Fibrinolytic activity and clotting factors in ischaemic heart disease in women

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Low fibrinolytic activity and raised levels of clotting factors have been linked with increased incidence of ischaemic heart disease in men.¹⁻³ Information in women, however, is confined to a relation of high fibrinogen concentrations with ischaemic heart disease in the Framingham study.³ This report describes the possible association of low fibrinolytic activity with fatal ischaemic heart disease in women.

Subjects, methods, and results

The Northwick Park heart study included 695 women aged 40-64 at entry in 1972-8. The methods and assessment of deaths attributed to ischaemic heart disease were as described for the men.¹ By the end of 1994, 74 women had died: 19 from ischaemic heart disease, 16 from other cardiovascular diseases, 28 from cancer, and 11 from other causes. Fibrinolytic activity is calculated as 100/(time to clot lysis in dilute whole blood (hours)),¹ and lysis time was measured in 17 of the women who died from ischaemic heart disease. Results have been adjusted to age 50.

Table 1 shows the women's mean entry values by cause of death. Those who died of ischaemic heart disease had significantly lower fibrinolytic activity and higher blood pressure than those who remained alive; those who died of other cardiovascular diseases also had higher blood pressure. Of the 17 women who died of ischaemic heart disease with results for lysis times (all of whom were postmenopausal at recruitment), 11 were current smokers. Smoking was associated with reduced fibrinolytic activity (that is, longer lysis times), especially in women smoking 15 or more cigarettes a day (fibrinolytic activity 23.3 units). Mean body mass index (weight (kg)/(height (m)²)) was 25.7 in those who died of ischaemic heart disease and 25.0 in survivors (P=0.4). Adjustment for smoking and body mass index (in addition to age) made little difference; fibrinolytic activity was 19.0 units in the women who died of ischaemic heart disease and 27.5 units in survivors (P=0.008).

Comment

The small numbers of deaths must be borne in mind when interpreting these findings. However, the differences in blood pressure between the women who died of cardiovascular disease and those who survived

are clear and as expected. The results in the women who died of ischaemic heart disease for cholesterol concentration and levels of factor VII and factor VIII are compatible with those from studies of men,^{1,4} though the differences compared with survivors were not significant. The small difference in the case of fibrinogen seems at odds with the significant difference in women in the Framingham study, which accrued a considerably larger number of events,³ and may be a reflection of the small number of women dying from ischaemic heart disease in our study.

The largest difference between those who died of ischaemic heart disease and survivors was in fibrinolytic activity. Low activity was specific for deaths from ischaemic heart disease; this is in accord with our prior hypothesis on fibrinolytic activity and is unlikely to be a chance finding. Measures of individual components of the fibrinolytic system such as tissue plasminogen activator and plasminogen activator inhibitor were not available when our study began in 1972. The dilute clot lysis time was therefore used as a global measure that was thought likely to be influenced by both activators and inhibitors. Another study has confirmed that dilute clot lysis time is substantially determined by tissue plasminogen activator and, particularly in women, by plasminogen activator inhibitor.⁵

We conclude that low fibrinolytic activity may play a part in fatal ischaemic heart disease in women as well as in men.

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Table 1—Mean (95% confidence interval) entry values in 695 women by cause of death and survival at follow up (values adjusted to age 50)

	Cause of death				
	Ischaemic heart disease (n=19)	Other cardiovascular diseases (n=16)	Cancer (n=28)	Other causes (n=11)	Survivors (n=621)
Fibrinolytic activity†	17.6 (12.9 to 24.2)***	28.7 (19.8 to 41.6)	29.1 (22.5 to 37.5)	27.7 (20.4 to 37.7)	27.3 (26.1 to 28.6)
Fibrinogen concentration (g/l)	3.38 (3.11 to 3.66)	3.08 (2.77 to 3.42)	3.31 (2.90 to 3.78)	3.30 (2.97 to 3.67)	3.31 (3.25 to 3.37)
Level of clotting factors (% of standard):					
Factor VII	119.5 (108.3 to 131.8)	120.4 (111.2 to 130.4)	106.8 (95.2 to 119.8)	131.4 (113.4 to 152.2)	112.5 (110.2 to 114.8)
Factor VIII	87.7 (75.4 to 102.0)	84.9 (77.4 to 93.0)	82.2 (72.5 to 93.1)	82.4 (74.6 to 90.9)	83.4 (80.9 to 86.0)
Systolic blood pressure (mm Hg)	148.0 (137.2 to 159.6)*	151.4 (138.5 to 165.5)**	135.8 (127.5 to 144.6)	121.3 (111.6 to 131.8)**	136.7 (135.1 to 138.3)
Cholesterol concentration (mmol/l)	6.57 (6.01 to 7.19)	6.06 (5.33 to 6.88)	6.10 (5.73 to 6.50)	6.30 (5.65 to 7.03).	6.26 (6.17 to 6.35)

Comparison with survivors (unpaired t test): *P = 0.02; **P = 0.01; ***P = 0.002.

†Calculated as 100/(time to clot lysis (hours)).