

Ischaemic Colitis: Practical Challenges and Evidence-Based Recommendations for Management

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ABSTRACT

Ischaemic colitis (IC) is a common condition with rising incidence and, in severe cases, a high mortality rate. Its presentation, severity and disease behaviour can vary widely and there exists significant heterogeneity in treatment strategies and resultant outcomes. In this article we explore practical challenges in the management of IC and where available, make evidence-based recommendations for its management based on a comprehensive review of available literature.

An optimal approach to initial management requires early recognition of the diagnosis followed by prompt and appropriate investigation. Ideally, this should involve the input of both gastroenterology and surgery. CT with intravenous and oral contrast is the imaging modality of choice. It can support a clinical diagnosis, define the severity and distribution of ischaemia and has prognostic value. In all but fulminant cases, this should be followed (within 48 hours) by lower GI endoscopy to reach the distal-most extent of the disease, providing endoscopic (and histological) confirmation. The mainstay of medical management is conservative/supportive treatment, with bowel rest, fluid resuscitation and antibiotics. Specific laboratory, radiological and endoscopic features are recognised to correlate with more severe disease, higher rates of surgical intervention and ultimately worse outcomes. These factors should be carefully considered when deciding on the need for and timing of surgical intervention.

KEY MESSAGES FOR CLINICAL PRACTICE

- Ischaemic colitis is common, rising in incidence, and is associated with a high mortality rate, especially in cases where surgical intervention is required
- CT with intravenous contrast is the imaging modality of choice. This should be followed by lower GI endoscopy (within 48 hours), aiming to reach the distal-most extent of the disease to achieve an endoscopic (and histologic) diagnosis.
- Isolated right colonic involvement is predictive of poorer outcomes, including higher rates of surgical intervention and death
- High-quality supportive/conservative treatment remains the backbone of medical therapy. Antibiotics are recommended but there is little evidence for the benefit of other pharmacological interventions.
- Surgical intervention should be considered in the setting of circulatory compromise, abdominal pain without rectal bleeding, pan-colonic or isolated right sided distribution and in patients with peritoneal signs.

INTRODUCTION

Ischaemic colitis (IC) represents the manifestations of compromised blood supply to the colon (ischaemia deriving from the Greek *iskhaimos* meaning “stopping blood”). When blood supply (however transiently) becomes insufficient to meet the metabolic demands of the colon, mucosal inflammation occurs, giving rise to ulceration and haemorrhage.

Inflammation stems from both direct ischaemic insult and reperfusion injury; the latter is caused by the release of reactive oxygen species and inflammatory cytokines during restoration of normal tissue perfusion(1), damage from which may exceed the direct effects of ischaemia. Bacterial translocation, intestinal vasospasm, and intestinal dysbiosis (from disruption of the gut microbiome) also contribute to tissue damage(2). Colonic ischaemia occurs in a top-down distribution; the mucosa, as the most metabolically active layer of the colon, is the first layer to be affected. Sloughing of villous tips and mucosal oedema are followed by submucosal haemorrhage and (eventually) transmural necrosis. Clinical manifestations are dependent upon the site and extent of ischaemic insult, but include abdominal pain, diarrhoea, melaena and rectal bleeding. The spectrum of severity ranges from self-limiting within days, to requiring emergency surgical resection.

IC should be differentiated from mesenteric ischaemia. Acute mesenteric ischaemia (AMI) represents complete loss of blood supply to a segment of bowel, leading to rapid necrosis and necessitating emergency laparotomy. It is usually due to acute thromboembolic arterial occlusion (often of the superior mesenteric artery). However, non-occlusive arterial AMI can also occur (generally in the setting of critical illness and haemodynamic compromise); less commonly, it may stem from mesenteric venous thrombosis (which may co-exist with chronic pancreatitis or portal hypertension)(3). Chronic mesenteric ischaemia (“mesenteric

angina”) involves intermittent crampy, post-prandial abdominal pain, typically within an hour of oral intake, over a period of at least 3 months.

IC is a relatively commonly encountered clinical syndrome (incidence of 22.9/100,000 person-years(4)), with substantial heterogeneity in clinical approach. There also exists variation in the specialty of clinicians responsible for managing IC patients; some cases are managed by surgeons, others by physicians (gastroenterologists). We, therefore, carried out a literature review in order to make evidence-based recommendations for the practical management of patients with IC.

METHODS

Our literature review search strategy and selection criteria can be found in the online supplementary material along with our Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram. Two reviewers (AH & TC) independently screened citations and abstracts before retrieving full-text publications of all potentially eligible articles.

AETIOLOGY

Consistently, old age (i.e. over 60), atherosclerosis, smoking, chronic kidney disease (CKD), and atrial fibrillation have been demonstrated to increase the risk of developing IC(5, 6).

Certain medications, such as NSAIDs and oestrogen therapy(7), also increase risk. There is interplay, of course, between these risk factors – patients with CKD have higher rates of diabetes mellitus, anaemia and hypertension(6); they also have changes in vascular elasticity, and haemodialysis can lead to microthrombus generation(5). Causes of IC can be

categorised into thromboembolic; haemodynamic insufficiency (often in the setting of a predisposing factor); iatrogenic; and drug-induced. Thromboembolic causes include atrial fibrillation, pro-thrombotic conditions such as anti-phospholipid syndrome (leading to both arterial and venous thromboemboli), and concurrent malignancy. Haemodynamic insufficiency (a “supply and demand” problem) occurs with cardiac failure, severe anaemia, hypovolaemia and septic shock; atherosclerosis (causing vascular narrowing) can be thought of as a predisposing factor to these. Iatrogenic IC can occur post-operatively during open abdominal aortic aneurysm (AAA) repair – either through cross-clamping of the aorta, or due to sacrifice of the inferior mesenteric artery due to its location in the aneurysmal sac. It can also arise through micro-emboli generated by disruption of aortic plaques during endovascular repair(8). Potential drug causes of IC are wide-ranging and include chemotherapeutic agents, vasopressors, oestrogen therapy, cocaine, amphetamines, ergotamine, antipsychotics and NSAIDs amongst others(9, 10). These agents should be specifically excluded when taking a history from patients with suspected IC.

CLINICAL FEATURES

Symptoms

IC is a clinical spectrum. The constellation of symptoms varies in relation to the anatomical distribution and severity of the colitis. The most common symptoms (with approximate prevalence) are abdominal pain (87%), PR bleeding (84%), and diarrhoea (56%)(11). PR bleeding is more common in left-sided colitis, and often absent in isolated right-sided colitis, where pain predominates. Bleeding usually manifests as fresh red blood PR, particularly when associated with distal colitis; melaena may occur with more proximal colonic involvement. The left colon is affected in around 75% of cases of IC, with approximately 25%

involving the splenic flexure; isolated right colon ischaemia (IRCI) occurs in around 10%(1). On examination, mild to moderate tenderness may be elicited, but usually without generalised peritonism. Pyrexia is uncommon, but if present may suggest infarction(1, 12).

Anatomical distribution

Typically, “watershed” areas of the colon are most frequently affected – these zones are at the junctions of vascular territories and have the least robust collateral blood supply(13). The splenic flexure is particularly susceptible to ischaemia(14) – Griffith’s point describes the point between territories formed by the middle colic branch of the superior mesenteric artery (SMA) and the right colic branch of the inferior mesenteric artery (IMA). Similarly vulnerable is Sudeck’s point, the junction between the last sigmoid branch and the superior rectal branch of the IMA in the rectosigmoid (Figure 1)(12). Collateral supply to the colon comes largely from the marginal artery of Drummond, which forms a vascular arcade connecting the SMA and IMA, and is subject to anatomical variants – in up to 5% of cases, blood supply from the marginal artery is absent at the splenic flexure(1). Furthermore, in up to 50% of cases the marginal artery is underdeveloped in the right colon(12), which may explain why the right colon may be vulnerable in low flow states and why some patients are more predisposed to right-sided involvement. The caecum is also felt to be a relative watershed area and rarely, isolated caecal involvement may occur. The rectum is usually spared in IC, as it receives collateral blood supply from the middle and inferior rectal arteries, which are branches of the internal iliac vessels rather than the IMA.

Prognostic factors

The most frequently cited factors to confer an unfavourable outcome in IC are the absence of rectal bleeding(15-17), and right-sided colonic involvement(4, 5, 15-17). Given other areas of the colon are more susceptible to ischaemic insult, right-sided involvement can be considered to be a marker of severity(18). Furthermore, IRCI can be the harbinger of incipient acute mesenteric ischaemia due to large vessel occlusion (given the area supplied by the SMA includes both distal small bowel and right colon)(19, 20).

Co-existent atrial fibrillation(21) and atherosclerotic disease(4) promote less favourable outcomes. Older patients and those with COPD also tend to have poorer outcomes(4), the latter likely owing in part to the cardiovascular sequelae of smoking. Other negative prognostic factors include CKD(5, 11), thrombocytopenia(5), high CRP(5), and high WCC(21). Unsurprisingly, examination findings of guarding or peritonism are linked to a poorer prognosis(15, 16).

GASTROINTESTINAL INVESTIGATION

Laboratory tests

All patients with suspected IC should have a basic workup including full blood count, renal profile, liver profile, CRP, serum lactate, coagulation studies, and group and save. Based on limited evidence, there doesn't currently appear to be any role for faecal markers of inflammation (e.g. calprotectin) in IC(22). Table 1 outlines laboratory findings indicative of more severe disease(19). In addition, initial investigations should also include faecal culture, clostridium difficile toxin assay and studies for ova, cysts and parasites(23).

Imaging

There is currently no standardised pathway for imaging in patients with IC; as a frequently misdiagnosed condition, it is often picked up as part of a workup for the “acute abdomen”, which usually includes CT. Where renal function allows, CT should be performed with intravenous contrast; formal CT angiography is not necessarily required unless AMI is suspected or IRCI is found. Oral contrast is not necessary and usually unhelpful, as it hinders assessment of bowel wall enhancement. Patients with IC demonstrate imaging features of colitis, such as bowel wall thickening and pericolic fat stranding; these are often seen in a segmental distribution, with the left colon most frequently involved(24). However, it must be noted that these imaging findings are non-specific; only approximately 15-39% of patients with bowel wall thickening on CT have been found to have endoscopic features of ischaemia(25). Figures 2 and 3 demonstrate common CT findings.

Concerning features on CT include right-sided involvement, colonic dilatation, pneumatosis and free abdominal fluid(26). Patients with severe disease necessitating surgical intervention and/or leading to death are five times as likely to have right-sided colonic involvement(18). Factors suggesting an alternative diagnosis include the absence of target sign (i.e. ring of submucosal oedema between enhancing mucosa and serosa), presence of a stricture upon presentation, and mucosal hyperenhancement; such findings might raise suspicion of Crohn’s disease(27). However, it is recognised that patients with established IC may develop strictures after the acute phase of the disease; in a case series of 8 such patients, a typical CT appearance was a single area of concentric wall thickening, with greater enhancement in the portal phase than arterial phase, and vasa recta prominence(28).

Ultrasound of the bowel can (with adequate expertise) also elicit the diagnosis, can differentiate between left and right sided disease(29), and represents a valid alternative for patients unable to tolerate contrast media for CT. Absence of flow on colour Doppler denotes more severe disease and confers poorer outcomes(30), as does lack of enhancement with microbubble ultrasound contrast medium. However, the inherent user dependency of ultrasound (combined with its lack of out-of-hours availability) renders CT the imaging modality of choice.

Endoscopy

Common endoscopic findings include scattered erythematous mucosa and petechial haemorrhages, with or without erosion and ulceration(31). Figure 4 demonstrates the single stripe sign (a single longitudinal strip of ulcerated or inflamed colon)(32). Features suggesting gangrenous transformation include dark and dusky mucosa, with blue-black mucosal nodules. There is a paucity of robust data regarding the correlation between endoscopic findings and clinical severity of disease. However, previous attempts have been made to risk stratify patients based on endoscopic findings with longitudinal recesses or erosions being considered lower risk and longitudinal or circumferential ulcers considered high risk. On this basis, patients with endoscopically severe IC have been found to have longer hospital stays, as well as higher background rates of ischaemic heart disease and connective tissue disorders(33).

The planned extent of lower GI endoscopy should be based upon the distribution of inflammation seen at CT – the American College of Gastroenterology (ACG) recommends termination of the examination upon reaching the distal-most extent of disease(23). As

most cases of IC involve the left colon, flexible sigmoidoscopy is usually sufficient to achieve an endoscopic and histopathological diagnosis, but where complete colonic evaluation is necessary, minimal insufflation using carbon dioxide (as opposed to air) is recommended(23). As there is evidence to suggest that the diagnostic yield reduces over time, early endoscopic examination is advocated within the first 48 hours(23).

As IC may mimic other conditions (such as colorectal malignancy) at endoscopy, histology is important to confirm the diagnosis and exclude alternative pathologies. The most commonly observed histological features are mucosal atrophy, hyperaemia, oedema and features of acute inflammation. Unsurprisingly, patients with gangrenous disease demonstrate both endoscopic and microscopic features of necrosis. Traditionally, “ghost cells” have been viewed as pathognomonic of colonic ischaemia – however, data suggest these to be an inconsistent and therefore unreliable finding(34).

CARDIOVASCULAR INVESTIGATION

Patients with IC often have cardiovascular risk factors, including atrial fibrillation, hypertension, and CKD. As such, they are more likely to have a potential cardiac precipitant of thromboembolic IC (e.g. arrhythmia or valvular abnormality), detectable by a combination of electrocardiography (ECG) and echocardiography. The most commonly observed cardiac abnormality is atrial fibrillation (either paroxysmal or sustained), which in one study occurred in 20% of patients with IC (n=60) – in the same cohort, 25% required anti-arrhythmic medication and 32% needed anticoagulation(35). All patients with suspected IC should have an ECG, and all patients with confirmed IC should receive an

echocardiogram. A Holter monitor should be considered to exclude paroxysmal arrhythmias.

MANAGEMENT

Treatment of IC comprises both medical and surgical components, and so patients should receive joint gastroenterology and surgical input. In mild cases, and in the absence of factors predictive of a need for operative intervention (table 1), emphasis lies on medical therapy. However, in borderline cases or where operative intervention appears necessary, patients require frequent surgical review to determine the optimal time for intervention; such patients may be best placed on a surgical ward with additional gastroenterology input. Our suggested algorithm for management can be seen in figure 5.

Medical management

The mainstay of medical management is careful supportive treatment, with correction of any precipitating factors. In addition to IV fluid resuscitation and blood glucose control (in diabetics), this generally consists of bowel rest and intravenous antibiotics(18). Bowel rest is achieved through fasting and in the presence of ileus, nasogastric tube placement. The duration of bowel rest will depend on severity and clinical response but in general, most improve within 2-3 days (although it is thought to take 1-2 weeks for the colon to heal)(23). As noted in the ACG clinical guideline, there is little robust evidence regarding antibiotic choice; consensus suggests combining anaerobic cover with a third-generation cephalosporin or fluoroquinolone(23). There is also a paucity of data regarding duration of antibiotic treatment, but expert consensus has suggested a pragmatic approach that involves review after 72 hours. If no clinical improvement is seen by this point, then

consultation with a microbiologist is recommended to help refine the antibiotic regimen. Where clinical improvement is seen, completion of a 7-day course has been advocated(23). In more severe cases where bowel rest is indicated and the course expected to be protracted, parenteral nutrition (PN) is indicated(23). Beyond antimicrobial cover, there are no comparative studies of medical therapies in IC, and there is no evidence to support the use of aminosaliclates, corticosteroids or immunomodulators. Prophylactic low molecular weight heparin is generally recommended but there is no established role for formal anticoagulation in the acute setting. Secondary prevention with antiplatelets and anticoagulants should, however, be considered at time of discharge; as there is a lack of evidence in support of specific risk-reducing medical therapies following an episode of IC, secondary prophylaxis should be tailored to individual thromboembolic risk factors. Aspirin, then, is appropriate for those with ischaemic heart disease, whereas Clopidogrel should be considered for patients with peripheral vascular disease or previous cerebrovascular disease; oral anticoagulants are recommended for patients with atrial fibrillation.

The thrust of monitoring for response to treatment should be through frequent clinical review (including abdominal examination) and careful monitoring of vital signs. In addition to worsening (or non-resolution) of symptoms, signs such as persistent fever and/or deterioration in biochemical markers (CRP, white cell count or lactate) should prompt re-investigation. This should include consideration of repeat CT scanning and endoscopic re-evaluation.

Surgical management

Certain factors have been identified that can indicate more severe disease, predict failure of conservative management and a need for surgery (table 1). The presence or absence of these can inform consideration of semi-elective surgical intervention in the face of probable non-resolution(5, 19, 20, 26, 33).

Table 1. Features associated with severe ischaemic colitis and failure of conservative management

Patient factors	Clinical features	Laboratory tests	Cross-sectional imaging
Male gender	Peritoneal signs evident	Anaemia	Free intra-peritoneal fluid
Pre-existing renal dysfunction	Absence of PR bleeding	Leucocytosis	Disease localised to or involving right colon
History of atrial fibrillation	Tachycardia	Hyponatraemia	
		Thrombocytopenia	
		Elevated CRP	
		Elevated serum lactate	

Depth of mural involvement can also be used to classify severity(36). Type 1 IC describes inflammation limited to the mucosa, with type 2 denoting muscularis layer involvement, and type 3 transmural inflammation. Depth of inflammation is best judged using cross-sectional CT imaging as endoscopy alone cannot reliably confirm or exclude transmural involvement(37). For patients with type 1 or 2 IC and no evidence of systemic compromise, conservative management is an appropriate initial approach. However, evidence suggests that in patients with type 2 IC and systemic compromise (i.e. circulatory collapse and/or

organ failure), operative intervention should be considered. Type 3 IC is generally accompanied by systemic compromise and necessitates surgery(38). Other factors that should prompt consideration of operative intervention include persistent abdominal pain without rectal bleeding, pan-colonic or isolated right sided distribution and the presence/development of peritoneal signs(16, 34, 39).

Surgical intervention in IC is associated with higher morbidity and mortality than patients managed conservatively (table 2). However, clearly selection bias exists here, as co-morbid patients with more severe disease are more likely to require surgery. Surgical intervention usually involves segmental resection and colostomy formation, with the average post-operative hospital stay typically lasting several weeks; many require intensive care admission. Table 3 demonstrates risk factors for post-operative mortality and such risk factors are understood to be additive(38, 40). Based on a study of 177 patients, the Ischemic Colitis Mortality Risk (ICMR) score was proposed (table 2, factors in bold). The number of factors present results in a score ranging from 0-5 with mortality rate estimates of 10.5%, 28.9%, 37.1%, 50.0%, 76.7% and 100.0% for each ascending stratification(40).

Table 2. Risk factors associated with increased post-operative mortality (factors in bold are included in the Ischemic Colitis Mortality Risk (ICMR) score(40))

Risk factors associated with increased post-operative mortality
Age >75
Multiple organ failure
ASA status \geq 4
Intra-operative blood loss > 500ml
Pre-operative lactate >2.5
Acute kidney injury
Pre-operative or intra-operative catecholamine use
Low output heart failure
Subtotal or total colectomy

Complications

Complications include perforation, abscess formation, and strictures. Perforation, which occurs in the context of transmural inflammation and sometimes gangrenous ischaemia, may be accompanied by sepsis, and requires laparotomy. Abscess formation generally occurs secondary to a (sometimes sealed, localised) perforation; percutaneous drainage may be necessary. Fulminant ischaemic pancolitis is rare(3), but is potentially life-threatening, and may also necessitate colectomy.

One key 'complication' of IC is the persistence of symptoms (in the absence of a fulminant decline) to the point where surgical resection is felt to be beneficial. This may be failure of diarrhoea or rectal bleeding to resolve within 1-2 weeks, persistent post-prandial pain, or the development of a protein-losing colopathy. The latter describes a constellation of ongoing weight loss, hypoalbuminaemia, inability to sustain oral intake, and failure to thrive

with conservative management. In most cases this will be a clinical diagnosis, but elevated faecal clearance of alpha-1-antitrypsin is supportive.

Post-inflammatory strictures can form following conservative management, and may occur in up to 10% of cases(41). As inflammation tends to be segmental (due to its vascular aetiology) strictures tend to be relatively long – as such, they are more likely to require surgical intervention, with either stricturoplasty or resection.

Post-operative complications of surgical intervention include anastomotic leak, rectal stump leak, stoma-related issues, malabsorption syndromes and short gut syndrome. Around 16% of patients will experience surgical complications, and these patients are often found to have ischaemic changes at the resection margins(42). Between 20-29% of patients will require second-look laparotomies, due to clinical deterioration or based upon findings during their initial laparotomy(40).

As noted, parenteral nutrition may be required – associated complications include line sepsis, deranged liver function tests, and refeeding syndrome.

Long term outcomes

Recurrence of IC is uncommon, with 5-year recurrence rates reported to be 10.5%; these patients appear to have a similar clinical presentation to index presentation(43). No clear data exist on long-term dysplastic risk following IC – most cases run an acute course, with relatively few resulting in a state of chronic inflammation which might predispose to dysplastic transformation (as is observed in ulcerative colitis, for example).

Table 3. Outcomes in ischaemic colitis

	Year	Number of patients	Management		In-patient mortality	
			Non-operative	Operative	Non-operative (%)	Operative (%)
Reissfelder et al	2011	177	0	177	-	85 (48)
Moszkowicz et al	2014	191	17	174	0 (0)	84 (48)
Medina et al	2004	53	35	18	0 (0)	5 (28)
Paterno et al	2010	253	205	48	10 (5)	16 (33)
Sadot et al	2014	117	96	21	3 (3)	2 (10)
Genstorfer et al	2014	100	-	100	-	54 (54)
Glauser et al	2011	49	45	4	0 (0)	1 (25)
Flobert et al	2000	60	39	21	3 (7)	4 (20)
Gilshtein et al	2018	63	50	13	12 (24)	6 (50)
Castleberry et al	2012	115	-	115	-	43 (37)
Anon et al	2005	69	54	15	1 (0.02)	7 (46)
Cosme et al	2013	135	123	12	4 (0.03)	4 (33)

CONCLUSIONS

The management of IC depends upon severity at presentation and the presence or absence of poor prognostic features; it is best delivered by a multidisciplinary team including both gastroenterologists and surgeons. Prompt recognition and appropriate investigation, initially with CT and then with lower GI endoscopy, is key to making the diagnosis and risk stratifying patients. Although the majority of cases will settle with conservative management, a minority will require operative intervention and the mortality amongst this group is high. An understanding of factors which predict surgical outcome is necessary in order to make crucial management decisions and counsel patients appropriately.

LICENCE FOR PUBLICATION

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ETHICAL APPROVAL

Ethical approval is not necessary for this type of review article.

CONTRIBUTIONS

AH, TC, MAS and GW were responsible for planning the content and structure of the article.

AH and TC drafted the manuscript, which MAS, AAP and GW critically reviewed and revised.

COMPETING INTERESTS

AH None declared

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AAP None declared

GW None declared

LEGEND

- Table 1.** Features associated with severe ischaemic colitis and need for operative management.
- Table 2.** Risk factors associated with mortality in post-operative patients (factors in bold are included in the Ischemic Colitis Mortality Risk (ICMR) score(40)).
- Table 3.** Outcomes in ischaemic colitis.
- Figure 1.** Arterial supply of the colon and the most common sites for ischaemic colitis. The colon receives blood from both the superior and inferior mesenteric arteries. However, there are weak points, or “watershed” areas, at the borders of the territory supplied by each of these arteries,5 such as the splenic flexure and the transverse portion of the colon. These watershed areas are most vulnerable to ischemia when blood flow decreases, as they have the fewest vascular collaterals. *Reproduced with permission from Trotter JM et al(32).*
- Figure 2.** CT images showing a) coronal views with mural thickening and submucosal oedema (arrow) with mild surrounding pericolic oedema and b) axial images demonstrating a sharp cut-off between normal proximal transverse colon and abnormal mid/distal transverse colon (arrow).
- Figure 3.** CT images demonstrating acute ischaemia on a background of chronic change due to chronic ischemia. The colon appears relatively featureless with loss of haustration and reduction in luminal calibre, with superadded mural thickening (arrow) and pericolic oedema (arrowhead) due to the acute insult.

Figure 4. Endoscopic findings of inflamed mucosa and single stripe sign (a single longitudinal strip of ulcerated or inflamed colon (arrow)) in segment of ischaemic colitis. *Reproduced with permission from Trotter JM et al(32).*

Figure 5. Algorithm for investigation and management of ischaemic colitis.

IRCI: Isolated right colonic ischaemia

*Risk factors for ischaemia: AF, smoking history, CKD, atherosclerosis, age>60, medications predisposing to IC

**Absence of rectal bleeding/right sided pain/symptoms of chronic mesenteric ischaemia

***Either systemic compromise (e.g. haemodynamic instability) or complications such as perforation

****Choice to commence TPN will be influenced by factors suggesting more severe disease and protracted course, such as: absence of rectal bleeding, peritonitis, IRCI or presence of biochemical markers of severity (anaemia, leucocytosis, thrombocytopenia, hyponatraemia, elevated CRP/lactate)

Supplementary figure 1. Search criteria and PRISMA flow chart for literature review

REFERENCE

1. Theodoropoulou A, Koutroubakis IE. Ischemic colitis: clinical practice in diagnosis and treatment. *World J Gastroenterol*. 2008;14(48):7302-8.
2. Nadatani Y, Watanabe T, Shimada S, Otani K, Tanigawa T, Fujiwara Y. Microbiome and intestinal ischemia/reperfusion injury. *J Clin Biochem Nutr*. 2018;63(1):26-32.
3. Schoots IG, Koffeman GI, Legemate DA, Levi M, van Gulik TM. Systematic review of survival after acute mesenteric ischaemia according to disease aetiology. *BJS*. 2004;91(1):17-27.
4. Yadav S, Dave M, Edakkanambeth Varayil J, Harmsen WS, Tremaine WJ, Zinsmeister AR, et al. A population-based study of incidence, risk factors, clinical spectrum, and outcomes of ischemic colitis. *Clin Gastroenterol Hepatol*. 2015;13(4):731-8 e1-6; quiz e41.
5. Choi SR, Jee SR, Song GA, Park SJ, Lee JH, Song CS, et al. Predictive Factors for Severe Outcomes in Ischemic Colitis. *Gut Liver*. 2015;9(6):761-6.
6. Lee TC, Wang HP, Chiu HM, Lien WC, Chen MJ, Yu LC, et al. Male gender and renal dysfunction are predictors of adverse outcome in nonpostoperative ischemic colitis patients. *J Clin Gastroenterol*. 2010;44(5):e96-100.
7. Newman JR, Cooper MA. Lower gastrointestinal bleeding and ischemic colitis. *Can J Gastroenterol*. 2002;16(9):597-600.
8. Lee MJ, Daniels SL, Drake TM, Adam IJ. Risk factors for ischaemic colitis after surgery for abdominal aortic aneurysm: a systematic review and observational meta-analysis. *Int J Colorectal Dis*. 2016;31(7):1273-81.
9. Hass DJ, Kozuch P, Brandt LJ. Pharmacologically mediated colon ischemia. *Am J Gastroenterol*. 2007;102(8):1765-80.

10. Longstreth GF, Yao JF. Diseases and drugs that increase risk of acute large bowel ischemia. *Clin Gastroenterol Hepatol*. 2010;8(1):49-54.
11. Longstreth GF, Yao JF. Epidemiology, clinical features, high-risk factors, and outcome of acute large bowel ischemia. *Clin Gastroenterol Hepatol*. 2009;7(10):1075-80 e1-2; quiz 23.
12. Baixauli J, Kiran RP, Delaney CP. Investigation and management of ischemic colitis. *Cleve Clin J Med*. 2003;70(11):920-1, 5-6, 8-30 passim.
13. Yamazaki T, Shirai Y, Tada T, Sasaki M, Sakai Y, Hatakeyama K. Ischemic colitis arising in watershed areas of the colonic blood supply: a report of two cases. *Surg Today*. 1997;27(5):460-2.
14. Robert JH, Mentha G, Rohner A. Ischaemic colitis: two distinct patterns of severity. *Gut*. 1993;34(1):4-6.
15. O'Neill S, Elder K, Harrison SJ, Yalamarthi S. Predictors of severity in ischaemic colitis. *Int J Colorectal Dis*. 2012;27(2):187-91.
16. Anon R, Bosca MM, Sanchiz V, Tosca J, Almela P, Amoros C, et al. Factors predicting poor prognosis in ischemic colitis. *World J Gastroenterol*. 2006;12(30):4875-8.
17. ten Heggeler LB, van Dam LJH, Bijlsma A, Visschedijk MC, Geelkerken RH, Meijssen MAC, et al. Colon ischemia: Right-sided colon involvement has a different presentation, etiology and worse outcome. A large retrospective cohort study in histology proven patients. *Best Practice & Research Clinical Gastroenterology*. 2017;31(1):111-7.
18. Medina C, Vilaseca J, Videla S, Fabra R, Armengol-Miro JR, Malagelada JR. Outcome of patients with ischemic colitis: review of fifty-three cases. *Dis Colon Rectum*. 2004;47(2):180-4.

19. Longstreth GF, Hye RJ. Right-Side Colon Ischemia: Clinical Features, Large Visceral Artery Occlusion, and Long-Term Follow-Up. *Perm J*. 2015;19(4):11-6.
20. Sotiriadis J, Brandt LJ, Behin DS, Southern WN. Ischemic colitis has a worse prognosis when isolated to the right side of the colon. *Am J Gastroenterol*. 2007;102(10):2247-52.
21. Sadot E, Telem DA, Cohen L, Arora M, Divino CM. Nonocclusive ischemic colitis: analysis of risk factors for severity. *Am Surg*. 2014;80(5):454-60.
22. Hsieh J, Brandt L. Fecal Calprotectin in Ischemic Colitis (IC): 438. *American Journal of Gastroenterology*. 2009;104:S164.
23. Brandt LJ, Feuerstadt P, Longstreth GF, Boley SJ, American College of G. ACG clinical guideline: epidemiology, risk factors, patterns of presentation, diagnosis, and management of colon ischemia (CI). *Am J Gastroenterol*. 2015;110(1):18-44; quiz 5.
24. Wiesner W, Morteale KJ, Glickman JN, Ji H, Khurana B, Ros PR. CT findings in isolated ischemic proctosigmoiditis. *Eur Radiol*. 2002;12(7):1762-7.
25. Al-Khowaiter SS, Brahmania M, Kim E, Madden M, Harris A, Yoshida EM, et al. Clinical and endoscopic significance of bowel-wall thickening reported on abdominal computed tomographies in symptomatic patients with no history of gastrointestinal disease. *Can Assoc Radiol J*. 2014;65(1):67-70.
26. Cruz C, Abujudeh HH, Nazarian RM, Thrall JH. Ischemic colitis: spectrum of CT findings, sites of involvement and severity. *Emerg Radiol*. 2015;22(4):357-65.
27. Chen M, Remer EM, Liu X, Lopez R, Shen B. Identification of the distinguishing features of Crohn's disease and ischemic colitis using computed tomographic enterography. *Gastroenterol Rep (Oxf)*. 2017;5(3):219-25.

28. Kim JS, Kim HJ, Hong SM, Park SH, Lee JS, Kim AY, et al. Post-Ischemic Bowel Stricture: CT Features in Eight Cases. *Korean J Radiol.* 2017;18(6):936-45.
29. Pastor-Juan MDR, Ripolles T, Marti-Bonmati L, Martinez MJ, Simo L, Gomez D, et al. Predictors of severity in ischemic colitis: Usefulness of early ultrasonography. *Eur J Radiol.* 2017;96:21-6.
30. Danse EM, Van Beers BE, Jamart J, Hoang P, Laterre PF, Thys FC, et al. Prognosis of ischemic colitis: comparison of color doppler sonography with early clinical and laboratory findings. *AJR Am J Roentgenol.* 2000;175(4):1151-4.
31. Zou X, Cao J, Yao Y, Liu W, Chen L. Endoscopic findings and clinicopathologic characteristics of ischemic colitis: a report of 85 cases. *Dig Dis Sci.* 2009;54(9):2009-15.
32. Trotter JM, Hunt L, Peter MB. Ischaemic colitis. *BMJ.* 2016;355:i6600.
33. Beppu K, Osada T, Nagahara A, Matsumoto K, Shibuya T, Sakamoto N, et al. Relationship between endoscopic findings and clinical severity in ischemic colitis. *Intern Med.* 2011;50(20):2263-7.
34. Montoro MA, Brandt LJ, Santolaria S, Gomollon F, Sanchez Puertolas B, Vera J, et al. Clinical patterns and outcomes of ischaemic colitis: results of the Working Group for the Study of Ischaemic Colitis in Spain (CIE study). *Scand J Gastroenterol.* 2011;46(2):236-46.
35. Hourmand-Ollivier I, Bouin M, Saloux E, Morello R, Rousselot P, Piquet MA, et al. Cardiac sources of embolism should be routinely screened in ischemic colitis. *Am J Gastroenterol.* 2003;98(7):1573-7.

36. Favier C, Bonneau HP, Tran Minh V, Devic J. [Endoscopic diagnosis of regressive ischemic colitis. Endoscopic, histologic and arteriographic correlations]. *Nouv Presse Med.* 1976;5(2):77-9.
37. Houe T, Thorboll JE, Sigild U, Liisberg-Larsen O, Schroeder TV. Can colonoscopy diagnose transmural ischaemic colitis after abdominal aortic surgery? An evidence-based approach. *Eur J Vasc Endovasc Surg.* 2000;19(3):304-7.
38. Moszkowicz D, Tresallet C, Mariani A, Lefevre JH, Godiris-Petit G, Noullet S, et al. Ischaemic colitis: indications, extent, and results of standardized emergency surgery. *Dig Liver Dis.* 2014;46(6):505-11.
39. Mosele M, Cardin F, Inelmen EM, Coin A, Perissinotto E, Sergi G, et al. Ischemic colitis in the elderly: predictors of the disease and prognostic factors to negative outcome. *Scand J Gastroenterol.* 2010;45(4):428-33.
40. Reissfelder C, Sweiti H, Antolovic D, Rahbari NN, Hofer S, Buchler MW, et al. Ischemic colitis: who will survive? *Surgery.* 2011;149(4):585-92.
41. Kim KH. Clinical characteristics of ischemic colitis according to the localization. *J Korean Soc Coloproctol.* 2011;27(6):275.
42. Genstorfer J, Schafer J, Kettelhack C, Oertli D, Rosenthal R. Surgery for ischemic colitis: outcome and risk factors for in-hospital mortality. *Int J Colorectal Dis.* 2014;29(4):493-503.
43. Cosme A, Montoro M, Santolaria S, Sanchez-Puertolas AB, Ponce M, Duran M, et al. Prognosis and follow-up of 135 patients with ischemic colitis over a five-year period. *World J Gastroenterol.* 2013;19(44):8042-6.