

Natural History of Asymptomatic Superior Mesenteric Arterial Stenosis Depends on Coeliac and Inferior Mesenteric Artery Status

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WHAT THIS PAPER ADDS

The latest European Society for Vascular Surgery recommendations for the management of asymptomatic superior mesenteric artery (SMA) stenosis remain unclear, based on the lack of data in the literature on the natural history of the SMA. This study confirms Mikkelsen's law — isolated SMA stenosis is associated with a low risk of mesenteric ischaemia. Patients with SMA stenosis associated with coeliac artery and/or inferior mesenteric artery seem to have a higher risk of developing mesenteric ischaemia. Considering the low life expectancy of these patients, optimisation of medical treatment is essential. The role of preventive revascularisation remains to be defined for patients with non-isolated SMA stenosis.

Objective: The benefit of preventive treatment for superior mesenteric artery (SMA) stenosis remains uncertain. The latest European Society for Vascular Surgery (ESVS) guidelines remain unclear given the lack of data in the literature. The aim of this study was to evaluate asymptomatic SMA stenosis prognosis according to the presence of associated coeliac artery (CA) and/or inferior mesenteric artery (IMA) stenosis.

Methods: This was a single academic centre retrospective study. The entire computed tomography (CT) database of a single tertiary hospital was reviewed from 2009 to 2016. Two groups were defined: patients with isolated > 70% SMA stenosis (group A) and patients with both SMA and CA and/or IMA > 70% stenosis (group B). Patient medical histories were reviewed to determine the occurrence of mesenteric disease (MD) defined as development of acute mesenteric ischaemia (AMI) or chronic mesenteric ischaemia (CMI).

Results: Seventy-seven patients were included. Median follow up was 39 months. There were 24 patients in group A and 53 patients in group B. In group B, eight (10.4%) patients developed MD with a median onset of 50 months. AMI occurred in five patients with a median of 33 months and CMI in three patients with a median of 88 months. Patients of group B developed more MD (0% vs. 15.1%; $p = .052$). The five year survival rate was 45% without significant difference between groups.

Conclusion: Patients with SMA stenosis associated with CA and/or IMA seem to have a higher risk of developing mesenteric ischaemia than patients with isolated SMA stenosis. Considering the low life expectancy of these patients, cardiovascular risk factor assessment and optimisation of medical treatment is essential. Preventive endovascular revascularisation could be discussed for patients with non-isolated > 70% SMA stenosis, taking into account life expectancy.

Keywords: Acute mesenteric ischaemia, Asymptomatic SMA stenosis, Chronic mesenteric ischaemia, Superior mesenteric artery

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INTRODUCTION

Acute mesenteric ischaemia (AMI) and chronic mesenteric ischaemia (CMI) account for 1% of patients admitted for acute abdominal syndrome.^{1–3} However, AMI mortality may be up to 93%.^{4–6} Mikkelsen law's, established in 1957

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on four CMI cases, concluded that at least two mesenteric arteries have to be diseased to develop mesenteric disease (MD).⁷ Thereafter, Thomas *et al.* published the clinical course of mesenteric arterial disease; however, among the 60 patients included with at least one > 50% mesenteric arterial stenotic lesion, only 23 patients had a stenosis affecting the superior mesenteric artery (SMA).⁸ Faced with this lack of scientific data, prophylactic SMA revascularisation is still debated. Indeed, according to the latest Guidelines of the European Society of Vascular Surgery (ESVS) 2017, “prophylactic revascularisation in patients with asymptomatic disease is controversial”.⁹ Likewise, with regard to the latest European guidelines from the United European Gastroenterology (UGE) 2020, while experts agree that revascularisation is not necessary in patients with asymptomatic single vessel stenosis, the decision not to intervene is less clear in asymptomatic patients with stenosis of all three mesenteric arteries.¹⁰ The aim of this study was to evaluate asymptomatic SMA stenosis prognosis according to the presence of associated coeliac artery (CA) and/or inferior mesenteric artery (IMA) stenosis.

MATERIALS AND METHODS

Study population

All computed tomography (CT) angiography performed in a single tertiary hospital centre between January 2009 and December 2016 was reviewed retrospectively when the report mentioned “stenosis” and “mesenteric”. These scans were scheduled exams (cancer, follow up or extension of lower extremity peripheral arterial disease [LE-PAD], follow up imaging after aortic endoprosthesis) or performed in emergency (polytrauma, chest or lower back pain, post-operative complication of digestive surgery, acute limb ischaemia). CT scans were performed on two different CT scanners; SOMATOM Sensation 64 Slice CT Scanner, (Siemens Healthineers, Germany) and IQON Philips spectral CT (Achieva, Philips Healthcare, Netherlands). Slice thickness values ranged from 1 to 2 mm and 120 to 140 mL of contrast injection (350 mg iodine/mL) were used for dual phase acquisition (arterial and portal). All patients suffering from atherosclerotic SMA occlusion or > 70% stenosis were included. Patients suffering from SMA stenosis related to inflammatory vasculitis or SMA dissection, patients with associated aortic pathology (aortic dissection, thoraco-abdominal aneurysm, coral reef aorta), and patients with CT scans performed for suspected AMI or CMI were excluded. Medical records were reviewed retrospectively to exclude patients with history of CMI or AMI at the time of the CT scan leading to inclusion.

CT scan analysis

The measurements were carried out using the Endosize program (Therenva SAS, Philadelphia, PA, USA), which is radiological software allowing centreline extraction. The degree of stenosis was determined by planimetric

measurements on CT angiography from the residual luminal diameter at the level of the stenosis (internal lumen to internal) and the total diameter (external to external) as follows: 1 - (residual diameter / total diameter). The rate of SMA stenosis was defined as follows: 70% – 90%, > 90%, occlusion. CT analysis determined the presence or not of CA or IMA > 70% stenosis or occlusion. The internal iliac arteries (IIA) were also studied and defined as follows: no significant lesion, unilateral > 70% stenosis, bilateral > 70% stenosis.

Two groups were defined: patients with isolated SMA stenosis (group A) and patients with both SMA stenosis and CA or/and IMA stenosis (group B).

Clinical characteristics

Clinical data for all included patients were collected through a review of medical records. Baseline demographic characteristics, cardiovascular risk factors (hypertension, diabetes, dyslipidaemia, smoking), history of coronary artery disease or stroke, renal function, as well as current medication use (antiplatelet, anticoagulant, or statin) were recorded. Chronic kidney failure (CKF) was based on glomerular filtration rate (GFR) using the Kidney Disease Outcomes Quality Initiative (K/DOQI) classification system.¹¹ Patients with chronic GFR < 30 mL/min/m² were considered to have severe chronic renal failure.

Outcome assessment

Outcome assessment of patients during follow up was focused on development of mesenteric disease (MD) defined as the occurrence of AMI or CMI according to the latest European Guidelines.⁹

The AMI diagnosis was established on a body of clinical (acute abdominal pain, diarrhoea, vomiting, rectal bleeding), biological (increased arterial lactic acid), and radiological evidence.^{9,12} CMI diagnosis was defined as the association of several of the following complaints: abdominal postprandial pain, weight loss or anorexia/fear of eating, diarrhoea.^{12,13} Differential diagnoses were ruled out. In both cases, the date and circumstances of the onset of symptoms, and the treatments undergone were recorded. Finally, the date and the cause of death were collected.

All information was obtained from medical records. If the latest entry in the medical record was older than six months, patients were contacted to verify the absence of MD history. The study protocol was approved by the local ethical committee.

Endpoints

The primary endpoint was the development of mesenteric disease (MD) defined as the occurrence of AMI or CMI according to the latest European Guidelines.⁹ The secondary endpoints were mortality from AMI and CMI and all cause deaths.

Table 1. Demographic and clinical data of 77 patients presenting with isolated (Group A) or non-isolated (Group B) superior mesenteric artery stenosis

Variable	Entire cohort (n = 77)	Group A (n = 24)	Group B (n = 53)	p value*
Age – y	79 (69–88)	72 (66–88)	80 (69–87)	.43
Male sex	53 (69)	14 (58)	39 (74)	.18
Hypertension	58 (75)	15 (63)	43 (81)	.079
Diabetes	31 (40)	9 (38)	22 (42)	.74
Dyslipidaemia	28 (36)	7 (29)	21 (40)	.38
Current smoker	22 (28)	6 (25)	15 (26)	.76
Ex-smoker ‡	30 (38)	8 (33)	22 (39)	.50
Coronary disease	26 (34)	5 (21)	21 (40)	.11
Stroke	12 (16)	6 (25)	6 (11)	.13
Atrial fibrillation	14 (18)	6 (25)	8 (15)	.30
CRF †	8 (9)	3 (13)	5 (9)	.70
GFR – mL/min/m ²	72 ± 29	79 ± 29	70 ± 29	.22
LE-PAD	52 (65)	15 (63)	37 (70)	.53
Statin	48 (62)	15 (63)	33 (62)	.98
Antiplatelets	60 (75)	15 (63)	45 (85)	.028
Anticoagulant	20 (25)	7 (29)	13 (25)	.67

Values are reported as n (%), mean ± standard deviation or median (interquartile range). CRF = chronic renal failure; GFR = glomerular filtration rate; LE-PAD = lower extremity peripheral arterial disease.

* Statistical analyses compare group A and B.

† CRF defined as glomerular filtration rate ≤ 30 mL/min/m².

‡ Ex-smoker was defined as smoking cessation ≥ 3 months.

Statistical analysis

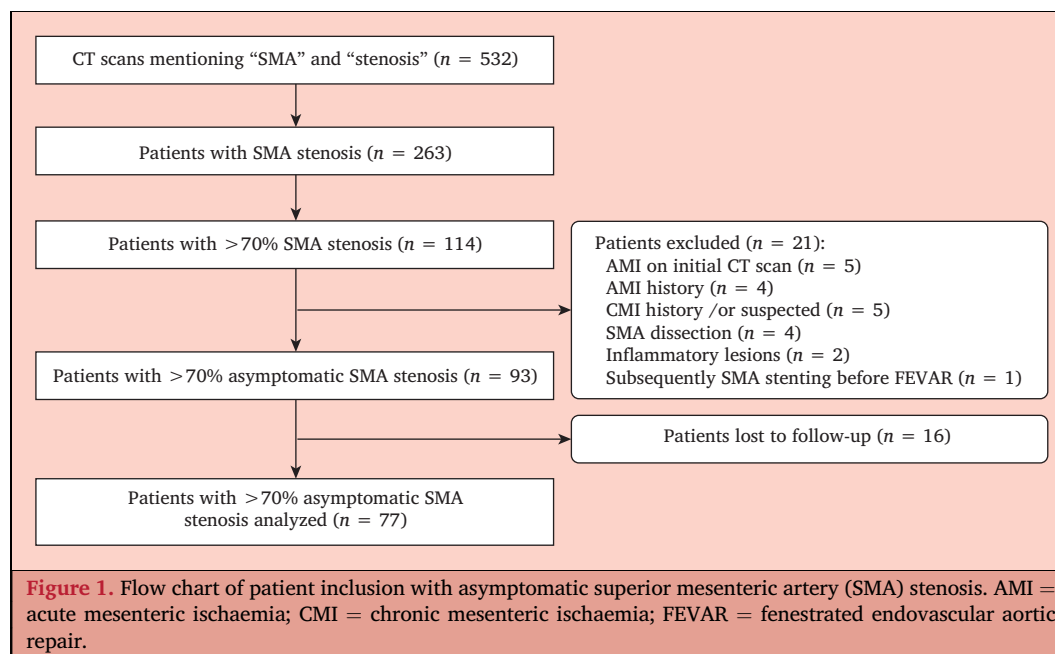
Data analysis was performed with XLSTAT.2019.1.2 (Addinsoft, Paris, France). Summary statistics were calculated, including means (± standard deviations, SD), medians (interquartile range, IQR) for continuous variables and proportions for categorical variables. Normality of continuous variables was tested using the Shapiro-Wilk test. Univariable analysis was performed using the unpaired *t* test or Mann–Whitney test for continuous variables and chi square or the Fischer's exact test for categorical data. The cumulative incidence

of mesenteric symptom development or death, respectively, were estimated by the Kaplan–Meier method. The comparison between two groups used the log rank test. A *p* < .05 was considered to be statistically significant.

RESULTS

Population

The review of all CT scans led to the inclusion of 77 patients as shown in Fig. 1. The mean age was 76 years with a



median of 79 years (IQR 69, 88) with a majority of male patients (69%). The study cohort included 54 patients with > 70% stenosis (70%), 17 patients with > 90% SMA stenosis (31%), and six patients with SMA occlusions (9%).

There were 24 patients in group A and 53 patients in group B. Demographic characteristics and patient comorbidities were stratified according to the two groups and summarised in Table 1. The groups were similar except for antiplatelet medication (63% vs. 85%; $p = .028$), which was more frequent in group B.

In group A there were 21 patients with > 70% SMA stenosis (88%), two patients with > 90% SMA stenosis (8%), and one patient with SMA occlusion (4%). Three patients (12%) suffered from unilateral IIA stenosis and five (21%) from bilateral IIA stenosis.

In group B there were 33 patients with > 70% SMA stenosis (62%), 15 patients with > 90% SMA stenosis (28%), and five patients with SMA occlusion (10%). Fourteen patients (26%) suffered from unilateral IIA stenosis and 22 (42%) from bilateral IIA stenosis. Twenty-nine patients of group B presented with bi-mesenteric arterial stenosis; 21 patients (72%) with SMA and IMA stenosis, and eight patients (28%) with SMA and CA stenosis. Twenty-four patients of group B suffered from tri-mesenteric arterial stenosis. The severity and location of mesenteric disease at entry is summarised in Table 2. There was no significant difference as to IIA stenosis prevalence between the two groups.

The median follow up of the whole cohort was 39 months (IQR 22, 63), and for group A 39 months (IQR 27, 51) and group B 39 months (IQR 20, 73). Five patients, one from group A and four from group B, died within three months of inclusion. The cause of death was cancer ($n = 3$),

Table 2. Severity and extent of digestive arterial disease for 77 patients presenting with isolated (Group A) or non-isolated (Group B) superior mesenteric artery stenosis

	Group A <i>n</i> = 24	Group B <i>n</i> = 53	<i>p</i> value
<i>Severity of SMA stenosis</i>			
70–90%	21 (88)	33 (62)	.032
90–99%	2 (8)	15 (28)	.074
Occlusion	1 (4)	5 (10)	.66
<i>Location of arterial lesions</i>			
SMA	24 (100)	0 (0)	<.001
SMA + CA	0 (0)	8 (15)	.052
SMA + IMA	0 (0)	21 (40)	<.001
SMA + CA + IMA	0 (0)	24 (45)	<.001
Unilateral IIA *	3 (12)	14 (26)	.24
Bilateral IIA *	5 (21)	22 (42)	.078

Data are presented as *n* (%). SMA = superior mesenteric artery; CA = coeliac artery; IMA = inferior mesenteric artery; IIA = internal iliac artery.

* Internal iliac arteries could not be evaluated in three cases: one in group A and two in group B including one acute mesenteric ischaemia and one chronic mesenteric ischaemia case.

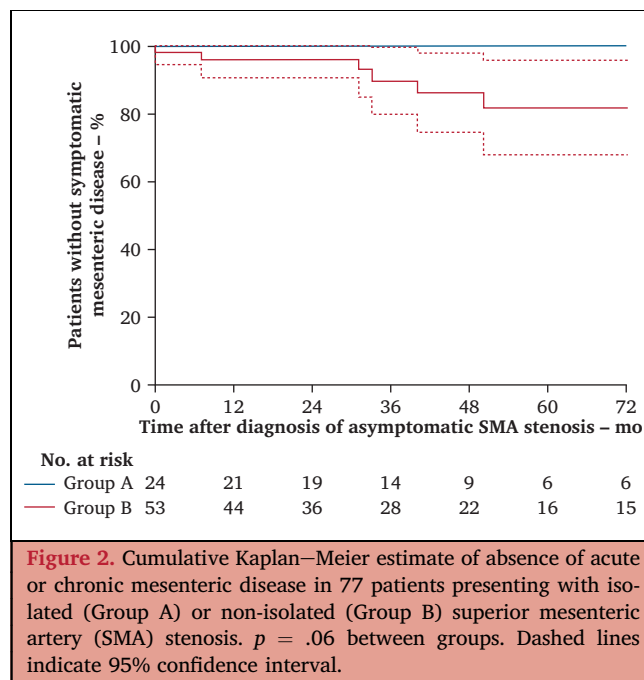


Figure 2. Cumulative Kaplan–Meier estimate of absence of acute or chronic mesenteric disease in 77 patients presenting with isolated (Group A) or non-isolated (Group B) superior mesenteric artery (SMA) stenosis. $p = .06$ between groups. Dashed lines indicate 95% confidence interval.

urinary ($n = 1$) or pulmonary ($n = 1$) infection complications. None of them presented with mesenteric symptoms.

Primary endpoint

Eight patients (10.4%) developed MD during follow up. All of the patients were in group B and onset occurred, on average at 42 months, with a median at 50 months (IQR 32, 80). The prevalence of MD was 0% in group A vs. 15.1% in group B ($p = .052$). The incidence of MD was 4% per year in group B and 2.8% in entire cohort. The freedom of cumulative incidence of MD for each group is shown in Fig. 2.

Secondary endpoints

Acute mesenteric ischaemia. AMI occurred in five patients (6.5%) at a median of 33 months (IQR 31, 40). The cases of AMI, the circumstances and time to onset of symptoms are summarised in Table 3. None of these patients had previous CMI symptoms. Prevalence of AMI was 0% in group A vs. 9.4% in group B ($p = .32$). The incidence of AMI was 0% per year in group A, 2.5% in group B, and 1.8% in the entire cohort.

Chronic mesenteric ischaemia. CMI occurred in three patients (3.9%) at a median of 88 months (IQR 73, 93). The cases of CMI, the time to onset of symptoms, and the management are summarised in Table 4. The prevalence of CMI was 0% in group A vs. 5.6% in group B ($p = .55$). The incidence of CMI was 0% per year in group A, 1.5% in group B, and 1.1% in the entire cohort.

Mortality. Overall the mortality rate was 52% and occurred at a mean of 25 and median 23 months (IQR 8, 39). Specific mortality from AMI was 5.2%. Mortality of

Table 3. Description of acute mesenteric ischaemia (AMI) cases within the 77 patients with previously diagnosed mesenteric artery stenosis

Patient	Initial lesion	Time – mo*	Lesion at AMI diagnosis†	Triggering factor for AMI (time‡)	Management	Result
1	SMA 70–90% IMA >70%	40	CA >70%† SMA occlusion† IMA >70%	Femoropopliteal bypass thrombectomy (few h)	Palliative care	Death
2	CA >70% SMA 70–90%	34	CA >70% SMA >90%†	Cardiac arrest (6 days)	Palliative care	Death
3	CA >70% SMA >90% IMA >70%	0.5	CA >70% SMA occlusion† IMA >70%	Acute Balthazar C Pancreatitis (8 days)	Re-implantation of the SMA on infrarenal aorta	Alive
4	CA >70% SMA 70–90% IMA >70%	32	CA occlusion† SMA >90%† IMA >70%	None	Palliative care	Death
5	CA >70% SMA >90% IMA >70%	8	CA >70% SMA occlusion† IMA >70%	Cardiac arrest (2 days)	Palliative care	Death

SMA = superior mesenteric artery; CA = coeliac artery; IMA = inferior mesenteric artery.

* Time between SMA stenosis diagnosis and onset of symptoms for AMI.

† Lesions that had evolved between the initial diagnosis and the diagnosis of AMI.

‡ Time between the triggering factor and AMI development.

patients with AMI was 80%. These deaths occurred within two days from the severity of intestinal necrosis. The mortality rates in the two groups were 50% in group A vs. 53% in group B ($p = .82$). The median time to death was 27 (IQR 10, 45) vs. 21 months (IQR 7, 34) ($p = .34$). For the tri-mesenteric vessel disease subgroup at entry ($n = 24$), global mortality increased to 67% ($n = 16$) related to cardiovascular comorbidities.

The other causes of death were two cancers, two pneumopathies, one urinary sepsis, two strokes, one neurological failure associated with hyperthermia, and four undetermined causes in group A. There were five cancers, two pneumopathies, one urinary sepsis, two digestive sepsis, one myocardial infarction, one acute leg ischaemia, one pancytopenia, and 11 undetermined causes in group B. Both cases of digestive sepsis underwent abdominal CT scan which showed mechanical intestinal obstruction: one sigmoid volvulus and one caused by abdominal adhesions.

Fig. 3 shows the survival curve of the entire cohort and for each group. The five year survival rate was 45%, with no significant difference between groups.

Factors related to mesenteric disease

Subgroup analyses comparing symptomatic to asymptomatic patients during follow up is shown in Table 5. Patients who developed MD were more often male ($p = .052$) and presented with more severe chronic renal failure ($\text{GFR} < 30 \text{ mL/min/m}^2$) ($p = .033$). Among symptomatic patients, five (63%) presented with 70% – 90% SMA stenosis and four (50%) with tri-mesenteric artery stenosis at entry. No symptomatic patient suffered from SMA occlusion at entry (Tables 3 and 4). All symptomatic patients presented with at least unilateral IIA stenosis.

Among the 24 patients with tri-mesenteric artery stenosis: three patients (12.5%) developed AMI, one patient (4.2%) developed CMI, and 16 patients (67%) died; two of which were AMI related deaths. Eighteen patients (75%)

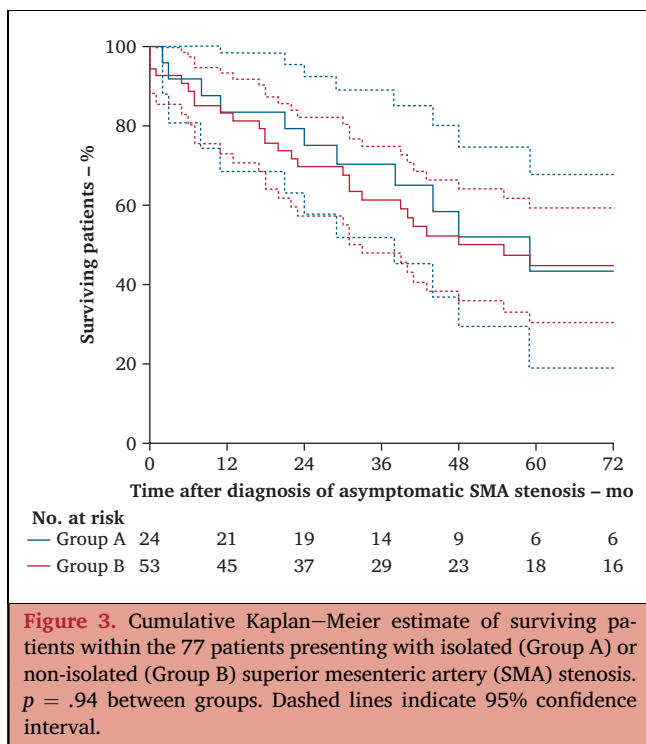
Table 4. Description of chronic mesenteric ischaemia (CMI) cases within the 77 patients with previously diagnosed mesenteric artery stenosis

Patient	Initial lesion	Time – mo*	Lesion at CMI diagnosis†	Management	Result	Follow up – mo
1	SMA 70–90% IMA >70%	50	SMA 70–90% IMA >70%	SMA stenting using covered metal stent	Alive, asymptomatic	64
2	SMA >90% IMA >70%	94	CA occlusion† SMA occlusion† IMA >70%	Parenteral nutrition Died before revascularisation	Death	99
3	CA >70% SMA 70–90% IMA >70%	74	CA >70% SMA 70–90% IMA >70%	Revascularisation refused by patient	Alive	88

SMA = superior mesenteric artery; CA = coeliac artery; IMA = inferior mesenteric artery; CMI = chronic mesenteric ischaemia.

* Time in months between SMA stenosis diagnosis and onset of symptoms for CMI.

† Lesions that had evolved between the initial diagnosis and the diagnosis for CMI.



developed MD and/or died during follow up. The incidence of AMI was 3.6% per year and CMI 1.2% per year in this subgroup.

DISCUSSION

Patients with an isolated SMA stenosis develop significantly less MD than patients with SMA stenosis associated with CA and/or IMA stenosis. This study retrospectively analysed the histories of 77 patients suffering from SMA stenosis with a median follow up of three years. To the present authors' knowledge, this is the largest asymptomatic SMA stenosis cohort in the literature. The cumulative incidence of MD appeared to be higher, without reaching the degree of significance, in patients with $> 70\%$ SMA stenosis associated with at least one other mesenteric artery stenosis. The prevalence increased to 16.7% in patients with trimesenteric artery stenosis. The incidence of AMI and CMI in the population with SMA stenosis was low; 1.8% and 1.1% per year, respectively. This risk increased to 2.5% and 1.5% per year when SMA stenosis was associated with CA and/or IMA stenosis.

In addition, AMI most often appears as a complication of another acute event. Indeed, in this study, four of the five AMI cases occurred secondary to an intercurrent event; two cardiac arrests, one acute pancreatitis, one vascular limb operation. If the development of a collateral network provides an adequate blood supply of the mesenteric territory and an absence of symptoms, an acute event can disturb this precarious vascular state at any time. Thus, as recommended by the UGE, "revascularisation should be considered in the event of stenosis of at least two digestive

arteries before any major abdominal surgery which includes the risk of ligation of the collateral circulation".¹⁰ In the present study, none of the five AMI cases occurred after abdominal surgery, but after acute intercurrent events responsible for low circulatory flow. Thus, in the present authors' opinion, preventive revascularisation should be considered in patients with non-isolated SMA stenosis, sufficient life expectancy and with favourable anatomy allowing SMA stenting without technical risk, to avoid AMI as a complication of any intercurrent event. In the same way, it seems appropriate to propose preventive revascularisation before any major elective surgery for which low circulatory flow or significant critical care is expected. Techniques have been developed to assess the status of gastrointestinal perfusion; tonometry and visible light spectroscopy (VLS).¹⁴ There could be a role for these tests in patients with multivessel disease scheduled for such major surgery to check gastrointestinal perfusion reserves and thus the likelihood of patients developing mesenteric ischaemia. Finally, during management of an unexpected acute event, these patients must be closely monitored, and the diagnosis of AMI made promptly in the event of any secondary deterioration.

Studies in the literature about the clinical course of asymptomatic SMA stenosis are rare. In 1954, Mikkelsen concluded from necropsies of four patients with CMI symptoms that at least two mesenteric arteries must be diseased to develop mesenteric disease.⁷ There was only one other study thereafter on the clinical course of asymptomatic mesenteric arterial stenosis; in 1998 Thomas *et al.* published a prospective study of 60 patients with at least one $> 50\%$ mesenteric artery stenosis (CA, SMA, or IMA) on aortogram. Four patients developed MD; one AMI and three CMI during an average follow up of 2.6 years. All of them suffered from tri-mesenteric artery stenosis. However, only 23 patients in the cohort had a $> 50\%$ SMA stenosis. Among them, only one patient presented with isolated SMA stenosis.⁸ The AMI prevalence in patients with non-isolated SMA stenosis was 4.5% vs. 9.4% in the present study cohort. This difference can be explained by the present study patients presenting with more severe SMA lesions and having longer follow up. Finally, the diagnosis of mesenteric arterial stenosis was made on an aortogram, which is probably less precise than CT scan for the assessment of presence and degree of mesenteric arterial stenosis.

In this study, all symptomatic patients were in group B; patients with isolated SMA stenosis appeared to be at very low risk of developing mesenteric disease. However, the two groups were similar with respect to demographics and clinical data, except for antiplatelet treatment which was higher in group B. These results can be explained by the anatomy of digestive vascularisation characterised by extensive collateralisation. Thus, the CA and the SMA are connected by the pancreaticoduodenal arteries (Rio Branco and by Bühler), the SMA and the IMA by the Riolan, the Villemain and the Drummond arcades.¹⁵ These anastomoses between the three main mesenteric arteries allow for

Table 5. Demographic and clinical data of symptomatic and asymptomatic patients presenting with superior mesenteric artery (SMA) stenosis

Variable	MD (n = 8)	AMI (n = 5)	CMI (n = 3)	Asymptomatic (n = 69)	p value*
Age – y	81 [66–89]	89 [79–90]	68 [64–75]	77 [69–87]	.93
Male sex	8 (100)	5 (100)	3 (100)	45 (65)	.052
Hypertension	7 (88)	4 (80)	3 (100)	51 (74)	.67
Diabetes	5 (63)	4 (80)	1 (33)	26 (38)	.26
Dyslipidaemia	3 (38)	1 (20)	2 (67)	25 (36)	1.0
Current smoker	3 (38)	2 (40)	1 (33)	18 (26)	.68
Ex-smoker †	3 (38)	2 (40)	1 (33)	27 (39)	1.0
Coronary disease	4 (50)	3 (60)	1 (33)	22 (32)	.43
Stroke	0 (0)	0 (0)	0 (0)	12 (17)	.34
Atrial fibrillation	0 (0)	0 (0)	0 (0)	14 (20)	.34
CRF ‡	3 (38)	2 (40)	1 (33)	5 (7)	.033
GFR – mL/min/m ²	50 (31)	51 (29)	49 (41)	75 (28)	.058
LE-PAD	5 (63)	4 (80)	1 (33)	47 (68)	.71
Statin	7 (88)	4 (80)	3 (100)	41 (59)	.25
Antiplatelets	6 (75)	3 (60)	3 (100)	54 (78)	1.0
Anticoagulant	2 (25)	2 (40)	0 (0)	18 (26)	1.0
Average no. of MAS	2.5	2.6	2.3	1.9	.023
SMA only	0 (0)	0 (0)	0 (0)	24 (29)	.052
+ CA stenosis	1 (13)	1 (20)	0 (0)	7 (10)	1.0
+ IMA stenosis	3 (38)	1 (20)	2 (66)	18 (26)	.68
Tri mesenteric stenosis	4 (57)	3 (60)	1 (33)	20 (29)	.25

Data are presented as n (%) or median (interquartile range) MD = mesenteric disease; AMI = acute mesenteric ischaemia; CMI = chronic mesenteric ischaemia; MAS = mesenteric artery stenosis; CRF = chronic renal failure; GFR = glomerular filtration rate; LE-PAD = lower extremity peripheral arterial disease; CA = coeliac artery; IMA = inferior mesenteric artery.

* Statistical analyses compare MD vs. asymptomatic subgroup.

† Ex-smoker defined as smoking cessation \geq 3 months.

‡ CRF defined as GFR \leq 30 mL/min/m².

sufficient blood supply in the event of proximal arterial occlusion. When SMA stenosis is isolated, progression of atheromatous disease leads to progressive occlusion and the anastomotic networks develop providing sufficient visceral blood supply.^{16,17} This vascular supply is compromised if the CA and/or IMA are also affected, leading to CMI when the diseased arteries fail to provide for increased blood demand during digestion, and AMI if blood supply becomes too low for intestinal viability. The IIAs participate to a lesser extent in bowel vascularisation via the middle and inferior rectal arteries. They are connected by collateral vessels with the superior rectal arteries branches of the IMA and consequently may participate in blood supply in case of chronic obliteration of the main digestive trunks. In this study, there was no significant difference between the two groups concerning IIA lesions, although all symptomatic patients had at least unilateral stenosis.

The degree of SMA stenosis did not seem to be a predictive factor in mesenteric disease; symptomatic patients in this cohort presented mostly with 70% – 90% SMA stenosis, less frequently $>$ 90% SMA stenosis, and there were no SMA occlusion cases at entry (Tables 3 and 4). In patients with SMA stenosis, vascularisation remains mainly dependent on the SMA which is dominant in mesenteric vascularisation.^{9,18,19} Collateral supply networks are poorly developed with a risk of mesenteric ischaemia in the event of acute SMA occlusion. Conversely, for asymptomatic SMA occlusion, collateral networks were largely developed

allowing sufficient blood supply. A considerable trigger factor is necessary to disrupt this compensated vascular state and lead to mesenteric symptoms.

This study highlighted the poor prognosis of this population. The five year survival rate for the whole cohort was 45%, with a trend to higher and earlier mortality in group B. Global mortality in the tri-mesenteric subgroup increased to 67%. In this subgroup, only 25% of patients were still alive without MD. Thomas *et al.* worked on the clinical course of asymptomatic mesenteric arterial stenosis and published an all cause mortality rate at 40% with a median follow up of 2.6 years.⁸ Patients with mesenteric atherosclerosis have a high cardiovascular risk as well as an increased risk of cancer because of common risk factors. These are the two main causes of death. These data show that, as recommended by the UGE 2020 guidelines, all patients with asymptomatic atherosclerotic stenosis of the mesenteric arteries, should be referred for an appropriate assessment of risk factors and initiation of optimal medical treatment.¹⁰ This high mortality led to follow up of $<$ 1 month in two patients who died of cancer and pulmonary sepsis. The decision was taken not to exclude these patients, which reflects the fragile state of this population in daily clinical practice.

Concerning the AMI prognosis in the cohort, 80% of patients were too severely affected to undergo surgical treatment. The results are consistent with those of Schoots.⁴ The prognosis of AMI is related to bowel viability,

which depends on the speed of management.^{1,5,20} Unfortunately, AMI diagnosis remains difficult and therefore is often delayed leading to extensive intestinal necrosis. This high AMI mortality rate associated with the risk of short bowel syndrome leads to the definition of a population that will benefit from preventive treatment.

In addition, systematic screening for mesenteric atherosclerotic lesions should be considered in patients treated for LE-PAD, carotid disease, or coronary disease, especially before surgery which might cause arterial decompensation. In this study, 65% of patients had a history of LE-PAD and 34% a history of coronary disease. Several studies have shown the high prevalence of coexisting atherosclerotic vascular diseases.²¹

The potential limitations of this study should be mentioned. First, the study is based on the inclusion of prevalent cases of SMA stenosis. There were no data on the age of the lesion at the time of inclusion. Thus, the risk of MD linked to SMA stenosis may be underestimated by the inclusion of patients with long standing asymptomatic stenosis, while the most threatening lesions are not included because they have already been symptomatic at the time of inclusion. Secondly, while CTA is the gold standard imaging test for the evaluation of mesenteric artery stenosis with very high sensitivity and specificity, the evaluation of the degree of stenosis of the mesenteric arteries could sometimes be less precise, for example, in the case of a heavily calcified lesion of the SMA or CA. In addition, the degree of mesenteric artery stenosis was evaluated by a single operator. Moreover, a large number of deaths were of undetermined cause with the majority in group B. This lack of data, mainly concerning deaths at home, can lead to an underestimation of the AMI incidence in patients of group B. Finally, this study was retrospective, generating bias linked to a retrospective data collection. The incidence of CMI was probably underestimated by the retrospective data collection from medical records. Furthermore, radiological evaluation of the evolution of mesenteric artery stenosis over time was not available.

This study confirmed the observations of Mikkelsen and Thomas, established on few patients several decades ago: patients with SMA stenosis associated with CA and/or IMA stenosis developed more AMI and CMI than patients with an isolated SMA stenosis. Considering the low life expectancy of these patients, the management of cardiovascular risk factors and the maximisation of medical treatment should be implemented for any patient with asymptomatic atherosclerotic mesenteric artery stenosis. Based on the present results, preventive revascularisation should not be offered to asymptomatic patients with isolated SMA stenosis. On the other hand, it could be discussed in patients presenting with SMA stenosis associated with CA and/or IMA stenosis, taking into account life expectancy and procedural risk. Preventive revascularisation could also be offered to patients for whom major surgery is planned to minimise the risk of post-operative mesenteric ischaemia.

However, considering the low life expectancy of this population, endovascular revascularisation using covered

metal stents should be preferred to open surgery because of its reduced post-operative morbi-mortality with satisfactory long term patency.^{22–26} A prospective study will be necessary to confirm these results. The low incidence of MD requires a large cohort with a long follow up. The low life expectancy of this population is a considerable obstacle to carrying out such a study, which seems impossible.

Conclusion

The high mortality of patients with asymptomatic SMA stenosis should lead to optimisation of medical treatment and control of cardiovascular risk factors for any patient with mesenteric arterial stenosis. The benefit of preventive revascularisation in patients with severe isolated SMA stenosis remains very uncertain given the absence of the occurrence of MD in this population. Preventive endovascular revascularisation could be discussed on a case by case basis for patients with SMA stenosis associated with CA and/or IMA arterial stenosis, taking into account life expectancy and procedural risk. Preventive revascularisation should be discussed more in patients with non-isolated SMA stenosis before any major surgery.

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CONFLICT OF INTEREST

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