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Adipokines and the risk of type 2 diabetes in healthy middle-aged men: the PRIME study

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Obesity is widely recognised as a major risk factor for type 2 diabetes[1,2]. Adipose tissue is known to secrete biologically active molecules known as adipokines[3], which have been implicated in the pathogenesis of type 2 diabetes[4,5]. However, results from prospective studies that have examined the relationship between adipokines and risk of type 2 diabetes have generally been inconsistent. Some of these prospective studies have also had relatively short follow-up periods, while others have failed to fully adjust for confounding factors. In addition, few UK-based prospective studies have examined the association between adipokines and the diagnosis of diabetes. The present study examined the association between adiponectin and leptin and the diagnosis of type 2 diabetes in non-diabetic men.

Between 1991 and 1994, baseline data were obtained from 2745 men aged 50–60 years. A fasting blood sample was analysed for concentrations of leptin, adiponectin, lipids, glucose and C-reactive protein (CRP). Self-report questionnaires were used to assess demographic, socio-economic and lifestyle characteristics. Clinical measurements included weight, height and blood pressure. Between 1991 and 2010, participants were contacted annually to complete a clinical event questionnaire in order to obtain information on new cases of diabetes.

During the 19-year follow-up there were 280 newly reported cases of diabetes. Men who developed diabetes during follow-up had significantly higher BMI, systolic and diastolic blood pressure, TAG, CRP, insulin resistance and adipokine concentrations at baseline than men who did not develop diabetes. The cumulative rate for developing diabetes at 5, 10 and 15 years was 1.1, 4.1 and 7.9%, respectively. A Cox regression model was used to assess the relative risk of diabetes according to adipokine concentrations. This showed that men in the lowest third for adiponectin and highest third for leptin had greater risk of developing diabetes after adjusting for confounding factors that included lifestyle and biological risk factors. Additional adjustment for insulin resistance did not alter the association between adiponectin and diabetes ($P<0.01$), but resulted in loss of significance for leptin ($P=0.98$).

Categories	Rate/1000 person years	Adjusted relative risk (95% CI)			
		Model 1	Model 2	Model 3	Model 4[a]
Adiponectin (μg/ml)					
<3.81 (*n* 686)	10.3	1.00***	1.00***	1.00***	1.00**
3.81–6.65 (*n* 685)	6.6	0.63 (0.47, 0.85)	0.65 (0.48, 0.87)	0.63 (0.47, 0.86)	0.69 (0.51, 0.94)
>6.65 (*n* 687)	2.5	0.23 (0.15, 0.35)	0.30 (0.19, 0.45)	0.29 (0.19, 0.44)	0.34 (0.22, 0.52)
Leptin (ng/ml)					
<2.99 (*n* 788)	2.2	1.00***	1.00***	1.00***	1.00**
2.99–6.10 (*n* 790)	5.3	2.32 (1.50, 3.58)	1.69 (1.08, 2.63)	1.68 (1.08, 2.61)	1.42 (0.91, 2.22)
>6.10 (*n* 787)	11.8	5.37 (3.60, 8.01)	2.71 (1.74, 4.22)	2.60 (1.66, 4.07)	2.01 (1.27, 3.18)

Model 1: adjusted for age; Model 2: adjusted for age and BMI; Model 3: adjusted for model 2 variables + alcohol status, smoking status, socio-economic status; Model 4: adjusted for model 3 variables + total cholesterol, TAG, systolic blood pressure, hypertension. [a]Further adjustment for HDL, CRP and physical activity had no significant influence on the results. $^{**}P<0.01$, $^{***}P<0.001$ for difference between thirds (Cox regression).

Low adiponectin concentrations were independently associated with higher risk of developing type 2 diabetes. Adipokine concentrations may be useful clinical indicators for identifying individuals at risk of developing type 2 diabetes. The findings support the need for further exploration of the relationship between adipokines and type 2 diabetes risk.

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