INTERDISCIPLINARY CONSENSUS STATEMENT ON THE DIAGNOSIS AND TREATMENT OF DIVERTICULAR DISEASE

Elaborated by a group of experts appointed by the Polish Society of Gastroenterology and Polish Society of Surgery:

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A. Definition and division

The diverticulum is usually a small, saccular prominence of the wall, externally to the lumen of the organ. It is considered as a pathology outside the fetal life (congenital or acquired). It can occur in different places, but most often is found in the colon. Due to their structure the diverticula may be divided into true-, and pseudodiverticula, which are in fact mucous membrane hernias covered with serous mucosa (1). The most common left colonic diverticula are considered as false, while the congenital right colonic diverticula are considered as true structures.

The first descriptions of colonic diverticula and their symptoms date back to the beginning of the eighteenth century (2). However, to this day there is no one commonly accepted classification. The most popular clinical classification distinguishes asymptomatic colon diverticulosis and symptomatic diverticular disease

of the colon, both uncomplicated and complicated. Acute complications include diverticulitis, abscess formation, bleeding and perforation, while chronic complications include colon stenosis and fistulas development (3, 4). In order to describe the stages of acute diverticulitis with colon perforation, a four-scale classification is used, introduced in 1978 by Hinchey et al. The above-mentioned determined the location and extent of the inflammatory infiltration, on the basis of the clinical and perioperative picture (tab. 1) (5). With the development of new imaging techniques novel classifications were elaborated, based on the radiological and endoscopic image. Table 2 presented Hansen and Stock's (1998) and Ambrosetti's classifications (2002) (6, 7).

Statement 1

Diverticula are considered as mucous membrane hernias through the colonic muscular membrane (pseudodiverticula). They are most commonly found in the sigmoid. The disease

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

Stage	Symptoms		
Ι	pericolic or phlegmonous abscess – limited lesions		
II	pelvic, mesogastric, or retroperitoneal abscess- diffuse lesions		
III	diffuse purulent peritonitis		
IV	fecal peritonitis		

Hansen and St	ock's classification on the basis of the clinical picture and additional investigations		
Stage	Description		
0	diverticulosis		
I uncomplicated acute diverticulitis (endoscopy: inflammation, computer tomo colon wall thickening)			
I acute, complicated diverticulitis			
II a phlegmonous abscess, tissue inflammation in the vicinity of the diverticule (computer tomography: inflammation of the surrounding fat tissue)			
II b	abscess, perforation		
II c	perforation (computer tomography: air or fluid)		
III	chronic, recurrent diverticulitis (endoscopy, computer tomography: stenosis, fistula)		
Ambrosetti's classificati	on on the basis of computer tomography		
Mild diverticulitis	segmental colon wall thickening ≥ 5 mm, surrounding fat tissue inflammation		
Severe diverticulitis	abscess air outside the gastrointestinal lumen, contrast outside the gastrointestinal lumen		

Table 2. Diverticulosis classifications used in clinical practice (6, 7)

may be divided into asymptomatic (diverticulosis), symptomatic (diverticular disease), as well as diverticulitis, both with early and late complications. The preferred four-scale classification elaborated by Hinchey et al. is used by surgeons to choose the method of treatment.

B. The etiology of diverticulosis

The etiology of diverticulosis is still not well understood. Risk factors for the development of diverticula include old age, low fiber diet, and connective tissue diseases (8). The role of the lifestyle and environmental factors are also emphasized. Theories responsible for the development of the disease include structural and functional disorders of the bowel, caused by improper innervation, neuromuscular abnormalities, smooth muscle fiber abnormalities, and connective tissue proliferation (9).

Diverticular incidence increases with patient age (10). While the disease is not frequent in patients before the age of 40 years, those in their seventh decade of life are diagnosed with the pathology in 50% of cases. The cause and effect relationship might be apparent, however, it is not attributed to the patients' age, but to the long-lasting exposure of the colonic wall to pathogenic factors. One of the abovementioned factors is the low-fiber diet, described in the sixties of the past century as a probable etiological factor responsible for diverticular development (11). This conclusion was assumed from the observation of demographic differences in the incidence of diverticular disease. The disease was frequently observed in highly-developed countries, being rare in Africa and Asia, where the diet is rich in vegetable fibers. Experimental data demonstrated that a low content vegetable fiber diet positively correlates with the development of diverticula in animals (12, 13). However, recent surveys undermine the importance of the diet in the development of colon diverticulosis (14).

Other environmental factors considered in the etiology of diverticulosis include red meat, alcohol, smoking, low physical activity, obesity and socioeconomic status. These factors have an impact on the occurrence of disease symptoms and complications. However, their contribution in the development of diverticulosis has yet to be established (8). For example, in a study published in 2010, only age >65 years was associated with diverticulosis development (15).

Statement 2

Considering the etiology of diverticulosis one should take into account the elderly age, diet, environmental factors and addictive substances. Previous studies, are however, ambiguous and do not entitle to recommend lifestyle modifications, as a prevention of diverticulosis.

C. Pathogenesis

The formation of colonic diverticula is observed when nutritional vessels (vasa recta) project through the mucous membrane. With age one may observe the change in the metabolism of the intestinal extracellular matrix. In case of diverticular disease one may observe changes in the composition of collagen and elastin. Collagen fibers are smaller and more densely arranged, and the connections between them more numerous and rigid, resulting in loss of elasticity. One may also observe the increased amount of elastin fibers in the longitudinal layer of the muscular membrane, which in consequence leads to segmental intestinal wall thickening and loss of elasticity. Increased rigidity facilitates the development of diverticulosis (9). In case of patients with diverticulosis one may also observe thickening of the circular layer of the muscular membrane. This is not associated with muscular cell proliferation, but with tissue reconstruction. As previously mentioned, there is an increased amount of elastin in the longitudinal layer of the muscular membrane. This leads to apparent intestinal shortening, and thus, its specific configuration, more susceptible to diverticulosis development (9).

Other pathogenic factors associated with the intestinal nervous system include the following:

- a) motor activity disturbances associated with the reduction of neural cells in visceral ganglia and Cajal cells (16-19),
- b) quantitative changes in the number of neuropeptides responsible for peristalsis, including increased levels of VIP, substance P, neuropeptide K, and galanin (20, 21, 22),
- c) reduced amount of glial-derived neurotrophic factor (GDNF) with secondary hipoganglionosis observed in patients with diverticulosis (9).

For some time now one highlights the role of chronic inflammation not only as a complication of diverticulosis, bot also as a causative factor. Depending on the intensity and duration of the inflammation in both the mucous membrane and surrounding tissues, one may observe a specific, chronic inflammatory infiltration of lymphocytes and plasmocytes with mucous membrane architecture disturbances, Paneth cell metaplasia, and formation of lymph nodules. Neurons and visceral ganglia are also subject to post-inflammatory structure changes, due to their location. It has been suggested that the proliferation of inflammatory cells is excessive, which increases the sensitivity to stimuli in patients with diverticular diseases resulting in chronic symptoms (23, 24). It is still not decided whether inflammation is the cause or consequence of diverticulosis.

Statement 3

The pathogenesis of the disease remains unclear. It is known that collagen and elastin structure disturbances play a role in the pathogenesis of diverticulosis leading towards intestinal shortening and stiffening. Abnormalities in the functioning of the visceral nervous system have also been proved leading to contractile dysfunction and abnormal sensitivity to stimuli. Minimum chronic inflammation of the intestinal wall and surrounding adipose tissue is responsible for the presence of disease symptoms and complications.

D. Epidemiology

Diverticulosis is one of the most common pathologies of the colon in the western population and is listed amongst the main reasons for outpatient visits and hospitalizations. Its incidence increases with age. Data concerning superiority gender are divergent, and depend on the study group. Most publications have shown that male patients predominate in case of subjects <50 years, between 50-70 years female patients slightly predominate, while in case of subjects > 70 years the domination of female patients is visible (25). In recent years there has been an increased incidence of symptomatic patients. It is estimated that diverticulitis concerns 10-25% of patients with diverticulosis, 25% with further complications (26).

In England during the past 10 years (1996-2006) the incidence of hospitalizations for diverticular disease has more than doubled (from 0.56 to 1.2 per 1000 inhabitants). At the same time one observed reduced average age of hospitalized patients (27). Thirty-day mortality amounted to 5.1%, while one-year mortality exceeded 14%, which is much higher than previously obtained data (nearly 3%). The highest mortality was observed in elderly patients with severe coexisting diseases.

Statement 4

Diverticular incidence increases with patient age. They are one of the most common diseases of the colon in western populations. Depending on the patient age group the disease affects more men or women, differences being statistically insignificant. The incidence of hospitalizations has increased, due to complications.

E. Diverticular disease in young patients

Based on the analysis of diverticular disease and diverticulosis incidence, their occurrence in young patients has increased. Whats more the recognition of the disease is also increased, since diverticulosis was, and is considered as a disease of the elderly. Some studies noted a 150% increase considering disease recognition in patients aged between 15 and 24 years, and an 84% increase in case of 18-44 year-olds (28, 29). The simplest explanation is the change in lifestyle, which occurred in recent decades. Available study results suggest that young patients with diagnosed diverticular disease have a higher body mass index (BMI), as compared to older patients. Such a trend is more pronounced in male patients. Data concerning the severity and recurrence of diverticulitis in young patients are contradictory. According to some studies the course of the disease is more aggressive, while others show no differences (30-33). In comparison to elderly patients younger subjects are more often hospitalized, which might be associated with initial misdiagnosis, such as appendicitis or gynecological diseases requiring surgical intervention (28).

Diverticula develop more often in children and young adults with congenital connective tissue disorders. The above-mentioned include: Marfan's syndrome (fibrilin gene mutation), Ehlers-Danlos's syndrome (collagen metabolism disturbances), Williams-Beuren's syndrome (elastin gene mutation), and many other rare syndromes. The cause of diverticulosis in the above-mentioned patients is believed to be associated with the improper structure of the connective tissue (32). Another common disorder in which diverticulosis develops is polycystic kidney disease (dominant type) observed in 50-80% of cases (34). In these patients diverticulosis should be considered during differential diagnosis of gastrointestinal symptoms. The diagnosis of asymptomatic disease does not affect prognosis.

Most female patients will end the reproductive period before the manifestation of the diverticular disease. Since the maternal age is increasing, diagnosis of complicated diverticu-

lar disease should be considered in case of differential diagnosis of abdominal pain or lower gastrointestinal bleeding in pregnant women. It should be remembered that in case of advanced pregnancy the anatomical relationships are changed, and typical lower quadrant pain may be located elsewhere in the abdomen. One report estimated the occurrence of diverticulitis in pregnant women at 1:6000 pregnancies (35). There are no statistical data concerning the need for surgical intervention in case of diverticulitis. However, 2% of pregnant women are subject to surgery (36, 37). Diagnostic imaging of diverticulosis should include examinations, which do not require exposure to radiation, such as ultrasound and MRI. In case of lower gastrointestinal bleeding sigmoidoscopy is safe (38). Some of the antibiotics used in the treatment of acute diverticulitis are contraindicated during pregnancy, which should be considered when undertaking therapeutic decisions. Rifaximin, which is not absorbed from the gastrointestinal tract could be a good alternative. However, due to lack of relevant studies, it is not recommended in pregnant women. Despite the lack of formal recommendations its seems that all pregnant women with diverticulitis require hospitalization (at least in the initial stage of the disease). Surgery in case of acute diverticulitis should be considered as a life-saving procedure (decisions are undertaken in case of conservative therapy failure and occurrence of severe complications).

Statement 5

One may observe an increase in the incidence of diverticulosis complications in young patients. Data concerning the severity of the disease and recurrence are inconclusive, and not require separate proceedings.

Diverticulitis should be considered in the diagnostics of abdominal pain in pregnant women. Ultrasound and MRI are the methods of choice. Patients require hospitalization taking into account therapy using antibiotics and analgesics allowed in pregnancy. Indications for surgery should only include direct life-threatening conditions for the pregnant woman.

F. Asymptomatic diverticulosis

Diverticulosis, the presence of colonic diverticula is a clinically silent condition. The physical examination and laboratory results are within normal limits. Diagnosis is usually accidental during colonoscopy or computer tomography. In the past, diverticulosis was diagnosed on the basis of an enema.

In patients with asymptomatic diverticulitis one may observe segmental colitis diagnosed in 2% of cases (39). The endoscopic image varies. Most often one may observe the presence of erythema, granulation, and superficial erosions or ulcerations. These lesions are focal, sometimes visible in one fold. They should be distinguished from diverticulitis, where the inflammatory process concerns the mucous membrane surrounding the infected diverticulum. The microscopic image resembles colitis ulcerosa or Crohn's disease, and the exclusion of both diseases requires additional examinations (40, 41).

Statement 6

Diverticulosis is an asymptomatic form of the disease, which does not require treatment or monitoring. Enteritis associated with diverticulosis is manifested by a different endoscopic and microscopic image, and requires differentiation with ischemic enteritis and non-specific inflammatory diseases. Microscopically diagnosed diverticulitis does not require treatment.

G. Diverticular disease

10-25% of patients with diverticulosis manifest symptoms. Most often one may observe uncomplicated diverticular disease manifested by the presence of recurrent abdominal pain, flatulence, defecation rhythm disturbances, without additional study deviations (42). Risk factors include a low-fiber diet, poor physical activity, and abdominal obesity (8), as well as rectal contraction hypersensitivity in patients with diverticular disease, as compared to subjects without symptoms and diverticula (11, 43). Recent studies draw attention to the chronic mild inflammation of the mucous membrane caused by microabrasions, secondary to the closure of the diverticular orifice by fecal masses and bacterial translocation to surrounding adipose tissues, where one may observe the stimulation of adipocytes and preadipocytes with the release of adipokin and chemokin (9, 24).

Diagnosis is based on the physical examination and additional study results. The physical

examination usually shows no abnormalities. Some patients complain of tenderness and resistance in the left iliac fossa (15, 42). In case of uncomplicated diverticular disease, laboratory markers of inflammation (ESR, CRP, WBC) are normal. The concentration of fecal calprotectin may be increased, which differentiates diverticular disease from diverticulosis or functional disturbances (44, 45). Considering imaging diagnostics one may use contrast enema, CT, and MR. Abdominal cavity plain film is no longer applicable (46). Barium enema remains a very good diagnostic method showing not only the presence of diverticula (oversized shadows), but also their cause (folds). The above-mentioned additionally enables to determine the size of the diverticula, their scope, and possible chronic complications (stenosis, fistulas) (41) Aqueous barium examinations are reserved for patients suspected of complications. Computer tomography is the most commonly used examination, due to its high sensitivity, specificity, reproducibility, and general availability. In order to increase method sensitivity one may administer rectal contrast before the examination (41). There are no data regarding the sensitivity and specificity of colonography by means of CT. Diagnosis of left lower quadrant abdominal pain should also consider endoscopy, although recent studies are inconclusive. In case of patients under the age of 50 years, sigmoidoscopy seems sufficient. Those above 50 years require full assessment of the colon, due to the possible coexistence of cancer (47).

Diverticular disease should be differentiated with many disorders associated with left iliac fossa pain (tabl. 3A). Due to the high incidence of IBS, differentiation usually concerns functional disturbances, where the nature of the symptoms is similar. It is postulated that these diseases overlap each other, especially since symptoms remain to be understood (15). Nevertheless, the population of patients with diverticular disease differs from patients diagnosed with functional disturbances. Patients with diverticulosis are older and one does not observe significant female predominance. The duration and location of pain differ between groups. Patients with functional disturbances complain of short, transient, diffuse pain, while those with diverticular disease complain of left lower quadrant abdominal pain lasting several weeks followed by an asymptomatic period of several months or years (59). As previously mentioned, laboratory results in case of functional disturbances show no abnormalities.

Prognosis in case of uncomplicated diverticular disease is favorable. The natural course is mild and complications are observed in a small percentage of patients, as confirmed by many studies. In case of one study the complication rate amounted to 1.4% during a fiveyear observation period (49).

Statement 7

Diverticular disease is characterized by abdominal pain, bloating, and defecation rhythm disturbances. The presence of diverticula is diagnosed by means of CT or contrast enema, which in case of uncomplicated diverticular disease remains a valuable diagnostic method. During differential diagnosis one should consider IBS, and due to clinical implications-colon cancer.

H. Diverticulitis

The most common complication of diverticular disease is acute diverticulitis, that is the presence of clinical, laboratory, and imaging markers of inflammation in patients with diverticulosis. Risk of diverticulitis is increased in case of a low fiber diet. A large populationbased EPIC study (47033 patients) evaluating the incidence of diverticular disease hospitalizations showed that patients on a high fiber diet were less likely to be hospitalized, as compared to those on a low fiber diet (50). Other risk factors include a diet rich in red meat, alcohol, smoking, limited physical activity, obesity, and socioeconomic status (8, 10). The pathogenesis of diverticulitis is similar to that of diverticular disease. Currently, attention is paid to the role of intestinal microbes and minimal inflammation, which became the target of modern treatment (51).

The main symptom of acute diverticulitis is sudden, rapidly intensifying pain, located in the lower left abdominal quadrant (possible diffuse pain). If diverticulitis is extensive and surrounding tissues and organs are infiltrated, one may observe pain upon movement (pelvic muscle involvement), and urinary system disturbances, as well as nausea, vomiting, constipation and urine retention, or on the contrary-diarrhea. Abdominal symptoms are usually accompanied by fever. The physical examination shows tenderness upon palpation in the left iliac fossa, sometimes local peritoneal and general infection symptoms. Laboratory examinations show elevated inflammatory markers (ESR, CRP, WBC, and fecal calprotectin) (44, 45). Computer tomography is the golden standard in the diagnosis of diverticulitis, its sensitivity and specificity being very high (46). Magnetic resonance is used less frequently, mainly due to the limited availability and higher costs. Transabdominal ultrasound is a good and cheap method used during initial diagnosis. Other radiological methods are of limited availability (52). Due to fear of complications, until recently, colonoscopy was contraindicated during acute diverticulitis (6 weeks since treatment initiation), and even now there are only isolated indications for its use (53, 54).

Computer tomography during the first episode of diverticulitis enables to confirm the diagnosis, determine its severity and extent, as well as exclude other complications. It also allows to plan invasive treatment (abscess drainage under ultrasound or CT control). The sensitivity of the examination is estimated at 79-99% (55). CT should include the abdominal cavity and pelvis. The examination should be contrast-enhanced, preferably with rectal contrast, as well (47). The most common abnormalities observed in case of diverticulitis include segmental bowel wall thickening (>3 mm) and indistinctness of fat tissue. When determining the severity of diverticulitis Ambrosetti's criteria are useful (tab. 2), correlating with the risk of surgery (7). Computer tomography is especially useful when diagnosing diverticula of the right half of the colon. Radiological differential diagnosis includes colorectal carcinoma, where one may observe wall thickening and fat tissue involvement. The ultrasound examination is easily accessible and inexpensive, the subjective evaluation of the result being its disadvantage. The sensitivity and specificity of the ultrasound examination in case of diverticulitis diagnosis amounted to 77-98% and 80-99%, respectively (52). Under ultrasound control one can perform puncture and drainage of the peridiverticular abscess. The examination does not burden the patient and does not require additional preparation. Thus, it is the method of choice in case of pregnant women with

suspicion of diverticulitis. The role of transvaginal and transrectal ultrasound is also underlined when evaluating disease complications.

As previously mentioned colonoscopy is not contraindicated in case of acute diverticulitis. Study results evaluating the safety of colonoscopy during hospitalization for diverticulitis are encouraging (53). During the examination one may observe mucous inflammation surrounding the diverticulum or segmental diverticulitis with a purulent exudate (41). There remains, however, the concern about the potential for exacerbation, especially perforation. Indications for colonoscopy are therefore quite narrow and should be limited to cases with prolonged symptoms, and management of bleeding. Another potential indication (recommended by some scientific societies) is to exclude colorectal cancer. The report published this year concerning the frequency of colorectal cancer in patients with diverticulosis found no indications for such management. Although the incidence of cancer in this group of patients was higher, as compared to the asymptomatic population (2.1% vs 0.68%), the above-mentioned should be rather compared to patients with gastrointestinal symptoms, where incidence of cancer is much higher (54, 56, 57).

Differentiation of acute diverticulitis was presented in table 3B. In 2007, study results were published evaluating the accuracy of the initial diagnosis established in the ER. Differential diagnosis of left lower quadrant abdominal pain with coexisting inflammatory symptoms, apart from diverticulitis, included unspecific abdominal pain, appendicitis, constipation, urinary tract infections, tumors, abdominal aortic aneurysm, and gynecological diseases (58). These diseases should be first considered.

Prognosis in case of diverticulitis depends on the course of the disease. Complications are rarely observed, although in recent years there has been an increase in their frequency. As previously mentioned, prior diverticulitis does not increase the risk of complications. The risk of recurrence ranges between 2-43% and tends to decline (59). In case of uncomplicated diverticulitis prognosis is favorable, which has been confirmed by recent publications (60, 61). Similar data are available concerning disease complications.

Table 3. Diverticular disease differentiation (15, 44,45, 48)

- / - /				
A. Uncomplicated				
IBS				
Habitual constipation				
Colorectal cancer				
Crohn's disease				
Colitis ulcerosa				
Ischemic colonitis				
Gastrointestinal tract infections				
Urinary tract infections				
Minor pelvis infections (women)				
Ovarian cyst				
B. Complicated				
Diseases as in part A				
Appendicitis				
Abdominal aortic aneurysm				
Hernia incarceration				
Pancreatitis				
Pyelonephritis				
Nephrolithiasis and ureterolithiasis				
Gynecological disorders				
Prostatitis				

Statement 8

Diverticulitis is the most common complication of diverticulosis. A low fiber diet has been proven to influence the development of the disease. The disease is manifested by acute pain located in the left iliac fossa with coexisting general symptoms of inflammation (fever, tachycardia, weakening, nausea). In case of severe inflammation one may observe limited or diffuse peritonitis. Computer tomography is the golden diagnostic method. Colonoscopy in case of acute diverticulitis should be limited to uncertain diagnostic cases, when suspecting a tumor or when treating complications. Differential diagnosis includes appendicitis, enteritis, urinary tract infections, colorectal cancer, abdominal aortic aneurysm, and gynecological diseases.

I. Conservative treatment

Table 4 presented the strategies of conservative treatment in case of diverticular disease.

a) ambulatory care:

- the asymptomatic disease does not require treatment. Lifestyle modifications are often recommended, such as the introduction of a diet rich in fiber, body weight reduction, ces-

		Symptomatic,	Benign and mild	Severe, uncomplicated
Type of	Asymptomatic diverticulosis	uncomplicated diverticular	8	diverticulitis, selected
disease		disease	diverticulitis	patient groups
Conservative treatment	without treatment	rifaximin spasmolytic drugs (anticholinergic) analgesics mesalazin (lack of evident data)	outpatient treatment spasmolytic drugs (anticholinergic) analgesics antipyretics oral antibiotics (rifaximin) or without antibiotics	hospitalization spasmolytic drugs (anticholinergic) analgesics antipyretics intravenous antibiotics 7-10 days followed by oral antibiotics 7-10 days (ambulatory) lmwh-prophylactic dose hydration intravenous
Diet	rich in fiber	bogatobłonnikowa / rich in fiber limitation: - red meat, - alcohol	protective diet, semi- fluid and fluid hydration	strict benign cases-fluid
Lifestyle modification	increased physical activity	body weight reduction increased physical activity cessation of smoking	work disability rest bed-chair lifestyle	hospitalization bedridden

Table 4. Conservative treatment of diverticular disease (62-67, 71)

sation of smoking, limited intake of red meat and alcohol, and increased physical activity. However, their is insufficient evidence concerning the above-mentioned.

- the aim of treating **uncomplicated di**verticular disease includes the following: control symptoms, cure the infection, prevent recurrence and limit complications. In case of benign and mild forms of the disease dietary modifications seem sufficient (fiber supplementation, protective diet). Simultaneously, antibiotics are recommended, in order to limit infection or bacterial growth, although there are no publications justifying such behavior (1). The most common bacteria isolated from such patients include Escherichia, Bacteroides and Clostridium strains, thus, treatment should include both aerobic and anaerobic. For more than twenty years the efficacy of rifaximin has been determined-practically a nonabsorbable antibiotic with a broad spectrum of activity (Gram-positive and Gram-negative bacteria, aerobes, anaerobes). Its efficacy, both in the treatment of symptoms and prevention of recurrence was confirmed by prospective studies. The meta-analysis of available publications showed the higher efficacy of rifaximin associated with a high-fiber diet, as compared to only a diet (62). Additionally, we observed a statistically significant improvement in the quality of life, considering patients subject to treatment (63). Therefore, since 2008, The

National Diverticulitis Study Group recommends cyclic rifaximin therapy (400 mg, twice daily for 7 days/month) in patients with symptomatic diverticular disease and without complications (64).

In recent years, the efficacy of mesalazin was also evaluated, used in the treatment of chronic inflammation. Several randomized studies, although without a control group showed the efficacy of such management. The largest study group (268 patients), which compared mesalazin with rifaximin demonstrated a significantly more common regression of symptoms in case of patients treated with mesalazin with a low recurrence rate in both groups (65). Another randomized study with the control group evaluated the role of mesalazin in the treatment of symptomatic diverticular disease. No differences were observed in comparison to placebo (66).

In conclusion, treatment of uncomplicated diverticular disease includes a diet rich in fiber and rifaximin. Data concerning mesalazin are heterogenous.

- The majority of patients with diagnosed **acute diverticulitis** and without complications may be subject to outpatient treatment. Terms of such treatment include the following: benign or mild course of the disease in patients well-tolerating hydration and oral medication, with easy access to medical care (in case of exacerbation or lack of improvement) (67). Such patients require oral, broad spectrum antibiotics for a period of 7 to 10 days. Improvement should be observed after 2-3 days, otherwise medical re-evaluation is required. Many antibiotics are used, most often ampicillin (with β -lactamase inhibitors), II generation cephalosporins, as well as ciprofloxacin or biseptol with metronidazol. During analgesic treatment morphine should be avoided, due to the possibility of smooth muscle contraction. After treatment of acute diverticulitis rifaximin may be used, in order to prevent recurrence. Studies from 1999-2007 show the efficacy of mesalazin in the prevention of diverticulitis recurrence. However, none were placebo-controlled (51).

Another issue is the need for antibiotics in case of patients with mild diverticulitis. In 2007 and 2011, study results were published comparing the course of diverticulitis in patients with various forms of the disease treated and untreated by means of antibiotics (68, 69). No statistically significant differences were observed between both groups. In 2012, multi-center randomization study results were published comprising more than 600 patients with diverticulitis diagnosed on the basis of computer tomography. Antibiotic therapy did not affect the duration of hospitalization, recurrence rate, and number of complications (70). Despite all the data there is still lack of guidelines affirming such management.

In conclusion, most patients with benign and mild diverticulitis may be subject to outpatient management, and some with the exclusion of antibiotics.

Statement 9

Asymptomatic diverticulitis does not require treatment. Lifestyle modifications are not supported by scientific evidence. Treatment of uncomplicated diverticular disease consists in a rich-fiber diet and rifaximin (2x400 mg for 7 days each month), which reduces the number of symptoms, recurrence and complication rates, improving the patients' quality of life. Systemic antibiotics are not applicable, due to the lack of studies confirming their efficacy and potential side effects. Routine use of mesalazin is not recommended in case of diverticular disease, and the role of probiotics is uncertain.

Benign or mild diverticulitis without severe concomitant diseases may be subject to outpatient treatment. Therapy consists in a protective diet, hydration, analgesic, antipyretic, and spasmolytic drugs. Several studies showed no differences considering the course of benign or mild diverticulitis in patients treated or not by means of antibiotics. Nevertheless, routine antibiotics are recommended. Ciprofloxacin and metronidazole are most commonly used. The withdrawal from antibiotic therapy might be considered in case of selected patients (young without coexisting diseases, easy access to medical centers). In order to prevent recurrence rifaximin might be used, while the role of mesalazin is uncertain.

b) hospital treatment

Severe diverticulitis requires hospitalization. Also, elderly patients with concomitant diseases or those on immunosuppressive therapy require intensive treatment (67). The above-mentioned patients should receive 7-10 days of broad spectrum intravenous antibiotics, followed by oral therapy. Patients in severe condition require a fluid or strict diet, intravenous hydration, and analgesic drugs. When suspecting additional complications a surgical consultation is indicated.

Gastroenterological and surgical recommendations do not mention anything about anticoagulation therapy in patients hospitalized, due to abdominal cavity inflammation and coexisting concomitant diseases. It seems, however, that the administration of prophylactic doses of LMWH is reasonable and consistent with cardiological guidelines (71).

Table 5 presented the antibiotics used in the treatment of diverticulitis.

Statement 10

Hospitalization is required in case of severe inflammation and ensuing complications, in elderly patients with concomitant diseases, and pregnant women. In addition to antibiotic therapy (usually intravenous), hydration, analgesic drugs, and a strict diet are important. LMWH prophylaxis is recommended. The surgical consultation should not be delayed.

J. Surgical treatment

Surgical treatment of patients with diverticulosis should be limited to those with complicated diverticulitis. Only a small group of patients with uncomplicated diverticulitis, in whom conservative therapy is ineffective or symptoms are more pronounced require surgi-

Medication	Contraindications	Side effects	Dosage, administration, combination	Duration of treatment
Amocillin with clavulo- nic acid	β-lactam allergy, liver failure	gastrointestinal (nausea, vomiting, diarrhea, C. difficile infection), allergy, hepatopathy	625 mg 2 x daily to 1 g 2 x daily <i>p.o.</i> depending on the severity; 1.2 g 3 or 4 x daily <i>i.v.</i> depending on the severity	8-10 days Severe: 8-10 days <i>i.v.</i> ,
Biseptol	pregnancy, allergy, liver, renal, bone marrow failure; attention with thiazi- des	gastrointestinal, skin allergy, bone marrow damage, liver infarction	960 mg (160+800) 2 x daily <i>p.o.</i> ; similar <i>i.v.</i> dosage; treatment in combination with metroni- dazol	10 days
Ciprofloxacin	pregnancy and lacta- tion, epilepsy, sun exposure	nausea, diarrhea, hepatopa- thy, renal failure, psycho- motor activity impairment	500 mg 2 x daily <i>p.o.</i> 200 mg 2 x daily <i>i.v.</i> ; treat- ment in combination with metronidazol	7-14 days
Metronidazol	I trimester of pregnan- cy and lactation, CNS diseases; hematological disorders	metallic taste, neuropathy and other neurological disorders, skin allergy	250 mg to 500 mg 3 x daily <i>p.o.</i> ; 500 mg 3 x daily <i>i.v.</i> in combination antibiotics against aerobes	7 days
Gentamicin	pregnancy and lacta- tion, renal failure, hearing disorders, parkinson's disease, miasthenia	neurotoxicity, ototoxicity, skin allergy	2-5 mg/ kg body weight- 3x BID <i>i.v.</i> ; In combination with metronidazol	7-10 days (maxi- mum)
Clindamicin	lactation, caution in liver and renal failure	bone marrow damage (agranulocytosis), Colitis ulcerosa, neuromuscular conduction inhibition, Cardiac arrest, venous thromboembolic disease	200 to 600 mg 3 x daily <i>p.o.</i> ; 200 to 400 mg 2-4 x daily <i>i.v</i> .	7-10 days
Rifaximin	pregnancy	abdominal pain, constipa- tion, ascites, sitophobia, dyspnoea, double vision, chest pain, hypertension	2 x 400 mg	7 days each month in the treatment of uncomplicated diverticular disease

Table 5. Antibiotics used in the treatment of diverticulitis

NZK - cardiac arrest, ŻChZZ - venous thromboembolic disease

cal intervention. It is estimated that in the American population, nearly 20% of patients require hospitalization, due to diverticular disease complications (72). The incidence of diverticulitis (stage I-IV, according to Hinchey et al.) ranged between 3.5 and 4.0/100 000/year (73). The incidence of lower gastrointestinal bleeding associated with colon diverticula amounted to 10/100 000/year (74). Differential diagnosis of bleeding should consider cancer.

a) Peridiverticular and minor pelvis abscess (stage I and II, according to Hinchey's scale)

Abscess development, as a complication of perforation in case of diagnosed diverticulitis depends on the ability of pericolonic tissues to limit the inflammatory process. Initially, one may observe inflammatory infiltration with ensuing formation of a purulent compartment. Abscesses on the ground of sigmoid diverticulitis account for nearly 23% of all intra-abdominal abscesses. It is estimated that approximately 15% of hospitalized patients with acute diverticulitis show characteristic CT features of an abscess (75, 76). In recent years, surgery was the only therapeutic method in case of patients with peridiverticular abscesses. The development of imaging methods and novel antibiotics contributed to the changes in treating these patients. Patients with small abscesses (<3 cm) may be subject to antibiotic therapy under constant clinical control (77). In case of patients with peridiverticular abscesses antibiotics and drainage under CT

control seem effective in 50-67% of patients. However, in case of abscesses located in the minor pelvis therapeutic efficacy is lower, ranging between 41-59%. Additionally, patients with minor pelvic abscesses require surgery more often during the initial hospitalization (75, 76). Some authors suggest the need to perform contrast X-ray examinations before removing the drain, in order to exclude fistula development (78).

Conservative treatment and drainage enable to postpone surgery. Thus, elective surgery is performed. The risk of stomy exteriorization during elective surgery is low. If patients with abscess presence require emergency colon resection the risk of stomy exteriorization is estimated at 80%, while mortality at 33% (79).

Statement 11

Abscesses <3 cm can be treated with antibiotics under constant clinical control. If technically possible, abscesses should be treated with antibiotics and subject to percutaneous drainage under ultrasound or CT control. The drains should be rinsed several times a day and removed when their content is clean. If the purulent content is present for a long period contrast X-ray examinations should be performed, in order to exclude intestinal fistula development (80, 81). In the absence of technical possibilities to perform intra-abdominal abscess puncture and drainage, the patient should be subject to laparotomy or laparoscopy with abscess drainage (81).

b) Purulent and fecal peritonitis (stage III and IV, according to Hinchey's scale)

Surgery is the therapeutic method of choice in case of complicated diverticulitis (stage III and IV, according to Hinchey's scale). Hartmann's procedure has successfully replaced the previously performed three-staged operations. Kronborg et al. evaluated early treatment results considering patients with purulent and fecal peritonitis. The authors' compared Hartmann's procedure with the simple stitching of the perforation and proximal colostomy exteriorization. Mortality was significantly lower in patients with purulent peritonitis subject to simple stitching of the perforation and colostomy, as compared to Hartmann's procedure. These differences were not observed in case of fecal peritonitis (82). In selected studies perioperative mortality of patients

subject to primary anastomosis was lower (10%), as compared to Hartmann's procedure (19%) (83). Another study showed no differences considering perioperative mortality (primary anastomosis (14.1%), Hartmann's procedure (14.4%) (84).

In recent years, many study results were published evaluating the efficacy of laparoscopic methods in the treatment of diverticulitis (stage III and IV, according to Hinchey's scale). Laparoscopic peritoneal cavity drainage is associated with a similar mortality rate and incidence of early complications, as in case of open surgery with stomy exteriorization (85, 86).

The laparoscopic method has a low complication rate estimated at 5%, and enables to shorten hospitalization and avoid stomy exteriorization (87).

Statement 12

Hartmann's procedure is the recognized method of treating Hinchey III and IV diverticulitis. In case of stage III, one may consider laparoscopic lavage and peritoneal drainage. In case of stage IV, Hartmann's procedure should be performed (80, 81).

c) Gastrointestinal tract perforation

In case of colon diverticulitis perforation to the peritoneal cavity is a rare complication. It is observed more often in patients with impaired immunity. Perforation to the peritoneal cavity significantly increases mortality, estimated at 30%. In most cases, Hartmann's procedure is the method of choice (1).

d) Elective resection

Laparoscopic technique

Elective colon resection, due to diverticular disease can be performed, both by means of laparoscopy and open surgery. Based on metaanalyses study results laparoscopy is associated with fewer complications and shorter hospitalization. The best time to perform laparoscopy is the period during which the patient has no acute symptoms, minimum 4-6 weeks since the last episode of inflammation (88).

The laparoscopic technique is not recommended in case of patients with complicated diverticulitis, being associated with a high percentage of complications and conversion to open surgery (88, 89). In case of complicated diverticulitis laparoscopy may be safely performed, only in experienced centers. In such cases the conversion rate, perioperative mortality, and complication rate are similar to results after laparoscopy performed in patients with uncomplicated diverticulitis. However, the abovementioned conclusion should not be generalized, since laparoscopic surgery in case of complicated diverticular disease is a major challenge and requires significant experience (90). *Level of colon anastomosis*

Anastomosis of the descending colon and rectum reduces the risk of diverticulitis recurrence. After excision of part of the sigmoid and simoidorectostomy the recurrence rate exceeds 12%. After excision of part of the sigmoid and colorectostomy the recurrence rate ranges between 2.8% and 6.7%. Thus, the level of the anastomosis is a proven risk factor of disease recurrence (91, 92).

Inferior mesenteric artery ligation

If it is possible and there is no suspicion of cancer, the inferior mesenteric artery should be preserved. The non-ligation of the artery reduces the risk of anastomotic leakage. In case of preserved inferior mesenteric artery the rate of clinically overt anastomotic leakage is estimated at 2.3%, (7% confirmed radiologically). When the artery is ligated the abovementioned rate increases to 10.4% (18.1%) (93). Inferior mesenteric artery ligation and lymphadenectomy should be performed, if cancer lesions have not been excluded.

Statement 13

Laparoscopic resection in case of complicated diverticulitis can be safely performed in centers with extensive experience. Elective surgery should be performed during the period free of symptoms, that is 4-6 weeks since the last episode of inflammation. In order to minimize the risk of anastomotic leakage colorectostomy should be performed. The inferior mesenteric artery should not be ligated. This does not apply in case of suspected colorectal cancer (80, 81, 91, 93).

e) Recurrent diverticulitis

Until recently it was thought that after two episodes of uncomplicated diverticulitis or one episode of complicated diverticulitis, elective colorectal surgery should be performed. This was intended to reduce the risk of complications in case of disease recurrence. However, one should bear in mind that elective surgery is also associated with risk of complications: mortality is estimated at 1-2.3%, disease recurrence at 2.6-10%, and risk of stomy exteriorization at 10% (94).

Recurrent diverticulitis is rarely observed (2% per year), thus, the risk of complicated

diverticulitis is much smaller than previously considered. The risk of increased complications in case of recurrence was not confirmed. The percentage of patients which required surgical intervention during initial diverticulitis amounted to 16%, while in case of recurrenceonly 6%. Perioperative mortality was 3% and 0%, respectively (95). Some authors are of the opinion that recurrent diverticulitis may protect from disease complications. In order to protect one patient from emergency surgery, 18 patients should be scheduled for elective surgery, after one episode of complicated diverticulitis (96).

Statement 14

The previously suggested need to perform elective surgery in case of recurrent diverticulitis has no influence on the reduction of mortality and number of complications, only increasing the costs of treatment (80, 81).

It is important to identify the patient groups with increased risk of recurrence and number of complications associated with recurrence. It is believed that young patients are at increased risk of recurrence in case of complicated diverticulitis. In order to protect one patient (<50 years) from emergency surgery, 13 elective operations should be performed with the risk of possible complications (96).

Factors five-fold increasing the risk of colon perforation during diverticulitis recurrence include:

- immunosuppressive drugs (chronic steroid therapy),
- chronic renal failure (stage III-V),
- COPD (stage III-IV).

In these patients, surgery should be considered after initial diverticulitis (97). In case of patients with impaired immunity subject to conservative treatment, due to complicated diverticulitis, mortality amounted to 56%, being significantly lower, as compared to patients undergoing surgery (23%) (98).

In patients with numerous and frequent recurrent diverticulitis one should consider elective surgery, taking into account the inconvenience of recurrence deteriorating the patients' quality of life. One should not forget that 75-78% of patients after elective surgery are asymptomatic, while the remaining complain of preoperative symptoms. Some of the clinical symptoms persisting after surgery are associated with anastomotic stenosis. Such patients can be effectively treated by means of endoscopic dilatation of the anastomosis (99).

f) Fistulas

In case of complicated diverticulitis fistulas are observed in 2-4% of patients. The peridiverticular abscess which was created on the basis of the perforated intestinal wall can spontaneously drain to the lumen of the adjacent organ or through the epidermis. The fistula canal is usually single, although in approximately 8% of patients one may observe several fistula canals. Fistulas are more common in male patients, as compared to women (2:1), in those after previous abdominal operations, and those with impaired immunity (100).

Fistulas in case of complicated diverticular disease:

- colovesical fistula concerning 65% of all fistulas,
- colovaginal fistula (25%),
- colovulvular fistula,
- ileocolic fistula.

We observed a clinical dependency concerning intra-abdominal fistulas:

- diverticular disease fistula- pneumaturia,
- neoplastic disease fistula- gastrointestinal symptoms, fecaluria, and hematuria,
- Crohn's disease fistula- pain, palpable tumor, pneumaturia (1, 100).

Patients with enterovesical fistulas suffer from urinary tract infections. Some authors are of the opinion that recurrent urinary tract infections do not affect the deterioration of renal functioning (80). Fistulas which develop as a consequence of diverticulitis should be subject to surgical treatment. One should always consider the patients' clinical condition and influence of the fistula on the overall functioning.

g) Gastrointestinal bleeding

Colon diverticula develop at the site of arterial vessel penetration into the intestinal wall. The arterial vessel is then at risk of injury, the vascular wall is ruptured, and one may observe bleeding.

One should always bear in mind, that apart from diverticulosis, hemorrhoids, and other non-neoplastic perianal diseases, colorectal cancer is also a common cause of lower gastrointestinal tract bleeding.

Diverticular disease is the major cause of massive, lower gastrointestinal tract bleeding (30-50% of cases). It is estimated that about

15% of patients with diverticulosis will sustain bleeding, at least once during their lifetime. Bleeding is usually sudden, painless, and profuse, and in 33% of cases requires hospitalization with blood transfusions. 70-80% of bleeding cases stop spontaneously. The use of nonsteroid anti-inflammatory drugs increases the risk of bleeding, and more than 50% of patients with active bleeding from the diverticula are on the above-mentioned (1, 101).

Diagnostic methods used in search of bleeding include: colonoscopy, selective angiography and radioisotope studies. The accuracy of the above-mentioned ranges between 24% and 91%. The source of bleeding is not determined in 30-40% of cases (102).

Colonoscopy is an important examination, allowing to exclude other reasons of bleeding (neoplastic disease as the cause of bleeding in 32% of patients).

Emergency surgery, due to diverticulosis bleeding enables to determine the source of hemorrhage in 90% of cases.

Indications to perform the procedure are as follows:

- hemodynamic instability,
- transfusion of > 6 blood units,
- recurrence of massive bleeding (1).
 Statement 15

Colon diverticula are often responsible for lower gastrointestinal tract bleeding (30-50% of cases). Diagnostic methods used in search of bleeding include colonoscopy, angiography, and radioisotope studies. In 70-80% of patients bleeding stops spontaneously. In selected cases interventional endoscopy is helpful. Surgery is performed in case of hemodynamic instability, despite massive transfusions and recurrence of bleeding.

h) Intestinal obstruction

Complete intestinal obstruction, due to diverticulitis is a rare complication affecting nearly 10% of all colon occlusions. Most often one may observe subileus, due to edema and intestinal wall contraction, as well as chronic enteritis and pericolonic tissue inflammation. Subileus may also result from the presence of pericolonic abscess compressing the intestinal wall. Recurrent infections lead towards intestinal fibrosis and lumen stenosis, and in consequence complete occlusion. In such cases it is important to determine whether obstruction is of inflammatory or neoplastic origin. The method of choice considering treatment of complete obstruction consists in bowel resection or proximal stomy exteriorization (80). Prosthesis implantation is not applicable, due to the very low efficiency of the procedure.

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