SUDDEN UNEXPECTED DEATH AS THE INITIAL MANIFESTATION OF CORONARY HEART DISEASE: CLINICAL AND PATHOLOGICAL OBSERVATIONS

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INTRODUCTION

In many areas of the world the major cause of non-traumatic sudden death (SD) is cardiovascular disease, specifically coronary heart disease (CHD). Attempts to prevent sudden death require identification of the factors associated with it. These factors need study in two groups of patients: (1) those with known CHD who suffer sudden death; (2) those whose initial manifestation of CHD was sudden death. The latter group may be designated more precisely as sudden, unexpected death (SUD) due to CHD. This report concerns the pathological findings and clinical features in residents of Rochester, Minnesota, who suffered sudden, unexpected death as the first known indication of coronary heart disease.

All deaths of residents of Rochester, Minnesota, over a 25 year period were reviewed to identify instances of coronary heart disease. Those in whom it was concluded that death was due to coronary heart disease and was sudden and un-expected form the basis for this report. Sudden death means that the interval from the apparent, onset of the fatal episode to death was one hour or less, and that there were no identi-fied symptoms of coronary (ischemic) heart disease for more than 24 hours prior to death. Unexpected death means that the patient had never had a clinical diagnosis of ischemic heart disease; thus, only patients who had seen a physician in recent years were included in the study. The families of the patients were interviewed to confirm these data and to obtain further information. The final diagnosis of death due to coronary heart disease was based upon the combination of historical factors, nature of final episode, findings of the attending physician at the terminal event, lack of any other known cause of death, and autopsy findings.

The magnitude of the problem of sudden unexpected death due to coronary heart disease is demonstrated by the fact that this was the initial manifestation of the disease in a little over 15 per cent of all patients with CHD in the 25 year study. The initial presentation of CHD was classical angina pectoris in about half of all patients and acute myo-cardial infarction in about one-third. Of the total of 2,352 patients with CHD studied, there were more males than females and SUD as the initial presentation was slightly more common in males than in females. In comparing the two decades, 1950 to 1959 and 1960 to 1969, in the 25 year time period, the proportion of instances of SUD did not change greatly although it was somewhat less in the later decade for both males and females.

Of the total of 398 instances of SUD due to CHD, 349 cases have been analyzed in detail. Autopsies had been per-formed on 286 of the 349 cases, an autopsy rate of 82 per cent. For each case, the heart, all histologic sections, and the autopsy protocol were personally reviewed. The path-ologic data is based upon our personal examination of the specimens.

The age and sex distribution of the 286 autopsied cases were similar to those of the total 349 cases (Table I). Based upon this finding and the high autopsy rate, it seemed logical to conclude that the pathologic features of the entire group were the same as those observed in the autopsied cases. There were more males by a ratio almost of 3:1. The most frequent age groups for both males and females were the sixth and seventh decades of life. The mean age for males was 58·3 years and for females was 64·4 years.

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PATHOLOGIC FINDINGS

The pathologic observations are based upon the 286 auto-psied cases. As would be anticipated, all had severe coronary artery disease (Table II). The frequency of involvement of specific arteries was similar in both males and females. The order of frequency of significant disease in the coronary arteries was left anterior descending, right coronary, left circumflex, and left main. The lattermost relatively un-commonly had significant disease. From our experience in many other studies, we define significant coronary arterial disease as greater than 50 per cent luminal stenosis. Coron-ary arterial thrombi superimposed on the significant athero-sclerotic disease were relatively infrequent even though careful search was made for them.

The myocardial findings were based upon both gross morphologic examination and histologic study by conven-tional pathologic techniques (Table III). It is recognized that more specialized histochemical and enzymatic studies probably would increase the frequency of abnormal findings. In over one-third of the cases, no ischemic myocardial lesions were found. Acute myocardial infarcts were present in 40 per cent; since this diagnosis was based upon conven-tional techniques, the onset of these episodes of infarction was prior to the last hour of life and, in most instances, prior to the last 24 hours of life. Rupture of an acute myocardial infarct had occurred in 7 per cent of the total group and this finding was statistically significantly more common in females than males. Over one-fifth of the cases had a typical scar of an old (healed) myocardial infarct. The infarcts were more frequently subendocardial than transmural in extent. Nearly 20 per cent of the group had more than one ischemic myocardial lesion.

CLINICAL FEATURES AND CORRELATIONS WITH PATHOLOGIC FINDINGS

To date, data on the risk factors of cigarette smoking, hypertension, obesity, and diabetes mellitus have been collected and analyzed (Table IV). Twelve per cent of the total of 349 patients had none of these factors whereas 56 per cent had more than one. Cigarette smoking was the most common factor in both sexes, being identified in two-thirds of all cases. It was significantly more common in males than females. Hypertension, present in over one-third of all cases, was significantly more frequent in females. Hypertension was defined as blood pressures of 160/95 or greater. Obesity was defined in a rather restrictive way and even so was present in about 40 per cent of the cases. Nine per cent of individuals were found to have had diabetes mellitus.

The presence or absence of these risk factors in relation to the pathologic findings in the 286 autopsied cases was examined (Table V). Thirty-four of the 286 (12 per cent) did not have any of these risk factors, which is the same percentage as the entire group. The average age at death was 3·7 years greater for the no risk-factor group (61·9 vs. 58·2 years). Relatively more males made up the no risk-factor group (M:F=4.7:1) than the risk-factor group (M:F=2.81). Coronary thrombi were somewhat more com-mon in the patients with risk factors and the scars of old infarcts were statistically significantly more frequent in this group.

Examination of the individual risk factors in relation to the pathologic findings (Table VI) showed that smoking was associated with slightly younger age at death then hyper-tension, obesity, or the total group. Relatively more males were in the smoking group and relatively more females in the hypertension group. Coronary arterial thrombi seemed slightly more frequent in smokers who also had more in-stances in which no ischemic myocardial lesion was found.

TABLE I

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Age and Sex Distribution

Age, yr.	All patients			Autopsy cases (82%)		
	M	F	Total	M	F	Total
20 - 29	1	0	1	1	0	1
30 - 39	6	1	7	6	1	7
40 - 49	33	4	37	30	4	34
50 - 59	99	22	121	86	19	105
60 - 69	96	51	147	82	39	121
>70	17	19	36	8	10	18
TOTAL	252 (75%)	97 (25%)	349	213 (74%)	73 (26%)	286
Mean age, yr	58·3	64·4	59·9	57·5	62·3	58·7

TABLE II

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Coronary Artery Disease

Artery	% of cases		
	Males (213 cases)	Females (73 cases)	Total (286 cases)
Left anterior descending	97	92	96 (9*)
Right coronary	80	78	79 (8*)
Left circumflex	67	64	66 (2*)
Left main	37	26	34 (0*)

* % with coronary thrombi.

TABLE III

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Myocardial Pathology

Myocardial infarct	% of cases		
	Males (213 cases)	Females (73 cases)	Total (286 cases)
None	39	33	38
Acute	41 (4*†)	37 (15*†)	40 (7*)
Old (scar)	20	30	22
More than one	18	20	19
Transmural	12	20	14
Subendocardial	49	47	48

* % of total group with ruptured acute myocardial infarct.
†Significant difference between sexes (P <0·05).

TABLE IV

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Identified Risk Factors

Factor	% of patients		
	Males (252 pts.)	Females (97 pts.)	Total (349 pts.)
None	14	8	12
Cigarette smoking*	69†	53†	65
Hypertension	26†	61†	36
Obesity	41	46	43
Diabetes mellitus	9	9	9
More than one of above	53	63	56

*Current smokers.
†Significant difference between sexes (P <0·05).

TABLE V

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Pathologic Findings and Risk Factors*

	No risk factor (34 cases)	One or more risk factors (252 cases)
Average age at death, yr.	61·9	58·2
Ratio of males to females	4·7:1	2·8:1
Coronary thrombi, %	9	19
Myocardial infarct, %		
None	47	37
Acute	44 (3‡)	39 (7‡)
Old (scar)	9†	24†
Transmural	15	13
Subendocardial	38	50

*Cigarette smoking, hypertension, obesity, and diabetes mellitus.
†Significant difference between groups (P <0·05).
‡% of total group with ruptured acute myocardial infarct.

TABLE VI

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Pathologic Findings and Risk Factors

	Smoking (55 cases)	Hypertension (18 cases)	Obesity (14 cases)	Total group (286 cases)
Average age at death, yr.	55·7	64·7	67·8	58·7
Ratio of males to females	6·9:1	1:1·3	3·7:1	2·9:1
Coronary thrombi, %	29	11	7	18
Myocardial infarct, % None	56	28	36	38
Acute	31 (2*)	39 (22*)	57 (7*)	40 (7*)
Old (scar)	13	33	7	22
Transmural	11	22	7	14
Subendocardial	33	50	57	48

*% of total group with ruptured acute myocardial infarct.

TABLE VII

SUDDEN UNEXPECTED DEATH DUE TO CORONARY HEART DISEASE
Pathologic Findings and Risk Factors*

	S & H (38 cases)	H & O (22 cases)	S & O (53 cases)	Total group (286 cases)
Average age at death, yr.	57·4	63·2	58·2	58·7
Ratio of males to females	2·5:1	1:1·4	7·8:1	2·9:1
Coronary thrombi, %	24	9	19	18
Myocardial infarct, % None‡	16	18	55	38
Acute	39 (13†)	37 (5†)	38 (2†)	40 (7†)
Old (scar)‡	45	45	7	22
Transmural	21	9	4	14
Subendocardial‡	63	73	41	48

*Cigarette smoking (S), hypertension (H), and obesity (O).
†% of total group with ruptured acute myocardial infarct.
‡Significant difference between groups (P <0·05).

The type of ischemic myocardial lesions present did not correlate clearly with these risk factors.

The risk factors were considered in various combinations and related to the pathologic features (Table VII). The combinations considered were smoking-hypertension, hypertension-obesity, and smoking-obesity. No marked differences in age at death were apparent among these groups. Males were relatively more frequent in the smoking-obesity group. The finding of no ischemic myocardial lesion was statistically significantly more common in the smoking-obesity risk factor combination and, as an apparent corollary to this observation, scars of old infarcts were uncommon in these cases. Subendocardial infarction was significantly more common in the smoking-hypertension and hypertension-obesity groups than in the other combination or the total series.

SUMMARY

Clinical-pathological correlative study of 349 instances of sudden unexpected death as the initial manifestation of coronary heart disease showed the following:

1. One or more of the risk factors of smoking, hypertension, obesity, and diabetes mellitus were present in 88 per cent of cases. Smoking was more common in males and hypertension was more common in females.

2. Severe coronary artery disease was present in all. The order by frequency of involvement of specific arteries was left anterior descending, right, and left circumflex coronary arteries. Coronary arterial thrombi were identified in 18 per cent.

3. Ischemic myocardial lesions were present in 62 per cent of the cases. More than one such lesion was found in 19 per cent. The lesions were acute infarct in 40 per cent, scar of an old infarct in 22 per cent, transmural infarcts in 14 per cent, and subendocardial infarcts in 48 per cent. Seven per cent of acute infarcts had ruptured.

4. The group with one or more of the risk factors had more coronary arterial thrombi and more old infarcts (scars). The no risk-factor group had relatively more men than women and was slightly older.

5. Smoking was more common among men and was associated with coronary arterial thrombi and an absence of myocardial lesions.

6. Hypertension was more common among women and was associated with ruptured acute infarct, more transmural infarcts and more old infarcts.