Recent myocardial infarction and the conduction system

A clinico-pathological correlation¹

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A clinico-pathological correlation has been attempted for 36 patients treated in a coronary care unit but dying from acute myocardial infarction.

Only few infarcts involving parts of the conduction system could be detected by serial sectioning. Minor infarcts of part of the conduction system and vacuolated conduction fibres could be present without electrocardiographic abnormalities.

The size of infarct and the maximum serum GOT activity had highly significant correlation.

Morphological studies of the conduction system in fresh myocardial infarction have been undertaken on selected series of patients with certain types of manifest arrhythmia, e.g. complete heart block (Davies, 1967; Sutton and Davies, 1968; Harper *et al.*, 1969). Little is known about the morphology of the conduction system in an unselected material of fresh myocardial infarction. With the introduction of coronary care units and electrocardiographic monitoring for acute myocardial infarction, the incidence of various arrhythmias has been observed to be very high (Julian and Oliver, 1968). Complete atrioventricular or bundle-branch block complicates approximately 5 per cent of subjects with acute infarction (Julian, Valentine, and Miller, 1964; Norris and Croxson, 1970). The establishment at this hospital of a coronary care unit with its continuous electrocardiographic monitoring provided us with the possibility of a clinico-pathological correlation for all patients dying from acute infarction.

Subjects and methods

Clinical studies The series consists of 36 consecutive patients with adequate clinical and pathological data, and the distribution by age is

shown in Table 1. Fifteen patients (40%) were older than 70 years of age. The average age for the series was 66.8 years. The mean age for the 128 patients admitted to the coronary care unit during 1969 was 64.0 years.

The previous cardiovascular diseases are listed in Table 2. Most of the patients had suffered from some cardiovascular disease and only 6 of the 36 patients appeared to be previously healthy.

All patients had been treated at the coronary care unit of this hospital. The admission policy for the coronary care unit was clinically suspected or verified myocardial infarction, which had developed during the preceding 48 hours. Patients with respiratory and circulatory arrest were not primarily brought to the coronary care unit but to a general intensive care unit. A patient with uncomplicated infarction was kept in the coronary care unit for at least 48 hours, and then moved to another room – without monitoring equipment – in the same ward and nursed by the same staff.

Electrocardiograms and pulse rate (from an ear probe) were monitored continuously.

A continuous tape recorder with a memory of 2 minutes was used. A 12-lead electrocardiogram was taken on admission and at least every morning and evening during the stay at the coronary care unit. Thereafter a full electrocardiogram was taken every day or every second day. Blood samples for routine laboratory tests were taken on admission and every morning. Radiographs of the heart and lungs were taken only when considered necessary but projections in recumbent position were not used.

Arrhythmias were treated according to generally accepted principles (Julian and Oliver, 1968). For cardiac insufficiency digitalis was usually administered and if necessary frusemide (Lasix)

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TABLE 1 *Age and sex*

Age (yr)	Men (21)	Women (15)	Total (36)
40-45	1	—	1
46-50	1	1	2
51-55	—	1	1
56-60	2	—	2
61-65	8	1	9
66-70	2	4	6
71-75	5	6	11
76-80	2	2	4
Mean age	65.5	68.5	66.8

was added. Anticoagulants (dicoumarol) were administered only when the risk of venous thrombosis was considered high.

Pathological studies A complete necropsy was performed on every subject. The coronary arteries were dissected out *in toto*, fixed in formalin, decalcified if necessary, and sectioned transversely at approximately 3 mm intervals. Several blocks were taken from each coronary artery for microscopical examination.

In the ventricular myocardium the size of old and recent infarcts was measured macro- and microscopically and expressed as a percentage of the left ventricular myocardium. In subendocardial infarcts an estimate was made of the depth of the infarcted area and a similar calculation of size of the infarct was made.

The conduction system was studied by the Hudson technique (1960, 1965). The whole conduction system – the areas of the sinus node, the atrioventricular node, and bundle-branches – were embedded and step-sectioned. Depending upon the pathological changes found in the specimens, selected blocks were serial sectioned; generally, some 100 sections were examined from each heart.

The sections were stained with the Verhoeff-van Gieson and the Mallory PTAH stains. The latter method gives an excellent staining of the cross-striation of the muscle cells (Voigt, 1967), the

damage of which is the first morphological sign of an infarction.

The morphological examinations were performed without detailed knowledge of the clinical and electrocardiographic recordings.

Results: general data

Cause of death The patients have been divided into various groups according to the dominating symptoms and findings before death (Table 3). More than half of the subjects died from pulmonary oedema and shock. Thirteen patients died in the ward outside the coronary care unit and 7 of them were not monitored at the moment of death.

The age of the myocardial infarction – calculated from the onset of pains until death – is shown in Table 4. About one-third of the patients died within the first 2 days.

Coronary vessels Thromboses were observed in 31 subjects and haemorrhage into an atheromatous plaque in one patient. Two subjects had severe atheromatosis and the lumen of the arteries was reduced to less than 5 and 2 per cent, respectively, of the cross-section area at the narrowest point of the artery. In one patient – despite the infarction – no stenosis could be observed in the coronary arteries; this was a 73-year-old woman with a large thyroid carcinoma, who developed respiratory arrest while being taken to hospital. The tissues of the coronary arteries from one patient were inadvertently destroyed.

Site of infarction The site of the infarction, as diagnosed by electrocardiogram, corresponded to the necropsy findings with few exceptions (Table 5). One patient had two separate recent infarcts, one anterior and one posterior, but only the posterior infarct could be detected on electrocardiograms. In 2 subjects the site of the infarct could not be determined by electrocardiogram since the patients died just after arrival at the hospital

TABLE 2 *Previous cardiovascular disease*

Disease	No. of patients (36)	Percentage
Myocardial infarction	7	19
Angina pectoris (> 1 mth)	20	56
Electrocardiographic signs of coronary insufficiency	3	8
Treatment for cardiac decompensation	14	39
Treatment for hypertension	6	17
No previous history of cardiac disease	6	17

The patients may be listed in more than one of the groups.

TABLE 3 *Clinical findings at death*

	No. of patients (36)	Percentage
Shock	8	22
Pulmonary oedema	12	33
Ventricular fibrillation	6	17
Asystole	3	8
Died unexpectedly; not examined at moment of death	7	19

TABLE 4 Age of myocardial infarction (onset of pains till death)

	0-24 hr	25-48 hr	3-7 dy	8-14 dy	15 dy
No. of patients	7	6	7	9	7

and before serial electrocardiograms were taken. In one of these patients and in a further subject, the exact site of the infarct could not be determined by the pathologist since small areas of infarcted tissue were scattered throughout the myocardium.

The papillary muscles to the mitral valve were normal in 29 hearts. In 6 subjects severe damage was present and in one patient only small areas were infarcted.

Size of infarct The extent of infarction is listed in Table 6. Subjects dying with small infarcts – less than 30 per cent of the left ventricular myocardium – were above the mean age for this series. Furthermore, hearts with small infarcts had a greater degree of diffuse myocardial fibrosis and in 4 of these 6 subjects the infarct was sited in the posterior wall. On the other hand, no correlation was found between these small infarcts and sex, mode of death (shock, arrhythmia, or myocardial insufficiency), or presence or absence of reinfarction.

The present series included 6 patients below 60 years of age. In 5 of these subjects the size of the myocardial infarction could be determined. Two patients had infarctions judged to be between 31 and 40 per cent of the left ventricular myocardium; both of these patients had essential hypercholesterolaemia. The remaining 3 patients had infarcts judged to involve 50 per cent or more of the left ventricular myocardium.

The size of the infarction was correlated

with all values of the different serum enzymes and the most interesting finding was the correlation with the maximal GOT (glutamic oxalacetic transaminase, Wroblewski-Ordell IE). Out of the 36 patients, 14 were excluded from this correlation since either no determinations were made during the peak period (24–48 hours) or the patients were very decompensated with increase in the GPT (glutamic pyruvic transaminase). In the remaining 22 patients there was a highly significant correlation between the size of the infarction and the maximum GOT activity ($r=0.853$, $P<0.001$). The equation or the regression line was size of infarction (in %) = $0.147 \times \text{GOT} + 19$. Since it is of great importance to know the size of a myocardial infarction this observation has initiated a more detailed study of the relation between changes in serum enzyme levels and size of infarction.

Pleural effusion A high frequency of pleural transudate was observed. The series comprised 36 patients and 17 of these had a total amount of pleural fluid exceeding 500 ml. The average amount in these 17 subjects was 1150 ml and the maximum in one patient was 3250 ml. A correlation was observed with, (1) the amount of diuretic drugs; higher doses given to patients with transudate indicating that the patients were in a poorer state than the others, (2) the site of the infarction; transudate tended to be more common in anterior infarction and, (3) infarction in the papillary muscles to the mitral valve; 5 out of 6 patients with such injuries had pleural effusion, though the average amount for these patients was comparatively low (500 ml). No correlation was found between the presence of transudate and the size of the infarct, heart weight, period in hospital, the mode of death (shock, arrhythmia, or myocardial insufficiency), kidney function, as judged by serum creatinine levels, or treatment for cardiac decompensation before the myocardial infarction.

TABLE 5 Site of recent infarction

Pathology	Electrocardiographic changes						Total
	Anterior	Diaphragmatic	Posterior	Lateral	Apical	Undetermined	
Anterior	16						17
Diaphragmatic		5				1	5
Posterior	1*		7				8
Lateral				3			3
Apical					2		2
Undetermined			1			1	2
Total	17	5	8	3	2	2	37

* Two separate acute infarctions: 1 anterior and 1 posterior.

TABLE 6 Myocardial infarction area in relation to total mass of left ventricular myocardium

Percentage	No. of patients (36)	Mean age
0-10	—	—
11-20	—	—
21-30	6	74
31-40	8	64
41-50	7	68
51-60	7	64
61-70	3	64
71-80	—	—
81-90	2	65
91-100	—	—
Undetermined (see text)	3	68

Miscellaneous Focal myocarditis characterized by lymphocyte infiltration between intact myocardial fibres and limited to the atria – not the ventricles – was observed in 3 of the 36 subjects. These 3 subjects did not have any other common clinical, laboratory, or pathological characteristics distinguishing them from the other subjects or fitting in with the so-called post-myocardial infarction syndrome.

Scattered infarcts of minor size were present in the atrial walls in 8 patients.

Cardiac rupture had occurred in 3 patients. In 2 subjects sinus rhythm in connexion with circulatory arrest suggested cardiac rupture. The third patient suddenly developed ventricular fibrillation followed by asystole after defibrillation. Rupture was not suspected clinically.

Pulmonary emboli were present in 4 patients; in 3 subjects the emboli were small and probably without clinical significance. The fourth patient died 42 days after the onset of the infarction. The major clinical problem was recurring secondary ventricular fibrillation. X-rays of the lungs showed a varying degree of pleural effusion and atelectasis. The patient was treated with anticoagulants, and the thrombotest value was held between 10 and 20 for more than two weeks.

Results: conduction system

Sinus node In Table 7 the morphological findings in the sinus node are considered in relation to the electrocardiographic recordings. Fibrosis of the sinus node was difficult to evaluate, since there is normally an increase in collagen fibres in the node with age (Lev, 1968). Slight fibrosis was not regarded as a pathological feature but the difference between

normal and pathological fibrosis was bound to be diffuse. It is not surprising to find that patients with fibrosis had sinus rhythm as well as various arrhythmias including atrial fibrillation. Recent infarction of the sinus node was observed in 4 subjects: one of these infarcts was quite small, 4 mm from the sinus node; this patient developed transitory atrial fibrillation for two days, 7 days after admission to hospital and 6 days before death.

One patient, with a pronounced atrial myocarditis, had atrial fibrillation but a normal sinus node, which seemed to provide a reasonable morphological explanation for the arrhythmia.

AV node, His bundle With few exceptions, the morphological findings in this region corresponded with the electrocardiographic observations (Table 8). Infarcts of this part of the conduction system were observed in three subjects; one of these infarcts was quite small and had not caused any arrhythmias. Seven subjects had vacuolated conduction fibres but none of them had electrocardiographic irregularities.

Bundle-branches There is close correspondence between electrocardiographic changes and the changes of the right and left bundle-branches (Tables 9 and 10). Minor fibrosis was present in the bundle-branches and most of these patients had a partial bundle-branch block. Six patients were regarded as having histologically normal bundle-branches but had partial or intermittent block. In at least 3 of these subjects, high doses of drugs, especially digitalis, may explain the electrocardiographic abnormality. In 2 subjects minor fibrosis was observed in the right bundle; one of them had a normal electrocardiogram and the other had a total bundle-branch block.

Infarction was observed in 11 bundle-branches. The infarct was small in 6 bundles and the electrocardiograms in these subjects were normal. When the infarction was larger the patients had partial or total bundle-branch block. Vacuolated conduction fibres without distinguishable myofibrils (Fig.) were seen in 9 bundle-branches. Infarcted myocardium in the vicinity of these conduction fibres was not a constant finding. According to common morphological criteria, these changes would be regarded as signs of early recent infarction (e.g. Davies, 1967). The electrocardiograms of these patients, however, were devoid of pathological features. We were unable to explain the cause of the vacuolization of the fibre and attempts will be made

TABLE 7 Clinico-pathological correlation of changes involving sinus node and atria

Pathology	Electrocardiographic changes						Total
	Sinus rhythm	Supra-ventricular ectopic beats	Different foci	Ectopic atrial rhythm	Supra-ventricular tachycardia	Atrial fibrillation	
Normal	14	3				1	18
Fibrosis	2	2	2	3	2	3	14
Infarction				1		3	4
Total	16	5	2	4	2	7	36

with different staining methods to see whether the fibres contain excessive amounts of lipid glycogen or other substances.

One patient deviated from the general picture (separately mentioned in the Tables). On arrival at the hospital, he had an acute anterior infarction and a right bundle-branch block. The patient died 16 days after admission and during his stay in hospital no changes were observed in the electrocardiogram apart from the usual infarct alterations. At necropsy, the infarct was confirmed but the left bundle was infarcted whereas the right bundle had a normal appearance. It should be pointed out, however, that only the first few centimetres of the right bundle were studied. The possibility of changes in the distal part of the bundle cannot be excluded. The discrepancy with the left bundle, however, cannot be explained.

Discussion

The size of the infarction was measured and is given as a percentage of the left ventricular myocardium. Our method is not as objective as the one described – during preparation of this paper – by Harnarayan *et al.* (1970). Since the size of the infarction was determined in an unchanged manner during this study it is unlikely that major differences occurred between the different subjects. There was a correlation between the size of the infarction and the maximum GOT value. Six subjects, all more than 70 years, average 74 years, died from an infarction involving less than 30 per cent of the left ventricular myocardium. A generalized diffuse myocardial fibrosis was also observed – besides the infarction – in all the hearts; this fibrosis must decrease the function of the rest of the myocardium, which seems to be a reasonable explanation for the death of patients with such relatively small myocardial infarctions and also explains the increased mortality in higher age groups (Swedish cooperative study, 1971).

Pleural effusion exceeding 500 ml was observed in half of the patients. The average amount was 1150 ml, a volume which is of clinical significance. The transudate was most likely a result of congestive heart failure as these patients had received higher doses of diuretics than subjects without pleural fluid. The exact cause of the effusion is difficult to explain. It might be supposed that patients with transudate would have had large infarcts but no correlation was observed between the percentile size of the infarction and the pleural fluid. Heikkilä (1967) pointed out that mitral insufficiency due to infarction of the papillary muscles is common in myocardial infarction. In the present series infarction of the papillary muscles was observed in 6 hearts and 5 of these patients had pleural effusion. In the remaining 12 patients other factors contributed to the pleural effusion.

In an experimental study, Mellins, Levine, and Fishman (1970) found that an increase in systemic capillary pressure was of greater importance to the development of pleural effusion than a pressure increase in the pulmonary capillaries. In myocardial infarction it is

TABLE 8 Clinico-pathological correlation of changes involving AV node and His bundle

Pathology	Electrocardiographic changes					Total
	Normal	AV block			AV dissociation	
		I	II	III		
Normal	21	3†				24
Fibrosis		1			1*	2
Infarction						
Small	1					1
Moderate			1	1		2
Large						1
Vacuolated fibres	5	1*			1*	7
Total	27	5	1	1	2	36

* High doses of drugs (digitalis and/or lignocaine).

† One subject with minor bilateral changes in the bundles and one patient had received high doses of drugs.

TABLE 9 Clinico-pathological correlation of changes involving the left bundle-branch

Pathology	Electrocardiographic changes			Total
	Normal	Block partial	Total	
Normal	14	3		17
Fibrosis		5		5
Partial			2	2
Total				
Infarction				
Small	3			3
Moderate		1		1
Large	1*		2	3
Vacuolated fibres	5			5
Total	23	9	4	36

* See text.

well known that patients often have right heart failure – causing an increase in the systemic capillary pressure – as well as a low oxygen tension. Decrease in oxygen saturation increases capillary permeability favouring a development of oedema/transudate. It is possible that these two factors – right heart failure and decreased oxygen tension – are the main cause of the pleural effusion. Whatever the cause of the transudate in the present series, it indicates that great attention must be paid to the possibility of pleural fluid. Even careful clinical observation seems to be inadequate to diagnose decompensation. In this series the

TABLE 10 Clinico-pathological correlation of changes involving right bundle-branch

Pathology	Electrocardiographic changes			Total
	Normal	Block total	Inter-mittent	
Normal	21	1*	3†	25
Fibrosis				
Partial	1	1		2
Total			1	1
Infarction				
Small	2		1†	3
Moderate	—	—	—	—
Large		1		1
Vacuolated fibres	4			4
Total	28	4	4	36

* See text.

† High doses of drugs (digitalis and/or lignocaine).

FIG. (a) Bundle-branch with evident vacuolization of the fibres. No electrocardiographic abnormality. (b) Normal bundle-branch for comparison.

pulmonary x-rays, taken at varying intervals, did not show any significant difference between patients with and patients without transudate.

There was generally good agreement between electrocardiographic changes and pathological findings in the conduction system. An exception to this rule is fibrosis in the sinus node, which was observed in 14 hearts. Three of these subjects had atrial fibrillation, 2 patients had sinus rhythm, and the remaining 9 subjects had different atrial arrhythmias. This difficulty in reconciling the clinico-pathological correlation depends upon the inability to distinguish between normal and pathological fibrosis in the node. Since the increase in the fibrosis is correlated with age, it seems natural that an imperfect correlation occurs in a series of aged patients.

The series comprises 36 patients and in each heart 4 different areas of the conduction system were examined (sinus node, AV node, and the two bundle-branches). Thus, a total of 144 parts of the conduction system was investigated and in only 18 areas could recent infarction be observed. In subjects who died after a long hospital stay, fibrosis in the con-

duction system could be attributed to circulatory disturbances in connexion with the onset of the myocardial infarction. The number of infarcted areas in the conduction system might, therefore, be somewhat higher than mentioned above but still there seem to be comparatively few infarcted parts of the conduction system in connexion with recent myocardial infarction. This could be due to a high resistance of the conducting tissues to anoxia or due to a fairly good filling of the coronary vessels to that region. The latter could depend upon either asynchronism in coronary filling between ventricles and atria or an extracardial coronary anastomoses (Moberg, 1968).

In the AV node bundle-branches 14 areas of recent infarction were observed. In 7 hearts the infarcted areas were small and involved only part of the node bundle-branch. None of the patients had electrocardiographic abnormalities. This finding – a small partial necrosis of the conduction system – could not be correlated with other types of arrhythmias, e.g. asystole or ventricular fibrillation. Infarction in this region of the conduction system had to be of moderate or large size to cause changes detectable in a 12-lead electrocardiogram. Our results are in accordance with those of Davies and Harris (1969) who found that in 'control' hearts up to 50 per cent of the left bundle-branch could be replaced by fibrosis without electrocardiographic abnormalities. This emphasizes the difficulty of predicting a partial bundle-branch block by histopathological examinations but gives rise to the clinically interesting observation that the conduction system can lose part of its conduction fibres, slowly or suddenly, without causing major clinical problems.

In 16 regions of the conduction system, vacuolated conduction fibres were observed. This morphological picture – where the myofibrils seem disintegrated – is what would be expected in early recent infarction. However, in none of these patients could any changes in the electrocardiogram be observed. The cause of the vacuolated conduction fibres is unknown. For the moment one can only say that the conduction system functioned adequately in these patients.

The findings mentioned above – the small infarcts and the vacuolated fibres – indicate that only a small part of all conduction fibres

is necessary for good clinical function. The results also show that great caution is necessary when making clinico-pathological correlations of changes in the conduction system.

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