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REVIEW

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Idiopathic mesenteric phlebosclerosis: a rare but important disease in Asian populations

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Abstract

Idiopathic mesenteric phlebosclerosis (IMP) is a rare form of ischemic colitis that predominantly impacts Asian populations. Despite some recognizable signs, there is a significant lack of awareness about IMP. In this review, we explore the etiology, pathogenesis, imaging manifestations, endoscopic traits, and therapeutic modalities of IMP. In addition, we discuss the deficiencies in the current comprehension of IMP and the potential research orientations in future.

Keywords Idiopathic mesenteric phlebosclerosis, Chinese herbal medicines, Ischemic colitis, Venous calcification, High venous pressure injury

Introduction

Idiopathic mesenteric phlebosclerosis (IMP) is a rare form of ischemic colitis characterized by calcification and obstruction of the mesenteric veins. The occurrence of IMP is associated with the long-term consumption of herbal medicines. The first reported case of this unique disease was in 1991 by Koyama et al. as Phlebosclerotic colitis (PC), subsequently identified and recognized as a distinct disease entity in 1993 [1, 2]. The reported incidence of IMP is very low, estimated at 0.01 per 100,000 individuals in Japan [3]. Despite the presence of specific imaging findings, this disease can often be misdiagnosed during the initial evaluation due to its low incidence and non-specific clinical presentations [4–8]. The available literature mainly comprises case reports, with some partial literature reviews showing contradictory conclusions and incomplete coverage [9, 10]. To gain a deeper understanding of IMP, a comprehensive review of the literature in English, Japanese, Korean, and Chinese over the past three decades was conducted, aiming to consolidate and summarize the clinical characteristics of this particular disease.

Epidemiology

IMP is more prevalent in Asian populations, with the majority of cases reported in East Asian countries such as China, Japan, and Korea. Only a small number of cases have been documented in Canada, Germany, the United States, and the United Kingdom [9, 11–15]. This distribution aligns with regions where Chinese herbal medicine consumption is common. Patients with IMP are typically in their middle age, within the age range of 31 to 86 years [16, 17]. Gender composition in IMP cases varies significantly by region. In Japan, there is an approximate ratio of 2:3 of male to female patients, as females are more inclined to use herbal remedies for chronic diseases [18]. Conversely, the proportion of male patients is higher in China, which has been linked to the consumption of herbal liquor among middle-aged Chinese men [9, 19]. Region-specific lifestyles or cultures may have influenced the development of the IMP. However, the predominant occurrence of cases in Asian populations implies the need to explore genetic susceptibility, a topic not yet addressed in relevant studies but crucial for future research.

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Clinical features

The clinical manifestations of IMP are non-specific. Common symptoms include abdominal pain, diarrhea, nausea, vomiting, and flatulence [20–22]. Some patients may also exhibit symptoms of complications such as gastrointestinal hemorrhage, intestinal obstruction, and colonic perforation [23–26]. It is important to note that around 10–20% of patients in the early stage show no clinical symptoms. These cases are often identified through routine examinations such as fecal occult blood tests, colonoscopies, and computed tomography (CT) [27, 28].

Laboratory findings

The most common laboratory abnormalities include elevated white blood cells, C-reactive protein (CRP), positive fecal occult blood, and anemia. However, these results are still not specific and do not correlate with disease severity [3, 22, 29–31]. Normal laboratory results cannot exclude IMP, particularly in asymptomatic patients [6]. Currently, there are no specific serum markers available for diagnosing IMP. This limitation may be attributed to the small sample size of cases, which renders marker screening unfeasible. This aspect also offers a promising direction for future research.

Radiographic examination

Plain films

Plain films can detect characteristic calcifications, which consist of multiple serpiginous, thread-like structures that run along and perpendicular to the colon frame, typically caused by calcifications of mesenteric veins (Fig. 1). Characteristic calcifications offer important diagnostic clues, aiding in the early identification of IMP [24, 32–35]. Additionally, plain films are instrumental in identifying potential complications such as intestinal obstruction and perforation [23, 36, 37].

Barium enema

Continuous ischemic colitis can lead to mucosal edema, distortion, and stenosis of the colon wall, so the double-contrast barium enema can reveal poor haustration, impaired wall distensibility, mucosal irregularity, serration in the ascending and transverse colon lumens, and thumbprinting [18, 23, 38–40].

Computed tomography (CT)

Abdominal CT is highly valuable for diagnosing IMP, for it provides detailed insights into the colonic wall, pericolic areas, and calcifications. It also helps evaluate serious complications such as peritonitis, bowel necrosis, and perforation [41] (Fig. 1). The CT imaging features

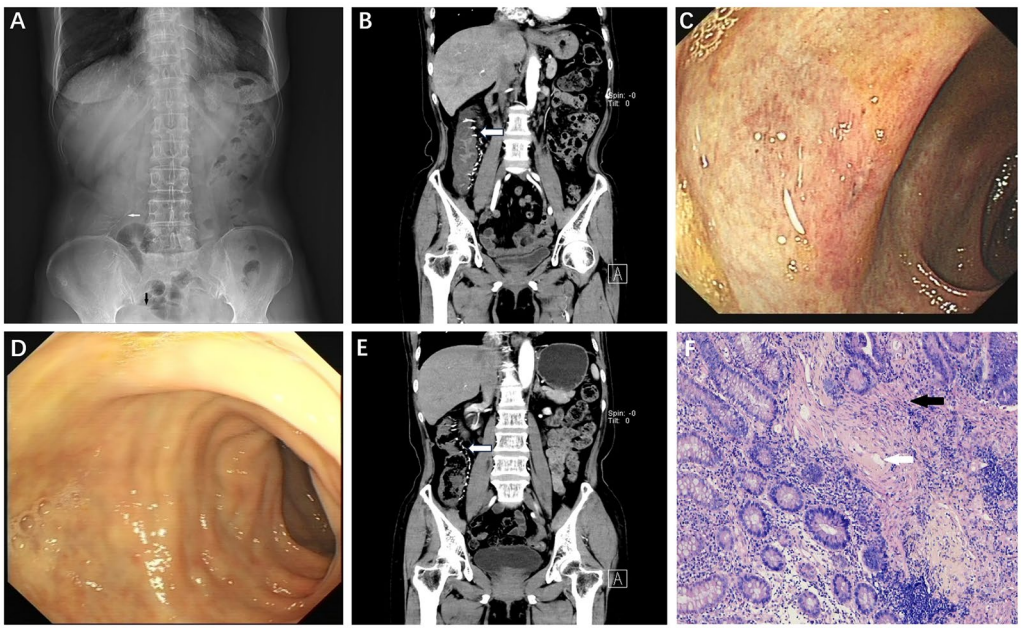

Figure1 A case from our institution's records. Thread-like calcification (white arrowhead) and intestinal obstruction (black arrowhead) on plain films (**A**). Prior to treatment, computed tomography revealed thickening and calcification (arrowhead) of the ascending colon (**B**). Colonoscopy showed dark purple discoloration and ulceration (arrowhead) of the mucosa pre-treatment (**C**). Repeat computed tomography and colonoscopy displayed healing ulcers with persistent dark purple mucosa (**D**), while bowel wall thickening resolved but mesenteric vein calcification persisted (**E**, arrowhead). Endoscopic biopsy specimens revealed inflammatory cell infiltration in the lamina propria, fibrous wall thickening, and hyalinization of small submucosal vessels (white arrowhead), along with collagenous fiber proliferation around the mesenteric vein (black arrowhead) (**F**, ×400)

of IMP as follows: (I) Lesions mainly occur in the colon, especially in the ileocecum, ascending colon, and transverse colon. Sometimes, lesions may extend to the rectum and potentially involve the entire colorectum. (II) Thread-like calcifications perpendicular to the intestinal wall, particularly in the superior mesenteric veins, are notable in imaging. Multi-planar reformatting (MPR) and Computed tomography angiography (CTA) are favorable for displaying the morphology of calcification. (III) The affected colonic wall is mainly thickened and pericolic fat stranding can be found in some cases. (IV) There is no thrombosis in the main trunk and branches of the superior and inferior mesenteric artery [42–45].

Superior mesenteric angiography

On arterial-phase images, irregularities and tortuosity of marginal arteries and vasa recta can be observed [46]. Moreover, delay-phase images often reveal dilated and convoluted veins, alongside a significant reduction in blood flow within the mesenteric vein [36, 47, 48]. However, in some cases, after achieving the primary goal of excluding arterial disease, the venous runoff was not further obtained, potentially overlooking important diagnostic information [11].

The barium enema is not commonly performed for IMP for its non-specific manifestations. Superior mesenteric angiography is typically conducted to rule out arterial disease. Plain film and abdominal CT scans are advised for all patients suspected of having IMP. However, due to differences in imaging conditions, plain films may not always show venous calcifications, and negative results do not definitively rule out the possibility of IMP [49]. Abdominal CT scans have been proven to be more effective in detecting calcification of mesenteric veins compared to plain films (66.9%), as they are able to reveal venous calcifications in almost all patients (91.2%). This high detection rate suggests a significantly higher sensitivity of CT scans in identifying venous calcification [27]. In summary, CT scans are considered the most valuable diagnostic tool for IMP due to its ability to provide detailed information on colonic wall, pericolic, and peritoneal calcifications, as well as assess potentially life-threatening complications [41]. However, in rare cases where venous calcification is also not visualized on CT scans, confirmation through pathological examination is necessary. Long-term follow-up studies of these cases have indicated a progressive increase in calcification of the venous wall over time, with obvious calcifications sometimes taking several years to form [21, 25, 50, 51]. This raises concerns about the effectiveness of using radiological investigations to diagnose patients with early IMP. Further research is needed to explore new non-invasive methods for detecting early cases.

Endoscopic examination

Colonoscopy

During colonoscopy, the most common and characteristic finding in patients with IMP is a dark purple discoloration of the mucosa in the colon. The affected areas are most prominent in the right colon, especially in the cecum and ascending colon, and gradually diminish toward the distal portion of the left colon [26, 29, 30, 42, 52–54] (Fig. 1). Nevertheless, lesions throughout the colorectal region can also be uncovered [55, 56]. Additional endoscopic findings may include mucosal edema, erythema, erosion, ulceration, rigidity of the colon wall, loss of normal haustra, luminal narrowing, and focal nodular surfaces, with one or more of these signs potentially present in a single patient [4, 19, 41, 57–60].

Endoscopic ultrasonography

Endoscopic ultrasonography (EUS) is not routinely performed for IMP; however, it can be considered when the diagnosis is challenging, as it exhibits high sensitivity to calcification [61]. EUS reveals a thickened wall at the site of the colonic lesion, with the thickness reaching approximately 2.5 times that of a normal colon wall. The most pronounced thickening is observed in the intrinsic muscle layer. Additionally, the boundary between the intrinsic muscle layer and the submucosal layer appears slightly blurred [62]. Multiple calcifications are also visible in the submucosal layer [29].

Performing a colonoscopy is safe in patients with IMP. After following the standard bowel preparation protocol, the rate of successful cecal insertion is over 97% and no colonoscopy-related complications have been reported [41, 63, 64]. However, in cases where the colon is severely narrowed, preventing further passage of the detector, the colonoscopy should be terminated immediately to prevent the risk of perforation [65]. It is worth noting that radiological examination findings do not always align with the colonoscopic findings. Notably, the extent of disease observed during the colonoscopy tends to extend more distally than what is revealed through radiological imaging. Therefore, accurate assessment of the extent of IMP via colonoscopy is crucial, particularly when surgical intervention is being considered [39]. Meanwhile, despite the significant advantages of EUS in visualizing submucosal structures and calcifications, its utilization among IMP patients remains minimal, with only a few documented cases in the literature. Current data do not clarify its value in early-stage cases where CT scans do not show calcification, nor its predictive role in disease progression and prognosis. But there is no doubt that the potential value of EUS in the diagnosis and treatment of IMP warrants further research and exploration.

Histopathological examination

Macroscopic findings

The large intestines, particularly the cecum and the ascending colon, exhibit a dark purple or brown-colored mucosal surface characterized by swelling and the absence of plicae semilunares. Additionally, there is a significant thickening of the colonic wall accompanied by sclerosis and edema [42, 53, 66, 67]. On the serosal surface, multiple convoluted blue-purple vessels and sclerosis nodules are typically observed [39, 68, 69].

Microscopic findings

The histologic hallmark is chronic ischemic colitis caused by fibrous thickening/sclerosis of the venous walls (Fig. 1), which is typically circumferential but sometimes eccentric. Microscopic findings are as follows: (I) Atrophic changes in glands and mucosal muscles are identified, along with ulceration and inflammation in the affected areas; (II) Fibrosis thickening with calcification and luminal stenosis in the vein wall; (III) Lamina propria and submucosal fibrosis; (IV) Foamy macrophages in the subserosa of the small vessel wall; (V) No thrombosis in the blood vessel; (VI) No active inflammation in the vascular lamina propria [3, 12, 42, 57, 67, 68, 70–73]. The deposition in the intestinal wall is negative in Congo red staining, which can be used in the differential diagnosis of amyloid deposits [74]. Kuo-Ming Chang proposed a hypothesis that fibrosis thickening and luminal stenosis in the vein wall are secondary to changes in the muscular layer of the vein wall. A unique type of coagulative necrosis is found in the muscular coats: the necrotic muscle fibers become pink ghost shadows with the absence of nuclear staining without fragmentation and removal as seen in classical coagulative necrosis. They named this type of necrosis "mummification," which, although not exhibiting features of apoptosis, is often obscured by subsequent fibrosis/sclerosis and dystrophic calcification [8]. Due to the distinct nature of this necrosis, a superficial review of sections only stained with H&E stain could mistakenly identify calcified vessels as arteries. Masson stain is recommended for recognizing hyperplastic collagen fibers, while EVG stain can be utilized to visualize elastic fibers in artery walls, aiding in the distinction between arteries and veins [7, 29, 51, 74, 75].

Obtaining sufficient diagnostic information from a single colonoscopic biopsy specimen is crucial. In some cases, observations may be limited to congestion and inflammatory cells, without indications of submucosal fibrosis or vascular wall thickening [24, 55]. This limitation can be influenced by factors such as the number of biopsy blocks, biopsy site, and depth of the biopsy. The exact biopsy site and the minimum number of biopsies necessary to meet diagnostic requirements remain unclear and may require validation through high-quality clinical studies and further research.

Etiology and pathogenesis

IMP is a non-thrombotic chronic intestinal ischemia syndrome [66, 76]. The pathogenesis of vein sclerosis remains poorly understood. The ingestion of specific chemicals and toxins that enter the bloodstream may significantly contribute to the pathophysiological process of IMP. Various risk factors are also hypothesized to play a role in the development of this condition [41, 76](Fig. 2).

Theory of high venous pressure injury

In 1999, Kitamura et al [77] reported a case of IMP with positive anti-centromere antibody, suggesting that collagen disease may be the underlying cause. Subsequently, numerous chronic diseases have been identified as risk factors for IMP, such as cardiovascular disease, chronic renal disease, cancer, chronic liver disease, diabetes mellitus, hyperlipidemia, rheumatism, and autoimmune disorders [19, 78–82]. More than 80% of IMP patients exhibit one or more of these chronic diseases. Researchers have postulated a theory that IMP may represent an adaptive response of the venous wall to prolonged and elevated venous blood pressure, a common hemodynamic alteration seen in various chronic diseases. Such conditions lead to increased venous blood pressure and abnormal shear stress, ultimately resulting in venous injury [45, 66]. Nevertheless, a subset of IMP patients do not exhibit any known risk factors at the onset, and the occurrence of IMP in individuals with diabetes, cirrhosis, and other chronic illnesses is notably rare [24, 29, 34, 53, 83]. This discrepancy challenges the validity of the hypothesis as a comprehensive explanation for the pathogenesis of IMP.

Theory of toxicity

In 2007, Chang summarized the clinicopathological features of 5 patients and found that long-term ingestion of Chinese herbal medicines may play a predominant role in the pathogenesis of IMP [8]. Subsequently, an increasing number of cases potentially related to herbal medicines have been reported. In Japan, a large-scale nationwide survey revealed that over 70% of IMP patients used herbal medicines [27]. Among the reported Chinese medicine prescriptions are Huanglian Jiedu Tang, Linggui Shugan Tang, Xinyi Qingfei Tang, Jingjie Lianqiao Tang, JiaWei XiaoYao San, Wu Jia Pi, and others [21, 22, 39, 54, 58, 67, 70, 71, 84, 85] (Table 1). Notably, most of the reported Chinese medicine prescriptions contain gardenia fruit (GF), which is the fruit of the plant Gardenia jasminoides J. Ellis and is considered a possible cause of IMP [18, 59, 86]. The GF extract and its primary active components exhibit a range of pharmacological

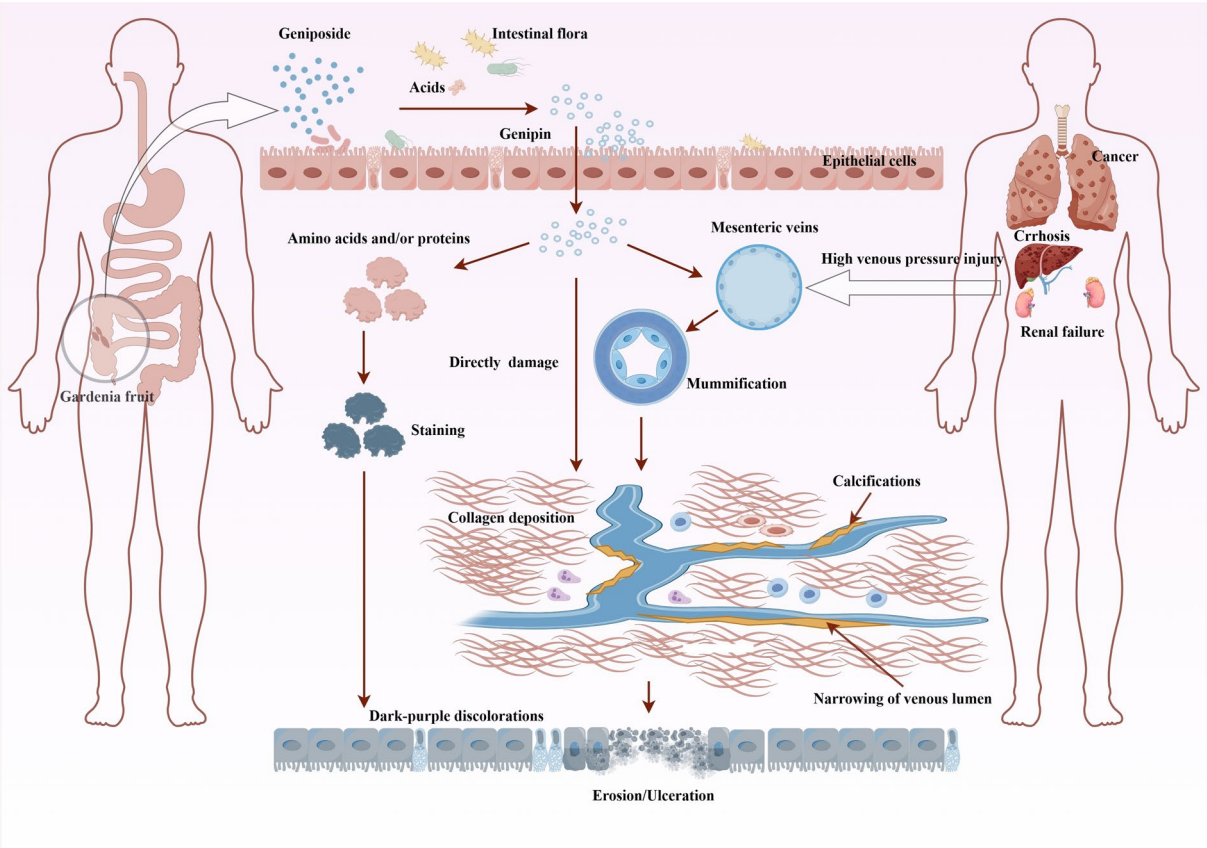

Figure2 The pathogenesis hypothesis of IMP. High venous pressure injury: chronic diseases lead to increased venous blood pressure and abnormal shear stress, resulting in venous injury. Toxicity mechanism: Geniposide is metabolized to genipin and is absorbed into the mesenteric veins, causing intimal hyperplasia and thickening and fibrosis of the venous wall, resulting in "mummification" changes. Genipin can act directly on the intestinal wall and also lead to formation of blue color, staining the vein and intestinal wall during absorption. Both high venous pressure and toxic substances can lead to calcification and obstruction of the veins, subsequently cause damage to the intestinal wall, forming erosions / ulcers and fibrosis of intestinal wall. By Figdraw

Table 1 Chinese medicine prescriptions that may be associated with IMP

Huanglian Jiedu Tang [23, 71]	Linggui Shugan Tang [7]
Xinyi Qingfei Tang [18]	Jingjie Lianqiao Tang [98]
Jiawei Xiaoyao San [18, 58]	Wu Jia Pi [3, 9]
An Zhong San [16]	Wu Ling San [16]
Chaihu Jia Longgu Muli Tang [16]	Guizhi Fuling Wan [16]
Yinchenhao Tang [16]	Xiao Chaihu Tang [98]
Wulin San [16]	Shiwei Baidu Tang [16]
Qingshang Fangfeng Tang [16]	Fangfeng Tongsheng San [21]
Banxia Houpo Tang [16]	Yiyiren Tang [16]
Jiawei Guipi Tang [51, 67]	Zhizi Jinhua Wan [99]
Zhizi Baipi Tang [49]	

properties, including liver protection, cholagogic effects, anti-inflammatory, antioxidant, neuroprotective, anti-diabetic, anti-apoptotic, and anti-tumor activities. However, high-dose consumption of GF can result in damage to multiple organs, such as the liver and kidneys [87, 88]. The toxicity mechanism of IMP is as follows: (I) Geniposide is the main component of GF, metabolized to genipin by intestinal flora, amino acids, and sulfuric acids. (II) Genipin, upon being absorbed into the mesenteric veins, leads to intimal hyperplasia, thickening, and fibrosis of the venous wall, causing "mummification" changes. This process ultimately results in the obstruction of the venous lumen, impairing reflux and leading to thickening and edema of the intestinal wall. (III) Genipin can directly damage the intestinal wall, leading to ulcer formation and fibrosis of the lamina propria. (IV) Genipin turns dark blue when it interacts with amino acids and/or proteins in the intestinal wall, possibly resulting in a dark blue or purple appearance during colonoscopy [9, 29]. In addition to GF, including licorice (glycyrrhizin), omanthus (baicalin), and poria cocos have been identified associated with IMP [16]. These glycosides are

metabolized by the beta-glucosidase of intestinal bacteria and are subsequently absorbed from the right colon as aglycones. The absorption of these aglycones may promote the release of oxygen reactive species, leading to tissue injury [38].

Although most patients with IMP have a history of consuming herbal medicines, only a small proportion of these patients have been diagnosed with IMP [59]. A review study analyzed the relationship between dosages of GF and IMP, revealing that the total oral dose of GF is more strongly correlated with IMP development than the duration of oral administration (in years). Specifically, excessive intake of GF, approximately 5,000 g, has been shown to contribute to and/or accelerate the onset of IMP [89]. Furthermore, in an animal experimentation study, rats that were fed 987 mg/kg of GF for 11 months exhibited reversible fibrosis in the colonic lamina propria, highlighting the significant role of the total oral dose of GF. Interestingly, the group of rats fed 459 mg/kg of GF did not show the same histopathological changes, underscoring the importance of the dosage in the development of IMP [90]. However, Hisanaga et al. had followed up a woman who had been taking Jia Wei Xiao Yao San for 13 years. By the third year of treatment, collagen fibers had started to accumulate around small blood vessels in the mucosa, with a total oral administration dose of GF amounting to 2340 g. Subsequently, by the sixth year, characteristic histopathological changes were evident in the mucosa, at a cumulative GF oral dose of 4380 g [74]. From this observation, it can be inferred that the actual minimum cumulative dose required for such effects may be lower.

Neither of the two existing pathogenesis hypotheses can fully explain the mechanism of IMP, and existing studies are predominantly retrospective and lack high-quality randomized controlled trials (RCTs) to provide a comprehensive understanding. Although some meaningful characteristic manifestations have been identified, these studies have been limited by small sample sizes and short durations in animal experiments. The challenges in elucidating the mechanisms of IMP occurrence and progression are multifold. First, the low incidence of IMP hinders the accumulation of robust data, while its protracted natural course requires considerable time to observe clinical changes, thus extending the research timeline [74, 89]. Furthermore, early diagnosis relies on invasive procedures like colonoscopy, which can impede patient compliance [89]. Additionally, the complex composition of traditional Chinese medicines (TCM) complicates the rapid identification of etiological components. The development of efficient animal modeling techniques holds promise for enhancing IMP research by providing a larger pool of subjects. Coupled with national health screening initiatives, such as national early gastrointestinal cancer screening, this approach may bolster sample sizes and lengthen study durations, ultimately yielding higher-quality research findings.

Diagnosis

The typical imaging findings play a crucial role in the diagnosis of IMP. Typical thread-like linear venous calcifications are observed along the colon wall through plain abdominal radiography and abdominal CT scanning [17, 18, 26, 45, 49, 74, 86]. Additionally, the typical colonoscopic presentation includes dark purple mucosa, although other features such as mucosal edema, erosion, and ulcerations may also be present with or without the dark purple mucosa [18, 26]. In some instances, patients may exhibit negative colonoscopy results and no definite calcifications identified in abdominal CT scans. In such cases, the diagnosis is confirmed through histopathological examination, which reveals marked fibrous thickening of the vascular wall and mild fibrosis in the submucosa [51]. Diagnosing this subset of cases, especially early IMP cases, is challenging due to non-specific clinical manifestations and laboratory results. Negative biopsies can complicate the reliance on invasive procedures for diagnosis.

Currently, there are no strictly validated diagnostic criteria for IMP. However, most literature adopts the following criteria: (1) the presence of typical manifestations of mesenteric venous calcification, (2) pathological examination revealing fibrous thickening of the venous wall and submucosal fibrosis, and (3) exclusion of other diseases. A diagnosis of IMP can be established if criteria 1 and/or 2 are met in conjunction with criterion 3. A history of Chinese herbal medicine use and distinct endoscopic mucosal changes can enhance diagnostic confidence. The symptoms of IMP may be easily mistaken for those of inflammatory bowel disease, atherosclerotic ischemic colitis, collagenous colitis, and other similar conditions. Nonetheless, the distinctive features of IMP, such as mesenteric vein calcification and fibrous thickening of the venous wall, do not occur in these other diseases, making them crucial differentiating factors [4, 45, 76]. Unfortunately, there is a lack of specific biochemical diagnostic markers to assist in the non-invasive diagnosis of IMP at an early stage. Developing such markers may represent the next significant advancement in research on this condition.

Treatment

Currently, there is no established standard treatment guideline for IMP. Treatment options are determined based on the patient's clinical symptoms and the recommendations of healthcare providers [41]. The therapeutic

approach for IMP includes both conservative management and surgical intervention [38].

Conservative management

Conservative management methods are recommended for IMP patients, with the primary suggestion being the discontinuation of Chinese herbal consumption as it may be linked to disease progression [38, 59, 79]. Asymptomatic patients may only require follow-up [45]. Other conservative measures include the use of antibiotics, probiotics, and bowel rest [19, 91]. Additionally, various therapeutic agents have been explored as potential treatments. In some cases, researchers have prescribed aspirin, warfarin, and low molecular weight heparin, which have led to clinical remission [12, 57, 92]. Mesalazine, a medication commonly used for inflammatory bowel disease, has also shown effectiveness in IMP patients [7, 54].

Surgical intervention

Surgical resection of the involved bowel segments has traditionally been the primary treatment approach. However, with an increasing number of studies on conservative treatment, surgical indications have become more stringent [45, 66]. Surgery is recommended for patients under specific conditions: (I) Severe complications like recurrent intestinal obstruction, massive hemorrhage, and perforation; (II) Persistent or recurrent symptoms despite conservative treatment; (III) IMP with colonic tumors [10, 25, 51, 53, 80]. Pre-surgical tattooing using colonoscopy can aid in determining an accurate excision line [67].

Studies have demonstrated that conservative treatment is safe and successful, with over 90% of patients achieving favorable outcomes [19, 45]. However, a small percentage of patients may still require surgery. Anticipating which patients with IMP may fail conservative therapy and require surgery presents challenges, and existing studies offer conflicting results. Lin et al. devised a calcification scoring system based on multidetector CT examinations [80]. The colon was divided into five segments, with the highest calcification score for each main mesenteric venous branch recorded and then totaled. The findings suggest that a cutoff value of 3.5 for the number of colonic segments with mesenteric venous calcification and 10.5 for the total calcification score can predict the necessity for surgery. Interestingly, colonic wall thickening and pericolic fat stranding were not helpful in identifying the need for surgery. Conversely, Ko et al. reported that a thicker colonic wall, more involved segments, and pericolic inflammation correlated with an increased likelihood of requiring surgical intervention [17]. The current studies present conflicting conclusions and are limited by the insufficient number of cases for validation. To address this challenge, exploring the potential use of suitable biochemical markers or developing a more effective scoring system through expanding the study sample size could offer new insights for improving patient management in IMP cases.

IMP and colonic cancer

The potential association between IMP and colonic cancer remains uncertain. To date, more than 10 cases of colorectal cancer coinciding with IMP have been reported in the literature [5, 29, 38, 51, 69, 70, 93]. Minami et al. conducted a comprehensive review of previously reported cases and observed that in 90% of the cases, colonic cancer was detected in the right colon, which was the most commonly affected area by IMP. Furthermore, they noted that 50% of the cases were associated with the usage of a Chinese herb containing genipin (GF). As a result, they concluded that there is indeed a noteworthy relationship between right-side colon cancer and IMP associated with GF [94]. Nevertheless, the majority of researchers have refrained from making definitive statements regarding the correlation between IMP and colonic cancer [38, 51]. More cases and further investigation are needed to evaluate the association between tumorigenesis of the colon and IMP [51]. Furthermore, considering the current research landscape, whether to include IMP patients in colorectal cancer screening programs requires a comprehensive evaluation of current evidence, integrating clinical guidelines, regional healthcare resource availability, and patient preferences within their specific healthcare systems.

IMP with early colonic cancer is a situation that requires special attention. Endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) are recommended for early colonic cancer and colonic adenoma. However, in patients with IMP, due to severe fibrosis of the submucosa around the lesion, submucosal injections are difficult. Additionally, dark purple discolorations of the mucosa also make blood vessels and muscles indiscernible [78]. Previous reports have indicated that most cases attempting ESD in IMP patients have resulted in surgery due to excessive difficulties or severe complications [18, 38, 78, 95]. Nonetheless, Kawasaki et al. successfully performed ESD on a patient with transverse colon cancer and IMP. They used a short-type ST Hood, which aided in the ESD procedure for IMP cases with significant submucosal fibrosis [70]. This successful case underscores the potential of using ESD in IMP patients. However, further evaluation is necessary to assess the safety and effectiveness of ESD in treating colonic epithelial tumors associated with IMP.

Prognosis

Patients with IMP generally have a benign prognosis, with most cases experiencing relief after comprehensive treatment and maintaining long-term stability [17, 55, 96, 97]. However, certain manifestations such as linear calcifications in the mesenteric vein area and bronze mucosa in the affected colon do not show improvement, even after discontinuing herbal medicine for months to years [17, 70] Fig. 1. A portion of IMP patients may exhibit an increase in colon wall thickness and more extensive involvement of colonic segments with distal extension to the left colon during follow-up. Despite these findings, conservative management approaches with a wait-and-watch strategy are usually deemed suitable, with only a minority of patients necessitating further interventions [17]. It should be emphasized that individuals with perforation or severe comorbidities face an elevated risk of mortality, with septic shock standing out as the primary cause of death [8, 42, 66].

Conclusions

IMP is a rare non-thrombotic chronic intestinal ischemia syndrome characterized by venous wall calcifications and fibrous thickening/sclerosis of the venous walls. Chemical exposure and other risk factors may contribute to its pathophysiology. This disease remains poorly understood, particularly its pathogenesis and association with colonic tumors. Challenges persist in early non-invasive diagnosis, endoscopic management of early-stage colon cancer, and surgical decision-making. Future research should prioritize developing animal models, identifying biomarkers, and establishing diagnostic and prognostic scoring systems.

Abbreviations

IMP	Idiopathic mesenteric phlebosclerosis
PC	Phlebosclerotic colitis
CT	Computed tomography
CRP	C-reactive protein
MPR	Multi-planar reformatting
CTA	Computed tomography angiography
EUS	Endoscopic ultrasonography
GF	Gardenia fruit
RCTs	Randomized controlled trials
ESD	Endoscopic submucosal dissection
EMR	Endoscopic mucosal resection

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Author contributions

X.T.H. and D.W. contributed to validation, wrote and reviewed the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

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Consent for publication

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Competing interests

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