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Incidence of Acute Thrombo-Embolic Occlusion of the Superior Mesenteric Artery—A Population-based Study

S. Acosta,[1*] M. Ögren,[2] N.-H. Sternby,[3] D. Bergqvist[4] and M. Björck[4]

Departments of [1]Surgery, Blekinge County Hospital, Karlskrona, [2]Community Medicine, [3]Pathology, Malmö, and [4]Vascular Surgery, Uppsala University Hospital, Uppsala, Sweden

Objective. *To determine the incidence of acute thrombo-embolic occlusion of the superior mesenteric artery (AOSMA) in a population-based study.*
Material. *All clinical (n = 23,446) and forensic (n = 7569) autopsies performed in the city of Malmö between 1970 and 1982 (population 264,000–230,000 inhabitants). The autopsy rate was 87%.*
Methods. *Calculation of the incidence of AOSMA with intestinal gangrene in those autopsies coded for bowel ischaemia (997/23,446 clinical and 9/7569 forensic autopsies). The operative procedures performed in 1970, 1976 and 1982 were also analysed.*
Results. *Two forensic and 211 clinical autopsies demonstrated AOSMA with intestinal gangrene. Previous suspicion of intestinal ischaemia was noted in only 33%. Sixteen patients were operated. The cause-specific mortality was 6.0/1000 deaths. The incidence was 8.6/100,000 person years, increasing exponentially with age ($p < 0.001$). Mortality was 93%.*
Conclusions. *The incidence and mortality of AOSMA is higher than previously reported from clinical series. There is seldom any suspicion of the diagnosis prior to death.*

Key Words: Superior mesenteric artery; Thrombo-embolism; Bowel ischaemia; Incidence; Autopsy.

Introduction

Acute thrombo-embolic occlusion of the superior mesenteric artery (AOSMA) has been recognized as a cause of intestinal necrosis and death since 1875.[1] Mortality remains high and was estimated at 62% in a recent study on an unselected population.[2] A contributing factor is the non-specific symptomatology in the early phase, and since it is said to be an uncommon condition,[3,4] the diagnosis may not appear in the forefront of the clinician's mind.[3–11] In a recent prospective study[2] on acute thrombo-embolic occlusion of the SMA, we estimated the annual incidence to be 5.3/100,000 person years. This may be an underestimate, since four of 24 patients were diagnosed at autopsy and the autopsy-rate was only 10%. Hence, an investigation on incidence in a population with a high autopsy rate was warranted.

The Department of Pathology, Malmö General Hospital, Sweden, has since long a special interest in arterial diseases,[12–14] and has been the central institute in epidemiological studies of atherosclerosis supported by both WHO and ISFC (International Society of Federation of Cardiology). Autopsies were carried out by a small number of senior pathologists, using a standardised technique and registration procedure. The registry has been a source for epidemiological research on other acute lethal conditions with diagnostic difficulties, such as pulmonary embolism,[15] ruptured abdominal aortic aneurysm[16] and acute pancreatitis.[17] The aim of the present study was to investigate the cause-specific mortality from AOSMA, and to assess, in a sample of the general population, the incidence of this disease.

Patients and methods

Between 1970 and 1982 the population of Malmö declined from 264,000 to 230,000 (Swedish Central Bureau of Statistics, SCB), but the elderly population, 80 years and above, increased from 6140 to 8890 (Fig. 1). During the study period 35,784 deaths occurred among the Malmö population (Malmö Statistical Year Books, 1970–1982). During this time 23,446 clinical autopsies, and 7588 forensic autopsies

*Corresponding author. Dr S. Acosta, Department of Surgery, Surgical Sciences, Uppsala, 371 85 Karlskrona, Sweden.

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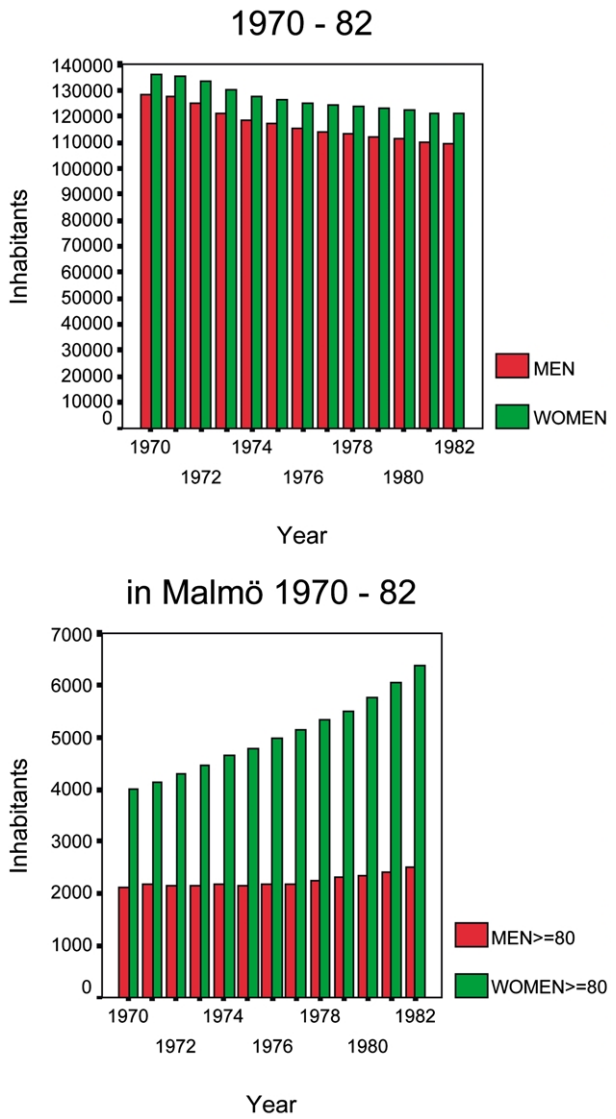

Fig. 1. The male and female population in Malmö 1970–1982. (a) Total population. (b) Octogenarians and beyond.

were performed, resulting in an 87% autopsy rate. Only patients where AOSMA resulted in a transmural gangrene of the intestine were included in this study.

All clinical autopsies were performed at the Department of Pathology, Malmö General Hospital using a standardised protocol. Findings were coded according to the Systematized Nomenclature of Pathology (the SNOP code), as defined by the College of American Pathologists in 1965. During the standardised examination of the SMA, the bowel was divided from the great mesenteric vessels at the mesenteric root, leaving the greater part of the mesentery attached to the bowel. The SMA was then opened from its aortic origin and checked for intra-luminal thrombus or embolus. The distal branches in the mesentery were also examined, especially if a short bowel segment showed signs of ischaemia. Patients with identified thrombus or embolus within the SMA and bowel infarction, or with embolisation at other sites and a simultaneous bowel infarction, and where the pathologist interpreted the bowel infarction as embolic, were defined as AOSMA.

Among 23,496 clinical autopsies, 997 cases were either coded for necrosis in the doudenum, small intestine, colon or rectum, and/or thromboembolism in a visceral artery. The protocols from all these 997 cases were identified and analysed. The case-records and autopsy records for these cases were analysed for clinical suspicion and autopsy confirmation of AOSMA. The SMA was not described in six patients with small bowel ischaemia and these cases were therefore excluded. According to current Swedish legislation, forensic autopsy is mandatory in cases of death occurring outside of hospitals. During the years 1970–1982, 7588 cases from Malmö were referred to the Institute of Forensic Medicine in Lund. In all 7569 (99.8%) cases were found and reviewed. The autopsy records of nine patients with bowel ischaemia were identified.

The Department of Surgery, Malmö General Hospital, was the sole referral hospital for the population of Malmö. All operations performed during the three sample years (1970, 1976 and 1982), were reviewed in order to identify patients who were diagnosed with AOSMA. The three sample years comprised 11,985/56,251 (21.3%) surgical procedures performed during the entire study period. Five hundred and thirty-seven patients with any one of the following diagnoses/operative interventions were identified: 'exploratative laparotomy', 'intestinal obstruction/ileus' or 'bowel resection' (not isolated colonic resections) in patients over 50 years, 'embolectomy', 'thrombectomy', 'second look' or 'mesenteric thrombus' at any age. In 12 patients (2%), the case-records were missing. Patients were considered to have AOSMA, if a revascularisation procedure was performed. Patients with intestinal gangrene and synchronous emboli or atrial fibrillation or a history of previous embolism, were also considered to have occlusive disease. At six operations a mesenteric venous thrombosis was identified, hence these cases were excluded.

The registry of operative procedures was cross-checked with the computerised in-patient registry, resulting in a validity of 100% for the registry of operative procedures and 71% for the in-patient registry.

Table 1. Autopsy-verified acute thrombo-embolic occlusion of the SMA: cause-specific mortality ratios in relation to age and gender.

Age group	Deaths 1970–1982			Autopsies 1970–1982			Deaths from SMA occlusion			Cause-specific mortality (95% CI)					
										/1000 autopsies			/1000 deaths		
	M	F	M + F	M	F	M + F	M	F	M + F	M	F	M + F	M	F	M + F
0–34	823	459	1282	719	410	1129	0	0	0	0.0 (0.0–5.1)	0.0 (0.0–9.0)	0.0 (0.0–3.3)	0.0 (0.0–4.5)	0.0 (0.0–8.0)	0.0 (0.0–2.9)
35–39	213	111	324	185	96	281	1	0	1	5.4 (0.1–30.1)	0.0 (0.0–38.4)	3.6 (0.1–19.8)	4.7 (0.1–26.2)	0.0 (0.0–33.2)	3.1 (0.1–17.2)
40–44	334	179	513	304	153	457	0	0	0	0.0 (0.0–12.1)	0.0 (0.0–24.1)	0.0 (0.0–8.1)	0.0 (0.0–11.0)	0.0 (0.0–20.6)	0.0 (0.0–7.2)
45–49	470	275	745	420	245	665	1	0	1	2.4 (0.1–13.3)	0.0 (0.0–15.1)	1.5 (0.0–8.4)	2.1 (0.1–11.9)	0.0 (0.0–13.4)	1.3 (0.0–7.5)
50–54	824	414	1238	740	365	1105	1	1	2	1.4 (0.0–7.5)	2.7 (0.1–15.3)	1.8 (0.2–6.5)	1.2 (0.0–6.8)	2.4 (0.1–13.5)	1.6 (0.2–5.8)
55–59	1294	629	1923	1130	554	1684	1	0	1	0.9 (0.0–4.9)	0.0 (0.0–6.7)	0.6 (0.0–3.3)	0.8 (0.0–4.3)	0.0 (0.0–5.9)	0.5 (0.0–2.9)
60–64	1906	935	2841	1692	803	2495	3	5	8	1.8 (0.4–5.2)	6.2 (2.0–14.5)	3.2 (1.4–6.3)	1.6 (0.3–4.6)	5.3 (1.7–12.5)	2.8 (1.2–5.5)
65–69	2736	1492	4228	2414	1294	3708	9	11	20	3.7 (1.7–7.1)	8.5 (4.2–15.2)	5.4 (3.0–7.9)	3.3 (1.5–6.2)	7.4 (3.7–13.2)	4.7 (2.7–6.8)
70–74	3074	2049	5123	2779	1812	4591	8	20	28	2.9 (1.2–5.7)	11.0 (6.2–15.9)	6.1 (3.8–8.4)	2.6 (1.1–5.1)	9.8 (5.5–14.0)	5.5 (3.4–7.5)
75–79	2944	2707	5651	2590	2350	4940	12	22	34	4.6 (2.4–8.1)	9.4 (5.4–13.3)	6.9 (4.6–9.2)	4.1 (2.1–7.1)	8.1 (4.7–11.5)	6.0 (4.0–8.0)
80–84	2306	3008	5314	2005	2566	4571	19	29	48	9.5 (5.2–13.7)	11.3 (7.2–15.4)	10.5 (7.5–13.5)	8.2 (4.5–11.9)	9.6 (6.1–13.1)	9.0 (6.5–11.6)
85-	2326	4196	6522	1985	3423	5408	18	52	70	9.1 (4.3–13.3)	15.2(11.1–19.3)	12.9 (9.9–16.0)	7.7 (4.2–11.3)	12.4 (9.0–15.8)	10.7 (8.2–13.2)
Total	19,250	16,454	35,704	16,963	14,071	31,034	73	140	213	4.3 (3.3–5.3)	9.9 (8.3–11.6)	6.9 (5.9–7.8)	3.8 (2.9–4.7)	8.5 (7.1–9.9)	6.0 (5.2–6.8)

This study was approved by the Research Ethics Committee of the University of Lund.

Statistical methods

Cause-specific mortality ratios were expressed as number of autopsy-verified deaths from acute thrombo-embolic SMA occlusion per thousand autopsies, and per thousand deaths, respectively, and analysed in relation to age and gender. In the analysis of incidence, autopsy-retrieved cases, and cases retrieved after operation only, were pooled. In order to render the figures comparable, each of the crude number of cases retrieved after operation only was divided by 0.213 (the proportion of operations 1970–1982 that was sampled).

Age- and gender-specific incidence rates were calculated using the population of Malmö in 1976 as the average (Table 3) and comprising a total of 3,122,860 person years. Rates were expressed as number of cases per 100,000 person years. Incidence rates in men and women were compared using indirect standardisation. Confidence intervals were calculated assuming a Poisson distribution of events, using the exact method for $N < 15$ and the normal approximation for larger N.[18] The relationship between incidence and age was evaluated using regression analysis with curvilinear modelling.

Results

Between 1970 and 1982, 211 and two cases of AOSMA leading to intestinal gangrene were identified at clinical and forensic autopsies, respectively, corresponding to a cause-specific mortality of 6.9/1000 autopsies (Table 1). The mortality increased with increasing age: 11.8/1000 autopsies occurring in octogenarians and beyond. AOSMA accounted for 6.0/1000 deaths (Table 1). No deaths from this cause were encountered below the age of 35. Among the 213 cases, the median age was 81 years (range 39–103), and 66% were women.

In the referral note for clinical autopsy, a suspicion of intestinal ischaemia was noted in 39, of those 174 patients managed non-operatively (22%), and in 30 of those 37 patients who underwent emergency abdominal surgery and subsequent autopsy (81%). In total, there was a documented suspicion of intestinal ischaemia in only 69 of the 211 cases (33%).

Sixteen patients, median age of 75 years (range 64–94), of whom nine were women, were diagnosed with AOSMA during an operative procedure in the years

Table 2. Incidence of autopsy-verified fatal acute thrombo-embolic occlusion of the SMA 1970–1982, in relation to age and gender.

Age group	Population at risk*			Autopsy-retrieved cases			Incidence (95% CI)/100,000 person years		
	M	F	M + F	M	F	M + F	M	F	M + F
0–34	54,696	52,814	107,510	0	0	0	0 (0.0–0.5)	0 (0.0–0.5)	0 (0.0–0.3)
35–39	6962	6599	13,561	1	0	1	1.1 (0.0–6.2)	0 (0.0–4.3)	0.6 (0.0–3.2)
40–44	6504	6638	13,142	0	0	0	0 (0.0–4.4)	0 (0.0–4.3)	0 (0.0–2.2)
45–49	7424	7617	15,041	1	0	1	1.0 (0.0–5.8)	0 (0.0–3.7)	0.5 (0.0–2.8)
50–54	8044	8927	16,971	1	1	2	1.0 (0.0–5.3)	0.9 (0.0–4.8)	0.9 (0.1–3.3)
55–59	8263	9114	17,377	1	0	1	0.9 (0.0–5.2)	0 (0.0–3.1)	0.4 (0.0–2.5)
60–64	7389	8604	15,993	3	5	8	3.1 (0.6–9.1)	4.5 (1.5–10.4)	3.8 (1.7–7.6)
65–69	6430	8353	14,783	9	11	20	10.8 (4.9–20.4)	10.1 (5.1–18.1)	10.4 (5.8–15.0)
70–74	4569	6720	11,289	8	20	28	13.5 (5.8–26.5)	22.9 (12.9–32.9)	19.1 (12.0–26.2)
75–79	2653	4753	7406	12	22	34	34.8 (18.0–60.8)	35.6 (20.7–50.5)	35.3 (23.4–47.2)
80–84	1344	2961	4305	19	29	48	108.7 (59.8–157.6)	75.3 (47.9–102.8)	85.8 (61.5–110.0)
85-	828	2014	2842	18	52	70	167.2 (90.0–244.5)	198.6 (144.6–252.6)	189.5 (145.1–233.9)
All	115,106	125,114	240,220	73	140	213	4.9 (3.8–6.0)	8.6 (7.2–10.0)	6.8 (5.9–7.7)

*The population of 1976 was defined as the average population in the analysis.

1970 ($n = 2$), 1976 ($n = 5$) or 1982 ($n = 9$). At operation, bowel resection ($n = 7$), explorative laparotomy ($n = 6$) and revascularisation of the SMA with bowel resection ($n = 3$), were performed. Four patients survived and 12 of the operated patients died, of whom eight did not undergo autopsy. Thus, 12 patients were not encountered at the autopsy registry in this sample, and the estimated total number of cases identified at operation only was calculated to 57 (12/0.21).

The incidence of autopsy-verified AOSMA was 6.8/100,000 person years (95% CI 5.9–7.7) (Table 2). The estimated overall incidence of fatal and non-fatal disease was 8.6 (95% CI 7.6–9.7) per 100,000 person years (Table 3). The estimated overall mortality was 93%. The proportions of cases diagnosed at autopsy only, operation and subsequent autopsy, and operation only, were 65, 14 and 21%, respectively. The incidence increased exponentially with age ($p < 0.001$) in both men and women, with approximately a doubling of the incidence per 5 year interval mounting up to a peak incidence of 217 (169–264) per 100,000 person years in the age category 85 and above (Table 3 and Fig. 2).

Discussion

Based on retrospective clinical series, it has been claimed that acute thrombo-embolic occlusion of the SMA is an uncommon condition.[3,4] However, assessments of incidence can only be made in population-based studies. Our finding of a steep increase of incidence with age, up to 217 cases per 100,000 person years in the age category 85 and above, underscores the previously demonstrated importance of age as a

Table 3. Incidence of acute thrombo-embolic occlusion of the SMA 1970–1982, in relation to age and gender.

Age group	Populationat risk*			Cases retrieved after operation only			All cases†			Incidence (95% CI)/100,000 person years		
	M	F	M + F	M	F	M + F	M	F	M + F	M	F	M + F
0–34	54,696	52,814	107,510	0	0	0	0	0	0	0 (0.0–0.5)	0 (0.0–0.5)	0 (0.0–0.3)
35–39	6962	6599	13,561	0	0	0	1	0	1	1.1 (0.0–6.2)	0 (0.0–4.3)	0.6 (0.0–3.2)
40–44	6504	6638	13,142	0	0	0	0	0	0	0 (0.0–4.4)	0 (0.0–4.3)	0 (0.0–2.2)
45–49	7424	7617	15,041	0	0	0	1	0	1	1.0 (0.0–5.8)	0 (0.0–3.7)	0.5 (0.0–2.8)
50–54	8044	8927	16,971	0	0	0	1	1	2	1.0 (0.0–5.3)	0.9 (0.0–4.8)	0.9 (0.1–3.3)
55–59	8263	9114	17,377	0	0	0	1	0	1	0.9 (0.0–5.2)	0 (0.0–3.1)	0.4 (0.0–2.5)
60–64	7389	8604	15,993	0	0	0	3	5	8	3.1 (0.6–9.1)	4.5 (1.5–10.4)	3.8 (1.7–7.6)
65–69	6430	8353	14,783	9	5	14	18	16	34	21.5 (11.6–31.5)	14.7 (7.5–22.0)	17.7 (11.7–23.6)
70–74	4569	6720	11,289	9	0	9	17	20	37	28.6 (15.0–42.2)	22.9 (12.9–32.9)	25.2 (17.1–33.3)
75–79	2653	4753	7406	5	5	10	17	27	44	49.3 (25.9–72.7)	43.7 (27.2–60.2)	45.7 (32.2–59.2)
80–84	1344	2961	4305	5	9	14	24	38	62	137.4 (82.4–192.3)	98.7 (67.3–130.1)	110.8 (83.2–138.4)
85-	828	2014	2842	5	5	10	23	57	80	213.7 (126.3–301.0)	217.7 (161.2–274.2)	216.5 (169.1–264.0)
All	115,106	125,114	240,220	33	24	57	106	164	270	7.1 (5.7–8.4)	10.1 (8.5–11.6)	8.6 (7.6–9.7)

*The population of 1976 was defined as the average population in the analysis.
†All cases defined as the sum of cases retrieved after operation only and autopsy-retrieved cases as stated in Table 2.

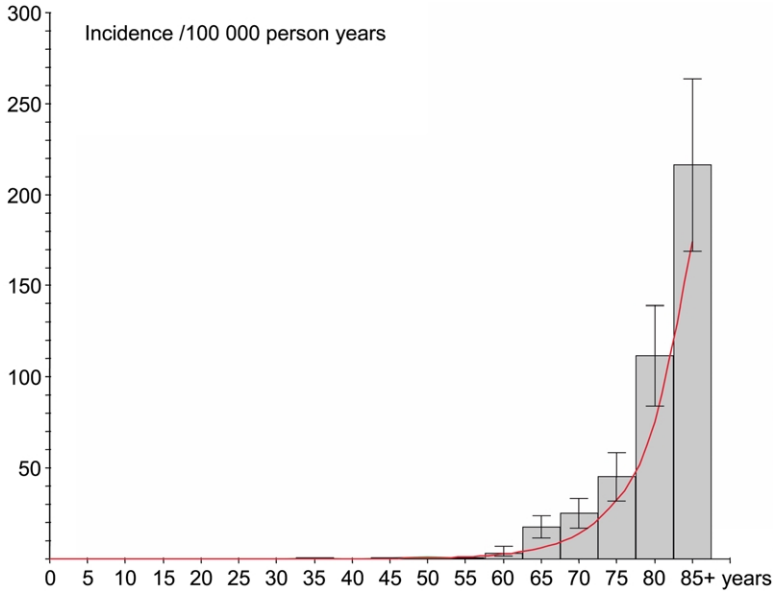

Fig. 2. Impact of age on the incidence of acute thrombo-embolic occlusion of the SMA. 95% CI within whiskers.

risk factor for this disease, which was the cause of death in a sizable 1.2% of the study population above age 80.[19,20] The higher rates found in this study compared with a previous study from Blekinge, Sweden,[2] cannot be attributed to differences in age distribution—the proportion of octogenarians were higher in the latter study—but most likely reflects the much lower autopsy rate of 10% in that study. The importance of a high autopsy-rate is also emphasised by the fact that in the present study, with an autopsy rate of 87%, a suspicion of bowel ischaemia was documented before death in only 22% of the cases managed non-operatively.

The incidence and mortality figures may still be somewhat underestimated, since in seven cases with fatal intestinal gangrene, the appearance of SMA was not described in the autopsy report, and these cases were excluded. Furthermore, although the autopsy-rate was high, e.g. 84% in patients 80 years and above, it was not 100%, and the possibility exists that the incidence was higher among those not undergoing autopsy. To diminish the risk of underestimation due to deaths outside hospital, we included forensic autopsies. As only two deaths occurred outside hospital, one can assume that most patients with acute SMA occlusion die in hospital. Autopsy rates among the elderly have declined considerably in Malmö.[21] To conduct a similar study today would be impossible, at least in Sweden, where changes in legislation and in public attitudes towards post-mortem examinations have decreased the autopsy-rate to only 15% in 2001.[22]

In a clinical setting it may be impossible to differentiate between occlusive and non-occlusive bowel ischaemia, unless the SMA is explored by angiography or by operation, which occurs rarely. Thus, investigators are dependent on indirect observations such as the presence of atrial fibrillation or synchronous emboli[2] or the anatomical distribution of the bowel ischaemia.[5] Therefore, data on the number of cases in clinical studies with occlusive disease of the SMA, may confound occlusive and non-occlusive disease, two distinctly different clinical entities. The high autopsy rate and the standardised procedure for invasive examination of the SMA in this study should ensure a comparably high validity and reliability in the assessment of aetiology of the bowel ischaemia.

Women predominated among the elderly in this study, and as in other studies on occlusion of the SMA, females were more affected than males.[2–7] This study has shown that the incidence rates do not differ significantly when age-standardised incidence and mortality rates are compared. With sufficient sample-size, and with a high autopsy-rate even among the most elderly, it has been possible for the first time to correct the confounding factor of women predominating in the elderly cohorts. This lack of gender difference is an interesting observation considering the fact that smoking and atherosclerotic disease has been shown to have a considerable male predominance in the Malmö population.[23] The gradual reduction of the male population from age 60 and above probably reflects an excess mortality from atherosclerotic and smoking-related disease,

predominantly from ischaemic heart disease, in men belonging to this generation.

In conclusion, the high autopsy rate in this study made it possible to report on the incidence of AOSMA in a population-based study. It was the cause of death in 1.2% of persons 80 years and above, and incidence rates for both men and women increased equally and exponentially with age. Suspicion of the diagnosis prior to death was seldom documented.

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