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Erythrocyte Sedimentation Rate, an Independent Predictor of Coronary Heart Disease in Men and Women

The Reykjavik Study

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The relation between erythrocyte sedimentation rate (ESR) and risk of developing coronary heart disease (CHD) or fatal cerebrovascular accident was assessed in a cohort of 7,988 men and 8,685 women who participated in The Reykjavik Study (Iceland). Cardiovascular risk assessment was based on characteristics at baseline, from 1967 to 1996. During an average follow-up of 19 and 20 years, 2,092 men and 801 women, respectively, developed CHD, and 251 men and 178 women died from cerebrovascular accident. For men, the fully adjusted increase in risk of developing CHD predicted by the top compared with the bottom quintile of ESR was 57% (hazard ratio = 1.57, 95% confidence interval: 1.38, 1.78; $p < 0.001$); for women, risk was increased by 49% (hazard ratio = 1.49, 95% confidence interval: 1.16, 1.90; $p < 0.001$). The increased risk after baseline ESR measurement was stable for up to 25 years for men and 20 years for women. The fully adjusted risk of death due to stroke predicted by increasing the ln(ESR + 1) by one standard deviation was increased by 15% for men ($p = 0.06$) and 16% for women ($p = 0.08$). In conclusion, ESR is a long-term independent predictor of CHD in both men and women. These findings support the evidence of an inflammatory process in atherosclerosis.

coronary disease; inflammation; risk factors

Abbreviations: CHD, coronary heart disease; CI, confidence interval; ESR, erythrocyte sedimentation rate; HR, hazard ratio.

It is evident that the traditionally known risk factors for coronary heart disease (CHD), including lipid abnormalities, high blood pressure, diabetes, and smoking, explain only a part of the risk associated with CHD (1). In recent years, the focus has been on the inflammatory nature of atherosclerosis, and this process has recently been reviewed extensively (2). In prospective population studies, sensitive markers of low-level inflammation such as fibrinogen and C-reactive protein have been found to be associated with future CHD rates, although it has been debated whether these acute-phase proteins are a consequence of the inflammatory changes or a part of the pathogenesis themselves (3, 4).

Erythrocyte sedimentation rate (ESR) is a widely used laboratory test, and this rate is found to be elevated in many acute and chronic disease states characterized by tissue necrosis and inflammation. It is an indicator of red cell aggregation and thus of blood viscosity. Only a few prospective studies with relatively few events have investigated the independent risk of erythrocyte sedimentation on subsequent CHD, and the results of these studies are conflicting (5–8). However, although some have demonstrated an increased risk of myocardial infarction and ischemic death for men, the sparse literature that exists on this risk factor in women has hitherto reported negative findings (7, 8).

Therefore, we assessed the value of erythrocyte sedimentation in predicting the development of future CHD in a prospective population cohort study, The Reykjavik Study. Participants were 16,673 men and women without a CHD diagnosis at baseline who were followed for up to 30 years.

MATERIALS AND METHODS

Study participants

The Reykjavik Study is a large, population-based cohort study that started in 1967. Men born in 1907–1934 and

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women born in 1908–1935, residing in the Reykjavik area and a few adjacent communities in Iceland on December 1, 1966, were classified by date and year of birth into six groups. A total of 19,390 persons attended, an overall response rate of approximately 70 percent for all those invited. The Reykjavik Study was performed in six stages: 1967–1969 (stage I), 1970–1972 (stage II), 1974–1979 (stage III), 1980–1984 (stage IV), 1985–1991 (stage V), and 1992–1996 (stage VI). The first group was invited to attend at all stages, the second group was invited to attend at two stages, and all other groups attended only once. The last stage included only those aged 70 years or older. Participants with a CHD diagnosis or an ESR of more than 50 mm/hour at study entry were excluded. In this analysis, only those data from the first examination of each participant were used, and the risk of developing CHD, as defined below, or dying from cerebrovascular accident was calculated. The follow-up period was from first attendance until December 31, 1998. The Reykjavik Study protocol was approved by the Data Protection Committee in Iceland and the Director General of Health.

Registration of CHD in study participants

In this study, the following endpoints were used to define CHD: acute myocardial infarction or sudden cardiac death as well as CHD evidenced by the need for percutaneous transluminal coronary angioplasty or coronary artery bypass graft. All episodes of myocardial infarction in the participants of The Reykjavik Study have been registered by the Icelandic Heart Association by gathering information from hospital records, death certificates, or necropsy reports and by using the World Health Organization's Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study criteria (9). Diagnostic criteria included symptoms, electrocardiograms, enzyme activities, and necropsy findings compatible with definite or possible myocardial infarction. Registrations included all occurrences of acute myocardial infarction and sudden ischemic cardiac death. A complete registry of all coronary artery bypass graft operations and percutaneous transluminal coronary angioplasties ever carried out on Icelanders is maintained at the Icelandic Heart Association and was used in this study to identify endpoints. The same two persons have carried out the registration of myocardial infarction, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft from the beginning. Registration of myocardial infarction was subjected to external quality control. The overall quality score for event registration was 1.9 (perfect score, 2.0) for Iceland in the MONICA study (10).

Additionally, we analyzed the data with respect to stroke death. To that end, causes of death were ascertained by reviewing all death certificates as well as all autopsy records of the participants (carried out for 55 percent of cases). Because of a computerized national roster that includes a unique personal identification number for each person and of low emigration (0.5 percent of those who ever attended), follow-up is nearly total.

Baseline data

The examination was carried out during two separate visits scheduled approximately 1 week apart. Blood was drawn during the first visit (after overnight fasting), height and weight were measured, and body mass index (weight (kg)/height $(m)^2$) was calculated. Blood pressure was measured in a supine position after 5 minutes of rest and was recorded to the nearest 2 mmHg; a mercury sphygmomanometer (Erkameter wall model; Richard Kallmeyer Nachforschung, Badtölz, Germany) was used. The cuffs had a 12 cm × 23 cm rubber bladder, and the total length of the cuff was 55 cm. A mean value of two blood pressure measurements from two separate visits was used for reference. A 12-lead electrocardiogram was administered and was coded according to the Minnesota code (11).

Blood sampling was conducted to measure serum total cholesterol level (mmol/liter), serum triglycerides (mmol/liter), blood glucose (mmol/liter), ESR (mm in the first hour), and hemoglobin level (g/dl). ESR was measured according to the Westergren method, as described in detail previously (12). In short, 4.5 ml of venous blood was sampled in a BD Vacutainer (Beckton, Dickinson and Company, Franklin Lakes, New Jersey) containing a 0.5-ml, 3.8 percent solution of sodium citrate. The test tube was mixed thoroughly immediately after blood sampling and again just before measuring, which took place within 2 hours after the blood was drawn. A standard 200-mm, Westergren-method glass tube was filled to the zero mark at the top, set in a vertical position, and left for 1 hour. The distance from the bottom of the surface of the miniscus to the top of the column was then measured, and the result was expressed as millimeters in the first hour. Room temperature at the place of measurement was registered and was used for corrections.

Information on smoking habits, use of antihypertensive medication (yes/no), personal history of diabetes (yes/no), level of education (level I: elementary school or less, level II: high school, level III: junior college, and level IV: university) (13), and leisure-time activity was obtained from a health questionnaire. Since physical activity after age 40 years has been shown to be the strongest protective factor for cardiovascular mortality, irrespective of the type of activity, we included this factor in our analysis (14). Furthermore, participants' CHD symptoms prior to study entry were registered on the basis of their answers to the Rose chest pain questionnaire (15), review of hospital records, physical examination, and the electrocardiogram. During the second visit, a physical examination was performed by a physician, including blood pressure measurement, as described above.

Statistical analysis

Patients were followed from entry into the study until occurrence of an endpoint, death from other causes, or December 31, 1998, whichever came first. Kaplan-Meier curves were constructed for CHD event-free survival according to quintiles of ESR in the age group 45–64 years. Pearson's correlation coefficients were computed to assess the association of the various confounding factors with ESR. A Cox proportional hazards model was applied to assess the predictive power of

TABLE 1. Baseline values* of risk factors† in the study population, The Reykjavik Study, Iceland, 1967–1996

Risk factor	Value (SD‡)	
	Men (n = 7,988)	Women (n = 8,685)
Age at examination (years)	51.9 (8.8)	53.4 (9.6)
Stage of the study (% of participants)		
I	24.7	24.7
II	24.1	22.8
III	23.0	21.1
IV	15.7	17.1
V	11.1	12.0
VI	1.4	2.2
Body mass index (weight (kg)/height (m)^2)	25.7 (3.4)	25.0 (4.2)
Cholesterol (mmol/liter)	6.36 (1.07)	6.57 (1.22)
Triglycerides (mmol/liter)	1.24 (0.69)	1.04 (0.52)
Systolic blood pressure (mmHg)	139 (18)	136 (20)
Antihypertensive drug use (%)	5.4	10.0
Glucose, fasting (mmol/liter)	4.59 (0.77)	4.36 (0.72)
Hemoglobin (g/dl)	15.1 (1.0)	13.5 (1.1)
Erythrocyte sedimentation rate (mm/hour) (median (range))	3 (0–50)	8 (0–50)
Physical activity after age 40 years (%)	16.0	17.2
Education (%)		
Elementary school	34.2	53.2
High school	44.5	38.4
Junior college	11.9	6.8
University	9.6	1.6
Smoking (%)		
Never	22.2	44.5
Former	23.9	15.2
Pipe/cigars	24.9	1.9
1–14 cigarettes/day	10.1	19.9
15–24 cigarettes/day	12.7	15.8
≥25 cigarettes/day	5.7	2.7

* Unless otherwise noted, all values are expressed as means.
† These factors were controlled for in subsequent analyses.
‡ SD, standard deviation.

ESR, measured at study entry, on the endpoints (CHD and death due to cerebrovascular accident). The distribution of ESR was very skewed to the right, so a logarithmic transformation was used (ln(ESR + 1)) because ESR can take the value of zero. For the same reason, a logarithmic transformation was performed for triglycerides. The analyses were conducted separately for each gender.

We calculated the hazard ratio of ln(ESR + 1) as a continuous variable and also according to quintiles of ESR, each compared with the lowest one. The hazard ratio was calculated by first adjusting only for age and study stage (I–VI), which refers to calendar period of entry into the study, and then after adjusting for all risk factors shown in table 1 using multivariable regression analysis. To examine whether the predictive power of ESR is mainly short term, the hazard ratio was calculated for 5-year time periods by using a Cox proportional hazards model. The fully adjusted log hazard ratio was generated for each 5-year time period after the baseline measurement, taking into account the occurrence of endpoints only during that specific time period. The regression line was computed as weighted least squares. Interaction was tested by adding the product of ln(ESR + 1) and each risk factor as an additional term in the regression and testing its independent predictive power. This testing produced nonsignificant results; thus, no adjustment for interaction was performed.

The significance level used was 0.05, two sided. We used the software package SPIDA (Statistical Package for Interactive Data Analysis) (16).

TABLE 2. Pearson's correlation coefficients for the relation between risk factors and ln(ESR* + 1), The Reykjavik Study, Iceland, 1967–1996

Risk factor	Men		Women	
	ln(ESR + 1) correlation coefficient	*p* value	ln(ESR + 1) correlation coefficient	*p* value
Age	0.14	<0.001	0.07	<0.001
Body mass index	0.04	<0.001	0.18	<0.001
Cholesterol	0.11	<0.001	0.19	<0.001
Systolic blood pressure	0.11	<0.001	0.16	<0.001
Antihypertensive drug use	0.08	<0.001	0.09	<0.001
Glucose, fasting	0.08	<0.001	0.17	<0.001
ln(triglycerides)	0.08	<0.001	0.17	<0.001
Hemoglobin	–0.27	<0.001	–0.15	<0.001
Smoking				
Pipe/cigars	–0.03	0.01	–0.01	0.44
1–14 cigarettes/day	0.02	0.08	0.01	0.47
15–24 cigarettes/day	0.07	<0.001	0.02	0.008
≥25 cigarettes/day	0.07	<0.001	0.03	<0.001
Education				
Junior high	–0.05	<0.001	–0.07	<0.001
Gymnasium	–0.02	0.02	–0.04	<0.001
University	–0.02	0.09	–0.08	0.003
Physical activity after age 40 years	–0.05	<0.001	–0.08	<0.001

* ESR, erythrocyte sedimentation rate.

RESULTS

A total of 9,328 men and 10,062 women participated in The Reykjavik Study. After exclusion of 1,309 men and 1,311 women with a CHD diagnosis at baseline and 31 men and 66 women with an ESR value of more than 50 mm/hour, 7,988 men and 8,685 women remained for analysis. Average follow-up was 19 years (range, 8 days–31 years) for men and 20 years (range, 8 days–31 years) for women.

Table 1 shows the baseline values for various CHD risk factors in the study population. The women compared favorably with the men with respect to triglycerides, systolic blood pressure, and smoking, which were all significantly higher in men. However, total cholesterol level was higher and use of antihypertensive drugs was more prevalent among women, and, compared with men, women had a lower level of education. In addition, ESR values were higher for women than for men (median, 8; range, 0–50 vs. median, 3; range, 0–50). As shown in figure 1, the distribution of ESR was skewed to the right. Furthermore, ESR increased significantly with age for both sexes—per year, 2.4 percent for men and 1.8 percent for women. As shown in table 2, all risk factors tested showed a significant correlation with ESR. Of these, the strongest correlation was found for hemoglobin level, cholesterol, triglycerides, and systolic blood pressure.

During follow-up, 2,092 men and 801 women developed CHD, as defined in the Materials and Methods section of this paper. As shown in figures 2 and 3, the probability of CHD-free survival for both men and women was poorest in the highest quintiles of ESR. The risk of developing CHD according to quintile of ESR is shown in table 3, first adjusted only for age and study stage and then fully adjusted for all risk factors shown in table 2. This analysis showed an increased risk with each increasing quintile of ESR relative to the first quintile for both men and women. For men, there was a 79 percent increased risk in the fifth quintile of ESR compared with the first one (hazard ratio (HR) = 1.79, 95 percent confidence interval (CI): 1.57, 2.04). After adjustment for all risk factors, risk increased significantly in the third, fourth, and fifth quintiles, corresponding to untransformed ESR values of 4 and above. The fully adjusted risk was increased 34 percent in the third quintile, 33 percent in the fourth quintile, and 54 percent in the fifth quintile of ESR. For women, the risk of CHD was doubled in the fifth quintile compared with the first one (HR = 2.03, 95 percent CI: 1.61, 2.56). After adjustment for all of the abovementioned risk factors, there was still a significant increase in risk of 49 percent (HR = 1.49, 95 percent CI: 1.16, 1.90) in the fifth quintile, corresponding to untransformed ESR values of 17 and above.

The increase in risk according to an increase of one standard deviation in ln(ESR + 1) was 23 percent (HR = 1.23, 95 percent CI: 1.18, 1.29; $p < 0.001$) for men and 33 percent (HR = 1.33, 95 percent CI: 1.23, 1.44; $p < 0.001$) for women when we adjusted for only age and study stage. After adjustment for all potential confounding risk factors shown in table

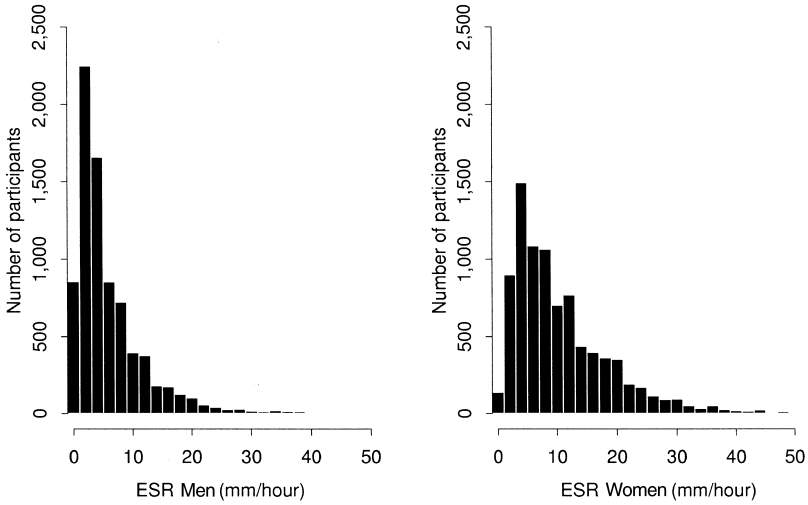

FIGURE 1. Histogram of the distribution of erythrocyte sedimentation rate (ESR) in men and women, The Reykjavik Study, Iceland, 1967–1996.

2, the increase of one standard deviation in ln(ESR + 1) was still associated with a significantly increased risk of CHD (HR = 1.17, 95 percent CI: 1.12, 1.23; $p < 0.001$ for men and HR = 1.18, 95 percent CI: 1.09, 1.28; $p < 0.001$ for women).

To examine the possible changes in the predictive power of ESR with time after measurement, a Cox proportional hazards model was used to calculate the risk in 5-year time periods, presented in figure 4. The increase in the fully adjusted risk was stable from the time of measurement during a follow-up period of 20 years for women and 25 years for men.

We also analyzed the risk of stroke mortality according to ESR. For men, the risk of death from stroke given an increase of one standard deviation in ln(ESR + 1) was increased by 23 percent (HR = 1.23, 95 percent CI: 1.08, 1.40); after adjustment for all risk factors, the risk was 15 percent (HR = 1.15, 95 percent CI: 0.99, 1.32). For women, the risk was increased by 21 percent (HR = 1.21, 95 percent CI: 1.04, 1.42); after full adjustment, the risk also increased not quite statistically significantly (HR = 1.16, 95 percent CI: 0.98, 1.37).

DISCUSSION

This prospective population study shows that ESR can independently predict the risk of developing CHD. An

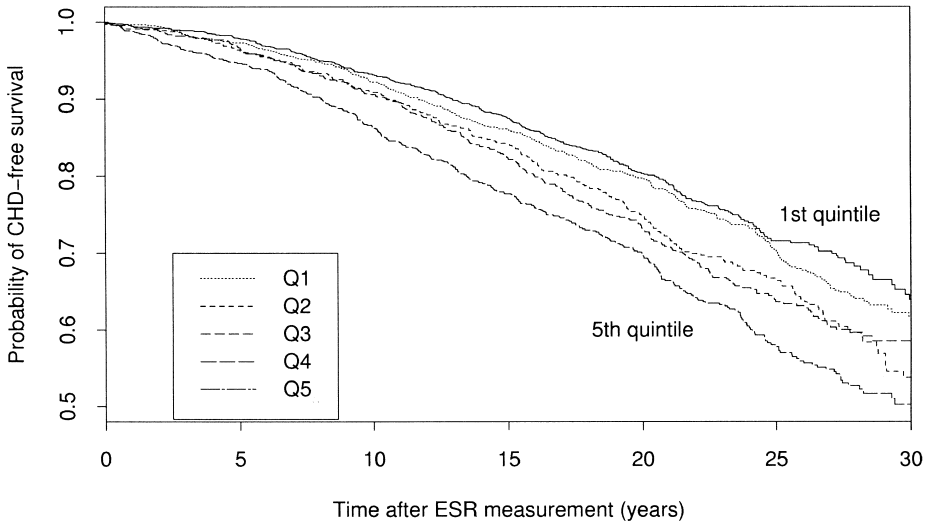

FIGURE 2. Kaplan-Meier estimates for coronary heart disease (CHD)-free survival according to baseline quintile (Q) of erythrocyte sedimentation rate (ESR) for men aged 45–64 years, The Reykjavik Study, Iceland, 1967–1996.

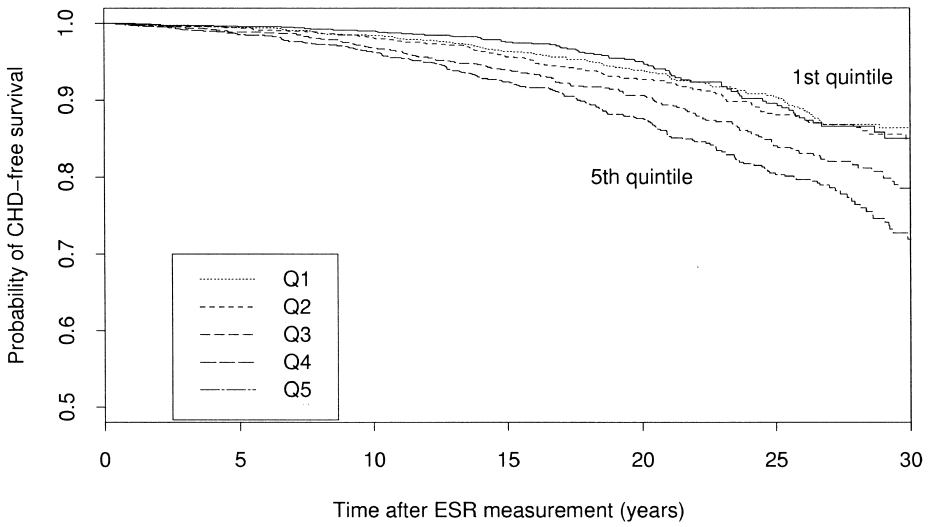

FIGURE 3. Kaplan-Meier estimates for coronary heart disease (CHD)-free survival according to baseline quintile (Q) of erythrocyte sedimentation rate (ESR) for women aged 45–64 years, The Reykjavik Study, Iceland, 1967–1996.

increase in ln(ESR + 1) of one standard deviation predicted independently a 17 percent increase for men and an 18 percent increase for women in the risk of developing CHD. For comparison, an increase in cholesterol of one standard deviation predicted independently a 34 percent increase in risk for men and a 27 percent increase in risk for women. ESR is therefore associated with approximately half of the increase in risk compared with cholesterol. Furthermore, we found that an increase of one standard deviation in ln(ESR + 1) increased the risk of death due to stroke by 23 percent ($p = 0.002$) for men and by 21 percent ($p < 0.001$) for women when adjusted for age and stage but that it decreased to 15 percent ($p = 0.06$) and 16 percent ($p = 0.08$), respectively, when adjusted for all risk factors. To our knowledge, no such data are available in the literature. We controlled for factors considered to influence ESR per se such as smoking, adiposity, socioeconomic indicators (as reflected by educational level), diabetes, and hemoglobin level as well as for other conventional CHD risk factors to minimize the effect of confounding.

To date, only four prospective population-based studies are known to have addressed the long-term predictive value of ESR in relation to the development of CHD. Two were rather small and reported negative findings (5, 6). In contrast, the Stockholm Prospective Study found erythrocyte sedimentation to be an independent risk factor for myocardial infarction (7). This study comprised 3,486 men followed up for 14 years and 171 incident cases of myocardial infarction. The First National Health and Nutrition Examination Survey in the United States (8) included 1,717 men and 2,003 women who developed a total of 1,462 endpoints during 15 years of follow-up. In this study, men aged 45–74 years with erythrocyte sedimentation in the upper quintile at baseline had an increased incidence of CHD (risk ratio = 1.32, 95 percent CI: 1.01, 1.72) compared with White men with erythrocyte sedimentation in the lowest quintile and,

TABLE 3. Hazard ratios for the risk of coronary heart disease* according to quintile of erythrocyte sedimentation rate, The Reykjavik Study, Iceland, 1967–1996

ESR† quintile	Men					Women				
	ESR cutoff values	HR† adjusted for age and year of study	95% CI†	HR fully adjusted‡	95% CI	ESR cutoff values	HR adjusted for age and year of study	95% CI	HR fully adjusted‡	95% CI
1	0–1	1.0				0–3	1.0		1.0	
2	2–3	1.14	1.00, 1.30	1.08	0.95, 1.24	4–6	1.03	0.80, 1.33	0.95	0.73, 1.23
3	4–5	1.40	1.21, 1.61	1.34	1.15, 1.55	7–10	1.17	0.91, 1.50	1.06	0.82, 1.37
4	6–9	1.50	1.31, 1.72	1.31	1.16, 1.54	11–16	1.55	1.21, 1.97	1.25	0.97, 1.61
5	≥10	1.79	1.57, 2.04	1.54	1.34, 1.78	≥17	2.03	1.61, 2.56	1.49	1.16, 1.90

* Myocardial infarction, coronary artery bypass graft, or percutaneous transluminal coronary angioplasty.
† ESR, erythrocyte sedimentation rate; HR, hazard ratio; CI, confidence interval.
‡ Refers to the multivariate risk after adjustment for all factors listed in table 2.

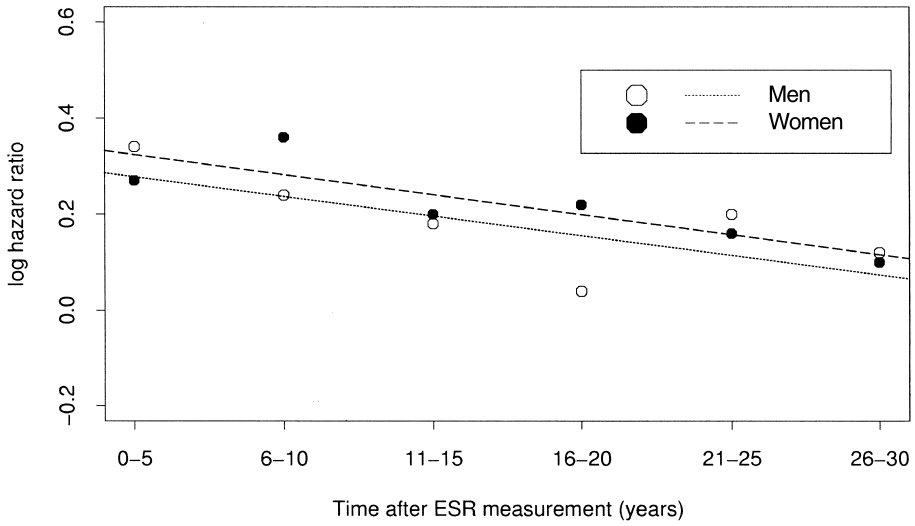

FIGURE 4. Log hazard ratio for the risk of developing coronary heart disease according to erythrocyte sedimentation rate (ESR) in six time periods after baseline ESR measurement for both men and women, The Reykjavik Study, Iceland, 1967–1996. Regression lines are weighted least squares.

furthermore, almost twice the risk of CHD death (risk ratio = 1.91, 95 percent CI: 1.23, 2.97). The corresponding risk ratios for women were not statistically significant: 1.21 (95 percent CI: 0.93, 1.58) and 1.15 (95 percent CI: 0.74, 1.79), respectively. Danesh et al. (17) combined the results of these four available studies and found that a comparison of persons whose erythrocyte sedimentation values were in the top third compared with the bottom third yielded a risk ratio of 1.33 (95 percent CI: 1.15, 1.54).

For comparison, in our study, the risk for persons whose ESR values were in the upper third compared with the bottom third was 1.40 (95 percent CI: 1.25, 1.57) for men (corresponding to an ESR value of ≥7) and 1.40 (95 percent CI: 1.17, 1.69) for women (corresponding to an ESR value of ≥12) after we adjusted for the classic CHD risk factors. To our knowledge, ours is the only study thus far to demonstrate an increased risk of CHD in relation to ESR for women. This finding reflects some of the strengths of the study, namely, the large number of both men and women who participated, a long follow-up, and an adequate number of endpoints that could be documented reliably.

A possible criticism is that a single measurement of ESR, known to vary with disease state, was used to predict CHD many years after the measurement was taken. Our analysis showed that the risk was quite stable after baseline ESR measurement for up to 25 years for men and 20 years for women. These results indicate that ESR not only is a short-term predictor of CHD, as would be expected if the risk was associated with acute disease at the time of measurement, but also predicts CHD in the long term. Similarly, C-reactive protein appears to predict risk over long time periods. Data from the prospective Physicians' Health Study showed that the increase in the risk of developing myocardial infarction predicted by C-reactive protein was stable over an 8- to 10-year follow-up period (3).

ESR values increased with age by 2.5 percent per year for men and 1.9 percent per year for women. No interaction was found between ESR and age (data not shown), indicating that the risk associated with ESR did not increase with advancing age. In addition, although women had higher ESR values than men did, the risk associated with ESR was not increased for women compared with men. These results are in line with recently published data from the Reykjavik cohort showing that various risk factors do not confer equal risk for women and men (18).

Note that the increase in risk of CHD was associated with ESR values in the normal range and increased with each increasing quintile. After correction for risk factors, sedimentation rate in the third, fourth, and fifth quintiles for men and in the fifth quintile for women was associated with a significantly increased risk. For comparison, in the First National Health and Nutrition Examination Survey, the association of elevated ESR was statistically significant for only those persons in the fifth quintile (8). The rate at which erythrocytes fall through plasma in 1 hour determines ESR and depends largely on the plasma concentration of macromolecules, particularly fibrinogen. Other determinants of ESR are the characteristics of the red blood cells (18). Markedly elevated ESR can be found in inflammatory states such as malignancies, infections, or collagen vascular diseases. Furthermore, ESR often becomes elevated following a myocardial infarction. In this study, we excluded persons whose ESR was above 50, which indicates concurrent illness.

Interpretation of the association between ESR in the normal range and CHD can be viewed as a result of persistent low-

level inflammation. Evidence from a broad range of studies demonstrates that atherosclerosis is a chronic inflammatory disease (2). Elevated plasma levels of several markers of the inflammatory cascade have been shown to predict future cardiovascular risk. Of these candidates, C-reactive protein and fibrinogen have been widely studied. A meta-analysis of 11 prospective studies including 1,953 CHD cases revealed that a measurement of C-reactive protein in the top third was associated with twice the risk of developing CHD (risk ratio = 2.0, 95 percent CI: 1.6, 2.5) when these cases were compared with those in the bottom third (19). Similar analysis of 18 prospective studies of fibrinogen, with 4,018 CHD cases, revealed a combined risk ratio of 1.8 (95 percent CI: 1.6, 2.0) for persons in the top third compared with those in the bottom third of the baseline measurements (20). Further evidence of the role of inflammation in atherosclerosis is the preventive effect of aspirin and statin therapy among persons with high C-reactive protein levels independent of the lipid-lowering effect (21, 22). Erythrocyte sedimentation rate is admittedly a more indirect marker of inflammation. Although fibrinogen is a major determinant of ESR, there is no precise correlation between sedimentation rates and fibrinogen concentrations; in one study, about one third of the values did not evidence a linear relation (23). We did not measure the fibrinogen level in our study cohort and consequently could not investigate how much of the effect of ESR could be explained by fibrinogen.

In conclusion, ESR in the normal range is an independent, long-term predictor of CHD in both men and women. These results support evidence of an inflammatory process in atherosclerosis that has been emerging as an important risk factor. Furthermore, this simple and inexpensive laboratory test with half the increase in risk compared with cholesterol may add to our ability to predict the risk of CHD in a multiple-variable risk-equation model.

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