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Incidence Rates of Arterial Occlusive Acute and Atherosclerotic Chronic Mesenteric Ischaemia: A Population Based Study Over a 15 Year Period

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WHAT THIS PAPER ADDS

This study reported age and sex specific incidence rates of arterial occlusive acute mesenteric ischaemia (AMI; 3.7/100 000 persons/year) divided between embolic and thrombotic aetiology, and of atherosclerotic chronic mesenteric ischaemia (CMI; 1.4/100 000 persons/year) in a well defined population in Finland. The study underlines that occlusive arterial AMI is a relatively common cause of acute abdomen in elderly emergency room patients. The incidence rates of embolic AMI and CMI were notably elevated in elderly females. Sex specific age standardised incidence rates did not differ significantly. The overall incidence of CMI was low, which may suggest underdiagnosis of this condition.

Objective: To determine contemporary incidence rates of acute mesenteric ischaemia (AMI) and chronic mesenteric ischaemia (CMI).

Methods: A single centre retrospective population based study. The study cohort included patients treated for AMI or CMI between 2009 and 2023 who lived in a well defined region of 250 000 inhabitants in Eastern Finland. Incidence rates with 95% confidence intervals (CIs) for arterial occlusive AMI and CMI were calculated, and stratified by age, sex, and aetiology. Age standardised incidence rates were compared between the sexes using indirect method. Venous and non-occlusive mesenteric ischaemia and median arcuate ligament syndrome were excluded.

Results: Within the study cohort, 141 patients had arterial occlusive AMI. Forty two patients (29.8%) had embolic AMI (15; 35.7% males and 27; 64.3% females) and 99 (70.2%) thrombotic AMI (50; 51% males and 49; 49% females). Fifty three patients had CMI due to atherosclerotic mesenteric artery disease (17; 32% males and 36; 68% females). The incidence rate of occlusive arterial AMI was 3.7/100 000 persons/year (95% CI 3.2 — 4.4) and 1.4/100 000 persons/year (95% CI 1.1 — 1.8) for CMI. In the population aged $\geq$ 70 years, the incidence rates were 18.4/100 000 persons/year (95% CI 15.1 — 22.1) for AMI and 7.0/100 000 persons/year (95% CI 5.1 — 9.4) for CMI. The incidence rates of embolic AMI and CMI in females were nearly twice as high as in males, whereas no sex related differences were observed in the incidence rates of thrombotic AMI. However, age standardised incidence rates did not statistically significantly differ between the sexes. There were three cases of embolic AMI, three cases of thrombotic AMI, and no cases of CMI in patients aged $<$ 60 years.

Conclusion: It is important to recognise AMI as a potential cause of acute abdominal pain in elderly emergency room patients. The incidence of atherosclerotic CMI was lower than previously reported.

Keywords: Acute mesenteric ischaemia, Chronic mesenteric ischaemia, Embolism, Epidemiology, Incidence, Thrombosis
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INTRODUCTION

Acute mesenteric ischaemia (AMI) incidence data are often reported as percentages of hospital admissions, which vary greatly depending on the population and diagnostic activity.[1,2] True population based data are surprisingly scarce. A meta-analysis published in 2022 included five studies that

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reported AMI incidence rates in the general population between years 1972 and 2013.[3] All aetiologies of AMI were included in the incidence rate calculation: arterial occlusive, non-occlusive, and venous mesenteric ischaemia. The estimated pooled incidence of AMI was 6.2/100 000 persons/year and varied from 0.7 to 14.1/100 000/year between the individual studies. A more recent study based on a nationwide hospital registry from Estonia found an incidence of 8.7/100 000/year for all aetiologies of AMI between 2016 and 2020 and 60.2/100 000/year for those >70 years of age.[4] Based on the systematic review, arterial occlusive AMI was the most common aetiology in approximately two thirds of the cases. A Finnish study of 470 AMI patients between 2006 and 2015 showed an incidence of 3.1/100 000/year for arterial occlusive AMI.[5] Specific incidence rates for embolic and thrombotic AMI are even less often reported.[6]

There is only one publication on the incidence of chronic mesenteric ischaemia (CMI) that is based on a well defined population. The data come from a large Dutch referral centre for CMI.[7] The estimated CMI incidence rate caused by atherosclerotic stenosis of the mesenteric arteries was 7.3/100 000 inhabitants/year.

In summary, seven publications report population based incidence rates of AMI[4–6,8–11] and one of CMI.[7] From a clinician's perspective, AMI and CMI incidence data are important in order to understand the likelihood of mesenteric ischaemia as a cause of acute or chronic abdominal symptoms in an individual patient. The likelihood varies significantly in patients of different ages and sex.[12] Hence, the aim of this study was to report age specific, sex specific, and aetiology specific incidence rates of arterial occlusive AMI and atherosclerotic CMI over a 15 year period in a well defined population in Finland.

MATERIALS AND METHODS

Study design and population

This was a retrospective single centre study. The study had an organisational permit. Formal informed consent was not required. This study adhered to the STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies. The study centre is an academic teaching hospital that is responsible for the treatment of a population of approximately 250 000 inhabitants in a well defined region in Eastern Finland. The hospital provides all levels of care for this population and serves as the only hospital in the area that treats patients with acute abdominal conditions. All patients living in the study area with acute abdomen are referred to the hospital from peripheral hospitals and healthcare units. In addition, the hospital is a tertiary referral centre for a wider population of approximately 850 000 inhabitants. However, referral patients who lived outside the study region of 250 000 inhabitants were excluded. Population data were extracted from the Statistics Finland database.

Study patients and determining the aetiology

Patients hospitalised with mesenteric ischaemia between years 2009 and 2023 were searched for from the electronic medical records, operation database, and radiology database using International Classification of Diseases (ICD-10) codes K55.x and Nordic Classification of Surgical Procedures codes for visceral artery procedures. A multidisciplinary team of the main investigator, an interventional radiologist, and a specialist in vascular surgery and gastrointestinal surgery evaluated the clinical data, imaging, operation reports, and pathology reports. The diagnosis of arterial occlusive AMI or CMI was confirmed, and the aetiology of occlusive AMI was categorised as embolism or thrombosis (including chronic atherosclerotic occlusion).

Acute or progressive abdominal symptoms, such as abdominal pain, diarrhoea, and vomiting, requiring immediate hospitalisation were pre-requisites for the diagnosis of AMI. Adequate computed tomography (CT), laparotomy, or autopsy findings were required to confirm the diagnosis. Both CTs with contrast enhancement in arterial and venous phases or venous phase alone (if arterial phase was missing) were accepted for analysis. Embolic AMI was defined as an oval shaped clot in the superior mesenteric artery (SMA) or coeliac axis (CA) on contrast enhanced CT without an underlying calcified stenosis. In cases with uncertainty between embolic and thrombotic aetiology, very acute onset of symptoms, atrial fibrillation without adequate anticoagulation, and synchronous embolic findings were indications of embolic aetiology. For cases of distal embolism in the marginal branches of the SMA, invisible on CT, the diagnosis was confirmed by an appropriate clinical presentation described above with segmental bowel necrosis at laparotomy, and findings of thromboembolic material in the small arteries of the mesentery in the pathology report. Thrombotic AMI was defined as a calcified stenosis with superimposed thrombotic clot in the SMA, with an appropriate acute clinical presentation. In addition, a chronic calcified occlusion of the SMA without an identifiable thrombotic clot, typically with concomitant occlusion or stenosis of the CA, was defined as thrombotic AMI given that the patient had clinical symptoms consistent with an acute on chronic AMI presentation. Symptom propagation leading to bowel necrosis or resolution of symptoms after successful revascularisation confirmed the acute on chronic presentation. High inflammatory markers and signs of intestinal injury on CT were also indications of AMI in acute on chronic cases.

CMI was defined as history of post-prandial abdominal pain with non-acute presentation, typically normal inflammatory markers and no signs of intestinal injury on CT. All patients with CMI had typically undergone a diagnostic workup consisting of CT angiography, endoscopic examinations, and a discussion between a gastrointestinal surgeon, interventional radiologist, and vascular surgeon, after which they underwent elective endovascular or open surgical revascularisation. Symptom resolution after successful revascularisation confirmed the diagnosis. The aetiology of CMI was atherosclerotic occlusion or severe stenosis of the SMA with or without concomitant stenosis or occlusion of the CA and IMA.

Median arcuate ligament syndrome was not included in this study. Patients with non-occlusive mesenteric ischaemia and

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venous mesenteric ischaemia were excluded. Moreover, patients with tumour infiltration of the mesenteric arteries, occlusion of the mesenteric arteries due to iatrogenic injury in a surgical procedure, as well as mesenteric hypoperfusion related to acute aortic dissection were excluded.

Statistical analysis

Incidence rates were calculated from the total number of events divided by person years. The incidence rates are presented as *n*/100 000 persons/year with 95% confidence intervals (CIs) calculated using MedCalc Confidence Interval for a rate calculator (MedCalc Software Ltd, Ostend, Belgium). The study population was stratified by sex, aetiology, and age (10 year intervals). Sex specific age standardised incidence rates with 95% CIs were calculated *ad hoc* using an indirect method. Standardisation population was the population of the study region, and the cases were from the data collection period.

RESULTS

Study patients and aetiology

During the 15 year period, 340 patients with arterial occlusive AMI or CMI were treated in the study hospital. The number of patients who lived outside the study region was 146, leaving 194 for the incidence analyses. Of these, 141 had AMI: 42 patients had embolic AMI, of whom 15 (35.7%) were male and 27 (64.3%) female; 99 patients had thrombotic AMI, of whom 50 (51%) were male and 49 (49%) female. The proportion of AMI patients with embolic aetiology was 30% and with thrombotic aetiology 70%. The embolus to thrombosis ratio in AMI was 1:2.4. Fifty three patients had CMI due to atherosclerotic mesenteric artery disease, of whom 17 (32%) were male and 36 (68%) female.

Of patients with embolic AMI, nine males (60%) and 17 females (63%) had atrial fibrillation at presentation. Six of the 17 females with atrial fibrillation and embolic AMI had adequate anticoagulation treatment (i.e., direct oral anticoagulant or warfarin with International Normalized Ratio 2.0 or more). None of the males with atrial fibrillation and embolic AMI had adequate anticoagulation.

Observations in the study population

The mean population at risk in the predefined district during the 15 year study period was 251 381 persons, of whom 124 308 (49.5%) were male and 127 073 (50.5%) female. The total population decreased from 253 605 to 247 689 during the study period (Fig. 1). The mean population aged $\geq$ 70 years was 41 026 (16.3% of the total population) increasing from 35 824 to 48 754. Of people aged $\geq$ 70 years, 17 097 (41.7%) were male and 23 930 (58.3%) female. The mean population aged $\geq$ 80 years was 15 578 (6.2% of the total population) increasing from 13 703 to 16 654; of whom 5 449 (35.0%) were male and 10 129 (65.0%) female.

The incidence rates of mesenteric ischaemia

The annual incidence of AMI and CMI varied sporadically (Fig. 2). The mean incidence rate of occlusive arterial AMI was 3.7/100 000 persons/year (95% CI 3.2 — 4.4) and 1.4/100 000 persons/year (95% CI 1.1 — 1.8) for CMI. In the population aged $\geq$ 70 years, the incidence rates were 18.4/100 000 persons/year (95% CI 15.1 — 22.1) for AMI and 7.0/100 000 persons/year (95% CI 5.1 — 9.4) for CMI. In the population aged $\geq$ 80 years, the corresponding incidence rates were 29.1/100 000 persons/year (95% CI 22.6 — 36.9) for AMI and 9.8/100 000 persons/year (95% CI 6.2 — 14.8) for CMI. The aetiology specific, sex specific, and age specific incidence rates are presented in Table 1. The comparison of incidence rates between the sexes did not reach statistical significance based on the CIs. However, the incidence rates of embolic AMI and CMI in females were nearly twice as high as in males in all age groups, whereas no sex related differences were observed in the incidence rates of thrombotic AMI. The incidence of AMI and CMI increased with age (Fig. 3). The increase in the incidence of occlusive AMI with age was more prominent in females than in males (Figs 4 and 5). There were three cases of embolic AMI, three cases of thrombotic AMI, and no cases of CMI in patients aged < 60 years. Since women predominated

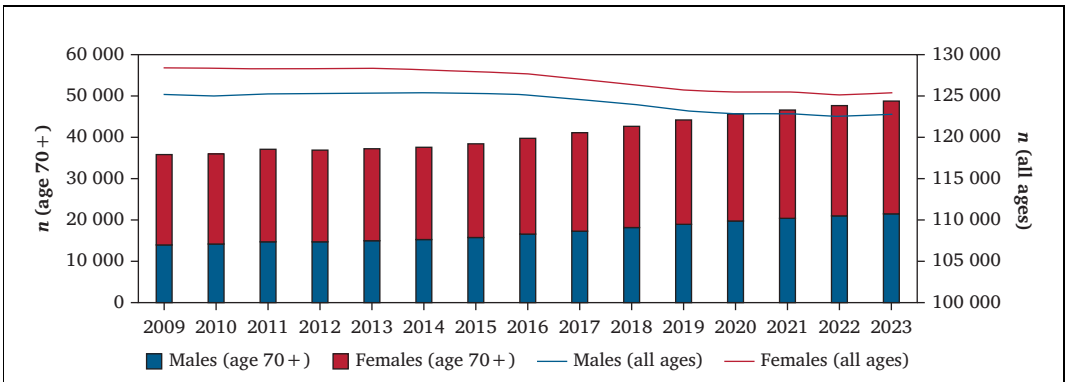

Figure 1. Yearly variation of the study population. Straight lines (red line for females and blue line for males, scale on the right side) show the total study population and its decline during the study period between years 2009 and 2023. The columns (red columns for females and blue columns for males, scale on the left side) show the number of population aged $\geq$ 70 years and its increase during the study period.

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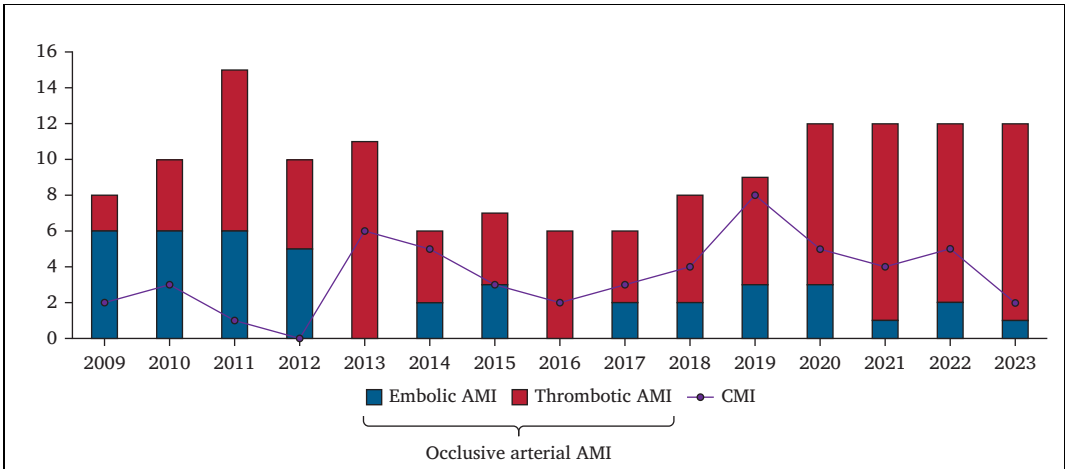

Figure 2. Yearly variation of the cases. The columns show the numbers of patients with occlusive arterial acute mesenteric ischaemia (AMI) each year during the study period (red column for thrombotic and blue column for embolic). The solid line shows the numbers of atherosclerotic chronic mesenteric ischaemia (CMI) each year.

in the elderly study population, an *ad hoc* analysis of the incidence rates with sex standardisation and age standardisation was performed; this showed no statistically significant differences between the sexes (Table 2).

DISCUSSION

Having detailed incidence data helps to identify patient groups that are likely to have AMI as the cause of acute abdominal pain in the emergency room and those who may have CMI as the cause of their persistent abdominal symptoms. The overall incidence of occlusive AMI in the present study (3.7/100 000/year) was similar to that which has recently been reported in Southern Finland (3.1/100 000/year).[5] This does not differ from the reports from other countries, suggesting that the AMI diagnostics in Finland are adequate in these two hospital regions.[3] The highest incidence of arterial occlusive AMI was reported four decades ago in Sweden, 8.6/100 000 persons/year.[8] This was based on a large autopsy cohort, as 87% of all those who died in the study population underwent autopsy. The autopsy rates then plummeted, and this may have contributed to the current lower incidence rates reported for AMI.[13] According to Statistics Finland (www.stat.fi), the autopsy rate in Finland was 18% in year 2020.

The incidence of atherosclerotic CMI in this study (1.4/100 000/year), however, was much lower than in the only previous population based study from the Netherlands (7.3/100 000/year).[7] In the Netherlands, all diagnostics and treatment of complicated CMI and median arcuate ligament syndrome are centralised in one specialised centre. In contrast, CMI may be vastly underdiagnosed in Finland, where the diagnostics and treatment occur in a dozen hospitals even though the population is less than one third of the Netherlands where the treatment is more centralised. In the Dutch study,

Table 1. Incidence rates of arterial occlusive acute mesenteric ischaemia (AMI) and atherosclerotic chronic mesenteric ischaemia (CMI) stratified by aetiology, sex, and age groups.

Incidence rates/100 000 persons/year	Both sexes	95% CI	Males	95% CI	Females	95% CI
All age groups						
Occlusive arterial AMI	3.74	3.15–4.41	3.49	2.69–4.44	3.99	3.14–4.99
Embolic AMI	1.11	0.80–1.51	0.80	0.45–1.33	1.42	0.93–2.06
Thrombotic AMI	2.63	2.13–3.20	2.68	1.99–3.54	2.57	1.90–3.40
Atherosclerotic CMI	1.41	1.05–1.84	0.91	0.53–1.46	1.89	1.32–2.61
People aged ≥70 years						
Occlusive arterial AMI	18.36	15.13–22.08	17.16	12.47–23.03	19.22	14.96–24.33
Embolic AMI	5.69	3.96–7.91	3.90	1.87–7.17	6.96	4.51–10.28
Thrombotic AMI	12.67	10.02–15.82	13.26	9.18–18.53	12.26	8.91–16.46
Atherosclerotic CMI	6.99	5.06–9.41	5.46	2.98–9.16	8.08	5.41–11.60
People aged ≥80 years						
Occlusive arterial AMI	29.10	22.60–36.89	23.24	14.00–36.29	32.25	23.86–42.64
Embolic AMI	10.27	6.58–15.28	4.89	0.13–12.53	13.16	8.04–20.33
Thrombotic AMI	18.83	13.68–25.28	18.35	10.27–30.26	19.09	12.78–27.41
Atherosclerotic CMI	9.84	6.24–14.77	6.12	1.99–14.27	11.85	7.02–18.72

Data are presented as *n*/100 000 persons/year with 95% CI. AMI = acute mesenteric ischaemia; CMI = chronic mesenteric ischaemia; CI = confidence interval.

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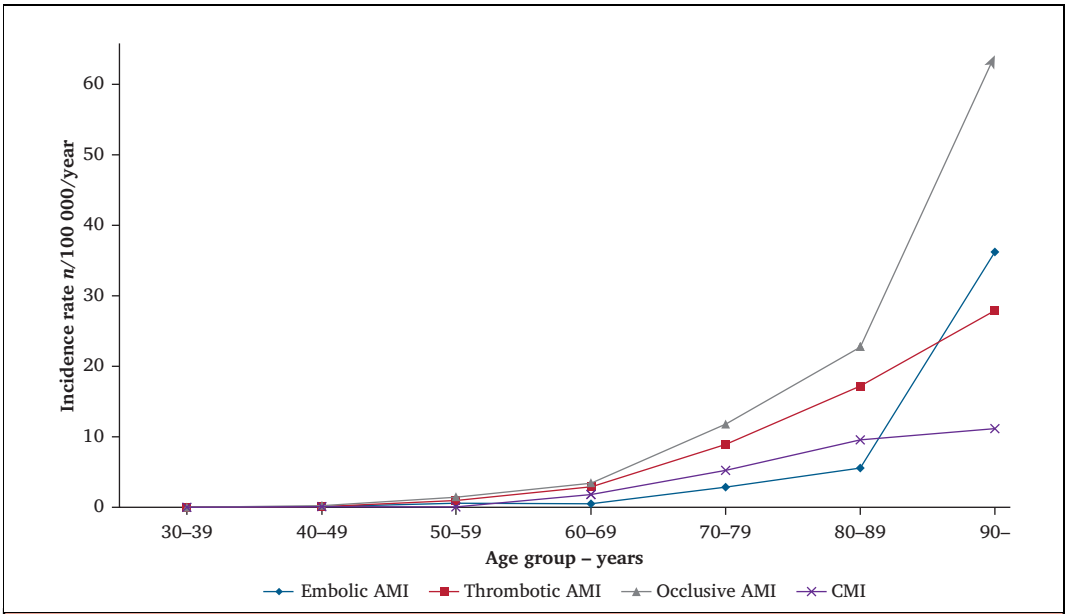

Figure 3. Age specific incidence rates of arterial occlusive acute mesenteric ischaemia (AMI; including embolic and thrombotic AMI) and atherosclerotic chronic mesenteric ischaemia (CMI) for males and females combined.

the diagnostic criterion for CMI was symptom resolution after revascularisation; taking this into account, their high incidence of CMI is reliable.

The incidence of both AMI and CMI was heavily associated with advanced age. The probability of AMI or CMI as a cause of abdominal symptoms was rare in patients aged <60 years. After the age of 70 years, the incidence of AMI and CMI starts to increase significantly. From the perspective of an acute care physician, it is important to understand that the diagnostic spectrum of acute abdomen is completely different in an 80 year old patient than in a 50 year old patient. In a 50 year old, the most probable specific diagnoses for acute abdominal pain are, for example, appendicitis, cholecystitis, pancreatitis, diverticulitis, or intestinal obstruction, whereas arterial occlusive AMI is a rarity.[14] For an 80 year old, AMI is more common than appendicitis or ruptured abdominal aortic aneurysm as the cause of acute abdomen.[6,12] These data encourage the liberal use of contrast enhanced CT in elderly patients with acute abdominal symptoms. The clinician should raise the suspicion of AMI especially in elderly patients with atrial fibrillation or other cardiovascular comorbidities. The suspicion of AMI in the imaging referral prompts the emergency room radiologist to choose the correct imaging modality with contrast enhancement in both arterial and

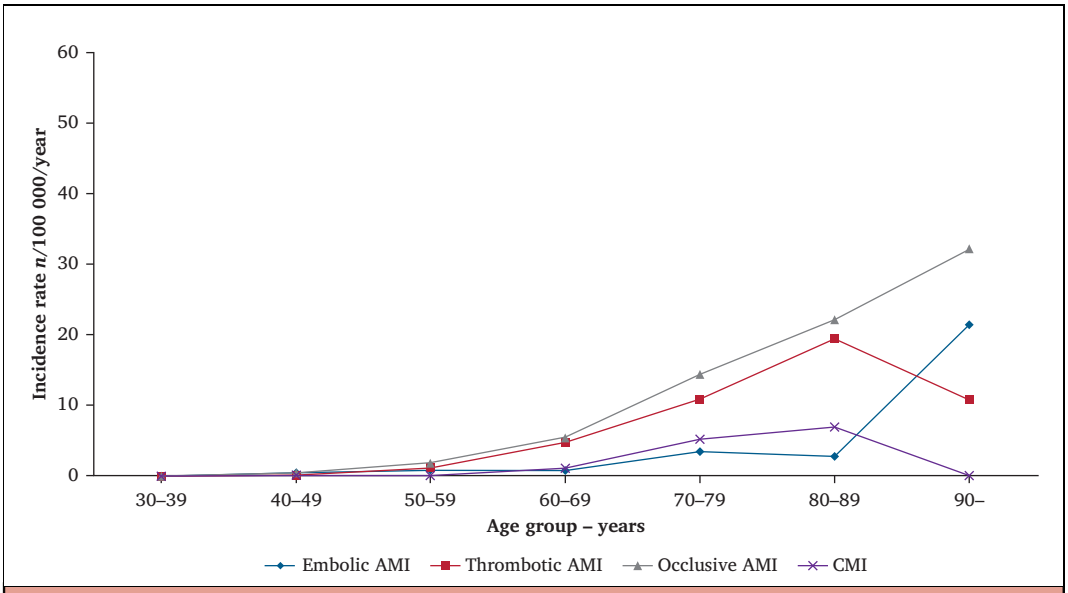

Figure 4. Age specific incidence rates of arterial occlusive acute mesenteric ischaemia (AMI; including embolic and thrombotic AMI) and atherosclerotic chronic mesenteric ischaemia (CMI) for males.

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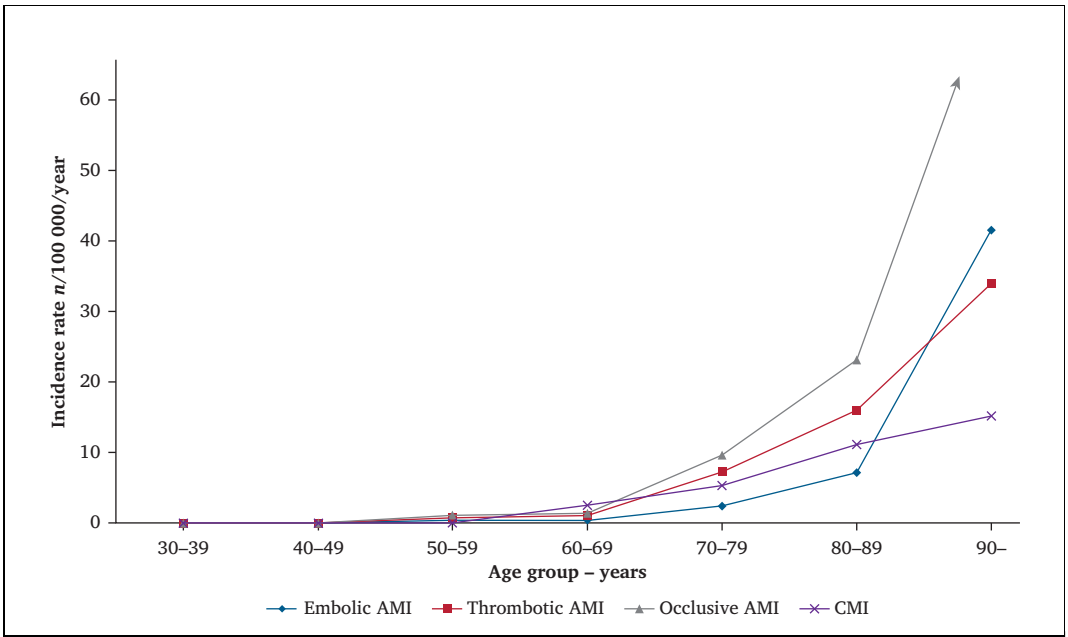

Figure 5. Age specific incidence rates of arterial occlusive acute mesenteric ischaemia (AMI; including embolic and thrombotic AMI) and atherosclerotic chronic mesenteric ischaemia (CMI) for females.

venous phases, to interpret the often vague signs of early intestinal ischaemia and to raise the suspicion of AMI in the imaging report.[15,16] It was noted that the age specific incidence of CMI declined in males aged $\geq$ 90 years (Fig. 4). One explanation may be that the number of men aged $\geq$ 90 years alive in the cohort was low.

Sex differences in the incidence of AMI have not been investigated recently. Case series of treated AMI patients without population based incidence calculations are biased by the predominance of female sex in the elderly population. The landmark paper by Acosta *et al.*, which reported age specific and sex specific population based incidence rates for AMI between 1970 and 1982 in Malmö, Sweden, showed no major differences in autopsy or operation verified incidence rates of AMI between males and females.[8,13] However, this study did not stratify the cohort based on the aetiology of occlusive arterial AMI (embolic *vs.* thrombotic). Atrial fibrillation is often associated with thromboembolism. The prevalence of atrial fibrillation increases with age and is higher in males than in females.[17] The focus of atrial fibrillation research has been on stroke prevention rather than peripheral thromboembolism. Regarding peripheral arterial embolic events, although there is no direct link to mesenteric artery embolism, a systematic review on upper limb arterial thromboembolism showed that female sex was a risk factor for upper limb thromboembolectomy.[18] A recent systematic review on pulmonary embolism showed that female sex was a risk factor for isolated pulmonary embolism, which subsequently was a risk factor for arterial thromboembolic events.[19] These associations were not shown for deep vein thrombosis related pulmonary embolism. A *post hoc* analysis of a randomised trial explored the influence of female sex in patients with atrial fibrillation and coronary artery disease; the risk of stroke or other embolic events was more than two times higher in females than in males.[20] In contrast, female sex was not considered a risk factor for arterial thromboembolism in patients with atrial fibrillation in a large national Danish registry study.[21] In the present study, atrial fibrillation was prevalent in both males and females with embolic AMI. In conclusion, the prevalence of atrial fibrillation may not explain why the incidence of embolic AMI was higher in females in this study. There may be sex differences in the risk of arterial embolism in some end organs in some patient groups for reasons that are still unknown.

The epidemiological reports on acute lower limb ischaemia typically do not report incidence rates for embolic and thrombotic

Table 2. Statistical analysis of differences in age standardised incidence rates between males and females for arterial occlusive acute mesenteric ischaemia (AMI) and atherosclerotic chronic mesenteric ischaemia (CMI).

Standardised incidence rates/100 000 persons/year	Males	Females	Rate	*p* value
Embolic AMI	1.05 (0.63–1.73)	1.16 (0.79–1.69)	1.10 (0.58–2.10)	.76
Thrombotic AMI	3.19 (2.42–4.21)	2.22 (1.68–2.94)	0.70 (0.47–1.04)	.072
Occlusive AMI	4.26 (3.34–5.43)	3.39 (2.71–4.24)	0.80 (0.57–1.12)	.18
Atherosclerotic CMI	1.08 (0.67–1.74)	1.64 (1.18–2.27)	1.52 (0.84–2.74)	.16

Data are presented as *n* (95% CI). AMI = acute mesenteric ischaemia; CMI = chronic mesenteric ischaemia; CI = confidence interval.

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aetiology separately.[22] Regarding the atherosclerotic aetiology of mesenteric ischaemia, no differences were observed between the sexes in the incidence of atherosclerotic (thrombotic) AMI in the present study. Yet, the incidence of atherosclerotic CMI was twice as high in females than males. Exactly the same male to female ratio was observed in the previous CMI epidemiological study by the Dutch Mesenteric Ischaemia Study Group.[7] The easiest explanation for the higher incidence of both embolic AMI and CMI in females is that females live longer, a known fact, which was also demonstrated in the present study population. The age standardised analysis of the incidence rates did not show statistically significant differences between the sexes. A larger population could potentially determine whether or not any true sex related differences exist. In particular, the number of elderly males was fairly low in the present study cohort.

Although the overall number of inhabitants within the study region decreased, the number of males and females aged $\geq$ 70 years increased during the 15 year study period. This reflects the ageing of the population in many Western countries. Women outnumber men at older ages in Europe. Based on the Eurostat database, in 2019, there were more than twice as many women aged $\geq$ 85 years than men of the same age. It may be expected that the incidence of atherosclerotic mesenteric vascular disease together with its complications will increase in the future.

Limitations and strengths

A number of patients with AMI treated between 2009 and 2013 have been part of a study cohort that has been published previously.[6] This previous study reported incidence rates for AMI with all aetiologies involved (non-occlusive, venous) together with other acute abdominal conditions. The present study focused on arterial occlusive AMI and included patients between 2009 and 2023. The limitations of this study are its retrospective nature, small population size limiting generalisation to the Western world, and reliance on the hospital incidence of AMI and CMI. The current low autopsy rates do not allow for such extensive studies as were performed in the 1970s and 1980s in Malmö, Sweden.[8,13] Even though several hospital registries were searched to involve all patients with AMI and CMI, it is possible that some cases may have been missed. At the start of the study period, the hospital radiologists and surgeons were regularly instructed and trained to raise early suspicion and detection of AMI and to use the correct diagnosis codes; however, the use of adequate ICD-10 codes has not been validated since 2009 – 2013.[23] The inclusion of non-occlusive mesenteric ischaemia and venous mesenteric ischaemia in this study was omitted because of the difficulty in the diagnosis and the unreliability of finding all these patients retrospectively due to the lack of definitive diagnosis codes. Furthermore, the differentiation between embolic and thrombotic AMI is sometimes not obvious. Therefore, a careful retrospective evaluation of all clinical data and imaging was done by a multidisciplinary team. The strengths of the study were that the population was well defined with population data available for both sexes and all different age groups for each of the study years. This enabled reporting accurate population based data, this study being the second to present such data for CMI. Furthermore, all patients were scrutinised for primary diagnosis of AMI or CMI by evaluating all available clinical and imaging data, not relying on unvalidated registry data.

Conclusion

This study emphasises that occlusive arterial AMI should be kept in mind as a potential cause of acute abdominal pain, especially in elderly emergency room patients. The crude embolic AMI and CMI incidence rates were notably elevated in elderly females. However, this may be explained by the predominance of females in the elderly study population. The overall incidence of CMI was lower than reported in the previous population based Dutch study.[7]

CONFLICT OF INTEREST

None.

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