UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

Facoltà di Medicina e Chirurgia

Corso di Laurea Magistrale in Medicina e Chirurgia
Dipartimento di Scienze Biomediche, Metaboliche e Neuroscienze
Struttura Complessa di Chirurgia Vascolare
Direttore Prof. Roberto Silingardi

CHRONIC AND ACUTE-ON-CHRONIC MESENTERIC ISCHEMIA AS DIFFERENT ENTITIES: OUTCOMES OF A 25-YEAR-PERIOD STUDY

Relatore:
Prof. Stefano Gennai

Correlatore
Dott. Nicola Leone

Tesi di laurea di:
Chiara Sghedoni

Anno accademico: 2024 – 2025

Alla mia famiglia, senza cui nulla
di tutto questo sarebbe stato possibile

INDEX

ABBREVIATIONS 1

1 INTRODUCTION 2

1.1 ANATOMY AND PHYSIOPATOLOGY OF VISCERAL CIRCULATION 2

1.2 MESENTERIC ISCHEMIA: A COMPLETE OVERVIEW 5

1.2.1 Epidemiology 5
1.2.2 Classification 7
1.2.3 Etiology 8
1.2.4 Natural history 15
1.2.5 Clinical findings 18
1.2.6 Diagnostic techniques 20

1.3 MANAGEMENT OF MESENTERIC ISCHEMIA 27

1.3.1 AMI management in patients not showing peritonitis signs 29
1.3.2 AMI management in patients with peritonitis 33
1.3.3 AMI management in patients with septic shock 36
1.3.4 AoCMI management 38
1.3.5 CMI management 39
1.3.6 Post-operative therapy 40

2 AIM OF THE STUDY 41

3 MATERIALS AND METHODS 41

3.1 PROTOCOL DESCRIPTION 41

3.2 STUDY COHORT 42

3.2.1 Inclusion and exclusion criteria 42

3.3 PROCEDURAL DATA 42

3.4 STUDY OUTCOMES 43

3.5 DEFINITIONS 43

3.6 STATISTICAL ANALYSIS 44

4 RESULTS 44

4.1 BASELINE CHARACTERISTICS OF THE POPULATION 46

4.1.1 Active medical treatment among the study population 48

4.2 PRIMARY OUTCOME 49

4.2.1 Perioperative mortality 50
4.2.2 Overall mortality 50
4.2.3 Pathology-related mortality 51

4.3 CTA FINDINGS AND INTRAOPERATIVE DATA 53

4.4 SECONDARY OUTCOMES 55

4.4.1 Estimates fraction of reintervention during follow-up 56
4.4.2 Predictor factors for reintervention during follow-up 59

5 DISCUSSION 60

5.1 MORTALITY AND SURVIVAL 61
5.2 REINTERVENTION RATES AND PREDICTORS 64
5.3 LIMITATIONS OF THE STUDY 66
5.4 FUTURE PERSPECTIVES 66
6 CONCLUSIONS 67
7 REFERENCES 68
8 RINGRAZIAMENTI 75

ABBREVIATIONS

α-GST α-glutathione S-transferase
AAA abdominal aortic aneurysm
ABGA arterial blood gas analysis
AE arterial embolism
AF atrial fibrillation
ARDS acute respiratory distress syndrome
AT arterial thrombosis
AMI acute mesenteric ischemia
AoCMI acute-on-chronic mesenteric ischemia
CA coeliac artery
CACS ceoeliac artery compression syndrome
CAD coronary artery disease
CKD chronic kidney disease
CMI chronic mesenteric ischemia
COPD chronic obstructive pulmonary disease
CRP C-reactive protein
CT computed tomography
CT coeliac trunk
CTA computed tomography angiography
CVD cardiovascular disease
DAPT dual antiplatelet therapy
DCS damage control surgery
DES drug eluting stent
DOACs direct oral anti-coagulants
DSA digital subtraction angiography
DUS duplex ultrasound/ultrasonography
ePTFE expanded polytetrafluoroethylene
ESVS European Society for Vascular Surgery
GSV great saphenous vein
IBD inflammatory bowel disease
ICG indocyanine green
I-FABP intestinal fatty acid binding protein
IL-6 interleukin 6
IQR interquartile range
IMA inferior mesenteric artery
IMV inferior mesenteric vein
IV intravenously
LDH lactate dehydrogenase
LMWH low-molecular weight heparin
MAL median arcuate ligament
MALS median arcuate ligament syndrome
MAS mesenteric artery stenoses
MOF multi organ failure
MRA magnetic resonance angiography
MVT mesenteric venous thrombosis
NOMI non-occlusive mesenteric ischemia
PAD peripheric artery disease
PTA percutaneous transluminal angioplasty
ROMS retrograde open mesenteric artery stenting
SAPT single antiplatelet therapy
SD standard deviation
SMA superior mesenteric artery
SMV superior mesenteric vein
TNF tumor necrosis factor
VKAs vitamin K antagonists
WBC white blood cells

1 INTRODUCTION

Chronic mesenteric ischemia (CMI) and acute-on-chronic mesenteric ischemia (AoCMI) have attracted growing clinical interest in recent years, largely due to the aging population and the global rise in atherosclerosis. Furthermore, the potentially fatal nature of both conditions, if not promptly recognized and treated, underscores the need for rapid diagnosis in order to ensure a more favorable prognosis[1].

Additional aspects that make CMI and AoCMI compelling subjects of investigation include the current absence of specific clinical and laboratory diagnostic markers[2,3], the remarkable advancements in therapeutic approaches—particularly in the field of endovascular techniques—and the fact that, especially in the case of AoCMI, the available literature remains highly fragmented.

1.1 ANATOMY AND PHYSIOPATOLOGY OF VISCERAL CIRCULATION

Vascularization of small and large intestines, as well as of several other abdominal organs, is ensured by three main arteries, all arising from the abdominal aorta. These arteries, arranged in an upward to downward orientation, are the coeliac artery (CA)—which branches into the left gastric artery, splenic artery, and common hepatic artery—followed by the superior mesenteric artery (SMA) and inferior mesenteric artery (IMA). Despite this general arrangement, the origin of these arteries can show considerable variability, particularly in the case of CA, which may alternatively originate from the distal thoracic aorta or proximal abdominal aorta.

The three aforementioned arteries form significant anastomoses that ensure robust collateralization of the splanchnic circulation, with noteworthy variability among individuals. This collateral network represents one of the most important self-protective mechanisms in cases of mesenteric ischemia[4]. Depending on the progression rate of the obstructive process, the entire visceral blood supply can be compensated by alternative vessels through this collateral circulation.

Further collateralization of this vascular network may develop in response to stenosis exceeding 70% in mesenteric arteries. Consequently, it is evident that in cases of chronic mesenteric ischemia, symptomatic manifestations typically arise only in the presence of

multi-vessel disease[4]. Conversely, conditions of acute mesenteric ischemia affecting an otherwise healthy vascular system, generally result in a pronounced and rapid onset of symptoms due to the delayed development of compensatory pathways.

The CA and the SMA are interconnected via the pancreaticoduodenal arteries. The SMA and the IMA, on the other hand, are linked centrally through the arcades of Riolan and Villemin, and peripherally via the marginal arcade of Drummond (*Figure 1*[5]). Villemin arcade is referred to as an accessory arcade, which may be found only in 10-20% of the population[1,6,7].

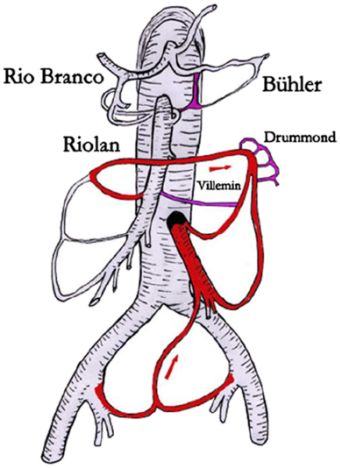


Figure 1. Collateral arcades between the main mesenteric arterial trunks

The celiac artery supplies blood to the esophagus—both diaphragmatic and abdominal segments—, to the liver via the common hepatic artery, to the gallbladder, to the stomach through the connection between the left and right gastric arteries and the left and right gastroepiploic arteries, to the spleen via the splenic artery, to the duodenum via branches of the gastroduodenal artery (itself a branch of the common hepatic artery), and to the superior portions of the pancreas through the pancreaticoduodenal arteries and branches of the splenic artery[8] (*Figure 2*[9]).

The SMA vascular territory includes the inferior portions of the duodenum and pancreas via the inferior pancreaticoduodenal artery; the jejunum and ileum through jejunal and ileal branches; the cecum via the ileocolic artery; the appendix; the ascending colon through the right colic artery; the right colic flexure; and the first half of the transverse colon via the middle colic artery[8] (*Figure 3*[10]).

As for the IMA, it provides vascular supply to the second half of the transverse colon, the left colic flexure, the descending colon, the sigmoid colon, and the rectum through its

terminal branches, namely the left colic artery, sigmoid arteries, and superior rectal artery[8] (*Figure 3*[10]).

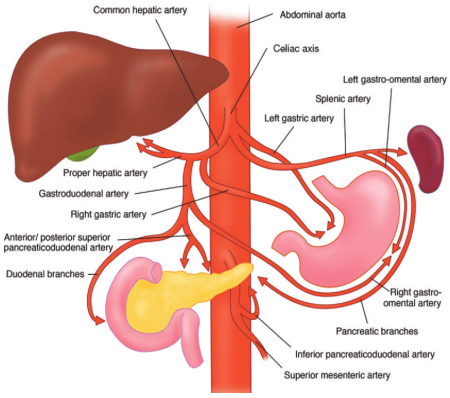


Figure 2. Coeliac artery: territory of vascular supply

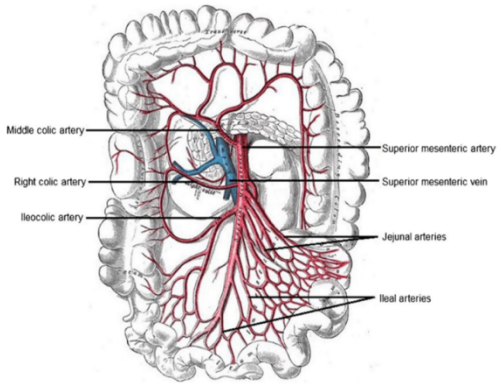


Figure 3. Frontal vision of mesenteric arteries and their branches

The origin of the superior mesenteric artery (SMA) from the aorta, approximately at the level of L1, creates a sharp angle that compresses the left renal vein. The initial segment of the artery is traversed by the neck of the pancreas and the splenic vein. Subsequently, the vessels pass over the uncinate process and the third portion of the duodenum before entering the root of the mesentery. Upon emerging beneath the pancreas, the SMA gives rise to the middle colic artery, which courses into the overlying root of the transverse mesocolon. Typically, the inferior pancreaticoduodenal artery is the first branch of the SMA on the right; however, it may also originate from the first jejunal branch. The jejunal and ileal branches arise from the left side, with their number ranging from 12 to 15. These branches form a series of arches and anastomoses at three or four levels, from which *vasa recta* and *vasa brevia* emerge to supply the intestinal wall and mucosa[7,11] (Table 1[12]).

Main artery	Main tributary arteries	Main areas supplied
Coeliac trunk	Common hepatic (branches: right gastric and gastroduodenal)	Liver; parts of stomach, duodenum and pancreas
	Splenic	Spleen; parts of stomach and pancreas
	Left gastric	Parts of stomach and lower oesophagus
Superior mesenteric artery	Inferior pancreaticoduodenal, intestinal (12–15 branches), ileocolic, right colic, middle colic	Small intestine, caecum, ascending colon, most of transverse colon; parts of duodenum and pancreas
Inferior mesenteric artery	Left colic, sigmoid, superior rectal	Descending and sigmoid colon; parts of transverse colon and rectum

Table 1. Arterial blood supply to the splanchnic region

At a microscopic level, a capillary network within the submucosal layer supplies blood to the intestinal villi, the most metabolically active region. In the event of reduced blood

flow, this network allows redistribution away from the mucosa while maintaining perfusion to the muscularis and serosa, resulting in ischemic necrosis of the superficial layer but preserving the overall structural integrity of the bowel (*Figure 4*[11]).

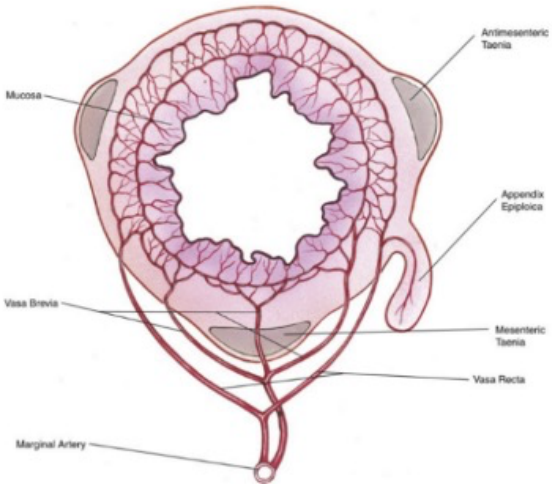


Figure 4. Intramural bowel vascularization

Furthermore, under normal conditions, only a small proportion of mesenteric capillaries are open, and oxygen demand can be met with as little as 20% of baseline blood flow, as the intestinal mucosa can extract increased amounts of oxygen during states of hypoperfusion[11,13,14].

1.2 MESENTERIC ISCHEMIA: A COMPLETE OVERVIEW

Mesenteric ischemia is a condition that arises when the mesenteric blood flow is inadequate to meet the vascular demands of the small and large bowel. As will be further discussed in the sections on classification and etiology, it can present as an acute, chronic, or acute-on-chronic process, and can result from a variety of underlying causes (e.g., cardioembolism, atherosclerosis, median arcuate ligament compression, etc.). This discrepancy between the pathological condition and the bowel's metabolic requirements leads to bowel necrosis and, if left untreated, may progress to peritonitis. CMI and AoCMI differ in terms of etiology, symptoms, and presentation. However, despite these differences, the underlying pathophysiological process is fundamentally the same: insufficient intestinal blood flow. The reason why symptoms tend to appear in postprandial time, especially after abundant and fatty meals, is because of the centralization of the blood volume at the splanchnic level. The increase in flow, associated with the potential presence of stenosis, leads to intense clinical manifestations.

1.2.1 Epidemiology

From an epidemiological perspective, mesenteric ischemia lacks reliable data. Accurately determining the true prevalence of the disease within the population proves challenging,

and the incidence rate appears to vary significantly depending on the type of mesenteric ischemia—whether acute, chronic, or acute-on-chronic—as well as on the underlying etiology (arterial, non-occlusive, or due to median arcuate ligament syndrome)[5].

With regard to AMI, the reported incidence ranges from 0.63 to 12.9 cases per 100,000 individuals per year[15]. This broad range underscores the existing uncertainty and divergence in the current literature. Some studies based on hospital admission data may underestimate the prevalence of AMI, whereas others—particularly those with high autopsy rates—report values approaching the upper limit of the cited range[5]. These findings suggest that a substantial number of AMI cases remain undiagnosed.
The epidemiology of AMI is closely linked to its root causes. According to studies, approximately two-thirds of AMI cases are attributable to thromboembolic occlusive causes, whereas non-occlusive mesenteric ischemia (NOMI) and mesenteric venous thrombosis (MVT) each account for roughly one-sixth of the cases.[16]

On the other hand, for CMI, the incidence rate can only be estimated and is generally reported to be approximately 3 cases per 100,000 individuals per year[15]; however, according to other studies, this figure may be significantly underestimated. Data from specialized centers in mesenteric ischemia suggest a much higher incidence, around 9.2 cases per 100,000 inhabitants. In the same study, incidence was shown to increase with advancing age, female sex, and underlying etiology. Atherosclerosis emerged as the most common cause, followed by median arcuate ligament syndrome (MALS) and non-occlusive chronic ischemia[17]. The discrepancy between sexes, with relative higher rate in females, might probably be attributable to different anatomic characteristics between the two genders: women generally have a lower angle of emergency of SMA, with a final more vertical course of the vessel[18].
A further condition that complicates the determination of the exact prevalence of CMI in the general population is that available data reflect only cases among treated patients. Despite the marked increase reported in recent years, this rise is likely attributable to a greater number of re-interventions rather than to a true increase in the incidence of the disease[5].

Turning to AoCMI, it is currently impossible, given the state of literature, to determine an exact incidence rate. AoCMI is generally regarded as a subset of AMI, and therefore

lacks dedicated studies. Due to the fragmented nature of the existing literature in this field, further research and studies should be encouraged and conducted.

1.2.2 Classification

Mesenteric pathologies can be classified in various ways, based on the presence or absence of symptoms, clinical presentation, and the specific vessel involved.

From a symptomatic perspective, mesenteric ischemia may present either as a symptomatic or asymptomatic condition. The nature of symptoms differs between acute and chronic forms. Acute mesenteric ischemia (AMI) typically occurs with severe abdominal pain as the predominant symptom, often described by healthcare professionals as a form of pain out of proportion relative to clinical findings[6]. If not promptly diagnosed and treated, this condition may culminate in bowel necrosis and, ultimately, peritonitis.[5] Additional common symptoms include nausea, vomiting, abdominal distension, and diarrhea.
Chronic mesenteric ischemia, on the other hand, is characterized by a constellation of symptoms commonly referred to as *angina abdominis*, which includes postprandial abdominal pain, significant unintentional weight loss over a short period (e.g., six months), food aversion, and diarrhea often lacking a clear organic cause[5,6].
A third possible clinical presentation is AoCMI, typically observed in patients with a history of abdominal angina who have recently experienced a worsening of their condition, such as more intense pain accompanied by partial or complete food refusal[5].

From a clinical standpoint, it is customary to distinguish AMI—defined as the sudden occlusion of a mesenteric artery resulting in the interruption of blood flow—from CMI, which is instead caused by a sustained reduction in mesenteric perfusion lasting at least three months[5]. Regarding AoCMI, the underlying pathophysiological mechanism is an acute hypoperfusion of the gastrointestinal tract superimposed on a pre-existing state of prolonged reduced blood flow, as previously described. This condition may arise from severe vasoconstriction or from an acute vascular occlusion due to events such as thrombosis or embolism. For this reason, it is also essential to distinguish between occlusive mesenteric ischemia and non-occlusive mesenteric ischemia (NOMI) as distinct physiopathological patterns of the disease.

Lastly, considering the specific vessel involved, mesenteric ischemia may result from altered blood flow in superior mesenteric artery (SMA), inferior mesenteric artery (IMA) or coeliac artery (CA).

1.2.3 Etiology

The etiologies of mesenteric ischemia vary significantly depending on the underlying pathophysiological mechanism. AMI may result from at least four distinct processes: acute mesenteric arterial embolism, acute mesenteric arterial thrombosis, non-occlusive mesenteric ischemia (NOMI), and mesenteric venous thrombosis (MVT).

Acute mesenteric arterial embolism (AE) occurs when an embolus obstructs the splanchnic circulation. An embolus can be defined as an intravascular mass—whether solid, liquid, or gaseous—that travels through the bloodstream from one site to another, ultimately lodging in a vessel too narrow to allow its passage, thereby causing vascular occlusion[19]. Emboli can be categorized according to their origin into thrombotic, gaseous, tumoral, septic, or fat types.

In the specific case of mesenteric ischemia, emboli most commonly originate from cardiac conditions such as atrial fibrillation (AF), left ventricular dysfunction with reduced ejection fraction, or endocarditis. Only in a minority of cases, they may originate from atherosclerotic plaques within the aorta[20]. Furthermore, mesenteric arterial embolism is frequently accompanied by embolic events in other visceral arteries, including the splenic and renal arteries[21].

SMA is the most frequently affected splanchnic artery, primarily due to its anatomical configuration. It originates from the aorta at a low angle and courses anteriorly over the horizontal portion of the duodenum; this structure facilitates the entry of emboli traveling through aorta. In certain cases, this anatomical relationship may lead to compression of the duodenum, resulting in SMA Syndrome, also known as Wilkie Syndrome. In this condition, the third portion of the duodenum becomes trapped between the aorta and the SMA. Additionally, due to its relatively large caliber, emboli commonly become lodged within the SMA approximately 3 to 10 cm distal to its origin[20].

Acute mesenteric arterial thrombosis (AT) instead, typically occurs as a result of a pre-existing atherosclerotic disease, upon which thrombus formation develops. The progressive narrowing caused by the atherosclerotic plaque gradually compromises blood flow, often leading to *angina abdominis* cohort of symptoms and promoting the formation of collateral circulation. Eventually, plaque evolution triggers the formation of an occlusive thrombus, leading to abrupt interruption of blood supply to the splanchnic territory. In terms of localization, thrombi usually form at the origin of the mesenteric artery—causing ostial occlusion—unlike emboli, which typically lodge in more distal segments[20] (Figure 5[22]). Additionally, while mesenteric embolic events are often associated with splenic and renal arteries obstruction, thrombotic occlusion more frequently involves CA[16]. It is therefore evident that acute mesenteric arterial thrombosis is more commonly a cause of AoCMI rather than of AMI.

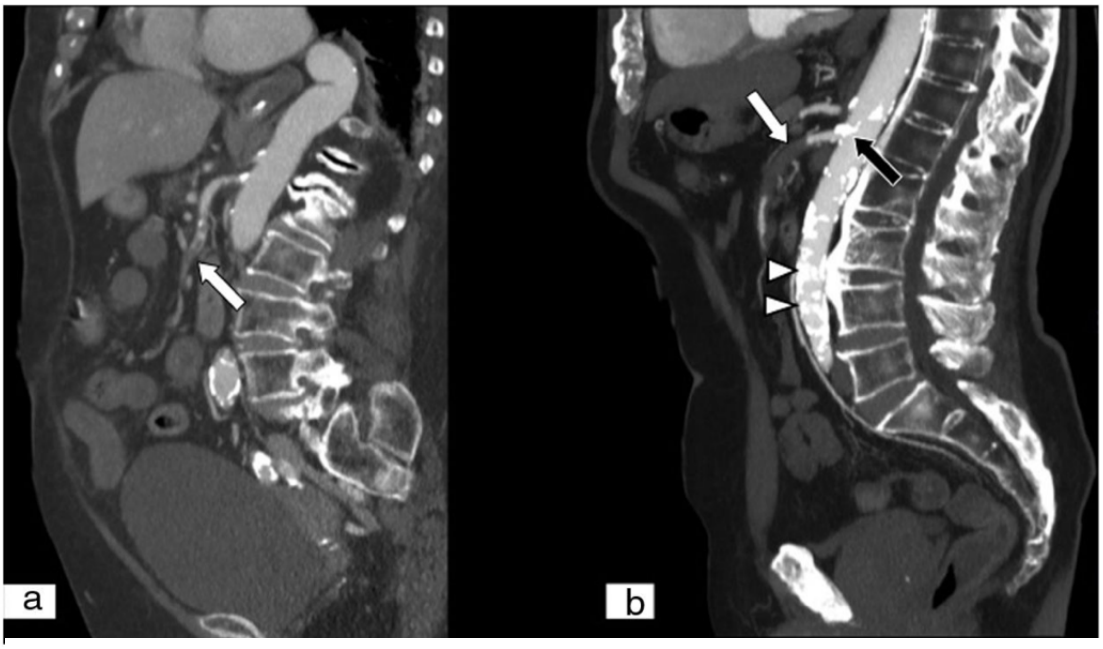


Figure 5. (A) SMA embolism in multiplanar reconstruction CT: distal localization of the embolus, (B) SMA thrombosis in multiplanar reconstruction CT: ostial localization of the thrombus

NOMI represents the third recognized etiology of AMI and results from either profound hypotension or intense vasoconstriction. Both conditions impair adequate perfusion of the splanchnic circulation, ultimately leading to intestinal ischemia. This pathophysiological state is commonly observed in clinical scenarios involving prolonged vasopressor use, severe cardiac failure, or multi-organ dysfunction syndrome in course of septic shock[20,23] (Figure 6[22]).

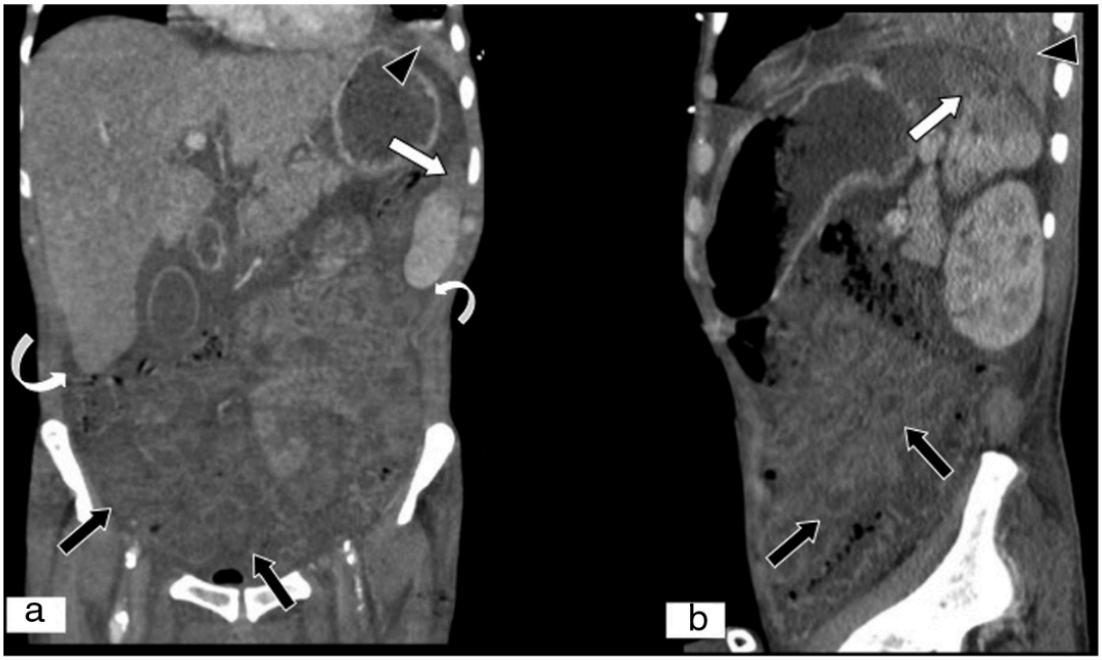


Figure 6. NOMI in a patient with septic shock in coronal MPR-CT (A) and sagittal MPR-CT (B)

Mesenteric venous thrombosis (MVT) represents the fourth major cause of mesenteric ischemia and differs fundamentally from arterial forms in its underlying mechanism. Unlike arterial obstruction, MVT induces ischemia through impaired venous outflow (Figure 7[22]). It accounts for approximately 20% of all AMI cases, with an estimated incidence of 2.7 per 100,000 person-years, showing no gender predilection[24].

The pathogenesis of MVT is best understood through Virchow's triad, which identifies three essential contributors to thrombus formation: hypercoagulability, blood flow stasis, and endothelial injury. Hypercoagulability may stem from inherited conditions such as Factor V Leiden mutation, prothrombin gene mutation, protein S deficiency, or antiphospholipid syndrome. However, acquired disorders also play a significant role and include inflammatory diseases involving the superior mesenteric vein (SMV), recent abdominal surgeries, malignancies (both solid tumors and hematologic cancers), and certain medications like oral contraceptives[1].

Stasis of venous blood flow is frequently related to portal hypertension, most commonly due to hepatic cirrhosis or severe right-sided heart failure. Anatomically, the portal vein is formed by the confluence of the SMV and the splenic vein, the latter having previously received the inferior mesenteric vein (IMV) along its course[10]. This vascular configuration helps explain how elevated portal pressure contributes to stasis in both the SMV and IMV. In congestive heart failure, by contrast, global impairment of venous return leads to systemic venous stasis, including within the mesenteric circulation.

Regarding the third element of Virchow's triad—endothelial injury—this may result from local inflammatory processes. Conditions such as acute pancreatitis or inflammatory bowel disease (IBD) can cause direct inflammation surrounding the mesenteric veins, thereby predisposing to thrombus formation[20,24].

Ultimately, in MVT, mesenteric ischemia arises from obstruction of venous outflow, preventing the normal drainage of blood from the intestinal wall into the portal circulation. This leads to third-space fluids accumulation, bowel wall edema, and microcirculatory dysfunction, which collectively contribute to ischemic injury of the gut.

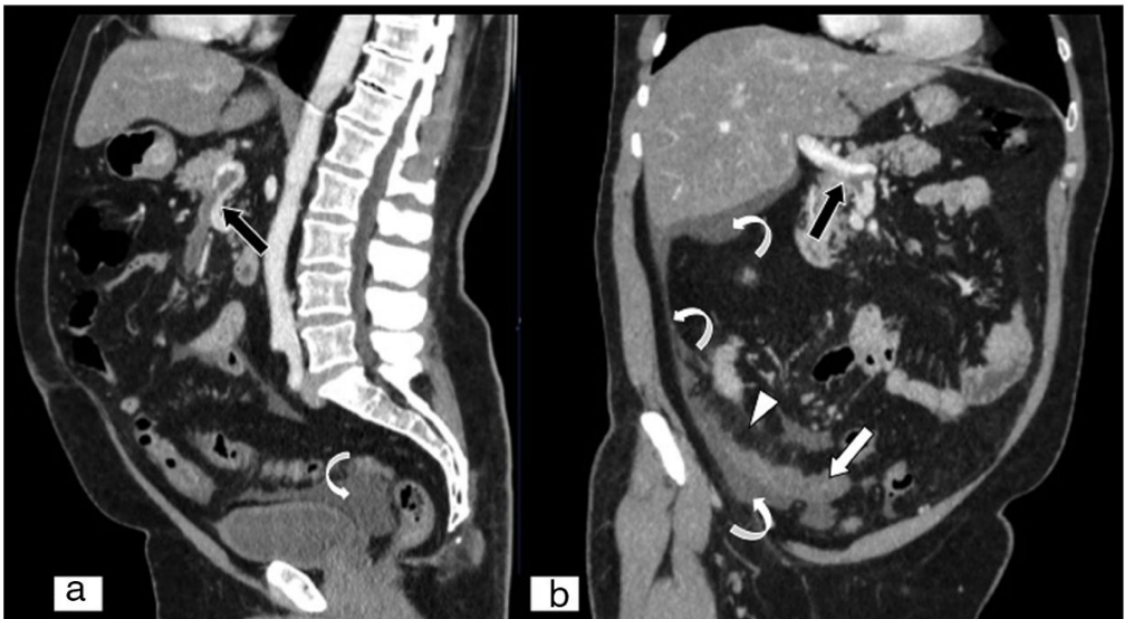


Figure 7. Mesenteric ischemia of venous origin in sagittal MPR-CT (A) and in oblique-coronal MPR-CT (B)

Risk factors for specific types of AMI are listed in the table below (Table 2[20]).

	Pathogenesis of AMI			
	Acute mesenteric arterial embolism	**Acute mesenteric arterial thrombosis**	**NOMI**	**Mesenteric venous thrombosis**
Risk factors	Atrial fibrillation recent MI cardiac thrombi Mitral valve disease Left ventricular aneurysm Endocarditis Previous embolic disease	Diffuse atherosclerotic disease Postprandial pain Weight loss	Cardiac failure Low flow states Multiorgan dysfunction Vasopressors Abdominal compartment syndrome	Portal hypertension history of VTE Oral Contraceptives Estrogen use Thrombophilia Pancreatitis
Clinical onset	Sudden strong abdominal pain, vomiting	Progressive or sudden abdominal pain, vomiting, diarrhea and/or melena	Progressive pain, mild	Nonspecific GI symptoms, abdominal distension, worsening of general condition
Vascular involvement	Main artery or branches of SMA	Celiac trunk, SMA, IMA origins	Superior mesenteric vein, progression to portal vein	Stenosis of SMA

Table 2. Risk factors for specific types of AMI

The etiology of AMI has significantly evolved in recent years. Historically, thromboembolic events accounted for approximately 66% of all cases. While they still

represent a major proportion, a redistribution within this category has occurred: arterial embolism has relatively declined to around 25%, whereas arterial thrombosis has increased to nearly 40%, compared to the previously reported 25–30%.

The decline in embolic events may be largely attributed to the widespread use of novel anticoagulant therapies—such as direct oral anticoagulants (DOACs)—which have substantially improved the management of conditions like atrial fibrillation (AF). Conversely, the rise in thrombotic cases likely reflects the global increase in atherosclerotic disease burden.

Additionally, non-occlusive mesenteric ischemia (NOMI), currently accounting for approximately 25% of AMI cases, also appears to be on a gradual upward trend[20,25].

All AMI etiologies are summarized in the diagram below (Diagram 1).

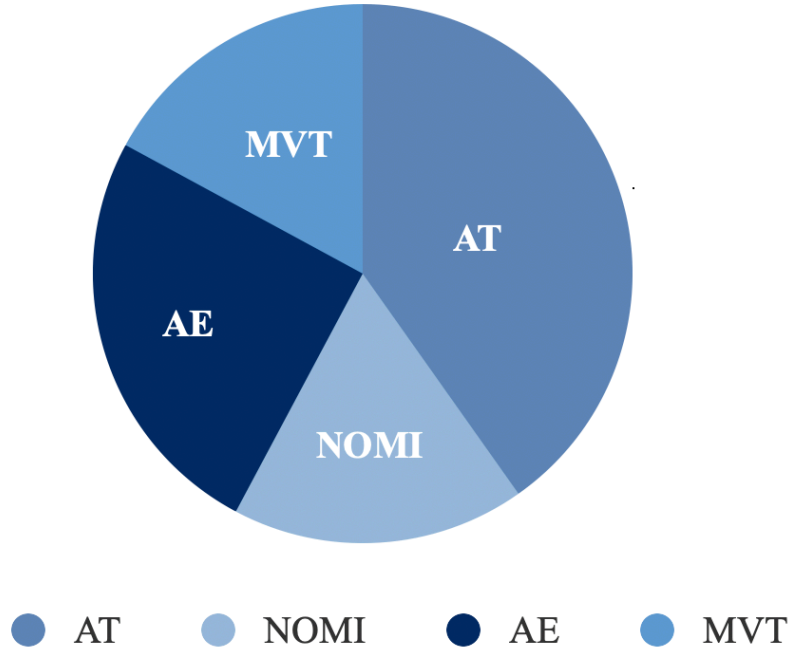


Diagram 1. AMI etiology incidences in the global population

With regard to AoCMI—considered as a distinct subset of AMI—the etiological mechanisms should be interpreted in line with those previously discussed. However, it is essential to emphasize that the acute ischemic event typically arises on a pre-existing chronic condition. Any of the four main pathophysiological mechanisms may underlie AoCMI, although acute mesenteric arterial thrombosis is the most frequently observed cause, largely due to its strong association with chronic atherosclerotic disease.

For what concerns CMI, despite the general belief that the only possible etiology is mesenteric artery stenosis (MAS) due to atherosclerosis, there are many others worth mentioning. Possible causes of CMI must include vasculitis, fibromuscular dysplasia, MALS—also referred to as coeliac axis compressive syndrome (CACS) or Dunbar syndrome—and NOMI[4]. In the following lines each condition will be further investigated.

MAS are the consequence of atherosclerotic disease which develops subsequently to the widely known cardiovascular risk factors: obesity, hypertension, smoking, hypercholesterolemia, diabetes, family history of cardiovascular disease (CVD), and contrary to what is observed in other vascular beds, female sex. The presence of these risk factors contributes both to the formation of MAS and to the reduction of splanchnic perfusion. Nevertheless, the prevalence of MAS far exceeds that of clinically manifest CMI, largely due to the development of collateral circulatory pathways. This disparity helps explain why many individuals with MAS do not experience symptoms associated with *angina abdominis*[4,26,27].

Fibromuscular dysplasia defined as an *"idiopathic, segmental, non-atherosclerotic and non-inflammatory disease of the musculature of the arterial walls, which leads to stenosis of small and medium-sized arteries"*[28] is, along with vasculitis (e.g., Takayasu's arteritis, Buerger's disease and autoimmune arteritis[2]), a more infrequent cause of CMI.

Median arcuate ligament syndrome (MALS) is a functional clinical condition caused by the dynamic and direct compression of the coeliac artery (CA) by the median arcuate ligament (MAL)[4,29]. Although the terms MALS and coeliac axis compression syndrome (CACS) are often used interchangeably, they are not entirely synonymous. MALS specifically refers to the clinical syndrome resulting from compression by the MAL, whereas CACS is a broader term indicating compression of the CA regardless of the underlying cause—which may include not only the MAL, but also enlarged lymph nodes, tumors, other vascular anomalies, or internal hernias (Figure 8[22]).

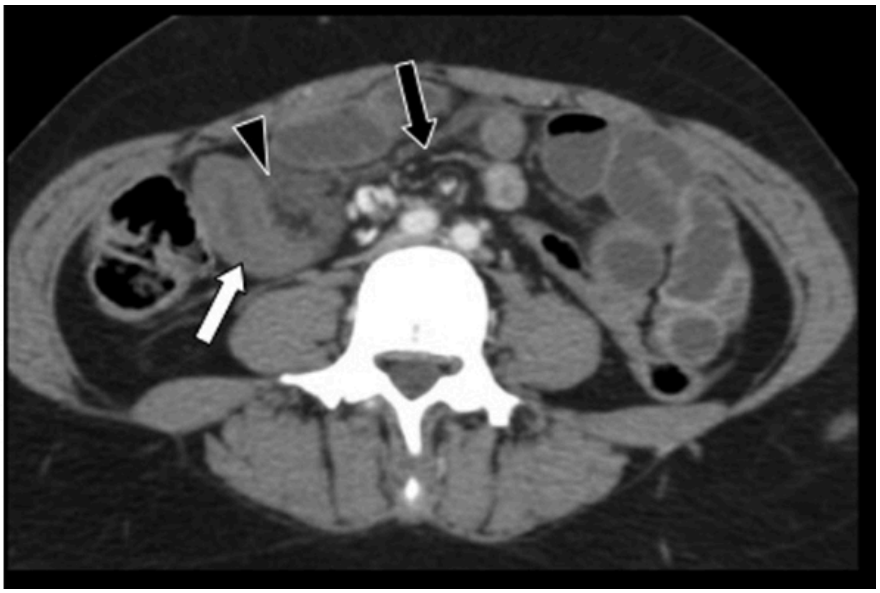


Figure 8. Coeliac axis compression by an internal hernia

The MAL is a fibrous band that connects the right and left diaphragmatic crura and typically lies superior to the origin of the CA. However, due to significant interindividual anatomical variability, a low-lying MAL or a high-origin CA can result in compression of the artery, leading to the characteristic symptoms of the syndrome[29]. This compression is dynamic in nature and tends to be more pronounced during the expiratory phase of respiration, due to the fact that during inspiration the ligament moves cranially and partially relieves the compression[1] (Figure 9[4]).

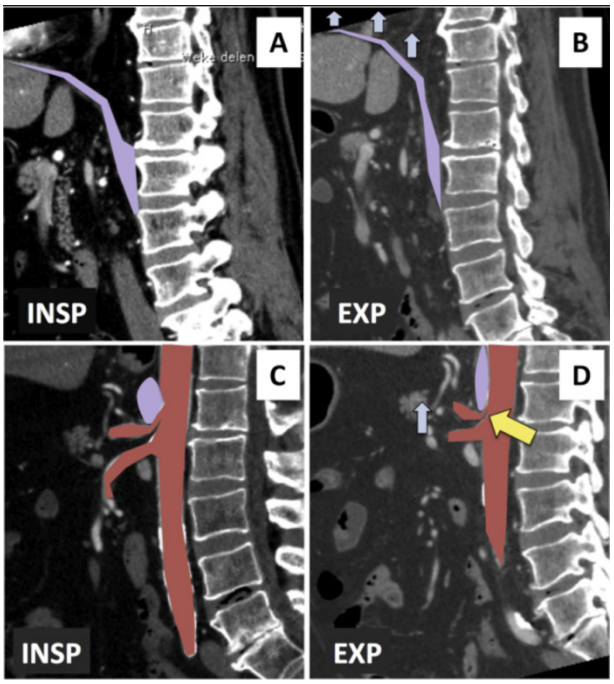


Figure 9. Median arcuate ligament syndrome: compression of the coeliac artery

The final potential etiology of CMI is NOMI, previously discussed in the context of AMI. In NOMI, mesenteric ischemia occurs despite the presence of anatomically normal arteries. As the name suggests, the underlying mechanism is non-occlusive and typically results from low-flow states. However, since we are dealing with CMI, it is important to distinguish these low-flow conditions from those causing AMI.

Non-obstructive CMI most commonly affects critically ill individuals, surgical patients—particularly those undergoing aortic procedures, in whom NOMI serves as an adverse prognostic factor[30]—and endurance athletes. Among critically ill patients, those at highest risk include individuals with heart failure, end-stage pulmonary disease, vasoconstrictive disorders, and Raynaud's phenomenon. All the aforementioned conditions impair oxygen delivery to the splanchnic circulation, creating a mismatch between supply and metabolic demand. This imbalance can result from structural deficits (e.g., cardiac or pulmonary failure) or functional issues, such as autonomic dysfunctions, which are frequently observed in endurance athletes and patients with Raynaud's phenomenon[2,4].

The association between non-occlusive CMI and endurance athletes is primarily attributed to the redistribution of blood flow toward active peripheral muscles. During sustained and intense physical activity, a significant reduction—up to nearly 80%—in splanchnic blood flow is essential to prioritize perfusion of the working musculature, where the metabolic demand is substantially higher. This physiological adaptation is finely regulated by the sympathetic nervous system, which maintains a subtle balance between central vasoconstriction and peripheral vasodilation[31].

Also referred to as "abdominal migraine", NOMI accounts for approximately 13–16% of CMI cases[2]. The term "migraine" emphasizes the functional component of the disorder, highlighting the characteristic presence of abdominal angina symptoms in the absence of vascular stenosis.

1.2.4 Natural history

A clear understanding of the natural history of mesenteric ischemia requires a preliminary overview of the normal physiology of splanchnic circulation. Under fasting conditions, approximately 20% of the total cardiac output is directed to the splanchnic circulation, with an oxygen extraction rate accounting for about 20–35% of whole-body oxygen consumption[4,12].

These values change notably in response to metabolic demands, particularly after food intake. Among the various types of meals, those rich in fats induce the greatest and most sustained increase in splanchnic blood flow, exceeding the responses observed after carbohydrate or protein consumption. The postprandial rise in blood flow, compared to the fasting state, ranges between 35% and 50%, depending on the specific vascular territory involved—namely the celiac artery (CA) or the superior mesenteric artery (SMA)[4].

Just as splanchnic blood flow increases in response to elevated metabolic needs, it is equally capable of rapid and significant reductions when blood must be redistributed to more metabolically active tissues. This adaptive response does not necessarily result in mesenteric ischemia, owing to the region's remarkable ability to enhance oxygen extraction, which can reach levels as high as 90%[12].

This finely tuned mechanism represents a crucial self-preservation strategy that prioritizes perfusion of vital organs such as brain, heart, and kidneys[4]. Indeed, during states of intense adrenergic stimulation—regardless of the underlying cause—splanchnic vasoconstriction is among the earliest physiological responses observed.

The regulation of splanchnic blood flow is governed by both intrinsic and extrinsic mechanisms. The intrinsic regulation involves metabolic and myogenic factors. From a metabolic perspective, the accumulation of metabolites—such as hydrogen ions, potassium, carbon dioxide, and adenosine—induces vasodilation and promotes hyperemia. Myogenic control, on the other hand, is mediated by arteriolar stretch receptors, which respond to sudden decreases in splanchnic perfusion pressure by lowering vascular resistance in order to preserve adequate blood flow.

Extrinsic regulation is primarily mediated by neural and humoral components (Table 3[32]). Vasoconstriction is induced through alpha-adrenergic sympathetic fibers and circulating catecholamines such as epinephrine and norepinephrine. In contrast, vasodilation is promoted by beta-adrenergic stimulation and several vasoactive substances including nitric oxide, leukotrienes, histamine, and acetylcholine[32].

Physiologic and Pharmacologic Factors Regulating Mesenteric Blood Flow (Extrinsic Regulatory System)

Decrease Blood Flow	Increase Blood Flow
Humoral (Endogenous and Exogenous)	
Epinephrine (high dose)	Epinephrine (low dose)
Norepinephrine (moderate to high dose)	Norepinephrine (low dose)
Dopamine (high dose)	Dopamine (low dose)
Phenylephrine	Dobutamine
Vasopressin	Sodium nitroprusside
Angiotensin II	Papaverine
Digoxin	Nitric oxide
Neural	
α-Adrenergic receptors	β-Adrenergic receptors
Dopaminergic receptors	

Table 3. Extrinsic system regulating factors

When splanchnic blood flow becomes insufficient to meet the metabolic demands of the small and large intestines, compensatory mechanisms aim to increase oxygen extraction. This adaptation allows the bowel to tolerate significant reductions in blood flow—up to 75%—for extended periods, sometimes lasting as long as twelve hours. However, in cases of complete vascular occlusion, mesenteric ischemia typically develops within six hours[1].

When the increase in oxygen extraction is no longer sufficient to meet metabolic needs, prolonged ischemia ensues. Microscopically, this is characterized by endothelial injury and disruption of the mucosal barrier. As previously describes, due to the specific architecture of the splanchnic capillary networks, the circulation is able to preserve the muscularis mucosa and serosa even under sustained ischemic conditions, at the expense of the superficial mucosal layers. At this level, most of the tissue damage is not caused by ischemia itself, but rather by the subsequent reperfusion. This process is driven primarily by reactive oxygen species and polymorphonuclear neutrophils. The detrimental role of oxygen in this context is underscored by the observation that antioxidants or xanthine oxidase inhibitors significantly reduce tissue injury following reperfusion[32].

Reperfusion also triggers the systemic release of inflammatory mediators such as interleukin-6 (IL-6) and tumor necrosis factor (TNF), which exert widespread effects. These cytokines contribute to systemic inflammation and can impair multiple organ systems: in the vascular system, they may induce shock and profound hypotension; in the lungs, they can lead to acute respiratory distress syndrome (ARDS); and in the abdomen,

once transmural necrosis occurs, they promote the development of peritonitis and acute abdomen, also due to bacterial translocation in case of lack of mucosal integrity. The convergence of these complications may ultimately lead to multi-organ failure (MOF)[33].

The aforementioned pathophysiological process is characteristic of both AMI and CMI. In AMI, it is a direct consequence of the abrupt vascular occlusion. For what concerns CMI, the same process develops either in the setting of an acute event occurring over a chronic condition (AoCMI), or in cases where the compensatory role of previously developed collateral circulations becomes insufficient to guarantee efficient perfusion. In all such scenarios, the disease progression follows the same pattern as described above.

1.2.5 Clinical findings

Clinically, mesenteric ischemia—AMI—lacks specific, pathognomonic signs[34]. Nonetheless, certain recurring patterns can be observed across its various subtypes. The clinical manifestations differ notably among the distinct forms of AMI—namely AE, AT, NOMI, and MVT—as well as in comparison to CMI.

In the case of AE, the clinical picture is typically characterized by a sudden onset of severe abdominal pain, spontaneous gastric emptying through vomiting and diarrhea, and the absence of significant abdominal findings on examination. This triad is highly suggestive and should raise suspicion. Considering AF as the leading risk factor for this condition, every patient with AF and severe abdominal pain should be investigated for AMI[5]. A hallmark of AE, also shared with AT, is the presence of pain that appears disproportionately severe relative to the minimal physical findings.
However, in AT, the abdominal pain may not present abruptly but tends to develop insidiously. It is often preceded by a chronic history of postprandial pain, progressive weight loss, and nausea. Gastrointestinal bleeding—manifesting as melena or other signs—can occur in both embolic and thrombotic events and is particularly indicative of colonic ischemia. The extent of ischemia is typically greater in AT due to the more proximal nature of occlusion, which is generally ostial in AT while distal in AE[33].

Regarding NOMI, it should be considered as a potential etiology in patients presenting with the triad of abdominal pain, abdominal distension, and signs of shock of unclear origin. The onset may be either acute or subacute, depending on the progression of the

underlying condition. Patients often experience clinical deterioration, and while not specific to AMI, intolerance to enteral nutrition should be considered a warning sign for the presence of the condition[33,35].

Mesenteric venous thrombosis (MVT), which may present acutely or sub-acutely, typically manifests with symptoms such as nausea and vomiting[33].
To summarize, all typical presentations are listed in the table below (Table 4[33]).

Cause	Presentation
Arterial embolism	Triad–sudden onset of pain, spontaneous gastric emptying (vomiting and diarrhea) with absence of physical signs.
Arterial thrombosis	Post-prandial pain, weight loss, nausea, insidious onset with progression to chronic pain
NOMI	Acute or subacute
Venous thrombosis	Acute or subacute, nausea and vomiting

Table 4. Characteristics associated with acute mesenteric ischemia

From a clinical perspective, AMI is often difficult to distinguish from ischemic colitis due to a significant overlap in symptoms. However, the key differentiating factor lies in the underlying conditions. Ischemic colitis typically occurs in the absence of persistent systemic hypoperfusion or chronic atherosclerotic disease and is not associated with occlusion of large vessels. Instead, it is more commonly linked to small vessel obstruction or prior aortic surgery involving sacrifice of the IMA. The relatively mild pathophysiology of ischemic colitis is further supported by the standard therapeutic approach, which usually consists of conservative measures such as antibiotic therapy, fluid resuscitation, and, in some cases, abdominal decompression—highlighting that the condition does not arise from severe vascular obstruction.

AoCMI, as other possible type of mesenteric ischemia, has the typical acute presentations depicted above, in relation to the causing process, occurring on an already chronic situation of post-prandial pain, weight loss and food fear. Acute or gradually worsening

abdominal pain should raise suspicion of AoCMI, especially in patients with a history of *angina abdominis* symptoms. In any situation where CMI symptoms are advancing, AoCMI should be highly suspected and treated if necessary[16].

Also, AMI and AoCMI are prevalent etiologies of acute abdomen and peritonitis in the elderly population. Although these conditions are often regarded as rare, they are more frequent causes of acute abdomen than appendicitis or ruptured abdominal aortic aneurysm (AAA) and are associated with higher mortality rates in emergency settings. Consequently, AMI should invariably be included in the differential diagnosis flowchart for acute abdomen cases in emergency departments[36,37].

CMI, as the final clinical presentation within the mesenteric ischemia spectrum, is characterized by a more defined and recognizable symptomatology. The typical symptom cluster includes postprandial pain localized to the mid-abdomen or epigastric region, usually beginning 20–30 minutes after eating and persisting for 1–2 hours, which can be referred to as *angina abdominis*. This hallmark symptom is commonly associated with significant weight loss over a short period (e.g., six months), food aversion, also known as sitophobia, and a range of less specific symptoms, such as persistent abdominal discomfort, nausea, vomiting, diarrhea or constipation, and gastrointestinal bleeding[2,3,5].

The classic diagnostic triad—postprandial pain, weight loss, and abdominal bruit—is particularly suggestive of CMI, with the abdominal bruit indicating the presence of turbulent flow due to stenotic or occluded mesenteric vessels. This cohort of symptoms may be found in 16-22% of people with CMI[2–4].

Therefore, unexplained weight loss in a patient with known severe peripheral arterial disease (PAD) should raise clinical suspicion and prompt further investigation for CMI[2,38,39].

1.2.6 Diagnostic techniques

Beyond clinical findings, the diagnosis of mesenteric ischemia—whether AMI, AoCMI, or CMI—relies on a combination of laboratory investigations and imaging studies. However, as consistently reported in literature, there is no established gold standard test nor any highly specific diagnostic biomarker[2,3].

For clarity and accuracy in the diagnostic approach, AMI and AoCMI should be discussed separately from CMI, as they have slightly different characteristics.

In the context of diagnosing AMI and AoCMI determined by embolism or thrombosis, laboratory tests play a crucial role. Some indicators that may be present in these conditions include increased serum lactate and D-dimer levels, neutrophilic leukocytosis, and metabolic acidosis at the arterial blood gas analysis (ABGA). With regard to metabolic acidosis, what can actually be observed in early phases at ABGA is metabolic alkalosis probably as a result of vomiting as one of the first manifestations of mesenteric ischemia[40]. Additional markers might involve hemoconcentration and elevated serum levels of amylase, lactate dehydrogenase (LDH), and aspartate aminotransferase (AST)[1]. However, as previously noted, none of these markers is highly accurate for diagnosis. The most significant early marker is D-dimer, which has high sensitivity but low specificity. Sensitivity refers to the test's ability to correctly identify individuals with the illness, meaning that a high sensitivity results in a very low rate of false negatives. Conversely, specificity is the test's ability to accurately identify healthy individuals who do not have the illness; high specificity leads to a very low rate of false positives. Given these characteristics, D-dimer is a valuable exclusion test. This implies that a negative D-dimer result, with normal values, typically rules out the chance of thromboembolic events[5,16].
Serum lactate is another plasma marker to be considered in the diagnostic work-up. Although it shares high sensitivity and low specificity with D-dimer—making it a potentially valuable exclusion marker—its diagnostic utility is limited by the time it takes to rise. Typically, serum lactate levels remain normal during the early stages of mesenteric ischemia and only begin to increase with the onset of bowel necrosis. Therefore, a normal lactate concentration does not exclude AMI, but may simply indicate that necrosis has not occurred yet[1,5,16]. To date, no reliable biomarker has been identified for detecting hypoperfusion in the early stages of AMI before irreversible bowel necrosis has developed[16]. Hence, there is a lack of accurate non-invasive modalities for the diagnosis of acute thromboembolic occlusion of the superior mesenteric artery[41].

Several efforts have been made to identify an ideal biomarker, with particular attention to the progression of necrosis from the mucosal layer—initially affected due to the microvascular architecture of the bowel wall—toward the serosa, which is typically spared in early stages. This pattern has been frequently studied in the search for

biomarkers indicative of mucosal necrosis, which could serve as early indicators of bowel injury while the condition remains potentially reversible through timely revascularization[42]. Following this direction some markers have been identified as promising candidates for the early detection of intestinal injury, including Intestinal Fatty Acid Binding Protein (I-FABP), α-glutathione S-transferase (α-GST), and D-lactate[42,43]. D-lactate is the isomer of L-lactate: while L-lactate is the common isomer produced in humans, D-lactate is the result of glycolysis carried out by bacteria in human colon, explaining its presence at the mucosal level[5]. The other two markers mentioned above are both located in the small intestine mucosa layer, being the former (I-FABP) a cytoplasmatic protein of jejunum and ileum enterocytes, while the latter (α-GST) a cytoplasmatic enzyme involved in cellular detoxification, with a key role in oxidation stress defense. All three molecules are located in the intestinal mucosa (Figure 10[42]) and can readily enter the bloodstream in case of mucosal damage. Although these markers may enhance early diagnosis of AMI and AoCMI, their specificity is limited, as elevated levels can also be observed in other conditions such as bacterial translocation and non-ischemic mucosal injury[42,43].

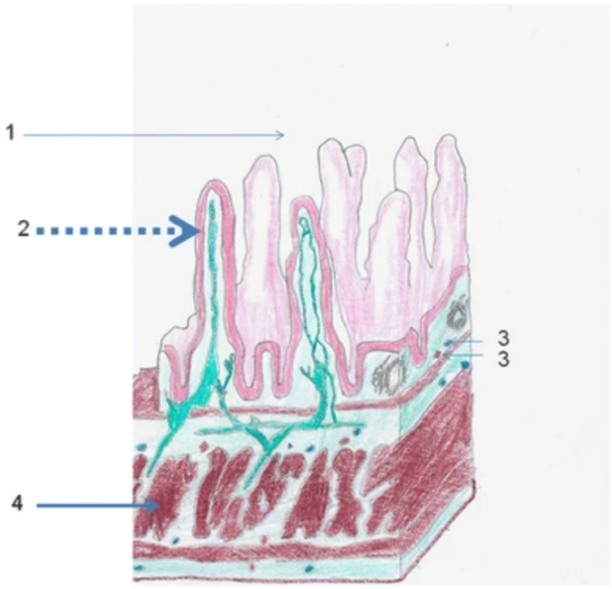


Figure 10. Proposed plasma biomarkers for AMI: 1. D-lactate in the lumen (long arrow), 2. I-FABP and α-GST in the epithelium (dotted arrow), 3. D-dimer in small arteries and veins (short arrows), 4. Creatine kinase in the muscular layer (thick arrow)

Given the complexity of establishing a prompt diagnosis, patients with AMI or AoCMI are frequently referred to multiple specialists before the underlying condition is recognized. Some are evaluated by cardiologists due to elevated troponin levels, while others are seen by internists for unexplained increases in serum amylase and

gastrointestinal symptoms such as vomiting and diarrhea. Therefore, it is vital to consider laboratory findings collectively rather than in isolation, in order to avoid misdirection from the correct diagnosis[5,16].

Considering that laboratory tests alone are insufficient to establish a definitive diagnosis of AE or AT, imaging plays a central role. Among the available modalities, technological advancements have positioned computed tomography angiography (CTA) as the current gold standard[5,16,40,44]. Plain abdominal radiographs are useful solely in cases where bowel perforation is suspected, while duplex ultrasound (DUS) is limited by its strong operator dependence and the time it requires[1,16]. As previously mentioned, contrast-enhanced CTA remains the only imaging modality capable of providing a definitive diagnosis of AE or AT, with each condition displaying distinct radiologic features.

In cases of embolism, distal occlusion is typically observed, often involving multiple vessels and they generally appear as "oval-shaped filling defects located within non-calcified arterial segments" as mentioned by current ESVS Clinical Practice Guidelines[5]. In cases of thrombosis, CTA imaging typically reveals the occlusion as a hypodense thrombus overlying a hyperdense, calcified atherosclerotic plaque[5].

CTA remains the crucial imaging to diagnose AMI due to its key advantages: it is a rapid imaging modality that does not require oral contrast—often poorly tolerated by patients with suspected mesenteric ischemia; the contrast is in fact administered intravenously (IV). For this reason, CTA should be performed even in patients with renal impairment, whether acute or chronic. Despite the potential risk of renal function worsening, its ability to precisely detect vascular occlusion makes it a life-saving diagnostic tool[1,5,45]. Furthermore, to ensure optimal diagnostic accuracy, the scan should be performed during both arterial and venous phases, with a slice thickness of 1 mm in the arterial phase[16]. The reliability of CTA is supported by several studies, reporting a sensitivity ranging from 73% to 100% and a specificity between 90% and 100%[23,46,47].

CTA not only enables the visualization of the exact site of occlusion in cases of AE or AT, but also reveals indirect signs suggestive of AMI progression toward bowel necrosis. These include intestinal pneumatosis (air within the bowel wall), wall oedema, gas in the porto-mesenteric venous system, and abnormal contrast enhancement of the bowel wall (Figures 11, 12[22]). Although these findings are not highly specific, being also present in other conditions such as intrabdominal infection, their presence should raise a strong clinical suspicion for AMI[1,48].

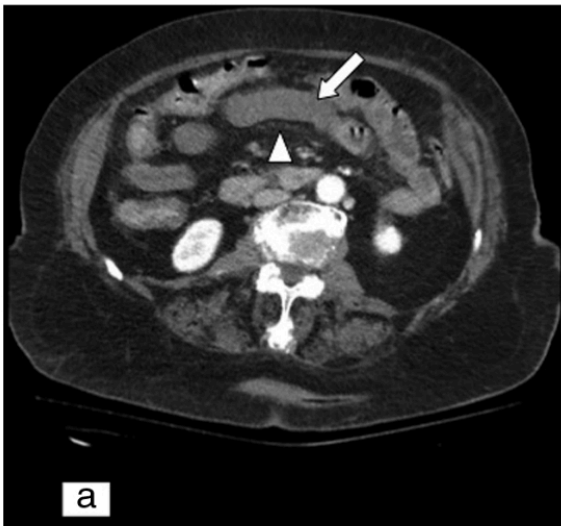


Figure 11. Abnormality in intestinal parietal uptake

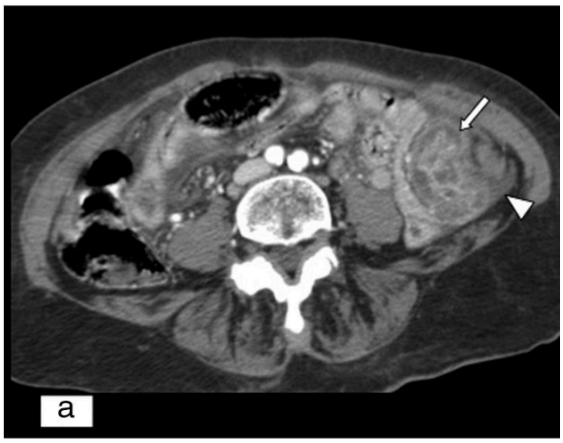


Figure 12. Oedema of the intestinal wall due to venous thrombosis

For what concerns NOMI its diagnosis is particularly challenging and should rely primarily on the patient's clinical condition, history, and physical findings. A high level of suspicion should raise in all cases of severe and global clinical deterioration, particularly in patients with a recent history of cardiac surgery or cardiopulmonary resuscitation[48].

Serum biomarkers may be considered in a similar way as in embolic or thrombotic causes of AMI, including D-dimer, serum lactate, white blood cell (WBC) count, metabolic acidosis, LDH, and AST. However, their diagnostic accuracy remains limited. In particular, the use of D-dimer, WBC count, and LDH is discouraged due to their low specificity in critically ill patients, where multiple confounding factors are often present. While I-FABP shows promise as an early diagnostic marker also for NOMI, further research is needed to validate its clinical utility[48].

Regarding imaging, the diagnostic role of CTA in NOMI is limited when compared to its established accuracy in embolic or thrombotic mesenteric ischemia and should not be used as first-line examination[30,48,49].

Angiography, especially in the form of digital subtraction angiography (DSA), has historically been the gold standard for diagnosing splanchnic vascular diseases, also having an operative-therapeutic role; its role has deeply evolved throughout the years. In the past, once NOMI was confirmed by DSA, the catheter was left in site and intra-arterial vasodilators were administered directly through it[49]. Even more recent studies have

investigated the use of vasodilators, like papaverine, in course of operative DSA as potential treatment to NOMI, but the use of such drugs in hemodynamically unstable patients remains a concern[48]. Nowadays, DSA is considered as a valid procedure to rule out the presence of occlusion[30].

On the other hand, endoscopy has gained recognition in this context due to its ability to directly visualize the intestinal mucosa, which is typically the first layer affected in mesenteric ischemia. However, despite this great advantage, it also presents limitations, as: risk of perforation in already compromised tissues, mucosal necrosis which may not always reflect deeper transmural damage, and large segments of the bowel remaining inaccessible to the procedure[30,48].

To summarize, in case of NOMI what drives the diagnosis is clinical suspicion, which can be followed by a routine panel of exams and even furnished with DSA or direct endoscopy.

In cases of MVT, diagnosis is based on an integrated assessment of risk factors, clinical presentation, laboratory parameters, and imaging. As with AE, AT, and NOMI, no specific laboratory biomarker has been identified for MVT; however, elevated WBC count, serum lactate, and D-dimer levels may orientate the suspicion. What is instead commonly found in such situations is the presence of genetic mutations affecting the coagulation cascade, such as Factor V Leiden or prothrombin gene mutation, as well as deficiencies in natural anticoagulants including antithrombin, protein C, and protein S[50]. Imaging, particularly CTA or contrast-enhanced magnetic resonance angiography (MRA) when promptly available[51], typically reveals extensive thrombosis within the porto-mesenteric venous system along with less evident nonspecific intestinal abnormalities[5,52] (Figure 13[5]).

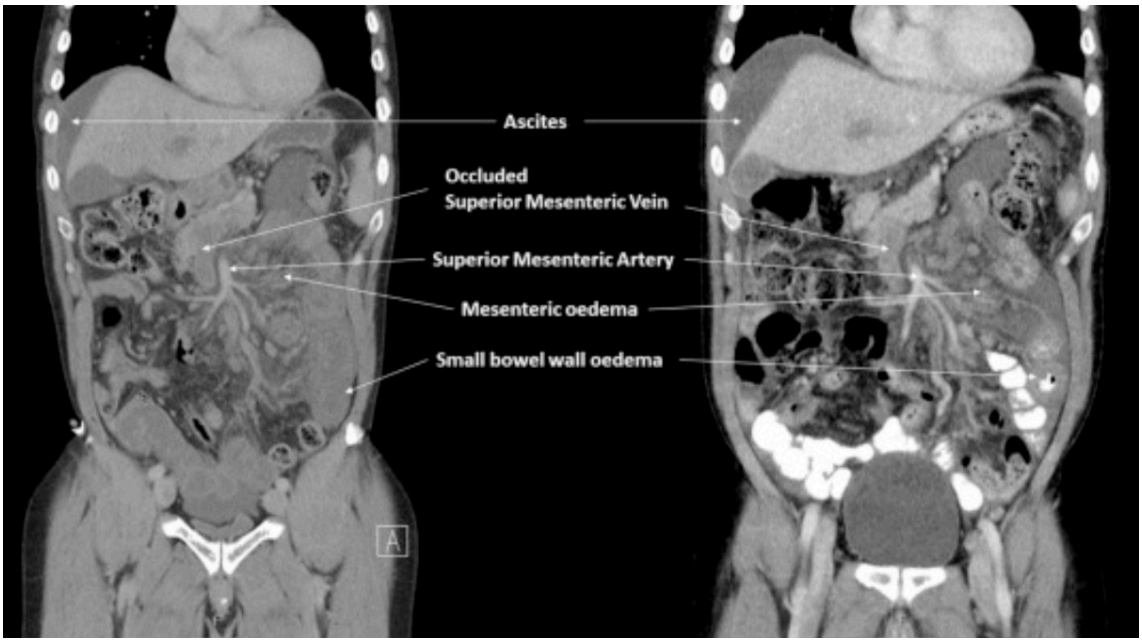


Figure 13. MVT and other common intestinal findings in abdomen CTA

Finally, the diagnostic approach to CMI should be addressed. As for laboratory findings, the situation resembles that described above. Several studies have explored the role of both early and late biomarkers, showing that I-FABP and D-dimer rise rapidly only once necrosis has occurred. Among the late markers are LDH, WBC count, C-reactive protein (CRP), and serum lactate, but as for the early ones they provide minimal diagnostic value[1,53]. While the former three are not directly related to the presence or absence of ischemia, the latter increases specifically in cases where bowel necrosis has already developed.

With regard to imaging, several modalities may be employed. As a first-line screening tool, DUS is advantageous due to the absence of radiation exposure, making it extremely safe. However, its main limitation lies in being highly operator-dependent and potentially time-consuming. Sensitivity and specificity are generally high, particularly when stenosis reaches or exceeds 70%. The gold standard diagnostic modality is CTA, alongside contrast enhanced MRA, with no significant differences reported between the two, owing to the absence of direct comparative data. Conversely, DSA is no longer widely used as a diagnostic tool and is instead primarily considered for interventional purposes. In suspected cases of MALS, dynamic imaging performed during both inspiratory and expiratory phases becomes particularly relevant[1–3].

1.3 MANAGEMENT OF MESENTERIC ISCHEMIA

The management of mesenteric ischemia is closely dependent on both the extent and severity of the condition. In cases of AMI, treatment typically involves a multi-step approach that may eventually require a damage control surgery (DCS) when no other viable options exist. The therapeutic strategy follows the widely accepted '3Rs rule', which states that in AMI the three fundamental steps are Resuscitation, Rapid diagnosis and Revascularization[54].

Initially, when the diagnosis of AMI is made, some early medicaments should be provided in a pre-operative setting. To rule out the chance of cardiovascular collapse during surgery, an intense fluid resuscitation with crystalloids should be carried out; this immediate pre-operative medical therapy is essential not only as cardiovascular support, but also to correct common electrolyte imbalances, such as hyperkalemia, which frequently accompanies bowel necrosis. Gastric decompression via nasogastric tube and the prompt administration of broad-spectrum antibiotics are also crucial, given the high risk of bacterial translocation across the compromised intestinal mucosa[1,20]. Antibiotic regimens typically combine cephalosporins and metronidazole, which are considered the most effective agents against abdominal bacteria[1].

Additionally, unless absolute contraindications such as active bleeding are present, IV unfractionated heparin should be administered as part of the best medical therapy. The use of vasopressors remains controversial, primarily due to the potential reduction of splanchnic perfusion generally associated with dobutamine, the most commonly used agent in this class. For this reason, vasopressors should be reserved for situations of critical hemodynamic instability[1,20].
Moreover, also bowel rest should be initiated as soon as the diagnosis is confirmed, with *nil per os* administration[55]. All patients with suspected AMI should undergo the aforementioned management protocol, typically referred to as supportive therapy.

Following pharmacological management, the most appropriate revascularization strategy must be selected. As first step involves the surgical team—along with other professionals involved in the multidisciplinary group—must determine whether the case regards AMI, AoCMI, or CMI.

In the context of AMI, it is critical to assess for the presence of peritonitis. When significant signs of peritonitis are identified, the preferred surgical approach is open laparotomy. This intervention aims to achieve three primary objectives: restoration of splanchnic blood flow, resection of all necrotic bowel segments, and preservation of any viable intestinal tissue[20].

The evaluation of bowel viability is conducted using various strategies, typically through a combination of the following methods: direct visual and tactile surgeon's assessment to determine the presence or absence of adequate blood flow, intraoperative DUS, fluorescein flowmetry, and indocyanine green (ICG) fluorescence imaging[20]. Indeed, the detection of peritonitis serves as a key factor in guiding the choice of the optimal surgical procedure, as illustrated in the figure below (Figure 14[1]). Visual and tactic signs of ischemic bowel necrosis are patchy cyanosis with bowel discoloration towards red-black shades, complete absence of peristalsis and pulsation in the mesentery[5].
DUS represents a non-invasive tool for intraoperative assessment of blood flow and is typically the first method employed, along with the surgeon's clinical judgment. Fluorescein flowmetry has been shown in multiple studies to effectively distinguish ischemic from viable bowel segments, both during early ischemic phases and in second-look procedures, by administering fluorescein dye and using ultraviolet light[56]. ICG operates through a similar mechanism; its use is strongly supported by evidence primarily in elective surgeries, and as some studies have shown, also in emergency procedures[57].

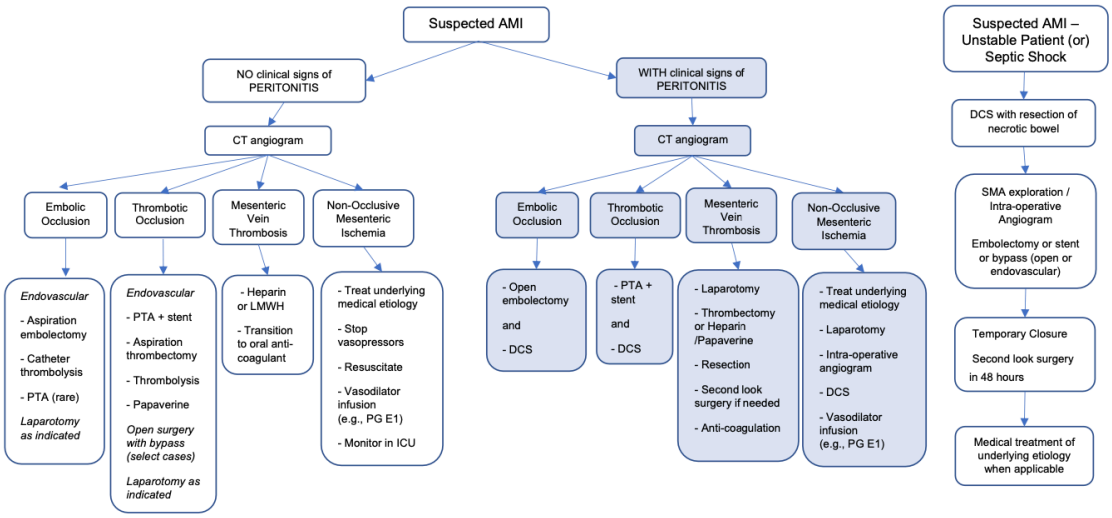


Figure 14. Correct approach flowchart to a patient with suspected AMI

The choice of treatment largely depends on the underlying pathophysiological mechanism.

1.3.1 AMI management in patients not showing peritonitis signs

In cases of arterial occlusive AMI without clinical signs of peritonitis, current literature strongly supports the use of endovascular approaches as initial treatment modality, given their association with lower in-hospital mortality compared to open surgery[58–60] and the high success rate which accounts for 94% for planned surgery[61].
For embolic occlusion, endovascular techniques may include aspiration embolectomy, catheter-directed thrombolysis—used both for AE and for AT—or percutaneous transluminal angioplasty (PTA). In cases of thrombotic occlusion, options such as PTA with or without stenting, aspiration thrombectomy, and direct intra-arterial administration of heparin or vasodilators (e.g., papaverine) can be considered[1].
In arterial occlusive AMI, the primary objectives are the removal of the obstruction and correction of any underlying stenosis, when present[62]. To better illustrate the surgical approaches in cases of embolism and thrombosis, the relevant procedures are briefly outlined below. Optimal treatment can be guaranteed both by endovascular and open surgery procedures.

When an endovascular procedure is carried out, a first evaluation of the accesses through the preoperative imaging—typically CTA—is compulsory; the femoral approach is generally preferred due to its anatomical convenience, while the brachial approach may be considered when the femoral route would result in unfavorable angulations[63].
An essential concept in revascularization is the distinction between antegrade and retrograde techniques: while the former highlights that the access to the vessels is conducted in the same direction of blood flow, the latter implies the opposite process, namely the access to the vessel is performed through a distal collateral branch.

Consequently, antegrade approaches to CA, SMA and IMA are typically achieved via femoral or brachial access, while retrograde procedures are usually performed through the collateral arcades, such as the arcade of Riolan. Generally, retrograde revascularization approaches are performed, especially in cases of CMI, when antegrade ones fail to restore the blood supply[64].

Moreover, in cases of severe ostial stenosis that cannot be approached via common femoral or brachial access, retrograde open mesenteric stenting (ROMS) should be considered. This hybrid technique involves a median laparotomy with direct access to the visceral arteries, allowing for rapid cannulation and subsequent stent placement (Figure 15[58]). It is particularly advantageous when intraoperative assessment of bowel viability is required.

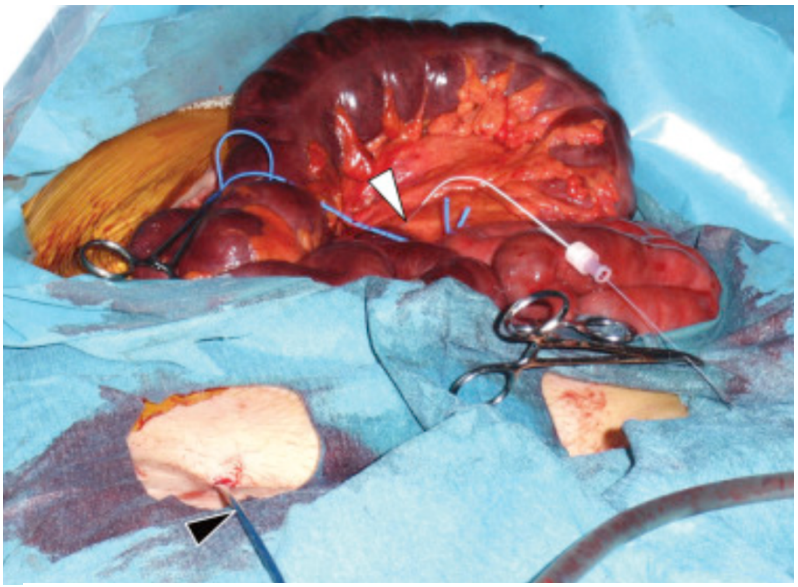


Figure 15. ROMS: retrograde recanalization of SMA during laparotomy

Aspiration embolectomy will be the first endovascular technique described for the treatment of arterial occlusive AMI, encompassing both AE and AT. This procedure is employed in the management of both conditions and involves mechanical or manual aspiration of the embolus using a catheter, which is advanced to the site of occlusion under fluoroscopic guidance. To ensure effective clot removal, multiple aspiration passes are typically required. As just said, this procedure is also used to resolve thrombotic conditions, but is important to underline that when the thrombus starts to become calcified, as happens in CMI, this option is no longer effective. The procedure is usually followed by a completion angiography to assess the technical success of the intervention[63] (Figure 16, 17[65]).

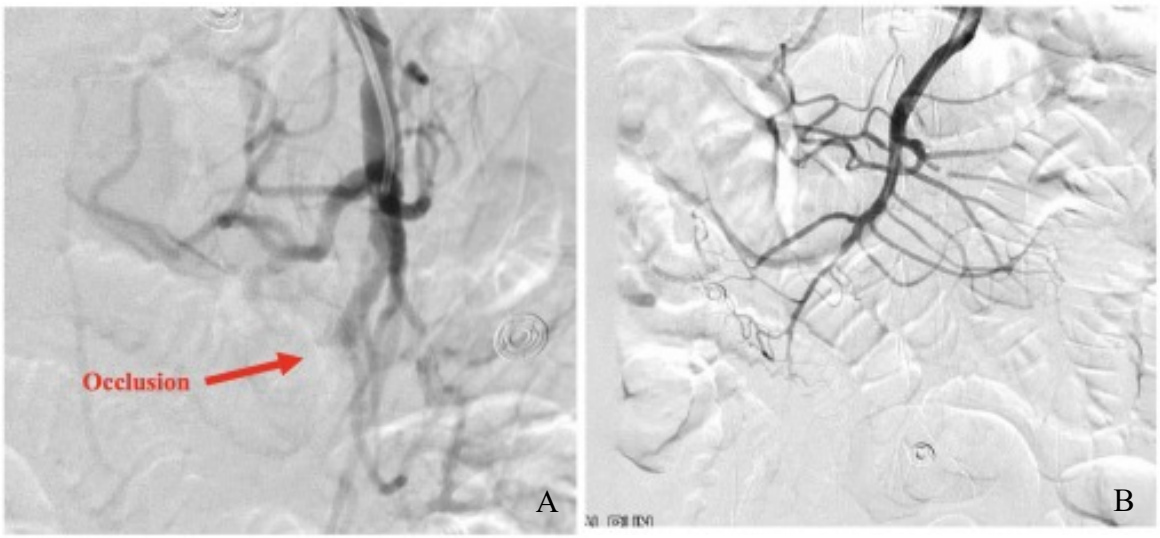


Figure 16. (A) Pre-operative DSA, (B) Excellent result after suction embolectomy performance

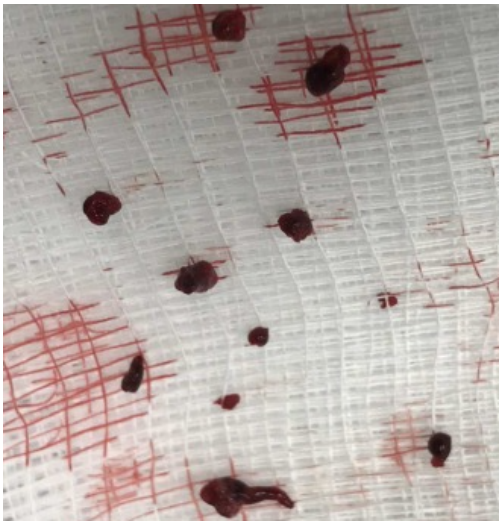


Figure 17. Clot volume removed via aspiration catheter

Catheter-directed thrombolysis represents a valuable adjunctive option in the management of AT, though it is rarely used as a standalone intervention. It is typically employed in combination with mechanical techniques. This approach carries specific limitations, primarily related to time constraints—which may be insufficient for effective reperfusion considering the patient's general conditions—and the risk of hemorrhagic complications. In particular, in all those cases in which bowel necrosis has already established, thrombolysis-induced bleeding can be fatal for the patient[63]. The procedure involves the administration of recombinant tissue plasminogen activator agents, such as urokinase, and is generally reserved for cases where mechanical methods, such as PTA with or without stenting, fail to re-establish adequate splanchnic perfusion[59].

In line with the above-mentioned procedure is the direct instillation of vasoactive drugs such as papaverine or prostaglandin E1 in occluded arteries. However, as previously noted, the use of such drugs in hemodynamically instable patients should be carefully evaluated due to the potential risks associated with their vasodilatory effects and is generally reserved to NOMI cases[48,66].

Another therapeutic option in the treatment of arterial occlusive AMI is PTA, which involves the advancement of a balloon catheter to the site of occlusion, followed by balloon inflation to compress the atherosclerotic plaque against the vessel wall. PTA is generally not performed alone due to its limited long-term durability and is typically followed by stent placement. Furthermore, considering the risk of dissection that PTA entails, delayed stenting can become technically challenging if it becomes necessary at a later stage[63].

As other option of management is stenting of the target vessel, which may be performed either as a primary procedure or following PTA. As extensively documented in current literature, stenting provides more durable reperfusion and yields better outcomes in cases of heavily calcified atherosclerotic plaques. Two main options are available: balloon-expandable stents (BES) and self-expandable stents (SES), each with distinct mechanical properties and indications. Selecting the appropriate type and size of the stent is crucial to achieving procedural success. BES are generally preferred, especially in calcified ostial occlusions, as nitinol SES may lack sufficient radial force to ensure optimal results. While the use of SES in splanchnic revascularization is limited to specific scenarios, no conclusive data demonstrate a clear superiority of BES over SES[63].
A completion angiography is routinely performed at the end of the procedure, similarly to aspiration embolectomy or thrombectomy, to confirm technical success. Given the potential risk of distal embolization during stenting, some studies have suggested the use of embolic protection devices (EPDs) during revascularization procedures to reduce the risk of peripheral ischemia[67].

After an arterial occlusive AMI all patients should be set in best medical therapy with statin, stop of smoking habit and single antiplatelet therapy to face potential atherosclerosis progress[5].

Regarding MVT, and still in the context of AMI without overt signs of peritonitis, initial treatment consists of anticoagulation with unfractionated heparin or low molecular weight heparin (LMWH). If anticoagulation alone fails to achieve clinical improvement, it may be followed by interventional procedures such as catheter-directed thrombolysis, arterial access via SMA, trans-jugular intrahepatic portosystemic shunting (TIPS), or percutaneous transhepatic thrombolysis. However, this presentation is relatively uncommon, as the presence of extensive collateral circulation often prevents mesenteric ischemia from occurring in isolated SMV thrombosis. In most cases, ischemia arises only when the portal vein is simultaneously involved.

Considering then NOMI, always in cases not presenting peritonitis signs, the treatment focuses on addressing the causing condition and interrupting any vasoactive agent administration that may exacerbate the condition. Additionally, intra-arterial infusion of medications such as papaverine, nitroglycerin, and prostaglandin E1 may be delivered to provide hemodynamic support, with the already mentioned concern[1,68]. Close patient monitoring is essential in this setting, given the well-documented persistence of splanchnic vasospasm even after the primary underlying factor has been corrected[49].

Surgical revascularization techniques—such as bypass grafting, thromboendarterectomy with patch angioplasty, and division with re-implantation of the occluded vessel—remain viable options for restoring adequate mesenteric blood flow. Nevertheless, when possible, an initial endovascular approach is generally preferred due to its less invasive nature. In cases where endovascular intervention is contraindicated, either relatively or absolutely, or when the surgical team deems open surgery more appropriate based on the patient's condition, these open techniques continue to represent valuable alternatives.

1.3.2 AMI management in patients with peritonitis

A completely different clinical scenario arises when the patient presents with clear signs of peritonitis, which necessitates an entirely different therapeutic approach—even when baseline conditions appear comparable. All patients exhibiting symptoms such as severe abdominal pain, abdominal distension, metabolic acidosis, and radiologic evidence of bowel ischemia should undergo exploratory laparotomy to assess for transmural necrosis and, if confirmed, proceed with bowel resection (Figure 18[58]). Nevertheless, if bowel

resection is required and the clinical conditions are permissive, attempt of revascularization should be performed before[1,58,69].

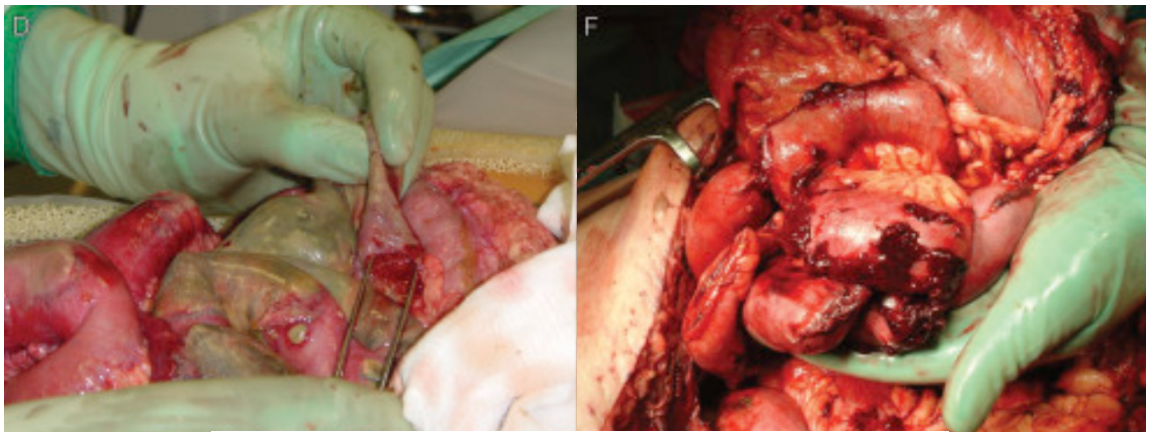


Figure 18. (D) Extensive transmural infarction with bowel perforation, (F) Multiple bowel resections performed with stapler

In the case of AE, open embolectomy is generally considered the first-line surgical intervention and it involves exposing the target vessel—typically SMA—followed by a transverse arteriotomy through which a Fogarty catheter is inserted to retrieve the embolus[69]. Upon completion, an intraoperative angiography, both with antero-posterior and lateral view, should be performed to assess the extent of reperfusion and confirm technical success.

For what concerns instead AT, PTA with stenting remains the leading therapeutic approach. Furthermore, in critically ill patients, several studies have emphasized the potential benefit of the above-mentioned hybrid strategy (ROMS)—combining exploratory laparotomy with subsequent retrograde endovascular revascularization of the SMA. This approach not only enables the restoration of mesenteric blood flow but also allows direct assessment of bowel viability. It has demonstrated high technical success and represents a valuable alternative to open surgical procedures, such as bypass, which may be associated with higher morbidity[63,70].

In both conditions, damage control surgery plays a crucial role. It consists of an emergency laparotomy with prompt resection of necrotic bowel segments, intentionally avoiding primary anastomosis; this should in fact be performed only in hemodynamically stable patients and in those where the extent of the resection is not only limited, but there is also high level of confidence that all the necrotic tissue has been removed. Abdomen is typically not definitively closed; instead, temporary abdominal closure is performed,

often using negative pressure wound therapy or, alternatively, only the skin may be approximated, leaving the fascial layers open to facilitate re-exploration[5]. A planned second-look surgery is then performed after 48 hours to reassess bowel viability and, if appropriate, proceed with definitive surgical reconstruction[1,5,71].

As for what happens in cases of MVT without clinical signs of peritonitis, also in the opposite condition systemic anticoagulation—often combined with local intra-operative heparin or papaverine venous instillation—remains the cornerstone of treatment. Systemic anticoagulation is always based on the administration of unfractionated heparine or LMWH, followed in second instance by vitamin K antagonists (VKAs) or direct oral anticoagulants (DOACs). If no clinical improvement is visible when the patient is under medical therapy endovascular or open surgical treatments should be provided. Nevertheless, laparotomy and DCS, with potential bowel resection and delayed reconstruction, continue to play a fundamental role in patient management[1].

For NOMI, patients should be taken to hybrid operating rooms where both open and endovascular techniques can be employed. The treatment strategy typically includes a combination of explorative laparotomy, intra-operative angiography with or without stent placement, intra-arterial infusion of vasoactive agents such as prostaglandin E1, correction of the underlying trigger, DCS, and resection of ischemic bowel segments if required[1,5].

In patients undergoing extensive bowel resections, there is a considerable risk of developing short bowel syndrome. Those at highest risk are individuals in whom less than 200 cm of functional intestine remains and when the condition manifests, it typically requires lifelong total parenteral nutrition to maintain adequate nutritional status and fluid balance[72].

1.3.3 AMI management in patients with septic shock

In patients manifesting signs and symptoms of hemodynamic instability or septic shock, the management strategy mirrors what mentioned for patients with signs of peritonitis, with DCS playing a central role. This approach typically involves bowel resection, preceded, if possible, by either open or endovascular revascularization, as required. The abdomen is generally left with temporary closure to allow for re-exploration after 48 hours, during which bowel viability is reassessed and, if appropriate, reconstructive procedures are completed.

When open surgical revascularization is indicated—which, in current practice, applies to a more limited subset of patients—options include thromboendarterectomy (TEA), open mechanical embolectomy using a Fogarty catheter, or arterial bypass. TEA entails opening the affected artery and removing the atherosclerotic plaque and any superimposed thrombus. In contrast, embolectomy consists of inserting a Fogarty catheter to retrieve the thrombus or embolus.

Arterial bypass is the third possible way to restore splanchnic blood flow, and without any doubt the most invasive; it may be performed using the autologous reversed great saphenous vein or a synthetic graft, most commonly polyethylene terephthalate or expanded polytetrafluoroethylene (ePTFE) as shown in the image below (Figure 19[73]). Bypass can both be performed in antegrade and retrograde direction in relation to the inflow source; in the former case it originates from distal-thoracic or supra-coeliac aorta, while in the latter it is based on infrarenal aorta or iliac arteries. Retrograde bypass technique is generally chosen in conditions of severe supra-coeliac aortic disease or pulmonary and cardiac impairment[5]. Therefore, the use of autologous vein is strongly recommended in case of bacterial contamination.
Finally, the underlying infective source responsible for the development of septic shock must be addressed and, where possible, treated[1].

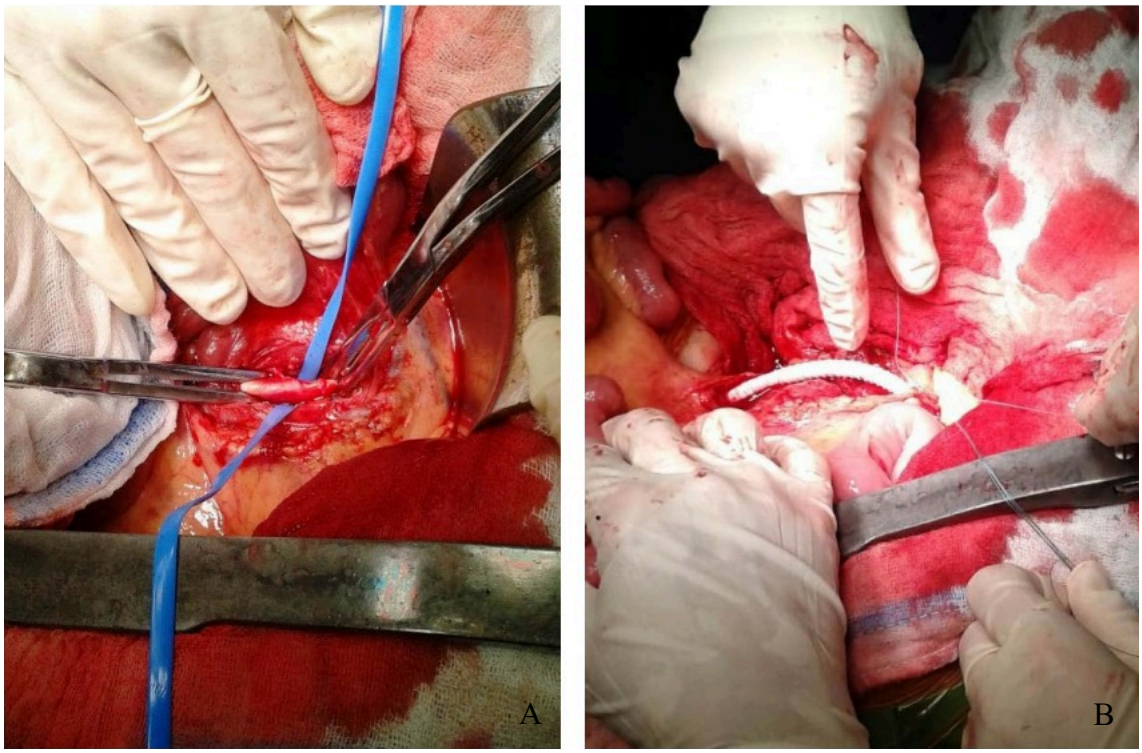


Figure 19. (A) SMA isolation for bypass, (B) Final aspect of aorto-mesenteric bypass performed with 5mm Gore-Tex prosthesis

A right external iliac artery–SMA bypass was recently performed at our center. The following images illustrate the tailoring of the bypass and the completion post-procedure DSA (Figure 20).

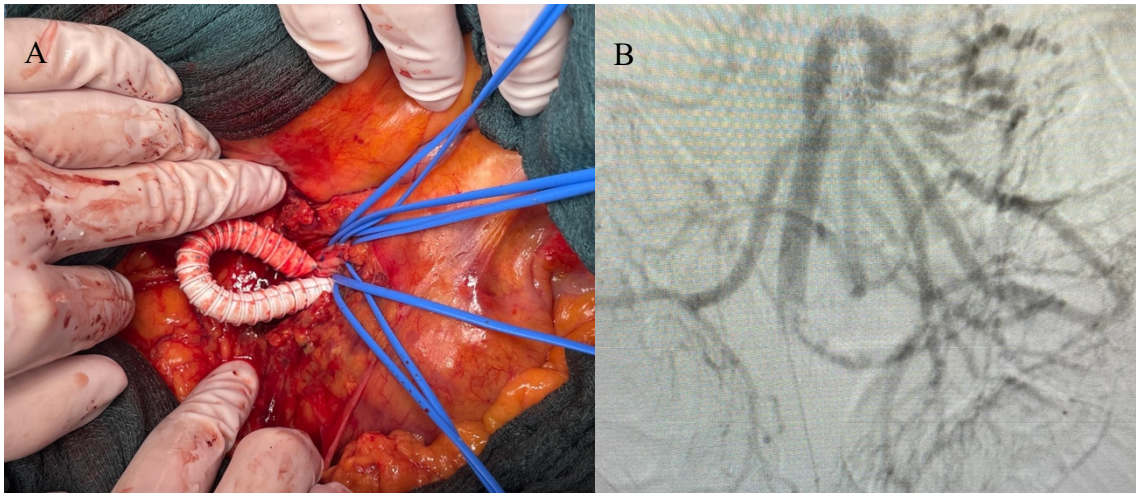


Figure 20. (A) Right external iliac artery-SMA bypass, (B) Completion post-procedure DSA

1.3.4 AoCMI management

When addressing AoCMI, the management options largely mirror those available for AMI, including both surgical and endovascular approaches. In the treatment of both AoCMI and CMI, open surgery is progressively losing its leading role, primarily due to the minimally invasive nature of endovascular procedures compared to open repair. In previous years, open surgery was still considered the gold standard, based on its reportedly superior long-term outcomes. However, recent meta-analyses have found no significant difference between surgical and endovascular treatments in terms of long-term results[74,75]. This has contributed to ongoing controversy in the literature regarding the optimal approach and for AoCMI, as well as for AMI and CMI, the choice between the two should be left to the surgical team and should be assessed in light of the clinical context.

The management of AoCMI starts with the prevention in all patients with CMI, including those who are still asymptomatic, given their risk of progressing to acute mesenteric ischemia. Therefore, all potential risk factors should be eliminated as a priority[76].

When the condition manifests, endovascular and surgical treatments are, as previously noted, largely the same as those used for AMI and CMI, with the main difference being the urgency typically required in AoCMI. While CMI is usually amenable to elective intervention, AMI and AoCMI often necessitate urgent or emergent procedures.

As a subtype of AMI, AoCMI may present with serious complications such as bowel perforation. In such cases, although open surgery—potentially involving a bypass—remains a viable option, the risk of infection associated with heterologous prosthetic material must be carefully considered[76]. If intraperitoneal bowel content loss is present and a bypass is required, the use of autologous vein grafts should be preferred.

An unresolved issue in the current literature concerns the indication for surgical intervention in completely asymptomatic patients with three-vessel mesenteric disease. In such cases, a thorough evaluation of both risks and potential benefits is warranted, as these patients often present with well-developed collateral circulation but also carry a significant risk of progressing to acute-on-chronic mesenteric ischemia[76].

1.3.5 CMI management

One of the major challenges in the management of CMI lies in accurately identifying patients who are likely to benefit from revascularization. Current literature strongly supports that, in cases of multi-vessel disease where alternative diagnoses have been ruled out by a multidisciplinary team, revascularization should not be postponed—not even to allow the patient to regain weight before surgery. Once patients exhibit definitive symptoms of *angina abdominis*—such as severe postprandial pain, abdominal distension, nausea, diarrhea, and significant weight loss—conservative treatment should not be proposed, and prompt revascularization should be carried out[3,5].

This may be achieved either through endovascular or open surgical approaches. However, in contemporary practice, open surgery is generally reserved for non-eligible patients for endovascular intervention or in whom endovascular procedures have already failed.

What is important to bear in mind is that open revascularization seems to be associated with superior long-term outcomes, whereas endovascular techniques often offer more rapid symptomatic relief. For this reason, the final therapeutic decision is typically left to the discretion of the surgical team[5,77,78].

The endovascular and open surgical options applicable in chronic mesenteric ischemia largely reflect those employed in the treatment of AMI, with PTA combined with stenting generally showing superior outcomes compared to PTA alone[3,5] especially in case of relatively short focal SMA occlusions. SMA is generally the most common target vessel, however recanalization of CA or IMA can be evaluated in case of chronic calcific occlusion of SMA, where no possible endovascular treatment would achieve the objective[5].

When it comes to open surgical techniques, the choice among them depends heavily on the patient's overall clinical condition. For example, elderly patients or those with significant dysfunction of major organs—such as cardiac, pulmonary, or renal impairment—are typically poor candidates for aortic-based procedures[78]. Surgery, moreover, is generally preferred when stenosis are non-atherosclerosis related such as in vasculitis, neurofibromatosis and mid-aortic syndrome[5,79].

In patients with CMI whose symptoms are attributable MALS, endovascular stenting of the affected vessel is generally associated with poor short-term outcomes. This is due to the fact that the underlying etiology is an extrinsic compression rather than an intrinsic vascular lesion. Therefore, the only effective treatment consists of surgical release of the MAL, eventually followed by open or endovascular revascularization in cases where symptoms of *angina abdominis* persist[3,80].

1.3.6 Post-operative therapy

Regardless of the underlying AMI subtype, patients should be placed on optimal medical therapy following the intervention. Initially, LMWH should be administered, followed by a transition to long-term anticoagulation once the immediate postoperative risk of reintervention has subsided. In thrombotic forms of AMI, antiplatelet therapy is recommended, whereas anticoagulation remains the preferred strategy for embolic cases, regardless of whether open or endovascular treatment was performed[58].

Specifically, following SMA stenting, low-dose clopidogrel should be continued for at least six to eight weeks, in combination with life-long aspirin to prevent acute stent thrombosis. However, due to the high-flow nature of the SMA, the necessity of DAPT remains a topic of ongoing debate in the literature[58].

As for MVT—although a less frequent entity—investigations into potential coagulation disorders should be considered. The duration of anticoagulation therapy depends on the type of precipitating factor: if the cause is transient, treatment may be limited in time, whereas in cases related to thrombophilia, life-long therapy is warranted due to the chronic nature of the condition[58].

2 AIM OF THE STUDY

As mentioned at the beginning of the present introduction, CMI and AoCMI represent two sides of the same coin, yet their markedly different features justify treating them as distinct entities. These differences encompass risk factors, diagnostic approaches, reintervention rates, and treatment strategies. Accordingly, the present study aims to investigate and compare targeted outcomes between the two groups, with the objective of elucidating the core distinctions underlying these conditions. Specifically, both overall and pathology-related mortality, estimates fraction of reintervention, and potential predictors of reintervention were analyzed for patients with CMI and AoCMI.

What prompted this comparative analysis is the notable lack of literature concerning AoCMI. Despite often being classified as a subgroup of AMI, AoCMI should arguably be considered a distinct clinical entity, as it exhibits pathophysiological and epidemiological characteristics that lie between those of AMI and CMI.

3 MATERIALS AND METHODS

3.1 PROTOCOL DESCRIPTION

A retrospective, observational, monocentric cohort study was conducted at the Vascular Surgery Unit of the University of Modena and Reggio Emilia.

A total of 68 patients—26 males (38.2%) and 42 females (61.8%)—treated at our center for either CMI or AoCMI between May 2000 and March 2025 were included in the analysis. For each patient, information about previous clinical history regarding specifically the presence or absence of hypertension, dyslipidemia, diabetes, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), AF, cancer, obesity (BMI > 30), and peripheral artery disease (PAD) was collected.

In addition, information on active medical therapy prior to surgery was gathered, including use of single or dual antiplatelet therapy (SAPT or DAPT), statins, antihypertensives, and anticoagulants.

The experimental protocol was conducted in accordance with the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013) and its most recent amendments. Good Clinical Practice guidelines were followed throughout the study. Informed consent was obtained from all capable patients.

3.2 STUDY COHORT

The study enrolled 68 patients, who underwent therapeutic procedures for AoCMI or CMI over a 25-year period, from January 2000 to March 2025. Both endovascular and open surgical interventions were equally considered.

3.2.1 Inclusion and exclusion criteria

Inclusion criteria thus consisted in:

- Patients treated for AoCMI and CMI in the period between January 2000 to March 2025
- Patients treated both with open or endovascular surgery
- Patients who underwent elective or urgent/emergent procedures

For what concerns exclusion criteria, instead, patients of the following categories were ruled out from the protocol:

- CMI secondary to MALS
- CMI secondary to CACS
- CMIs or AoCMIs secondary to branches occlusions, such as after Branched Endovascular Aneurysm Repair (BEVAR) or Fenestrated Endovascular Aneurysm Repair (FEVAR)
- All AMI cases

3.3 PROCEDURAL DATA

Data were collected in a dedicated database and included patient comorbidities, event onset, stenosis characteristics (length, pre- and post-stenotic diameters), intraoperative findings and materials used, follow-up duration, clinical and radiological technical success at follow-up and the number and nature of any reinterventions.

All measurements were performed using EndoSize software (Therenva, Rennes, France).

For morphological assessment, preoperative CTA scans were analyzed.

Radiological technical success during follow-up was evaluated using CTA, DUS, or MRA, according to the one available.

3.4 STUDY OUTCOMES

The primary outcome of the present study was to assess survival in both CMI and AoCMI groups, with separate evaluations of overall and pathology-related survival. Secondary outcomes included the estimates fraction of reintervention during follow-up and the identification of predictors for reintervention in both cohorts.

3.5 DEFINITIONS

Perioperative mortality was also evaluated as part of the survival analysis. It was defined as any patient death occurring within 30 days of the procedure or during the same hospital stay, even if longer than one month. This approach allowed the identification of disease-related deaths, including those resulting from procedure-related complications that prolonged hospitalization.

Regarding reinterventions, these were defined as any subsequent procedure performed on the same visceral vessel due to complications such as re-occlusion.

Mortality was classified as pathology-related or non-pathology-related based on the primary event leading to the patient's death.

Technical success was defined as the proper execution and completion of the endovascular or surgical procedure. Clinical success at follow-up referred to the absence of symptoms attributable to CMI or AoCMI.

Stenosis severity was categorized according to the percentage of luminal occlusion as follows:

- Grade 0: <50%
- Grade 1: 50–75%
- Grade 2: 75-99%
- Grade 3: complete occlusion

A stenosis was classified as calcified only when calcifications involved more than 50% of the plaque.

As for symptom onset, cases were considered acute when symptoms had developed within the previous 24 hours, and chronic when symptoms had persisted for more than three months. Intermediate presentations were assessed individually based on the specific characteristics of symptom evolution.

3.6 STATISTICAL ANALYSIS

Mean ± standard deviation and median (interquartile range [IQR]) were used to describe normally and non-normally distributed continuous variables. The Shapiro–Wilk test was used to assess the distribution of normality.

Categorical variables were expressed as frequencies and percentages. Between-group comparisons of continuous and categorical data were performed using Student's t test, or Wilcoxon rank test for skewed variables, and chi-square test, respectively.

Kaplan-Meier survival analysis and log-rank tests were performed to compare mortality and reinterventions during follow-up. Variables suspected to be predictors of reintervention during follow-up were tested with a univariable Cox proportional hazard regression model; those with a p value < 0.20 were included in a multivariable model.

All tests were two sided with a 95% confidence interval (CI); a p-value < 0.05 was considered statistically significant. Analysis was carried out using STATA 18 (STATA, College Station, TX, USA).

4 RESULTS

The present study included 68 patients who underwent a splanchnic circulation recanalization procedure between January 2000 and March 2025 at the Vascular Surgery Unit of the University of Modena and Reggio Emilia. Among these, 47 procedures were performed to treat CMI and 21 to address AoCMI.

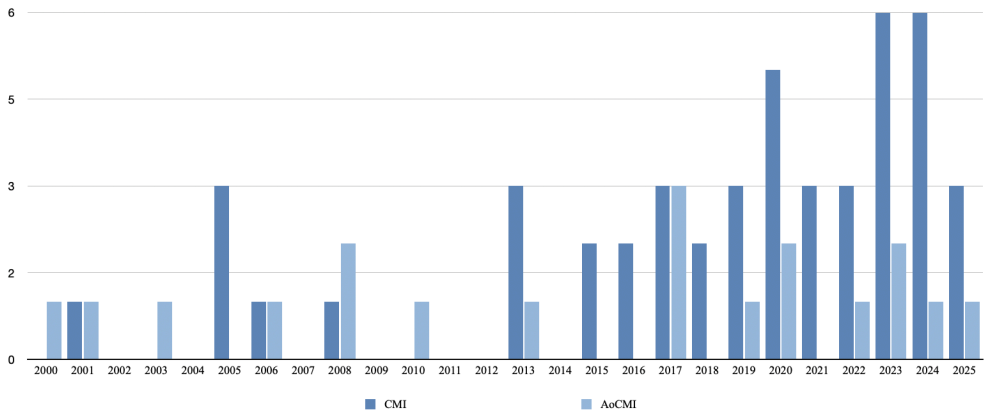
Overall, 17.6% of the interventions were conducted in an urgency or emergency setting, with different rates between the two groups: 10.6% in CMI and 33.3% in AoCMI. For

patients with AoCMI who were not managed in an emergency setting, surgery was scheduled within 48 hours of hospital admission. The vast majority of procedures were performed using an endovascular approach, accounting for 89.6% of cases overall, with a similar distribution in both CMI (93.6%) and AoCMI (80.0%) patients, as reported in the table below (Table 5).

Globally the interventions performed, as first-line procedures, thus excluding all reinterventions, were:

- 6 PTAs alone
- 27 PTAs with stenting
- 23 primary stentings
- 2 endovascular thrombectomies
- 1 ineffective endovascular recanalization due to severe stenosis
- 1 bypass in autologous saphenous vein
- 3 bypasses in prosthesis (ePTFE)
- 3 recanalization procedures via Fogarty catheter
- 1 superior mesenteric artery reimplantation

In terms of time distribution, the number of interventions per year both for CMI and AoCMI group are shown in the following graphics and table (Diagram 2).



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
CMI	0	1	0	0	0	3	1	0	1	0	0	0	0	3	0	2	2	3	2	3	5	3	3	6	6	3
AoCMI	1	1	0	1	0	0	1	0	2	0	1	0	0	1	0	0	0	3	0	1	2	0	1	2	1	1

Diagram 2. Number of interventions for CMI and AoCMI per-year

Technical success at completion of the procedure were achieved in 86.8% of cases, with comparable rates in the CMI and AoCMI groups, accounting for 87.2% and 85.7%, respectively, as reported in Table 5.

The median overall follow-up duration was 38.6 months, being specifically 38 months for CMI group and 39.9 months for AoCMI group.

All results reported in this paragraph have a P value greater than 0.05, indicating that they are meaningful only within our sample and cannot be generalized to the broader population.

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
Urgent setting	12 (17.6%)	5 (10.6%)	7 (33.3%)	0.023
Endovascular approach	60 (89.6%)	44 (93.6%)	16 (80.0%)	0.095
Tech success	59 (86.8%)	41 (87.2%)	18 (85.7%)	0.864

Table 5. Urgency, approach and technical procedure characteristics in both groups (CMI and AoCMI)

4.1 BASELINE CHARACTERISTICS OF THE POPULATION

According to the characteristics and comorbidities, the population analyzed consisted of 26 males, which accounted for the 38.2% of the whole amount of patients, while when referred to single CMI and AoCMI groups males were found to be significantly higher in AoCMI, accounting for 42.9% of all AoCMI cases; however, these prevalence rates, being non-statistically significative (P = 0.600), have value only in our sample.

Of all 68 patients, 41.2% had current or past smoking habit with a relatively higher association of smoke with CMI, in which groups there was 46.8% smokers, rather than in AoCMI, group in which only 28.6% of smokers are counted (P = 0.364).

Hypertension was highly prevalent in the study population, affecting 73.5% of the overall sample. Notably, it was almost twice as common in the CMI group (85.1%) compared to the AoCMI group (47.6%), a difference that was statistically significant (P = 0.001).

A similar pattern was observed for dyslipidemia, which showed an overall prevalence of 50.0%, but was significantly more frequent in the CMI group (59.6%) than in the AoCMI group (28.6%) (P = 0.018).

Regarding diabetes, the overall prevalence in the study sample was 17.7%, with similar rates observed in the CMI (19.2%) and AoCMI (14.3%) groups (P = 0.627).

A comparable trend was noted for a history of coronary artery disease, which was almost equally distributed between the two groups, with prevalences of 29.8% in CMI and 28.6% in AoCMI, and an overall prevalence of 29.4% in the total sample (P = 0.919).

COPD was another of the comorbidities investigated during the collection of data, with a coherent distribution among the three groups. In the study population it accounted for 17.7%, showing no significant differences in the groups of CMI and AoCMI where 17% and 19.1% had history of COPD in their medical record (P = 0.840).

Chronic kidney disease (CKD) was present in 17.7% of the overall study population, with a prevalence of 14.9% among patients with CMI. In contrast, nearly one in four patients (23.8%) in the AoCMI group had CKD as a comorbidity (P = 0.373).

Atrial fibrillation (AF) was significantly more prevalent in the AoCMI group (38.1%) compared to 17.0% in CMI patients, reflecting a similar trend observed in the general sample population (23.5%) (P = 0.058).

The prevalence of a history of past or active malignancies differed notably between groups: it affected 23.4% of CMI patients but was observed in only 9.5% of those with AoCMI (P = 0.179).

Obesity was reported in 5.9% of the total study cohort, with a marked difference between groups—2.1% in CMI patients and 14.3% in those with AoCMI. This difference was statistically significant and therefore generalizable beyond the analyzed cohort (P = 0.049).

Finally, peripheral artery disease (PAD) was commonly reported across the study population, consistent with the high rate of previous revascularization procedures. In total, 31.3% of patients had undergone at least one intervention for PAD, typically involving the carotid or iliac/femoral arteries. The prevalence was comparable between the two groups, at 31.9% in CMI and 30.0% in AoCMI (P = 0.877).

For greater clarity, all the information reported above, are summarized in the Table below (Table 6).

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
Male sex	26 (38.2%)	17 (36.2%)	9 (42.9%)	0.600
Smoking habit (current or past)	28 (41.2%)	22 (46.8%)	6 (28.6%)	0.364
Hypertension	50 (73.5%)	40 (85.1%)	10 (47.6%)	0.001
Dyslipidemia	34 (50.0%)	28 (59.6%)	6 (28.6%)	0.018
Diabetes	12 (17.7%)	9 (19.2%)	3 (14.3%)	0.627
Coronary artery disease	20 (29.4%)	14 (29.8%)	6 (28.6%)	0.919
COPD	12 (17.7%)	8 (17.0%)	4 (19.1%)	0.840
Chronic Kidney Disease	12 (17.7%)	7 (14.9%)	5 (23.8%)	0.373
Atrial Fibrillation	16 (23.5%)	8 (17.0%)	8 (38.1%)	0.058
Cancer	13 (19.1%)	11 (23.4%)	2 (9.5%)	0.179
Obesity	4 (5.9%)	1 (2.1%)	3 (14.3%)	0.049
Previous surgery for PAD (limbs/carotids)	21 (31.3%)	15 (31.9%)	6 (30.0%)	0.877

Table 6. Baseline characteristics of the population

4.1.1 Active medical treatment among the study population

Similarly, the active medical treatment prior to the ischemic event was assessed for each of the 68 patients included in the study. Findings revealed that 48.9% of patients in the CMI group were on single antiplatelet therapy before the onset of mesenteric ischemia, compared to 42.9% in the AoCMI group (P = 0.643).

Double antiplatelet therapy was administered to 12.8% of CMI patients, whereas no patients in the AoCMI group received this treatment (P = 0.086).

With regard to antihypertensive medications, 72.3% of the CMI group and 52.4% of the AoCMI group were under treatment, roughly mirroring the distribution of hypertension within the study population (P = 0.108). However, this also highlights that not all hypertensive patients were receiving therapy, and conversely, not all patients on antihypertensives had a documented diagnosis of hypertension.

Statin therapy was prescribed in 47.1% of the overall cohort, with a significantly different distribution between groups: 57.5% in the CMI group versus 23.8% in the AoCMI group (P = 0.010).

Anticoagulant treatment showed a uniform distribution both in the entire sample (20.6%) and across the two subgroups: 21.3% in the CMI group and 19.1% in the AoCMI group (P = 0.834).

Except for statin usage, none of the other treatment variables reached statistical significance; therefore, they should be considered representative solely of this study cohort.
All the above-mentioned information is detailed in the following table (Table 7).

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
SAPT	32 (47.1%)	23 (48.9%)	9 (42.9%)	0.643
DAPT	6 (8.8%)	6 (12.8%)	0 (0.0%)	0.086
Anti-hypertensives	45 (66.2%)	34 (72.3%)	11 (52.4%)	0.108
Statins	32 (47.1%)	27 (57.5%)	5 (23.8%)	0.010
Antithrombotics	14 (20.6%)	10 (21.3%)	4 (19.1%)	0.834

Table 7. Active medical treatment in the study cohort

4.2 PRIMARY OUTCOME

The primary outcome of the present study was to assess mortality, and thus survival rates, for what concerns perioperative, overall and pathology-related mortality.

4.2.1 Perioperative mortality

Regarding perioperative death our study showed an overall amount of 6 people which accounted for 8.8% of the whole study cohort. Of the aforementioned 6 patients, 2 were referrable to the CMI group (4.3%), while 4 to the AoCMI group (19.1%), showing a significant higher mortality in the latter group rather than in the former (P = 0.047) as reported in Table 8.

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
Perioperative death	6 (8.8%)	2 (4.3%)	4 (19.1%)	0.047

Table 8. Perioperative mortality

4.2.2 Overall mortality

Our findings reveal that the total number of deaths, excluding perioperative ones, was 18 in the CMI group and 9 in the AoCMI group, corresponding to 38.2% and 42.8% of overall mortality, respectively, indicating a higher overall death rate in the AoCMI cohort.

When evaluating mortality over time, the one-year overall mortality was 8.5% in the CMI group and 37.5% in the AoCMI group, yielding corresponding survival rates of 91.5% (95% CI: 75.9%–97.2%) and 62.5% (95% CI: 31.7%–82.5%).

At two years, mortality in the CMI group rose to 22.2%, while the AoCMI group remained at 37.5%, with survival rates of 77.8% (95% CI: 58.6%–88.8%) and 62.5% (95% CI: 31.7%–82.5%), respectively.

By the third year, cumulative mortality reached 26.1% in the CMI group and 53.1% in the AoCMI group. These values remained stable at years four and five for AoCMI, while in the CMI group, mortality continued to increase, reaching 39.5% at year four and 45% at year five. Corresponding survival rates were 73.9% (95% CI: 54.1%–86.2%) for CMI vs. 46.9% (95% CI: 19.6%–70.3%) for AoCMI at year three, 60.5% (95% CI: 39.3%–76.3%) at year four, and 55% (95% CI: 33.3%–72.3%) at year five for CMI.

All these data are summarized in the following table (Table 9) and graphically represented in the Kaplan–Meier survival curve (Figure 21), which displays survival estimates at

predefined time points (1, 2, 3, 4, and 5 years), stratified by clinical onset (CMI vs. AoCMI).

As shown by the Kaplan–Meier survival curve, the confidence intervals of the two study groups—CMI and AoCMI—overlap. The implications of this observation will be further addressed in the Discussion section.

	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	Std. Error CMI	Std. Error AoCMI
1st year	91.5% (95% CI: 75.9%-97.2%)	62.5% (95% CI: 31.7%-82.5%)	4.7%	13.4%
2nd year	77.8% (95% CI: 58.6%-88.8%)	62.5% (95% CI: 31.7%-82.5%)	7.5%	13.4%
3rd year	73.9% (95% CI: 54.1%-86.2%)	46.9% (95% CI: 19.6%-70.3%)	8.1%	13.9%
4th year	60.5% (95% CI: 39.3%-76.3%)	46.9% (95% CI: 19.6%-70.3%)	9.6%	13.9%
5th year	55% (95% CI: 33.3%-72.3%)	46.9% (95% CI: 19.6%-70.3%)	10.2%	13.9%

Table 9. Estimates survival rates at predefined time points (1, 2, 3, 4, 5 years), stratified by clinical onset (CMI vs. AoCMI)

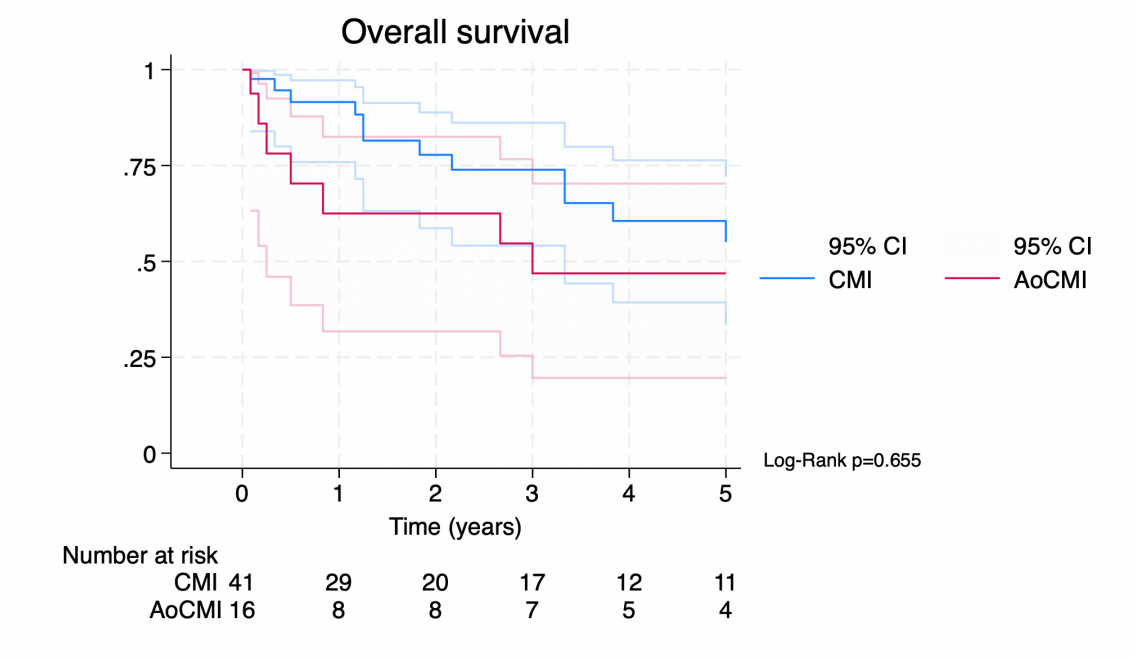


Figure 21. Kaplan-Meier survival curve for both study groups (CMI vs. AoCMI)

4.2.3 Pathology-related mortality

Our data showed that visceral vessel-related deaths occurred in 5 patients in both the CMI and AoCMI groups, corresponding to 10.6% in the former and 23.8% in the latter.

Analyzing the time-based trend, disease-related mortality at one-year post-procedure was 3.1% in the CMI group and 23.3% in the AoCMI group, with corresponding freedom from pathology-related death of 96.9% (95% CI: 80.4%–99.6%) and 76.7% (95% CI: 43.1%–91.9%), respectively. These figures remained unchanged in the second year, showing a stable mortality and survival pattern.

In the CMI group, the pathology-related mortality continued to be stable at year three. In contrast, AoCMI-related mortality rose to 42.5% by the third year, with freedom from pathology-related death decreasing to 57.5% (95% CI: 25.3%–80.1%), a value that remained unchanged at both fourth- and fifth-year follow-up.

In the CMI group, disease-related mortality increased to 12.9% at year four and remained unchanged at year five. Thus, CMI patients demonstrated a higher rate of freedom from pathology-related death at five years compared to AoCMI: 87.1% (95% CI: 64.1%–95.8%) versus 57.5% (95% CI: 25.3%–80.1%).

For better clarity, all the aforementioned information is reported in the following table (Table 10) and graphically displayed in the Kaplan–Meier survival curve (Figure 22), which shows non-pathology-related death estimates at predefined time points (1, 2, 3, 4, and 5 years), stratified by clinical onset (CMI vs. AoCMI).

As for overall mortality, in the Kaplan–Meier survival curve, the confidence intervals of the two study groups—CMI and AoCMI—overlap. The implications of this observation will be further addressed in the Discussion section.

	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	Std. Error CMI	Std. Error AoCMI
1st year	96.9% (95% CI: 80.4%-99.6%)	76.7% (95% CI: 43.1%-91.9%)	2.9%	11.9%
2nd year	92.6% (95% CI: 72.8%-98.1%)	76.7% (95% CI: 43.1%-91.9%)	5.2%	11.9%
3rd year	92.6% (95% CI: 72.8%-98.1%)	57.5% (95% CI: 25.3%-80.1%)	5.2%	14.8%
4th year	87.1% (95% CI: 64.1%-95.8%)	57.5% (95% CI: 25.3%-80.1%)	7.2%	14.8%
5th year	87.1% (95% CI: 64.1%-95.8%)	57.5% (95% CI: 25.3%-80.1%)	7.2%	14.8%

Table 10. Estimates non-pathology related death rates at predefined time points (1, 2, 3, 4, 5 years), stratified by clinical onset (CMI vs. AoCMI)

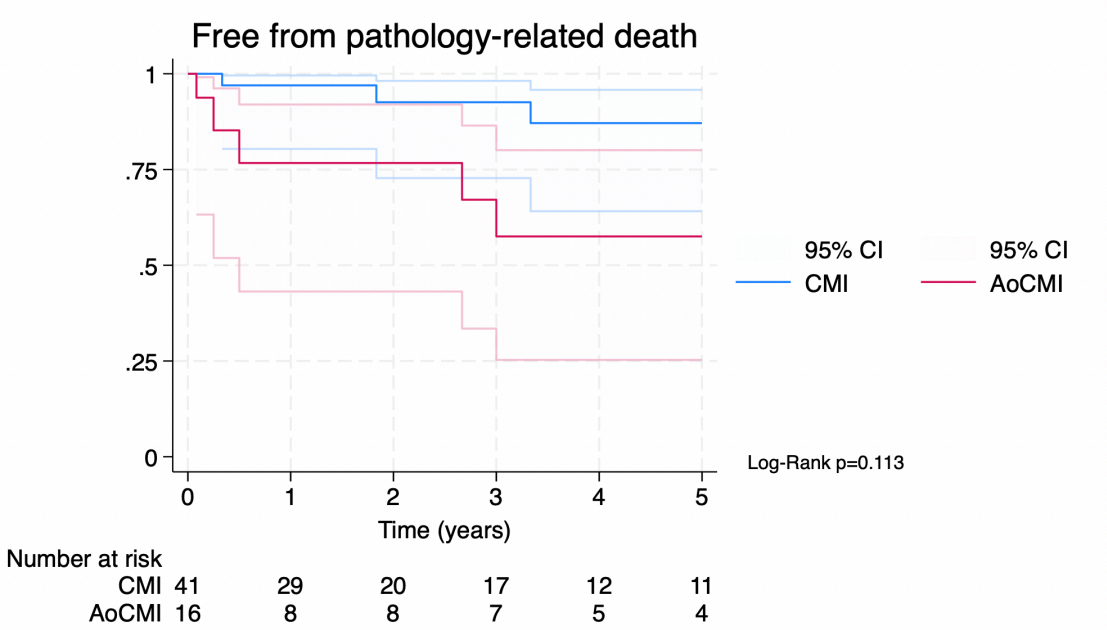


Figure 22. Kaplan-Meier free from pathology-related death curve for both study groups (CMI and AoCMI)

4.3 CTA FINDINGS AND INTRAOPERATIVE DATA

Another set of data collected and analyzed included CTA findings and intraoperative observations.

Firstly, it is worth noting the distribution of treated vessels within the overall study population. Among all procedures performed, 39.7% involved the coeliac trunk (CT), 58.8% the SMA, and 1.5% the IMA, highlighting a marked predominance of SMA-targeted interventions. This finding was statistically significant, with a P value of 0.044.

When stratified by study group, the distribution of vessel-specific interventions was as follows:

- CT: 48.9% in the CMI group versus 19.1% in the AoCMI group
- SMA: 48.9% in the CMI group versus 80.9% in the AoCMI group
- IMA: 2.2% in the CMI group versus none in the AoCMI group

Regarding lesion characteristics, 86.6% of all stenoses were ostial, with similar distributions between the groups: 87.2% in the CMI group and 85.0% in the AoCMI group (P = 0.806).

Calcified lesions were found in 52.3% of the total cohort, with comparable proportions in the two groups—52.2% in CMI and 52.6% in AoCMI (P = 0.973).

Conversely, a statistically significant difference emerged concerning the presence of bowel necrosis, which was assessed either indirectly by CT imaging signs or directly when exploratory laparotomy was performed. Overall, bowel necrosis was observed in 22.4% of the study population. However, its prevalence was markedly higher in the AoCMI group (45.0%) compared to only 12.8% in the CMI group (P = 0.004). The significance of this P value supports and allows the generalizability of the finding to the broader population.

Moreover, referring back to the previously defined classification of stenosis grade, our analysis revealed the following distribution:

- Grade 0 (<50%)**:** observed infrequently across both groups—6.5% in the CMI group and 10.0% in the AoCMI group
- Grade 1 (50–75%)**:** also rare, detected in 2.2% of CMI patients and in none of the AoCMI cases
- Grade 2 (75–99%)**:** more common, seen in 47.8% of CMI cases and 25.0% of AoCMI cases
- Grade 3 (complete occlusion)**:** predominant in both groups—43.5% in CMI and 65.0% in AoCMI

As evidenced by these findings, most stenoses were either grade 2 or 3, with grade 2 lesions more prevalent in the CMI group and grade 3 in the AoCMI group (P = 0.293).

Regarding other lesion characteristics, the median post-stenotic diameter was 6.5 mm (IQR: 5.4–7.1) in the CMI group and 6.7 mm (IQR: 5.0–7.2) in the AoCMI group (P = 0.988). The median lesion length was 12.1 mm (IQR: 6.9–22.0) for CMI and 19.4 mm (IQR: 8.2–27.0) for AoCMI patients (P = 0.229).
These values are expressed as median and interquartile range (IQR).

Two final worth-mentioning findings include the prevalence of a second severe stenosis in another visceral vessel and the corresponding rate of treatment. An at least second visceral lesion was identified in 68.1% of CMI patients and 71.4% of those in the AoCMI group (P = 0.783), yet only 8.5% of CMI and 15.0% of AoCMI patients underwent treatment for both lesions during the initial procedure (P = 0.228).

As indicated by the respective P values, except for bowel necrosis and the distribution of target vessels, all other comparisons did not reach statistical significance and should thus be interpreted as descriptive of this specific study-cohort.

All the above-mentioned information is summarized in the table below (Table 11).

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
CT signs of bowel lesions	15 (22.4%)	6 (12.8%)	9 (45.0%)	0.004
Vessel treated				0.044
CT	27 (39.7%)	23 (48.9%)	4 (19.1%)	
SMA	40 (58.8%)	23 (48.9%)	17 (80.9%)	
IMA	1 (1.5%)	1 (2.2%)	0 (0.0%)	
Ostial pathology	58 (86.6%)	41(87.2%)	17 (85.0%)	0.806
Calcified lesion	34 (52.3%)	24 (52.2%)	10 (52.6%)	0.973
Stenosis grade				0.293
<50%	5 (7.6%)	3 (6.5%)	2 (10.0%)	
50-75%	1 (1.5%)	1 (2.2%)	0 (0.0%)	
75-99%	27 (47.8%)	22 (47.8%)	5 (25.0%)	
Occlusion	33 (50.0%)	20 (43.5%)	13 (65.0%)	
Post-lesion diameter (mm)	6.5 (5.2 – 7.2)	6.5 (5.4 – 7.1)	6.7 (5 – 7.2)	0.988
Lesion lenght (mm)	13.3 (6.9 – 22.9)	12.1 (6.9 – 22)	19.4 (8.2 – 27)	0.229
Severe stenosis of other visceral vessel(s)	47 (69.1%)	32 (68.1%)	15 (71.4%)	0.783
Second vessel treated	7 (10.4%)	4 (8.5%)	3 (15.0%)	0.228

Table 11. CTA findings and intraoperative data in both groups (CMI and AoCMI

4.4 SECONDARY OUTCOMES

As previously discussed in earlier chapters, beyond the primary objective of evaluating mortality in all its aspects—including perioperative, overall, and pathology-related death—the present study also aimed to estimate reintervention rates and identify potential

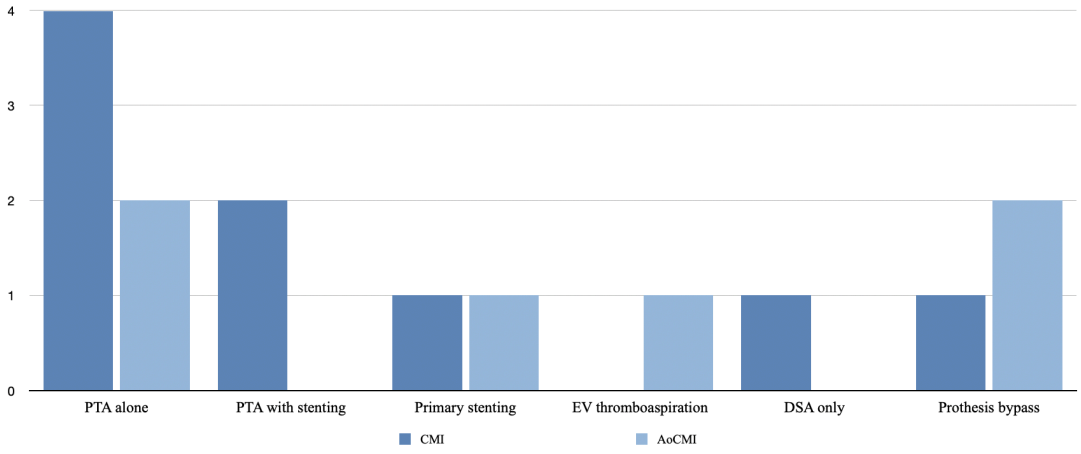
and promising predictors of reintervention during follow-up in both groups. These objectives were therefore designated as secondary outcomes of the research.

4.4.1 Estimates fraction of reintervention during follow-up

Our data show that 9 patients in the CMI group (19.1%) and 6 in the AoCMI group (28.6%) required a second procedure due to complications, indicating a higher rate of reintervention in the latter group. To assess reintervention rates, only the first reintervention was taken into account.

Specifically, among the 15 patients who underwent a second procedure, the types of interventions performed were distributed as follows (Diagram 3):

- 6 PTA-alone
- 2 PTA with stenting
- 2 primary stenting
- 1 endovascular thrombo-aspiration
- 1 diagnostic DSA due to failed stent cannulation
- 3 prosthesis bypass (ePTFE)



	CMI	AoCMI
PTA alone	4	2
PTA with stenting	2	0
Primary stenting	1	1
EV thromboaspiration	0	1
DSA only	1	0
Prothesis bypass	1	2

Diagram 3. Types of reintervention procedures in both groups (CMI and AoCMI)

Reintervention rates were analyzed over time using a Kaplan–Meier curve and predefined time points, following the same approach used for mortality assessment.

Our findings revealed that, although at one-year post-procedure the proportion of patients free from reintervention was similar in both groups—approximately 87%, with thus a reintervention incidence average of 13%—differences emerged over time. By the five-year mark, patients with CMI exhibited a higher cumulative risk of reintervention (35.1%) compared to 27.1% in the AoCMI group. This corresponded to a freedom from reintervention of 64.9% (95% CI: 39.1%–81.9%) in the CMI group and 72.9% (95% CI: 27.6%–92.5%) in the AoCMI group.

Specifically, at one year, freedom from reintervention was 87.1% (95% CI: 64.9%–97.9%) in the CMI group and 87.3% (95% CI: 38.7%–98.1%) in the AoCMI group. For AoCMI patients, this value remained unchanged through the second year, while for CMI patients, reintervention incidence increased to 27%, resulting in 73% freedom from reintervention (95% CI: 50.7%–86.5%). This rate remained stable at both the third and fourth year for CMI group.

In the AoCMI group, estimated reintervention rates rose to 27.1% at third year and remained constant through the fourth and fifth years, with corresponding freedom from reintervention of 72.9% (95% CI: 27.6%–92.5%).

At the five-year follow-up, cumulative reintervention risk in the CMI group reached 35.1%, with freedom from reintervention of 64.9% (95% CI: 39.1%–81.9%).

All the aforementioned data are listed in the table below (Table 12) and graphically represented in the Kaplan-Meier curve beneath (Figure 23).

As for overall mortality, in the Kaplan–Meier survival curve, the confidence intervals of the two study groups—CMI and AoCMI—overlap. The implications of this observation will be further addressed in the Discussion section.

	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	Std. Error CMI	Std. Error AoCMI
1st year	87.1% (95% CI: 64.9%-97.9%)	87.3% (95% CI: 38.7%-98.1%)	6.0%	11.7%
2nd year	73.0% (95% CI: 50.7%-86.5%)	87.3% (95% CI: 38.7%-98.1%)	9.0%	11.7%
3rd year	73.0% (95% CI: 50.7%-86.5%)	72.9% (95% CI: 27.6%-92.5%)	9.0%	16.5%
4th year	73.0% (95% CI: 50.7%-86.5%)	72.9% (95% CI: 27.6%-92.5%)	9.0%	16.5%
5th year	64.9% (95% CI: 39.1%-81.9%)	72.9% (95% CI: 27.6%-92.5%)	11.0%	16.5%

Table 12. Free from reintervention rates in both groups (CMI and AoCMI)

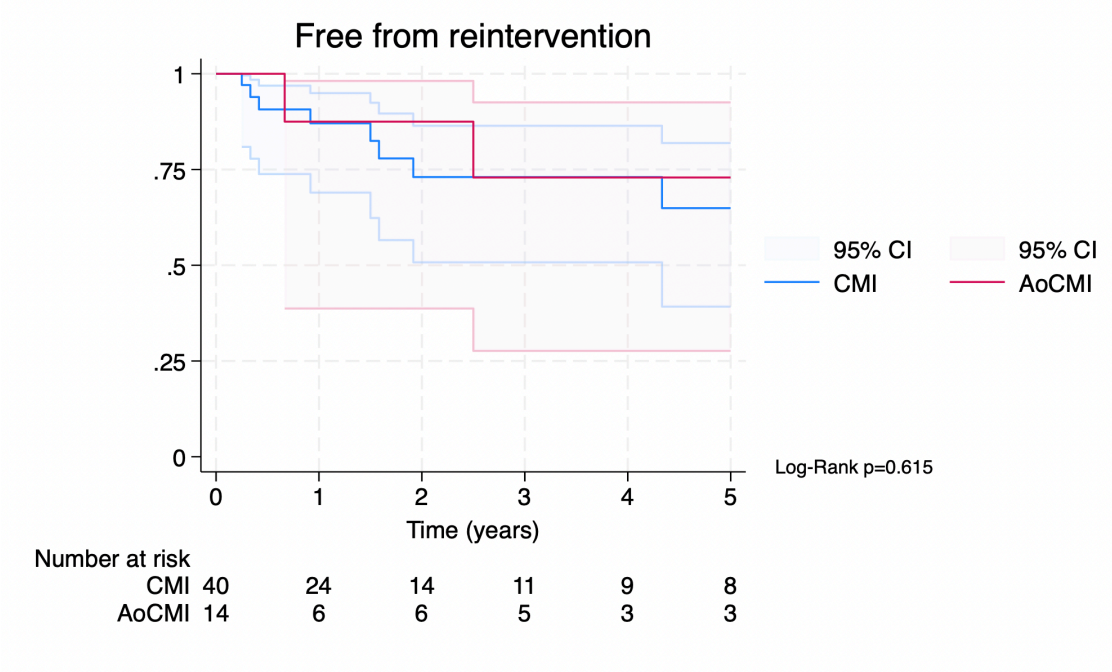


Figure 23. Kaplan-Meier free from reintervention curve for both study groups (CMI and AoCMI)

Moreover, the mean follow-up duration for CMI patients was 38 months—slightly more than three years—while for AoCMI patients it was marginally longer, with an average of 39.9 months (P = 0.898), as reported in table below (Table 13).

Regarding the time to first reintervention, CMI patients typically underwent a second procedure after an average of 59.7 months, corresponding to nearly five years from the initial intervention. In contrast, AoCMI patients experienced a shorter interval between procedures, with a mean time to reintervention of 15 months, approximately one and a half years (P = 0.116), as shown in Table 13.

	Total (N 68) n-mean/median (%-SD/IQR)	CMI (N 47; 69.1%) n-mean/median (%-SD/IQR)	AoCMI (N 21; 30.9%) n-mean/median (%-SD/IQR)	P value
Follow-up time (months)	38.6 (57.6)	38 (50.9)	39.9 (71.8)	0.898
Time to first reintervention (months)	32.9 (53.5)	59.7 (78.6)	15 (16.1)	0.116

Table 13. Follow-up duration and time to first reintervention for both groups (CMI and AoCMI)

4.4.2 Predictor factors for reintervention during follow-up

To identify potential predictors of reintervention during follow-up, a Cox proportional hazards regression model was applied.
Several factors were included in the univariate analysis as potentially contributing to the development of visceral vessel stenosis and subsequent mesenteric ischemia: male sex, active or past smoking habit, dyslipidemia, involvement of the SMA as the target vessel, distal lesion localization, calcified stenosis, post-stenosis diameter, lesion length, and performance of PTA alone as initial procedure. Their respective hazard ratios and 95% confidence intervals are reported in the table below for the sake of formal completeness**.**

Among these variables, those with a P value of approximately 0.20 in univariate analysis were then entered into the multivariate model to identify independent predictors of reintervention. The variables selected for multivariate analysis were male sex, smoking habit, presence of a calcified lesion, and performance of PTA alone as the first revascularization strategy.

What emerged from our analysis is that three of the four variables included in the multivariate model independently play a role in determining the hazard of reintervention, either as risk or protective factors.

Specifically, active or past smoking habit emerged as a significant risk factor, associated with a threefold increased hazard of requiring reintervention compared to non-smokers, (HR: 3.0; 95% CI: 1.2–6.9; P = 0.012).

Likewise, undergoing PTA alone as the initial revascularization procedure was strongly associated with a markedly increased risk of reintervention, showing a ninefold higher

hazard compared to alternative treatment strategies (HR: 9.2; 95% CI: 2.0–43.2; P = 0.005).

Conversely, the presence of calcified lesions appeared to act as a protective factor, significantly reducing the risk of reintervention (HR: 0.1; 95% CI: 0.02–0.6; P = 0.012).

Finally, male sex, due to its P value of 0.204, did not show a statistically significant association with reintervention risk (P = 0.204).

All the above-mentioned information is summarized in the table below (Table 14). The implication of such results will be further addressed in the Discussion section.

Risk Factor	Univariate analysis (HR – 95% CI)	P value	Multivariate analysis (HR – 95% CI)	P value
Male	0.4 (0.1-1.4)	0.147	0.3 (0.1-1.18)	0.204
Smoke	1.7 (0.8-3.3)	0.154	3.0 (1.2-6.9)	0.012
Dyslipidemia	2.4 (0.7-8.2)	0.154		
SMA	0.8 (0.2-2.7)	0.684		
Distal localization	2.2 (0.6-8.4)	0.262		
Calcific	0.4 (0.1-1.9)	0.243	0.1 (0.02-0.6)	0.012
Diameter post-lesion	1.0 (0.7-1.5)	0.809		
Lesion lenght	1.0 (0.9-1.0)	0.884		
PTA alone	3.6 (1.1-12.1)	0.036	9.2 (2.0-43.2)	0.005

Table 14. Cox proportional hazard regression model for reintervention during follow-up

5 DISCUSSION

As outlined in the previous sections of this work, the study aimed to drew a comparison between CMI and AoCMI patients in terms of overall, perioperative, and pathology-related mortality, as well as to assess the estimated rate of reintervention in both groups. Furthermore, it sought to identify potential predictors of reintervention during follow-up.

Regarding baseline characteristics, our cohort was consistent with current literature, which reports a predominance of female patients affected by mesenteric ischemia—particularly in cases of CMI[17,18]. In our study, 38.2% of the patients were male and 61.8% female. This disparity was even more pronounced within the CMI subgroup, with 36.2% males and 63.8% females.

Moreover, AF was present in 23.5% of the overall study population, with a significantly higher prevalence in the AoCMI group (38.1%) compared to the CMI group (17.0%). This finding underscores the greater incidence of arterial embolism in AoCMI, where embolism of cardiac origin is often the underlying cause, in contrast to the more atherosclerotic etiology typically observed in CMI[16]. Therefore, this finding approaches statistical significance, suggesting that the reported percentages may be reasonably generalizable to the broader population.

In addition, in terms of target vessels treated, SMA emerged as the most frequently addressed visceral artery in our study population; not only this finding shows statistical significance (P = 0.044), but is also in accordance with existing literature[5]. It was the target vessel treated in 58.8% of all procedures, compared to 39.7% for CT and 1.5% for IMA.

5.1 MORTALITY AND SURVIVAL

In our study, mortality—and consequently survival—was evaluated in terms of perioperative, overall, and pathology-related death rates. Specifically, perioperative mortality accounted for 6 patients (8.8% of the total cohort), with a higher incidence in AoCMI compared to CMI (19.1% vs 4.3%, respectively). This present finding, which reached statistical significance (P = 0.047), confirmed what previously published in literature, suggesting an increased number of fatalities amongst AoCMI patients.

The elevated perioperative mortality observed in AoCMI patients may be attributed to multiple clinical, surgical, and pathophysiological factors. At the time of diagnosis and intervention, patients with CMI are generally in stable condition, whereas AoCMI patients often present in hemodynamic instability, hypovolemic shock, lactic acidosis, and multi-organ failure, with inadequate collateral compensation. Additionally, while CMI is typically diagnosed electively, AoCMI—being a subset of AMI—requires rapid identification in emergency settings, often leading to misdiagnosis due to limited time for comprehensive clinical evaluation.

This also affects surgical management: CMI patients typically undergo scheduled, elective procedures, while AoCMI cases often require urgent or emergent interventions, sometimes in presence of bowel necrosis or other major complications, resulting in more complex intraoperative scenarios.

Moreover, although the greater perioperative mortality in AoCMI is well supported by literature and the specific figures observed in our study are approximately in line with such meta-analysis and systematic reviews, they lack stratification between perioperative mortality following open versus endovascular procedures—an aspect extensively investigated in the current literature. In particular, several studies report a 30-day mortality rate of 17.2% after endovascular treatment, rising to 38.5% following open surgery[5]. Regarding CMI instead, the 30-days mortality rates showed no significant differences between the endovascular and open surgery group, with a perioperative death rate ranging from 0.7% to 12.5% in relation to the patient's comorbidities: the former figure represents low-risk patients, while the latter the ones with two or three major comorbidities[77].

In terms of overall mortality, our results—represented through a Kaplan-Meier survival curve—revealed an overlap of the 95% confidence intervals between the CMI and AoCMI groups, indicating the uncertainty in definitively interpreting the observed survival trends. Furthermore, the Log-Rank test, employed to formally assess the global significance of the difference between the curves, yielded a P value of 0.655, confirming the absence of statistical significance. Such findings are probably due to the limited sample size and to the few follow-up data according to the retrospective nature of the research.

In our population, overall survival at one-year post-procedure was significantly higher in CMI patients (91.5%; 95% CI: 75.9%–97.2%) compared to those with AoCMI (62.5%; 95% CI: 31.7%–82.5%).

Although survival declined over time in both groups, a greater cumulative loss was observed in the CMI cohort at the five-year follow-up. Specifically, five-year survival was 55% in the CMI group (95% CI: 33.3%–72.3%) versus 46.9% in AoCMI. Despite AoCMI patients exhibiting lower survival at each predefined time point (1, 2, 3, 4, and 5 years), the decline in the CMI group appeared steeper. This observation may be attributed either to the larger sample size in the CMI group or to potential biases in data collection. Although the differences in overall survival—and consequently in mortality—did not reach statistical significance, our findings are partially consistent with existing literature. Some studies, always stratifying data by treatment modality (endovascular vs. open surgery), report five-year survival in AMI patients ranging between 30–40%[5,81].

The slightly higher rate of 46.9% observed in our cohort may be explained by the fact that we considered AoCMI patients, who, unlike those with AMI, often develop abundant collateral circulation, potentially accounting for the reduced mortality.

Regarding CMI, long-term survival is frequently reported according to the completeness of revascularization. Literature describes significantly higher long-terms survival rates than those observed in our study, with ten-year survival reaching up to 88% for complete and 76% for incomplete revascularization in some studies[5]. In contrast, our 55% 5-years survival finding likely reflects the high burden of comorbidities in the study population, which may not be representative of the general CMI cohort. Moreover, our analysis only included treated patients, who typically present with more advanced disease and worse clinical status.

Ultimately, concerning pathology-related mortality, this parameter was, similarly to other forms of mortality, significantly higher in the AoCMI population, both in absolute terms and across the analyzed time points. However, as observed for overall mortality and survival, the Kaplan-Meier analysis revealed no statistically significant difference between the two groups, with overlapping 95% confidence intervals and a P value of 0.113 (Log-Rank test); therefore, this finding cannot be confidently generalized to the general population.

Nevertheless, pathology-related mortality appeared consistently higher in the AoCMI group at each time point, with 76.7% (95% CI: 43.1%-91.9%) of patients free from pathology-related death at the one-year follow-up, compared to 96.9% (95% CI: 80.4%-99.6%) in the CMI group. Survival rates continued to decline over time in both cohorts, reaching five-year estimates of 57.5% (95% CI: 25.3%-80.1%) for AoCMI patients and 87.1% (95% CI: 64.1%-95.8%) for those with CMI.
The more pronounced decline observed in the AoCMI group may be attributed to the more severe clinical condition of acute patients, as previously discussed, or potentially to population bias; given that the study cohort may not fully represent the general population, it is possible that, by chance, the AoCMI group included a higher proportion of elderly patients with greater comorbidity burden and more advanced disease stages.

5.2 REINTERVENTION RATES AND PREDICTORS

When analyzing reintervention rates, the previously mentioned consideration regarding the statistical significance of our findings must be reiterated. In the Kaplan-Meier analysis, the 95% confidence intervals overlapped (Log-Rank P = 0.615), thereby precluding any interpretation of the observed trend as representative of the general population due to the absence of statistical significance.
At the one-year follow-up, both groups demonstrated a similar reintervention incidence of approximately 13%. However, over time, CMI patients exhibited a higher cumulative risk, with reintervention rates, reaching 35.1% at five years compared to 27.1% in the AoCMI group.

This increased cumulative risk in CMI patients may be attributed to their longer survival; as they live longer, they are more likely to experience restenosis and symptom recurrence, ultimately necessitating additional procedures.
Indeed, mesenteric reinterventions are associated not only with low mortality rates (3%), as reported in several studies, but also with significant symptom improvement (92%)[5].
In this context, the chronic nature of CMI, often characterized by recurrent postprandial symptoms, increases the likelihood of reintervention. Some studies have indicated that approximately 36% of CMI patients develop restenosis within two and a half years following the initial procedure[5], thereby requiring subsequent intervention to alleviate symptoms.
Nevertheless, our data are challenging to compare with existing literature, as most studies primarily focus on comparing open versus endovascular procedures, with reintervention rates defined in relation to the initial technique employed — a variable that was not the primary focus of our investigation.

Regarding our analysis of predictors for reintervention during follow-up, both a history of active or past smoking habit and the use of PTA alone as initial revascularization procedure emerged as significant factors. Based on our Cox proportional hazard regression model, each was independently associated with an increased risk of requiring a second procedure: smoking was associated with a threefold higher risk (HR = 3.0; 95% CI: 1.2–6.9), while initial treatment with PTA alone carried a ninefold increase in risk (HR = 9.2; 95% CI: 2.0–43.2). These findings align with existing literature, as smoking

is a well-established risk factor for atherosclerosis—the principal etiology of both CMI and AoCMI, whose progression may cause the need of a second intervention—while PTA alone is increasingly avoided as a first-line treatment due to its renowned limitations in long-term efficacy[3,5].

On the other hand, the presence of calcific stenosis emerged from our Cox proportional hazard regression model as a protective factor against the risk of reintervention (HR = 01.; 95% CI: 1.2-6.9). A definitive explanation for this finding is still lacking in our study. In fact, some studies in literature have shown that severely calcified lesions are generally associated with a higher risk of distal embolization during surgical procedures, particularly during endovascular interventions[82]. Although severely calcified stenoses are typically well-managed with primary stenting, the risk of distal embolization—which may necessitate a second procedure—remains.

However, the role of previously treated calcified lesions—whether potentially protective or detrimental—in the setting of subsequent interventions has not been extensively addressed in the literature.

One possible hypothesis to explain our finding is that, in cases of extremely calcified lesions, the underlying etiology of mesenteric ischemia is more often thrombosis. These lesions are typically managed with primary stenting[82], which often involves DAPT as postoperative best medical therapy, at least for a limited period of time[5]. This more aggressive secondary prevention, along with a better control of the overall risk factors, may contribute to the lower risk of reintervention observed in these patients. Conversely, when vessels are non-calcified, embolism represents a more frequent etiology of mesenteric ischemia. These cases are rarely treated with stenting and thus do not require DAPT. Although such patients are usually managed with anticoagulation, the advanced age of this population often results in contraindications to anticoagulant therapy, leading to treatment discontinuation. This may promote disease relapse and consequently increase the likelihood of reintervention.

The above-mentioned explanation remains merely hypothetical, and our finding may also be influenced by biases related to sample size or to the limited representativeness of our study cohort. For this reason, further research specifically addressing this aspect is required.

5.3 LIMITATIONS OF THE STUDY

The primary limitation of the present study lies in its retrospective design, which inherently exposes it to selection bias—as the study population may not fully reflect the general population—and to data collection bias. Retrospective studies, in fact, heavily rely on available clinical records, which may be incomplete, not entirely accurate for the study objectives, or gathered using non-standardized methods. These issues contribute to the limited ability of such studies to establish a clear and direct causal relationship.

Secondly, the monocentric nature of the research resulted in a limited sample size, with only 68 patients included in the cohort. Such a small number may hinder the achievement of statistically significant results and, even when significance is reached, the reliability of the findings remains limited due to potential numerical bias.

Thirdly, the study was based on data collected over a 25-year period, from May 2000 to March 2025. Such an extended timeframe may introduce confounding elements due to the evolution of technologies and therapeutic approaches. In the early years, our data show a higher prevalence of open surgical procedures, which later shifted in favor of endovascular techniques. The introduction of thrombo-aspiration marked yet another turning point. The inclusion of data spanning such distinct procedural eras within a single study may have compromised the overall consistency and quality of the results.

Ultimately, our sample only included patients with CMI and AoCMI who underwent treatment over the 25-year study period. As a result, the reported mortality rates—whether overall or pathology-related—may not be representative of the general population, since all patients on whom no vascular surgical procedure have been performed, due to factors such as lack of surgical indication, multiple and severe comorbidities, or misdiagnosis, were not captured in the analysis.

5.4 FUTURE PERSPECTIVES

Future research on this topic should specifically focus on AoCMI, given the current substantial gap in the literature addressing this condition. AoCMI can no longer be

regarded as a mere subtype of AMI, as aspects ranging from pathophysiology to mortality outcomes, management, and reintervention must be interpreted within the context of an acute event superimposed on a chronic established condition.

Moreover, the most noteworthy finding of our study was the identification of calcific lesions as potential protective factors against reinterventions. Since this aspect has been scarcely explored in the existing literature, it warrants further investigation through appropriately designed studies. Although our finding reached statistical significance, we cannot ascertain whether it reflects a true protective effect or is influenced by potential biases; for this very reason, it could serve as a primary outcome in future research.

6 CONCLUSIONS

In conclusion, in response to our first question we can state that AMI and AoCMI are actually two different entities. AMI, in fact, showed significantly worse outcomes and should consequently, not be, clinically and scientifically, considered within the CMI plethora.

In terms of mortality—whether perioperative, overall, or disease-related—AoCMI patients showed higher rates than CMI ones.

As for secondary outcomes, the estimates fraction of reintervention rates over time appeared to be higher in the CMI group, likely due to their longer survival and the comparatively lower disease burden associated with CMI versus AoCMI.

Regarding predictors of reintervention during follow-up, both active or previous smoking habit and the use of PTA alone as the initial revascularization strategy were associated with an increased risk of a secondary procedure, in line with current literature. Conversely, the presence of calcific lesions emerged as a protective factor against the need for reintervention. Further investigation is required to better understand this latter finding.

Given the marked differences between CMI and AoCMI, further research is required to compare AoCMI with AMI.

7 REFERENCES

1. Gnanapandithan K, Feuerstadt P. **Review Article: Mesenteric Ischemia.** *Curr Gastroenterol Rep*. 2020;22(4):17. doi:10.1007/s11894-020-0754-x

2. Sardar P, White CJ. **Chronic mesenteric ischemia: Diagnosis and management.** *Prog Cardiovasc Dis*. 2021;65:71-75. doi:10.1016/j.pcad.2021.03.002

3. van Dijk LJ, van Noord D, de Vries AC, et al. **Clinical management of chronic mesenteric ischemia.** *United Eur Gastroenterol J*. 2019;7(2):179-188. doi:10.1177/2050640618817698

4. Kolkman JJ, Geelkerken RH. **Diagnosis and treatment of chronic mesenteric ischemia: An update.** *Best Pract Res Clin Gastroenterol*. 2017;31(1):49-57. doi:10.1016/j.bpg.2017.01.003

5. Björck M, Koelemay M, Acosta S, et al. **Editor's Choice – Management of the Diseases of Mesenteric Arteries and Veins: Clinical Practice Guidelines of the European Society of Vascular Surgery (ESVS)**. *Eur J Vasc Endovasc Surg*. 2017;53(4):460-510. doi:10.1016/j.ejvs.2017.01.010

6. Olson MC, Fletcher JG, Nagpal P, Froemming AT, Khandelwal A. **Mesenteric ischemia: what the radiologist needs to know.** *Cardiovasc Diagn Ther*. 2019;9(Suppl 1):S74-S87. doi:10.21037/cdt.2018.09.06

7. Gary GW, R. James V. ***Anatomic Exposures in Vascular Surgery*.** IV. Wolters Kluwer; 2020.

8. Gilroy AM, MacPherson BR, Ross LM. ***Prometheus, Atlas of Anatomy*. II.** EdiSES; 2012.

9. **The Celiac Axis Revisited: Anatomic Variants, Pathologic Features, and Implications for Modern Endovascular Management.** ResearchGate. Accessed May 7, 2025. https://www.researchgate.net/publication/275049967_The_Celiac_Axis_Revisited_Anatomic_Variants_Pathologic_Features_and_Implications_for_Modern_Endovascular_Management

10. Gray H. ***Gray's Anatomy. The Anatomical Basis of Clinical Practice*. Vol 2.** 41st ed. Elsevier; 2016.

11. Uflacker A, Guimaraes M. ***Uflacker's Atlas of Vascular Anatomy. An Angiographic Approach*. III.** Wolters Kluwer; 2020.

12. Takala J. **Determinants of splanchnic blood flow.** *Br J Anaesth*. 1996;77(1):50-58. doi:10.1093/bja/77.1.50

13. Sidawy AN, Perler BA. ***Rutherford's Vascular Surgery and Endovascular Therapy*.** Vol 2. 10th ed. Elsevier; 2022.

14. Parks DA, Jacobson ED. **Physiology of the splanchnic circulation.** *Arch Intern Med*. 1985;145(7):1278-1281.

15. Oehler H, Eichler K, Derwich W, Schnitzbauer AA, Schreckenbach T. **[Epidemiology and diagnostics of mesenteric ischemia].** *Chir Heidelb Ger*. 2024;95(5):347-352. doi:10.1007/s00104-023-02021-6

16. Kärkkäinen JM, Acosta S. **Acute mesenteric ischemia (part I) - Incidence, etiologies, and how to improve early diagnosis.** *Best Pract Res Clin Gastroenterol*. 2017;31(1):15-25. doi:10.1016/j.bpg.2016.10.018

17. Terlouw LG, Verbeten M, van Noord D, et al. **The Incidence of Chronic Mesenteric Ischemia in the Well-Defined Region of a Dutch Mesenteric Ischemia Expert Center.** *Clin Transl Gastroenterol*. 2020;11(8):e00200. doi:10.14309/ctg.0000000000000200

18. Xhepa G, Vanzulli A, Sciacqua LV, et al. **Advancements in Treatment Strategies for Chronic Mesenteric Ischemia: A Comprehensive Review.** *J Clin Med*. 2023;12(22):7112. doi:10.3390/jcm12227112

19. Kumar V, Abbas AK, Aster JC. ***Robbins & Cotran Pathologic Basis of Disease*.** Tenth. Elsevier; 2020.

20. Bala M, Catena F, Kashuk J, et al. **Acute mesenteric ischemia: updated guidelines of the World Society of Emergency Surgery.** *World J Emerg Surg WJES*. 2022;17(1):54. doi:10.1186/s13017-022-00443-x

21. Acosta S, Ögren M, Sternby NH, Bergqvist D, Björck M. **Clinical Implications for the Management of Acute Thromboembolic Occlusion of the Superior Mesenteric Artery: Autopsy Findings in 213 Patients.** *Ann Surg*. 2005;241(3):516. doi:10.1097/01.sla.0000154269.52294.57

22. Navas-Campo R, Moreno-Caballero L, Ezponda Casajús A, Muñoz DI. **Acute mesenteric ischemia: a review of the main imaging techniques and signs.** *Radiologia*. 2020;62(5):336-348. doi:10.1016/j.rx.2020.02.001

23. Aschoff AJ, Stuber G, Becker BW, et al. **Evaluation of acute mesenteric ischemia: accuracy of biphasic mesenteric multi-detector CT angiography.** *Abdom Imaging*. 2009;34(3):345-357. doi:10.1007/s00261-008-9392-8

24. Acosta S, Salim S. **Management of Acute Mesenteric Venous Thrombosis: A Systematic Review of Contemporary Studies.** *Scand J Surg SJS Off Organ Finn Surg Soc Scand Surg Soc*. 2021;110(2):123-129. doi:10.1177/1457496920969084

25. Acosta-Mérida MA, Marchena-Gómez J, Saavedra-Santana P, Silvestre-Rodríguez J, Artiles-Armas M, Callejón-Cara MM. **Surgical Outcomes in Acute Mesenteric Ischemia: Has Anything Changed Over the Years?** *World J Surg*. 2020;44(1):100-107. doi:10.1007/s00268-019-05183-9

26. Sana A, van Noord D, Mensink PBF, et al. **Patients with chronic**

gastrointestinal ischemia have a higher cardiovascular disease risk and mortality. *Atherosclerosis*. 2012;224(1):235-241. doi:10.1016/j.atherosclerosis.2012.07.007

27. Veenstra RP, ter Steege RWF, Geelkerken RH, Huisman AB, Kolkman JJ. **The Cardiovascular Risk Profile of Atherosclerotic Gastrointestinal Ischemia Is Different from Other Vascular Beds.** *Am J Med*. 2012;125(4):394-398. doi:10.1016/j.amjmed.2011.09.013

28. Gornik HL, Persu A, Adlam D, et al. **First International Consensus on the diagnosis and management of fibromuscular dysplasia.** *Vasc Med Lond Engl*. 2019;24(2):164-189. doi:10.1177/1358863X18821816

29. Goodall R, Langridge B, Onida S, Ellis M, Lane T, Davies AH. **Median arcuate ligament syndrome.** *J Vasc Surg*. 2020;71(6):2170-2176. doi:10.1016/j.jvs.2019.11.012

30. Kolkman JJ, Mensink PBF. **Non-occlusive mesenteric ischaemia: a common disorder in gastroenterology and intensive care.** *Best Pract Res Clin Gastroenterol*. 2003;17(3):457-473. doi:10.1016/S1521-6918(03)00021-0

31. ter Steege RWF, Kolkman JJ. **Review article: the pathophysiology and management of gastrointestinal symptoms during physical exercise, and the role of splanchnic blood flow.** *Aliment Pharmacol Ther*. 2012;35(5):516-528. doi:10.1111/j.1365-2036.2011.04980.x

32. Oldenburg WA, Lau LL, Rodenberg TJ, Edmonds HJ, Burger CD. **Acute mesenteric ischemia: a clinical review.** *Arch Intern Med*. 2004;164(10):1054-1062. doi:10.1001/archinte.164.10.1054

33. Lendzion RJ, Frahm-Jensen G, Keck J. **Acute Mesenteric Ischemia.** *Clin Colon Rectal Surg*. 2022;35(3):227-236. doi:10.1055/s-0042-1743283

34. Reintam Blaser A, Jakob SM, Starkopf J. **Gastrointestinal failure in the ICU.** *Curr Opin Crit Care*. 2016;22(2):128-141. doi:10.1097/MCC.0000000000000286

35. Reintam Blaser A, Acosta S, Arabi YM. **A clinical approach to acute mesenteric ischemia.** *Curr Opin Crit Care*. 2021;27(2):183-192. doi:10.1097/MCC.0000000000000802

36. Yu H, Kirkpatrick IDC. **An Update on Acute Mesenteric Ischemia.** *Can Assoc Radiol J J Assoc Can Radiol*. 2023;74(1):160-171. doi:10.1177/08465371221094280

37. Kärkkäinen JM. **Acute Mesenteric Ischemia: A Challenge for the Acute Care Surgeon.** *Scand J Surg SJS Off Organ Finn Surg Soc Scand Surg Soc*. 2021;110(2):150-158. doi:10.1177/14574969211007590

38. Loffroy R, Guiu B, Cercueil JP, Krausé D. **Chronic mesenteric ischemia: efficacy and outcome of endovascular therapy.** *Abdom Imaging*. 2010;35(3):306-314. doi:10.1007/s00261-009-9515-x

39. Cappell MS. INTESTINAL (MESENTERIC) VASCULOPATHY II: **Ischemic**

Colitis and Chronic Mesenteric Ischemia. *Gastroenterol Clin North Am*. 1998;27(4):827-860. doi:10.1016/S0889-8553(05)70034-0

40. van den Heijkant TC, Aerts BAC, Teijink JA, Buurman WA, Luyer MDP. **Challenges in diagnosing mesenteric ischemia.** *World J Gastroenterol*. 2013;19(9):1338-1341. doi:10.3748/wjg.v19.i9.1338

41. Acosta S, Nilsson TK, Björck M. **D-dimer testing in patients with suspected acute thromboembolic occlusion of the superior mesenteric artery.** *Br J Surg*. 2004;91(8):991-994. doi:10.1002/bjs.4645

42. S A, T N. **Current status on plasma biomarkers for acute mesenteric ischemia.** *J Thromb Thrombolysis*. 2012;33(4). doi:10.1007/s11239-011-0660-z

43. Evennett NJ, Petrov MS, Mittal A, Windsor JA. **Systematic review and pooled estimates for the diagnostic accuracy of serological markers for intestinal ischemia.** *World J Surg*. 2009;33(7):1374-1383. doi:10.1007/s00268-009-0074-7

44. Brandt LJ, Boley SJ. **AGA technical review on intestinal ischemia.** American Gastrointestinal Association. *Gastroenterology*. 2000;118(5):954-968. doi:10.1016/s0016-5085(00)70183-1

45. Acosta S, Björnsson S, Ekberg O, Resch T. **CT Angiography Followed by Endovascular Intervention for Acute Superior Mesenteric Artery Occlusion does not Increase Risk of Contrast-Induced Renal Failure.** *Eur J Vasc Endovasc Surg*. 2010;39(6):726-730. doi:10.1016/j.ejvs.2010.01.017

46. Barmase M, Kang M, Wig J, Kochhar R, Gupta R, Khandelwal N. **Role of multidetector CT angiography in the evaluation of suspected mesenteric ischemia.** *Eur J Radiol*. 2011;80(3):e582-e587. doi:10.1016/j.ejrad.2011.09.015

47. Yikilmaz A, Karahan OI, Senol S, Tuna IS, Akyildiz HY. **Value of multislice computed tomography in the diagnosis of acute mesenteric ischemia.** *Eur J Radiol*. 2011;80(2):297-302. doi:10.1016/j.ejrad.2010.07.016

48. Bourcier S, Klug J, Nguyen LS. **Non-occlusive mesenteric ischemia: Diagnostic challenges and perspectives in the era of artificial intelligence.** *World J Gastroenterol*. 2021;27(26):4088-4103. doi:10.3748/wjg.v27.i26.4088

49. Trompeter M, Brazda T, Remy CT, Vestring T, Reimer P. **Non-occlusive mesenteric ischemia: etiology, diagnosis, and interventional therapy.** *Eur Radiol*. 2002;12(5):1179-1187. doi:10.1007/s00330-001-1220-2

50. Amitrano L, Brancaccio V, Guardascione MA, et al. **High prevalence of thrombophilic genotypes in patients with acute mesenteric vein thrombosis.** *Am J Gastroenterol*. 2001;96(1):146-149. doi:10.1111/j.1572-0241.2001.03465.x

51. Rajesh S, Mukund A, Arora A. **Imaging Diagnosis of Splanchnic Venous Thrombosis.** *Gastroenterol Res Pract*. 2015;2015:101029. doi:10.1155/2015/101029

52. Acosta S, Alhadad A, Svensson P, Ekberg O. **Epidemiology, risk and prognostic factors in mesenteric venous thrombosis.** *Br J Surg*. 2008;95(10):1245-1251. doi:10.1002/bjs.6319

53. van Noord D, Mensink PBF, de Knegt RJ, et al. **Serum markers and intestinal mucosal injury in chronic gastrointestinal ischemia.** *Dig Dis Sci*. 2011;56(2):506-512. doi:10.1007/s10620-010-1303-5

54. Tilsed JVT, Casamassima A, Kurihara H, et al. **ESTES guidelines: acute mesenteric ischaemia.** *Eur J Trauma Emerg Surg Off Publ Eur Trauma Soc*. 2016;42(2):253-270. doi:10.1007/s00068-016-0634-0

55. Kim SH, Hwang HY, Kim MJ, Park KJ, Kim KB. **Early laparoscopic exploration for acute mesenteric ischemia after cardiac surgery.** *Acute Crit Care*. 2020;35(3):213-217. doi:10.4266/acc.2018.00423

56. Paral J, Ferko A, Plodr M, et al. **Laparoscopic diagnostics of acute bowel ischemia using ultraviolet light and fluorescein dye: an experimental study.** *Surg Laparosc Endosc Percutan Tech*. 2007;17(4):291-295. doi:10.1097/SLE.0b013e3180dc9376

57. Liot E, Assalino M, Buchs NC, et al. **Does near-infrared (NIR) fluorescence angiography modify operative strategy during emergency procedures?** *Surg Endosc*. 2018;32(10):4351-4356. doi:10.1007/s00464-018-6226-9

58. Kärkkäinen JM, Acosta S. **Acute mesenteric ischemia (Part II) - Vascular and endovascular surgical approaches.** *Best Pract Res Clin Gastroenterol*. 2017;31(1):27-38. doi:10.1016/j.bpg.2016.11.003

59. Kärkkäinen JM, Lehtimäki TT, Saari P, et al. **Endovascular Therapy as a Primary Revascularization Modality in Acute Mesenteric Ischemia.** *Cardiovasc Intervent Radiol*. 2015;38(5):1119-1129. doi:10.1007/s00270-015-1064-9

60. Salsano G, Salsano A, Sportelli E, et al. **What is the Best Revascularization Strategy for Acute Occlusive Arterial Mesenteric Ischemia: Systematic Review and Meta-analysis.** *Cardiovasc Intervent Radiol*. 2018;41(1):27-36. doi:10.1007/s00270-017-1749-3

61. Heiss P, Loewenhardt B, Manke C, et al. **Primary percutaneous aspiration and thrombolysis for the treatment of acute embolic superior mesenteric artery occlusion.** *Eur Radiol*. 2010;20(12):2948-2958. doi:10.1007/s00330-010-1859-7

62. Sakamoto T, Kubota T, Funakoshi H, Lefor AK. **Multidisciplinary management of acute mesenteric ischemia: Surgery and endovascular intervention.** *World J Gastrointest Surg*. 2021;13(8):806-813. doi:10.4240/wjgs.v13.i8.806

63. Resch TA, Acosta S, Sonesson B. **Endovascular techniques in acute arterial mesenteric ischemia.** *Semin Vasc Surg*. 2010;23(1):29-35. doi:10.1053/j.semvascsurg.2009.12.004

64. Kersjes WH, Hesse A. **Percutaneous retrograde revascularization of chronic occlusions of the superior mesenteric artery via collaterals of the celiac artery.** *CVIR Endovasc*. 2020;3:81. doi:10.1186/s42155-020-00170-x

65. Mak AK, Andraska EA, Reitz KM, Chaer R, Eslami MH, Avgerinos E. **A single institutional experience with suction thrombectomy in acute mesenteric ischemia.** *Ann Vasc Surg Brief Rep Innov*. 2022;2(2):100070. doi:10.1016/j.avsurg.2022.100070

66. Expert Panel on Interventional Radiology, Lam A, Kim YJ, et al. ACR **Appropriateness Criteria® Radiologic Management of Mesenteric Ischemia: 2022 Update.** *J Am Coll Radiol JACR*. 2022;19(11S):S433-S444. doi:10.1016/j.jacr.2022.09.006

67. Mendes BC, Oderich GS, Tallarita T, et al. **Superior mesenteric artery stenting using embolic protection device for treatment of acute or chronic mesenteric ischemia.** *J Vasc Surg*. 2018;68(4):1071-1078. doi:10.1016/j.jvs.2017.12.076

68. Klotz S, Vestring T, Rötker J, Schmidt C, Scheld HH, Schmid C. **Diagnosis and treatment of nonocclusive mesenteric ischemia after open heart surgery.** *Ann Thorac Surg*. 2001;72(5):1583-1586. doi:10.1016/s0003-4975(01)03179-4

69. Acosta S. **Surgical management of peritonitis secondary to acute superior mesenteric artery occlusion**. *World J Gastroenterol*. 2014;20(29):9936-9941. doi:10.3748/wjg.v20.i29.9936

70. Wyers MC, Powell RJ, Nolan BW, Cronenwett JL. **Retrograde mesenteric stenting during laparotomy for acute occlusive mesenteric ischemia.** *J Vasc Surg*. 2007;45(2):269-275. doi:10.1016/j.jvs.2006.10.047

71. Acosta S, Kärkkäinen J. **Open abdomen in acute mesenteric ischemia.** *Anaesthesiol Intensive Ther*. 2019;51(2):159-162. doi:10.5114/ait.2019.86280

72. Bering J, DiBaise JK. **Short bowel syndrome: Complications and management.** *Nutr Clin Pract Off Publ Am Soc Parenter Enter Nutr*. 2023;38 Suppl 1:S46-S58. doi:10.1002/ncp.10978

73. Mocian A, Russu E, Kaller R, Mureșan A. **Aorto-mesenteric Bypass for the Treatment of Chronic Mesenteric Ischemia.** *J Interdiscip Med*. 2019;4(2):101-103. doi:10.2478/jim-2019-0012

74. Cai W, Li X, Shu C, et al. **Comparison of Clinical Outcomes of Endovascular Versus Open Revascularization for Chronic Mesenteric Ischemia: A Meta-analysis.** *Ann Vasc Surg*. 2015;29(5):934-940. doi:10.1016/j.avsg.2015.01.010

75. Altintas Ü, Lawaetz M, de la Motte L, et al. **Endovascular Treatment of Chronic and Acute on Chronic Mesenteric Ischaemia: Results From a National Cohort of 245 Cases.** *Eur J Vasc Endovasc Surg*. 2021;61(4):603-611. doi:10.1016/j.ejvs.2021.01.003

76. Terlouw LG, Moelker A, Abrahamsen J, et al. **European guidelines on chronic**

mesenteric ischaemia - joint United European Gastroenterology, European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Gastrointestinal and Abdominal Radiology, Netherlands Association of Hepatogastroenterologists, Hellenic Society of Gastroenterology, Cardiovascular and Interventional Radiological Society of Europe, and Dutch Mesenteric Ischemia Study group clinical guidelines on the diagnosis and treatment of patients with chronic mesenteric ischaemia. *United Eur Gastroenterol J*. 2020;8(4):371-395. doi:10.1177/2050640620916681

77. Oderich GS, Bower TC, Sullivan TM, Bjarnason H, Cha S, Gloviczki P. **Open versus endovascular revascularization for chronic mesenteric ischemia: Risk-stratified outcomes.** *J Vasc Surg*. 2009;49(6):1472-1479.e3. doi:10.1016/j.jvs.2009.02.006

78. Oderich GS, Gloviczki P, Bower TC. **Open Surgical Treatment for Chronic Mesenteric Ischemia in the Endovascular Era: When It is Necessary and What is the Preferred Technique?** *Semin Vasc Surg*. 2010;23(1):36-46. doi:10.1053/j.semvascsurg.2009.12.005

79. Rits Y, Oderich GS, Bower TC, et al. **Interventions for mesenteric vasculitis.** *J Vasc Surg*. 2010;51(2):392-400.e2. doi:10.1016/j.jvs.2009.08.082

80. Iqbal S, Chaudhary M. **Median arcuate ligament syndrome (Dunbar syndrome).** *Cardiovasc Diagn Ther*. 2021;11(5):1172-1176. doi:10.21037/cdt-20-846

81. Block TA, Acosta S, Björck M. **Endovascular and open surgery for acute occlusion of the superior mesenteric artery.** *J Vasc Surg*. 2010;52(4):959-966. doi:10.1016/j.jvs.2010.05.084

82. Mastoraki A, Mastoraki S, Tziava E, et al. **Mesenteric ischemia: Pathogenesis and challenging diagnostic and therapeutic modalities.** *World J Gastrointest Pathophysiol*. 2016;7(1):125-130. doi:10.4291/wjgp.v7.i1.125

8 RINGRAZIAMENTI

Mi approccio alla scrittura di questa ultima pagina dopo la stesura integrale di questa tesi in lingua inglese; scriverò in italiano, affinché il cuore possa parlare liberamente, senza vincoli né sintattici, né di forma.

In primo luogo, devo ringraziare i Professori Gennai e Silingardi e tutti i professionisti dell'Unità Operativa di Chirurgia vascolare, che hanno reso questo progetto fattibile, credendo in me e aiutandomi con passione e gentilezza nei momenti di bisogno. Un grazie speciale va al Dott. Leone e a Giovanni, che da vicino hanno vissuto e permesso ogni piccolo sviluppo di questa tesi, dalla sua nascita, fino al suo completamento; senza di voi non starei scrivendo questa ultima pagina.

Ora è giunto il momento di ringraziare le persone che invece, hanno permesso il compimento di questo percorso, nonché la stesura di questa tesi, non con l'aiuto medico-scientifico, ma con quello dell'amore. Ringrazierò ognuno di voi, a modo mio, un po' *unconventional* e lo farò iniziando dal raccontare qualcosa di me; spero di non dilungarmi troppo.

Nel corso di questi lunghissimi (e dall'altra parte brevissimi) sei anni ho sostenuto 80 esami, ognuno dei quali sempre preceduto da un rituale che doveva essere portato a termine con la stessa precisione maniacale: sempre gli stessi pantaloni, sempre la stessa camicia, sempre la stessa canzone ascoltata e cantata con voce tremolante mentre in macchina mi recavo in Università, sempre la stessa ansia, sempre la stessa paura di non aver fatto abbastanza, sempre la stessa maniacale attenzione a non tralasciare mai nessun argomento, sempre lo stesso senso del dovere, sempre lo stesso senso di responsabilità. La canzone ascoltata in macchina era rigorosamente *'Ain't no mountain high enough'*, che cita: *"Non esiste una montagna sufficientemente alta, una valle sufficientemente profonda, un fiume sufficientemente largo, che possa impedirmi di arrivare a te";* quel punto di arrivo è questo momento, questa laurea, che sogno, immagino e bramo dal giorno in cui sono andata a fare il test di Medicina, e oggi posso dirlo… ce l'abbiamo fatta.

Ecco, tutte le persone che conoscono, almeno in parte, la Chiara che ho appena raccontato, meritano il più profondo dei miei ringraziamenti, perché sono stati tasselli imprescindibili per la riuscita di questa avventura.

Ringrazio Monica, Stefano e Andrea, che hanno permesso in ogni modo che io potessi vivere e affrontare questo percorso nel migliore modo possibile, senza mai dovermi preoccupare di nulla, se non di studiare. Cari ragazzi, siete le mie colonne portanti.

Ringrazio tutta la mia famiglia, che ha vissuto questo percorso e questo traguardo con un'empatia e una solidarietà che mai mi sarei potuta aspettare, nemmeno nei miei sogni più belli. Ringrazio chi non c'è più, per aver contribuito a fare di me la donna che sono. Anche se non siete qui oggi, siete sempre con me.

Ringrazio i miei amici, sia tutti quelli vecchi, tra cui non posso non menzionare Elisabetta e Gianluca (scusa, Sacco, sennò non capisci), sia quelli nuovi Emma ed Alberto; siete le persone che hanno visto, sopportato e sostenuto tutti i momenti belli e tutti i momenti i brutti. Senza la vostra vicinanza e amicizia non sarebbe stata la stessa cosa. Ringrazio Laura, che ha preparato insieme a me ognuno di quegli 80 esami citati sopra, che ha condiviso con me le ansie pre-esame più irrazionali e che mi ha tranquillizzata ogni volta che ne avevo bisogno. Ringrazio tutti quelli che hanno passeggiato con me in questi sei anni.

Un grazie al piccolo Gin, che meriterebbe una laurea tutta sua per tutte le volte che non l'ho portato al parco per studiare e per tutti gli esami che mi ha sentito ripetere.

Per ultimo ringrazio te, L, che hai rifatto gli ultimi due anni di università ascoltandomi ripetere ogni esame, che hai pianto e gioito insieme a me per ogni paura e per ogni successo. Incontrarti è stato il regalo migliore che la vita potesse farmi.

Per sempre vostra,

Chiara