Systematic review

Systematic review of survival after acute mesenteric ischaemia according to disease aetiology

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Background: **Differentiation of acute mesenteric ischaemia on the basis of aetiology is of great importance because of variation in disease progression, response to treatment and outcome. The aim of this study was to analyse the published data on survival following acute mesenteric ischaemia over the past four decades in relation to disease aetiology and mode of treatment.**
Method: **A systematic review of the available literature from 1966 to 2002 was performed.**
Results: **Quantitative analysis of data derived from 45 observational studies containing 3692 patients with acute mesenteric ischaemia showed that the prognosis after acute mesenteric venous thrombosis is better than that following acute arterial mesenteric ischaemia; the prognosis after mesenteric arterial embolism is better than that after arterial thrombosis or non-occlusive ischaemia; the mortality rate following surgical treatment of arterial embolism and venous thrombosis (54·1 and 32·1 per cent respectively) is less than that after surgery for arterial thrombosis and non-occlusive ischaemia (77·4 and 72·7 per cent respectively); and the overall survival after acute mesenteric ischaemia has improved over the past four decades.**
Conclusion: **There are large differences in prognosis after acute mesenteric ischaemia depending on aetiology. Surgical treatment of arterial embolism has improved outcome whereas the mortality rate following surgery for arterial thrombosis and non-occlusive ischaemia remains poor.**

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Introduction

Despite considerable advances in medical diagnosis and treatment over the past four decades, mesenteric vascular occlusion still has a poor prognosis with an in-hospital mortality rate of 59–93 per cent[1]. The pessimistic view offered by Cokkinis more than 75 years ago[2], namely that '...the diagnosis is impossible, the prognosis hopeless and the treatment useless...', seems to remain valid up to the present day. Whether an aggressive approach to acute mesenteric ischaemia, consisting of early diagnosis, restoration of arterial perfusion to the ischaemic intestine, resection of the necrotic intestine, second-look laparotomy and supportive intensive care[3], has improved survival during the past decades is unclear from the literature[4,5]. Several factors underlie this uncertainty. The aetiology of acute mesenteric ischaemia is often undefined in reported studies, as the correct diagnosis can usually only be confirmed at autopsy. This information is often not available. Furthermore, the relative infrequency of acute mesenteric ischaemia (1–2 per 1000 hospital admissions)[6] and the varied clinical presentation constitute an almost insurmountable obstacle to undertaking randomized or case–control trials.

Mesenteric ischaemia can be classified grossly into ischaemia of thrombotic or non-thrombotic origin. Non-occlusive mesenteric ischaemia, the dominant non-thrombotic cause of acute mesenteric ischaemia, results from low-flow states (for example cardiogenic shock, sepsis, hypovolaemia) whereas thrombotic conditions include arterial embolism, arterial thrombosis and mesenteric venous thrombosis.

Systematic evaluation of research results, even if only observational data and small case series are available, is necessary to move forward, certainly in view of the impact of improved imaging and current thrombolytic strategies. The aim of this systematic analysis of the literature

on acute mesenteric ischaemia was to investigate the relationships between disease aetiology (arterial embolism, arterial thrombosis, venous thrombosis and non-occlusive mesenteric ischaemia), mode of treatment and mortality.

Patients and methods

Inclusion and exclusion criteria

Studies were eligible for inclusion if patients with acute mesenteric ischaemia were divided into aetiological subsets (arterial embolism, arterial thrombosis, venous thrombosis and non-occlusive mesenteric ischaemia) and reported in conjunction with in-hospital mortality rates. Studies that reported data concerning only one aetiological subset were excluded, because they focused on aspects other than aetiology and mortality, such as patient and clinical characteristics, risk factors and diagnostic methods. Patients with acute mesenteric ischaemia secondary to arteritis, mechanical obstruction, adhesion or aortic aneurysm repair, or caused by occlusion of the inferior mesenteric artery (ischaemic colitis), were excluded. Studies dealing with chronic mesenteric ischaemia were also excluded. All studies included had to provide information on the methods used to ascertain the diagnosis (angiography, laparotomy, histopathology or autopsy).

Search strategy

Two authors independently performed a formal computer-assisted search of the medical databases Medline (January 1966 to January 2002, search updated to August 2002), Cochrane Database of Systematic Reviews, Cochrane Clinical Trial Register and Embase (January 1988 to January 2002). Keywords and medical subject heading (MeSH) terms used were 'mesenteric vascular occlusion', 'mesentery' and 'ischemia', limited to 'human' studies; clinical studies written in English, Spanish, German, French and Italian were identified. A manual cross-reference search of the eligible papers was performed to identify additional relevant articles. Data quoted as unpublished or data from abstracts were not used.

Data collection

Two authors independently assessed the selected studies and extracted data on study design (retrospective, prospective), population, aetiology and outcome measures, and judged whether the publication met the stated inclusion criteria. Retrospective data were defined as those extracted from patient charts or routine data sources. Prospective data were defined as specific information the collection of which started before disease diagnosis in specified patients. Disagreements concerning inclusion of studies and data extraction were resolved by group discussion. The checklist proposed by the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group[7] was used as a guideline for performing this quantitative analysis. Observational studies were defined as reports that used data from existing databases, cross-sectional studies, case series, case–control studies, or studies with a historical control or a cohort design[7].

Aetiological subsets

Patient data from each study were divided into the following aetiological subsets: superior mesenteric artery embolism, superior mesenteric artery thrombosis, mesenteric venous thrombosis and non-occlusive mesenteric ischaemia. When no distinction in aetiological origin was made between superior mesenteric artery embolism and artery thrombosis, patients were included in the group 'artery embolism and artery thrombosis'.

Mortality

Mortality was defined as in-hospital death, and was categorized according to the defined aetiological subsets and analysed from 1966 to 2002. The median years of the inclusion period of each included study were used as independent variables in the regression analysis.

Treatment strategy

To discriminate between the outcomes of various treatment strategies, data on treatment modalities (when available) were divided into treatment subsets: 'supportive care', 'exploratory laparotomy', 'resection', 'revascularization' and 'revascularization with resection'. Patients were included in the group 'resection, revascularization or both' when type of surgical intervention was not clearly stated. Supportive care was defined as conservative treatment without diagnostic or surgical intervention. Supportive care was used in patients who refused surgery, in patients who did not qualify for operation, or in those whose condition improved during diagnostic follow-up. A diagnostic exploratory laparotomy only was performed when total necrosis of the small and large bowel was found, in which case resection would be incompatible with life. Patients who were included in the subset 'resection' underwent resection of varying lengths of small bowel with or without large bowel resection during primary laparotomy or subsequent relaparotomy. The subset 'revascularization' included patients who underwent embolectomy, thrombectomy, patch angioplasty, endarterectomy or aortoiliac–mesenteric bypass with or

without autologous material. The authors were not able to specify the subdivision of each individual surgical procedure, owing to lack of data. Patients who were included in the subset 'revascularization and resection' underwent revascularization of the splanchnic circulation and subsequent resection of part of the large and/or small bowel, during the same operation or during subsequent relaparotomy.

Prognostic studies

Prognostic studies which contained all patients with acute mesenteric ischaemia, including those treated with supportive care or diagnosed at autopsy, were distinguished from prognostic studies in which patients treated with supportive care were not included. This subdivision was made on the assumption that inclusion of patients treated with supportive care only, who were most often moribund or not eligible for interventional treatment, might influence survival negatively.

Statistical analysis

The primary outcome measure was the in-hospital mortality rate according to aetiological subsets in the individual studies. A relative risk for mortality was calculated. The statistical heterogeneity of the included studies was assessed with the χ^2 test with $k - 1$ degrees of freedom. Estimates of mortality risk in the aetiological subsets were expressed as pooled relative risks using either the fixed-effects model according to Mantel and Haenszel[8] or the random-effects model according to DerSimonian and Laird[9], depending on the degree of heterogeneity of the included studies. When significant heterogeneity was found, the random-effects method was used to calculate the pooled relative risk. *P* values were calculated with the χ^2 test; $P < 0{\cdot}050$ was considered statistically significant. Data analysis was performed using Review Manager® 4.1 software (Cochrane Collaboration, Oxford, UK).

Results

Excluded studies

The initial search yielded 933 articles of which 863 did not meet the inclusion criteria. The majority of the excluded papers covered a variety of topics, including diagnostic modalities and treatment strategies. Other excluded articles comprised review articles, articles on chronic mesenteric ischaemia or papers lacking data on aetiology. Retrieval of the 70 candidate papers led to the exclusion of a further 25 because of insufficient data on aetiology[10–21], unclear primary endpoints[22–27], publication of the same dataset in two languages[28], or because data on acute and chronic mesenteric ischaemia or bowel strangulation[29–34] was published.

Included studies

The 45 studies[35–79] included in the analysis are listed chronologically in *Table 1*. Only observational studies were identified, of which one was prospective and 44 were retrospective case series, published between 1967 and 2002. The total number of patients was 3692 with a female : male ratio of 1·06.

Clinical characteristics

The median (range) ages of patients in the different aetiological subsets were comparable: 69 (60–75) years for those with arterial embolism ($n = 280$), 71 (59–78) years for patients with arterial thrombosis ($n = 264$), 70 (43–74) years for patients with venous thrombosis ($n = 108$) and 69 (57–76) years for patients with non-occlusive mesenteric ischaemia ($n = 152$). In the subsets of arterial embolism, arterial thrombosis and non-occlusive mesenteric ischaemia, there were more females than males, but the female : male ratios in these subsets were not significantly different (χ^2 test): 1·23 for arterial embolism ($n = 268$), 1·46 for arterial thrombosis ($n = 244$), 0·78 for venous thrombosis ($n = 41$) and 1·17 for non-occlusive mesenteric ischaemia ($n = 117$).

Mortality

Mortality was expressed as in-hospital death in all studies. The overall mortality rates of patients within the aetiological subsets in the two groups of prognostic studies, either with or without patients treated with supportive care, were mean (range) 74 (33–95) and 64 (24–85) per cent respectively (*Table 2*). Mean mortality rates for the aetiological subsets in the two groups were 71 (36–100) and 66 (18–88) per cent for arterial embolism, 87 (33–100) and 70 (27–100) per cent for arterial thrombosis, 44 (0–100) and 44 (25–69) per cent for venous thrombosis, and 80 (17–100) and 70 (50–83) per cent for non-occlusive ischaemia, respectively. Mortality rates within the aetiological subsets of the group of studies that included patients treated with supportive care were higher than those in the group that excluded such patients (except for patients with mesenteric venous thrombosis); however, the latter group comprised solely studies from the past 25 years.

The results of quantitative analysis of in-hospital mortality according to disease aetiology, as measured by the pooled relative risks of two aetiological subsets,

Table 1 Characteristics of patients included in studies of acute mesenteric ischemia

Reference	Year	Country	Inclusion period	No. of patients	Sex ratio (F : M)	Age (years)*	Study design
Prognostic studies of acute mesenteric ischaemia including patients receiving supportive care							
Ottinger and Austen[35]	1967	USA	1960–1965	128	79 : 49	74 (3–95)	Retrospective
Schennach and Dorfmann[36]	1972	Austria	1964–1971	32	—	—	Retrospective
Slater and Elliott[37]	1972	USA	1961–1971	18	7 : 11	67 (50–94)	Retrospective
Bergan *et al.*[38]	1975	USA	1955–1974	48	26 : 22	—	Retrospective
Havia and Inberg[39]	1975	Germany	1957–1971	82	42 : 40	70 (30–88)	Retrospective
Hansen and Christoffersen[40]	1976	Denmark	1964–1973	56	29 : 27	69	Retrospective
Smith and Patterson[41]	1976	USA	1968–1973	23	13 : 10	—	Retrospective
Boley *et al.*[42]	1977	USA	1972–1976	33	—	(51–88)	Retrospective
Kairaluoma *et al.*[43]	1977	Finland	1961–1974	51	19 : 32	65 (40–90)	Retrospective
Vellar and Doyle[44]	1977	Australia	1958–1975	52	28 : 24	—	Retrospective
Hertzer *et al.*[45]	1978	USA	1968–1977	10	6 : 4	60 (47–79)†	Retrospective
Krausz and Manny[46]	1978	Israel	1952–1976	40	15 : 25	(17–84)	Retrospective
Ottinger[47]	1978	USA	1964–1975	103	65 : 38	70†	Retrospective
Rogers *et al.*[48]	1982	USA	1955–1981	11	7 : 4	61 (34–74)	Retrospective
Sachs *et al.*[49]	1982	USA	1965–1980	44	21 : 23	67 (40–86)	Retrospective
Andersson *et al.*[50]	1984	Sweden	1969–1982	60	29 : 31	78 (56–92)	Retrospective
Koveker *et al.*[51]	1985	Germany	1979–1984	39	21 : 18	72	Retrospective
Bergan *et al.*[52]	1987	USA	1983–1986	20	9 : 11	70 (31–84)	Retrospective
Clavien *et al.*[53]	1987	Switzerland	1968–1984	81	44 : 37	71 (27–89)†	Retrospective
Giulini *et al.*[54]	1987	Italy	1982–1986	34	15 : 19	73 (43–84)	Retrospective
Wilson *et al.*[55]	1987	UK	1973–1984	102	56 : 46	66 (38–89)	Retrospective
Mishima[56]	1988	Japan	1981–1985	163	—	—	Retrospective
Kach and Largiader[57]	1989	Switzerland	1976–1987	45	24 : 21	71	Retrospective
Inderbitzi *et al.*[58]	1992	Switzerland	1973–1990	100	54 : 46	72 (44–89)†	Retrospective
Järvinen *et al.*[59]	1994	Finland	1972–1990	214	106 : 108	75 (50–98)†	Retrospective
Voltolini *et al.*[60]	1996	Italy	1979–1992	47	33 : 47	72 (47–88)	Retrospective
Czerny *et al.*[61]	1997	Austria	1979–1996	145	70 : 75	68 (45–86)	Retrospective
Ritz *et al.*[62]	1997	Germany	1979–1995	141	80 : 61	72 (31–93)†	Retrospective
Duron *et al.*[63]	1998	France	1980–1985	492	249 : 243	70 (18–96)	Retrospective
			1990–1995	305	157 : 148	71 (16–102)	Retrospective
Urayama *et al.*[64]	1998	Japan	1978–1995	39	14 : 25	62	Retrospective
Mamode *et al.*[65]	1999	UK	1987–1993	57	35 : 22	68 (37–91)	Retrospective
Endean *et al.*[66]	2001	USA	1993–2000	58	32 : 26	61 (20–91)	Retrospective
Subtotal				2873	1385 : 1293		
Prognostic studies of acute mesenteric ischaemia excluding patients receiving supportive care							
Rius *et al.*[67]	1979	Spain	1967–1977	46	19 : 27	65 (24–90)	Retrospective
Braun[68]	1985	Germany	1974–1984	52	33 : 19	73	Retrospective
Riemenschneider *et al.*[69]	1987	Germany	1966–1986	105	57 : 48	71	Retrospective
Sitges-Serra *et al.*[70]	1987	Spain	1976–1985	83	30 : 53	67	Retrospective
Macarone Palmieri *et al.*[71]	1989	Italy	1977–1988	64	34 : 30	70 (24–92)	Retrospective
Levy *et al.*[72]	1990	Israel	1977–1987	45	—	—	Retrospective
Bottger *et al.*[73]	1991	Germany	1985–1989	46	22 : 24	67	Prospective
Grothues *et al.*[74]	1996	Germany	1972–1993	90	36 : 54	57	Retrospective
Newman *et al.*[75]	1998	USA	1990–1996	71	—	—	Retrospective
Meyer *et al.*[76]	1998	Germany	1988–1994	35	19 : 16	71 (43–95)†	Retrospective
Bjorck *et al.*[77]	2002	Sweden	1987–1998	60	35 : 25	76 (35–90)†	Retrospective
Luther *et al.*[78]	2002	Germany	1979–2002	64	31 : 33	64 (30–89)†	Retrospective
Park *et al.*[79]	2002	USA	1990–1996	58	36 : 22	67 (35–96)	Retrospective
Subtotal				819	352 : 351		
Total				3692	1737 : 1644		

*Values are mean or †median (range).

Table 2 In-hospital deaths according to aetiology of acute mesenteric ischaemia over the past four decades

		Mortality rate					
Reference	Year	AE and AT	AE	AT	VT	NMI	Overall
Prognostic studies of acute mesenteric ischaemia including patients receiving supportive care							
35	1967		22 of 29 (75·8)	21 of 22 (95)	8 of 10 (80)	67 of 67 (100)	118 of 128 (92·2)
36	1972		13 of 18 (72·2)	11 of 11 (100)	0 of 0	3 of 3 (100)	27 of 32 (84·4)
37	1972		1 of 1 (100)	3 of 3 (100)	2 of 3 (6·7)	7 of 7 (100)	17 of 18 (94·4)*
38	1975		23 of 33 (69·7)	15 of 15 (100)	Excl.	Excl.	38 of 48 (79·2)
39	1975		50 of 52 (96·2)	18 of 20 (90·0)	8 of 10 (80·0)	Excl.	76 of 82 (92.7)
40	1976		7 of 7 (100)	31 of 32 (96·9)	5 of 8 (62·5)	0 of 0	53 of 56 (94·6)*
41	1976		6 of 7 (85·7)	9 of 10 (90·0)	3 of 3 (100)	3 of 3 (100)	21 of 23 (91·3)
42	1977		9 of 16 (56·3)	1 of 3 (33·3)	0 of 1 (0)	4 of 13 (30·8)	14 of 33 (42·4)
43	1977		10 of 11 (90·9)	19 of 21 (90·5)	0 of 1 (0)	6 of 14 (42·9)	38 of 51 (74·5)*
44	1977		6 of 9 (66·7)	31 of 32 (96·9)	3 of 5 (60·0)	4 of 6 (66·7)	44 of 52 (84·6)
45	1978		4 of 7 (57·1)	2 of 2 (100)	0 of 0	1 of 1 (100)	7 of 10 (70·0)
46	1978		12 of 17 (70·6)	19 of 23 (82·6)	0 of 0	0 of 0	31 of 40 (77·5)
47	1978		44 of 57 (77·2)	44 of 46 (95·7)	Excl.	Excl.	88 of 103 (85·4)
48	1982		5 of 8 (62·5)	1 of 1 (100)	0 of 0	2 of 2 (100)	8 of 11 (72·7)
49	1982		9 of 14 (64·3)	12 of 12 (100)	4 of 11 (36·4)	5 of 7 (71·4)	30 of 44 (68·2)
50	1984	45 of 53 (84·9)			4 of 7 (57·1)	0 of 0	49 of 60 (81·7)
51	1985		16 of 19 (84·2)	12 of 13 (92·3)	1 of 2 (50·0)	4 of 5 (80·0)	33 of 39 (84·6)
52	1987		5 of 6 (83·3)	6 of 8 (75·0)	0 of 0	6 of 6 (100)	17 of 20 (85·0)
53	1987		28 of 33 (84·8)	14 of 15 (93·3)	5 of 9 (55·6)	10 of 15 (66·7)	61 of 81 (75·3)*
54	1987		8 of 12 (66·7)	4 of 6 (66·7)	1 of 1 (100)	3 of 5 (60·0)	25 of 34 (73·5)*
55	1987		32 of 34 (94·1)	25 of 27 (92·6)	Excl.	24 of 24 (100)	94 of 102 (92·2)*
56	1988	76 of 120 (63·3)			11 of 19 (57·9)	19 of 24 (79·2)	106 of 163 (65·0)
57	1989		11 of 16 (68·8)	10 of 12 (83·3)	1 of 5 (20·0)	2 of 4 (50·0)	27 of 45 (60·0)*
58	1992		39 of 55 (70·9)	14 of 15 (93·3)	6 of 19 (31·6)	4 of 6 (66·7)	68 of 100 (68·0)
59	1994		56 of 67 (83·6)	119 of 127 (93·7)	2 of 4 (50·0)	0 of 0	176 of 214 (82·2)*
60	1996		5 of 14 (35·7)	18 of 20 (90·0)	2 of 4 (50·0)	9 of 9 (100)	34 of 47 (72·3)
61	1997		43 of 93 (46·2)	28 of 40 (70·0)	3 of 5 (60·0)	5 of 7 (71·4)	79 of 145 (54·5)
62	1997		53 of 77 (68·8)	22 of 30 (73·3)	10 of 16 (62·5)	15 of 18 (83·3)	100 of 141 (70·9)
63	1998		41 of 68 (60·3)	88 of 99 (88·9)	25 of 49 (51·0)	100 of 122 (82·6)	380 of 492 (77·2)*
			34 of 55 (61·8)	35 of 56 (62·5)	9 of 47 (19·1)	57 of 77 (74·0)	185 of 305 (60·7)*
64	1998	10 of 25 (40·0)			1 of 8 (12·5)	1 of 6 (16·7)	13 of 39 (33·3)
65	1999		9 of 12 (75·0)	16 of 18 (88·9)	2 of 4 (50·0)	6 of 8 (75·0)	46 of 57 (80·7)*
66	2001		13 of 22 (59·1)	13 of 21 (61·9)	2 of 15 (13·3)	Excl.	28 of 58 (48·2)
Subtotal		131 of 198 (66·2)	614 of 869 (70·7)	661 of 760 (87·0)	118 of 266 (44·4)	367 of 459 (80·0)	2123 of 2873 (73·9)*
Prognostic studies of acute mesenteric ischaemia excluding patients receiving supportive care							
67	1979		3 of 5 (60·0)	27 of 27 (100)	5 of 8 (62·5)	4 of 6 (66·7)	39 of 46 (84·7)
68	1985	32 of 49 (65·3)			Excl.	Excl.	33 of 52 (63·5)
69	1987		23 of 26 (88·5)	32 of 40 (80·0)	22 of 32 (68·8)	Excl.	83 of 105 (79·0)*
70	1987		4 of 6 (66·7)	16 of 19 (84·2)	2 of 7 (28·6)	2 of 3 (66·7)	59 of 83 (71·1)*
71	1989		8 of 10 (80·0)	17 of 20 (85·0)	3 of 8 (37·5)	10 of 13 (76·9)	51 of 64 (79·7)*
72	1990		3 of 17 (17·6)	3 of 11 (27·3)	5 of 17 (29·4)	0 of 0	11 of 45 (24·4)
73	1991		7 of 10 (70·0)	10 of 17 (58·8)	6 of 17 (35·3)	1 of 2 (50·0)	24 of 46 (52·2)
74	1996		16 of 21 (76·2)	22 of 27 (81·5)	11 of 30 (36·7)	10 of 12 (83·3)	59 of 90 (65·6)
75	1998		9 of 11 (81·8)	9 of 13 (69·2)	1 of 4 (25·0)	27 of 43 (62·8)	46 of 71 (64·8)
76	1998	22 of 35 (62·9)			Excl.	Excl.	22 of 35 (62·9)
77	2002	31 of 60 (51·7)			Excl.	Excl.	31 of 60 (51·7)
78	2002		14 of 18 (77·8)	13 of 19 (68·4)	3 of 9 (33·3)	4 of 5 (80·0)	43 of 64 (67·2)*
79	2002		5 of 16 (31·3)	12 of 37 (32·4)	Excl.	4 of 5 (80·0)	21 of 58 (36·2)
Subtotal		85 of 144 (59·0)	92 of 140 (66·0)	161 of 230 (70·0)	58 of 132 (44·0)	62 of 89 (70·0)	522 of 819 (63·7)*
Total		216 of 342 (63·2)	705 of 1010 (69·8)	812 of 980 (82·9)	177 of 394 (44·9)	434 of 556 (78·1)	2645 of 3692 (71·6)*

Values in parenthese are percentages AE, superior mesenteric artery embolism; AT, superior mesenteric artery thrombosis; VT, mesenteric vein thrombosis; NMI, non-occlusive mesenteric ischaemia; AE and AT, superior mesenteric artery embolism and superior mesenteric artery thrombosis included together; Excl, excluded. *Patients with aetiology of acute mesenteric ischaemia unknown or other than AE, AT, VT or NMI are included.

Table 3 Pooled relative risks of in-hospital death in relation to aetiology of acute mesenteric ischaemia

Aetiology	Mortality rate	Relative risk	*P**
Prognostic studies including patients receiving supportive care[35–66]			
AE *versus* AT	619 of 874 *versus* 661 of 760	0·85 (0·78, 0·92)	< 0·001
AE *versus* NMI	414 of 619 *versus* 347 of 429	0·86 (0·78, 0·95)	0·004
AT *versus* NMI	402 of 476 *versus* 347 of 429	1·01 (0·92, 1·10)	0·842
AE *versus* VT	481 of 694 *versus* 102 of 232	1·32 (1·05, 1·65)	0·020
AT *versus* VT	538 of 627 *versus* 102 of 232	1·59 (1·23, 2·05)	< 0·001
NMI *versus* VT	331 of 423 *versus* 97 of 222	1·47 (1·22, 1·78)	< 0·001
Prognostic studies excluding patients receiving supportive care[67–79]			
AE *versus* AT	93 of 140 *versus* 161 of 230	1·02 (0·90, 1·16)	0·734
AE *versus* NMI	66 of 97 *versus* 62 of 87	1·00 (0·82, 1·21)	1·000
AT *versus* NMI	126 of 179 *versus* 63 of 89	0·99 (0·79, 1·24)	0·936
AE *versus* VT	87 of 124 *versus* 58 of 132	1·56 (1·21, 2·03)	< 0·001
AT *versus* VT	149 of 193 *versus* 58 of 132	1·62 (1·25, 2·09)	< 0·001
NMI *versus* VT	58 of 84 *versus* 31 of 83	1·91 (1·36, 2·70)	< 0·001
All prognostic studies[35–79]			
AE *versus* AT	711 of 1014 *versus* 822 of 990	0·88 (0·82, 0·94)	< 0·001
AE *versus* NMI	480 of 716 *versus* 409 of 518	0·88 (0·80, 0·97)	0·007
AT *versus* NMI	528 of 655 *versus* 409 of 518	1·01 (0·93, 1·09)	0·865
AE *versus* VT	568 of 818 *versus* 160 of 364	1·38 (1·10, 1·66)	< 0·001
AT *versus* VT	677 of 810 *versus* 160 of 364	1·60 (1·32, 1·95)	< 0·001
NMI *versus* VT	389 of 507 *versus* 128 of 305	1·54 (1·32, 1·80)	< 0·001

Values in parentheses are 95 per cent confidence intervals. AE, superior mesenteric artery embolism; AT, superior mesenteric artery thrombosis; VT, mesenteric vein thrombosis; NMI, non-occlusive mesenteric ischaemia. *χ^2 test.

Table 4 Treatment and associated in-hospital death according to aetiology of acute mesenteric ischaemia

	Mortality rate					
Treatment	AE and AT	AE	AT	VT	NMI	Overall
Non-surgical treatment						
Supportive care	27 of 29 (93·1)	47 of 50 (94·0)	36 of 36 (100)	11 of 13 (84·6)	68 of 79 (86·1)	189 of 207 (91·3)
Explorative laparotomy	52 of 52 (100)	88 of 90 (97·8)	123 of 124 (99·2)	16 of 18 (88·9)	48 of 49 (98·0)	327 of 333 (98·2)
Subtotal	79 of 81 (97·5)	135 of 140 (96·4)	159 of 160 (99·4)	27 of 31 (87·1)	116 of 128 (90·6)	516 of 540 (95·6)
Surgical treatment						
Resection	62 of 109 (56·9)	39 of 81 (48·1)	65 of 85 (76·5)	29 of 78 (37·2)	32 of 44 (72·8)	227 of 397 (57·2)
Revascularization	14 of 31 (45·2)	40 of 67 (59·7)	22 of 30 (73·3)	2 of 11 (18·2)	0 of 0	78 of 139 (56·1)
Revascularization + resection	20 of 36 (53·6)	32 of 54 (59·3)	16 of 19 (84·2)	1 of 2 (50·0)	0 of 0	69 of 111 (62·2)
Resection, revascularization or both (not specified)	31 of 60 (51·7)	14 of 29 (48·3)	24 of 30 (80·0)	4 of 21 (19·0)	0 of 0	73 of 140 (52·1)
Subtotal	127 of 236 (53·8)	125 of 231 (54·1)	127 of 164 (77·4)	36 of 112 (32·1)	32 of 44 (72·7)	447 of 787 (56·8)
Total	206 of 317 (65·0)	260 of 371 (70·1)	286 of 324 (88·3)	63 of 143 (44·0)	148 of 172 (86·0)	963 of 1327 (72·6)

Values in parentheses are percentages. AE, superior mesenteric artery embolism; AT, superior mesenteric artery thrombosis; VT, mesenteric vein thrombosis; NMI, non-occlusive mesenteric ischaemia; AE and AT, superior mesenteric artery embolism and superior mesenteric artery thrombosis included together.

are presented in *Table 3*. The pooled mortality risk for mesenteric arterial thrombosis was equivalent to that for non-occlusive mesenteric ischaemia in both sets of studies. The pooled mortality risk from mesenteric arterial emboli was less than that from arterial thrombosis or non-occlusive mesenteric ischaemia. The pooled mortality risk from venous thrombosis was lower than that from arterial causes of acute mesenteric ischaemia in both sets.

The mortality rates for each aetiological subset over the past four decades, obtained from weighted mortality rates

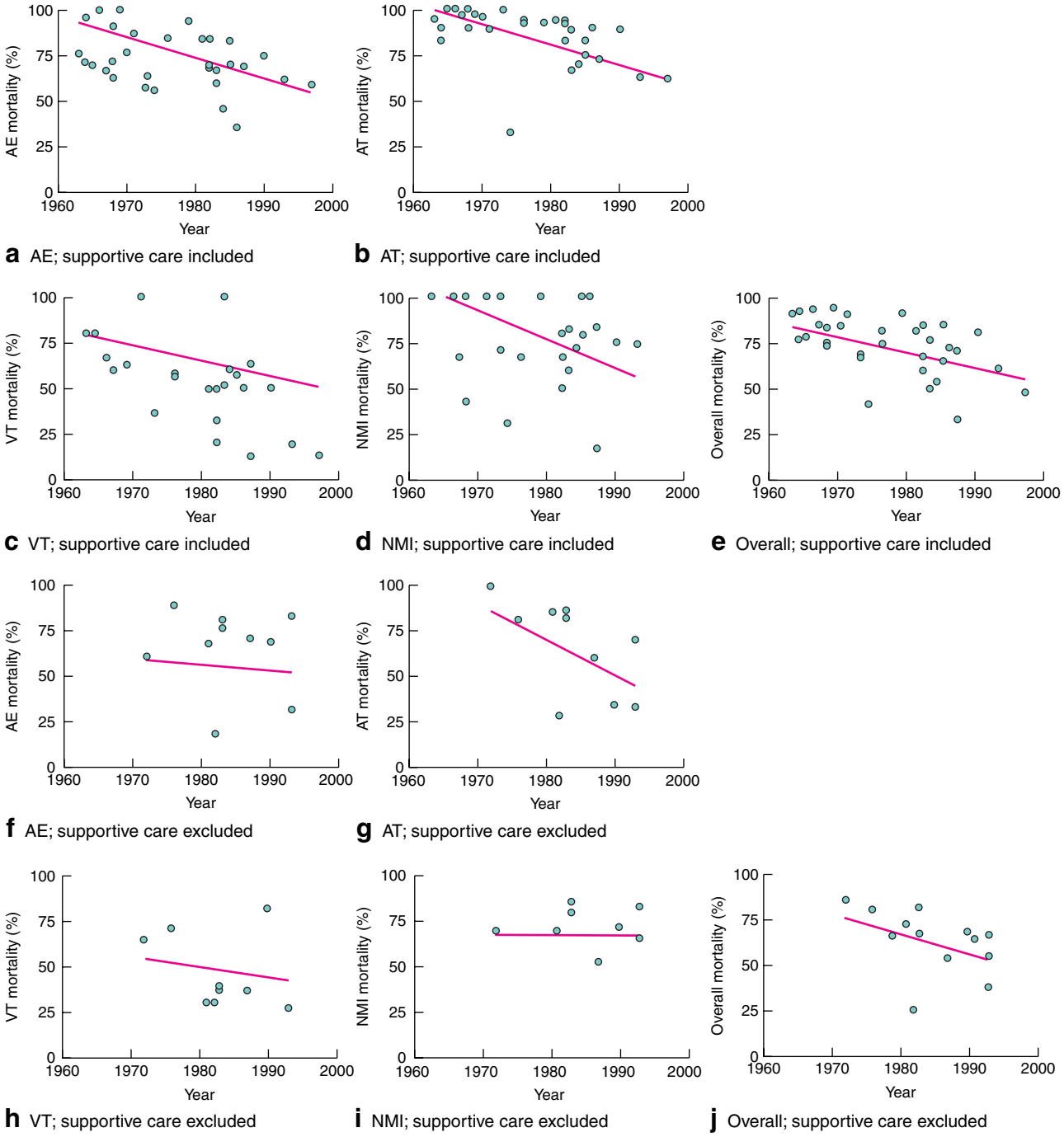

Fig. 1 Trends in in-hospital mortality rate with time in relation to aetiology of acute mesenteric ischaemia. The median of the inclusion period of each included study was used in regression analysis, along with in-hospital mortality rates weighted according to the number of patients included in the study. AE, superior mesenteric artery embolism; AT, superior mesenteric artery thrombosis; VT, mesenteric vein thrombosis; NMI, non-occlusive mesenteric ischaemia; overall, mortality rates for all aetiological subsets combined

and the median year of the inclusion period, are shown in *Fig. 1*. In both groups, overall mortality rate, and also the mortality rates for the individual aetiological subsets of acute mesenteric ischaemia, demonstrated a declining trend over the past four decades.

Surgical treatment

Table 4 shows mortality rates of acute mesenteric ischaemia following surgical and non-surgical treatment according to the aetiological subsets. From the surgical perspective, it is necessary to analyse mortality rates following surgical treatment while excluding moribund patients or patients in whom the diagnosis was made at autopsy. Observational studies that included patients who did not receive surgical treatment[35–66] may obscure the effectiveness of surgical intervention. Therefore, patients were classified into treatment modalities and categorized into non-surgical or surgical treatment according to disease aetiology.

For non-surgical treatment, the mortality rates of the different aetiological subsets varied between 87·1 and 99·4 per cent. In some patients clinical symptoms improved during supportive care and they did not therefore undergo surgical exploration, which may account for the few survivors. Patients who underwent explorative laparotomy for diagnosis only ('open-and-close procedure') died in almost all cases from massive bowel infarction. Some patients in whom intestinal ischaemia was observed in the absence of mesenteric infarction survived.

Following surgical treatment the mortality rates associated with venous thrombosis and arterial embolism improved from 44·0 to 32·1 per cent and from 70·1 to 54·1 per cent respectively, whereas the mortality rates of mesenteric arterial thrombosis (77·4 per cent) and non-occlusive mesenteric ischaemia (72·7 per cent) remained poor. Mesenteric revascularization conferred no benefit over resection alone, except in patients in whom acute mesenteric ischaemia was caused by venous thrombosis.

Discussion

Because of the low incidence and broad spectrum of acute mesenteric ischaemia, randomized or case–control trials are lacking and preclude an analysis with a higher level of evidence than can be extracted from observational data. A quantitative analysis of observational data was therefore performed to assess mortality and prognosis in relation to aetiological causes of acute mesenteric ischaemia over the past four decades. Most of the studies assessed calculated a mortality rate based on data compiled from all aetiological subsets taken together. This has the drawback of obscuring differences in clinical presentation and characteristics, diagnostic investigation, disease progression, mortality and response to therapeutic modalities that are specific to disease aetiology. Despite the limitations and careful interpretation of observational data, the results of this quantitative analysis of individual aetiological subsets show clearly the better prognosis of acute mesenteric venous thrombosis compared with arterial causes of acute mesenteric ischaemia; the better prognosis of mesenteric arterial embolism compared with arterial thrombosis and non-occlusive ischaemia; the improved prognosis of venous thrombosis and arterial embolism following surgical treatment while the mortality rate associated with mesenteric arterial thrombosis and non-occlusive mesenteric ischaemia remained poor; and the improved overall survival of patients with acute mesenteric ischaemia over the past four decades.

The survival benefit for patients with acute mesenteric venous thrombosis compared with those suffering arterial mesenteric occlusion may be explained by the usually limited segmental bowel infarction and the need for limited intestinal resection[80]. Whether acute arterial occlusion is of embolic or thrombotic origin may not influence the timing of diagnosis and outcome; however, the difference in mortality rate after surgery for embolic and thrombotic arterial occlusion (54·1 *versus* 77·4 per cent respectively) indicates a far worse prognosis for mesenteric arterial thrombosis. Mesenteric arterial thrombosis is most often superimposed on atherosclerosis at the origin of the superior mesenteric artery. The poor prognosis of patients with mesenteric arterial thrombosis is most likely due to the proximal location of the occlusion that is associated with extensive bowel infarction and the need for extended bowel resection[47]. In contrast, mesenteric arterial embolism occludes the mesenteric vessels at different levels of the mesenteric vascular tree resulting in varying areas of mesenteric infarction[47]. For non-occlusive mesenteric ischaemia, revascularization procedures are not appropriate because the underlying problem is a low-flow state. The mortality rate of these patients will remain high in spite of supportive circulatory treatment and bowel resection, if the underlying cause of mesenteric hypocirculation is not treated adequately.

In addition to distinguishing disease aetiology, therapeutic modalities were categorized into non-surgical or surgical treatment groups. Non-surgical treatment (supportive care and diagnostic explorative laparotomy) was followed by death in almost all cases, the diagnosis being established when the patient was in a moribund state or

at autopsy. This emphasizes the importance of early diagnosis and treatment[1,5]. Regarding surgical treatment, two findings were notable. As expected, the mortality rates were lower after surgical than non-surgical treatment. However, the mortality from mesenteric arterial thrombosis and non-occlusive mesenteric ischaemia remained high even after surgical treatment (resection, revascularization or both) (77·4 and 72·7 per cent respectively), whereas the in-hospital mortality rate associated with arterial embolism and venous thrombosis had decreased to 54·1 and 32·1 per cent respectively.

Patients who underwent revascularization with or without resection appeared to fare even worse than patients who underwent bowel resection only. This might be explained by the varying prognosis of different revascularization procedures. Relatively small revascularization procedures, for example thrombectomy or embolectomy without subsequent bowel resection, are undertaken when the disease is diagnosed early and there is no transmural bowel necrosis, and may therefore be associated with decreased mortality. On the other hand, large revascularization procedures, such as aortoiliac–mesenteric bypass surgery, are used when there is intestinal vascular insufficiency and may result in increased mortality. Unfortunately, incomplete data made it impossible to distinguish between the various revascularization procedures.

Whether advances in diagnostic tests and therapeutic strategies have improved survival over time is difficult to determine, in part because of the infrequency of acute mesenteric ischaemia and the paucity of data regarding outcome. Over the past decade reviews and expert opinion have disagreed as to whether improvements in mortality from acute mesenteric ischaemia have occurred[1]. However, in several studies data encompassing two inclusion periods showed improved survival[63,72,81]. Furthermore, investigation of each aetiological subset in this study, using weighted mortality rates, demonstrated a declining trend in mortality over the past four decades. Whether this trend derives from publication bias, improvements in treatment strategy or from early diagnosis remains a matter of debate. There is no doubt that early diagnosis decreases mortality[54,58,67,68,71]. The authors were unable to obtain data from published studies on patient and doctor delay, and its relation to mortality. Diagnosis is still often delayed, mainly as a result of the non-specific nature of clinical symptoms during the early phase of acute mesenteric ischaemia and limitations in current diagnostic techniques[82]. The declining mortality of acute mesenteric ischaemia over the past four decades is therefore probably attributable to better management of the disease, with improvements in surgical interventions and perioperative and postoperative supportive intensive care.

Survival after acute mesenteric ischaemia varied between the different aetiological subsets. The mortality rate after surgical treatment of arterial embolism and venous thrombosis has improved whereas that after surgery for arterial thrombosis and non-occlusive ischaemia remains poor. Although the statement offered by Cokkinis more than 75 years ago may to some degree still apply, there is now room for more optimism and it might be said that 'the diagnosis of acute mesenteric ischaemia is possible, and, in some cases, the treatment is useful and the prognosis hopeful'.

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