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Chronic atherosclerotic mesenteric ischemia (CMI)

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Abstract

Chronic mesenteric ischemia (CMI) is most likely caused by atherosclerosis and less frequently by external compression and vasculitis. Symptomatic CMI is an uncommon, potentially under-diagnosed condition caused by fixed stenoses or occlusion of, in most conditions, at least two visceral arteries. If only one of the three major bowel-providing arteries – the celiac trunk, and the superior and inferior mesenteric arteries – is affected, the patient is usually asymptomatic due to a tight collateral network. The only exception is the celiac artery compression syndrome which represents primarily a compression syndrome of celiac plexus nerves by the arcuate ligament in conjunction with a compression of the celiac trunk. CMI of atherosclerotic origin is associated with a high morbidity and mortality. During the last decade, endovascular revascularization has replaced surgical revascularization as the therapy of choice in most centers. This article reviews the most relevant clinical aspects of the disease and the current practice of diagnosis and treatment of CMI.

Keywords

angioplasty; celiac artery compression syndrome; chronic mesenteric ischemia; revascularization; stent

Introduction

Acute mesenteric ischemia is usually caused by embolism resulting in bowel infarction characterized by a typical acute onset of diffuse abdominal pain with still high mortality rates of 70–90% despite immediate surgery or endovascular therapy.[1–4] In contrast, symptomatic chronic mesenteric ischemia (CMI) is an uncommon, potentially under-diagnosed condition caused by fixed stenoses or occlusion of, in most conditions, at least two visceral arteries. CMI is – independent of the etiology – characterized by frequently unrecognized unspecific symptoms such as diffuse postprandial abdominal pain, diarrhea induced by ischemic enteritis, and unintended weight loss.[5,6] Owing to the unspecific symptoms, it needs often years until the correct diagnosis is established.[7]

Stenosis of one and even two visceral vessels is usually well tolerated because of the abundant collateral circulation between the celiac trunk, the superior mesenteric artery, and the inferior mesenteric artery − the latter connected to branches of the internal iliac arteries. Atherosclerosis is the first cause of CMI (95%). Typically, patients affected by CMI have diffuse atherosclerotic vascular disease including coronary artery disease. Non-atherosclerotic causes of CMI such as fibromuscular disease, celiac artery compression syndrome (compression of the celiac trunk by the arcuate ligament; Figures 1 and 2A) and vasculitis will not be discussed in this review.

During the last decade, endovascular therapy has replaced surgery as the first-line revascularization strategy.

Clinical presentation

Patients with CMI usually present with abdominal angina, a clinical syndrome characterized by painful abdominal cramps and colic occurring typically during the postprandial phase.[6,8] Patients may suffer from ischemic gastropathy and enteropathy, a condition characterized by the fear of food, nausea, vomiting, diarrhea, symptoms of malabsorption, and unintended progressive weight loss.[7,9] Table 1 summarizes the differential diagnoses.

Natural history

The incidence of CMI in the general population is approximately 1/100,000 per year.[10] In patients with known atherosclerotic disease, the prevalence of CMI may range from 8% to 70% and a greater than 50% stenosis of more than one splanchnic artery may be detected in up to 15% of cases.[11] In patients with abdominal aortic aneurysm, aortoiliac

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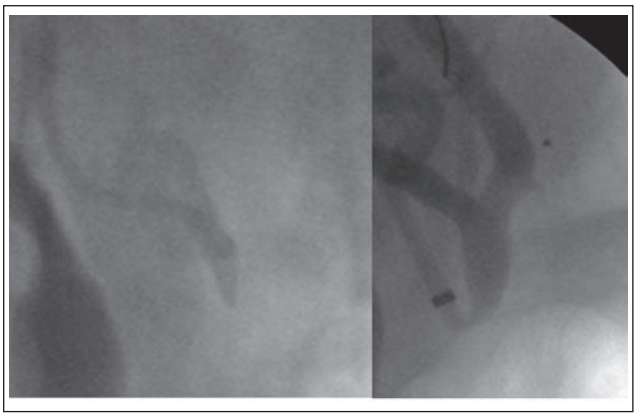

Figure 1. External compression of celiac artery.

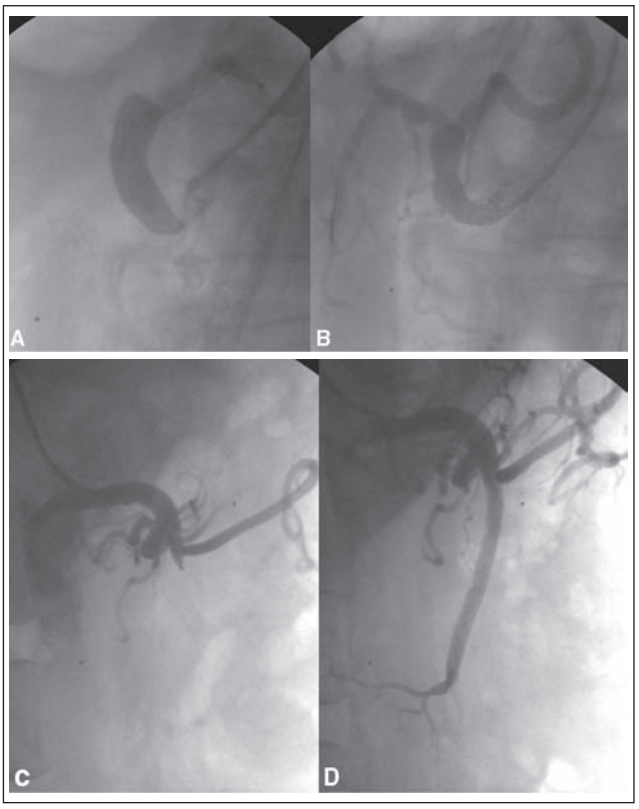

Figure 2. Stenosis of celiac trunk suspicious for external compression before (A) and after stent implantation (B); chronic embolic occlusion of the main stem of the superior mesenteric artery (C) and after stent revascularization (D, sigmoid arteries missing).

occlusive disease, and lower extremity vascular disease, a significant stenosis of at least one of the three visceral arteries may be found in 40%, 29%, and 25% of the cases, respectively. Predisposing conditions for the development of CMI include arterial hypertension, diabetes mellitus, and hypercholesterolemia. Untreated, symptomatic CMI may lead to starvation, bowel infarction, and death. Even in the absence of symptoms, CMI is associated with a cardiovascular mortality rate of up to 40% within 6 years depending on the severity of the disease.[11–14] The likely explanation for this finding is that those patients invariably have advanced systemic atherosclerotic disease. Another recent report about the prevalence of asymptomatic CMI in free-living elderly patients in the United States, found no association between the presence of mild disease and cardiovascular mortality.[15] A subgroup of 553 participants of the Cardiovascular Health Study underwent visceral duplex ultrasonography; 97 (17.5%) had disease of the celiac trunk or superior mesenteric artery. At a mean follow-up of 6½ years, 20 participants with CMI representing 20.6% of the CMI cohort and 93 without CMI representing 20.4% of the non-CMI cohort had died (relative risk, 1.01; 95% confidence interval, 0.66–1.55). No deaths were attributed to intestinal infarction. No association existed between the presence of CMI and prevalent cardiovascular disease, all-cause mortality, or adverse cardiovascular events. Interestingly, no participant reported symptoms or weight loss consistent with CMI. This finding might be explained by the results of another report by the same study group.[16] Most of these study participants had isolated celiac trunk stenosis. Superior mesenteric artery disease was present in only 2.5% of the population but was associated with renal artery stenosis and weight loss. Lesions of the superior mesenteric artery were uncommon in the cohort, yet the association with weight loss suggested that superior mesenteric artery stenosis may have important clinical significance. It cannot be ruled out that in a significant proportion of the individuals identified with celiac trunk disease this lesion was caused by external compression. This compression syndrome is not associated with an increased risk of mortality.

Table 1. Differential diagnoses of CMI (modified according to ref. 40)

Presenting symptom	Suspicious diagnosis	Diagnostic procedure
Batch-wise upper abdominal pain	Duodenic ulcer, gastritis, gastric dyspepsia	Endoscopy
Chronic recurrent upper abdominal pain	Cholecystitis, pancreatitis, pancreas carcinoma, gastric ulcer, gastric carcinoma	Blood tests, abdominal sonography, X-ray, CT or MR scan, endoscopy
Permanent upper abdominal pain	Gastric carcinoma, hepatic diseases, hematoma, tumor, abscess	Blood tests, abdominal sonography, X-ray, CT or MR scan, endoscopy
Lower abdominal pain	Crohn's disease, diverticulitis, colo-rectal carcinoma, irritable colon	Blood tests, abdominal sonography, X-ray, CT or MR scan, endoscopy, functional testings
Peri-umbilical pain	Intestinal obstruction, malabsorption syndrome, ischemic disease	Blood tests, abdominal sonography, X-ray, CT or MR scan, endoscopy, angiography

Diagnostic strategy

Color duplex ultrasound has become the screening method of choice for CMI. In the majority of patients, sufficient visibility of the arteries is given despite frequently seen trapped air in the frame of the colon. Table 2 lists the duplex criteria for significant stenosis or occlusion for each affected vessel. The most commonly used duplex criteria for significant visceral disease are for the celiac trunk a peak systolic velocity greater than 200 cm/s or superior mesenteric artery peak systolic velocity greater than 275 cm/s.[17–21]

CT-angiography and gadolinium-enhanced MR-angiography are useful initial tests for supporting the clinical diagnosis of symptomatic CMI if duplex ultrasound is inconclusive (as in approximately 10% of the cases due to bowel gas shadowing effects).[22–27] CMI can be diagnosed by a test for actual ischemia. Recently, gastrointestinal 24-hour tonometry has been validated as a diagnostic test to detect splanchnic ischemia and to guide treatment.[28]

Ischemic colitis is frequently diagnosed by histology following biopsy during bowel endoscopy.[29] Intra-arterial digital subtracted angiography is still considered the diagnostic gold standard even if multi-slice CT reconstructions offer a better three-dimensional understanding of the vessel anatomy, especially for planning the interventional access.[30]

Prognostic stratification

Five-year mortality in asymptomatic patients with CMI is up to 40%; if all three main visceral arteries are affected it is up to 86%.[8] Five-year mortality of untreated symptomatic CMI is close to 100%. Thus, all patients with symptomatic CMI should undergo revascularization and asymptomatic patients with significant three-vessel visceral arterial stenosis should be considered, in addition to cardiovascular risk factor management, for prophylactic visceral arterial reconstruction. Visceral arterial reconstruction should be routine when these patients undergo aortic reconstruction for aneurysm or occlusive disease.[8]

However, no indication is given in asymptomatic patients with single-vessel disease – in particular, in those with celiac trunk involvement.[15]

Table 2. Duplex criteria for a significant visceral artery stenosis (patients in a fasting condition)

Vessel [reference]	Duplex criterion for a > 70% stenosis or occlusion
Celiac trunk [18]	PSV ≥ 200 cm/s or no flow signal
Superior mesenteric artery [18]	PSV ≥ 275 cm/s or no flow signal
Inferior mesenteric artery [17]	PSV > 200 cm/s, EDV > 25 cm/s, and MAR > 2.5

PSV, peak systolic velocity; EDV, end-diastolic velocity; MAR, mesenteric to aortic ratio.

Treatment

Current literature recommends conservative treatment in patients with asymptomatic disease, even if Thomas et al.[6] reported a high progression rate to symptomatic disease and a high mortality rate – especially in patients with at least two significantly affected mesenteric arteries (Figure 3). Medical treatment includes all aspects of secondary preventive drug treatment including statins, antiplatelet therapy, blood pressure control, lowering HbA1c to less than 7%, and smoking cessation. So far, no controlled data exist to justify this recommendation. Patients with symptoms that can be attributed to CMI should be revascularized.

Recent reports have suggested that angioplasty (PTA), with and without stenting (PTA/S), may have a lower perioperative mortality rate than open surgery for revascularization of CMI.[31–34] Retrospective data from a US nationwide inpatient sample analysis extending from 1988 to 2006, including 22,413 individuals treated for CMI, suggested a lower mortality rate associated with PTA/S than with surgical bypass (3.7% vs 15.4%, $p < 0.001$; Table 3).[31] In addition, bowel resection was less frequently encountered in the endovascular group than in the surgical group treated for CMI (3% vs 7%, $p < 0.01$; Table 3). This subgroup of

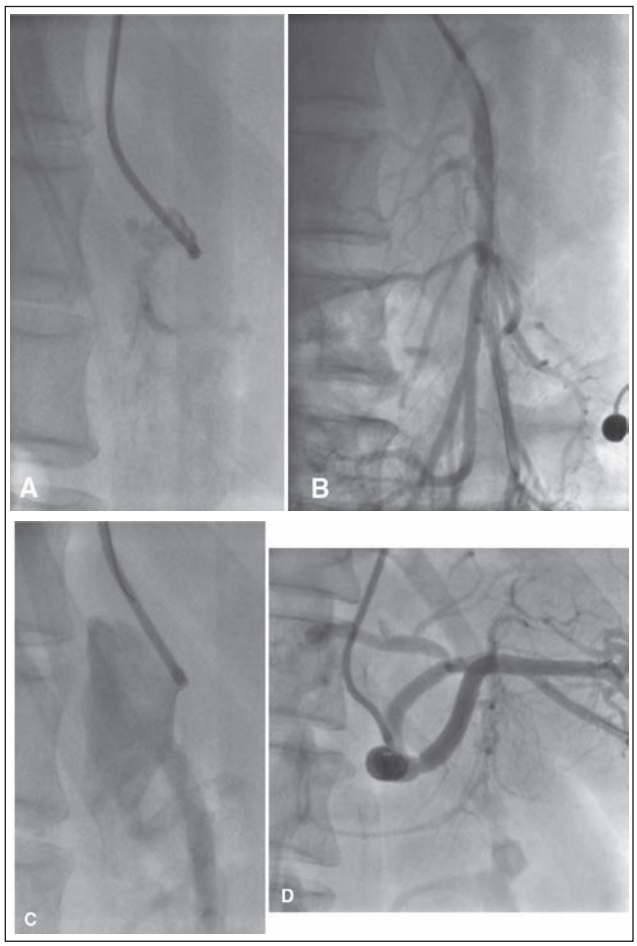

Figure 3. Chronic total occlusion of the superior mesenteric artery and the celiac trunk of unknown origin before (A and C) and after revascularization (B and D).

Table 3. (A) Mortality and morbidity in all patients and in patients with bowel resection: angioplasty versus surgery and (B) complications and length of hospital stay: angioplasty versus surgery (2000–2006 [according to ref. 31])

(A)	Chronic mesenteric ischemia			Acute mesenteric ischemia		
	PTA/S	Surgery[a]	*p*-value	PTA/S	Surgery[a]	*p*-value
All patients	3.7%	15.4%	< 0.001	15.6%	38.6%	< 0.001
Bowel resection	3%	7%	< 0.05	28.8%	46.5%	< 0.01
(B)	Chronic mesenteric ischemia			Acute mesenteric ischemia		
	PTA/S	Bypass	*p*-value	PTA/S	Bypass	*p*-value
Complication						
Cardiac	0.7%	5.6%	< 0.001	2.1%	9.3%	< 0.001
Respiratory	0.3%	5.7%	< 0.001	1.1%	8.8%	< 0.001
LOS, median (range), days	5 (0–94)	11 (1–135)	< 0.001	9 (0–104)	14 (1–27)	< 0.001

[a]Surgery includes bypass, endarterectomy, or embolectomy.
PTA/S, angioplasty with or without stenting; LOS, length of stay.

patients showed a high in-hospital mortality rate for both repair types (25% and 54%, respectively). Overall, these results have to be interpreted with caution because it is possible that patients with CMI undergoing surgery may have an advanced stage of the visceral and/or the systemic atherosclerotic disease. Nevertheless, the lower in-hospital mortality rate documented in patients treated with PTA/S confirms that PTA/S is an appropriate therapy for selected patients with CMI. In addition, the high prevalence of coronary disease in this patient population confers high attractiveness to the endovascular approach.

Accordingly, PTA/S is being used with increasing frequency for revascularization of patients with CMI. Longitudinal data are needed to determine the durability of this benefit. The greater proportion of patients undergoing bowel resection with bypass for acute mesenteric disease suggests a more advanced level of ischemia in this group, making comparison with PTA/S difficult. However, PTA/S may be useful in selected patients with acute mesenteric disease and appropriate anatomy (Figure 2). So far no randomized controlled data are available.

The technical success of endovascular revascularization of mesenteric lesions is 81–100% and even in the presence of total occlusions the success rate exceeds 80%.[35–39] Owing to the aorto-ostial location of most lesions, stenting has become the endovascular procedure of choice (Figures 2, 3 and 4). Symptom relief following revascularization is reported to be up to 100%, with recurrence in cases of restenosis, which is more frequent as compared to renal stenting (29–40%).[35–39] Even if no controlled data support the strategy, in accordance with renal stenting, dual antiplatelet therapy for 4 weeks post procedure has become the standard of care. Duplex sonographic follow-up every 6–12 months is recommended. The use of drug eluting stents, flared stent devices (e.g. Archstent™, SquareOne) or drug eluting balloons in conjunction with bare metal stents has not yet been evaluated in larger series and cannot yet be recommended outside of controlled protocols. The treatment strategy of instent restenosis (Figure 5) is not yet defined. Different strategies such as POBA (plain old balloon angioplasty), stent-in-stent, drug eluting stent placement and the use of drug-coated stents are under evaluation.

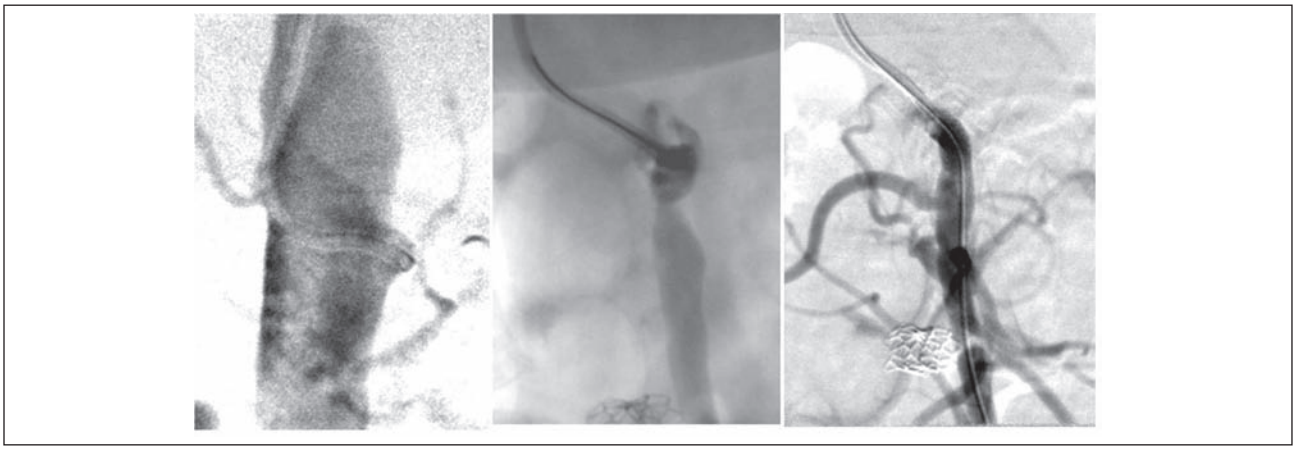

Figure 4. Transbrachial recanalization of a chronic total occlusion of a superior mesenteric artery: (A) short stump of the occluded SMA; (B) after wire recanalization; (C) final result after stent placement.

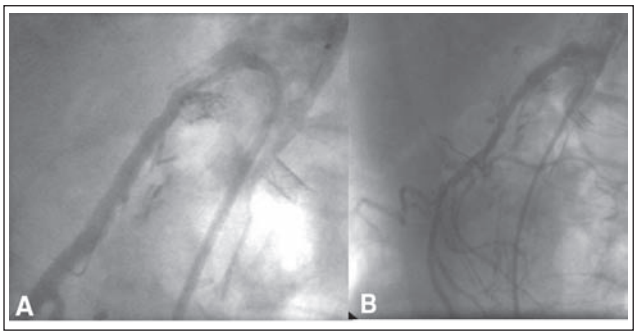

Figure 5. Instent restenosis of superior mesenteric artery (A) and result after instent placement of a drug eluting stent (B).

Besides the individual patient preference, anatomic considerations might guide the choice between surgical reconstruction and PTA/S. Patients with aneurismal disease in conjunction with CMI should undergo surgical reconstruction as well as patients with total occlusions without visible stump. Symptomatic celiac artery compression syndrome indicates surgical lysis of the diaphragmatic crura and reconstruction of the celiac trunk if appropriate. In all other cases, due to its less invasive nature, endovascular revascularization should be the first-line treatment strategy of choice. Considering the high likelihood of restenosis, especially after endovascular therapy, revascularization of at least two vessels should be the revascularization strategy.

Postinterventional care

Owing to the relatively high likelihood of restenosis, particularly after endovascular reconstruction, after mesenteric revascularization patients should be included in a tight surveillance program, initially at least every 6 months including duplex ultrasound, if appropriate, for early detection of restenosis. Moreover, these patients must be enrolled in a close surveillance program for cardiovascular diseases considering myocardial infarction as the main cause of mortality in this patient cohort.

The postinterventional drug regimen usually consists of dual antiplatelet therapy after endovascular therapy, including clopidogrel 75 mg per day for 4 weeks and aspirin 100–325 mg per day for life. After surgical reconstruction, single administration is considered to be sufficient for prevention of graft thrombosis.

Summary

CMI is a potentially underdiagnosed disease with potentially increasing prevalence during the next decade due to demographic changes with increasing life expectancy. Advanced stages of CMI disease with significant two- or three-vessel disease are associated with an increased cardiovascular and intestinal mortality and are thus an indication for revascularization, even if asymptomatic. Duplex ultrasonography has become the primary screening method for CMI; if inconclusive, MR- or CT-angiography are appropriate alternative diagnostic tools.

In patients anatomically suited for endovascular revascularization, percutaneous revascularization has replaced surgical revascularization as the first-line therapeutic strategy, even if patency rates are in favor of surgical revascularization (Table 4).

Table 4. Primary patency rates following surgical and interventional revascularization[41]

	Surgery	Angioplasty ± stent
1 year	89% (78–100)	74% (58–100)
3 years	65% (64–100)	na
5 years	59% (57–92)	na
Mean	37 (1–264) months	20 (1–23) months
follow-up	87% (76–100)	77% (63–100)

Numbers in parentheses represent range.

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