Non-fatal healed transmural myocardial infarction and fatal non-cardiac disease

Qualification and quantification of coronary arterial narrowing and of left ventricular scarring in 18 necropsy patients

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SUMMARY A qualitative and quantitative analysis of the amount of myocardial scarring and the degree and extent of coronary arterial narrowing by atherosclerotic plaque in the entire lengths of each of the four majorepicardial coronary arteries is described in 18 necropsy patients with healed transmural myocardial infarcts and death from a non-cardiac condition. An average of 30 per cent of the basal half and 38 per cent of the apical half of the left ventricular wall was scarred. The nine patients with clinical evidence of previous acute myocardial infarction tended to have larger left ventricular scars than the nine patients without such evidence but the difference was not significant. An average of 26 cm (51.5 mm segments) of coronary artery were examined from each patient and 25 cm (49.5 mm segments) from each of 19 control subjects. Of 924 segments examined in the 18 patients, 292 (32%) were 76 to 100 per cent narrowed in cross-sectional area (controls=5); 321 (35%) were 51 to 75 per cent narrowed (controls=34%); 210 (23%) were 26 to 50 per cent narrowed (controls=44%), and 101 (11%) were 0 to 25 per cent narrowed (controls=17%). The extent of severe narrowing of 75 per cent or more was similar (25%) in the left anterior descending and left circumflex coronary arteries; the right was the most severely narrowed artery and the left main was not severely narrowed in any patient. Excluding, then, the left main artery, the amount of severe narrowing in the proximal and distal halves of the other three vessels was similar. The amount of severe narrowing was not related to the age at death or to heart weight, but was greater in patients with hypertension or with a history of acute myocardial infarction.

Much is now known about the amount of left ventricular damage and the extent of coronary arterial narrowing present in patients dying either suddenly, or with acute myocardial infarction, or with chronic congestive cardiac failure after the healing of an acute infarction, but information on these two points is lacking in patients with old healed infarcts who subsequently die of non-cardiac conditions. The present report attempts to fill this void by describing the findings in 18 such patients, all of whom died at least two years after their acute myocardial infarction.

Patients and methods

Eighteen patients were studied. All fulfilled the
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following criteria: (1) death from a non-cardiac cause; (2) a previous healed myocardial infarction involving at some point > 50 per cent of the thickness of the left ventricular wall; (3) an absence of left ventricular myocardial necrosis; (4) no clinical evidence of congestive cardiac failure; (5) normal sized right and left ventricular cavities; (6) no cardiac surgery having been undertaken; and (7) no other cardiac disease present. Clinical details are set out in Table 1. Nine had a history of acute myocardial infarcts in the past, four of them (cases 2, 3, 6, and 9) having had two acute infarcts documented clinically. Three patients had had angina pectoris. Nineteen age and sex matched control subjects were also studied. All fulfilled the following criteria: (1) death from a non-cardiac condition; (2) no symptoms suggesting myocardial ischaemia

Non-fatal healed myocardial infarction

Table 1 Clinical and morphological observations in 18 patients with non-fatal healed transmural myocardial infarcts and fatal non-cardiac conditions

Case no.	Age (y)	Sex	Interval (years) 1st AMI to death	Angina pectoris	Hyper-tension	Diabetes	Total serum cholesterol (mg/100 ml)*	Heart weight (g)	Percentage LV wall scarred		No. 5 mm CA segments examined	No. (%) 5 mm segments > 75% narrowed	No. CA > 75% narrowed	Cause of death
									Apical	Basal				
Clinically apparent acute myocardial infarct														
1	60	M	22	0	+	0	325	540	0	30	56	17 (30)	3	Hodgkin's disease
2	62	M	13	0	+	0	—	520	25	20	63	6 (9)	1	Bowel infarct
3	63	M	8	0	0	0	—	420	35	30	37	14 (38)	2	Trauma
4	63	M	10	0	—	0	—	510	100	35	57	16 (28)	3	Trauma
5	65	M	14	0	0	0	—	310	25	30	55	6 (11)	1	Carcinoma, lung
6	73	F	2	0	—	+	—	535	45	25	42	25 (59)	3	Carcinoma, colon
7	78	M	5	+	+	0	—	475	35	50	43	11 (26)	1	Renal failure
8	78	M	6	0	0	+	—	430	35	30	64	36 (56)	3	Carcinoma, pancreas
9	80	M	16	0	+	0	—	420	100	60	44	17 (39)	2	Carcinoma, lung
Clinically silent acute myocardial infarct														
10	50	M	—	+	+	0	—	510	100	60	75	21 (28)	3	Acute pancreatitis
11	55	M	—	+	+	0	252	380	0	35	40	22 (55)	3	Carcinoma, mouth
12	57	M	—	0	0	0	180	310	20	15	40	5 (13)	2	Hodgkin's disease
13	62	M	—†	0	0	0	—	500	25	25	48	10 (21)	2	Carcinoma, lung
14	64	F	—	0	+	+	—	360	0	15	73	21 (29)	2	Stroke
15	65	M	—	0	+	0	220	365	20	25	49	24 (49)	3	Carcinoma, lung
16	66	M	—	0	0	0	185	370	25	20	57	10 (18)	2	Carcinoma, pancreas
17	69	F	—	0	0	0	—	310	100	20	50	9 (18)	2	Carcinoma, mouth
18	72	M	—	0	0	+	—	490	0	25	31	4 (13)	1	Stroke

Abbreviations: AMI, acute myocardial infarction; CA, coronary arteries. Hypertension = > 140 systolic or > 90 mmHg diastolic.

*For conversion to SI units multiply by 0.0259 to arrive at mmol/l.

†Electrocardiogram 19 years before death showed changes typical of a healed myocardial infarct.

or cardiac dysfunction; (3) no systemic hypertension (blood pressure > 140 mmHg systolic and/or > 90 mmHg diastolic); (4) no cardiomegaly; (5) no left ventricular fibrosis or necrosis; and (6) no history of mediastinal irradiation. Seven of the 19 had died of carcinoma (pancreas two, ovary two, prostate two, tongue one); five of leukaemia; six of lymphoma; and one of sideroblastic anaemia.

The coronary arteries in the 18 patients and 19 control subjects were studied in a similar fashion. The hearts were fixed in 10 per cent formalin for at least one day. The four major epicardial coronary arteries (right, left main, left anterior descending, and left circumflex) were removed intact, x-rayed (Fig. 1), decalcified, and then cut transversely to their longitudinal axes into segments 5 mm in length. Each segment was labelled sequentially either from its aortic ostium or from its origin from the left main coronary artery. The segments were dehydrated and embedded in paraffin, and at least two histological sections were cut from each and stained, one by haematoxylin and eosin and the other by the Movat method. The degree of luminal narrowing within the internal elastic membrane by atherosclerotic plaque was based on histological examination of the Movat stained cross-sections magnified 25 to 50 times. The percentage of cross-sectional area luminal narrowing of each section was graded into four categories: 0 to 25, 26 to 50,

51 to 75, and 76 to 100. As a check, the degree of cross-sectional narrowing in three of the 18 patients was measured by planimetry and a 96 per cent agreement was found between this and the visual estimation on microscopy.

The location and the extent of left ventricular scarring was determined after cutting the ventricles at approximately 1 cm intervals beginning at the left ventricular apex and extending to about 2 cm caudal to the posterior atrioventricular sulcus. The ventricular incisions were made parallel to the posterior atrioventricular sulcus. In most cases six slices of the ventricles were examined, including three from the basal half and three from the apical half. The extent of left ventricular scarring was determined by circumferential measurement of it in one of the three apical slices and in one of the three basal slices, choosing the one with the maximal amount of scarring in each group. The percentage of scarring was determined by dividing the circumferential length of the transmural scar by the total circumference of the slice (including the ventricular septum).

Results

In the 18 patients, 71 major epicardial coronary arteries were examined (right, left main, left anterior descending, and left circumflex). The left

Fig. 1 Radiograph of the major epicardial coronary arteries after removing them from the heart at necropsy. Calcific deposits are present in all of them. The short segment is the left main coronary artery.

main was not examined in one patient. In the 19 control subjects 74 major coronary arteries were examined (the left main was not examined in two subjects). Four patients had one, seven had two, and seven had three of their four major coronary arteries narrowed 76 to 100 per cent in cross-sectional area by atherosclerotic plaque. Thus, of the possible 71 major coronary arteries studied, 39 (55%) were narrowed to this extent, an average of 2.2 per patient. If the left main coronary artery is excluded the percentage rises to 72, that is 39 of the 54 other major coronary arteries. In the 10 control subjects one had three arteries narrowed by >75 per cent in cross-sectional area, three had two,

Table 2 Summary of number of 5 mm long segments of major epicardial coronary artery examined

Coronary artery	Number (range [mean]) of 5 mm segments per patient	
	Patients (18)	Controls (19)
Right	6-28 (16.7)	11-37 (19.7)
Left main	1-6 (2.0)	1-3 (1.6)
Left anterior descending	8-39 (19.4)	10-32 (18.1)
Left circumflex	3-24 (11.4)	3-29 (10.1)
Total segments of four coronary arteries per patient	24-67 (49.5)	27-75 (49.4)

and six had one. Thus, of 74 major coronary arteries studied, 15 (20%) were narrowed to this extent, an average of 0.8 per control subject. If the left main is excluded, the percentage rises to 27, that is 15 of the 55 other major coronary arteries studied.

None of the patients or the control subjects had a thrombus in any of the four major coronary arteries.

The numbers of 5 mm long segments of coronary arteries examined are summarised in Tables 2 and 3, and in Fig. 2. Of the 924 segments examined in the 18 patients, 292 segments (32%) were 76 to 100 per cent narrowed in cross-sectional area (controls=5%, $p < 0.005$), 321 (35%) were 51 to 75 per cent narrowed (controls=34%), 210 (23%) were 26 to 50 per cent narrowed (controls=44% $p < 0.005$), and 101 (11%) were 0 to 25 per cent narrowed (controls=17%). In the patients the percentage

Fig. 2 Number and percentage of 5 mm segments of all four major coronary arteries narrowed to various degrees in the 18 study patients and in the 19 control subjects.

Table 3 Number and percentage of 5 mm segments of four major epicardial coronary arteries showing the four grades of cross-sectional luminal narrowing

Per cent cross-sectional area luminal narrowing											
Coronary artery	0-25			26-50		51-75		76-100		Totals	
	P	C		P	C	P	C	P	C	P	C
Left main*	No.	5	7	13	12	17	9	0	0	35	28
	%	(14)	(25)	(37)	(43)	(49)	(32)	0	0	(100)	(100)
Left anterior descending	No.	58	49	92	157	123	111	92	27	365	344
	%	(16)	(14)	(25)	(46)	(34)	(32)	(25)	(8)	(100)	(100)
Left circumflex	No.	24	51	56	63	74	75	62	4	216	193
	%	(11)	(26)	(26)	(33)	(34)	(39)	(29)	(2)	(100)	(100)
Right	No.	14	50	49	181	107	127	138	17	308	375
	%	(5)	(13)	(16)	(48)	(35)	(34)	(45)	(5)	(100)	(100)
Totals	No.	101	157	210	413	321	322	292	48	924	940
	%	(11)	(17)	(23)	(44)	(35)	(34)	(32)	(5)	(100)	(100)

*Sections not examined in one patient and in two control subjects.
Abbreviations: P, patients; C, control subjects.

of segments narrowed was similar at all levels of severity in the left anterior descending and left circumflex coronary arteries, the right coronary artery showed the highest incidence of severe narrowing, and the left main was not severely narrowed in any patient. In the control subjects the incidence of narrowing in each of the four major coronary arteries was similar at the four categories of narrowing and was not significantly different at any level (Fig. 3). The percentage of segments

narrowed 76 to 100 per cent in cross-sectional area was significantly higher in the proximal half of the right and left anterior descending coronary arteries than it was distally (Fig. 4).

The weight of the heart, the location of the healed myocardial infarcts, and the amount of left ventricular scarring are summarised in Tables 1 and 4 and illustrated in Fig. 5 to 8. The heart weight was normal (<400 g in men and <350 g in women) in six and increased in 12 patients. The

Fig. 3 Percentage of 5 mm segments of each of the four major coronary arteries narrowed to various degrees in the 18 patients (left) and in the 19 control subjects (right).

Table 4 Location of transmural left ventricular scar and percentage of 5 mm segments of four major coronary arteries narrowed 51 to 75 per cent and 76 to 100 per cent in cross-sectional area by atherosclerotic plaque

Case no.*	Percentage LV wall scarred		Dominant posterior coronary artery	No. 5 mm segments	Percentage 5 mm segments narrowed 51–75 per cent in cross-sectional area				Percentage 5 mm segments narrowed 76 to 100 per cent in cross-sectional area			
	Apical half	Basal half			R	LM	LAD	LC	R	LM	LAD	LC
Posterior wall												
14	0	15	R	73	21	37	19	30	79	0	6	0
18	0	25	LC	31	86	100	92	64	0	0	0	36
1	0	30	R	56	29	0	38	40	59	0	12	40
11	0	35	R	40	15	100	71	30	62	0	20	70
12	20	15	R	40	22	—	42	23	22	0	0	54
16	25	20	R	57	62	0	22	0	0	0	28	0
13	25	25	R	48	39	0	17	45	33	0	0	36
5	25	30	R	55	36	100	45	33	27	0	0	0
3	35	30	R	37	19	100	80	48	81	0	0	12
8	35	30	R	64	36	50	23	42	54	0	77	34
6	45	25	R	42	33	0	13	55	44	0	87	45
7	35	50	R	43	10	0	23	0	90	0	0	0
4	100	35	R	57	65	100	33	58	25	0	29	33
9	100	60	R	44	54	100	43	70	81	0	0	12
Anterior wall												
2	25	20	LC	63	6	0	14	17	0	0	27	0
15	20	25	R	49	39	100	26	30	61	0	32	70
17	100	20	LC	50	33	50	33	33	17	0	33	0
10	100	60	R	75	29	0	46	28	48	0	18	72

Abbreviations: LAD, left anterior descending coronary artery; LC, left circumflex coronary artery; LM, left main coronary artery; LV, left ventricular; R, right coronary artery.

*The case number corresponds to the case number in Table 1. The patients are listed in order of progressively increased amounts of left ventricular scarring.

Fig. 4 Percentage of 5 mm segments of the right, left anterior descending, and left circumflex coronary arteries narrowed 76-100% in cross-sectional area in the proximal and distal halves of each of the 3 arteries in the 18 patients.

most frequent location of the transmural infarcts was the posterior wall of the left ventricle (14 patients). In four patients the infarct involved only the basal half of the left ventricle. One patient (case 10, Table 1) had a small left ventricular thrombus (about 1 cm in diameter) and he had been in septic

Table 5 Mean percentage of segments in four major coronary arteries narrowed > 75 per cent in cross-sectional area in 18 patients: comparison of four clinical or morphological indices

Indices analysed	No. of patients	Mean percentage (± standard error) of coronary segments narrowed > 75% in cross-sectional area	p value
Age (y)			
46-65	10	27 ± 4	> 0.05
> 65	8	33 ± 7	
History of acute myocardial infarction			
Present	9	35 ± 6	< 0.05
Absent	9	24 ± 4	
Systemic hypertension			
Present	8	38 ± 5	< 0.05
Absent	8	25 ± 5	
Heart weight			
Increased*	12	31 ± 4	> 0.05
Normal	6	26 ± 8	

* > 400 g in men and > 350 g in women.

Fig. 5 Transverse slices of the cardiac ventricles in case 1 (*a* and *a*¹) and in case 7 (Table 1) (*b* and *b*¹). Transverse slices of the cardiac ventricles illustrating transmural healed posterior wall myocardial infarcts. *a*¹ and *b*¹ are close-up views of the slices from *a* and *b* enclosed by the interrupted line. The most apical portion of the heart in *b* is not shown.

shock for several days before death from acute pancreatitis.

The relation between the site of the left ventricular transmural scar and the amount of coronary narrowing in each of the 18 patients is tabulated in Table 5. In nine of the 14 with *posterior* wall scars, the dominant posterior perfusing coronary artery (right in 13; left circumflex in one) had a higher percentage of segments severely narrowed (>75%) than the left anterior descending coronary artery. In two of the four patients with *anterior* wall scars, the left anterior descending coronary artery had a higher percentage of segments severely narrowed (>75%) than the dominant posterior perfusing coronary artery (right in two, left circumflex in

two). The location of the transmural scar, therefore, did not necessarily indicate which of the coronary arteries was most narrowed.

Table 5 shows the relation of age, hypertension, a history of infarction, and heart weight in the 18 patients to the mean percentage of coronary segments severely narrowed (>75%). The second and third of these were significantly correlated ($p < 0.05$).

Comments

Although none of the 18 patients died from coronary heart disease, and only three had angina, the

Fig. 6 Single transverse slices of cardiac ventricles in case 3 (a) and in case 5 (Table 1) (b), showing transmural posterior wall healed myocardial infarcts in each.

amount of coronary narrowing they had was extensive. Two or three of the four major epicardial coronary arteries examined were narrowed by more than 75 per cent in cross-sectional area by atherosclerotic plaques in 14 of them. In none, however, was the left main coronary artery narrowed to this extent. Furthermore, the total length of these major arteries so severely narrowed was considerable—292 of the 924 5 mm long segments of artery examined (32%) compared with 5 per cent in the control subjects. Another 321 segments (35%) were narrowed in cross-sectional area to between 51 and 75 per cent. Thus, 61 per cent of the total length of the four major coronary arteries were more than 50 per cent narrowed in cross-sectional area by atherosclerotic plaque. Only 11 per cent of the segments were 25 per cent narrowed or less.

Even in the four patients in whom only one major coronary artery was more than 75 per cent narrowed, plaque was extensive, with that degree of narrowing being present in between 27 and 90 per cent of

segments examined. Such extensive coronary narrowing is similar to that observed in patients with fatal acute myocardial infarcts¹ and sudden coronary death² but less than that found in patients with unstable angina pectoris.³

Fig. 7 Transverse slides (a) of the cardiac ventricles in case 15 (Table 1); this patient has a healed transmural anteroseptal myocardial infarct. The close-up (b) is of the slice enclosed by the interrupted line in a.

Fig. 8 Transverse slices of the cardiac ventricles in case 16 (a and a') and in case 18 (Table 1) (b and b') showing healed posterior wall transmural myocardial infarcts. a' and b' are close-up slices of the slices in a and b enclosed by the interrupted line.

Comparison of the two groups of patients with and without a previous clinical history of acute myocardial infarction disclosed a significant difference between them. Severe narrowing ($>75\%$) was more extensive in the former, $35 \text{ per cent} \pm 6$ of the 5 mm segments compared with 24 ± 4 .

Although none of our patients died from cardiac disease, the sizes of the left ventricular scars at necropsy were surprisingly large. With the left ventricle arbitrarily divided into two halves, apical and basal, the amount of scarring in the basal half ranged from 15 to 60 per cent (mean 30) and that in the apical half, from 0 to 100 per cent (mean 38%). The nine patients with an overt previous acute myocardial infarction also had larger myocardial scars on average than the nine without this history, but the difference was not significant.

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