Electrocardiography (ECG)

BRHS Baseline examination 1978-80 (Q1)

Electrocardiography 1978-80 (Q1)

Included in the clinical measurements made at the baseline physical examination in 1978–1980 (Q1) was a resting electrocardiogram which was carried out using three orthogonal leads, as derived from the modified axial lead system.

Details of the methods used are described in the following two publications:

References

1. Shaper AG, Cook DG, Walker M, Macfarlane PW. Prevalence of ischaemic heart disease in middle aged British men. British Heart Journal 1984; 51(6): 595-605. (Appendix 1)

2. Whincup PH, Wannamethee G, Macfarlane PW, Walker M, Shaper AG. Resting electrocardiogram and risk of coronary heart disease in middle-aged British men. Journal of Cardiovascular Risk 1995; 2(6):533-543. (Appendix 2)

BRHS Baseline 1978-80 (Q1) ECG variables

Variable Description		Category labels/units	BRHS VARIABLE NAME	Method
Heart Rate		39-145, 999=missing	q1ECG_heart_rate	
Rhythm		0-53, 99=missing	q1ECG_rhythm	see Refs
		Arrythmia diagnoses		
Code	P?	PRINT OUT		
0		SINUS RHYTHM		
1		PROBABLE SINUS RHYTHM		
2		SINUS ARRHYTIMIA		
3	x	ATRIAL FIBRILLATION		
4	x	ATRIAL FIBRILLATION & VENTRICULAR EXTRASYSTOLES		
5	x	PROBABLE ATRIAL FIBRILLATION		
6		SINUS RHYTHM & SUPRAVENTICULAR EXTRASYSTOLES		
7		SINUS RHYTHM & VENTRICULAR EXTRASYSTOLES		
10	x	ATRIAL FIBRILLATION WITH COMPLETE HEART BLOCK		
11		ATRIAL TACHYCARDIA WITH VARYING BLOCK		
12	x	RECIPROCAL RHYTHM		
		SECOND DEGREE N:1 CONSTANT A-V BLOCK		
	x	THIRD DEGREE COMPLETE A-V BLOCK		
	x	JUNCTIONAL RHYTHM		
16		CORONARY SINUS RHYTHM		
17	x	SUPRAVENTICULAR TACHYCARDIA		
20	x	VENTRICULAR TACHYCARDIA		
21		SECOND DEGREE A-V BLOCK WITH DROPPED BEATS		
22	x	SECOND DEGREE A-V BLOCK WITH WENCKEBACH PERIODS		
23		ATRIAL TACHYCARDIA WITH N:1 BLOCK		
24		WANDERING SINUS PACEMAKER		
25	x	ACCELERATED INIOVENTICULAR RHYTHM		
26	x	ATRIAL FLUTTER WITH N:1 BLOCK		
27	x	A-V DISSOCIATION		
30		SINUS RHYTHM & VENTICULAR ESCAPE BEATS		
31		SINUS RHYTHM & SUPAVENTRICULAR ESCAPE BEATS		

Rhythm codes / cont.				
Variable Description / cont.		**Category labels/units**	**BRHS VARIABLE NAME**	**Method**
32	x	ATRIAL FLUTTER WITH VARYING BLOCK BIGEMINAL RHYTHM ATRIAL FLUTTER WITH COMPLETE BLOCK ATRIAL TACHYCARDIA & COMPLETE BLOCK		
36 37 40 41 42 43 44 45 46 47 50 51 52	x x x	ATRIAL FLUTTER & VENTRICULAR EXTRASYSTOLES ATRIAL FIBRILLATION & A-V DISSOCIATION PROBABLE ATRIAL FIBRILLATION & VENTRICULAR EXTRASYSTOLES COUPLED ATRIAL EXTRASYSTOLES SECOND DEGREE SINO-ATRIAL BLOCK WITH DROPPED BEATS SINUS RHYTHM & ATRIAL EXTRASYSTOLES PACEMAKER UNCLASSIFIED ARRHYTHMIA PROBABLE SINUS ARRHYTIMIA SINUS RHYTHM & INTERPOLATED VENTRICULAR EXTTRASYSTOLES SINUS RHYTHM & ABERRANTLY CONDUCTED SUPRAVENTRICULAR EXTRASYSTOLES PROBABLE SINUS RHYTHM & ATRIAL EXTRASYSTOLES ATRIAL FLUTTER EQUIVOCAL ST JUNCTIONAL DEPRESSION = BOX 26 AS 1		
PR Interval		1=short 2=normal 3=prolonged 9=missing	q1ECG_PR_Interval	see Refs
Myocardial Infarction Type - X anterolateral		1= acute 2= old 3= possible 4= unspecified 9= missing, 0= ?	q1ECG_MI_x_anteroL	see Refs
Myocardial Infarction Type - Y inferior		1= acute 2= old 3= possible 4= unspecified 9= missing	q1ECG_MI_y_inferior	see Refs

Variable Description / cont.		Category labels/units	BRHS VARIABLE NAME	Method
Myocardial Infarction Type - Z anteroseptal		1= acute 2= old 3= possible 4= unspecified 9= missing	q1ECG_MI_z_anteroS	see Refs
Myocardial Ischaemia Type		1= consistent with MI 2= suggestive of MI 3= equivocal of MI 4= unspecified 9= missing	q1ECG_MIsch_Type	
Myocardial Ischaemia Type - leads		1= anterolateral X 2= Y inferior 3= Z anteroseptal 4= X & Y inferolateral 5= X & Z anterior 6= Y & Z inferior & anteroseptal 7= X, Y, & Z widespread 9=missing	q1ECG_MIsch_Leads	see Refs
Left Venticular Hypertrophy(LVH)		4= possible 4 points 5= probable, 5 points 6= definite > 6 points 7= unspecified 9=missing 0=? Data entry error?	q1ECG_LVH	see Refs
Right Venticular Hypertrophy(RVH)		4= possible 4 points 5= probable, 5 points 6= definite > 6 points 7= unspecified 9=missing	q1ECG_RVH	see Refs
Bi Venticular Hypertrophy		4= possible 4 points 5= probable, 5 points 6= definite > 6 points 7= unspecified 9=missing	q1ECG_BIVH	see Refs

Variable Description / cont.		Category labels/units	BRHS VARIABLE NAME	Method
Conduction Defects		1= LBBB 2= RBBB 3= Incomplete RBBB 4= IVCD 5= WPW 6= Left anterior hemiblock 9= missing	q1ECG_CD	see Refs
ST Segment Changes		1= Non Specific ST changes 2= Moderate ST elevation 3= Marked ST segment displacements 4= 1&2 5= 1&3 9 = missing	q1ECG_ST_Seg_change	see Refs
AXIS - deviation		1= Right axis deviation (RAD) 2= Left axis deviation (LAD) 9= missing	q1ECG_Axis_Dev	see Refs
AXIS - Cardiac rotation		1= Clockwise cardiac rotation 2= Counter Clockwise cardiac rotation 9= mizssing	q1ECG_Axis_CRotation	see Refs
Atrial Abnormalities		1= Atrial Hypertrophy 2= Atrial Abnormality 3= P pulmonale 4= 1 & 3 9=missing	q1ECG_Atrial_Abnormal	see Refs
Miscellaneous		1= Large T wave amplitudes 2= Low Voltage complexes 9= missing	q1ECG_Miscel	see Refs
QT Interval		1=short 3=prolonged 9=missing	q1ECG_QT_Int	see Refs

Variable Description / cont.		Category labels/units	BRHS VARIABLE NAME	Method
Normal		1= Normal 2= Abnormal 9=missing	q1ECG_Normal	see Refs
12 Lead ECG		1= Coded from 12-lead ECG 9=missing, 0=? Possibly a data entry error?	q1ECG_12Lead_ECG	see Refs

MI or Ischaemia grade using ECG Minnesota codes

Derived variables Description/cont.	Value label	BRHS Variable name	Method
MI or Ischaemia grade using Minnesota codes from ECG	1 = None 2 = Possible Ischaemia 3 = Definite Ischaemia 4 = Possible MI 5 = Definite MI	q1ECG_mish	See derivation below

1. Derivation method of q1ECG_mish

Code	Meaning	Definition
1	None	
2	Possible Ischaemia	coded 2 or 3 in Myocardial Ischaemia Type (*q1ECG_MIsch_Type*) or coded 1(LBBB) in Conduction Defects (q1ECG_CD)
3	Definite Ischaemia	coded 1 in Myocardial Ischaemia Type (*q1ECG_MIsch_Type*)
4	Possible MI	coded 3 in Myocardial Infarction Type - X anterolateral, Myocardial Infarction Type - Y inferior, Myocardial Infarction Type - Z anteroseptal. (q1ECG_MI_x_anteroL, q1ECG_MI_y_inferior, q1ECG_MI_z_anteroS)
5	Definite MI	coded 1 or 2 or 4 in Myocardial Infarction Type - X anterolateral, Myocardial Infarction Type - Y inferior, Myocardial Infarction Type - Z anteroseptal. (*q1ECG_MI_x_anteroL, q1ECG_MI_y_inferior, q1ECG_MI_z_anteroS*)

A hierarchy was imposed so that a man with both definite MI and definite Ischaemia is coded to the higher code, definite MI

2. ECG methods

References

1. ***Shaper AG, Cook DG, Walker M, Macfarlane PW. Prevalence of ischaemic heart disease in middle aged British men. British Heart Journal 1984; 51(6): 595-605. (Appendix 1)***

2. ***Whincup PH, Wannamethee G, Macfarlane PW, Walker M, Shaper AG. Resting electrocardiogram and risk of coronary heart disease in middle-aged British men. Journal of Cardiovascular Risk 1995; 2(6):533-543. (Appendix 2)***

"Each man had a resting electrocardiogram carried out using three orthogonal leads, as derived from the modified axial lead system [14]. The signals were recorded on electromagnetic tapes that were analysed by computer in the Department of Medical Cardiology in Glasgow. On occasions when technical problems occurred (400 cases), a 12-lead electrocardiogram was recorded using a Hewlett-Packard 151 5B (Boise, Idaho, USA) machine and referred for visual analysis.

Interpretation of electrocardiograms

Details of the criteria used for interpreting the orthogonal three-lead electrocardiogram have been published elsewhere [15-17]. The validity of the method in comparison with the standard 12-lead electrocardiogram has been reported [18]. The definitions of abnormalities using this system of classification and their relationships to the Minnesota Code [10] are outlined below. In the present study myocardial ischaemia and infarction are treated as exclusive categories, so that each subject can appear only once in the analysis. The diagnosis of myocardial infarction is made on the basis of a broad Q wave in any lead together with a Q : R amplitude ratio greater than 1 : 3 if the Q wave is in the anterolateral (X) or inferior (Y) leads. The division into definite and possible myocardial infarction depends on the width of the Q wave and the magnitude of the Q : R amplitude ratio. The Minnesota Code classifies Q and QS patterns for three sites: inferior, anteroseptal and anterolateral. These sites equate closely to the three orthogonal leads used in the present system: X for anterolateral, Y for inferior and Z for anteroseptal. Definite myocardial infarction in the present study equates closely with Minnesota Codes 1-1 and 1-2-1 to 1-2-6. Possible myocardial infarction in the present study equates with Minnesota codes 1-2-7, 1-2-8 and 1-3.

A combination of ST segment depression and T wave changes (negativity or low positivity) in the three-lead electrocardiogram is used to report myocardial ischaemia. Although the Minnesota Code treats the S segment and T wave separately, there are considerable similarities between the methods. However, the degree of ST junctional depression required for definite abnormality by the Minnesota Code (in excess of 0.1 mV) is greater than that required by the three-lead system (0.06 mV), which, however, also requires the ST segment to be flat or downward sloping. Thus a three-lead electrocardiogram showing definite myocardial ischaemia equates with Minnesota Codes 4-1 or 5-1, while those three-lead electrocardiographic appearances regarded as possible myocardial ischaemia equate with Minnesota Codes 4-1, 4-2, 5-2 and 5-3.

The diagnosis of ventricular hypertrophy was made on the basis of R wave amplitude, ST-T abnormalities and abnormal QRS vector orientation. A scoring system was used 1171, with six points representing definite hypertrophy and four to five points representing possible or probable hypertrophy. Definite left ventricular hyper- trophy equates with Minnesota Code 3-1, while possible or probable hypertrophy equates with Code 3-3. Right ventricular hypertrophy equates with Minnesota Code 3-2; possible and probable right ventricular hypertrophy have no Minnesota Code equivalent. Diagnosis of left ventricular strain was based on the presence of ST depression in lead X of at least 0.06niV accompanied by T wave inversion in excess of 0.1 mV. Conduction defects are consistent in the 3- and 12-lead systems. Left bundle branch block corresponds to Minnesota Code 7-1-1, while right bundle branch block corresponds to 7-2-1 and incomplete right bundle branch block to 7-3. Intraventricular conduction defect is equivalent to 7-4, while left anterior hemiblock corresponds to 7-7.

Left axis deviation was defined as a QRS frontal axis between + 240 and + 360 degrees, right axis deviation as a QRS frontal axis between + 75 and + 180 degrees.

ST elevation corresponds to STj > 0.1 mV and ST mid-point >0.08 mV in leads X or Y; tall T waves correspond to a T vector magnitude >0.80mV or a T wave > 0.50 mV in lead Z.

All QT intervals were corrected for heart rate. Prolongation was defined as a QTc interval > 0.43 s and shortening as a QTc interval <0.30s, occurring in all leads.

Arrhythmias were diagnosed using a complex diagnostic tree, and were then checked by an experienced electro-cardiographer. Sinus rhythm, coronary sinus rhythm and sinus arrhythmia were all accepted as normal rhythms.[1] "

Br Heart J 1984; 51: 595–605

Prevalence of ischaemic heart disease in middle aged British men

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SUMMARY The prevalence of ischaemic heart disease was determined by an administered questionnaire and electrocardiography in 7735 men aged 40–59 years drawn at random from general practices in 24 British towns. Overall, one quarter of these men had some evidence of ischaemic heart disease on questionnaire or electrocardiogram or both. On questionnaire, 14% of men had possible myocardial infarction or angina, with considerable overlap of the two syndromes. The prevalence of possible myocardial infarction combined with angina and of definite angina only showed a fourfold increase over the age range studied.

Electrocardiographic evidence of ischaemic heart disease (definite or possible) was present in 15% of men, there being myocardial infarction in 4·2% and myocardial ischaemia in 10·3%. Electrocardiographic evidence of myocardial infarction increased fourfold over the age range studied. There was considerable overlap of questionnaire and electrocardiographic evidence of ischaemic heart disease. Nevertheless, more than half of those with possible myocardial infarction combined with angina had no resting electrocardiographic evidence of ischaemic heart disease, and half of those with definite myocardial infarction on electrocardiogram had no history of chest pain at any time. This national population based study strongly suggests that the prevalence of ischaemic heart disease in middle aged British men is greater than has been indicated by previous studies based on occupational groups.

Ischaemic heart disease is a major cause of incapacity and death in middle aged and elderly men and women in Great Britain. There are reasonably sound data on deaths due to ischaemic heart disease[1] but less information regarding its prevalence—that is, the proportion of people in the community with symptoms or signs of ischaemic heart disease or both. Several major prevalence studies of ischaemic heart disease have been carried out, usually based on one geographic area[2] and often restricted to one occupational group.[3] It is difficult to generalise from such studies to the British population at large, as there are considerable geographic and socioeconomic variations in cardiovascular disease mortality.[4–6] Information from heart attack registers suggests that these variations affect non-fatal as well as fatal ischaemic heart disease events, and thus the prevalence of the disease is likely to show as much geographic variation as its mortality.[7,8] The British Regional Heart Study is concerned with such geographic variations in cardiovascular disease and includes a survey of middle aged men in 24 British towns.[9,10] The present report, based on the findings of this study, describes the overall prevalence of ischaemic heart disease as determined by an administered questionnaire and electrocardiography. A companion report (p 606) analyses the ability of subjects in this study to recall a diagnosis of ischaemic heart disease made by a doctor.[11] Further reports will deal with the effects of social class and town of residence on the prevalence of ischaemic heart disease and with the relation between its prevalence and those factors which might contribute to the development of the disorder.

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Subjects and methods

The British Regional Heart Study includes 7735 men aged 40–59 years randomly selected from the age-sex

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registers of group general practices in 24 towns in England, Wales, and Scotland. The criteria for selecting the town, the general practice, and the subjects, as well as the methods of data collection, have been reported previously.[10] In brief, the 24 towns were primarily selected from those with populations of 50 000–100 000 (1971 Census). They were chosen to represent the full range of cardiovascular disease mortality and included towns in all the major standard regions. The general practice selected in each town was required to have a social class distribution representative of the men of that town.

From each age-sex register some 420 men aged 40–59 years were selected at random to produce five-year age groups of equal size. The list of names was reviewed by the doctors in the practice, who were asked to exclude those whom they considered could not participate because of severe mental or physical disability. It was emphasised that no attempt should be made to exclude subjects with cardiovascular problems, and close scrutiny of the returned annotated lists reduced the exclusions to approximately 6 to 10 per practice. The remaining subjects were invited to take part in the study in a letter signed by their general practitioner, and on average 78% of those invited attended for examination.

A mobile research team of three nurses administered to each man an extensive questionnaire which included questions on chest pain and medical history. The questions on chest pain were based on the WHO questionnaire,[12] but they are not identical. Copies of the questionnaire are available on request. Electrocardiograms were recorded in analogue form on magnetic tape using the three orthogonal leads as derived from the modified axial lead system.[13] They were simultaneously reviewed on an oscilloscope in order to detect major acute abnormalities, which were reported to the general practitioner. The completed tapes for each town were sent to the collaborating centre in Glasgow for replay to a computer system for analysis and interpretation.[14 15] On those occasions (n=400) when technical problems occurred with the recording 12 lead electrocardiograms were obtained on a Hewlett Packard (1515-B) machine and sent to the centre for visual analysis.

TERMINOLOGY

The prevalence of ischaemic heart disease was measured in several ways in this study. In order to make it clear which method is being referred to at any particular time the suffixes (Q) and (ECG) are used whenever necessary to refer respectively to the questionnaire on chest pain and to the electrocardiographic findings. Each of these two methods of determining prevalence has a variable level of certainty, which may be expressed by terms such as "definite" or "possible." As the clinical diagnosis of angina is based on symptoms it seems reasonable to apply these two grades of diagnostic certainty to the information elicited by administered questionnaire. On the other hand, the diagnosis of myocardial infarction is usually based on symptoms or signs or both (for example, enzyme response, electrocardiographic changes), and it thus seems inappropriate to use the term "definite myocardial infarction" when referring purely to a response to a question about prolonged severe chest pain. We, therefore, use the term "possible myocardial infarction (Q)" for the category of greatest certainty. This is well established in epidemiological use.[12] In electrocardiography, where precise measurements and criteria are used, it is reasonable to use the terms "definite" and "possible." Definite angina (Q) and possible angina and myocardial infarction (Q) may be combined as ischaemic heart disease (Q). The electrocardiographic findings of myocardial infarction (definite or possible) and myocardial ischaemia (definite or possible) may be combined as ischaemic heart disease (ECG). The term "ischaemic heart disease" without a suffix is used in the general sense.

CRITERIA AND CATEGORIES

Myocardial infarction (Q)

Possible myocardial infarction (Q)—Subjects were regarded as having had a possible myocardial infarction if (*a*) they answered yes to "Have you ever had a severe pain in your chest lasting for half an hour or more?" and (*b*) the distribution of pain included positions 4 or 5 or 8 (Fig. 1). They were also asked whether they had seen a doctor because of this pain.

Other prolonged severe chest pain—The subject answered yes to the above question, but the distribution of the pain did not include position 4 or 5 or 8. They

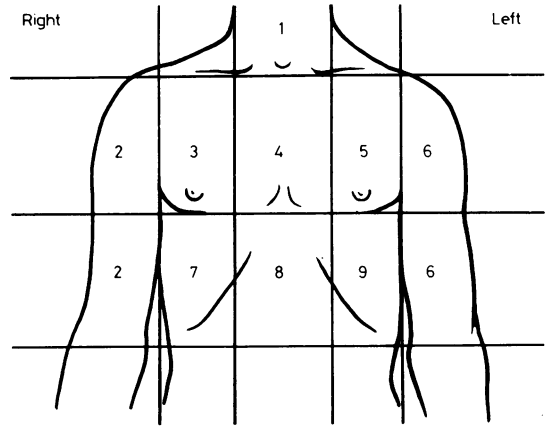

Fig. 1 *Diagram showing sites of chest pain.*

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were also asked whether they had seen a doctor because of this pain.

No prolonged severe chest pain.

Angina (Q)

Definite angina (Q)—The questions relating to angina followed the inquiry into severe chest pain. Subjects were regarded as having definite angina if they answered yes to (*a*) "Do you ever have any pain or discomfort in your chest?" and (*b*) "When you walk uphill or hurry, does this produce pain?"; in addition, four additional criteria had to be satisfied: (i) the distribution of pain included position 4 or 5 or 8; (ii) the subject slowed down or stopped walking when the pain occurred; (iii) the pain went away if he stood still and (iv) did so in less than 10 minutes. These criteria denote definite angina grade 1. If, in addition, the chest pain was produced by walking at an ordinary pace on the level it was regarded as grade 2. Four subjects with chest pain on the level, but not on walking uphill or hurrying, were included in grade 1 as they satisfied all the four additional criteria.

Possible angina (Q)—Chest pain was present on exertion (walking uphill or hurrying) but did not fulfil all four of the additional criteria. Possible angina was also separated into grades 1 and 2. Nine of these subjects said they had chest pain on the level but not on walking uphill or hurrying and were included in grade 1.

Chest pain (not on exertion)—The subject answered yes to the question "Do you ever have any pain or discomfort in your chest?" but it was not related to exertion.

No chest pain.

Electrocardiogram

Details of the criteria used in interpreting the three orthogonal lead electrocardiogram have already been published.[14-16] In the following sections an explanation is given of the system of classification used in this study, and an outline is offered of possible relations between this system and the Minnesota Code,[12] which is widely used for classifying the 12 lead electrocardiogram. It must be emphasised that the comparison can be only an approximation. For the purposes of this study, a system of exclusive categories is used in ranking order so that each man can appear once only in the analysis of findings.

Myocardial infarction (ECG)—In the three orthogonal lead electrocardiogram the diagnosis of myocardial infarction is made on the basis of a broad Q wave in any of the leads together with a Q : R amplitude ratio greater than 1/3 if the Q wave is in the anterolateral (X) or inferior (Y) leads. The anteroseptal (Z) lead of the three orthogonal lead electrocardiogram in this system should be considered equivalent to lead V2 or V3. Q and QS patterns are expressed as definite or possible myocardial infarction, depending on the width of the Q wave and the magnitude of the Q : R amplitude ratio. The Minnesota Code classifies Q and QS patterns using varying criteria for anterolateral, inferior, and anterior sites. These equate almost on a one-to-one basis with the three orthogonal lead electrocardiogram—namely, X anterolateral, Y inferior, and Z anteroseptal. If changes occur in leads X and Z the infarct is regarded as anterior. In this study definite myocardial infarction (three lead) equates essentially with Minnesota Code 1.1 and most of 1.2 (1.2.1 and 1.2.2). Possible myocardial infarction (three lead) basically equates with Minnesota Code 1.2.7/8 and 1.3.

Myocardial ischaemia (ECG)—A combination of ST segment and T wave changes in the three lead electrocardiogram is used to report myocardial ischaemia. Although the Minnesota Code treats the ST segment and T wave separately, there are considerable similarities between the three and 12 lead coding schemes. As with infarction, three basic areas are identified, and the degree of certainty of diagnosis is related either to the amount of ST depression or to the extent of T wave negativity or low positivity. The major difference between the system would be that the Minnesota Codes 4.1 and 5.1 require more ST depression or T wave negativity to be present than the criteria used for the three orthogonal lead electrocardiogram. For example, Minnesota Code 4.1.2 requires ST junctional depression in excess of 0·1 mV, whereas the three orthogonal lead system requires ST depression in excess of 0·06 mV for a report of definitely abnormal ST segment, in addition to requiring the ST segment to be flat or downward sloping. Thus a three lead electrocardiogram regarded as showing definite myocardial ischaemia equates with Minnesota Code 4.1 or 5.1, whereas those three lead electrocardiographic appearances regarded as possible myocardial ischaemia equate with Minnesota Codes 4.1, 4.2, 5.2, and 5.3.

Other categories—These are not dealt with in detail in this report. The major conduction defects correspond completely in the three orthogonal and the 12 lead electrocardiograms. In the present study the presence of left bundle branch block is regarded as evidence of possible myocardial ischaemia. Atrial fibrillation and certain atrioventricular conduction defects are not regarded as evidence of myocardial ischaemia, although this has been done in some other studies. Ventricular hypertrophy is not regarded as evidence of ischaemic heart disease and will be reported in detail in later publications concerned with blood pressure and hypertension. T wave abnormalities occurring in the anterolateral lead X in the presence of left ventricular hypertrophy (that is, the so called left ven-

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tricular strain pattern) were subsumed in the electrocardiographic diagnosis of left ventricular hypertrophy and not reported separately as "myocardial ischaemia."

Results

POSSIBLE MYOCARDIAL INFARCTION (Q)

A history of prolonged severe chest pain in an appropriate site, such as might occur in acute myocardial infarction, was recorded in 706 men—that is, 9·1% of all men had possible myocardial infarction (Q). A similar chest pain occurring in an inappropriate site, predominantly site 9, was recorded in a further 80 men—that is, 1·0% of all men.

ANGINA (Q)

One third (2582) of the men admitted to having chest pain at some time, and in one quarter (607) of these the chest pain was related to exertion (Fig. 2). Definite angina was present in 367 men (307 grade 1, 60 grade 2)—that is, 4·8% of all men. Possible angina was present in a further 240 men (205 grade 1, 35 grade 2)—that is, 3·1% of all men. Two thirds of those with possible angina (158/240) satisfied three of the four additional criteria. In both definite and possible categories there were five to six times as many men with grade 1 as with grade 2 angina.

POSSIBLE MYOCARDIAL INFARCTION (Q) AND ANGINA (Q)

It was possible for the men to respond independently to the questions on possible myocardial infarction and angina, and Table 1 shows the relation between responses to these two areas of inquiry.

The men with a history of possible myocardial infarction were far more likely to have angina (definite or possible) than those with no such history (31% *v* 5%). Those with "other" severe chest pain—that is, in an inappropriate site—had an intermediate frequency of angina (14%). Similarly, men with angina (definite or possible) were far more likely to have a history of possible myocardial infarction than those with no chest pain (32–47% *v* 6%). Those with non-exertional chest pain had a frequency of possible myocardial infarction (9%) similar to that seen in men without angina. It is important to note that men with possible angina have rates of possible myocardial infarction similar to those observed in men with definite angina. Overall, 1094 (14·2%) men had some evidence of ischaemic heart disease on questionnaire, and Table 2 summarises the information in Table 1.

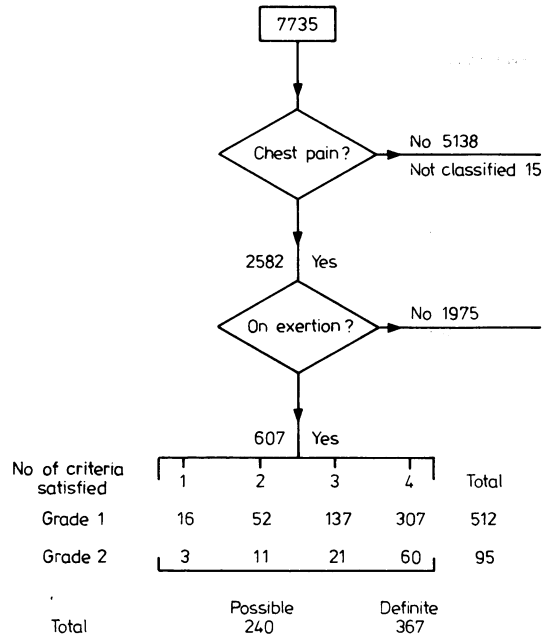

Fig. 2 *Flow chart showing response to questions on chest pain (angina) from 7735 subjects.*

ELECTROCARDIOGRAPHIC EVIDENCE OF ISCHAEMIC HEART DISEASE

The exclusive ranking system of determining the elec-

Table 1 *Relation between angina (Q) and possible myocardial infarction (Q). Figures are numbers of subjects*

Questionnaire categories	*Possible myocardial infarction*	*"Other" severe chest pain*	*No severe chest pain*	*Total No*	*% With possible myocardial infarction*
Definite angina					
Grade 2	28	0	32	60	47
Grade 1	109	2	196	307	36
Possible angina					
Grade 2	14	2	19	35	40
Grade 1	65	7	133	205	32
Chest pain (not on exertion)	181	24	1770	1975	9
No chest pain	306	45	4786	5137	6
Total	703	80	6936	7719*	9
% With angina (definite/possible)	31	14	5	8	—

*Data missing on possible myocardial infarction in one subject and on angina in 15.

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Table 2 *Ischaemic heart disease on questionnaire and electrocardiography*

	No	%
Questionnaire		
Possible myocardial infarction and angina*	216	2·8
Possible myocardial infarction only	487	6·3
Angina only		
Definite	230	3·0
Possible	161	2·1
Ischaemic heart disease (Q)	1094	14·2
Electrocardiography†		
Myocardial infarction		
Definite	242	3·1
Possible	86	1·1
Myocardial ischaemia		
Definite	257	3·3
Possible	541	7·0
Ischaemic heart disease (ECG)	1126	14·6

*Definite or possible.
†ECG evidence missing for eight subjects

trocardiographic status of each man (see methods) means that each individual can appear in only one category. Overall, 1126 (14·6%) men were regarded as having evidence of ischaemic heart disease on the electrocardiogram (Table 2). Nineteen men with left bundle branch block are included in "possible myocardial ischaemia."

ELECTROCARDIOGRAPHIC AND QUESTIONNAIRE EVIDENCE OF ISCHAEMIC HEART DISEASE

There is considerable overlap between the electrocardiographic findings and the prevalence of possible myocardial infarction (Q) and angina (Q). Table 3 shows the proportion of those with symptoms of ischaemic heart disease on questionnaire who have electrocardiographic evidence of ischaemic heart disease. Those with possible myocardial infarction combined with angina (Q) have the highest rate of electrocardiographic abnormalities (45%), but even in this group of men, who are likely to have severe atherosclerosis and ischaemic heart disease, more than half have no resting electrocardiographic evidence of ischaemic heart disease. Men with possible myocardial infarction (Q) only, definite angina (Q) only, or possible angina (Q) only have similar rates of ischaemic heart disease (ECG). Men with "other chest pain" (non-exertional chest pain or prolonged severe chest pain in an inappropriate site) have the same frequency of ischaemic heart disease (ECG) as those with "no chest pain."

Table 3 also shows the proportion of those with electrocardiographic abnormalities who have symptoms of ischaemic heart disease on administered questionnaire. Of those with definite myocardial infarction (ECG), 51% have a history of ischaemic heart disease (Q)—that is, almost half of these men give no history of severe chest pain at any time or of angina. The men with other electrocardiographic abnormalities (possible myocardial infarction, definite or possible myocardial ischaemia) have lower rates of positive response to the questionnaire. From the data in Table 3, it can be calculated that men with any electrocardiographic evidence of ischaemic heart disease are more than twice as likely to respond positively to the chest pain questionnaire as those with no electrocardiographic evidence of ischaemic heart disease (315/1124 (28%) *v* 778/6587 (12%)).

OVERALL PREVALENCE OF ISCHAEMIC HEART DISEASE

From the detailed information in Table 3 a number of diagnostic categories relevant to the prevalence of ischaemic heart disease may be derived. At the one extreme there is a group of 49 men with definite myocardial infarction (ECG) together with question-

Table 3 *Relation between the evidence for ischaemic heart disease (IHD) on electrocardiography and on questionnaire. Figures are numbers of subjects*

Questionnaire	*Electrocardiography*							
	Myocardial infarction		*Myocardial ischaemia*		*IHD (ECG)*	*No IHD (ECG)*	*Total*	*% With IHD (ECG)*
	Definite	*Possible*	*Definite*	*Possible*				
Possible MI and angina	49	7	24	18	98	118	216	45
Possible MI only	53	7	31	29	120	366	486	25
Definite angina only	13	4	12	31	60	170	230	26
Possible angina only	9	2	9	17	37	124	161	23
Other chest pain	33	18	55	111	217	1619	1836†	12
No chest pain	85	48	126	333	592	4190	4782	12
Total	242	86	257	539	1124	6587	7711*	15
% With IHD (Q)	51	23	30	18	28	12	14	—

MI, myocardial infarction.
*Data missing on possible infarction (Q) or angina (Q) in 16 subjects and ECG evidence missing on eight subjects.
†Comprises those men with chest pain not on exertion (1770), severe chest pain in an inappropriate site (45), and those with both of these symptoms (24); missing ECG or questionnaire (3).

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Table 4 *Prevalence of ischaemic heart disease by electrocardiographic (ECG) and questionnaire (Q) categories. Figures are numbers of subjects*

	No	%	Total No (%)
ECG and Q			315 (4·1)
ECG only			809 (10·5)
Definite myocardial infarction	118	1·5	
Possible MI or definite ischaemia	247	3·2	
Possible ischaemia	444	5·8	
Q only			778 (10·1)
Possible MI and angina	118	1·5	
Possible MI or angina	660	8·6	
Total			1902 (24·7)

naire evidence of possible myocardial infarction and angina. At the other extreme are 333 men with possible myocardial ischaemia (ECG) and no history of any chest pain.

Overall, 1902 (24·7%) of the men had some evidence of ischaemic heart disease by questionnaire or electrocardiography or both. The data in Table 4 are presented in a manner which allows prevalence to be viewed at several levels. In a prospective study of this kind we are concerned with the prognostic significance of all these categories, and even with other subcategories which may be derived from Table 3.

AGE AND THE PREVALENCE OF ISCHAEMIC HEART DISEASE

Questionnaire

The prevalence of possible myocardial infarction combined with angina and of definite angina only increase progressively with age, rising almost fourfold over the four successive five-year age groups (Table 5). Possible myocardial infarction only and possible angina only do not show the same progressive increase in prevalence with age, although there is about a 50% increase in prevalence from the 40–49 year age group to the 50–59 year age group. "Other chest pain" (non-exertional chest pain or severe chest pain in an inappropriate site) shows a small but progressive decline with increasing age.

Table 5 *Prevalence of various diagnostic categories of ischaemic heart disease by age group. Figures are percentages of subjects*

	Age group (yr)			
Diagnostic category	40–44 (n=1838)	45–49 (n=1898)	50–54 (n=1974)	55–59 (n=2025)
Questionnaire (Q):				
Possible MI and angina	1·1	2·2	3·5	4·2
Possible MI only	4·5	5·7	7·7	7·2
Definite angina only	1·4	2·2	3·1	5·1
Possible angina only	1·5	1·6	2·6	2·5
Other chest pain	27·5	26·2	22·1	20·0
Electrocardiogram (ECG):				
Myocardial infarction	1·7	3·3	5·2	6·6
Myocardial ischaemia	8·8	8·1	11·2	12·9
Combined:				
Q or ECG	17·6	21·1	28·0	31·2
Q and ECG	2·3	3·4	7·0	9·3

MI, myocardial infarction.

Electrocardiogram

Myocardial infarction (definite and possible) increases progressively with age, with a fourfold rise in prevalence over the age range. Myocardial ischaemia shows only a small increase with age—namely, 8·5% below 50 years and 12·1% in the 50–59 year age group.

Overall prevalence

The overall prevalence of ischaemic heart disease, using electrocardiographic or questionnaire evidence, almost doubles over the age range covered in this study—that is, from 17·6% to 31·2%. The percentage of men with both electrocardiographic and questionnaire evidence of ischaemic heart disease increases fourfold—that is, from 2·3% to 9·3%. These findings suggest that not only is the overall prevalence increasing with age, but there is simultaneously a considerable and disproportionate increase in the proportion of men with severe ischaemic heart disease.

For the purposes of internal validation of the questionnaire, it is of interest to observe the proportion of subjects with some electrocardiographic evidence of ischaemic heart disease in each questionnaire category by age (ischaemic heart disease (ECG)) (Table 6). Men with possible myocardial infarction and angina (Q) show a high rate of ischaemic heart disease (ECG) in all age groups and a twofold increase from the youngest to the oldest group. The men with possible myocardial infarction (Q) only show rates of ischaemic heart disease (ECG) similar to the total study population in those under 50 years, but the rates of ischaemic heart disease (ECG) are considerably increased in the older subjects. For men with angina (Q) only (definite and possible) the pattern of ischaemic heart disease (ECG) is similar to that seen for possible myocardial infarction (Q) alone with a

Table 6 *Percentage of men with electrocardiographic evidence of ischaemic heart disease in questionnaire categories by age*

	Age range (yr)			
Diagnostic category	40–44 (n=1838)	45–49 (n=1898)	50–54 (n=1974)	55–59 (n=2025)
All subjects	10	11	16	20
Possible MI and angina*	29	38	46	53
Possible MI only	14	13	26	38
Angina* only	17	12	27	32

MI, myocardial infarction.
*Definite and possible.

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considerable increase in the rate of ischaemic heart disease (ECG) in the men aged 50 years or more.

Discussion

The main purpose of the prevalence data from the Regional Heart Study is to provide the background for a prospective study of cardiovascular events taking place in these men. Such events can be related to the many variables measured at the original examination, including the usual "risk factors" and the prevalence criteria derived from the questionnaire and the electrocardiogram. They are also useful for exploring the relations between existing ischaemic heart disease in the men and their measured characteristics, as part of the search for causal factors. Furthermore, they may be used for assessing the present size of the problem of ischaemic heart disease in the community and for determining the facilities likely to be required by those affected by the disorder.

The reliability of the prevalence data depends almost entirely on the validity of the methods used—that is, the questionnaire and the electrocardiogram. The questionnaire used in this study was originally developed for detecting the presence or absence of angina or a history of possible myocardial infarction in population studies and was not primarily intended for use on individual patients.[17] Nevertheless, from the earliest days of assessing the significance of answers to the questionnaire it became clear that positive answers in population groups and individuals contributed to the prognosis as much as positive findings on electrocardiography.[18] Rose and his colleagues interviewed 1136 men in 1961 using the standardised questionnaire and in 1962 they reinterviewed 995 of these men.[18] The prevalence rates for angina were 3·3% in 1961 and 3·4% in 1962, but the men who made up the totals were not the same in the two years. Although the vast majority of men were consistent in their replies on the two occasions (94% negative, 2% positive), approximately half of those with angina in 1961 (19/33) did not have angina in 1962, and half of those with angina in 1962 (14/32) had not had angina in 1961. Men with consistently positive answers for either angina or possible myocardial infarction in both 1961 and 1962 were more likely to have electrocardiographic changes of ischaemia than those whose answers were not consistent. Even those who answered positively one year and negatively the other year were more likely to have electrocardiographic changes than the men who gave consistently negative answers. There seems to be little doubt that this questionnaire is a powerful tool for detecting individuals and groups with ischaemic heart disease and at high risk of further episodes such as acute myocardial infarction or sudden death.

In an extended study of the same 1136 men based on four examinations over a four year period, the period prevalence of angina remained constant at around 4% but with a great deal of flux among the "angina positive" group.[19] The majority were positive on only a single occasion. On follow up, however, 59% of the clinical coronary events had been preceded by a positive response to the questionnaire (angina or possible myocardial infarction) and 80% by either a positive questionnaire or a positive electrocardiogram. Relatively few of these earlier manifestations would have been recognised apart from the survey, and the physician in charge would have concluded that a major illness had occurred without prior warning. This makes for a particularly difficult situation in defining what is an "old" and a "new" case of ischaemic heart disease and suggests that the definition of incidence may be more arbitrary than is realised.

POSSIBLE MYOCARDIAL INFARCTION (Q)

The questionnaire administered to the 7735 men in the present study indicates that about 1 in 10 have experienced prolonged severe chest pain such as might occur in acute myocardial infarction. Men with such a history were five to six times as likely to have angina on questionnaire as men who had not experienced such chest pain and were five times as likely to have electrocardiographic changes of myocardial infarction or definite myocardial ischaemia. These findings strongly suggest that a high proportion of men with a history of possible myocardial infarction (Q) actually have ischaemic heart disease.

ANGINA (Q)

Chest pain is an extremely common symptom, but the criteria which have to be satisfied before a diagnosis of definite angina is made in this study are exacting. Possible angina appears to be very similar to definite angina in its association with possible myocardial infarction (Q) and with evidence of ischaemic heart disease on electrocardiography. For the purposes of assessing the prevalence of angina in these men it therefore seems reasonable to combine the definite and possible categories as angina (Q). About 8% of these middle aged men have angina and one in three of those with angina also have a history of possible myocardial infarction (Q).

ELECTROCARDIOGRAPHY

The relation of electrocardiographic finding to the risk of ischaemic heart disease has been well documented.[20] A recent review of three epidemiological studies in Chicago[21] has shown that major electrocardiographic abnormalities retain a significant relation to mortality even when age, diastolic blood pressure, serum cholesterol concentration, relative weight, and cigarette smoking are taken into consideration. In two of these Chicago studies minor elec-

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trocardiographic changes also showed an independent relation to mortality. The electrocardiograms in these studies were classified using the Minnesota Code, a system originally developed during the 1950s for use in epidemiological studies in order to provide for the "reporting of findings in uniform, clearly defined and objective terms with the least risk of confusion with regard to interpretation."[22] The orthogonal three lead systems developed in the 1960s considerably reduce the electrical distortion inherent in the conventional 12 lead electrocardiogram and by reduction of redundant information facilitate the analysis of electrocardiograms by computer. A classification system suitable for epidemiological investigations has recently been proposed[23] but was not available at the time of this study.

A recent comparative study provides information on the validity of the three lead orthogonal systems in the diagnosis of ischaemic heart disease.[24] In 90 patients undergoing coronary arteriography both three lead orthogonal and 12 lead electrocardiograms were used to examine ST-T wave abnormalities in relation to the presence of arterial obstruction. The X lead (anterolateral) was compared with leads I, V5, and V6, the Y lead (inferior) with aVF and lead II, and the Z lead (anteroseptal) with V2 and V3 of the 12 lead electrocardiogram. The 12 lead electrocardiogram was interpreted by two cardiologists. The overall agreement between the two systems was relatively high. The three orthogonal lead system had a somewhat greater sensitivity than the 12 lead system, with a slightly lower specificity in the anteroseptal and inferior leads. Nevertheless, the predictive value was very similar for the two systems, about 80% for anterolateral leads, 86% for anteroseptal leads, and 90% for inferior leads.

It should perhaps be emphasised that both systems merely help to describe and categorise the electrocardiographic findings; they do not provide a diagnosis. It should also be emphasised that in this study the terms "definite" and "possible," as applied to myocardial ischaemia (ECG), essentially indicate the severity of the ST-T changes. It must also be remembered that an exclusive categorisation system was used and that secondary ST-T abnormalities such as occur in ventricular hypertrophy and right bundle branch block were not regarded as evidence of myocardial ischaemia (ECG). Furthermore, while ST-T change can be due to many causes, in the male population aged 40–59 years under study, none of whom was acutely ill, the most likely cause of a primary ST-T change is myocardial ischaemia.

When the men have been followed for the development of clinical ischaemic heart disease it will be possible to assign levels of risk to the various categories of electrocardiographic findings as in other studies. At present it is feasible only to report on the prevalence of the findings and their relation to the information obtained on questionnaire. It is of interest and concern that, of the 241 men with definite myocardial infarction on electrocardiograms, only half had a history of possible myocardial infarction or angina or both on questionnaire. This lends further support to the widely accepted concept of unrecognised (silent) myocardial infarction[25] and emphasises the need for objective methods of determining the prevalence of ischaemic heart disease in populations and in assessing the cardiovascular status of individuals.

COMPARISON WITH OTHER STUDIES

It would be useful to compare the findings in a study of this kind with those derived from similar studies in the same population on previous occasions. Unfortunately, there are no similar studies based on subjects recruited from general practices spread widely over Great Britain, but there are two major studies which provide comparable data.

The Whitehall Study of cardiorespiratory disease and diabetes was based on 18 403 male civil servants aged 40–64 years working in selected government departments within about two miles of Whitehall, London.[3 26] The men were examined over a two and a half year period in 1967 to 1969 and the response rate was 77%, ranging from 58% among messengers to 87% among senior grades. They completed a self-administered questionnaire, which included questions on chest pain (possible myocardial infarction, angina), and had an electrocardiogram, in which only the six limb leads were recorded. The prevalence of ischaemic heart disease was expressed in terms of the presence of angina (Q) and possible myocardial infarction (Q) and by Minnesota Code items indicative of myocardial ischaemia (1.1–1.3, 4.1–4.4, 5.1–5.3, 7.1).

The WHO Collaborative Trial in the Multifactorial Prevention of Coronary Heart Disease included a United Kingdom group (The UK Heart Disease Prevention Project (UKHDPP)) of 18 210 men aged 40–59 years employed in 24 large industrial groups, mainly factories.[27] They represent a cross section of light, medium, and heavy industry. The study included all men regardless of their work activity and they were examined between 1971 and 1973.

These two studies record similar prevalences of the various manifestations of ischaemic heart disease and both show a lower prevalence than the Regional Heart Study (Table 7). In the Regional Heart Study data (Table 7) angina (Q) includes possible angina, whereas this group may have been excluded in the Whitehall angina category. In both the Whitehall Study and the UKHDPP there is relatively little over-

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Table 7 *Prevalence of ischaemic heart disease (IHD) in the Whitehall Study,[26] the UK Heart Disease Prevention Project (UKHDPP),[27] and the British Regional Heart Study (RHS). Figures are percentages of subjects*

Diagnostic category	*Whitehall (1967–9)*	*UKHDPP (1971–3)*	*RHS (1978–80)*
Angina (Q)	4·3	3·6	7·9
Possible MI (Q)	6·5	6·6	9·1
IHD (Q)	10·4	—	14·2
IHD (ECG) major	0·5*	0·9†	3·1
IHD (ECG) other	5·0	6·9	11·4
Any suspect IHD	14·1	—	24·7

MI, myocardial infarction.
*Minnesota Code 1.1–1.2.
†Minnesota Code 1.1–1.3.

lap between a positive history on questionnaire and electrocardiographic evidence of ischaemic heart disease. In the UKHDPP 23% of those with angina (Q) and 5% of those with possible myocardial infarction (Q) had some electrocardiographic evidence of ischaemic heart disease. The corresponding figures for the Whitehall Study were 17% and 13% and for the Regional Heart Study 32% and 31%. An issue which must be considered in contrasting the electrocardiographic findings from these two studies with those of the Regional Heart Study concerns the sensitivity of the three lead orthogonal system compared with that of the 12 lead electrocardiogram. We have already indicated (see methods) that the orthogonal system requires less ST depression or T wave negativity for categorisation as myocardial ischaemia. Nevertheless, close comparison of the criteria used in the three lead and 12 lead systems indicates that all the categories of ischaemic heart disease (ECG) used in this presentation can be represented by an appropriate Minnesota Code. A factor which could account to a considerable extent for a lower prevalence of ischaemic heart disease in these other two studies is the "healthy worker" effect.[28] Although men in the Whitehall Study were encouraged to attend regardless of whether or not they were currently under medical care, it is likely that those who suffered from ischaemic heart disease may have retired on medical grounds. Use of the limb leads only will lead to at least a 25% loss of information on myocardial ischaemia, and this loss is likely to be as high as 50% for Q : QS items.[29] In the Whitehall Study, there is an unusual social class distribution, with social class III (manual) entirely unrepresented and with under-representation of social classes IV and V.[30] This could also lead to some reduction in the prevalence of ischaemic heart disease in the study population.

The Whitehall Study is based on London, which has a low mortality rate for cardiovascular disease relative to Britain as a whole. The UKHDPP excludes the north of England and Scotland, which have relatively high mortality rates for cardiovascular disease. By contrast the Regional Heart Study includes men from all major geographic regions of Great Britain and adequately represents the social class composition of the male population. Only a very few men were excluded from the study by their general practitioners and the design of the study precludes the "healthy worker" effect seen in studies of occupational groups.

HEART ATTACK REGISTERS

Heart attack registers have been maintained in a number of countries over the past 10 years, including several registers in British towns.[7 8 31] These have provided valuable information on the frequency and natural history of heart attacks in different communities, and in particular have emphasised the prognostic importance of the previous history of cardiovascular disease. In the Tower Hamlets study in East London half of those suffering heart attacks had a previous history of ischaemic heart disease, and an appreciable minority were already unfit for work, mainly because of recognised cardiovascular disease.[8]

The WHO International Collaborative Study with heart attack registers in 19 European centres, as well as Australia (Perth) and Israel (Tel-Aviv), covered a population of 3·6 million men and women aged 20–64 years.[32] In this study, two thirds of the men and four fifths of the women were already suffering from some form of cardiovascular disease by the time they experienced acute myocardial infarction or sudden death. The commonest preceding histories were hypertension, angina, and myocardial infarction.

The findings in the heart attack registers relate to the attempts we will make to determine the strength of the relations between risk factors and the frequency of ischaemic heart disease events. We have already noted in the Chicago epidemiological studies that electrocardiographic abnormalities have a relation to mortality independent of the established risk factors.[21] There is also considerable evidence that the risk of death or recurrent myocardial infarction in those who have already experienced a myocardial infarction depends more on their age and the severity of the initial episode (manifest to some degree by the electrocardiographic changes) than on the level of the conventional risk factors such as smoking, hypertension, or raised serum cholesterol concentrations.[33 34] These factors retain an independent effect but to a lesser extent than in those initially free of ischaemic heart disease.

CONCLUSIONS

The Regional Heart Study aims to explain the pronounced regional variations in cardiovascular disease mortality in Great Britain and to determine the causes

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of ischaemic heart disease. It is based on a survey of 7735 middle aged men recruited from general practices in 24 towns, and these men are being followed for morbidity and mortality over a five to 10 year period. The prognostic importance of their baseline personal characteristics will be determined by relating these potential "risk factors" to cardiovascular events taking place after the initial examination. In this report the criteria for determining the existence of ischaemic heart disease have been established, and the prevalence of ischaemic heart disease by these criteria has been presented. There is strong evidence from other studies that existing ischaemic heart disease is a potent risk factor for further episodes of ischaemic heart disease and that this may outweigh that associated with the conventional risk factors. Clearly, it is of paramount importance in the Regional Heart Study to categorise each subject by his previous/existing ischaemic heart disease as well as by determining his status for other personal and environmental risk factors. The prevalence criteria can be viewed as "risk factors" or as established ischaemic heart disease, and this dual possiblity emphasises the arbitrary nature of incidence in studies of this kind. In the Regional Heart Study we will be able to determine the relative risk of the many characteristics measured in subjects with a wide range of evidence of ischaemic heart disease. At the one extreme are those with definite myocardial infarction (ECG) plus possible myocardial infarction (Q) and angina (Q); at the other extreme are those with a normal electrocardiogram and no history of any chest pain. The relative risk of hypertension, cigarette smoking, or raised serum cholesterol concentrations in these extreme groups is likely to be different, and the determination of such relative risks is critical to a rational approach to the management and prevention of ischaemic heart disease.

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Resting electrocardiogram and risk of coronary heart disease in middle-aged British men

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Objective: To examine the relation between resting electrocardiographic (ECG) abnormalities and risk of coronary heart disease (CHD).

Design and setting: This was a prospective study of 7735 middle-aged men aged 40–59 years at entry (British Regional Heart Study). At baseline assessment each man completed a modified World Health Organization (WHO) (Rose) chest-pain questionnaire, gave details of his medical history and had a three-lead orthogonal electrocardiogram recorded. 'Symptomatic CHD' refers to a history of anginal chest pain and/or a prolonged episode of central chest pain on WHO questionnaire and/or recall of a doctor diagnosis of CHD (angina or myocardial infarction).

Main outcome measures: These were the first major CHD events, i.e. fatal CHD and non-fatal myocardial infarction, occurring during 9.5 years of follow-up.

Results: Of 611 first major CHD events during follow-up, 243 (40%) were fatal. After adjustment for age, other ECG abnormalities and symptomatic CHD, the ECG abnormalities most strongly associated with risk of a major CHD event were definite myocardial infarction (relative risk 2.5; 95% confidence interval 1.8–7.5) and definite myocardial ischaemia (1.9; 1.1–2.9). Other ECG abnormalities independently associated with a statistically significant increase in risk were left ventricular hypertrophy (2.2; 1.5–3.3), left axis deviation (1.3; 1.1–1.6) and ectopic beats, particularly if these were ventricular (1.6; 1.1–2.4). Three ECG abnormalities associated with a marked increase in CHD case-fatality rate were pre-existing myocardial infarction (67%), major conduction defect (71%) and arrhythmia (67%); the rate in men with none of these abnormalities was 32%. The relative risks associated with each ECG abnormality were similar in men with and without symptomatic CHD. The increase in risk in the presence of symptomatic CHD (2.4-fold) and ECG evidence of definite myocardial infarction (2.5-fold) was similar; the presence of both factors increased risk more than six-fold. The most serious ECG abnormalities – definite myocardial infarction and ischaemia – were useful predictors of future major CHD events only in men with symptomatic CHD.

Conclusion: The prognostic importance of major ECG abnormalities is strongly influenced by the presence of symptomatic CHD. In men with symptomatic CHD the resting electrocardiogram may help to define a group at high risk who may benefit from intervention. However, it has little or no value as a screening tool in middle-aged men without symptomatic CHD.

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Introduction

The role of the resting electrocardiogram in patients with established heart disease is well recognized [1]. However, during the past 20 years, the resting electrocardiogram has been used increasingly in health screening and particularly in the assessment of occupational fitness [2]. Its use may further increase with the recognition

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that strategies for the prevention of coronary heart disease need to focus on individuals at high risk of coronary heart disease rather than on the general population [3,4]. The value of the electrocardiogram as a screening test depends on the prevalence and the prognostic importance of electrocardiographic abnormalities in apparently healthy subjects, as well as in those with established coronary heart disease. Although several reports have examined the importance of electrocardiographic abnormalities in middle-aged individuals [5–7], few have examined the prevalence and independent prognostic importance of specific electrocardiographic abnormalities separately in subjects with and without symptoms of coronary heart disease. In a preliminary report we described the univariate relationships between electrocardiographic abnormalities and major coronary heart disease [8]. In the present paper we report on the prevalence and independent prognostic importance of specific electrocardiographic abnormalities in middle-aged British men, distinguishing between subjects with and without evidence of coronary heart disease, and examine the potential value of the resting electrocardiogram as a screening tool.

Subjects and methods

The British Regional Heart Study includes 7735 men aged 40–59 years at initial examination, randomly selected from the age–sex registers of one general practice in each of 24 towns in England, Wales and Scotland (response rate 78%). The criteria for selecting the town, the general practice and the subjects, as well as the methods of data collection, have been reported elsewhere [9].

Initial assessment

A team of three nurses administered to each man a questionnaire that included questions on chest pain and medical history, measured blood pressure and recorded an electrocardiogram. The questions on chest pain were based on those used in the World Health Organization (Rose) questionnaire [10] with minor modifications [11,12]. The questions on medical history included enquiry about recall of a previous diagnosis by a doctor of illnesses including coronary heart disease (angina, heart attack, coronary thrombosis and myocardial infarction). In the present report, a group of men with symptomatic coronary heart disease were defined, who fulfilled at least one of the following criteria: chest pain on exertion, even when not fulfilling all the additional criteria for angina [12]; a history of severe central or left-sided chest pain of at least 30 min duration – a possible myocardial infarction; recall of a previous doctor diagnosis of coronary heart disease (angina, heart attack, coronary thrombosis or myocardial infarction). Measurement of blood pressure was carried out twice in succession with the man seated and his arm supported on a cushion, using the London School of Hygiene sphygmomanometer (Cinetronics Ltd, Mildenhall, England). The mean of the two readings was used in all analyses and adjustment made for observer variation within each town [13]. In the present report hypertension is defined as a systolic blood pressure of > 160 mmHg or a diastolic pressure > 90 mmHg or current use of antihypertensive medication.

Electrocardiography

Each man had a resting electrocardiogram carried out using three orthogonal leads, as derived from the modified axial lead system [14]. The signals were recorded on electromagnetic tapes that were analysed by computer in the Department of Medical Cardiology in Glasgow. On occasions when technical problems occurred (400 cases), a 12-lead electrocardiogram was recorded using a Hewlett-Packard 1515B (Boise, Idaho, USA) machine and referred for visual analysis.

Interpretation of electrocardiograms

Details of the criteria used for interpreting the orthogonal three-lead electrocardiogram have been published elsewhere [15-17]. The validity of the method in comparison with the standard 12-lead electrocardiogram has been reported [18]. The definitions of abnormalities using this system of classification and their relationships to the Minnesota Code [10] are outlined below.

In the present study myocardial ischaemia and infarction are treated as exclusive categories, so that each subject can appear only once in the analysis. The diagnosis of myocardial infarction is made on the basis of a broad Q wave in any lead together with a Q : R amplitude ratio greater than 1 : 3 if the Q wave is in the anterolateral (X) or inferior (Y) leads. The division into definite and possible myocardial infarction depends on the width of the Q wave and the magnitude of the Q : R amplitude ratio. The Minnesota Code classifies Q and QS patterns for three sites: inferior, anteroseptal and anterolateral. These sites equate closely to the three orthogonal leads used in the present system: X for anterolateral, Y for inferior and Z for anteroseptal. Definite myocardial infarction in the present study equates closely with Minnesota Codes 1-1 and 1-2-1 to 1-2-6. Possible myocardial infarction in the present study equates with Minnesota codes 1-2-7, 1-2-8 and 1-3.

A combination of ST segment depression and T wave changes (negativity or low positivity) in the three-lead electrocardiogram is used to report myocardial ischaemia. Although the Minnesota Code treats the ST segment and T wave separately, there are considerable similarities between the methods. However, the degree of ST junctional depression required for definite abnormality by the Minnesota Code (in excess of 0.1 mV) is greater than that required by the three-lead system (0.06 mV), which, however, also requires the ST segment to be flat or downward sloping. Thus a three-lead electrocardiogram showing definite myocardial ischaemia equates with Minnesota Codes 4-1 or 5-1, while those three-lead electrocardiographic appearances regarded as

possible myocardial ischaemia equate with Minnesota Codes 4-1, 4-2, 5-2 and 5-3.

The diagnosis of ventricular hypertrophy was made on the basis of R wave amplitude, ST–T abnormalities and abnormal QRS vector orientation. A scoring system was used [17], with six points representing definite hypertrophy and four to five points representing possible or probable hypertrophy. Definite left ventricular hypertrophy equates with Minnesota Code 3-1, while possible or probable hypertrophy equates with Code 3-3. Right ventricular hypertrophy equates with Minnesota Code 3-2; possible and probable right ventricular hypertrophy have no Minnesota Code equivalent. Diagnosis of left ventricular strain was based on the presence of ST depression in lead X of at least 0.06 mV accompanied by T wave inversion in excess of 0.1 mV.

Conduction defects are consistent in the 3- and 12-lead systems. Left bundle branch block corresponds to Minnesota Code 7-1-1, while right bundle branch block corresponds to 7-2-1 and incomplete right bundle branch block to 7-3. Intraventricular conduction defect is equivalent to 7-4, while left anterior hemiblock corresponds to 7-7.

Left axis deviation was defined as a QRS frontal axis between +240 and +360 degrees, right axis deviation as a QRS frontal axis between +75 and +180 degrees.

ST elevation corresponds to STj >0.1 mV and ST mid-point >0.08 mV in leads X or Y; tall T waves correspond to a T vector magnitude >0.80 mV or a T wave >0.50 mV in lead Z.

All QT intervals were corrected for heart rate. Prolongation was defined as a QT_c interval >0.43 s and shortening as a QT_c interval <0.30 s, occurring in all leads.

Arrhythmias were diagnosed using a complex diagnostic tree, and were then checked by an experienced electrocardiographer. Sinus rhythm, coronary sinus rhythm and sinus arrhythmia were all accepted as normal rhythms.

Follow-up

All men were followed up for all-cause mortality and for major cardiovascular morbidity (particularly non-fatal myocardial infarction) for 9.5 years. Information on death was obtained by the established 'tagging' procedure carried out by the National Health Service Central Registers in Southport (for England and Wales) and Edinburgh (for Scotland), which provided information on the date and causes of death from the death certificate. Information on non-fatal myocardial infarction was obtained from follow-up reports provided by the patient's general practitioner and by annual reviews of the patient's notes. A fatal coronary heart disease event was defined as a death coded to ICD 410-414. A diagnosis of non-fatal myocardial infarction was based on an event associated with a combination of at least two of: severe prolonged chest pain; electrocardiographic evidence of myocardial infarction at the time of the event; cardiac enzyme abnormalities, with survival for at least 28 days [19]. The results presented here are based on the first major coronary heart disease event during the follow-up period. Thus, a non-fatal myocardial infarction followed months or years later by a fatal coronary heart disease event is categorized as a non-fatal episode.

Statistical methods

Multiple logistic regression was used to obtain relative odds adjusted for age, each of the other electrocardiographic abnormalities and symptomatic coronary heart disease. Age was fitted as a continuous variable. The different electrocardiographic abnormalities were fitted as categorical variables. The presence of myocardial ischaemia or infarction was fitted as four dummy variables for the five groups (no abnormality; possible myocardial ischaemia; definite myocardial ischaemia; possible myocardial infarction; definite myocardial infarction). Left ventricular hypertrophy was fitted as three dummy variables for the four groups (none; 4–5 points; 6 points; 6 points with left ventricular strain). Conduction defects were fitted as two dummy variables for three groups (none; left bundle branch block + left anterior hemiblock + intraventricular conduction defect; right bundle branch block). Axis deviation (none; left; right) and QT interval (normal; short; long) were treated similarly. Arrhythmias were treated as three dummy variables for the four groups (none; supraventricular extrasystoles; ventricular extrasystoles; atrial fibrillation/flutter). ST elevation and tall T waves were treated as dichotomous variables; symptomatic coronary heart disease was treated similarly. Chi-square tests were used to test for differences in the prevalence of symptomatic coronary heart disease and hypertension in the presence and absence of electrocardiographic abnormalities (Table 1). For electrocardiographic abnormalities with different levels (myocardial ischaemia/infarction, ventricular hypertrophy, conduction defects, arrhythmias), the different levels have been included in a chi-square test on n−1 degrees of freedom.

Results

Electrocardiographic data were available for 7727 of the 7735 men. During the 9.5 year follow-up period a total of 611 first events were recorded (8.3/1000 per year), of which 243 (39.7%) were fatal.

Prevalence of electrocardiographic abnormalities

Table 1 shows the prevalence of each electrocardiographic abnormality and the proportion of men with symptomatic coronary heart disease (as defined above) in each category. Apart from axis deviation, myocardial ischaemia and myocardial infarction are the commonest electrocardiographic abnormalities (present in 14.3% of all men), followed by tall T waves (6.6%), left ventricular hypertrophy (6.3%) and arrhythmias (4.8%). Electrocardiographic abnormalities significantly

Table 1. Prevalence of electrocardiographic abnormalities: association with symptomatic ischaemic heart disease and hypertension.

Electrocardiographic abnormality	No. of men	Prevalence rate (%)	% with symptoms (n = 1158)	% with hypertension (n = 2682)
Myocardial ischaemia and infarction				
Possible ischaemia	525	6.8	18.9**	48.4**
Definite ischaemia	257	3.3	30.7**	53.3**
Possible infarction	86	1.1	25.6**	44.2**
Definite infarction	242	3.1	57.4**	50.4**
Left ventricular (LV) hypertrophy				
4–5 points	244	3.2	14.3**	53.3**
6 points				
All cases	220	2.8	20.5**	52.9**
With LV strain	23	0.3	39.1**	91.0**
Right ventricular hypertrophy				
4–5 points	106	1.4	18.9NS	32.1NS
6 points	34	0.4	20.5NS	52.9NS
Conduction defect (CD)				
Left bundle branch block	18	0.2	16.7NS	61.1NS
Intraventricular CD	50	0.6	22.0NS	38.0NS
Left anterior hemiblock	6	0.1	33.0NS	67.0NS
Right bundle branch block	67	0.8	20.8NS	28.4NS
Axis deviation				
Right	545	7.1	16.9NS	25.3NS
Left	942	12.1	19.5**	51.9**
S-T elevation	179	2.3	14.9NS	24.0*
Tall T-wave	510	6.6	12.0*	30.2*
Q-T interval				
Short	76	0.9	22.0NS	43.4NS
Long	56	0.7	19.6NS	25.0NS
P-R interval				
Short	720	9.3	14.1NS	33.6NS
Long	7	0.1	–	–
Arrhythmias				
Supraventricular extrasystoles	113	1.5	15.0**	33.6*
Ventricular extrasystoles	202	2.6	20.3**	45.1*
Atrial fibrillation/flutter	56	0.7	35.7**	46.4*
All subjects	7727	100	15.0	34.7

P values are based on chi-square tests comparing the odds of symptoms or hypertension in those with or without each electrocardiographic (ECG) abnormality. Where indicated, related ECG categories have been grouped for testing. *$P<0.05$; **$P<0.001$; NS, not significant.

associated with symptomatic coronary heart disease were myocardial ischaemia and infarction (particularly when definite), left ventricular hypertrophy, left axis deviation and arrhythmias, particularly ventricular extrasystoles and atrial fibrillation/flutter. The same abnormalities were also significantly associated with the presence of hypertension. Tall T waves were significantly less common in subjects with symptomatic coronary heart disease than in those without, while both tall T waves and ST segment elevation were less common in hypertensive subjects.

Electrocardiographic abnormalities and rate of coronary heart disease events

Table 2 shows the rate of major coronary heart disease events associated with each abnormality and the proportion of these that were fatal within 28 days. Evidence of myocardial ischaemia and myocardial infarction (particularly when definite) were most strongly related to the rate of subsequent coronary heart disease events. Left ventricular hypertrophy (particularly when associated with strain), major conduction defects (left bundle branch block, left anterior hemiblock and intraventricular conduction defect) and left axis deviation were also associated with a significantly increased rate of subsequent major coronary heart disease events. Right ventricular hypertrophy, right bundle branch block and right axis deviation appeared to have little or no influence on prognosis. The presence of tall T waves appeared to be associated with a lower than average rate of subsequent coronary heart disease events, while the Q-T interval showed little or no association with risk. Both ventricular extrasystoles and atrial fibrillation/flutter were associated with a significantly increased risk of coronary heart disease. Electrocardiographic evidence of myocardial ischaemia or infarction was strongly associated with an increased case fatality rate ($P<0.0001$). High case-fatality rates were also observed with conduction defects (left bundle branch block, left anterior hemiblock and intraventricular conduction defect) and with arrhythmias. However, the numbers of deaths in these groups are very small and the increases do not achieve statistical significance.

In order to assess the independent contribution of those abnormalities that were significantly related to the rate

Table 2. Electrocardiographic abnormalities, rate of major ischaemic heart disease (IHD) events (per 1000 per year) and associated case fatality rates.

	Men (n)	Major IHD event rate per 1000 per year (n)	% Case fatality rate (no. deaths)
Myocardial ischaemia and infarction			
None	6617	6.8 (431)	34 (147)
Possible ischaemia	525	11.8 (59)**	49 (29)
Definite ischaemia	257	18.0 (44)**	39 (17)
Possible infarction	86	12.2 (10) NS	50 (5)
Definite infarction	242	29.2 (67)**	67 (45)
Left ventricular (LV) hypertrophy			
None	7263	8.0 (554)	40 (219)
4–5 points	244	8.6 (20) NS	30 (6)
6 points			
All cases	220	17.7 (37)**	47 (18)
With LV strain	23	32.0 (7)**	71 (5)
Right ventricular hypertrophy			
None	7114	8.3 (596)	40 (236)
4–5 points	106	10.9 (11) NS	45 (5)
6 points	34	12.4 (4) NS	50 (2)
Conduction defect (CD)			
None	7586	7.7 (591)	39 (230)
LBBB, LAH, IVCD	74	18.9 (14)**	71 (10)
RBBB	67	8.9 (6) NS	17 (1)
Axis deviation			
None	6240	7.5 (442)	38 (169)
Right	545	8.1 (52) NS	36 (15)
Left	942	14.2 (127)**	46 (59)
S-T elevation			
None	7548	8.4 (604)	39 (238)
Yes	179	4.5 (8) NS	63 (5)
Tall T-wave			
No	7217	7.3 (502)	48 (239)
Yes	510	3.9 (19)**	21 (4)
Q-T interval			
Normal	7595	9.3 (597)	40 (236)
Short	76	11.1 (8) NS	63 (5)
Long	56	12.3 (6) NS	33 (2)
Arrhythmias			
None	7325	8.0 (557)	39 (217)
Supraventricular extrasystoles	113	11.9 (11) NS	73 (8)
Ventricular extrasystoles	202	16.6 (32)**	63 (20)
Atrial fibrillation/ flutter	56	20.6 (11)**	73 (8)

L(R)BBB, left (right) bundle branch block; LAH, left anterior hemiblock; IVCD, intraventricular conduction defect. *$P<0.05$; **$P<0.001$; NS, not significant.

of coronary heart disease events during the follow-up period, three factors need to be taken into account. First, age is related both to the prevalence of electrocardiographic abnormalities and to coronary heart disease incidence. Second, several abnormalities are strongly associated with the presence of symptomatic coronary heart disease (Table 1), which is itself a risk factor for further coronary heart disease events. Third, several of the electrocardiographic abnormalities described are not independent of one another. In particular, left ventricular hypertrophy, conduction defects, left axis deviation and the presence of arrhythmia are all associated with the presence of definite myocardial ischaemia or infarction (Table 3).

Table 3. Inter-relationships of electrocardiographic (ECG) myocardial ischaemia and myocardial infarction with other ECG abnormalities.

	ECG evidence of myocardial ischaemia or myocardial infarction		
	None	Definite myocardial ischaemia	Definite myocardial infarction
Left ventricular hypertrophy	5.6	9.0	8.3
Right ventricular hypertrophy	2.0	0.7	0.0
Conduction defect (LBBB, LAH, IVCD)	0.8	1.2	4.1
Left axis deviation	10.2	18.7	43.4
Arrhythmias	4.5	8.5	14.5

Figures show the percentages of men who have each ECG abnormality according to their grade of myocardial ischaemia or infarction. LBBB, left bundle branch block; LAH, left anterior hemiblock; IVCD, intraventricular conduction defect.

To allow the independent contribution of each electrocardiographic abnormality to coronary heart disease risk to be examined, a series of adjustments were carried out (Table 4). Relative risks were adjusted for age alone (column A), for age and other electrocardiographic abnormalities (column B) and for age, other electrocardiographic abnormalities and symptomatic coronary heart disease (column C). When the effect of other electrocardiographic abnormalities is taken into account (column B), myocardial ischaemia and infarction and left ventricular hypertrophy remain strong, independent predictors of risk. The influence of conduction defects, left axis deviation and arrhythmias on prognosis is attenuated, although left axis deviation and ventricular extrasystoles remain statistically significant. The relationship of tall T waves to a lower risk of heart attack is unaffected by adjustment for other electrocardiographic abnormalities. Taking into account symptomatic coronary heart disease as well as age and other electrocardiographic abnormalities (column C) produces further attenuation of the risks associated with myocardial ischaemia and infarction and left ventricular hypertrophy, although these remain statistically significant.

Influence of symptomatic coronary heart disease on the prognosis of electrocardiographic abnormalities

Relative risk

The influence of symptomatic coronary heart disease on the relative risks associated with each electrocardiographic abnormality has been examined separately in those with and without a history of cardiac symptoms on World Health Organization (Rose) chest pain questionnaire and/or recall of a doctor diagnosis of coronary heart disease (Table 5). The relative risk associated with each electrocardiographic abnormality is broadly similar in those with and without symptoms. Although relative risk estimates for possible ischaemia

Table 4. Electrocardiographic (ECG) abnormalities and relative odds of ischaemic heart disease, with adjustment for age and for other ECG abnormalities.

	Adjustment		
	A	B	C
Myocardial ischaemia and infarction			
None	1.0	1.0	1.0
Possible ischaemia	1.7 (1.2, 2.2)	1.6 (1.2, 2.2)	1.5 (1.1, 2.1)
Definite ischaemia	2.7 (1.9, 3.8)	2.3 (1.9, 3.8)	1.9 (1.1, 2.9)
Possible infarction	1.5 (0.8, 2.9)	1.4 (0.8, 2.9)	1.2 (0.6, 2.5)
Definite infarction	4.5 (3.3, 6.0)	3.7 (3.3, 6.0)	2.5 (1.8, 7.5)
Left ventricular (LV) hypertrophy			
None	1.0	1.0	1.0
4–5 points	1.1 (0.7, 1.8)	1.0	1.1
6 points			
All cases	2.2 (1.5, 3.3)	1.9 (1.3, 2.8)	1.9 (1.3, 2.8)
With LV strain	3.9 (1.6, 9.9)	3.4 (1.3, 8.8)	2.2 (0.8, 6.2)
Right ventricular hypertrophy			
None	1.0	1.0	
≥4 points	1.4 (0.7, 2.7)	1.6 (0.9, 3.1)	1.6 (0.9, 3.1)
Conduction defect			
None	1.0	1.0	
LBBB, LAH, IVCD	2.4 (1.3, 4.3)	1.7 (0.9, 3.2)	1.7 (0.9, 3.2)
RBBB	1.0 (0.4, 2.2)	1.0 (0.4, 2.4)	1.0 (0.4, 2.4)
Axis rotation			
None	1.0	1.0	1.0
Right	1.2 (0.8, 1.4)	1.0	1.0
Left	1.8 (1.4, 2.1)	1.3 (1.1, 1.6)	1.3 (1.1, 1.6)
S-T elevation			
No	1.0	1.0	
Yes	0.6 (0.3, 1.2)	0.7 (0.3, 1.5)	0.7 (0.3, 1.5)
Large T-wave			
No	1.0	1.0	
Yes	0.5 (0.3, 0.8)	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)
Q-T interval			
Normal	1.0	1.0	
Short	1.3 (0.6, 2.8)	1.1 (0.5, 2.4)	
Long	1.6 (0.7, 3.8)	1.6 (0.6, 3.6)	1.5 (0.6, 3.6)
Arrhythmias			
None	1.0	1.0	1.0
Supraventricular extrasystoles	1.2 (0.6, 2.3)	1.1 (0.6, 2.1)	1.1 (0.6, 2.1)
Ventricular extrasystoles	2.0 (1.3, 2.9)	1.6 (1.1, 2.4)	1.6 (1.1, 2.4)
Atrial fibrillation/flutter	2.9 (1.4, 5.8)	1.8 (0.9, 3.8)	1.5 (0.7, 3.2)

Figures represent relative risk (95% confidence limits). A, adjusted for age only; B, adjusted for age and other ECG abnormalities; C, adjusted for age, other ECG abnormalities amd symptomatic ischaemic heart disease. L(R)BBB, left (right) bundle branch block; LAH, left anterior hemiblock; IVCD, intraventricular conduction defect.

and definite myocardial infarction, left ventricular hypertrophy, conduction defects and left axis deviation are slightly higher in subjects with cardiac symptoms, statistical tests for interaction were negative for all these abnormalities.

Absolute risk

Because absolute risk, rather than relative risk, is the most important guide to prognosis in the individual subject [20], the absolute risk associated with the presence of two of the most important electrocardiographic abnormalities – definite myocardial ischaemia and definite myocardial infarction – has been examined separately in the presence and absence of symptomatic coronary heart disease (Fig. 1). For subjects with symptomatic coronary heart disease, the risk of coronary heart disease events is approximately 2.4 times greater than it is for those without symptomatic coronary heart disease, for each category of electrocardiographic abnormality. The only group of subjects without symptomatic coronary heart disease who have an absolute risk comparable with that of subjects with symptomatic coronary heart disease and a normal electrocardiogram are those men with electrocardiographic evidence of definite myocardial infarction. For subjects with both symptomatic coronary heart disease and electrocardiographic evidence of definite myocardial infarction, the absolute risk of coronary heart disease is more than six times higher than that of men without symptomatic coronary heart disease and with a normal electrocardiogram.

Table 5. Electrocardiographic (ECG) abnormalities and adjusted relative odds of ischaemic heart disease, in men with and without symptomatic ischaemic heart disease separately.

	Symptomatic ischaemic heart disease	
	No (n = 6569)	Yes (n = 1158)
No abnormality	1.0	1.0
Myocardial ischaemia and infarction		
Possible ischaemia	1.4	1.9
Definite ischaemia	2.1	1.9
Possible infarction	1.2	1.2
Definite infarction	2.1	2.6
LV hypertrophy ≥6 points	1.8	2.3
RV hypertrophy ≥4 points	2.0	1.0
Conduction defect	1.3	2.6
Left axis deviation	1.2	1.6
Tall T-wave	0.6	0.4
Arrhythmia		
Supraventricular extrasystoles	1.6	0.5
Ventricular extrasystoles	1.6	1.9
Atrial fibrillation/flutter	2.7	0.9

L(R)V, left (right) ventricular. Relative risks are calculated within each group of men with or without symptomatic ischaemic heart disease. Results are based on 1158 men with and 6569 men without symptomatic ischaemic heart disease and are adjusted for age and the presence of other ECG abnormalities.

Table 6. Prevalence (percentage in parenthses) of electrocardiographic (ECG) myocardial ischaemia and infarction in men with and without symptomatic ischaemic heart disease (IHD).

Age-group (years)	No symptomatic IHD (n = 6569)	Symptomatic IHD (n = 1158)
40–44	62/1676 (3.7)	19/162 (11.7)
45–49	55/1660 (3.3)	24/233 (10.3)
50–54	85/1622 (5.2)	71/350 (20.3)
55–59	79/1611 (4.9)	104/413 (25.2)
All	281/6569 (4.3)	218/1158 (18.8)

Prevalence, yield and predictive value of definite myocardial infarction and ischaemia: the influence of symptomatic coronary heart disease

To assess the value of the resting electrocardiogram as a screening instrument for future major coronary heart disease events, we have examined a combination of two electrocardiographic abnormalities – definite myocardial ischaemia and definite myocardial infarction – that have high relative risks of a major coronary heart disease event and are relatively common. The relevant characteristics here are the prevalence (which provides a measure of the occurrence of the abnormality on screening), the yield of major coronary heart disease events (defined as the proportion of major coronary heart disease events occurring during follow-up in which these electrocardiographic abnormalities were

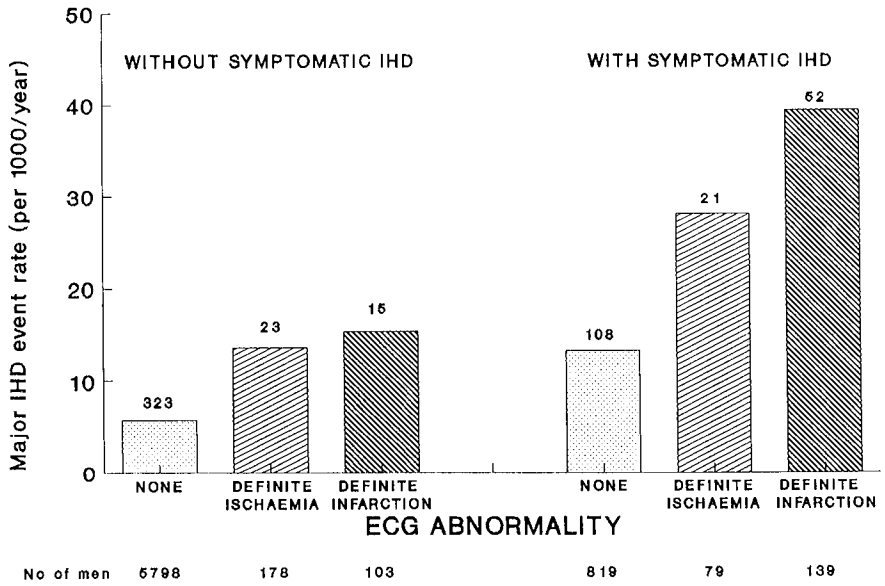

Fig. 1. Electrocardiographic (ECG) evidence of definite myocardial ischaemia, definite myocardial infarction and risk of a major ischaemic heart disease (IHD) event (per 1000 per year) in men with and without symptomatic IHD. Number of events in each group is shown above the bar.

Table 7. Yield and rate of major ischaemic heart disease (IHD) events in men aged 40–59 years with definite electrocardiographic evidence of myocardial ischaemia or infarction.

	No symptomatic IHD (n = 6569)		Symptomatic IHD (n = 1158)	
Follow-up (years)	Yield [n/total (%)]	Rate*	Yield [n/total (%)]	Rate*
5.0	19/184 (10.3)	13.5	44/115 (38.2)	40.3
9.5	38/401 (9.5)	14.2	73/210 (34.8)	35.2

*Per 1000 per year.

present, which provides a measure of the sensitivity of the electrocardiogram) and the major coronary heart disease event rate in men with these electrocardiographic abnormalities (which provides a measure of the predictive value of the electrocardiogram). Because the validity of screening instruments may vary with the level of risk in the screened population [21], men with and without symptomatic coronary heart disease have been examined separately for two lengths of follow-up, 5.0 and 9.5 years (Tables 6 and 7).

Men without symptomatic coronary heart disease

In men without symptomatic coronary heart disease, the combined prevalence rate of these two abnormalities is low, particularly in the younger age groups, and only rises to 5% in subjects over 50 years of age. Moreover, the yield of major coronary heart disease events associated with the combined electrocardiographic abnormalities is small and the major coronary heart disease event rate in subjects with these abnormalities is very low. These findings are consistent at both 5.0 and 9.5 years of follow-up.

Men with symptomatic coronary heart disease

The prevalence rate of the combined electrocardiographic abnormalities is very much higher in this group of men, exceeding 10% in men under 50 years of age and rising to 25.2% in the 55–59 year age-group. Similarly, the yield of major coronary heart disease events associated with the combined electrocardiographic abnormalities is substantially greater (38.2% at 5 years, falling to 34.8% at 9.5 years), while the rate of major coronary heart disease events in men with the electrocardiographic abnormalities is markedly higher (40.3/1000 per year at 5 years, falling to 35.2/1000 per year at 9.5 years).

Discussion

The present study explored the prevalence of electrocardiographic abnormalities in a representative sample of middle-aged men, using a three orthogonal lead system, and subsequent risk of major coronary heart disease events. The validity of the orthogonal lead system has been examined, particularly in relation to the standard 12-lead electrocardiogram [18,22]. For major electrocardiographic abnormalities (for example, myocardial infarction), both the sensitivity and the specificity of the three-lead orthogonal electrocardiogram are greater than 90% [18,22]. The prevalence rates of myocardial ischaemia and infarction in the present study are markedly greater than those in other British population studies, notably the Whitehall Study [5] and the United Kingdom Heart Disease Prevention Project [23]. Some of these differences may reflect differences in methodology (the Whitehall Study used limb leads only, which almost certainly resulted in loss of information [24]. The differences may also reflect the variations in occupational, social and geographic selection of the different cohorts, in particular the 'healthy worker effect' [25]. The prevalence of definite and possible left ventricular hypertrophy in our study population is remarkably similar to estimates from the Framingham Study [26].

Risks associated with electrocardiographic abnormalities

Myocardial ischaemia and infarction, left ventricular hypertrophy, major conduction defects

Earlier reports have suggested that major electrocardiographic abnormalities are associated with at least a two-fold increase in risk of subsequent coronary heart disease events [6,7]. The approximately four-fold unadjusted increase in coronary heart disease risk associated with electrocardiographic evidence of definite myocardial infarction is similar to that observed in the Whitehall Study [5]. However, the results presented here suggest that an important component of risk is accounted for by co-existing symptomatic coronary heart disease. After adjustment for this factor, the relative risk associated with definite myocardial infarction is substantially reduced. The two-fold increase in risk associated with definite left ventricular hypertrophy is close to the estimates obtained in the Framingham Study [26,27] and the Honolulu Heart Study [7]. Left ventricular hypertrophy with strain is associated with a particularly marked increase in risk similar in magnitude to that of definite myocardial infarction. The more than two-fold increase in risk associated with left bundle branch block closely parallels the findings in the Whitehall Study [5]. The observation that electrocardiographic signs of established ventricular damage (myocardial infarction, major conduction defect) are associated with an increased case fatality rate in subsequent myocardial infarction is consistent with earlier reports [5,28,29].

Arrhythmias

Earlier studies examining the relationship between ventricular extrasystoles and coronary heart disease have produced conflicting results. The present study suggests that frequent ventricular extrasystoles (three or more detected by an 8 s rhythm strip) are associated with an increased risk of subsequent major coronary heart disease events, and with an increased case-fatality rate, in

subjects both with and without symptomatic coronary heart disease. While such a relationship between ventricular extrasystoles on the resting electrocardiogram and coronary heart disease mortality rate has not been observed in some studies [30], observations in others have been consistent with the present findings. In the Busselton Study, a relationship between ventricular extrasystoles and coronary heart disease mortality was observed that was most marked when the frequency of ventricular extrasystoles was high, namely at least 10% of all beats [28]. A slight but non-significant increase in coronary heart disease mortality was associated with ventricular extrasystoles in the Whitehall Study [5]. In the Tecumseh Study [31], ventricular extrasystoles were associated with sudden cardiac death, a finding also observed in the present study [32], but other cardiac endpoints were not reported. An association between atrial fibrillation, increased coronary heart disease risk and increased case-fatality in the event of myocardial infarction is well recognized [5,6,33].

Other electrocardiographic abnormalities

The absence of any influence of right bundle branch block on long-term prognosis is consistent with findings from the Whitehall Study [5] and the Honolulu Heart Study [7], although there is some evidence that newly acquired right bundle branch block may exert an adverse influence on prognosis [34]. The absence of a strong relationship between Q-T interval prolongation and prognosis is consistent with a report from the Framingham Study [35]. The association between tall-peaked T waves and low rates of coronary heart disease mortality has not been widely reported. The only association between this T wave characteristic and major cardiovascular risk factors observed in the present study was with physical activity: tall-peaked T waves occurred in 10.6% of subjects taking vigorous exercise but in only 3.4% of those who were inactive. No association was observed with alcohol intake or with other major risk factors.

Clinical implications

Definite myocardial infarction, definite myocardial ischaemia and left ventricular hypertrophy with strain are the electrocardiographic abnormalities most strongly related to the incidence of major coronary heart disease events. However, to assess the absolute risk faced by an individual patient, the additional information provided by the presence or absence of symptomatic coronary heart disease is critical. In particular, it is important to note that the absolute risk of coronary heart disease associated with even the most serious electrocardiographic abnormalities in subjects without symptomatic coronary heart disease (15.4/1000 per year) barely exceeds that of subjects with symptomatic coronary heart disease and a normal electrocardiogram (13.9/1000 per year). When both symptomatic coronary heart disease and the electrocardiogram are taken into account, it is possible to define a group with an coronary heart disease rate of 39.4/1000 per year, more than six times greater than that of subjects without symptomatic coronary heart disease and with a normal electrocardiogram (5.8/1000 per year).

Is the resting electrocardiogram a useful screening tool?

In men without symptomatic coronary heart disease, the resting electrocardiogram has limited value as a screening test. The prevalence of important prognostic abnormalities (definite myocardial ischaemia and infarction) is low in this group of men, especially in those below 50 years of age. Moreover, these abnormalities in combination identify only about 10% of major coronary heart disease events occurring both during the next 5 years and during the next 9.5 years. Finally, the rate of major coronary heart disease events occurring in the men identified by the test is not very high (approximately 14/1000 per year), suggesting that the predictive value of the test is limited. Hence, the resting electrocardiogram is not an effective screening tool in men without symptomatic coronary heart disease – a conclusion consistent with that of earlier reports [36,37]. A more sensitive method for identifying future major coronary heart disease events in this population is the use of a multivariate scoring system, of the kind described elsewhere [38,39]. The use of a system based on age, parental history, diabetes, cigarette smoking, systolic blood pressure and total cholesterol can identify more than half of all major coronary heart disease events occurring during a 5-year follow-up period in men without symptomatic coronary heart disease; the inclusion of electrocardiographic abnormalities in such systems adds little to the precision of high risk identification [Whincup PH, unpublished data].

In men with symptomatic coronary heart disease the prevalence of major electrocardiographic abnormalities (definite myocardial ischaemia and infarction) is more than three times greater than it is in men without symptomatic disease. Furthermore, the proportion of future major coronary heart disease events identified by these abnormalities and the rate of major coronary heart disease events in men with an abnormal electrocardiogram are both very much greater. The resting electrocardiogram can therefore identify a subgroup of men with symptomatic heart disease who are at particularly high risk of future major coronary events. Identification of these individuals may be particularly valuable with the increasing recognition that subjects at exceptionally high risk of coronary heart disease mortality (> 3.0% per annum) may benefit from specific interventions, particularly treatment with lipid-lowering drugs [40]. In the present study, men aged between 40 and 59 years with symptomatic coronary heart disease and electrocardiographic evidence of definite myocardial infarction (2.8% of the total study population) had an annual death rate from coronary heart disease of 2.7% – a rate approaching, but not quite reaching, the specified mortality rate of 3.0% per annum. In this context, the resting electrocardiogram would help with

risk stratification, but further separation, using age and current risk factor levels (which continue to influence prognosis even in the presence of established coronary heart disease [41]) would also be needed.

Conclusion

Major electrocardiographic abnormalities are associated with an increase in risk of coronary heart disease, in men both with and without symptomatic coronary heart disease. However, the prognostic importance of major electrocardiographic abnormalities is strongly influenced by the presence of symptomatic coronary heart disease, which should be taken into account in assessment. In men with symptomatic coronary heart disease, the resting electrocardiogram may help to define a group at exceptionally high risk who may gain particular benefit from intervention. In men without symptomatic coronary heart disease, the resting electrocardiogram appears to have little or no value as a screening test.

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