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Prevalence and prognostic implications of the metabolic syndrome in community-based patients with type 1 diabetes: The Fremantle Diabetes Study☆,☆☆

Timothy M.E. Davis *, David G. Bruce, Wendy A. Davis

School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Western Australia, Australia

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Abstract

To determine whether the metabolic syndrome (MS) predicts fatal outcome in type 1 diabetes, we assessed prospective data from 127 patients from the observational community-based Fremantle Diabetes Study. Causes of death were classified as cardiac or other. The mean ± S.D. age of the patients was 42.0 ± 15.7 years and 57.5% were male. MS defined by the World Health Organisation (WHO), National Cholesterol Education Program's Adult Treatment Panel (ATP) III and the International Diabetes Federation (IDF) consensus definitions was present in 44.9, 42.1 and 39.4% of patients, respectively. There were 29 deaths (22.8%) during a mean of 11.0 years of follow-up, 55% of which were cardiac. In Cox proportional hazards models incorporating all plausible contributory variables (including individual MS components), none of the definitions was independently associated with cardiac or all-cause death ($p \geq 0.49$ in each case). When component variables were removed, the WHO definition weakly predicted cardiac death ($p = 0.045$). Microalbuminuria was a significant predictor of cardiac mortality ($p \leq 0.001$). A minority of our community-based type 1 patients had the MS and its presence did not add significant prognostic predictive value to conventional vascular risk factors.

Keywords: Type 1 diabetes; Metabolic syndrome; Cardiac death; All-cause mortality

1. Introduction

Although the subject of debate [2], insulin resistance has been considered a prime determinant of the metabolic syndrome (MS), a cluster of risk factors strongly associated with cardiovascular disease (see Table 1). There is also evidence that insulin resistance can accelerate the development of type 1 diabetes in antibody-positive individuals [3]. Since cardiovascular disease is a major cause of death in type 1 diabetes [4,5], it could be hypothesised that the MS is present in a significant proportion of patients and that its presence is associated with an increased risk of cardiovascular death.

A recent hospital-based US study has examined the relationship between MS and diabetes-related mortality in type 1 patients diagnosed in childhood [6]. Regardless of how MS was defined, the individual component variables were better predictors of outcome than the MS

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* Corresponding author at: School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, PO Box 480, Fremantle, Western Australia 6959, Australia. Tel.: +61 8 9431 3229; fax: +61 8 9431 2977.
E-mail address: tdavis@cyllene.uwa.edu.au (T.M.E. Davis).

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Table 1
Metabolic Syndrome criteria developed by the World Health Organisation (WHO), National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATPIII), and the International Diabetes Federation (IDF) consensus group

	WHO	NCEP ATPIII	IDF
Obesity	Waist-to-hip ratio >0.90 in men, >0.85 in women and/or BMI >30 kg/m^2	Waist circumference >102 cm in men, >88 cm in women	Waist circumference >94 cm in European men, >90 cm in Asian men, >80 cm in women*
Plasma glucose (mmol/L)	Diabetes, impaired glucose tolerance, impaired fasting glucose or insulin resistance by clamp*	≥6.1*	≥5.6 or previous diagnosis of impaired glucose tolerance or diabetes
Serum triglycerides (mmol/L)	≥1.7**	≥1.7	≥1.7
Serum HDL-cholesterol (mmol/L)	<0.9 in men, <1.0 in women	<1.04 in men, <1.29 in women	<1.04 in men, <1.29 in women
Blood pressure (mmHg)	≥140/90 or treated hypertension	≥130/85 or treated hypertension	≥130/85 or treated hypertension
Other	Urinary albumin excretion rate >20 μg/min or albumin:creatinine ratio >30 mg/g	–	–

Three factors are required in each case with obligatory components indicated by an asterisk (*); ** either a raised serum triglyceride or low serum HDL-cholesterol constitutes one factor under the WHO definition.

itself [6]. However, the representative nature of this sample is questionable since the prevalence of the MS was substantially lower than in other community-based type 1 cohorts [7]. In addition, diabetes-related deaths (the numbers of which were not revealed [6]) included those from microvascular complications as well as the macrovascular events with which the MS is conventionally associated [5]. A recent sub-study from the Diabetes Control and Complications Trial (DCCT) did not employ death as an endpoint but also found the MS to be a relatively poor predictor of macrovascular complications [8].

The results of these studies leave open the question as to whether the presence of MS in community-based patients with type 1 diabetes diagnosed at any age is a strong and independent predictor of cardiovascular and all-cause mortality, and thus a valuable part of the assessment and directed management of adult type 1 patients. We have, therefore, examined this question in a well-characterised community-based patient cohort.

2. Materials and methods

2.1. Subjects

The Fremantle Diabetes Study (FDS) was an observational study in a community of 120,097 people in the state of Western Australia [9,10]. The study protocol was approved by the Fremantle Hospital Human Rights Committee and all subjects gave informed consent before participation. Descriptions of recruitment, sample characteristics including classification of diabetes type and details of non-recruited patients have been published elsewhere [9]. We identified 2258 subjects between 1993 and 1996 and recruited 1426 (63%) to the FDS.

Patients were classified as having type 1 diabetes if they were (i) aged <40 years and commenced insulin at diagnosis, or (ii) diagnosed between 40 and 60 years of age, on insulin therapy at diagnosis and study entry, and non-obese (body mass index (BMI) <30 kg/m^2). Where possible, case records were consulted for confirmatory evidence including ketonaemia, autoantibody status and serum/plasma insulin/C-peptide concentrations [9]. There were 127 (8.9%) patients in the FDS cohort identified as having type 1 diabetes [11].

2.2. Clinical assessment

At baseline and annual reviews, a comprehensive history was taken, a physical examination was performed. Fasting blood and urine samples were taken for standard biochemical tests measured using automated methods [12]. Body mass index (BMI) was calculated from each patient's height and weight, and a waist-to-hip ratio was calculated from the waist circumference (measured in the mid-axillary line midway between the highest point of the iliac crest and lowest point of the costal margin) and hip circumference (at the widest point of the gluteal muscles).

Complications were identified using standard criteria [13]. Microalbuminuria was defined as an urinary albumin:creatinine ratio (ACR) ≥3.0 mg/mmol on a first-morning sample, neuropathy as a score >2/8 on the Michigan Neuropathy Screening Instrument clinical portion [14], and retinopathy as any grade in one/both eyes on direct/indirect ophthalmoscopy and/or detailed specialist assessment. Self-report and hospitalizations were used to identify cerebrovascular disease (stroke, transient ischaemic attack) and coronary heart disease (myocardial infarction, angina, coronary revascularization). Peripheral arterial disease was defined as an ankle:brachial index ≤0.9 or diabetes-related amputation.

We classified the MS using criteria developed by (i) the World Health Organisation (WHO) [15], (ii) National Cholesterol Education Program's Adult Treatment Panel (ATP) III