



Risk Factors and Management of Diverticulitis

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Abstract

Diverticulitis is a type of gastrointestinal disorder that develops when the mucosa herniates through the muscular wall of the colon forming a sac like pouch known as diverticula. Development of diverticula can present as asymptomatic, known as diverticulosis or symptomatic, known as diverticulitis. Within the gut, the flora plays an essential role in providing a barrier to pathogenic organisms. Scientists believe that the chronic inflammation related to diverticulitis is a result of an imbalance in the normal gut flora. There are many risk factors associated with diverticulitis including genetic predisposition, dietary and lifestyle factors. Individuals aged sixty-five and older have a significantly higher risk of developing a diverticular disease, however new research has shown that the greatest increase in percentage of individuals diagnosed with diverticulitis are individuals age 50 years and younger. With irreversible damage being done on the gut microbe, scientists have developed several possible treatments of diverticulitis with antibiotics, anti-inflammatory and probiotic drugs. A combination of these treatments helps to eliminate recurrence of diverticulitis.

Keywords: Computed Tomography; Diverticulitis; Diagnosis; Genetic Component; Risk Factor

Abbreviations: CT: Computed Tomography.

Introduction

Diverticulitis, a common type of gastrointestinal disorder, is characterized by the inflammation of the colon. The development of diverticulitis occurs when the mucosa herniates through the muscular wall of the colon, forming a sac like pouch, known as the diverticulum [1]. In the absence of symptoms associated with formation of diverticula, the disease is referred to as, diverticulosis. However, once symptoms onset, the disease is termed diverticulitis [2]. Most people with diverticula remain asymptomatic, with roughly 20% of people beginning to experience symptoms, thus acquiring diverticulitis [3]. Although clinical presentations of diverticulitis can vary, individuals with left sided diverticulitis commonly

experience left lower quadrant pain, which is accompanied by a fever and leukocytosis. Left sided diverticulitis is the most common form in westernized cultures; however other forms exist and vary in clinical presentation of the disease. Additionally, patients may also experience nausea, vomiting, changes in bowel movements and painful urination [4]. In roughly 12% of individuals with diverticulitis complications may occur. These complications include phlegmon, abscesses, bowel obstruction, peritonitis, and fistulas [5]. Right sided diverticulitis is not common in westernized countries and is hard to distinguish between an acute appendicitis.

The most common age groups of individuals affected by a diverticular disease are adults age 65 and older. However, recent studies have shown that the number of younger individuals presenting with diverticulitis is increasing. In industrialized countries more than two-thirds

of adults will develop some extent of diverticular disease, with nonindustrialized rural areas containing the highest prevalence of the disorder [6].

The primary function of the gut is to absorb nutrients that are essential for other organs and the processes they carry out. The large surface area of the gut allows for absorption of nutrients and is riddled with numerous amounts of gut micro biomes. These microbes play an imperative role in the immune system. Gut homeostasis is achieved by the physical barrier that the epithelial layer provides against micro flora [7]. Chronic inflammation related to diverticulitis may result from an imbalance of this normal gut flora⁵. Research has shown that dietary factors can disrupt the overall homeostasis of the gut microbe, thus affecting the overall immune system of the individual, leading to an impaired digestive system [7].

Although genetic factors play somewhat of a role in the development of diverticulitis, dietary and lifestyle factors are also primary contributors to this disorder. Lifestyle factors affecting the development of diverticulitis include level of physical activity, obesity, smoking, and intake of medications such as NSAIDs and steroids. While dietary factors such as level of fiber consumption and consumption of high levels of unprocessed red meat contribute to the development of diverticulitis [8]. The primary purpose of this review article is to examine the essential risk factors contributing to diverticulitis and how to prevent recurrence of the disease as well as how to manage symptoms associated with the disease.

Diagnosis

There are several ways to assess and diagnose a patient with suspected diverticulitis. A patient usually presents with constant abdominal pain in the left lower quadrant. During examination, the healthcare provider should examine for symptom severity and evidence of peritonitis. Additionally, blood work should be obtained, since leukocytosis presents in 55% of patients with acute diverticulitis. Although imaging studies are not necessary for patients presenting with mild symptoms, ultrasonography, MRI, and CT scan can be performed to confirm the diagnosis [9].

An imaging study known as computed tomography (CT) is the most commonly used imaging study in the diagnosis and identification of the stage of diverticulitis an individual has. Roughly two-thirds of patients with acute colonic diverticulitis have an uncomplicated form of diverticulitis. Patients that present with acute uncomplicated diverticulitis are typically initiated on a course of antibiotics, although this is not always necessary. Uncomplicated diverticulitis

can typically be treated in an outpatient setting, unless complication or symptoms become worse. Computed tomography is able to improve patient selection for a more aggressive type of treatment by identifying the stage of diverticulitis. Failure to properly treat uncomplicated diverticulitis can possibly lead to the development of complicated diverticulitis [10]. Uncomplicated diverticulitis characteristically shows thickening of the colonic wall, whereas complicated diverticulitis is associated with abscesses or fistulas and obstruction or perforations of the colonic wall, often requiring surgical intervention [11].

Risk factors

There are many factors that play a role in the development of diverticulitis. As with other diseases, there is a heavy genetic component that contributes to the development of diverticulitis. In addition to genetic components, there are a variety of external factors contributing to the disease as well. Diet is a huge factor that contributes to diverticulitis, with fiber intake and red meat consumption playing the largest role. Additionally, medications such as steroids and anti-inflammatories, such as NSAIDs increase and individuals' risk for developing diverticulitis.

Genetic component

Both genetic and environmental factors put an individual at risk of developing diverticulitis. Previous twin studies have shown that genetic predisposition to diverticulosis accounts for 40-53% of all cases. Variation in the Laminin beta 4 (LAMB4) nucleotide is thought to contribute to colonic dysmotility that is associated with diverticulitis. Laminins are a type of heterotrimeric protein that is important in influencing cellular differentiation, migration and cellular adhesion. Laminins are vital for the maintenance and survival of tissues, and with malformation they can lead to defective formation of muscles [12]. Although the exact function of LAMB4 is still unknown, it is thought to play a role in regulating the intrinsic nervous system. When a mutation occurs in the genes that encode for laminins, there is a reduced expression of LAMB4. Reduced level of LAMB4 can cause alterations in the innervation of the intrinsic nervous system. Scientist believes that by altering the innervation of the intrinsic nervous system, the digestive system is not able to function normally and can lead to the development of diverticulitis [13].

Age

Diverticulitis is commonly found in individuals over the age of 65. The reason the risk associated with diverticulitis increases with age is due to the degeneration of the mucosal

wall. As the mucosal wall degenerates, protrusions through the mucosa are more likely to occur due to increased colonic pressure. This results in bulging points of weakness, which can typically be found at the insertion point of the vasa recta [14]. However, based on a population study of individuals diagnosed with diverticulitis from 1980 to 2007 in Rochester, New York, the incidence rate grew the largest in individuals younger than 50 years old. However, those younger than 50 were observed to have a less severe form of diverticulitis, more recurrence and a higher rate of survival due to complications [15].

Fiber Intake

The most important lifestyle associated risk factor with diverticulitis is the lack of dietary fiber in an individual's diet. Not eating enough fiber can cause a buildup of waste in the colon, leading to constipation, putting strain on the walls of your colon. This causes an increase in pressure on the colon. Increasing the pressure against the colon results in weak areas of the colon, causing diverticula. Previous studies observing a vegetarian diet with high levels of dietary fiber versus a non-vegetarian diet with dietary fiber intake shows that vegetarians had a 31% lower risk of developing diverticulitis compared to meat-eaters. Individuals who consumed greater quantities of dietary fiber had an overall decrease of 41% risk of developing diverticulitis, when compared to individuals consuming less fiber [16]. Further studies examining middle aged women with the highest level of fruit and vegetable intake, both vegetarians and meat eaters respectively, showed a 30% decreased risk for developing diverticulitis. Among men, a similar trend was observed [8].

Meat Consumption

Another dietary risk factor for development of diverticulitis is the consumption of red meat. A study consisting of 86 individuals diagnosed with right sided diverticulitis compared to 106 controls (individuals that do not currently have diverticulitis) found that the individuals that consumed red meat at least once per day had a twenty five times greater risk of developing diverticulitis compared to those who ate red meat less than once a week [17]. Additionally, another study in diet shows that a more western diet consistent of high consumption of red and processed meat, refined grains, sweets, french fries, and high-fat dairy has a greater risk of developing diverticulitis than a diet high in fruit, vegetables and grains [18].

Medications

Multiple medications can be associated to an increase risk for diverticulitis. One of the major classes of medications

increasing risk for diverticulitis is the regular use of NSAIDs and other anti-inflammatory medications [19]. Chronic uses of NSAIDs are associated with diverticular bleeding. Previous studies have shown that in Men who are chronic NSAID users (take more than twice a week) had the greatest risk for developing diverticulitis. Interestingly enough, those who regularly took a baby aspirin (81 mg daily) were at higher risk for diverticular bleeding but not for development of diverticulitis overall [20].

Management

In recent years, studies of individuals with diverticulitis have found that irreversible damage can occur in the gut microbe, which is crucial for the persistence of diverticulitis related symptoms. Pharmacologic treatments for diverticulitis include but are not limited to dietary fiber intake, antibiotics, probiotics and other anti-inflammatory drugs. Several treatments for diverticulitis are currently recommended; however, their effectiveness are still highly debated among the medical community [21].

Antibiotics

One of these treatments includes the use of the antibiotic rifaximin. Rifaximin has direct and indirect anti-inflammatory properties [22]. Rifaximin is able to control symptoms of small intestine bacterial overgrowth induced by diverticulitis, by inhibiting transcription factors and cytokines. Inhibition of these transcriptional factors and cytokines cause a reduction in the severity of bacterial growth, adhesion and translocation in the gut [21]. In a retrospective study of 142 individuals, after only one cycle of rifaximin individuals with diverticulitis saw significant reduction in abdominal pain, tenderness, bloating and disturbances in bowel habit. The study administered 3 cycles of rifaximin, quantified as a dosage of 2 x 400 mg tablets daily for 3 days, over the course of three months. After the third cycle was complete, the severity of symptoms associated with diverticulitis decreased with over 75% of participants reporting no abdominal pain at all [23].

Another study of 176 individuals with right colonic uncomplicated diverticulitis received a combination of intravenous and oral antibiotics of metronidazole and cefmetazole. Individuals were broken down into two groups, one containing 87 individuals and the other 89. One group received the combination of antibiotics only once, where the second group received the same antibiotics for 4 consecutive days in a row. This study concluded that the administration of antibiotics in the single day treatment was just as effective as the 4 consecutive day treatment in the prevention and recurrence of right colonic uncomplicated diverticulitis [24].

Anti-inflammatory

Another highly talked about type of anti-inflammatory used in the treatment and prevention of diverticulitis is mesalamine. Mesalamine is thought to exhibit an inhibitory effect on the inflammation cascade by reducing the production of interleukin, although the exact mechanism of action is uncertain [25]. Treatment with mesalamine is generally well tolerated with individuals experiencing mild to moderate side effects that range from hair loss to diarrhea. However, based on a comprehensive study comparing all studies where mesalamine was used as a treatment for diverticulitis, no evidence showed vast improvement while using mesalamine alone. In fact, one-third of the individuals being studied had a recurrence of diverticulitis [26].

Probiotics

Additionally, it is believed that probiotics can play a vital role in the treatment of diverticulitis. However, use of antibiotics and anti-inflammatory medication are preferred over treatment with probiotics. Probiotics are a type of live microorganism that in large quantities can alter the host microbe without significant increase to antibiotic resistance.

Probiotics are believed to work in several different ways. Probiotics have shown to inhibit pathogen adherence, improve defense of the mucosa, and cause stimulation of the immune system by pro and anti-inflammatory cytokines [27]. Recent studies investigated the effectiveness of probiotics in the treatment of symptomatic uncomplicated diverticulitis. The results proved that several strains of probiotics were all effective in the treatment of diverticulitis [14].

Surgical Intervention

Another treatment if necessary is through surgical intervention. Surgical management of diverticulitis has been questioned. However, in cases where a patient exhibits severe complicated diverticulitis with obstruction, surgical intervention is sometimes necessary [28]. With bowel obstruction, fecal matter must be removed usually through aspiration or a large suction device. Upon removal of the fecal matter, a laparoscopic technique is used to repair the damaged colon or peritoneum [29]. Emergent surgical intervention is often accompanied by an unfavorable rate of mortality. Due to complications in this type of surgery, physicians often opt for a less invasive treatment through use of antibiotics and anti-inflammatory drugs [30].

It is important to note that no one therapy alone can treat diverticulitis. Often a combination of therapies needs to be utilized in order to reduce symptoms and prevent

recurrence of diverticulitis. Recurrent diverticulitis can cause significant complications often requiring surgical intervention. Currently there are no appropriate means in determining which individuals will develop recurrent diverticulitis. However, several retrospective studies have aimed at categorizing cases into groups of low risk and high-risk individuals for developing recurrent diverticulitis [31].

Conclusion

Despite diverticulosis being very common, many individuals live asymptotically for the entirety of their life. Studies have shown that genetic predisposition, environmental factors such as diet and age can all increase risk for developing diverticulitis. Alteration and overgrowth of the intestinal microbe is a vital determinant in the development of diverticulitis. Several ways of treatment for acute diverticulitis include administration of antibiotics, anti-inflammatories, probiotics and as a last route when necessary, surgical intervention. As people continue to change their lifestyle habits, the rate of diverticulitis continues to increase worldwide. As the rate of diverticulitis increase, the amount of research being done to provide an accurate treatment plan continues to prevent recurrence and lead to complicated diverticulosis.

Occasionally conflicting research has been published on the treatment and management of diverticulitis. Some scientist argues that fiber intake and administration of antibiotics are ineffective methods of treatment and prevention of recurrent diverticulitis. Additional long-term research, following a patient's treatment plan with antibiotics, anti-inflammatories or probiotics needs to be conducted. Following larger groups of individuals over a long period of time will aid in the determinant of effective treatment once diverticulitis symptoms onset. The primary goal of treatment is to prevent recurrence of diverticulitis. As the number of episodes of diverticulitis increase, patient's risk of having severe complications also increases. As we know, genetic predisposition plays a significant role in the development of diverticulitis. Further research should be conducted on the genes and its pathway that results in the development of diverticulitis. Through gene mapping, scientist may be able to regulate gene expression of diverticulitis and inhibition of the genes itself. Although LAMB4 is thought to play a role in development of diverticulitis, the exact mechanism and role LAMB4 plays in the development of diverticulitis is still questioned. Continuing to study this protein may provide more information into exactly how reduced levels of LAMB4 contribute to development of diverticulitis. With additional research scientist may eventually be able to increase expression of this protein, reducing its contribution to the development of diverticulitis.

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