Colonic ischaemia, commonly referred to as ischaemic colitis, is the most common type of intestinal ischaemia. The term "ischaemic colitis" was used by Marston (1966) with three typical patterns of injury described: transient reversible ischaemia, ischaemic ulcers with stricturing, and gangrenous ischaemic colitis. Dominant presenting symptoms were colicky abdominal pain, vomiting, bloody diarrhoea, and hematochezia. Patients often have minimal signs on clinical examination. Most patients were diagnosed at colonoscopy. Two regions that are believed to be anatomically vulnerable to ischemic disease are "Griffith’s point", at the splenic flexure and "Sudeck’s critical point", of the Drummond marginal artery. Clinically, ischaemic colitis is classified as non-gangrenous or gangrenous.

Non-gangrenous ischaemic colitis involves the mucosa and submucosa and accounts for 80–85 percent of all cases of ischaemic colitis. Non-gangrenous ischaemic colitis is further subclassified into transient, reversible ischaemic colitis with a less severe form of injury and chronic, non-reversible ischaemic colitis, which includes chronic colitis and stricture and has a more severe form of injury.

Gangrenous ischaemic colitis accounts for the remaining 15–20 percent of cases and manifests as the most severe form of injury. It includes acute fulminant ischaemia with transmural infarction that may progress to necrosis and death. Specific indications for operation include peritonitis, perforation, recurrent fever or sepsis, clinical deterioration in patients refractory to medical management.

Relative indications include fulminant colitis, massive hemorrhage, chronic protein losing colopathy, and symptomatic ischaemic stricture.

Key words: ischaemic colitis, ischaemia, colon, mesenteric circulation.

INTRODUCTION

Colonic ischemia is usually the result of a sudden and most often temporary reduction in blood flow that is insufficient to meet the metabolic demands of the affected regions of the colon. Ischemic colitis is the most frequent form of ischemic injury to the gastrointestinal tract and the second most common cause of lower gastrointestinal bleeding.

Historically, colonic injury as the result of hypoperfusion was described by Boley et al in 1963 and in 1966, Marston et al established the term ischaemic colitis, reported on the three stages of ischemic colitis and described the natural history of the disease.

It has been estimated that ischaemic colitis is the most prevalent form of all gastrointestinal ischaemic disease, accounting for approximately 50-60 percent, and that it accounts for roughly 1 in 2000 acute admissions to hospital.

The incidence of ischaemic colitis in general populations ranges from 4.5 to 44 cases per 100 000 person-years. The risk increases two to four times with conditions like irritable bowel syndrome or chronic obstructive pulmonary disease.

ETIOLOGY

Ischaemic colitis etiologically can be divided into two categories, occlusive and non-occlusive. In occlusive disease, the cause of ischemia is a mechanical obstruction of the colon blood vessel. Non-occlusive ischemic colitis can be caused by a low flow state or a sudden, sometimes unexplained state of vasoconstriction. It is obvious that any pre-existing vascular disease can be an important factor in non-occlusive ischaemic colitis.

Causes of colonic ischaemia are listed in the Table 1. Occlusive ischaemia can be the result of arterial or venous obstruction, although the venous one is not so frequent. Arterial obstruction is most frequently caused by an em-
bolus or a thrombus, but occasionally may be related to trauma or, in the case of aortic reconstructive surgery, by ligation of the inferior mesenteric artery in the absence of good collaterals. In some prospective studies the incidence of colonic ischaemia following elective aortic surgery varies between 5 and 10 percent. However, the incidence in patients undergoing emergency surgery for ruptured abdominal aortic aneurysm is much higher and colonic ischaemia may be seen in as many as 60 percent of these patients.

More common form is non-occlusive colonic ischemia that most commonly affects the "watershed" areas of the colon that have limited collateral circulation such as the splenic flexure and rectosigmoid junction. A study of more than 1000 patients with ischemic colitis demonstrated that the left colon was involved in approximately 75 percent of patients, with about one-quarter of lesions affecting the splenic flexure. The rectum was involved in only 5 percent of patients, which can be explained because of collateralization of the inferior mesenteric artery with the systemic circulation through the hemorrhoidal vessels.

Non-occlusive ischaemia is a condition with still not completely explained pathophysiology. There is a group of patients in which this disease appears to occur spontaneously, without any identifiable reason. In others, conditions as cardiac failure, haemorrhage, sepsis or dehydration cause hypotension or shock, thus limiting mesenteric blood flow and causing ischaemic colitis. Medicaments with vasoconstrictive properties may be responsible for some cases of non-occlusive ischaemia. Some medicaments that also can cause colonic ischaemia are digitalis, diuretics, oestrogen, cocaine, pseudoephedrine and non-steroidal anti-inflammatory drugs. Patients with diabetes and those with chronic renal failure, on dialysis are known to be at increased risk of non-occlusive ischaemia, probably the result of the accompanying vascular disorder. Rarely, colonic distension associated with an obstructing colon cancer or severe constipation can result in ischaemic colitis proximal to the obstruction. In these cases the increased intramural pressure results in venous stasis, which eventually impairs the arterial supply, resulting in ischaemia.

**PATHOPHYSIOLOGY OF ISCHAEMIC COLITIS**

There is a number of factors that can be included in the hypoperfusion state that causes ischaemic colitis. Some of them are: general haemodynamic state, the degree of atherosclerosis, the existence of collateral circulation, neurogenic, humoral and local control mechanisms of vascular resistance. Abnormal products of cellular metabolism before and after reperfusion of an ischaemic segment are also important agents in the genesis of ischaemic colitis. It is logical to conclude that acute occlusion or hypoperfusion of a large mesenteric vessel usually results in transmural gangrenous ischaemia, on the other hand, acute occlusion of the intramural vessels can usually result in intramural, partial, non-gangrenous ischaemia. However, depending on the severity of occlusion or hypoperfusion, there are exceptions in both cases. The first tissue layer to demonstrate signs of ischaemia is colonic mucosa because of its metabolic activity. After the onset of ischaemia, ultrastructural changes occur within 10 minutes and cellular damage is extensive by 30 minutes. Sloughing of the colonic mucosa is followed by its oedema, submucosal haemorrhage and finally by transmural necrosis.

The first sign of intestinal ischaemia is hypermotility, that results in the feeling of severe abdominal pain, even though the ischaemic damage may be limited to the mucosa at this stage. As the ischaemia progresses, motor activity will cease and bacterial translocation will start along with consequential peritonitis.

A factor that can often be responsible for aggravating intestinal ischaemia is the phenomenon of vasospasm.
Ischemic colitis is by no means confined to the area of the splenic flexure and there does not appear to be any area of the colon that is entirely protected. Even the rectum, which is normally well perfused from both the inferior mesenteric and iliac arteries, can be involved in some cases. In a review of 1024 patients in the literature, Reeders et al. found the incidence to be as follows: right colon, 8 percent; transverse colon, 15 percent; splenic flexure, 23 percent; descending colon, 27 percent; and sigmoid colon, 23 percent. Rectal ischemia has been described in 4 percent of the cases in the above review. In a review of 250 cases of colonic ischemia, the left colon was, also, most commonly affected, and the frequency of involvement of all sites was as follows: right colon 12 percent, transverse colon and splenic flexure 17%, splenic flexure alone descending colon or sigmoid 40 percent, rectum 6 percent still, this distribution does not appear to be confirmed in other reports, for example, Longo et al. reported in their series that the anatomic distribution of disease was different than that usually reported with ischemic colitis: right colon, 46 percent; splenic flexure, 4 percent; descending colon, 7 percent; rectosigmoid, 40 percent; and pancolitis, 8 percent. Furthermore, one of the studies conducted on 273 biopsy proven ischemic colitides that demonstrated the prevalence of right-sided colitis (26 percent right-sided vs. 74 percent others) also showed notably worse prognosis and outcome in these patients. One factor that may predispose elderly patients to colonic ischemia is related to age-related tortuosity of the colic arteries was observed, with the vessels supplying blood to the colon becoming more tortuous with advancing age. It is hypothesized that this increased tortuosity may result in increased vascular resistance, a possible predisposing condition for ischemia.

**CLASSIFICATION**

The three degrees of severity of ischemic colitis as classified by Marston et al. include transient ischemia, ischemic stricture as a late consequence of a partial-thickness injury, and the gangrenous form. Gangrenous form is seen in 15% to 20% of all ischemic colitis cases. Of the 80 percent to 85 percent of non-gangrenous cases, most are transient and reversible. Chronic damage in the form of persistent segmental colitis occurs in 20 to 25 percent and strictures in 10 to 15 percent of cases. The transient form is characterized by its reversibility and is associated with mucosal edema, congestion, superficial ulcerations, and petechiae. Gradually, if perfusion is restored at this stage, the blood is resorbed, and the edema resolves with full recovery in 1 to 2 weeks. The ischemic stricture represents a partial-thickness injury that involves the mucosa and muscular layers and results in consequential fibrosis and narrowing of the lumen over a period of weeks to months. Dilatation proximal to the stricture suggests that the stricture may be significant, while the presence of a simple asymptomatic stricture may not be of clinical importance.
Gangrenous ischemic colitis is characterized by full-thickness necrosis and infarction. Gross examination reveals the segment to be dilated with gray-green or black discoloration (Picture 1). Patients with gangrenous form are prone to life-threatening complications such as perforation, sepsis which are absolute indications for immediate surgical treatment.

HISTOPATHOLOGY

The transient form of ischemic colitis is characterized by the changes that are confined predominantly to the mucosa and submucosa and consist of an intense inflammatory reaction with superficial devitalizing of the mucosa, submucosal hemorrhage, and edema (Picture 2). In the case of the structuring form, marked fibrosis is seen within the muscularis, the mucosa is replaced by granulation tissue, and hemosiderin-filled macrophages are present. Gangrenous ischemic colitis is characterized by intense inflammation with transmural necrosis (Picture 3).

DIAGNOSIS

History and physical examination

Unfortunately, despite the existence of several distinct forms of this disease, presented symptoms are often very similar and when considered alone, non-specific. So, the clinical setting of these symptoms is often equally important and should raise the physician’s suspicion of the existence of ischemic colitis. The typical patient is elderly one with one or more accompanying risk factors such as atherosclerosis, congestive or ischemic heart disease, a recent hypertensive episode and/or taking certain vasoactive medications. However, there are reports of colonic ischemia affecting young patients, usually secondary to drugs or profound hypotension. A careful history should be taken to try and identify these potential risk factors.

Abdominal pain is one of the most common symptoms of colonic ischemia, being present in almost 80 percent of patients. In patients where the ischemic damage is localized to the mucosa, the afferent autonomic nerves transmit visceral pain, not accurately localized and, when arising from the left colon and rectum, it is typically localized in the left lower quadrant of the abdomen. Visceral pain arising from the right colon is often localized in the central regions of the abdomen. Part of this visceral pain is the result of increased tension in the bowel wall caused by intense hypermotility and spasmodic contractions of the ischemic colon. This intestinal hypermotility often manifests as abdominal cramps. In the case of transmural ischemia, the pain will be caused by parietal peritoneum irritation with evident peritoneal signs. These peritoneal signs may be localized or diffuse depending on the severity of the disease. Other symptoms of ischemic colitis include diarrhea (54 percent), abdominal distention (63 percent) and nausea/vomiting (51 percent). Rectal bleeding is usually mild and can vary from bright red (with left-sided ischemia) to maroon blood (with right-sided ischemia) mixed with the stool. The bleeding is usually self-limiting and transfusion is rarely required.

Patients are usually haemodynamically stable with no sign of peritonitis because of the fact that most patients do not have transmural disease. However, when the disease is transmural, patients present with very serious clinical picture.

Laboratory tests

In patients with ischemic colitis, laboratory tests are most commonly non-specific. Leucocytosis is almost always present, especially with more advanced disease. Electrolyte and renal function abnormalities secondary to dehydration may also be seen. Up to date, there’s no reliable, specific biochemical marker. Creatinine kinase, alkaline phosphatase, lactate dehydrogenase, diamine oxidase and inorganic phosphate are among the biochemical markers that have been examined with no evident success. Lange and Jackel reported that a raised serum lactate concentration is the best marker for mesenteric ischaemia. In a study of 85 patients with acute abdominal symptoms, the authors found that a raised plasma lactate concentration was always a sign of a life-threatening condition and usually indicated the need for an emergency operation. As a marker of mesenteric ischemia, its sensitivity was 100 percent and its specificity was 42 percent. Still, serum lactate levels rise with intestinal ischemia. However, any and all tissue hypoxia will result in its production and the fact is that lactate, produced by the ischemic gut, is extracted from the portal circulation by the liver. Thus, in the early stage of intestinal ischemia, serum lactate levels may be normal.

There were studies that assessed measuring of serum levels of the stereoisomer D-lactate. D-Lactate is produced only by bacteria, especially in the colon, as a normal product of bacterial fermentation. Serum baseline levels of D-lactate are very low in healthy humans, probably the effect of an intact colonic mucosal barrier. With colonic ischemia, intestinal permeability increases, allowing D-lactate to enter the circulation. Since the liver is unable to metabolize D-lactate, it has the potential to be an early marker of intestinal ischemia. When serum D-lactate level was measured in patients undergoing abdominal aortic aneurysm repair, the sensitivity and specificity in predicting colonic ischemia was 82 and 77 percent, respectively. Further confirmation of these findings is required.

Radiological examinations

Upright and supine roentograms of the abdomen are mostly non-informative in cases of colonic ischaemia. However, they should be performed in case of visceral perforation or bowel obstruction. The findings are usually non-specific, and include bowel dilatation and air-filled bowel loops. In approximately 20 percent of patients, more specific findings of colonic ischaemia may be seen, such as thumb printing (from submucosal oedema and haemorrhage) and mural thickening. Findings of barium enemas can be predictive of ischemic colitis, but often they do not exclude other forms of colitis. Because of that and the fact that distension of the colon with air may compress intramural blood vessels and further decrease blood
low, this radiological examination should rarely be used in patients where there is a reasonable suspicion of ische-
mic colitis. Also, if barium is used in the examination, then subsequent endoscopic, computed tomography (CT) and angiographic assessment of the colon can be very dif-
ficult as a result of the retained barium.

CT imaging can be used in the diagnosis of patients with abdominal pain of unknown aetiology. It is a very useful for ruling out other diagnoses and may provide evi-
dence in favor of ischaemic colitis. Segmental bowel wall thickening is seen in most cases and can be graded as mild (3—6 mm), moderate (6—12 mm) and severe (12 mm). In a study of 54 cases of ischaemic colitis, the average wall thickness of the ischaemic area was 8 mm, mild to moderate ascites was present in 37 percent and intramural pneumatosis was only seen in 6 percent. An attempt was made to use the severity of the CT findings to predict the severity and prognosis of the ischaemic disease. However, an important finding of this study was that CT findings did not correlate with, nor did they predict, the develop-
ment of bowel infarction.

Non-invasive Doppler sonography has been validated as a useful tool for detecting intestinal ischaemia both in ani-
mals and in humans. The use of colour Doppler has fur-
ther enhanced the utility of this diagnostic tool. The ab-
seence of arterial flow in the wall of the ischaemic colon on initial colour Doppler sonography is not only diagnos-
tic, but is also predictive of an unfavorable outcome. As
this technique becomes more widely available, it may in-
deed play a greater role in the diagnosis of ischaemic coli-
tis.

Mesenteric angiography does not play a large role in the
diagnosis of ischaemic colitis. When the disease is thought to involve the left colon, mesenteric angiography may identify evidence of atherosclerotic vascular disease, but it seldom identifies an acute arterial obstruction as the cause of the colonic ischaemia. In cases of non-occlusive ischaemia, by the time the angiogram is performed, blood flow to the colon is usually restored and, thus, the angiogram will be normal. With suspected right-sided is-
chaemic disease, and in cases were colonoscopy can't provide the proof of ischaemic colitis there may be a role for angiography, in particular if acute mesenteric ischae-
mia is suspected.

More recently, magnetic resonance imaging (MRI) and indium-III white cell scans have been employed in the di-
agnosis of ischaemic colitis.

**Endoscopic examinations**

Colonoscopic assessment of the mucosa is a very sensi-
tive and specific method of evaluating the colon for is-
chaemia. Visual inspection of the mucosa will not always
allow the physician to make a firm diagnosis, the ability
to biopsy allows the differentiation of inflammatory, in-
fected and ischaemic colitis. With early ischaemia, the
mucosa may appear pale and oedematous with inter-
spersed areas of hyperemia. With more significant ischae-
mia there will be evidence of submucosal oedema and haemorrhage, characterized by blue or black nodules pro-
truding into the lumen of the bowel. It is these nodules
that correspond to the thumbprinting of the bowel. These
submucosal les-
sions are seen most frequently in the first 2—3 days after
the onset of ischaemia and resolve quickly. Also, it has
been shown that histological findings consistent with
those of ischaemic colitis are most frequently observed on
the first day and less frequently later on. So, colonoscopy
should be performed as early as possible and, preferably,
within the first 3 days after the onset of symptoms to en-
sure the best diagnostic potential. Since colonoscopy only
visualizes the mucosa, it is not able to distinguish mucosal
from full thickness ischaemia.

Care must be taken not to over insufflate the colon,

The majority of patients with ischaemic colitis present
with mild form, non-transmural disease. Their clinical
presentation is not serious, consisting of mainly abdomi-
nal pain with no peritonitis or signs of sepsis. These pa-
tients can be managed on an outpatient basis with liquid
diet, close observation, and antibiotics. More serious
cases require hospitalization, and more aggressive treat-
ment that includes bowel rest, nasogastric suction, and in-
travenous fluid replacement. Factors that may be contrib-
uting to the ischaemia should, wherever possible, be cor-
corrected. Cardiac function and oxygen delivery should be optimized and, if possible, medications known to induce mesenteric vasoconstriction should be withdrawn. Broad-
spectrum antibiotics, that cover both aerobic and anaero-
bic coliform bacteria, should be administered. Although
there is no good evidence that antibiotic coverage is bene-
ficial, it is logical to conclude that the bowel wall perme-
ability with the potential for bacterial translocation is in-
creased by ischaemia. Patients should be closely ob-
served for the signs of complications. If the patient be-
comes septic or develops peritoneal signs, urgent laparo-
tomy is indicated. These patients may have a fever, leuko-
cytosis and evidence of free intra-peritoneal air on roent-
gograms. At the time of surgery, all of the ischaemic colon
should be resected with a margin of normal healthy bowel.
Judging the extent of ischaemia intra-operatively may be
difficult, as the surgeon may find that the serosa
appears healthy even in the presence of underlying mu-
cosal infarction. Intra-operative colonoscopy and mucosal
inspection of the resected bowel segment may prove use-
ful to ensure that all parts of ischaemic colon have been
included in the resection. When a segmental resection for
right-sided colonic ischaemia is performed, a primary
anastomosis may be considered, especially if the surgeon
djudges the distal colonic margin to be well perfused and
provided the patient is haemodynamically stable. How-
ever, if there are any concerns about the stability of the
patient and/or the vascular perfusion of the remaining co-

Ishemični kolitis


Ključne reči: ishemični kolitis, ishemičnost, kolon, mezenterična cirkulacija.

REFERENCES