V A R I A

POLISH INTERDISCIPLINARY CONSENSUS ON DIAGNOSTICS AND TREATMENT OF COLONIC DIVERTICULOSIS (2015)

Developed by an expert group established by the Polish Society of Gastroenterology and the
Association of Polish Surgeons

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A. Introduction

In the two years that have passed since the publication of the first Polish Interdisciplinary Consensus on diagnostics and treatment of diverticulosis, results of tens of studies concerning aetiology, epidemiology, and treatment of diverticulosis have been published, significant enough to make update of the previous recommendations necessary.

As with any recommendations, it should be reminded that these are only general guidelines based on scientific evidence and each decision concerning a specific patient should be taken by a doctor who would take into account all circumstances concerning the health and condition of that patient.

B. Definitions and classification

Diverticulum is usually a small sac-like external protrusion of an organ wall. Except in foetal life, it is a pathological lesion (congenital or acquired). Diverticula may develop at various sites, but most often they affect the large intestine. With respect to the structure, diverticula may be classified as true, i.e. those involving all layers of the organ wall, or false (pseudodiverticula), being actually mucosal pouches covered with serous membrane (1). The most common diverticula of the left hemicolon are acquired false diverticula, while rare and usually congenital diverticula of the right hemicolon are true diverticula.

First descriptions of colonic diverticula and symptoms they may cause were published in the beginning of the 18th century (2). Despite that, there is still no uniform, universally accepted classification. In the most commonly used clinical classification, asymptomatic colonic diverticulosis, symptomatic uncomplicated diverticular disease, and diverticulitis with its complications are discerned. Acute complications include diverticulitis which in turn may be complicated by development of abscess, bleeding, or perforation; chronic complications include development of colonic stenosis and fistulae (3, 4). Acute diverticulitis with perforation is classified into four stages according to a system introduced in 1978 by Hinchey et al. in which location and extensiveness of the inflammatory infiltration is assessed based on clinical features and intraoperative findings

(tab. 1) (5). As new imaging methods were developed, other classifications, taking into account radiological and endoscopic findings, were proposed. Systems still in use include those of Hansen and Stock (1998) or Ambrosetti (2002), presented in tab. 2 (6, 7); however, clinical classification (uncomplicated diverticulosis) was not included in these tables.

Statement 1

Diverticula develop as a result of herniation of the mucosa through the colonic muscular layer (pseudodiverticula). They are most commonly observed in the sigmoid colon. Manifestations of the disease include asymptomatic diverticulosis, symptomatic uncomplicated diverticular disease, and diverticulitis with its

Table 1. Classification of acute diverticulitis with perforation according to Hinchey et al. (5).

Stage	Symptoms
I	Pericolonic abscess or phlegmon – localised lesions
II	Pelvic, mesogastric, or retroperitoneal abscess – diffuse lesions
III	Generalised purulent peritonitis
IV	Generalised faecal peritonitis

Table 2. Classifications of diverticulosis used in clinical practice (6,7)

Hansen and Stock's classification based on the clinical manifestation and additional tests	
Stage	Description
0	Diverticulosis
I	Uncomplicated acute diverticulitis (endoscopy: inflammation, CT: thickening of the colonic wall)
II	Acute complicated diverticulitis
II a	Phlegmon, peridiverticulitis (CT: inflammation involving the surrounding adipose tissue)
II b	Abscess, sealed perforation
II c	Free perforation (CT: air or fluid)
III	Chronic recurrent diverticulitis (endoscopy, CT: stenosis, fistula)
Ambrosetti's classification based on the CT findings	
Mild diverticulitis	Localised colonic wall thickening ≥ 5 mm, inflammation involving the surrounding adipose tissue
Severe diverticulitis	Abscess, extraluminal air, extraluminal contrast medium

CT – computed tomography

early and long-term complications. The recommended four-stage classification of complicated diverticulitis proposed by Hinchey et al. is used by surgeons to select the appropriate treatment.

C. Aetiology of diverticulosis

The aetiology of diverticulosis is still not well known. The risk factors for development of diverticulosis include: old age, low-fibre diet, and connective tissue diseases (8). The role of the lifestyle and environmental factors is also stressed. In theoretic models of pathogenesis of the disease, structural and functional intestinal disorders due to abnormal innervation, impaired neuromuscular transduction, disturbed architecture of smooth muscle fibres in the intestinal wall, or connective tissue proliferation are taken into account (9).

The prevalence of diverticulosis increases with age (10). The disease is uncommon before the age of 40, while in the 7th decade of life more than 50% of people are affected. However, a cause and effect relationship may be apparent only – the cause may not be the old age itself but a long time during which the colonic wall is exposed to pathogenic factors. One of these factors is low-fibre diet, first described in the 1960s as a probable aetiological factor for development of diverticulosis (11). This proposition was based on observed demographic differences in the prevalence of diverticulosis, a condition common in highly developed countries and rare in Africa and Asia, where diet is rich in vegetable fibres. Data from experimental studies demonstrated a positive correlation between low content of vegetable fibres in diet and development of diverticula in animals (12, 13). However, recent surveys brought into question the role of low-fibre diet in development of colonic diverticulitis (14).

Other environmental factors taken into account in the aetiology of diverticulosis include red meat, alcohol, and cigarettes, as well as low physical activity, obesity, and low socioeconomic status. Those factors affect the prevalence of symptoms and complications of the disease; however, their effect on development of diverticula has not been demonstrated (8). For instance, in a study published in 2010, only the age > 65 years was a factor associated with development of diverticula (15).

Statement 2

In the aetiology of diverticulosis, apart from old age, environmental factors such as diet, exercise, and stimulants, are taken into account. However, the evidence obtained so far is inconclusive and insufficient to recommend dietary modifications as a method of prevention of diverticulosis.

D. Pathogenesis of diverticulosis

Colonic diverticula develop as a result of pushing of the mucosa through openings containing nutrition vessels *(vasa recta)*. With age, the metabolism of components of the extracellular matrix in the intestinal wall changes. In diverticulosis, structural changes are observed in the two most important components, i.e. collagen and elastin. Collagen fibres are smaller are more densely packed, with more numerous and stiffer junctions, resulting in reduced elasticity. The number of elastin fibres in the longitudinal muscular layer is also increased, resulting in segmental thickening of the intestinal wall and loss of elasticity. This contributes to development of diverticula (9). In patients with diverticulosis, the circular muscular layer is often also thickened. This is not due to proliferation of muscle cells, but to changes in tissue architecture. These result in apparent shortening of the intestine and increased haustrations which make the intestine more susceptible to development of diverticula (9).

Other pathogenic factors associated with the intestinal nervous system include:

a) impaired motility due to reduced number of neurons in the visceral ganglia and cells of Cajal (16-19);
b) quantitative alterations in neuropeptides regulating peristalsis, including increased concentrations of VIP, substance P, neuropeptide K, and galanin (20-22);
c) decreased amount of glial cell-derived neurotrophic factor (GDNF) with secondary hypoganglionosis observed in patients with diverticulosis (9).

For some time, the role of chronic inflammation has been stressed, not only as a complication of diverticulosis, but also as its cause. Depending on the intensity and duration of the inflammatory process, both in the mucosa and in adjacent tissues a specific, sometimes persistent inflammatory infiltration of lymphocytes and plasmatic cells in the lamina propria with tissue architecture disturbance, Paneth cell metaplasia, and formation of lymphatic nodules. Due to their location, neurons and visceral ganglia are also involved in post-inflammatory structural changes. It has been suggested that proliferation of inflammatory cells is excessive, resulting in increased sensitivity to stimuli in individuals with diverticulosis (23, 24). However, the question whether inflammation is a cause or a consequence of diverticulosis remains unanswered.

Statement 3

The pathogenesis of diverticulosis is unknown. Structural abnormalities of collagen and elastin are known to stiffen and shorten the intestine, thus facilitating pushing the mucosa through sites of reduced resistance and formation of diverticula. Abnormalities in functioning of the visceral nervous system at all levels of conduction, leading to contractility disorders and abnormal susceptibility to stimuli, have also been demonstrated. For some time, the role of minimal chronic inflammation and changes in the intestinal microbiota have also been stressed.

E. Epidemiology

In Western world, diverticulosis is one of the most common diseases involving the large intestine and is listed among the main causes of outpatient visits and hospitalisations. Its prevalence increases with age. Data concerning sex distribution are inconsistent and depend on the age of the investigated group. Most studies demonstrated that in patients below 50 years of age the condition was more common in men, between 50 and 70 years it became slightly more common in women, and over 70 years it was diagnosed predominantly in women (25).

Until recently, it was assumed that diverticulitis developed in 10-25% of patients with diverticulosis, of whom one fourth suffered from further complications (26). However, according to the most recent data, published in 2013, radiologically or surgically confirmed diverticulitis was found only in 1% of the subjects observed for 11 years. Certain clinical symptoms and signs were present in 4.3% (27). Therefore, it should be stated that the actual

proportion of patients with diverticulosis who develop complications has not been precisely estimated and further, prospective studies are required.

Epidemiological data, obtained both from European and American healthcare systems, indicate increasing incidence of hospitalisation due to diverticulosis over the last decades. In England, over 10 years (1996-2006) the incidence of hospitalisation due to diverticulosis increased more than twice (from 0.56 to 1.2 per 1000 inhabitants), and in the USA – by 26% in 7 years. At the same time, the mean age of hospitalised patients decreased. The 30-day mortality rate also increased to 4-5.1%. The highest mortality rate was observed in elderly patients with severe concomitant diseases (28, 29).

Statement 4

The prevalence of diverticulosis increases with age. In Western world, diverticulosis is one of the most common diseases involving the large intestine. Depending on the age group, the disease may be more likely to affect men or women; however, the differences are not significant. The incidence of hospitalisation due to complications of the disease also increases.

Diverticulosis in young patients

The prevalence of diverticulosis and diverticulitis in young individuals increases. However, this may be due to the condition being diagnosed more often, as diverticulosis was considered a disease of the old age and therefore the appropriate diagnostic tests were applied only in the elderly. In some studies, an increase in the number of diagnosed cases by 150% was noted in the age group 15-24 years and by 84% in patients aged 18-44 years (30, 31). The most obvious explanation is the change of lifestyle observed over the recent decades. The available evidence suggests that the body mass index (BMI) of young individuals diagnosed with diverticulosis is higher than that of older patients. This trend is more pronounced in men than in women. Data concerning the severity and recurrence rate of diverticulitis in young patients are inconsistent. While some studies suggested a more aggressive course of the disease, other studies dem-

onstrated no differences (32-35). In comparison with elderly patients, young individuals are more often hospitalised, which may be due to erroneous initial diagnosis, e.g. appendicitis or gynaecological conditions requiring surgical intervention (30).

Diverticula develop more often in children and young adults with connective tissue diseases. These include: Marfan syndrome (a mutation in the fibrillin gene), Ehlers-Danlos syndrome (defective collagen metabolism), Williams-Beuren syndrome (a mutation in the elastin gene), and other, even less common syndromes. Abnormal connective tissue structure is considered the main cause of formation of diverticula in those patients (34). Another common disease associated with development of diverticulosis in 50-80% of cases is polycystic kidney disease (dominant type) (36). In such patients, diverticular disease should be taken into account in differential diagnosis of gastrointestinal symptoms and signs. The diagnosis of asymptomatic disease has no effect on the patient's prognosis.

Most women are beyond their childbearing age at the time of the first manifestation of diverticulosis. However, as pregnancy at older age becomes more common, the diagnosis of symptomatic diverticular disease should be taken into account in differential diagnosis of abdominal pain or lower gastrointestinal bleeding in pregnant women. It should be also remembered that advanced pregnancy is associated with altered anatomic relationships and pain typically located in the lower left quadrant may be present in another part of the abdomen. In one of the reports, the estimated prevalence of diverticulitis in pregnant women was 1:6000 gestations (37). No statistical data concerning the frequency of surgical interventions due to diverticulitis are available; however, it is known that ca. 2% of pregnant women undergo surgery (38, 39). Imaging diagnostics of diverticulosis should be based on tests not requiring exposure to X-rays, i.e. USG and MRI. However, if computed tomography is necessary for specific reasons, it should be performed (40). Sigmoidoscopy is a safe method in patients with lower gastrointestinal bleeding (41). Some antibiotics used in treatment of acute diverticulitis are contraindicated in pregnancy; this must be taken into account when therapeutic decisions are made. Rifaximin may be a good agent as it is

not absorbed from the gastrointestinal tract; however, due to the lack of appropriate studies, its use in pregnant women is at present not recommended. Despite the lack of formal studies, it seems that all pregnant women with diverticulitis require hospitalisation (at least in the initial phase of the disease). Surgical interventions in acute diverticulitis should be considered only in life-threatening conditions (i.e. after failure of conservative treatment and in the case of severe complications).

Statement 5

Increased prevalence of complications of diverticulosis in young adults has been observed. Data concerning severity of the course and recurrences of the disease are inconclusive and no specific management is recommended in this group of patients.

Diverticulitis should be taken into account in diagnostics of abdominal pain in pregnant women. In this group of patients, USG and/or MRI are the methods of choice. Treatment should be administered at the hospital and include antibiotics and analgesics admissible in pregnancy. Only direct threat to the pregnant woman's life should be considered an indication for surgical treatment.

F. Diverticulosis

Diverticulosis, or the presence of colonic diverticula, is a clinically silent condition. No abnormalities are found on physical examination or in the results of laboratory tests. The diagnosis is established accidentally, during colonoscopy or computed tomography. Previously, diverticulosis was most commonly diagnosed based on a double-contrast barium enema.

In patients without symptoms or signs of diverticulitis, segmental colitis (present in ca. 2% of patients) may be revealed (42). Endoscopic presentation may vary; the most commonly reported lesions include reddening, granulation, and superficial erosions or ulceration in the colonic segment in which diverticula are present (the diverticular ostium being spared). These lesions are focal; sometimes only one fold is involved. They should be distinguished from diverticulitis in which the inflammatory process involves the mucosa of the affected diverticulum. Microscopic examination may reveal lesions similar to those observed in colitis ulcerosa or Crohn's disease; exclusion of these conditions requires additional tests (including microscopic examination of samples obtained from other parts of the intestine) (43, 44).

Statement 6

Diverticulosis is asymptomatic condition requiring neither treatment nor monitoring. Inflammation found on microscopic examination only also requires no treatment.

G. Symptomatic uncomplicated diverticular disease

It is estimated that ca. 20% of patients with diverticulosis suffer from abdominal symptoms. These usually include mild, recurrent abdominal pain, flatulence, and changes in bowel habits, without abnormalities in diagnostic tests (45). Risk factors for development of symptoms include: low-fibre diet, low physical activity, and obesity, especially abdominal (8). Excessive sensitivity to rectal dilation in patients with diverticular disease in comparison with asymptomatic individuals and those without diverticula was also suggested (11, 46). Changes in the intestinal microflora constitute a possible mechanism responsible for local mild inflammation. In patients with symptomatic uncomplicated diverticular disease, excessive bacterial growth, increased by faecal retention in the diverticula, may contribute to chronic, local mild inflammation. This results in bacterial translocation to the adjacent adipose tissue, and stimulation of adipocytes and preadipocytes with the release of adipokines and chemokines, leading to sensitisation of afferent and efferent neurons. These changes may lead to smooth muscle hypertrophy and increased visceral sensitivity, and these in turn – to development of symptoms (47, 48).

The diagnosis is based on physical examination and the results of additional diagnostic tests. Usually, no abnormalities are found on physical examination. In some patients, tenderness or resistance in the left hypogastrium may be found (15, 45). In symptomatic, uncomplicated diverticular disease, laboratory markers of inflammation (ESR, CRP, leukocytosis)

remain normal. The concentration of calprotectin in the stools may be elevated, distinguishing symptomatic uncomplicated diverticular disease from diverticulosis or functional disorders (49, 50). Imaging diagnostic tests include double-contrast barium enema, computed tomography, and, more and more often, magnetic resonance. Plain abdominal radiography is no longer used (51). Contrast (especially barium) enema remains a valuable diagnostic test in this form of the disease, revealing not only the presence of diverticula (as protruding barium collections), but also their cause (i.e. folds). This test makes it also possible to assess the size and scope of diverticula, as well as possible chronic complications (i.e. stenosis, fistulae) (44). Water contrast media should be used in patients in whom complications are suspected. At present, computed tomography is the most widely used method, due to its high sensitivity and specificity, reproducibility, and general availability; CT makes it also possible to exclude other conditions. In order to increase sensitivity, a contrast medium may be administered rectally prior to the test (44). No data concerning the sensitivity or specificity of colonography by means of computed tomography are available. In diagnostics of pain in the left lower abdominal quadrant, endoscopic evaluation is still recommended; however, this is not a test of choice in diagnostics of diverticulosis and should not be recommended in this indication. Nevertheless, it should be remembered that in patients over 50 years of age colonoscopy should be proposed as a screening test for colorectal cancer (52).

Symptomatic uncomplicated diverticular disease should be differentiated from numerous other diseases in which pain in the left hypogastrium may be present (tab. 3A). In practice, due to high prevalence of the irritable bowel syndrome, functional disorders producing similar symptoms should in the first place be taken into account in differential diagnostics. Overlapping of these conditions is also suggested, especially as the causes of symptoms are not well understood (15). Nevertheless, the population of patients with diverticular disease differs from patients with functional disorders. Patients with diverticulosis are older and no significant female predominance is observed. The groups differ with respect to the duration and location of pain.

Patients with functional disorders suffer from short, often recurrent, episodes of diffuse pain, while in diverticular disease pain is localised in the left hypogastrium and may last for weeks, with asymptomatic periods lasting months or even years (53). As discussed above, abnormal laboratory test results that may be present in diverticular disease are absent in functional disorders.

The prognosis in symptomatic uncomplicated diverticular disease is favourable. The natural course of the disease is mild and complications are observed in a small proportion of patients, as confirmed in numerous studies. In one study, the complication rate in a 5-year observation period was only 1.4% (54).

Statement 7

Symptomatic uncomplicated diverticular disease is associated with abdominal pain, flatulence, and changes in bowel habits. The presence of diverticula may be confirmed using computed tomography or a double-contrast barium enema, remaining a valuable diagnostic method in uncomplicated diverticular disease. In differential diagnostics, the irritable bowel syndrome should be taken into account due to its high prevalence, and colorectal cancer – due to its clinical implications.

Table 3. Differentiation of diverticulosis
(15, 44, 45, 48)

A. Symptomatic uncomplicated diverticular disease
Irritable bowel syndrome
Habitual constipation
Colorectal cancer
Crohn's disease
Ulcerative colitis
Ischaemic colitis
Gastrointestinal tract infection
Urinary tract infection
B. Pelvic inflammatory disease (women)
Ovarian cyst
Diverticulitis
Diseases listed under A
Appendicitis
Abdominal aortic aneurysm
Incarcerated hernia
Pancreatitis
Pyelonephritis
Nephrolithiasis and ureterolithiasis
Gynaecological diseases
Prostatitis

H. Uncomplicated diverticulitis

The most common complication of diverticular disease is acute diverticulitis, i.e. the presence of clinical, laboratory, and imaging signs of inflammation in patients with diverticulosis. Numerous prospective studies have confirmed the effect of low-fibre diet on development of the symptoms. In a 6-year prospective observational study (published in 2014) in which more than 690,000 enrolled patients made no changes in their diet during the study, the risk of hospitalisation or death due to diverticular disease was statistically significantly lower in the group with the highest dietary fibre content. For the first time, attention was paid and differences were proven in the prevalence of symptoms depending on the fibre source. It turned out that risk reduction concerned only those individuals whose diet was rich in soluble fibre (55). Other risk factors (discussed above) include: diet rich in red meat, alcohol, cigarette smoking, limited physical activity, obesity, and low socioeconomic status (8, 10). In pathogenesis of inflammation, the same factors are stressed as those involved in development of diverticular disease. At present, minimal chronic inflammation (discussed above) and changes in the intestinal microbiota are considered the most important factors (56). It is known that composition of the intestinal microbiota changes with the disease. In 2014, the results of a study evaluating such changes in the case of diverticulitis were published. The demonstrated changes regarded mainly *Proteobacteria* strains (57). Both abnormalities became targets of modern treatment methods.

The main symptom of acute diverticulitis is sudden, quickly increasing pain, localised usually in the left lower abdominal quadrant (diffuse pain may also be present). In the case of extensive diverticulitis with involvement of the surrounding tissues and organs, pain on movement (pelvic muscle involvement) and urinary system disorders may be present. In severe disease, nausea or vomiting, accompanied by accumulation of gas and stools or diarrhoea, may develop. Abdominal symptoms are usually accompanied by fever. On physical examination, tenderness in the left hypogastrium is found, sometimes with local peritoneal signs and general signs of infection. Laboratory test results reveal elevation of all inflammatory markers (i.e. ESR, CRP, leuko-cytosis with neutrophilia, and calprotectin in the stools) (49, 50). The "gold standard" in diagnostics of diverticulitis is computed tomography due to its high sensitivity and specificity in this condition (51). Magnetic resonance imaging is used less often, mainly due to its limited availability and higher cost. Abdominal ultrasonography is a very good and cheap method used in initial diagnostics; in many cases, this may be the main imaging method. The applicability of other radiological methods is limited (58). Until recently, colonoscopy was contraindicated in the acute phase (i.e. within 6 weeks from treatment introduction) due to possible complications; even now, it is indicated in selected cases only (59, 60).

Computed tomography in the first episode makes it possible to establish a diagnosis, determine the severity and extensiveness of inflammation, and exclude other complications. Its sensitivity is estimated at 79-99% (61). The CT scans should visualise the whole abdominal cavity and pelvis. A contrast medium should be administered intravenously; for best results, water contrast media should also be administered orally and rectally (52). The most common abnormalities found in diverticulitis include segmental thickening of the intestinal wall (over 3 mm) and indistinct contours of the adipose tissue. The Ambrosetti criteria may be helpful in evaluation of severity of the disease (tab. 2) that correlates with the risk of surgery (7). Computed tomography plays a particularly important role in diagnostics of diverticulosis of the right hemicolon. In radiologic differential diagnostics, colorectal cancer is usually taken into account, as intestinal wall thickening and involvement of the adipose tissue may be signs of a tumour. Ultrasound examination is an easily available and cheap method; however, subjective assessment of its results is a disadvantage. The sensitivity and specificity of graduated pressure USG in diagnostics of diverticulitis were 77-98% and 80-99%, respectively (58). Ultrasound examination puts no additional burden on the patient and does not require administration of additional agents. Therefore, it is the method of choice in pregnant women with suspected diverticulitis. The role of vaginal and rectal ultrasonography in the assessment of disease complications is also stressed.

As mentioned above, colonoscopy is not absolutely contraindicated in acute diverticu-

litis. The results of studies evaluating the safety of colonoscopy during hospitalisation due to diverticulitis are encouraging (59). Colonoscopy may reveal inflammation of the mucosa surrounding the diverticulum or involving the whole intestinal segment, with purulent exudate (44). However, the risk of exacerbation or even perforation must not be neglected. The range of indications for colonoscopy is therefore quite narrow and its application should be limited to cases with prolonged symptoms or to the treatment of bleeding. Another indication mentioned only by certain scientific societies is the exclusion of colorectal cancer. However, a recently published systematic review evaluating the prevalence of colorectal cancer in patients with diverticulosis did not confirm this indication. Although the prevalence of cancer in this group of patients was higher than in asymptomatic individuals (2.1% vs 0.68%), this group should rather be compared with patients having gastrointestinal symptoms in whom the prevalence of cancer is much higher (60, 62, 63).

Differential diagnostics of uncomplicated diverticulitis is presented in tab. 3B. In 2007, results of a study evaluating accuracy of the initial diagnosis established in the emergency room were published. Apart from diverticulitis, differential diagnostics of pain in the left lower abdominal quadrant associated with symptoms and signs of inflammation most commonly included unspecific abdominal pain, appendicitis, constipation, urinary tract infection, a neoplasm, abdominal aortic aneurysm, and a gynaecological disease (64). These conditions should be taken into account in the first place.

Prognosis in diverticulitis depends on the course of the disease. Complications are relatively rare, although their incidence increased in recent years. As mentioned above, an episode of diverticulitis in the past does not increase the risk of development of complications. The risk of recurrence ranges from 2% to 43%, with a declining trend (53). Prognosis in uncomplicated diverticulitis is favourable (65, 66).

Statement 8

Diverticulitis is the most common complication of diverticulosis. A negative effect of diet with low content of soluble fibre on the occurrence of symptoms has been demonstrated. Symp-

toms of the disease include intense pain, usually in the left hypogastrium, accompanied by general symptoms of inflammation (fever, tachycardia, weakness, and nausea). The condition may develop into severe inflammation with symptoms and signs of limited or diffuse peritonitis. The diagnostic "gold standard" is computed tomography. The use of colonoscopy in acute diverticulitis should be limited to cases in which the diagnosis is uncertain, a neoplasm is suspected, or treatment of complications is necessary. Differential diagnostics includes appendicitis, enterocolitis, colorectal cancer, urinary tract infection, aortic aneurysm, and gynaecological diseases.

Other forms of the disease are discussed in the surgical part.

I. Conservative treatment of specific forms of diverticular disease

Strategies of conservative treatment of specific forms of diverticular disease are presented in tab. 4.

a. Outpatient treatment

- **Asymptomatic diverticulosis** requires no treatment. Lifestyle modifications, such as diet with increased fibre content, body weight reduction, smoking cessation, decrease of consumption of red meat and alcohol, and increase of physical activity are often recommended, although there is no sufficient evidence for such recommendations.

- The aims of treatment of **symptomatic uncomplicated diverticular disease** are: symptom relief, infection cure, prevention of recurrence, and reduction of complications. In mild and moderate forms, dietary modifications (i.e. supplementation of soluble fibre and easily digestible diet) are sufficient. Until recently, parallel systemic antibiotic treatment was recommended, although there was no study evidence to support it (1). At present, we have convincing data (see below) to demonstrate that such an approach was inappropriate and systemic antibiotics should not be routinely recommended in symptomatic uncomplicated diverticular disease (67). Therefore, at present the only medication with which

Table 4. Strategies of conservative treatment of specific forms of diverticular disease (62-67,71)

Form	Asymptomatic diverticulosis	Symptomatic uncomplicated diverticular disease	Mild to moderate uncomplicated diverticulitis	Severe uncomplicated diverticulitis, refractory to treatment, specific patient groups
Main symptoms	None – accidental diagnosis during tests performed for other causes.	Recurrent abdominal pain, flatulence, changes in bowel habits. Normal results of additional tests (except calprotectin in the stools).	Severe, long-term abdominal pain (left lower quadrant), fever, other general symptoms. Abnormal results of additional (imaging and laboratory) tests.	Severe abdominal pain, high fever, impaired peristalsis, haemodynamic and fluid/electrolyte imbalance.
Causal treatment	No treatment	Cyclic rifaximin Antispasmodic (anticholinergic) agents Analgesics	Outpatient treatment Antispasmodic (anticholinergic) agents Analgesics Antipyretic agents No antibiotics or oral antibiotics	Hospital treatment Antispasmodic (anticholinergic) agents Analgesics Antipyretic agents Intravenous antibiotics for 7-10 days, followed by oral antibiotics for 7-10 days (in outpatient settings) low-molecular-weight heparins (prophylactic dose) I.V. hydration
Diet	Rich in soluble fibre	Rich in fibre Limited consumption of: - red meat - alcohol	Easily digestible, semi-liquid, or liquid diet Hydration	Strict Liquid in less severe cases
Lifestyle modifications	Increased physical activity	Body weight reduction Increased physical activity Smoking cessation	Sick leave Rest Bed-chair lifestyle	Hospitalisation Bedridden
Prevention of recurrence (including lifestyle modifications)	Not applicable	Cyclic rifaximin (all symptoms) Mesalazin (pain)	Cyclic rifaximin	Cyclic rifaximin

all objectives of treatment of symptomatic uncomplicated diverticular disease is rifaximin – a wide-spectrum (including Gram-positive as well as Gram-negative and aerobic as well as anaerobic bacteria), topically active antibiotic, not absorbed from the gastrointestinal tract. Its effectiveness, both in symptomatic treatment and in the prevention of recurrence, was confirmed by prospective studies, including meta-analyses (68). In addition, statistically significant improvement of the quality of life of treated patients was demonstrated (69). Most studies concerned cyclic treatment with rifaximin (400 mg twice daily, 7 days per month, up to 12 months) and this is the correct method of its administration (70).

In recent years, the efficacy of mesalazin, used in treatment of chronic inflammation, has also been investigated. However, in some studies evaluating its effect on symptoms of diverticular disease, no differences in comparison with placebo were demonstrated (71). The efficacy of mesalazin in prevention of symptom recurrence in patients with symptomatic uncomplicated diverticular disease was also evaluated, and only reduced intensity of long-term pain was demonstrated. Due to heterogeneity of the studies, the indications for mesalazin use cannot be clearly defined. Taking into account its adverse effects, decisions as to its use should be made with due care (72,73).

In summary, treatment of symptomatic, uncomplicated diverticular disease includes diet rich in soluble vegetable fibres, and rifaximin. Data concerning the use of mesalazin are inconsistent.

- Most patients diagnosed with **acute uncomplicated diverticulitis**, without additional comorbidities, may be treated in outpatient settings. This is possible in patients with

mild to moderate disease who tolerate hydration and oral medications, and have easy access to medical care (should their condition worsen or no improvement be observed) (74). Until recently, in all patients diagnosed with diverticulitis oral systemic wide-spectrum antibiotic treatment for 7-10 days was recommended. Such an approach was not evidence-based and in many cases its effects were negative due to complications of antibiotic therapy and increasing bacterial resistance (56).

In 2007 and 2011, results of studies comparing the course of various forms of diverticulitis in patients treated and not treated with antibiotics were published (75,76). No significant differences between the groups were demonstrated. In 2012, the results of a multicentre randomised trial were published in which more than 600 patients with diverticulitis diagnosed based on computed tomography were enrolled. It was demonstrated that antibiotic treatment had no effect on duration of hospitalisation or the risk of recurrence or complications (77). The ultimate evidence was provided by the DIABOLO study. It was a prospective, multicentre study in which 528 patients, treated with antibiotics or observed, were enrolled. No differences with respect to the proportion of patients cured, treatment duration, or the risk of recurrence or complications (93.2% vs 89.3%; 12 vs 14 days; 3.0% vs 3.4%; and 2.3% vs 3.8%, respectively) were demonstrated, regardless of the treatment applied (67). Therefore, it should be stated that in patients with mild to moderate uncomplicated diverticulitis the decision concerning antibiotic therapy should be made individually, taking into account the presence of symptoms, concomitant diseases, and preferences of the physician and patient. Most patients may and should receive symptomatic treatment, without the use of antibiotics.

In summary, patients with mild to moderate diverticulitis may be treated in outpatient settings, in most cases without systemic antibiotics.

In order to prevent complications, after completion of treatment of acute diverticulitis, rifaximin may be used as its efficacy has been demonstrated in several randomised prospective studies (66, 78). The efficacy of mesalazin in the prevention of recurrence after diverticulitis has also been studied for more than 10 years. In the last two years, the results of seven double-blind, placebo-controlled studies were published. In 6 of them, no superiority of mesalazin in the prevention of recurrence was demonstrated (72, 79-82). The largest studies, i.e. PREVENT 1 and PREVENT 2, published in 2014, demonstrated no superiority of mesalazin over placebo in 1182 patients. Therefore, mesalazin is not recommended in the prevention of recurrence of diverticulitis (82).

Statement 9a

Asymptomatic diverticulosis requires no treatment. There is no evidence to support recommendations concerning lifestyle modifications.

Statement 9b

In treatment of **symptomatic uncomplicated diverticular disease**, the recommendations include diet rich in soluble fibre and rifaximin (2 x 400 mg for 7 days per month, up to 12 months) which alleviates all symptoms, reduces the risk of recurrence or complications, and improves the quality of life. Mesalazin reduces the risk of recurrence of pain. Systemic antibiotics should not be applied due to the lack of studies to demonstrate their efficacy and to their potential adverse effects.

Statement 9c

Mild to moderate uncomplicated **diverticulitis** in patients without severe concomitant diseases should be treated in outpatient settings. The treatment includes easily digestible or liquid diet, hydration, and analgesic, antipyretic and antispasmodic medications. Numerous properly designed trials demonstrated no differences in the course of mild to moderate diverticulitis in patients treated or not treated with antibiotics. Therefore, routine use of systemic antibiotics is not recommended.
In the prevention of recurrence of diverticulitis, rifaximin is recommended, while mesalazin is not recommended in this indication.

b. Hospital treatment

Severe diverticulitis requires treatment in inpatient settings. Also elderly patients with numerous or severe concomitant diseases, or receiving immunosuppressive treatment, require more intensive care (74). In these groups, intravenous wide-spectrum antibiotics for 7-10

days are recommended, with subsequent oral treatment. Patients in more serious general condition require liquid or strict diet, intravenous hydration, and analgesic. If additional complications are suspected, surgical consultation is advisable.

It was demonstrated that diverticulitis increases the risk of venous thromboembolism. Therefore, application of low-molecular-weight heparin in prophylactic doses is justified and consistent with cardiological guidelines (83, 84).

Antibiotics used in treatment of diverticulitis are presented in tab. 5.

Statement 10

Hospitalisation is required in patients with severe or complicated diverticulitis, in elderly patients with concomitant diseases, and in pregnant women. Apart from antibiotic therapy (usually intravenous), hydration, strict diet, and the use of analgesics are important. The application of prophylactic doses of low-molecular-weight heparin is recommended. Surgical consultation is advisable.

J. Surgical treatment

Surgical treatment in patients with colonic diverticulosis should be limited to patients with complicated diverticulitis. Only a small group of patients with uncomplicated diverticulitis in whom conservative treatment is ineffective or the symptoms of diverticulitis increase require surgical intervention. It is estimated that in the USA ca. 20% of patients require hospitalisation due to complications of diverticular disease (85). The incidence of Hinchey I-IV diverticulitis is 3.5 to 4.0/100,000/year (86). The incidence of lower gastrointestinal bleeding due to colonic diverticulosis is 10/100,000/year (87). It should be additionally stressed that in differential diagnostics neoplastic aetiology of the disease must be excluded.

a. Peridiverticular and pelvic abscess (Hinchey I and II)

Abscess development as a complication of perforation due to diverticulitis depends on the ability of pericolonic tissues to confine the inflammatory process. Initially, inflammatory infiltration is formed, followed by development of a purulent lesion. Abscesses due to sigmoid diverticulitis constitute ca. 23% of all intra-abdominal abscesses. It is estimated that signs of an abscess are present on CT scans in ca. 15% of patients hospitalised due to acute diverticulitis (88, 89). Previously, surgical intervention was the only therapeutic option in patients with peridiverticular abscesses. Development of new imaging methods and antibiotic therapy regimens changed the treatment paradigm in such patients. Patients with small abscesses, i.e. less than 3 cm in diameter, may be treated with antibiotics only, provided that they are continuously monitored (90). In patients with peridiverticular abscesses > 3 cm in diameter, antibiotic therapy and USG/CT-guided drainage is effective in 50-67% of patients. However, in abscesses located in the small pelvis the efficacy is slightly lower, i.e. 41-59%. In addition, patients with abscesses in the small pelvis are more likely to require surgical intervention during initial hospitalisation (88, 89).

Conservative treatment and drainage make it possible to delay surgery and perform it as an elective procedure. The risk of stoma exteriorisation during an elective surgical procedure is small. If urgent colon resection is required due to abscesses, the risk of stoma exteriorisation is as high as 80%, and mortality – 33% (91).

Statement 11

Abscesses < 3 cm may be treated with antibiotics only, provided that the patient is continuously monitored. If technically feasible, abscesses > 3 cm should be treated with antibiotics and USG/CT-guided percutaneous drainage. If puncture and drainage of intra-abdominal abscesses is technically impossible, laparotomy or laparoscopy with abscess drainage should be performed (92).

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b. Purulent or faecal peritonitis (Hinchey III and IV)

Surgery is the treatment method of choice in patients with Hinchey III or IV complicated diverticulitis. The Hartmann's procedure successfully replaced previously performed three-stage procedures. In certain studies, periop-

Table 5. Antibiotics used in treatment of diverticulitis

Product	Main contraindications	Main AE	Dosage and method of administration combinations	Treatment duration
Amoxicillin with clavulanic acid	Allergy to ß-lactams, impaired liver function	GI (nausea, vomiting, diarrhoea, *C. difficile* infection), allergy, hepatopathy	From 625 mg b.i.d. to 1 g b.i.d. *p.o.* depending on severity; 1,2 g 3 or 4 times per day *i.v.* depending on severity	Mild to moderate: 8-10 days Severe: 8-10 days *i.v.,* followed by 14 days *p.o.*
Trimethoprim/sulfamethoxazole	Pregnancy, allergy to sulfonamides, liver, kidney, or bone marrow failure; thiazides – carefully	GI, skin hypersensitivity reactions bone marrow damage, hepatic infarction	960 mg (160 + 800) b.i.d. *p.o.*; the same dosage *i.v.*; treatment in combination with metronidazole only	10 days
Ciprofloxacin	Pregnancy and lactation, epilepsy, exposure to sunlight	Nausea, diarrhoea, hepatopathy, impaired kidney function, impaired psychomotor ability	500 mg b.i.d. *p.o.*; 200 mg b.i.d. *i.v.* (use carefully due to selection of resistant strains); treatment in combination with metronidazole only	7-14 days
Metronidazole	Pregnancy (1st trimester) and lactation, serious and active diseases of the CNS; hematopoiesis disorders	Metallic taste in the mouth, neuropathies and other neurological disorders, skin allergy	From 250 mg to 500 mg t.i.d. *p.o.*; 500 mg t.i.d. *i.v.*; in combination with anti-aerobic antibiotics only	7 days
Gentamycin	Pregnancy and lactation, kidney failure, hearing disorders, Parkinson's disease, myasthenia gravis	Neurotoxicity, ototoxicity, skin allergy	2-5 mg per kg body weight, usually divided into 3 doses *i.v.;* in combination with metronidazole only	7-10 days (maximum)
Clindamycin	Lactation, carefully in liver or kidney failure	Bone marrow damage (including agranulocytosis), pseudomembranous colitis, inhibition of neuromuscular transduction sudden cardiac arrest, venous thromboembolism	From 200 mg to 600 mg t.i.d. *p.o.*; from 200 mg to 400 mg 2-4 times per day *p.o.*;	7-10 days

erative mortality following primary anastomosis was lower (10%) than after the Hartmann's procedure (19%) (93). In another study, no differences in perioperative mortality were observed in patients after resection with primary anastomosis (14.1%) in comparison with those who underwent the Hartmann's procedure (14.4%) (94).

In the recent years, results of studies evaluating the efficacy of laparoscopic methods in treatment of patients with Hinchey III diverticulitis were published. Laparoscopic washing and drainage of the peritoneal cavity are associated with mortality and risk of early complications similar to those observed after open resection with stoma exteriorisation (95, 96).

The laparoscopic method is associated with a low risk of complications (ca. 5%), and makes it possible to shorten hospitalisation and avoid stoma exteriorisation (87). Prospective studies evaluating the efficacy and safety of this method are ongoing.

Statement 12

In Hinchey III diverticulitis, the Hartmann's procedure is the established treatment method. In highly experienced centres, resection

with primary anastomosis (with or without a protective ileostomy) or laparoscopic procedures (washing and drainage or resection procedures) are admissible. In Hinchey IV diverticulitis, laparotomy with the Hartmann's procedure should be performed (92, 98).

c. Perforation of the gastrointestinal tract

Perforation to the peritoneal cavity is a rare complication of colonic diverticulitis. Perforation to the peritoneal cavity significantly increases mortality – up to 30%. The treatment method of choice is surgical intervention, i.e. the Hartmann's procedure (1).

d. Assumptions for elective resection

Laparoscopic technique

Elective colon resection due to diverticular disease may be performed in either laparoscopic or open surgery settings. Based on meta-analyses of non-randomised studies, it may be stated that laparoscopic procedures are associated with a lower risk of complications and shorter hospitalisation. The best time for laparoscopic surgery is the period in which the patient presents no symptoms or signs of acute diverticulitis, i.e. minimum 4-6 weeks after the last episode (99). Prior to elective surgery, one-week therapy with rifaximin (2 x 400 mg for 7 days) may be considered in order to reduce the risk of postoperative complications (68).

Laparoscopic surgery is not recommended in patients with complicated diverticulitis as it is associated with a high risk of complications and conversion (99,100). In complicated diverticulitis, laparoscopic surgery may be safely applied only in highly experienced centres (101).

Level of colonic anastomosis

An anastomosis between the descending colon and the rectum reduces the risk of recurrent diverticulitis. The recurrence rate after partial sigmoidectomy and creation of an anastomosis between the descending colon and the distal sigmoid colon exceeds 12%.

After sigmoidectomy and creation of an anastomosis between the descending colon and the rectum, the recurrence rate is much lower and ranges from 2.8% to 6.7%. The level of anastomosis is a proven risk factor of recurrence and therefore complete sigmoidectomy with creation of an anastomosis between the descending colon and the rectum is recommended (102,103).

Inferior mesenteric artery ligation

If it is possible and there is no suspicion of cancer, the inferior mesenteric artery should be preserved. This reduces the risk of anastomotic leakage. If the inferior mesenteric artery is preserved, the risk of a clinically overt anastomotic leakage is 2.3% (7% radiologically confirmed), while in patients with ligated artery this proportion increases to 10.4% (18.1%) (104). However, ligation of the inferior mesenteric artery and lymphadenectomy must be performed if neoplastic lesions have not been excluded.

Statement 13

In complicated diverticulitis, laparoscopic resection may be safely performed in highly experienced centres. Elective resection should be performed when no disease symptoms are present, i.e. 4-6 weeks after the last episode of diverticulitis. In order to minimise the risk of anastomotic leak, the anastomosis should be created between the descending colon and the rectum (and not the sigmoid colon). The inferior mesenteric artery should not be ligated. This principle is not applicable if colorectal cancer is suspected (92, 98, 102, 104).

e. Recurrent diverticulitis

Until recently, two episodes of uncomplicated diverticulitis or one episode of complicated diverticulitis were considered sufficient reason for elective colon resection. The aim was to reduce the risk of complications in case of a subsequent recurrence. However, it must be remembered that elective resection is also associated with complications: the mortality rate is 1-2.3%, the recurrence rate – 2.6-10%, and the risk of stoma exteriorisation during the procedure – 10% (105).

Recurrent diverticulitis is a rare condition (ca. 2% annually) and therefore the risk of complicated recurrent diverticulitis is much lower than previously thought. Increased risk of complications with subsequent recurrences of diverticulitis was also not confirmed. It was observed that the proportion of patients who required surgery during the first episode of diverticulitis was ca. 16%, while in recurrent diverticulitis – only 6%. The perioperative mortality rate was 3% and 0%, respectively (106). In order to prevent complications, rifaximin may be used as its efficacy was confirmed in several prospective randomised studies (68). Mesalazin is not recommended in the prevention of recurrence (82).

Identification of patients at a higher risk of recurrence and related complications is an important issue.

Factors significantly increasing the risk of colonic perforation in recurrent diverticulitis include:
– immunosuppressive treatment (including chronic steroid therapy);
– chronic kidney disease;
– chronic obstructive pulmonary disease.

In such patients, resection should be considered after the first episode of diverticulitis (107). In immunocompromised patients who receive conservative treatment due to complications of diverticulitis, the mortality rate is as high as 56%, but is significantly lower in patients undergoing surgical treatment (23%) (108).

In patients with numerous, frequent recurrences, elective resection should be considered, taking into account the burden of recurrences and their effect on the quality of life. It should be remembered that after elective surgery 75-78% of patients remain free of disease symptoms, and in the remaining patients only a part of previous symptoms is present. Certain clinical symptoms that persist after the procedure are due to anastomotic stenosis. Such patients may be successfully treated with endoscopic dilation of the anastomosis (109).

Statement 14

Previously recommended elective surgery in recurrent diverticulitis has no effect on mortality or the risk of complications, while it increases treatment cost (92,98). Elective surgery should be considered in patients with persistent symptoms refractory to conservative treatment and those in whom a malignancy cannot be unequivocally excluded.

f. Fistulae

In complicated diverticulitis, fistulae develop in 2-4% of patients. A peridiverticular abscess formed as a result of intestinal wall perforation may open itself spontaneously into the lumen of an adjacent organ or outwards through the skin. A fistula usually consists of a single channel, but in ca. 8% of patients multiple channels develop. Fistulae are more common in men than in women (2:1), in patients who underwent abdominal surgery in the past, and in immunocompromised patients (110).

In complicated diverticular disease, the following types of fistulae may develop:
– colovesical fistula – nearly 65% of fistulae in this condition,
– colovaginal fistula (25%)
– colocutaneous fistula,
– coloenteric fistula.

Fistulae that developed as a complication of diverticulitis require surgical treatment.

g. Gastrointestinal bleeding

Diverticular disease is one of the most common causes of massive lower gastrointestinal bleeding (30-50% of cases). It is estimated that ca. 15% of patients with diverticulosis will bleed at least once in their life. Bleeding is usually sudden, painless, and profuse; in 33% of cases, hospitalisation and urgent blood transfusion is required. In 70-80% of cases, bleeding stops spontaneously. The use of non-steroidal anti-inflammatory drugs increases the risk of bleeding, and more than 50% of patients with active bleeding from diverticula receives those agents (1, 111).

Diagnostic methods used to identify the source of bleeding include: colonoscopy, selective angiography (including angio-CT), and radionuclide tests. The accuracy of those studies ranges from 24% to 91% (112).

Indications for urgent surgery include:
– haemodynamic instability refractory to conservative treatment,

– the necessity of transfusion of > 6 units of erythrocyte concentrate,
– recurrent haemorrhage (1).

However, it must always be remembered that, apart from the haemorrhoidal disease and other non-malignant rectal conditions, colorectal cancer is also a frequent cause of lower gastrointestinal bleeding.

Statement 15

Colonic diverticular disease is a common cause of massive lower gastrointestinal bleeding (30-50% of cases). Diagnostic methods used to identify the source of bleeding include: colonoscopy, selective angiography (including angio-CT), and radionuclide tests. In 70-80% of cases, bleeding stops spontaneously. In some cases, endoscopic treatment is helpful. Surgery is performed in patients haemodynamically unstable despite blood transfusion and those with recurrent bleeding.

h. Intestinal obstruction

Complete intestinal obstruction due to diverticulitis is a rare complication, seen in less than 10% of all cases of colonic obstruction. Most commonly, the mechanism is subileus due to oedema and spasm of the intestinal wall as well as chronic inflammatory lesions in the intestinal wall and the surrounding tissues. Subileus may also be due to the presence of a pericolonic abscess compressing the intestinal wall. Recurrent inflammatory lesions lead to fibrosis of the intestinal wall and lumen stenosis which may result in complete obstruction. In such cases, it is essential (although often difficult) to determine whether the cause of obstruction is inflammation or malignancy.

In complete obstruction, the method of choice is bowel resection and/or stoma exteriorisation (98).

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