Papers

Prognosis of angina with and without a diagnosis: 11 year follow up in the Whitehall II prospective cohort study

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Abstract

Objective To investigate the prognosis of angina among people with and without diagnosis by a doctor and an abnormal cardiovascular test result.

Design Prospective cohort study with a median follow up of 11 years.

Setting 20 civil service departments originally located in London.

Participants 10 308 civil servants aged 35-55 years at baseline.

Main outcome measures Recurrent reports of angina; quality of life (SF-36 physical functioning); non-fatal myocardial infarction; death from any cause (n = 344).

Results 1158 (11.4%) participants developed angina, and 813 (70%) had no evidence of diagnosis by a doctor at the time of the initial report. Participants without a diagnosis had an increased risk of impaired physical functioning (age and sex adjusted odds ratio of 2.36 (95% confidence interval 1.91 to 2.90)) compared with those who had neither angina nor myocardial infarction throughout follow up. Among reported cases of angina without a diagnosis, the 15.5% with an abnormality on a study electrocardiogram had an increased risk of death (hazard ratio 2.37 (1.16 to 4.87)). These effects were similar in magnitude to those in participants with a diagnosis of angina.

Conclusion Undiagnosed angina was common and had an adverse impact on prognosis comparable to that of diagnosed angina, particularly among people with electrocardiographic abnormalities. Efforts to improve prognosis among people with angina should take account of this submerged clinical iceberg.

Introduction

During a period of declining incidence of myocardial infarction, the prevalence of angina remains high, and consultations for angina in primary care have increased.[1] Government and professional bodies increasingly emphasise the importance of systematic identification and investigation of people with new onset angina on the basis of an assessment of prognosis.[2–4]

However, people with angina do not necessarily seek medical care.[5–7] The size and prognosis of this group has not been assessed in a contemporary prospective cohort. Population based studies show that the combination of angina identified by questionnaire and an abnormality on a resting electrocardiogram identifies groups with increased risk of death.[8 9] Whether this risk is confined to patients who have sought medical care and have a diagnosis from a doctor (visible clinical iceberg) or if it extends to those without a diagnosis by a doctor (submerged clinical iceberg) is not known.[10] The impact of undiagnosed angina on recurrent reports of angina and physical functioning is unclear.

Our objective therefore was to investigate the prognosis of angina among people with and without a diagnosis by a doctor and an abnormal cardiovascular test result. We defined prognosis by four outcomes: death, myocardial infarction, recurrent reports of angina, and functional status.

Method

Participants

We invited all non-industrial civil servants aged 35-55 years working in the London offices of 20 departments to participate in this study. The final cohort consisted of 10 308 participants (3413 women) with an overall response rate of 73%.[11] We obtained written informed consent from participants to examine clinical records. Participants completed questionnaires at five phases of data collection between 1985 and 1999 (fig A on bmj.com). At phase 5, 7830 participants completed a questionnaire (76% response rate from phase 1). At each phase we used the seven item Rose angina questionnaire to define angina independent of contact with medical care.[12]

Diagnosis of angina by a doctor

We obtained evidence of a diagnosis of angina from questionnaire items on diagnosis (four items), investigation (two items), and treatment (two items) (see bmj.com). We examined general practitioner and hospital records for details of diagnoses and abnormal test results among participants reporting positively on any of these eight questionnaire items. We also sought clinical records where the civil service gave a reason for sickness absence as angina or myocardial infarction or when the spell of absence exceeded 21 days.

Abnormal test results

Regardless of contact with medical care, we investigated each participant with a resting 12 lead

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Additional tables, figures, and questionnaire items appear on bmj.com

electrocardiogram at phases 1, 3, and 5. We defined abnormal results as Q waves (Minnesota codes 1-1 to 1-3), ST depression (4-1 to 4-4), inverted T waves (5-1 to 5-3), or left bundle branch block (7-1).[13] Additionally, among participants who had sought medical care, we defined abnormal test results as the presence of one or more diseased vessels at coronary angiography or ≥ 1 mm ST depression on exercise electrocardiogram or a reversible defect on stress imaging.

Outcomes: classification of angina and recurrent reports

We classified angina according to evidence of diagnosis by a doctor and the presence of an abnormal test result (table 1). We made chronological listings of each item of epidemiological and clinical record data. We coded pairwise combinations of evidence from two columns in the table in a hierarchy starting from a clinical record of diagnosis of angina plus an abnormal coronary angiogram at the top (first row) down to angina identified by the Rose angina questionnaire ("Rose angina") plus a normal study electrocardiogram at the bottom (last row). Two independent coders assigned dated codes for each report of angina. In the rare event of disagreement a third coder adjudicated. We defined a report of angina at each date that new evidence became available, but we allocated only one code, the highest, within any 28 day period. For participants reporting Rose angina at follow up but not at the previous phase, we used the mid-point date as the date of the report.

Outcomes: mortality, non-fatal myocardial infarction and physical functioning

Almost all (99.9%) participants were flagged at the NHS Central Registry, which notified us of dates of death. We defined non-fatal myocardial infarction by following the MONICA criteria of typical symptoms, enzyme abnormalities, and electrocardiographic changes.[14] We assessed physical functioning at phase 5 in 6839 participants by using the 10 item scale of the SF-36 health survey.[15 16] This scale asks: "Does your health now limit you in these [10 different] activities?" The activities range from running, through climbing stairs, to bathing and dressing. The scale ranges from 0 (worst) to 100 (best) and has previously been validated against risk factors, severity of angina, and time on an exercise electrocardiogram.[16 17]

Statistical analysis

We compared participants with four categories of angina, defined by the presence or absence of a diagnosis by a doctor or an abnormal test result, with participants who did not have angina or a myocardial infarction throughout follow up. All analyses concern incident angina among people without previous myocardial infarction. We excluded from all analyses 102 participants with angina or myocardial infarction (n = 224 reports) before phase 1 and 15 participants not flagged at the Central Registry. By 31 December 1999, 344 deaths had occurred among the remaining 10 191 participants (2.9 per 1000 person years). To examine the prognosis of participants after their first report of angina, we calculated the risk (probability) of specified events occurring in the next five years from their rate of occurrence. We calculated person years of survival by using the date of phase 1 and the dates of angina events and death or censoring at the end of 1999. We described the relation between types of angina and subsequent mortality with hazard ratios and 95% confidence intervals, calculated by using time dependent Cox's proportional hazards models that allowed for transitions during the follow up period, but only to a more severe category of angina. Thus the numbers of participants in the categories of angina in tables 1 and 4 differ. We defined impaired SF-36 physical functioning as below the lowest sex specific quartile (< 86 for men and < 71 for women) and used logistic regression to determine odds ratios of impaired physical functioning.

Results

Table 1 shows that 1158 (11.4%) of 10 191 participants developed angina. We found 2772 reports of angina, so 1614 (58%) of angina reports were recurrent (fig B on bmj.com).

Recurrent angina and non-fatal myocardial infarction

At the time of the first report of angina, 718/970 (74%) participants had no evidence of a diagnosis of angina by a doctor (table 2). Of these, 470 (65%) reported angina again during follow up and remained without a diagnosis. Among participants with an abnormal test result, the absolute risk of non-fatal myocardial infarc-

Table 1 Classification of angina according to evidence of diagnosis by doctor and abnormal test result

Evidence of diagnosis of angina by doctor?	Abnormal test result?	Epidemiological study data		Clinical record data		No of participants (total=1158)	No of reports* (total=2772)
		Self report questionnaire	Abnormal test result: study ECG	Diagnosis	Abnormal test result		
Yes ("visible iceberg")	Yes	—	—	Angina	Coronary angiography†	134	178
		—	—	Angina	Exercise ECG‡	65	76
		—	Abnormal§	Angina	—	51	63
		Diagnosis of angina or use of nitrate	Abnormal§	—	—	105	170
	No	—	Normal	Angina	—	125	147
		Diagnosis of angina, use of nitrate, or sickness absence	Normal	—	—	252	405
No ("submerged iceberg")	Yes	Rose angina	Abnormal§	—	—	174	268
	No	Rose angina	Normal	—	—	768	1465

ECG=electrocardiogram.

*One participant may have more than one report of angina.

†One or more diseased vessel on coronary angiography.

‡≥1 mm horizontal or downward sloping ST depression on exercise ECG or reversible deficit on stress imaging.

§Minnesota codes 1-1 to 1-3 (Q waves), 4-1 to 4-4 (ST depression), 5-1 to 5-3 (T wave inversion), or 7-1 (left bundle branch block) in most recent ECG.

Table 2 Percentage risk (number) of most serious* subsequent event over five years in participants with angina as a first report

				Type of most serious event over five years' follow up				
					Angina			
				Diagnosis by doctor		No diagnosis by doctor		
Type of first report†	No of participants	Death from any cause	Myocardial infarction	Abnormal test (any)	No abnormal test	Abnormal test (study ECG)	No abnormal test	None
Angina (diagnosis by doctor):								
Abnormal test (any)	80	0.13 (8)	0.16 (10)	0.26 (17)	0.16 (10)	0.07 (4)	0.02 (1)	0.20 (30)
No abnormal test	172	0.03 (5)	0.17 (27)	0.24 (39)	0.21 (34)	0.01 (2)	0.03 (5)	0.31 (60)
Angina (no diagnosis by doctor):								
Abnormal test (study ECG)	85	0.10 (7)	0.15 (11)	0.11 (8)	0.00 (0)	0.46 (42)	0.01 (1)	0.17 (16)
No abnormal test	633	0.04 (22)	0.07 (36)	0.05 (24)	0.05 (24)	0.07 (34)	0.54 (393)	0.18 (100)
No angina or myocardial infarction throughout follow up	9066	0.01 (297)	NA	NA	NA	NA	NA	0.99 (8769)

ECG=electrocardiogram; NA=not applicable.
*Seriousness of event ranged from death (most serious), through myocardial infarction and angina with diagnosis by doctor, to angina without diagnosis by doctor (least serious). First events occurring at or after phase 5 have been excluded.
†In 155 participants the first event was myocardial infarction.

tion was similar in those without a diagnosis by a doctor (15%) and those with a diagnosis (16%).

Impaired physical functioning
Participants with angina had an increased risk of impaired physical functioning at phase 5 (mean follow up seven years) compared with participants who did not have angina or myocardial infarction throughout follow up (table 3). The age and sex adjusted odds ratio was similar in participants without a diagnosis by a doctor (2.36 (95% confidence interval 1.91 to 2.90)) and those with a diagnosis (3.19 (2.25 to 4.53)). Separate analyses showed that the prospective impact of angina on functional impairment was the same in women and men (table A on bmj.com). Angina diagnosed within the seven years before functional assessment had a similar impact on functional impairment to angina diagnosed earlier (table B on bmj.com). As the median year of phase 5 was 1998, this approximates to diagnoses before or after 1991.

Survival
Mortality was increased in people with undiagnosed angina and an abnormal test result, compared with participants with neither angina nor myocardial infarction (table 4). Abnormal study electrocardiograms occurred in 268/1733 (15.5%) reported cases of undiagnosed angina (table 1). The age and sex adjusted hazard ratio for mortality in this group was 2.37 (1.16 to 4.87, P=0.02). Among participants with a diagnosis by a doctor, we found some evidence for adverse survival in those with an abnormal test result (hazard ratio 1.83 (0.95 to 3.52, P=0.07)).

Discussion

In this population based study, followed throughout the 1990s, more than half of people with angina had no evidence of diagnosis by a doctor. Among this group, an abnormal study electrocardiogram was common and was associated with worse survival. The increased risk of death and non-fatal myocardial infarction in people with angina and an abnormal test result was similar in magnitude in participants with and without a diagnosis. Recurrent reports of angina and impaired physical functioning were common in the undiagnosed group. The consistency of our

findings across all four outcomes provides evidence for a prognostically important submerged clinical iceberg of people with angina.

Angina without a diagnosis
No previous prospective studies during the 1990s have estimated the frequency and prognosis of angina without diagnosis by a doctor. Primary care consultations for angina rose between 1981 and 1991,[1] during a period of declining incidence of myocardial infarction. Most patients with symptoms of acute myocardial infarction seek medical care and obtain a diagnosis from a doctor—the submerged clinical iceberg is small. Our study shows that this is not true for angina. Our findings indicate that primary care disease registers, required by national policy,[2] are underestimating the

Table 3 Impaired physical functioning at phase 5 by type of first angina report

Type of first angina report	No of participants	No with poor physical functioning	Odds ratio (95% CI) adjusted for age and sex
No angina or myocardial infarction throughout follow up	6200	1374	1.00
Angina (diagnosis by doctor):			
Abnormal test (any)	53	24	2.29 (1.32 to 3.98)
No abnormal test	133	68	3.19 (2.25 to 4.53)
Angina (no diagnosis by doctor):			
Abnormal test (study electrocardiogram)	39	18	2.75 (1.45 to 5.22)
No abnormal test	414	169	2.36 (1.91 to 2.90)

Table 4 All cause mortality by type of angina report

Type of angina report	No of participants†	No of deaths	Rate* per 1000 person years at risk	Hazard ratio* (95% CI)
No angina or myocardial infarction throughout follow up	8949	296	2.6	1.00
Angina (diagnosis by doctor):				
Abnormal test (any)	201	10	4.9	1.83 (0.95 to 3.52)
No abnormal test	231	5	2.4	0.90 (0.37 to 2.21)
Angina (no diagnosis by doctor):				
Abnormal test (study electrocardiogram)	150	8	6.0	2.37 (1.16 to 4.87)
No abnormal test	706	20	2.8	1.12 (0.71 to 1.78)

*Adjusted for age and sex.
†No of participants contributing person years in each category of angina.

burden of angina in the general population. Consistent with a previous study,[18] employment grade did not influence the probability of having a diagnosis (data not shown).

Several reasons exist for a lack of diagnosis. A person with angina may not seek medical care. Little is known about factors predicting uptake of medical care and the negotiation of a diagnosis.[7] Once medical care has been sought, the doctor may miss or not record the diagnosis—a group that this study was not able to identify. If this were an important reason for the lack of diagnosis then the adverse prognosis suggests a need for improvements in the diagnostic ability of clinicians.

Prognosis of angina

A strength of our study lies in the repeated assessments of angina status made over prolonged follow up. An estimated 60% of the undiagnosed group reported angina again but remained without a diagnosis over five years of follow up. The British regional heart study found that Rose angina reported on two occasions was associated with a greater risk of fatal and non-fatal myocardial infarction than was angina reported on only one occasion.[6] Recurrent reports of angina may represent severe disease or ongoing ischaemia, as Rose proposed.[19]

As physical exercise is a common precipitant of angina, impairments in physical activities of everyday living constitute a major dimension of prognosis of angina. The presence of angina at baseline was associated with worse physical functioning at follow up, as assessed by a generic measure of health related quality of life. Importantly, this effect was similar in people with and without a diagnosis from a doctor and among both women and men.

We investigated all participants with resting electrocardiography and found adverse survival in people with angina without a diagnosis from a doctor in the presence of an abnormal resting electrocardiogram. Importantly, this effect was similar in magnitude (doubling of mortality) in those people with diagnosed angina who had an abnormal test result. Although many general practices have facilities for electrocardiography, the prognostic importance of common abnormalities is underappreciated.[8]

Impact of medical care and policy implications

Secondary prevention and revascularisation improve outcomes in angina, but only in people with a diagnosis. Underuse of investigation and treatment, widespread in the United States and the United Kingdom,[20 21] may have an adverse effect on outcomes.[22] We found no evidence that the impact of diagnosed angina on long term functional impairment improved over time. Guidelines in the United States and the United Kingdom recommend that all people with angina should undergo resting electrocardiography in order to identify high risk groups for further investigation and treatment.[2 4] The cost effectiveness of systematic case finding (with questionnaire) and risk assessment (with electrocardiography) of people with angina in the general population awaits investigation.

Conclusion

Among people with angina, a submerged clinical iceberg is associated with adverse prognosis across a range of outcomes. Reducing the population burden of

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What is already known on this topic

Systematic identification and investigation of people with angina is recommended by government and professional bodies

Many people with angina do not seek medical care, but the size and prognosis of this group has not been prospectively investigated in a contemporary cohort

What this study adds

Over half of participants with angina remained without a diagnosis on follow up

Physical functioning was impaired to a similar degree in people with and without a diagnosis of angina

Among people with an abnormal test result, the impact on mortality was similar in those with and without a diagnosis

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angina requires consideration of people who have yet to be given a diagnosis.

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