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(REVIEW ARTICLE)



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Abstract

Diverticula are protrusions that resemble sacs in the colon's wall. Acute or chronic problems are experienced by 4% of diverticula patients. Diverticulosis development has been linked in large part to the western way of life. Colonic diverticular disease has become more common. Obesity, smoking, and inadequate fibre consumption are risk factors for the illness. Most of the time, surgery is not necessary to treat this; however, if the bleeding is significant, angiography and endovascular intervention may be helpful. Ureteral catheters should be considered when a patient has undergone radiation therapy, resurgery, or preoperative imaging reveals an abnormal anatomy. Oral antibiotics can help prevent surgical site infections after an elective colon resection, according to studies. Using nonabsorbable oral antibiotics like erythromycin, neomycin, and metronidazole reduces surgical site infections overall.

Keywords: Diverticula; Risk factors; Lifestyle; Nutrition; Antibiotics

1. Introduction

Diverticula, that is, sac-like protrusions in the wall of large bowel are the most frequent anatomical alteration in the human colon. Due to alterations which produce inflammation of diverticula of the colon. The anatomy of the colon wall, including loss of elasticity function and deposition of immature collagen fibres in the extracellular matrix, which are implicated in the formation of diverticula. For many years, the western lifestyle has been considered a key factor for the development of diverticulosis.

2. Colonic diverticular disease

The outcome of changes in diet and lifestyle also influences the colonic diverticulosis. Recently, the incidence of diverticulitis has been rising, particularly in young individuals. Approximately 4% of patients with diverticula develop acute or chronic complications including perforation, abscess and fistula [1]. The aetiology of the diverticulosis is poorly understood involving low fibre intake , changes in colonic pressure, motility and wall structure ,smoking, non-steroidal anti-inflammatory drugs(NSAIDs),physical inactivity and obesity are identified as risk factors for diverticulitis, and also has the potential for causing serious complications [2]. This review will discuss the common symptoms, pathogenesis, complications, risk factors, current diagnostic techniques ,treatment of colonic diverticular [3].

2.1. Asymptomatic diverticulosis

Asymptomatic diverticulosis is often an incidental finding in patients undergoing imaging for other indications. However, the clinical significance of such findings is unclear as there is no indication for treatment or further follow-up for patients with asymptomatic diverticulosis [4].

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2.2. Symptomatic uncomplicated diverticular disease

Diverticular illness with symptoms has been divided into a number of unique categories in recent years. These include symptomatic uncomplicated diverticular disease, segmental colitis associated with diverticulosis (SCAD), and chronic recurrent diverticulitis (SUDD). In the absence of acute diverticulitis symptoms, SUDD is characterized as chronic diverticulosis with accompanying chronic abdominal discomfort. It's possible that the illness processes associated with SUDD and irritable bowel syndrome (IBS), which also includes visceral hypersensitivity, share comparable pathophysiologic underpinnings. Clemens et al. conducted a study on this and discovered that the SUDD patient exhibited hyperalgesia in the sigmoid colon with diverticula. In terms of altered intestinal motility, SUDD is furthermore likened to IBS. Even though there were no irregularities in the enteric neuronal population, Bassotti et al. showed that individuals with diverticulosis have less colonic interstitial cells of Cajal (ICC) and enteric glial cells. He hypothesised that a shortfall in ICC causes a decrease in colonic electrical slow wave activity, which causes slower transit, and proposes that this is because of their involvement in controlling intestine motor function. At this time, it is unknown if SUDD and IBS have a same aetiology or whether people with IBS are more likely to develop diverticulosis and, thus, be classified as having SUDD if they experience persistent stomach discomfort [5-8].

2.3. Diverticulitis

Diverticulitis results from an inflamed diverticulum. Either an acute or chronic process may manifest. The most frequent side effect of diverticulosis, which affects 10% to 25% of patients, is diverticulitis. The occlusion of the diverticulum sac by a fecalith, which results in low-grade inflammation, congestion, and additional obstruction due to irritation of the mucosa, is the pathophysiology of diverticulitis. Diverticulitis can also be divided into simple and complex cases. Typically, abscesses, fistulas, obstructions, and/or perforations arise as a result of complicated diverticulitis. The choice of whether to admit a patient to the hospital is crucial in the therapy of diverticulitis. According to the American Society for Colon and Rectal Surgery (ASCRS), numerous aspects, such as inability to accept oral intake and discomfort level, are taken into consideration [9,10].



Figure 1 Various Complications of Diverticular Disease

2.4. Abscess

The development of phlegmon and abscesses may be caused by diverticulitis. The most used method for evaluating abscesses and phlegmon is CT. Phlegmon is shown as a spherical or ovular inflammatory mass next to diverticulitis, with heterogenous contrast enhancement, whereas an abscess often appears as a loculated fluid collection with air in it. In up to 30% of people with acute diverticulitis, abscesses may be found. An inflammatory and ischemic condition of the appendices called epiploic appendagitis causes peri colonic fat to strand on a CT scan. In epiploic appendicitis, contrast-enhanced CT shows a central focal region of thin-high density rim around the abscessed fat. In epiploic appendagitis the Inflammation is localized on the antimesenteric while Diverticulitis the Inflammation is localized in the mesocolon. Treatment for abscess (Table 1)

Table 1 Treatment approach for abscess based on lesion size

Lesion size	Management
below 3 cm	Conservative management
more than 3 cm	Surgical intervention

According to the Hinchey classification complicated diverticulitis is classified below



Figure 2 Phases of Complicated DD

The liver is the most common remote site of abscess formation. The mortality rate in case of pylephlebitis and liver abscess formation can be as high. Multiphasic imaging may aid in differentiating an abscess from other malignant lesions. A tuboovarian abscess may complicate acute diverticulitis of a sigmoid colon due to its close proximity to the adnexa, and it was assessed by Sonographic technique. It may be of higher yield when performed via the routes such as transrectal or transvaginal. This method highlights the anatomical connection between the diverticulitis and the abscess. Since tuboovarian abscesses frequently present as a complicated multiloculated adnexal mass, making the diagnosis with CT may be difficult [11-18].

2.5. Perforation

Diverticulitis can become perforated as a result of severe bowel wall layer inflammation, necrosis, and loss of intestinal wall integrity. Colonic diverticulitis nearly often results in a perforation on the left side, which may lead to the creation of a local abscess and fistula. Acute stomach discomfort, nausea, and vomiting are common signs of intraperitoneal perforation. Retroperitoneal air can develop if the second and third duodenal segments, as well as the ascending and descending sigmoid colon segments, are perforated. Delayed diagnosis in such individuals leading to consequences that might be fatal. On upright abdominal X-rays, subdiaphragmatic free air may be seen in the presence of perforated diverticulitis. It is difficult to evaluate the perforated diverticulitis using sonographic methods. The detection of free air is substantially better suited to multidetector computed tomography Focused gut wall discontinuities, extraluminal gas, and extraluminal enteric contrast agent leaking are direct indicators of perforation on MDCT. As indirect signs of perforation, it is possible to observe aberrant gut wall augmentation, perivisceral fat stranding, and abscess development. Endovascular air bubbles in the mesenteric veins, portal vein, and bowel segments can be found using CT scans. After having their first diverticulitis episode, people with poor health and those who take steroids are more vulnerable to perforation and subsequent peritonitis [19- 28].

2.6. Fistula [29-36]

Because of the abscess, the immediate neighbour's anatomic structure's wall integrity encourages the development of fistulas. Some of the areas implicated in fistula creation are the urinary bladder, ureter, other nearby intestine segments, gallbladder, uterus, fallopian tubes, vagina, skin, and the perianal.

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1.	Coloenteric fistula	fistula Secondary to diverticulitis differ from those seen in Crohn's disease.	
	Location	Fistula occurs generally between the terminal ileum and right anterior surface of the bladder.	
2.	Colovesical fistula	It is present as free air in the bladder along with thickening of the adjacent bladder wall.	
	Common symptoms	Lower urinary tract infection and the presence of stool or air in the urine.	
	Diagnosis	Administration of rectal contrast may be helpful for outlining the exact point of the fistula tract	
	Location	Located in the left posterior portion of the bladder, which is in close anatomic location with the sigmoid colon.	
3.	Colouterine fistula	Manifest with myometrial abscess formation.	
	Diagnosis	CT may demonstrate air bubbles within the uterine cavity, MRI and sonohysterography were also reported to be helpful in detecting colouterine fistula.	

Table 2 Diverticulitis fistulas and its Diagnosis

2.7. Pylephlebitis

Pylephlebitis and the damaged colonic segment have a cordial relation. It is an uncommon intraabdominal infection consequence also known as ascending septic thrombophlebitis. The most frequent kind of infectious thrombosis found in patients is in the superior mesenteric vein, followed by the portal vein and inferior mesenteric vein. The most frequent underlying cause of portal venous system and septic thrombophlebitis is diverticulitis. Appendicitis, necrotizing pancreatitis, intestinal perforation, pelvic infection, and inflammatory bowel disease are other underlying conditions that can result in pylephlebitis. The most typical pathogens responsible for these individuals' illnesses are Bacteroides fragilis and Escherichia coli. Thrombosis from sigmoid diverticulitis causes further propagation along the IMV and the portal vein. The term for this condition is ascending thrombophlebitis. The first modality usually used in individuals with diverticulitis and pylephlebitis is a proper CT procedure. The endoluminal thrombus is typically directly seen to make the diagnosis as a filling defect in the contrast-filled mesenteric veins. As a sign of aberrant hepatic perfusion in the event of portal vein thrombosis, the liver may show central or peripheral hypoattenuating regions. CT protocols Biphasic injection which nicely, depicts both the arterial and venous structures of the mesentery. A reliable diagnosis of an endoluminal thrombus can be made using curved planar, coronal, and sagittal reformatted images. Diverticulitis may also be accompanied with septic thrombosis in the inferior vena cava, which can lead to cavitary pulmonary nodules and septic pulmonary emboli. To stop embolic abscess development in distant organs, early identification, antimicrobial therapy, and concurrent anticoagulation are crucial [37-41].

2.8. Bowel obstructions

Diverticulitis patients rarely suffer serious intestinal obstruction; nevertheless, they may experience partial blockage due to edema in the intestinal wall, peripheral inflammation, or abscess development. In the majority of instances, intramuscular fibrosis found in the chronic phase may also result in blockage. The most frequent observation in these patients is uneven wall thickening with upstream bowel dilatation. An obstructive malignant tumor in the colon is the primary differential diagnosis in patients of acute diverticulitis. The presence of a diverticulum in the affected segment is the most useful indicator of diverticulitis, however this finding cannot be used to clearly rule out colon cancer since diverticulosis without any signs of active inflammation is also quite common in the general population. Concentric wall thickening is more typical of acute diverticulitis, whereas eccentric wall thickening is more typical with colonic cancer. Acute diverticulitis is less prevalent than perilesional mesenteric lymph nodes with a short axis diameter more than 10 mm in colon cancer. Diverticulitis of the rectum is quite uncommon. Even though jejunal diverticulitis is uncommon, it frequently manifests as epiploic band adhesion, which leads to internal hernia. A kind of diverticulitis known as chronic diverticulitis is characterized by symptoms including stomach discomfort that last for months to years. Chronic inflammatory alterations and related dense fibrosis may result in intestinal blockage. The intestinal segment most frequently impacted by this type is the sigmoid colon. Additionally, the affected segment narrows, producing tapered edges with diverticula as well as connected and hypothesized folds. Circumferential constriction of the affected segment is caused by the colonic wall's persistent inflammation, fibrosis, and surrounding pericolic fat [42-46].

2.9. Bleeding

Lower gastrointestinal hemorrhage can be seen in up to a smaller number of patients with colonic diverticulosis. Diverticulitis and non-complicated diverticulosis both have a tendency to bleed because the outpouchings, or diverticula, mainly appear where the vessels puncture the muscularis layer of the colonic wall. In patients who have a clinical suspicion of gastrointestinal bleeding on CT, oral contrast should not be utilized because it might mask the active contrast extravasation from the damaged artery. On unenhanced CT scans, bleeding from colonic diverticulitis may be seen. If the flow rate of the bleeding is copious enough, contrast-enhanced CT images taken during the arterial phase can show active extravascular contrast extravasation into the diverticulum and intestine lumen. Another indication of active bleeding from the diverticulitis in these situations is increasing contrast pooling in the gut lumen [47-49].

2.10. Segmental Colitis

It is a type of active chronic inflammation that resembles inflammatory bowel disease It is also called as Segmental colitis associated with diverticulosis (SCAD). It mostly appears in the sigmoid colon affected by diverticular disease with sparing of the rectum and proximal colon. The prevalence of SCAD is higher in men, with a mean age of above 60 years. However, SCAD has also been reported in younger patients. Only a few cases of SCAD have been reported in Asian countries [50-53].

3. Pathophysiological mechanisms

Numerous factors, including genetics, fibre consumption, vitamin D levels, obesity, and physical activity have been researched and may have an impact on the development of the illness. Other factors include colonic wall shape, colonic motility, and heredity [54].

3.1. Colonic motility

Diverticulosis is thought to be caused by uncoordinated contractions and excessive pressure, which are caused by denervation of myenteric plexus neurones and a reduction in myenteric glial cells and interstitial cells of Caja, according to several studies [55]. Painter discovered Morphine's intrasigmoid pressure high-pressure responses create extremely high pressures in the sigmoid with divertieula and, as a result, should not be administered to people with divertieular illness [56]. Painter demonstrated that simultaneous contraction of the segmental wall under very high pressure might lead to mucosal herniation using cineradiography and pressure measurement. Colonie diverticula are caused by the mucosa herniating through weakened areas of the muscle wall. Therefore, while pulling at a stool, intraluminal pressure can easily increase and lead to a rupture in this area. A peri diverticular abscess, a perforation, the development of a phlegmon, adhesions, the creation of a fistula, and, if scarring takes place, the development of a stenosis are all possible outcomes of rupture [57].

3.2. Genetic factors

Recent investigations have shown that genetic factors play a role in the development of diverticular hospitalization. Diverticulosis often affects the left colon in Western nations, but it typically affects the right colon in Asian nations. When twin siblings were compared to the general population, the Danish twin research discovered a relative risk for diverticulosis among twin siblings [58]. The chances ratio of getting the condition if one twin was afflicted was higher for monozygotic and lower for dizygotic twins among a total of 2296 twins with a diagnosis of DD in the Swedish Twin Registry, which was cross-linked with the Swedish Inpatient Registry. Both studies suggest that together with other general variables, heredity contributes to DD at a rate of 40% [59]. Additionally, several inherited diseases of the connective tissue have been connected with DD and diverticulosis: Ehlers-Danlos syndrome type IV, Williams-Beuren syndrome, polycystic kidney disease, Coffin-Lowry syndrome, and Marfan syndrome [60].

3.2.1. Ehlers-Danlos syndrome type IV

It is a hereditary connective tissue disorder characterised by spontaneous ruptures of the intestines and major arteries and problems in collagen production [61]. Increased prevalence of DD in EDS type IV is revealed by studies [62].

3.2.2. Williams-Beuren syndrome

DD can appear at a young age and is a rare neurodevelopmental condition that also causes gastro-oesophageal reflux, constipation, rectal prolapse, and hernias [63].

3.2.3. Polycystic Kidney Disease

PKD1, PKD2, and PKD3 gene mutations can all result in cystic kidney disease [64]. Diverticulitis in the right colon is much more common and severe in people with the mutant ADPKD gene [65].

3.2.4. Coffin-Lowry syndrome

Mutations in RPS6KA3 are the etiology of an X-chromosomal semi-dominant genetic disorder characterised by mental retardation, auditory and visual impairments. Diverticulitis may be more likely to occur in some people [66].

3.2.5. Marfan syndrome

It is an autosomal dominant characteristic with issues in the heart valves and aorta. Marfan syndrome type 1 may have a greater frequency of diverticulosis than Marfan syndrome type 2, however this is currently unclear [67,68].

3.3. Significance of dietary fiber

Diverticulosis was mostly caused by a diet lacking in fibre, which raised intracolonic pressures [69]. Less frequent bowel movements and firm stools were linked to a lower risk of diverticulosis, according to previous research on the interaction between bowel habits and dietary fibre intake in the development of asymptomatic diverticulosis [70]. Aldoori et al. investigated the relationship between dietary fibre and symptomatic diverticular disease and discovered that symptomatic diverticular disease is more common in people who consume less dietary fibre [71]. Based in large part on this information, the American Gastroenterology Association recently concluded that increasing fibre intake can reduce the complications associated with diverticular disease. It might be wise to re-evaluate the advice to stay away from certain meals in order to avoid diverticular issues [72]. In comparison to a high consumption of fruits, vegetables, whole grains, legumes, poultry, and fish, a high intake of red and processed meats, refined grains, sweets, French fries, and high-fat dairy products was positively related with an elevated risk of diverticulitis [73].

3.4. Function of vitamin D

Diverticular illness has recently been studied in relation to vitamin D. Patients with simple diverticulosis and those who required hospitalisation for diverticulitis had their prediagnostic levels of vitamin D (25-OH) compared in a cohort study. The results of this investigation point to a possible role for vitamin D deficiency in the aetiology of diverticulitis and indicate that lower blood vitamin D levels may be associated with a higher risk of severe diverticulitis, but larger cohort studies would be required to confirm this [74].

3.5. Obesity

With rising obesity rates over the past few decades, diverticular disease has become more common [75]. Numerous gastrointestinal conditions, including diverticulitis, have been linked to obesity. The risk of diverticulitis has been positively correlated with body mass index, waist circumference, and waist-to-hip ratio in several sizable prospective studies [76-78]. Numerous investigations have been made to determine how obesity affects alterations in the gut microbiota in both human and mouse models in an effort to understand how obesity contributes to diverticular disease [79-81].

3.6. Physical exercise

By decreasing transit time, inflammation, and colon pressures, it may lower the risk of colon cancer as well as several other gastrointestinal problems. Additionally helpful in diverticular illness, these hypothesised mechanisms [82,83]. However, this correlation was only observed with severe exercise, such as jogging, cycling, using a ski machine, swimming laps, playing tennis, squash, or other racquet sports [84].

3.7. NSAIDs /Diverticulum risk and aspirin

Aspirin is well-known NSAID that might induce difficulties in the upper gastrointestinal system. Additionally, some drugs have been linked to decreased gastrointestinal damage. Nearly all major gastrointestinal side effects linked to NSAIDs [85-90]. Diverticulitis and its consequences are increasingly being linked to ulcers and diverticular disease [91]. NSAID regular users have a greater risk of diverticulitis, but aspirin regular users had a slightly lower risk. Aspirin and other NSAIDs have the potential to cause diverticular problems through a number of different routes. The colon is hypothesised to be harmed by NSAIDs, such as aspirin, by direct topical irritation and/or reduced prostaglandin production, which compromises mucosal integrity, increases permeability, and allows the entry of bacteria and other toxins [92]. High prevalence of diverticular condition and NSAID usage, particularly in the elderly, these findings have

significant clinical and public health implications. Diverticulosis patients, especially those who have had past difficulties, should carefully consider their analgesic treatments. Future research is required to more accurately pinpoint and create mitigation plans for the lower gastrointestinal toxicity of NSAIDs [93,94].

4. Treatment

4.1. Veggie/fiber-rich diet

An increasing collection of scientific research shows that healthy vegetarian diets have unique advantages over healthy alternatives that include a lot of meat and other animal products. Vegetarian diets have previously been compared to plant proteins, iron, zinc, calcium, micronutrients, vitamin A, n-3 fatty acids, and iodine. Vegetarian diets are helpful in the prevention and treatment of several ailments, including diverticular disease, gallstones, and autoimmune diseases. as well as heart events, hypertension, diabetes, bowel cancer, osteoporosis, renal disease, and dementia. Vegetarian diets provide potential health advantages, including the treatment and prevention of many medical conditions, as demonstrated by the existing database of vegetarian studies [95]. In addition to greater quantities of carbohydrates, dietary fibre, magnesium, potassium, folate, and antioxidants including vitamins C and E and phytochemicals, vegetarian diets also have lower levels of saturated fat, cholesterol, and animal protein [96]. Numerous medical practitioners recommend a high-fiber diet, or fibre supplements, which continue to be the first-line treatments for SUDD [97]. A recent comprehensive study discovered strong evidence in favour of a high-fiber diet in the management of DD [98]. Peery et al. momentarily discovered that those who consume a lot of soluble fiber had a greater chance of developing diverticulosis [99]. The risk of various chronic complications, is lowered by eating enough fibre [100]. Protein, unsaturated fats, fibre, vitamins, minerals, and other micronutrients may all be found in large quantities in nuts. Nuts may be a crucial component of a diet that promotes health, according to compelling data. A diet rich in nuts may offer protection from a number of common illnesses, such as cholelithiasis, colon and prostate cancer, diabetes, cardiovascular disease, and diabetes mellitus. [101-111].

4.2. Diverticulitis with antibiotic use

Rifaximin, an intestinal absorption oral antibiotic with a wide range of effects, has been studied and used to treat SUDD [112]. It has a wide range of effects that include eradicating Gram-positive and -negative bacteria as well as aerobes and anaerobes [113]. The newest AGA guidelines suggest against the use of rifaximin as an agent to reduce diverticulitis recurrence [114]. Rifaximin 800 mg/ with GM 2g (or) 4g/day for 7 days, administered to individuals, resulting in a reduction in SUDD symptoms, according to Papi et al. and Latella et al [115-116]. Therefore, the most recent recommendations advise using of rifaximin as a preventative measure for diverticulitis recurrence [117].

4.3. Mesalazine

Mesalazine, sometimes referred to as mesalamine is a medication used to treat ulcerative colitis and Crohn's disease as well as other inflammatory bowel disorders. Another alternative for the treatment of SUDD is mesalazine. Mesalazine works on the gastrointestinal epithelium via the active metabolite of 5-ASA and suppresses the synthesis of interleukin-1, free radicals, and certain important components of the inflammatory cascade, including COX, TX-synthetase, and PAF-synthetase. It also possesses intrinsic antioxidant action [118]. In a randomized, double-blind, multicentered trial with 1,182 patients, Raskin et al. examined the effectiveness of mesalamine in preventing diverticulitis from recurring. Mesalamine should not be advised for the prevention of recurrent diverticulitis, according to the results, which revealed that it did not lower the risk of diverticulitis recurrence, latency to recurrence, or the number of patients needing surgery [119]. It is yet unclear whether or not this drug can help SUDD sufferers with their symptoms.

4.4. Probiotics

Diverticular and peri-diverticular inflammation, increased exposure to intraluminal antigens and toxins, as well as alterations in the bacterial ecology, may result from bacterial overgrowth in the diverticula [120]. In order to manage colonic inflammation, the colonic flora may be therapeutically altered. As a third option, probiotics can be used to treat SUDD. Living microorganisms known as probiotics have additional health advantages for their hosts beyond those provided by inherited basic nutrients. Probiotics have physio-pathological effects that include decreasing pathogen adhesion, enhancing IgA production in Peyer's patches, boosting immune system function, and blocking the release of both pro-inflammatory and anti-inflammatory cytokines [121]. A more dated paper published by Giaccari et al. evaluated the effect of rifaximin, together with lactobacilli was well tolerated and could reduce both GI symptoms and occurrence of SUDD in those patients [122].



Figure 3 Modern treatment approaches for Diverticular inflammation

Overall, 88% of patients were symptom free after 2 years of treatment, while mesalazine plus L. casei resulted to be the best treatment [123]. In contrast to antibiotic treatment, probiotics are a less invasive and more physiological approach to treat the microbial dysbiosis in patients with diverticular disease. The most widely used probiotic mixtures contain Lactobacilli and Bifidobacteria, sometimes yeasts are also used with good clinical results [124].

4.5. Physical activity

Physical activity has been studied in many gastrointestinal disorders and proposed to reduce risk of colon cancer and other gastrointestinal disorder through decreased transit time, inflammation and/or colon pressure [125,126]. Men who exercised the most had a 25% reduction in risk of diverticulitis, and a 46% risk reduction of diverticular bleeding when compared to men who exercised the least after adjustment for age, study period, diet, BMI, and NSAID and aspirin use [127]. Williams et al. studied over thousands of male and female runners above 50 years of age and concluded that the risk of reported diverticular disease decreased linearly with the number of kilometers run per week and with cardiorespiratory fitness [128]. So, running was the only specific activity to significantly reduce the risk of diverticular complications. A prospective cohort study of Swedish women also found that physical inactivity increased the risk of diverticular disease requiring hospitalization [129].

5. Surgical treatment

For individuals who experience recurring bouts of acute diverticulitis, surgical intervention is still frequently required. [130]. Diverticulitis is potentially fatal if there is generalised peritonitis, uncontrolled visceral perforation, severe uncontrollable sepsis, a huge, infected abscess that cannot be drained or reached, intestinal obstruction, or perforation. Severe symptoms that call for immediate surgery [131]. In fact, in accordance with ASCRS recommendations [132] along with several additional rules, [133] after one or two diverticulitis episodes that are well documented, elective resections should be taken into consideration. Resection Elective Patients who experienced an episode of acute, uncomplicated diverticulitis were treated non-operatively and had marginal rates of complications or the need for immediate surgery (6%). Following recovery from simple acute diverticulitis, an elective sigmoid colectomy should be recommended based on clinical practise guidelines developed by the Clinical Practice Guideline Task Force of the American Society of Colon and Rectal Surgeons. [134-139]. Immunosuppressed Elective Resection When treated for acute diverticulitis alone with medical therapy, patients who require chronic corticosteroid therapy are more likely to fail medical care and have a high death risk. Additionally, individuals with collagen-vascular disease or chronic renal failure are at a higher risk of developing complex and recurring diverticulitis. Additionally, they are more likely to need urgent surgery [140,142]. Elective or semi-elective resection is recommended following an episode of complicated diverticulitis coupled with a fistula of any kind colocutaneous, colovesical, colovaginal [143]. After an elective resection, morbidity is prevalent, and surgery does not completely reduce the chance of diverticulitis recurrence [144].

6. Robotic and laparoscopic surgery

The American Society of Colon and Rectal Surgeons have recommended a laparoscopic approach for elective colectomy with short-term benefit include, the decreased length of stay, decreased ileus, decreased intraoperative blood loss, and decreased pain. Long-term benefits include up to a decrease in incisional hernias. However, laparoscopic surgery is performed by an experienced surgeon trained in laparoscopic surgery [145-148]. Surgery for colon and rectal surgery has continued to expand over the last decade beyond laparoscopic and hand-assist surgery and now includes robotic

surgery. Robotic colectomy has been shown in the literature to be a safe and comparable alternative to laparoscopic surgery [149-152]. Advantages include surgeon-controlled, three-dimensional, high-definition optics, stable platform, improved strength, articulating instruments, and decreased rate of conversion to an open procedure.

6.1. Percutaneous treatment

For individuals with a significant diverticular abscess, radiologically guided percutaneous drainage recommended by the American Society of Colon and Rectal Surgeons (ASCRS) is often the best course of action [153]. When an abscess is larger than 5 cm in diameter and involves the pelvis, surgery is more likely to be required [154]. Last but not least, colonic diverticular disease is another often occurring factor in acute lower gastrointestinal bleeding [155]. The majority of the time, this may be controlled without surgery, but if the bleeding is severe, angiography and endovascular intervention may be beneficial [156]. When a patient has received radiation therapy, resurgery, or preoperative imaging shows aberrant anatomy, ureteral catheters should be taken into consideration. [157,158]. After an elective colon resection, research has shown that the administration of oral antibiotics helps reduce surgery site infections. Overall surgical site infections are reduced by using nonabsorbable oral antibiotics as erythromycin, neomycin, and metronidazole [159-162].

7. Conclusion

The best techniques to treat acute diverticulitis are a hotly contested issue right now. Controlled studies have demonstrated that the use of antibiotics for acute, uncomplicated diverticulitis neither hastens healing nor shields against complications or recurrence. Future clinical trials looking at antibiotic treatment in individuals with acute diverticulitis need to offer more individualized approaches. Despite the fact that an RCT indicated that both rifaximin and mesalazine were unsuccessful for secondary diverticulitis prevention. It is surprising, especially in light of the fact that mesalazine is likewise helpful in the primary prevention of acute diverticulitis and that both medications reduce the symptoms of SUDD in placebo-controlled studies. To sum up, DD is a complex illness in which the best patient stratification based on the disease's severity may ensure therapy effectiveness. Recent classifications in radiology and endoscopy may be the best method for achieving this goal. Furthermore, in order to have a customized treatment plan, prospective trials using this categorization are critically needed.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors declares no conflict of interest.

References

- [1] Tursi A, Scarpignato C, Strate LL, Lanas A, Kruis W, Lahat A et al.. Colonic diverticular disease. Nat Rev Dis Primers. 2020;6(1):20.
- [2] Cao Y, Strate LL, Keeley BR, Tam I, Wu K, Giovannucci EL, Chan AT. Meat intake and risk of diverticulitis among men. Gut 2018; 67 (3): 466-472
- [3] Rangan V, Lamont JT. Small bowel diverticulosis: pathogenesis, clinical management, and new concepts. Curr Gastroenterol Rep. 2020; 22(1):4.
- [4] Bhucket TP, Stollman NH. Diverticular disease of the colon. In: Feldman M, Friedman LS, Brandt LJ, editors. Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management. 2014; 10th ed. Vol. 2.
- [5] Peery AF, Sandler RS. Diverticular disease: reconsidering conventional wisdom. Clin Gastroenterol Hepatol. 2013; 11(12):1532-7.

- [6] Strate LL, Modi R, Cohen E, Spiegel BM. Diverticular disease as a chronic illness: evolving epidemiologic and clinical insights. Am J Gastroenterol. 2012; 107(10):1486-93.
- [7] Clemens CH, Samsom M, Roelofs J, van Berge Henegouwen GP, Smout AJ. Colorectal visceral perception in diverticular disease. Gut. 2004; 53(5):717-22.
- [8] Bassotti G, Battaglia E, Bellone G, Dughera L, Fisogni S, Zambelli C. Interstitial cells of Cajal, enteric nerves, and glial cells in colonic diverticular disease. J Clin Pathol. 2005; 58(9):973-7.
- [9] Bhucket TP, Stollman NH. Diverticular disease of the colon. In: Feldman M, Friedman LS, Brandt LJ, editors. Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management. 2014; 10th ed. Vol. 2.
- [10] Parks TG. Natural history of diverticular disease of the colon. Clin Gastroenterol. 1975; 4(1):53-69.
- [11] Sessa B, Galluzzo M, Ianniello S, Pinto A, Trinci M, Miele V. Acute perforated diverticulitis: assessment with multidetector computed tomography. Semin Ultrasound CT MR. 2016;37(1):37-48.
- [12] Hulnick DH, Megibow AJ, Balthazar EJ, Naidich DP, Bosniak MA. Computed tomography in the evaluation of diverticulitis. Radiology. 1984;152(2):491-5.
- [13] Singh AK, Gervais DA, Hahn PF, Rhea J, Mueller PR. CT of acute appendagitis. AJR Am J Roentgenol. 2004; 183(5):1303-7.
- [14] Singh AK, Gervais DA, Hahn PF, Sagar P, Mueller PR, Novelline RA. Acute epiploic appendagitis and its mimics. RadioGraphics. 2005; 25(6):1521-34.
- [15] Destigter KK, Keating DP. Imaging update: acute colonic diverticulitis. Clin Colon Rect Surg. 2009; 22(3):147-55.
- [16] Tuncer ZS, Boyraz G, Yücel SÖ, Selçuk I, Yazicioğlu A. Tuboovarian abscess due to colonic diverticulitis in a virgin patient with morbid obesity: a case report. Case Rep Med. 2012;413185.
- [17] Jeong SW, Jang JY, Lee TH, Kim HG, Hong SW, Park SH. Cryptogenic pyogenic liver abscess as the herald of colon cancer. J Gastroenterol Hepatol. 2012; 27(2):248-55.
- [18] Plemmons RM, Dooley DP, Longfield RN. Septic thrombophlebitis of the portal vein (pylephlebitis): diagnosis and management in the modern era. Clin Infect Dis. 1995; 21(5):1114-20.
- [19] Puylaert JB. Ultrasound of colon diverticulitis. Dig Dis. 2012; 30(1):56-9.
- [20] Werner A, Diehl SJ, Farag-Soliman M, Düber C. Multi-slice spiral CT in routine diagnosis of suspected acute leftsided colonic diverticulitis: a prospective study of 120 patients. Eur Radiol. 2003; 13(12):2596-603.
- [21] Stoker J, van Randen A, Laméris W, Boermeester MA. Imaging patients with acute abdominal pain. Radiology. 2009;253(1):31-46.
- [22] West AB, Losada M. The pathology of diverticulosis coli. J Clin Gastroenterol. 2004; 38(5); Suppl 1:S11-6.
- [23] Kim SH, Shin SS, Jeong YY, Heo SH, Kim JW, Kang HK JYY. Gastrointestinal tract perforation: MDCT findings according to the perforation sites. Korean J Radiol. 2009; 10(1):63-70.
- [24] Schreyer AG, Layer G, Guidlines for diverticular disease and diverticulitis: diagnosis, classification, and therapy for the radiologist. RöFo. 2015; 187(8):676-84.
- [25] Sessa B, Galluzzo M, Ianniello S, Pinto A, Trinci M, Miele V. Acute perforated diverticulitis: assessment with multidetector computed tomography. Semin Ultrasound CT MR. 2016; 37(1):37-48.
- [26] Weizman AV, Nguyen GC. Diverticular disease: epidemiology and management. Can J Gastroenterol. 2011; 25(7):385-9.
- [27] Fosi S, Giuricin V, Girardi V, Di Caprera E, Costanzo E, Di Trapano R. Subcutaneous emphysema, pneumomediastinum, pneumoretroperitoneum, and pneumoscrotum: unusual complications of acute perforated diverticulitis. Case Rep Radiol. 2014; 2014;431563.
- [28] Choi PW. Pneumomediastinum caused by colonic diverticulitis perforation. J Korean Surg Soc. 2011; 80; Suppl 1:S17-20.
- [29] Puylaert JB. Ultrasound of colon diverticulitis. Dig Dis. 2012; 30(1):56-9.
- [30] Sessa B, Galluzzo M, Ianniello S, Pinto A, Trinci M, Miele V. Acute perforated diverticulitis: assessment with multidetector computed tomography. Semin Ultrasound CT MR. 2016; 37(1):37-48.

- [31] Horton KM, Corl FM, Fishman EK. CT evaluation of the colon: inflammatory disease. RadioGraphics. 2000; 20(2):399-418.
- [32] Suros J, Lee RA. Pneumoretroperitoneum, pneumomediastinum and subcutaneous emphysema. Complications of acute, perforated diverticulitis. Minn Med. 1973; 56(9):747-9.
- [33] Maddu KK, Mittal P, Shuaib W, Tewari A, Ibraheem O, Khosa F. Colorectal emergencies and related complications: a comprehensive imaging review-imaging of colitis and complications. AJR. 2014; 203(6):1205-16.
- [34] Choi PW. Colouterine fistula caused by diverticulitis of the sigmoid colon. J Korean Soc Coloproctol. 2012; 28(6):321-4.
- [35] Kassab A, El-Bialy G, Hashesh H, Callen P. Magnetic resonance imaging and hysteroscopy to diagnose colo-uterine fistula: a rare complication of diverticulitis. J Obstet Gynaecol Res. 2008; 34(1):117-20.
- [36] Takada T, Nakagawa S, Hashimoto K, Sone K, Kugu K, Kozuma S . Preoperative diagnosis of colouterine fistula secondary to diverticulitis by sonohysterography with contrast medium. Ultrasound Obstet Gynecol. 2004; 24(6):682-3.
- [37] Jeong SW, Jang JY, Lee TH, Kim HG, Hong SW, Park SH et al. Cryptogenic pyogenic liver abscess as the herald of colon cancer. J Gastroenterol Hepatol. 2012; 27(2):248-55.
- [38] Bazan F, Busto M. IMAGES IN CLINICAL MEDICINE. Pylephlebitis as a complication of diverticulitis. N Engl J Med. 2015; 373(23):2270.
- [39] Kanellopoulou T, Alexopoulou A, Theodossiades G, Koskinas J, Archimandritis AJ. Pylephlebitis: an overview of non-cirrhotic cases and factors related to outcome. Scand J Infect Dis. 2010; 42(11-12):804-11.
- [40] Mailleux P, Maldague P, Coulier B. Pyleophlebitis complicating peridiverticulitis without hepatic abscess: early detection with contrast-enhanced CT of the abdomen. JBR–BTR. 2012; 95(1):13-4.
- [41] Işik M, Çinar E, Cemal Kizilarslanoğlu MC, Özbek E, Etgül S, Kiraz S. A confusing case: pulmonary lesions including cavities, isolated left heart endocarditis and inferior vena cava thrombosis in a patient with perforated diverticulitis. Rheumatol Int. 2013; 33(8):2179-81.
- [42] Sessa B, Galluzzo M, Ianniello S, Pinto A, Trinci M, Miele V. Acute perforated diverticulitis: assessment with multidetector computed tomography. Semin Ultrasound CT MR. 2016; 37(1):37-48.
- [43] Destigter KK, Keating DP. Imaging update: acute colonic diverticulitis. Clin Colon Rect Surg. 2009; 22(3):147-55.
- [44] Shen SH, Chen JD, Tiu CM, Chou YH, Chiang JH, Chang CY et al. Differentiating colonic diverticulitis from colon cancer: the value of computed tomography in the emergency setting. J Chin Med Assoc. 2005; 68(9):411-8.
- [45] Sheiman L, Levine MS, Levin AA, Hogan J, Rubesin SE, Furth EE. Chronic diverticulitis: clinical, radiographic, and pathologic findings. AJR. 2008; 191(2):522-8.
- [46] Stollman N, Raskin JB. Diverticular disease of the colon. Lancet. 2004; 363(9409):631-9.
- [47] Maykel JA, Opelka FG. Colonic diverticulosis and diverticular hemorrhage. Clin Colon Rect Surg. 2004; 17(3):195-204.
- [48] Horton KM, Corl FM, Fishman EK. CT evaluation of the colon: inflammatory disease. RadioGraphics. 2000; 20(2):399-418.
- [49] Suros J, Lee RA. Pneumoretroperitoneum, pneumomediastinum and subcutaneous emphysema. Complications of acute, perforated diverticulitis. Minn Med. 1973; 56(9):747-9.
- [50] Lamps LW, Knapple WL. Diverticular disease-associated segmental colitis. Clin Gastroenterol Hepatol. 2007; 5(1):27-31.
- [51] Tursi A, Elisei W, Brandimarte G, Giorgetti GM, Lecca PG, Di Cesare L. The endoscopic spectrum of segmental colitis associated with diverticulosis. Colorectal Dis. 2010; 12(5):464-70.
- [52] Imperiali G, Meucci G, Alvisi C, Fasoli R, Ferrara A, Girelli CM et al. Segmental colitis associated with diverticula: a prospective study. [Gruppo di Studio per le Malattie Infiammatorie Intestinali (GSMII)]. Am J Gastroenterol. 2000; 95(4):1014-6.
- [53] Mann NS, Hoda KK. Segmental colitis associated with diverticulosis: systematic evaluation of 486 cases with meta-analysis. Hepato-Gastroenterology. 2012; 59(119):2119-21.

- [54] Rezapour M, Ali S, Stollman N. Diverticular disease: an update on pathogenesis and management. Gut Liver Rezapour1. 2018; 12(2, March):125-32.
- [55] Tursi A, Papa A, Danese S. Review article: the pathophysiology and medical management of diverticulosis and diverticular disease of the colon. Aliment Pharmacol Ther. 2015; 42(6):664-84.
- [56] Sethbhakdi S. Pathogenesis of colonic diverticulitis and diverticulosis. Postgrad Med. 1976; 60(6):76-81.
- [57] The pathology of diverticulosis coli A. Brian West, MD, and Mariela Losada, MD J Clin Gastroenterol. May/June 2004; Vol. 38. Suppl 1.
- [58] Rezapour M, Ali S, Stollman N. Diverticular disease: an update on pathogenesis and management. Gut Liver. 2018; 12(2, March):125-32.
- [59] Tursi A, Papa A, Danese S. Review article: the pathophysiology and medical management of diverticulosis and diverticular disease of the colon. Aliment Pharmacol Ther. 2015; 42(6):664-84.
- [60] Bläker H, Funke B, Hausser I, Hackert T, Schirmacher P, Autschbach F. Pathology of the large intestine in patients with vascular type Ehlers-Danlos syndrome. Virchows Arch. 2007; 450(6):713-7.
- [61] Lindor NM, Bristow J. Tenascin-X deficiency in autosomal recessive Ehlers-Danlos syndrome. Am J Med Genet A. 2005; 135(1):75-80.
- [62] Beighton PH, Murdoch JL, Votteler T. Gastrointestinal complications of the Ehlers-Danlos syndrome. Gut. 1969; 10(12):1004-8.
- [63] Partsch CJ, Siebert R, Caliebe A, Gosch A, Wessel A, Pankau R. Sigmoid diverticulitis in patients with Williams-Beuren syndrome: A relatively high prevalence and high complication rate in young adults with the syndrome. Am J Med Genet A. 2005; 137(1):52-4.
- [64] Scheff RT, Zuckerman G, Harter H, Delmez J, Koehler R. Diverticular disease in patients with chronic renal failure due to polycystic kidney disease. Ann Intern Med. 1980; 92(2 Pt 1):202-4.
- [65] Lederman ED, McCoy G, Conti DJ, Lee EC. Diverticulitis and polycystic kidney disease. Am Surg. 2000; 66(2):200-3.
- [66] Machin GA, Walther GL, Fraser VM. Autopsy findings in two adult siblings with Coffin-Lowry syndrome. Am J Med Genet Suppl. 1987; 3:303-9.
- [67] Eliashar R, Sichel JY, Biron A, Dano I. Multiple gastrointestinal complications in Marfan syndrome. Postgrad Med J. 1998; 74(874):495-7.
- [68] Suster SM, Ronnen M, Bubis JJ. Diverticulosis coli in association with Marfan's syndrome. Arch Intern Med. 1984; 144(1):203.
- [69] Painter NS. The cause of diverticular disease of the colon, its symptoms and its complications: review and hypothesis. J R Coll Surg Edinb. 1985; 30(2):118-22.
- [70] Peery AF, Sandler RS, Ahnen DJ, Galanko JA, Holm AN, Shaukat A, et al. Constipation and a lowfiber diet are not associated with diverticulosis. Clin Gastroenterol Hepatol. 2013; 11(12):1622-7.
- [71] Aldoori WH, Giovannucci EL, Rockett HR, Sampson L, Rimm EB, Willett WC. A prospective study of dietary fiber types and symptomatic diverticular disease in men. J Nutr. 1998; 128(4):714-9.
- [72] Stollman N, Smalley W, Hirano I, AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the management of acute diverticulitis. Gastroenterology. 2015; 149(7):1944-9.
- [73] Strate LL, Keeley BR, Cao Y, Wu K, Giovannucci EL, Chan AT. Western dietary pattern increases, and prudent dietary pattern decreases, risk of incident diverticulitis in a prospective cohort study. Gastroenterology. 2017; 152(5):1023-1030.
- [74] Maguire LH, Song M, Strate LE, Giovannucci EL, Chan AT. Higher serum levels of vitamin D are associated with a reduced risk of diverticulitis. Clin Gastroenterol Hepatol. 2013; 11(12):1631-5.
- [75] Strate LL, Liu YL, Aldoori WH, Syngal S, Giovannucci EL. Obesity increases the risks of diverticulitis and diverticular bleeding. Gastroenterology. 2009; 136(1):115-122.
- [76] Strate LL, Liu YL, Aldoori WH, Giovannucci EL. Physical activity decreases diverticular complications. Am J Gastroenterol. 2009; 104(5):1221-30.

- [77] Rosemar A, Angerås U, Rosengren A. Body mass index and diverticular disease: a 28-year follow-up study in men. Dis Colon Rectum. 2008;51(4):450-5.
- [78] Hjern F, Wolk A, Håkansson N. Obesity, physical inactivity, and colonic diverticular disease requiring hospitalization in women: a prospective cohort study. Am J Gastroenterol. 2012; 107(2):296-302.
- [79] Ly NP, Litonjua A, Gold DR, Celedón JC. Gut microbiota, probiotics, and vitamin D: interrelated exposures influencing allergy, asthma, and obesity? J Allergy Clin Immunol. 2011; 127(5):1087-94; quiz 1095.
- [80] Ley RE, Bäckhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JI. Obesity alters gut microbial ecology. Proc Natl Acad Sci U S A. 2005; 102(31):11070-5.
- [81] Turnbaugh PJ, Backhed F, Fulton L, Gordon JI. Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome. Cell Host Microbe. 2008; 3(4):213-23.
- [82] Colditz GA, Cannuscio CC, Frazier AL. Physical activity and reduced risk of colon cancer: implications for prevention. Cancer Causes Control. 1997; 8(4):649-67.
- [83] Oliveria SA, Christos PJ. The epidemiology of physical activity and cancer. Ann N Y Acad Sci. 1997; 833:79-90.
- [84] Chasan-Taber S, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. Epidemiology. 1996; 7(1):81-6.
- [85] Lanas A, Sekar MC, Hirschowitz BI. Objective evidence of aspirin use in both ulcer and non-ulcer upper and lower gastrointestinal bleeding. Gastroenterology. 1992; 103(3):862-9.
- [86] Lanas A, Serrano P, Bajador E, Esteva F, Benito R, Sáinz R. Evidence of aspirin use in both upper and lower gastrointestinal perforation. Gastroenterology. 1997; 112(3):683-9.
- [87] Langman MJ, Morgan L, Worrall A. Use of anti-inflammatory drugs by patients admitted with small or large bowel perforations and haemorrhage. Br Med J (Clin Res Ed). 1985; 290(6465):347-9.
- [88] Chan FK, Hung LC, Suen BY, Wu JC, Lee KC, Leung VK, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. N Engl J Med. 2002; 347(26):2104-10.
- [89] Laine L, Connors LG, Reicin A, Hawkey CJ, Burgos-Vargas R, Schnitzer TJ, et al. Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use. Gastroenterology. 2003; 124(2):288-92.
- [90] Laine L, Curtis SP, Langman M, et al. Lower gastrointestinal events in a double-blind trial of the cyclo-oxygenase-2 selective CLINICAL- alimentary TRACT 1432 Strate ET AL GASTROENTEROLOGY Vol. 140, 5 inhibitor etoricoxib and the traditional nonsteroidal anti-inflammatory drug diclofenac. Gastroenterology. 2008; 135:1517-25.
- [91] Kvasnovsky CL, Papagrigoriadis S, Bjarnason I. Increased diverticular complications with nonsteriodal antiinflammatory drugs and other medications: a systematic review and meta-analysis. Colorectal Dis. 2014; 16(6):189-96.
- [92] Lanas A, Sopeña F. Nonsteroidal anti-inflammatory drugs and lower gastrointestinal complications. Gastroenterol Clin North Am. 2009; 38(2):333-52.
- [93] Shaheen NJ, Hansen RA, Morgan DR, Gangarosa LM, Ringel Y, Thiny MT, et al. The burden of gastrointestinal and liver diseases, 2006. Am J Gastroenterol. 2006; 101(9):2128-38.
- [94] Talley NJ, Evans JM, Fleming KC, Harmsen WS, Zinsmeister AR, Melton LJ. Nonsteroidal anti-inflammatory drugs and dyspepsia in the elderly. Dig Dis Sci. 1995; 40(6):1345-50.
- [95] Leitzmann C. Nutrition ecology: the contribution of vegetarian diets. Am J Clin Nutr. 2003; 78(3); Suppl: 657S-9S.
- [96] American Dietetic Association (ADA) and dietetics of Canada (DOC): position of the ADA and DOC. J Am Diet Assoc. 2003;103(6):748-65. doi: 10.1053/jada.2003.50142.
- [97] World Gastroenterology Organization (WGO) practice guidelines. Diverticular disease. Available from: http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/07_diverticular_disease pdf [accessed Apr 15 2008]. Vol. 2007; 2007.
- [98] Ünlü C, Daniels L, Vrouenraets BC, Boermeester MA. A systematic review of high-fibre dietary therapy in diverticular disease. Int J Colorectal Dis. 2012; 27(4):419-27.

- [99] Peery AF, Barrett PR, Park D, Rogers AJ, Galanko JA, Martin CF, et al. A high-fiber diet does not protect against asymptomatic diverticulosis. Gastroenterology. 2012; 142(2):266-72.
- [100] Painter NS, Burkitt DP. Diverticular disease of the colon: a deficiency disease of Western civilization. Br Med J. 1971; 2(5759):450-4.
- [101] Albert CM, Gaziano JM, Willett WC, Manson JE. Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study. Arch Intern Med. 2002; 162(12):1382-7.
- [102] Hu FB, Stampfer MJ, Manson JE, Rimm EB, Colditz GA, Rosner BA, et al. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. BMJ. 1998; 317(7169):1341-5.
- [103] Jenab M, Ferrari P, Slimani N, Norat T, Casagrande C, Overad K, et al. Association of nut and seed intake with colorectal cancer risk in the European Prospective Investigation into Cancer and Nutrition. Cancer Epidemiol Biomarkers Prev. 2004; 13(10):1595-603.
- [104] Jiang R, Jacobs DR Jr, Mayer-Davis E, Szklo M, Herrington D, Jenny NS, et al. Nut and seed consumption and inflammatory markers in the multi-ethnic study of atherosclerosis. Am J Epidemiol. 2006; 163(3):222-31.
- [105] Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and peanut butter consumption and risk of type 2 diabetes in women. JAMA. 2002; 288(20):2554-60.
- [106] Tsai CJ, Leitzmann MF, Hu FB, Willett WC, Giovannucci EL. A prospective cohort study of nut consumption and the risk of gallstone disease in men. Am J Epidemiol. 2004; 160(10):961-8.
- [107] Hu FB, Stampfer MJ. Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence. Curr Atheroscler Rep. 1999; 1(3):204-9.
- [108] Sabaté J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. Am J Clin Nutr. 1999; 70(3);Suppl:500S-3S.
- [109] Hebert JR, Hurley TG, Olendzki BC, Teas J, Ma Y, Hampl JS. Nutritional and socioeconomic factors in relation to prostate cancer mortality: a cross-national study. J Natl Cancer Inst. 1998; 90(21):1637-47.
- [110] Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: findings from casecontrol studies in Canada. Nutr Cancer. 1999; 34(2):173-84.
- [111] Mills PK, Beeson WL, Phillips RL, Fraser GE. Cohort study of diet, lifestyle, and prostate cancer in Adventist men. Cancer. 1989; 64(3):598-604.
- [112] Qualified health claims: letter of enforcement discretion—nuts and coronary heart disease. Food and Drug Administration Center for Food Safety and Applied Nutrition. http://www.cfsan; July 14, 2003 [cited Jul 24, 2008].
- [113] Papi C, Ciaco A, Koch M, Capurso L. Efficacy of Rifaximin in the treatment of symptomatic diverticular disease of the colon: a multicentre double-blind placebo-controlled trial. Aliment Pharmacol Ther. 1995; 9(1):33-9.
- [114] Lamanna A, Orsi A. In vitro activity of Rifaximin and rifampicin against some anaerobic bacteria. Chemioterapia. 1984; 3(6):365-7.
- [115] Stollman N, Smalley W, Hirano I, AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the management of acute diverticulitis. Gastroenterology. 2015; 149(7):1944-9.
- [116] Papi C, Ciaco A, Koch M, Capurso L. Efficacy of Rifaximin on symptoms of uncomplicated diverticular disease of the colon: a pilot multicentre open trial. Diverticular disease study group. Ital J Gastroenterol. 1992; 24(8):452-6.
- [117] Latella G, Pimpo MT, Sottili S, Zippi M, Viscido A, Chiaramonte M, et al. Rifaximin improves symptoms of acquired uncomplicated diverticular disease of the colon. Int J Colorectal Dis. 2003; 18(1):55-62.
- [118] Stollman N, Smalley W, Hirano I, AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the management of acute diverticulitis. Gastroenterology. 2015; 149(7):1944-9.
- [119] MacDermott RP. Progress in understanding the mechanisms of action of 5-aminosalicylic acid. Am J Gastroenterol. 2000; 95(12):3343-5.

- [120] Raskin JB, Kamm MA, Jamal MM, Márquez J, Melzer E, Schoen RE, et al. Mesalamine did not prevent recurrent diverticulitis in phase 3 controlled trials. Gastroenterology. 2014; 147(4):793-802.
- [121] [Humes DJ, Spiller RC. Review article: the pathogenesis and management of acute colonic diverticulitis. Aliment Pharmacol Ther. 2014; 39(4):359-70.
- [122] Bermudez-Brito M, Plaza-Dıaz J, Muñoz-Quezada S, Gómez-Llorente C, Gil A, ~ et al. Probiotic mechanism of action. Ann Nutr Metab. 2012; 61(2):160-74.
- [123] Giaccari S, Tronci S, Falconieri M, Ferrieri A. Long-term treatment with Rifaximin and lactobacilli in postdiverticuliticstenoses of the colon. Riv Eur Sci Med Farmacol. 1993; 15(1):29-34.
- [124] Tursi A, Brandimarte G, Giorgetti GM, Elisei W. Mesalazine and/or Lactobacillus casei in maintaining long-term remission of symptomatic uncomplicated diverticular disease of the colon. Hepato-Gastroenterology. 2008; 55(84):916-20.
- [125] Scarpignato C. Bertelé A & Tursi A probiotics for the treatment of symptomatic uncomplicated diverticular disease. J Clin Gastroenterol. 2016; 50;Suppl 1:S70-3.
- [126] Colditz GA, Cannuscio CC, Frazier AL. Physical activity and reduced risk of colon cancer: implications for prevention. Cancer Causes Control. 1997; 8(4):649-67.
- [127] Leitzmann MF, Rimm EB, Willett WC, Spiegelman D, Grodstein F, Stampfer MJ, et al. Recreational physical activity and the risk of cholecystectomy in women. N Engl J Med. 1999; 341(11):777-84.
- [128] Strate LL, Liu YL, Aldoori WH, Giovannucci EL. Physical activity decreases diverticular complications. Am J Gastroenterol. 2009; 104(5):1221-30.
- [129] Williams PT. Incident diverticular disease is inversely related to vigorous physical activity. Med Sci Sports Exerc. 2009; 41(5):1042-7.
- [130] Hjern F, Wolk A, Håkansson N. Obesity, physical inactivity, and colonic diverticular disease requiring hospitalization in women: a prospective cohort study. Am J Gastroenterol. 2012; 107(2):296-302.
- [131] Gralista P, Moris D, Vailas M, Angelou A, Petrou A, Felekouras E, et al. Laparoscopic approach in colonic diverticulitis: dispelling myths and misperceptions. Surg Laparosc Endosc Percutan Tech. 2017; 27(2):73-82.
- [132] Jacobs DO. Clinical practice. Diverticulitis. N Engl J Med. 2007; 357(20):2057-66.
- [133] Pemberton JH. Acute Colonic Diverticulitis: Medical Management. UpToDate; 2017 [cited Jun 1, 2017]. Available from: http://www.uptodate.com.
- [134] Feingold D, Steele SR, Lee S, Kaiser A, Boushey R, Buie WD, et al. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014; 57(3):284-94.
- [135] Andersen JC, Bundgaard L, Elbrønd H, Laurberg S, Walker LR, Støvring J et al. Danish national guidelines for treatment of diverticular disease. Dan Med J. 2012; 59(5):C4453.
- [136] Feingold D, Steele SR, Lee S, Kaiser A, Boushey R, Buie WD, et al. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014; 57(3):284-94.
- [137] Hall JF, Roberts PL, Ricciardi R, Read T, Scheirey C, Wald C, et al. Long-term follow-up after an initial episode of diverticulitis: what are the predictors of recurrence? Dis Colon Rectum. 2011; 54(3):283-8.
- [138] Eglinton T, Nguyen T, Raniga S, Dixon L, Dobbs B, Frizelle FA. Patterns of recurrence in patients with acute diverticulitis. Br J Surg. 2010; 97(6):952-7.
- [139] Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. Arch Surg. 2005; 140(7):681-5.
- [140] Broderick-Villa G, Burchette RJ, Collins JC, Abbas MA, Haigh PI. Hospitalization for acute diverticulitis does not mandate routine elective colectomy. Arch Surg. 2005; 140(06):576-81.
- [141] Holmer C, Lehmann KS, Engelmann S, Gröne J, Buhr HJ, Ritz JP. Long-term outcome after conservative and surgical treatment of acute sigmoid diverticulitis. Langenbecks Arch Surg. 2011; 396(6):825-32.
- [142] Hwang SS, Cannom RR, Abbas MA, Etzioni D. Diverticulitis in transplant patients and patients on chronic corticosteroid therapy: a systematic review. Dis Colon Rectum. 2010; 53(12):1699-707.

- [143] Klarenbeek BR, Samuels M, van der Wal MA, van der Peet DL, Meijerink WJ, Cuesta MA. Indications for elective sigmoid resection in diverticular disease. Ann Surg. 2010; 251(4):670-4.
- [144] Feingold D, Steele SR, Lee S, Kaiser A, Boushey R, Buie WD, et al. Practice parameters for the treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014; 57(3):284-94.
- [145] Strate LL, Peery AF, Neumann I. American Gastroenterological Association institute technical review on the management of acute diverticulitis. Gastroenterology. 2015; 149(7):1950-1976.e12.
- [146] Masoomi H, Buchberg B, Nguyen B, Tung V, Stamos MJ, Mills S. Outcomes of laparoscopic versus open colectomy in elective surgery for diverticulitis. World J Surg. 2011; 35(9):2143-8.
- [147] 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.
- [148] Gervaz P, Inan I, Perneger T, Schiffer E, Morel P. A prospective, randomized, single-blind comparison of laparoscopic versus open sigmoid colectomy for diverticulitis. Ann Surg. 2010; 252(1):3-8.
- [149] Schwenk W, Haase O, Neudecker J, Müller JM. Short term benefits for laparoscopic colorectal resection. Cochrane Database Syst Rev. 2005; 03(3):CD003145.
- [150] Maeso S, Reza M, Mayol JA, Blasco JA, Guerra M, Andradas E, et al. Efficacyof the DaVinci surgical system in abdominal surgery compared with that of laparoscopy: a systematic review and meta-analysis. Ann Surg. 2010; 252(2):254-62.
- [151] Antoniou SA, Antoniou GA, Koch OO, Pointner R, Granderath FA. Robot-assisted laparoscopic surgery of the colon and rectum. Surg Endosc. 2012; 26(1):1-11.
- [152] Delaney CP, Lynch AC, Senagore AJ, Fazio VW. Comparison of robotically performed and traditional laparoscopic colorectal surgery. Dis Colon Rectum. 2003; 46(12):1633-9.
- [153] Zimmern A, Prasad L, Desouza A, Marecik S, Park J, Abcarian H. Robotic colon and rectal surgery: a series of 131 cases. World J Surg. 2010; 34(8):1954-8.
- [154] Rafferty J, Shellito P, Hyman NH, Buie WD, Standards Committee of American Society of Colon and Rectal Surgeons. Practice parameters for sigmoid diverticulitis. Dis Colon Rectum. 2006; 49(7):939-44.
- [155] Egger B, Peter MK, Candinas D. Persistent symptoms after elective sigmoid resection for diverticulitis. Dis Colon Rectum. 2008; 51(7):1044-8.
- [156] Machicado GA, Jensen DM. Acute and chronic management of lower gastrointestinal bleeding: cost-effective approaches. Gastroenterologist. 1997; 5(3):189-201.
- [157] Fozard JB, Armitage NC, Schofield JB, Jones OM, Association of Coloproctology of Great Britain and Ireland. ACPGBI position statement on elective resection for diverticulitis. Colorectal Dis. 2011; 13; Suppl 3:1-11.
- [158] Shaheen NJ, Hansen RA, Morgan DR, Gangarosa LM, Ringel Y, Thiny MT, et al. The burden of gastrointestinal and liver diseases, 2006. Am J Gastroenterol. 2006; 101(9):2128-38.
- [159] Pokala N, Delaney CP, Kiran RP, Bast J, Angermeier K, Fazio VW. A randomized controlled trial comparing simultaneous intraoperative vs sequential prophylactic ureteric catheter insertion in re-operative and complicated colorectal surgery. Int J Colorectal Dis. 2007; 22(6):683-7.
- [160] Fry DE. Colon preparation and surgical site infection. Am J Surg. 2011; 202(2):225-32.
- [161] Hayashi MS, Wilson SE. Is there a current role for preoperative non-absorbable oral antimicrobial agents for prophylaxis of infection after colorectal surgery? Surg Infect (Larchmt). 2009; 10(3):285-8.
- [162] Englesbe MJ, Brooks L, Kubus J, Luchtefeld M, Lynch J, Senagore A, et al. A statewide assessment of surgical site infection following colectomy: the role of oral antibiotics. Ann Surg. 2010; 252(3):514-9.