-drained abscess or symptomatic stricture. Significantly more complications, higher pain scores and longer hospital stay were found among patients openly operated, but operating time was significantly longer in the laparoscopic group and conversion rate was 19.2 %. Quality of life assessed on Short Form-36 was significantly better after 6 weeks, but no difference was found after 6 month. Total costs were equal (85-87).
In a single-centre study, which included 54 openly and 59 laparoscopic operated cases, the inclusion criteria were two episodes of uncomplicated diverticulitis or one episode of complicated diverticulitis, significantly lower pain scores, shorter time to bowel function, shorter hospital stay and longer operating time were found, but complication rates were equal. There were no cases of anastomotic leaks or mortality and the conversion rate was 8.5 %. The long-term results were equal, except the cosmetic outcome, in favour of laparoscopy. No difference was found considering ventral hernia, patient satisfaction, quality of life (GIQLI-score) or total costs (88,89).
A meta-analysis of several non-randomized studies suggests a reduction in hospital stay and complications in favour of the laparoscopic technique (90). The British-Irish guideline recommends laparoscopic resection in centres with appropriate expertise (38).
The evidence for the use of laparoscopic technique for elective surgery of complicated cases is not so good; conversion rate seems to be higher (91,92). However the British-Irish guidelines recommends laparoscopic technique used in centres possessing the appropriate expertise (38).
A larger prospective database study has shown that laparoscopic resection for complicated diverticulitis is feasible in expert hands. The study included 387 cases of uncomplicated recurrent diverticulitis and 113 complicated cases with abscess, fistula or stricture, all operated laparoscopic. The left flexure was taken down routinely. Neither conversion rate (2.1 % vs. 5.3 %), morbidity (10.9 % vs. 11.5 %) nor mortality (0 % vs. 0.9 %) differed significantly (93). Such excellent results can probably not be applied generally.
According to a prospective study of Reissfelder et al. *the optimal time for elective laparoscopic surgery* seems to be in an inflammation-free interval (94). The study compared early laparoscopic resection (5-8 days after antibiotic therapy) with later laparoscopic resection in an inflammation-free period (4-6 weeks after initial hospitalization). The indications for surgery were acute recurrent diverticulitis, complicated diverticulitis or first attack in immunosuppressed cases. In the period 1999 – 2001 116 patients were operated in the first group and in the period 2002 – 2005 94 patients in the second group. Abdominal wall abscess (19/116 vs. 5/94), anastomotic leaks (8/116 vs. 0/94) and conversion (9/116 vs. 1/94) were all significantly more common during early elective surgery. Due to the study design bias is likely, i.e. it cannot be ruled out, that the results reflect an effect of a learning curve.
Anastomosis on to the rectum appears to reduce the frequency of recurrence. In a retrospective series of all patient undergoing surgery for diverticulitis 501 had anastomosis. Recurrence of diverticulitis (diagnosed clinically) occurred with a frequency of 12.5 % (40/321) by colosigmoidal anastomosis compared to 6.7 % (12/180) by colorectal anastomosis, $p<0.05$ (95). In a retrospective study of 236 patients, who were electively operated for diverticilitis, the sole determinant for recurrence (confirmed by CT or colonic contrast enema) were level of anastomosis in regression analysis (96). Thus, 12.5 % had recurrence by colosigmoidal anastomosis versus 2.8 % by colorectal anastomosis, p=0.03.
Regarding the level of the proximal resection there is no evidence for resection of all diverticulum-bearing bowel, but it is recommended that resection is done in soft compliant bowel (38,97).
No clear evidence exists concerning routinely mobilization of the left colonic flexure.

The inferior mesenteric artery should be preserved whenever possible, since lymph node dissection is not needed unless cancer is suspected. In a randomized study of patient who underwent colonic resection for diverticulitis anastomotic leaks occurred more often when the vessel were divided. The difference was significant both clinically (2.3 % vs. 10.4 %) and radiologically (7 % vs. 18.1 %), p=0.02 (98).
If it is unclear whether there is a malignant genesis operation must be done according to the recommendations of the Danish Colorectal Cancer Group (DCCG), with a central mesocolic dissection and ligation of vessels.

Conclusion:
Laparoscopic surgery for recurrent diverticulitis should be preferred to open surgery if the expertise is held (evidence Ib).
Laparoscopic surgery for chronic complicated diverticulitis (fistula, stricture) should be preferred to open surgery if the expertise is held (evidence III).
Elective laparoscopic surgery should be performed in an inflammation-free interval (evidence III).
By resection for diverticulitis recurrence occurs more often at colosigmoidal anastomosis compared to colorectal anastomosis (evidence III).
It is not necessary to resect all diverticulum-bearing proximal bowel, but the anastomosis should be made in a soft, compliant area (evidence IV).
It is unclear if mobilization of the left flexure is necessary.
In resection for diverticulitis anastomotic leaks occur rarer if the inferior mesenteric artery is preserved (evidence Ib).

Recommendation:
Laparoscopic resection for recurrent diverticulitis (grade A) and complicated chronic diverticulitis (grade B) is recommended in centres with the appropriate laparoscopic expertise.
Elective laparoscopic surgery should be performed in an inflammation-free interval (grade C).
By resection for diverticulitis anastomosis on to the rectum is recommended (grade B).
Proximal resection boundary should be in soft, compliant bowel, but not necessary free from diverticula (grade C).
The left flexure may be mobilized either routinely or selectively (grade C).
The inferior mesenteric artery should be preserved if malignancy is ruled out preoperatively (grade A).
If malignancy is not ruled out, surgery should follow DCCGs guideline for oncological resection of sigmoid cancer (grade C).

Conservative treatment for uncomplicated symptomatic diverticular disease
The cornerstone of the conservative treatment of uncomplicated symptomatic diverticular disease has traditionally been a high fibre diet with supplements of bran or psyllium husk, but evidence for this is not solid.
A cross-over study, involving 20 patients with symptomatic diverticular disease reported by Taylor et al. in 1976, found that 18 g bran tablets daily reduced symptom scores, increased stool volume, reduced transit time and normalized myoelectric activity more than a high fibre diet or a combination of bulk laxatives and antispasmodics (99). In a small randomized controlled trial by Brodribb (100), which included 18 patients with symptomatic diverticular disease, the effect of a fibre supplement of 6.1 g per day were evaluated on a relatively broad symptom score. Fibre supplement gave a significant reduction in total symptom score.
In a double blind randomized cross-over study by Ornstein et al., including 58 patients with uncomplicated symptomatic diverticular disease, in which a daily supplement of bran (6.99 g fibre) or psyllium (9.04 g fibre) were compared with placebo (2.34 g fibre), fibre supplements only had a significant effect on constipation symptoms (101).
There is evidence that antibiotic therapy has an effect on symptomatic uncomplicated diverticular disease:
A meta-analysis - including 1660 patients in 4 randomized trials, in which only one was blinded - indicates that cyclic administered rifaximin (400 mg bid, 7 days /month) plus fibre relieves symptoms in symptomatic uncomplicated diverticular disease better than fibre supplements alone, as the rate difference (RD) after one year of treatment with rifaximin was 29 % (95 % CI:0.245-0.336) and NNT = 3. Assessed on the frequency of diverticulitis no clinical relevant effect was found as NNT were 59 (RD ÷1.9 %(95 % CI:÷0.034-÷0.0057))(102). Rifaximin is an orally antibiotic with low systemic absorption (<1 %). The suggested possible mechanisms of action are reduced proliferation of the intestinal flora causing less gas formation and reduced bacterial degradation of fibre. Rifaximin has a minimal potential for bacterial resistance, a low risk of side effects and of pharmacological interaction.

Conclusion:
Studies of fibre supplements in the conservative treatment of uncomplicated symptomatic diverticular disease are ambiguous, but evidence suggests a beneficial effect (evidence 1b).
In uncomplicated symptomatic diverticular disease cyclic rifaximin plus fibre provide symptomatic relief to 1 of 3 (evidence Ia).

Recommendation:
Fibre supplements are recommended when treating uncomplicated symptomatic diverticular disease conservatively (grade B).
Cyclic rifaximin plus fibre may have a place in the therapeutic armamentarium when dealing with uncomplicated symptomatic diverticular disease (grade A).

Need for elective surgery:

1) Need for elective resection following acute diverticulitis
Until a few years ago elective sigmoid resection was recommended after two cases of uncomplicated or one case of complicated acute diverticulitis, in order to reduce morbidity and mortality by relapse. Numerous reports have shown these risks including risk of colostomy increased by acute compared to elective resection. However, elective resections carry a risk of recurrence of 2.6 to 10 %, a risk of mortality of 1 to 2.3 % and a risk of stoma of approximately 10 % (103).
These factors must therefore be weighed against the anticipated risk of relapse of complicated diverticulitis and the expected complications addressing this. Scientific contributions in the area are characterized by low evidence, but data from recent years has resulted in increased reservations about prophylactic sigmoid colectomy. This may essentially be attributed to the following:

1) Recurrent diverticulitis is relatively rare and further more often uncomplicated than previously assumed; therefore the prognosis is per se better.
Of the conservatively treated cases of acute diverticulitis 2-50 % gets relapse at follow-up of 5-10 years. The risk of relapse is estimated to 2 % per year (104). It was earlier thought that the risk of complicated courses of diverticulitis increased at relapse, but

recent data argue against this, thus Pittet et al. (105) found that 16 % of cases with first time diverticulitis were operated acutely compared to 6 % of relapsed cases. The incidence of conservative treatment failure was similar in both groups (10 %). The 30-day mortality for first time diverticulitis was 3 % opposed to 0 % at relapse.
Correspondingly a lower mortality of 2.5 % was found by recurrences compared to 10 % at the first episode of diverticulitis was reported by Somasekar et al. (106).
Interestingly, the majority of patients presenting with severe diverticulitis lack a history of the disease (107). It actually seems as if recurrent diverticulitis may protect against complications of the disease (103).
In a large retrospective observational study of 25,058 cases of diverticulitis 80.3 % had conservative treatment. Of these 19 % experienced relapse, which were treated operatively in 18.1 %, corresponding to that the predicted relapse rate demanding surgery after a single case of conservatively treated diverticulitis was as low as 5.5 % (108). Thus to prevent one patient from needing emergency surgery for diverticulitis, 18 patients, recovering from an initial episode of diverticulitis, should undergo elective operation.
Based on this large registry study from Washington from the period 1987-2001, the mortality risk can be estimated 10-foldly increased if everyone not primarily operated with acute diverticulitis were offered elective surgery. The estimate is based on the following assumptions: 20,136 individuals were treated conservatively during the first hospitalization for diverticulitis - of these 692 needed emergency surgery for recurrent diverticulitis with a mortality of 3.1 % (0.031x692 = 21 deaths) compared with a mortality of 1.1 % by elective surgery (0.011x20,136 = 221 deaths).
Despite the fact that expert opinions and guidelines previously recommended elective resection following to attacks of diverticulitis, such strategy has shown no benefit on mortality, morbidity, quality of life or stoma risk and carries significant and probably unnecessary costs to society (109,110). In fact after recovering from an episode of diverticulitis the risk of an individual requiring an urgent Hartmann's procedure is only one in 2000 patient-years of follow-up.
No randomized studies exist able to advice whether to offer operation or not after one or more cases of diverticulitis.

2) Improved diagnostics and new treatment modalities have reduced the morbidity in treatment of complicated diverticulitis.
According to several studies about 20 % of first time diverticulitis previously was treated surgically. This percentage seems declining, possibly due to introduction of routine CT staging, improved access to CT or US guided abscess drainage and laparoscopic lavage combined with antibiotics as standard treatment for purulent peritonitis.
A retrospective register survey from Canada comprising 685,390 cases of diverticulitis has indeed shown a rising incidence of discharges with a diagnosis of diverticulitis in the period 1991 to 2005, but a decline in the proportion having a resection both in uncomplicated (from 18 to 14 %) as well as in complicated cases (from 71 to 56 %). An increase in admissions with abscess from 6 to 10 % was noted, but the frequency of perforated cases remained constantly 1.5 % over 15 years (111).
In a smaller Swedish study after the introduction of modern treatment principles only 5 % needed acute resection and additionally 5 % in the following 3 years. Mortality was only found among patients with faecal peritonitis (112).
The induction of laparoscopic lavage in the treatment of perforated diverticulitis appears to have a substantially lower morbidity and mortality when compared with resection strategies (83).
The fact, that the risk of recurrence of complicated diverticulitis is lower and treatment complications fewer than previously thought, led the American Society of Colon and Rectal Surgeons to a change in recommendations in 2006, so that the question of elective resection should be evaluated individually and not based on previous numbers of diverticulitis (97).

2) Who is at increased risk for relapse?
We are generally unable to anticipate which cases of diverticulitis that will relapse; but there seems to be an increased risk of relapse in patients with a pelvic abscess treated conservatively with/without CT-guided drainage (46,54).
It was earlier assumed that young age at onset increased the risk of complicated recurrence of diverticulitis, thus supporting a recommendation for elective resection.
In a study by Broderick-Villa et al. older age was associated with a lower risk of recurrence (RR 0.68 (95 % CI:0.53-0.87), age ≥50 years vs. <50 years)(104). The previously mentioned large register study from Washington found that younger patients (<50 years) had greater risk of recurrence than older patients (27 % vs. 17 %, p<0.001) and more often underwent emergency resection or colostomy at relapse (7.5 % vs. 5 %, p<0.001)(108). But even in a population under age 50 it would be necessary to operate 13 individuals to avoid one acute resection and/or colostomy. Furthermore mortality by emergency surgery in younger patients (< 50 years) was only 0.2 % as opposed to 3.4 % in older patients (p<0.001). In a study by Hjern et al. no significant age impact on recurrence was found, but type 2 error could not be excluded (112).
In a retrospective study the need for colectomy significantly correlated with low serum albumin levels, glucocorticoid use and chronic obstructive pulmonary disease (113). In an American cohort analysis, risk factor analysis showed that patients having one or more of the following conditions: use of immunosuppressive therapy, chronic renal failure or collagen-vascular disease, had a 5-fold greater risk of perforation in recurrent episodes of diverticulitis, therefore elective resection should be considered (114). In a systematic review of the clinical course of diverticular disease in immunosuppressed patients the incidence of acute diverticulitis was 1 % in general, but 8 % in patients with known diverticular disease. Mortality from acute diverticulitis in these patients was 23% when treated surgically and 56% when treated medically. The authors found further research needed to define whether these risks constitute a mandate for screening and prophylactic sigmoid colectomy (115).

3) Resection for chronic diverticulitis or symptomatic uncomplicated diverticular disease
For frequently recurring or prolonged diverticulitis cases resection may be considered, if the condition is unacceptable to the patient, provided accept of the risks of elective resection.
Patients with atypical "smouldering" diverticular disease, presenting with chronic symptoms but without diverticulitis, who underwent sigmoid resection, experienced complete resolution of symptoms in 76.5 % with 88 % being pain free, according to a publication from the Mayo Clinic (116). Pathological examination of resected specimens showed in 76 % of cases acute or chronic inflammation.

In a collection of long-term results of surgery for diverticulitis comprising 7 studies 78 % (508/655) became asymptomatic after sigmoid resection (117). Similarly Egger et al. found that 25 % suffered persistent symptoms after elective sigmoid resection for diverticulitis (118). In this regard no difference was found between patients operated openly or laparoscopic.
Persistent symptoms after resection may occasionally be due to anastomotic stenosis. Ambrosetti et al. found 17.6 % anastomotic stenosis in patients who underwent elective laparoscopic sigmoidectomy with a stapled anastomosis, all treated successfully with endoscopic dilatation (119).
A randomized multicenter study has since 2010 been conducted in Holland comparing elective resection with conservative treatment if symptoms persist after an episode of diverticulitis or by frequently recurrent diverticulitis (120).

4) Need for surgery for chronic complicated diverticulitis
The evidence for treatment of chronic complicated diverticulitis with fistula or stricture is based on case reports and small series. The condition usually presents with chronic symptoms and treatment needs is electively. It is important to consider whether comorbidity represents a contraindication to surgery, since many of these conditions may be treated conservatively or with a proximal relieving colostomy. In cases of a non-resectional strategy malignancy must be excluded and if this is not possible resection is recommended.
Fistulas occur most commonly to the bladder, to other intestinal segments, to the skin and in hysterectomized women to the closed vagina.
Patients with colovesical fistulas uniformly have urinary tract infection and often the pathognomonic symptoms pneumaturia and/or fecaluria. In a retrospective study of 50 patients diagnosed with colovesical fistula not a single documented case of septicaemia were found and likewise no significant decline in renal function were found in cases with fistula present for more than 6 months (121).
Strictures caused by diverticulitis can not normally be dealt with successfully with endoscopic stenting, leaving resection or proximal relieving stoma as the therapeutic option.

Conclusion:
The risk of stoma and severe complications is higher in acute than in elective surgery (evidence IIb).
Recurrent diverticulitis seems to be associated with less complication risk than primary cases (evidence III).
Diverticulitis onset before age 50 seems to be associated with an increased risk of relapse and need for emergency surgery at relapse (evidence III).
There is no evidence for routine elective resection after a single case of acute diverticulitis, even in younger patients (evidence IIa).
Individuals on immunosuppressive therapy, with chronic renal failure or having inflammatory connective tissue disease are at greater risk of recurrence and severe complications (evidence III).
In chronic symptomatic uncomplicated diverticular disease not amenable to conservative measures 3 of 4 benefits from resection (evidence III).
In case of fistula or stenosis treatment must be individualized (evidence IV).

Recommendation:
Elective resection is not routinely recommended for neither uncomplicated nor complicated cases of diverticulitis, even in younger patients (grade B).
Any recommendation for routine resection following multiple cases of diverticulitis must await results of randomized studies (grade C).
In individuals on immunosuppressive therapy, with chronic renal failure or having inflammatory connective tissue disease elective resection may be justified (grade B).
In chronic symptomatic uncomplicated diverticular disease or by frequent relapse, resection can be considered if the condition is intolerable (grade C).
In complicated diverticulitis with fistula or stenosis resection is recommended if the patient's condition allows this (grade C).
If malignancy can not be ruled out preoperative staging and oncological resection according to the DCCG guidelines is recommended (grade C).

SUMMARY
In order to elaborate evidence–based, national Danish guidelines for the treatment of diverticular disease the literature was reviewed concerning the epidemiology, staging, diagnosis and treatment of diverticular disease in all its aspects.
The presence of colonic diverticula, which is considered to be a mucosal herniation through the intestinal muscle wall, is inversely correlated to the intake of dietary fibre. Other factors in the genesis of diverticular disease may be physical inactivity, obesity, and use of NSAIDs or acetaminophen. Diverticulosis is most common in Western countries with a prevalence of 5% in the population aged 30-39 years and 60% in the part of the population > 80 years. The incidence of hospitalization for acute diverticulitis is 71/100,000 and the incidence of complicated diverticulitis is 3.5-4/100,000.
Acute diverticulitis is conveniently divided into uncomplicated and complicated diverticulitis. Complicated diverticulitis is staged by the Hinchey classification 1-4 (1: mesocolic/pericolic abscess, 2: pelvic abscess, 3: purulent peritonitis, 4: faecal peritonitis). Diverticulitis is suspected in case of lower left quadrant abdominal pain and tenderness associated with fever and raised WBC and/or CRP; but the clinical diagnosis is not sufficiently precise. Abdominal CT confirms the diagnosis and enables the classification of the disease according to Hinchey. The distinction between Hinchey 3 and 4 is done by laparoscopy or, when not possible, by laparotomy.
Uncomplicated diverticulitis is treated by conservative means. There is no evidence of any beneficial effect of antibiotics in uncomplicated diverticulitis; but antibiotics may be used in selected cases depending on the overall condition of the patients and the severity of the infection.
Abscess formation is best treated by US- or CT-guided drainage in combination with antibiotics. When the abscess is < 3 cm in diameter, drainage may be unnecessary, and only antibiotics should be instituted.
The surgical treatment of acute perforated diverticulitis has interchanged between resection and non-resection strategies: The three-stage procedure dominating in the beginning of the 20th century was later replaced by the Hartmann procedure or, alternatively, resection of the sigmoid with primary anastomosis. Lately a non-resection strategy consisting of laparoscopy with peritoneal lavage and drainage has been introduced in the treatment of Hinchey stage 3 disease. Evidence so far for the lavage regime is promising, comparing favourably with resection strategies, but lacking in solid proof by randomized, controlled investigations.

In recent years, morbidity has declined in complicated diverticulitis due to improved diagnostics and new treatment modalities. Recurrent diverticulitis is relatively rare and furthermore often uncomplicated than previously assumed. Elective surgery in diverticular disease should probably be limited to symptomatic cases not amenable to conservative measures, since prophylactic resection of the sigmoid, evaluated from present evidence, confers unnecessary risks in terms of morbidity and mortality to the individual as well as unnecessary costs to society. Any recommendation for routine resection following multiple cases of diverticulitis should await results of randomized studies.
Laparoscopic resection is preferred in case of need for elective surgery. When malignancy is ruled out preoperatively, a sigmoid resection with preservation of the inferior mesenteric artery, oral division of colon in soft compliant tissue and anastomosis to upper rectum is recommended.
Fistulae to bladder or vagina, or stenosis of the colon may be dealt with according to symptoms and comorbidity. Resection of the diseased segment of colon is preferred when possible and safe; alternatively, a diverting stoma can be the best solution.

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