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Does vital exhaustion increase the risk of type 2 diabetes? A prospective study

Sasia Volden[a,*], Cathrine Lawaetz Wimmelmann[b,c], Trine Flensborg-Madsen[b,c]

[a] The Copenhagen City Heart Study, Hovedvejen, entrance 5, 1st floor, Frederiksberg Hospital, 2000 Frederiksberg, Denmark
[b] Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, Building 05 1353 Copenhagen, Denmark
[c] Center for Healthy Aging, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen, Denmark

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ABSTRACT

Background: There is evidence that both stress and depression have a causal relationship with type 2 diabetes suggesting that vital exhaustion (VE) too could be a risk factor. The association between VE and type 2 diabetes has, however, not been investigated prospectively.

Aim: To prospectively investigate whether VE is associated with an increased risk of type 2 diabetes in a Danish population.

Methods: A prospective cohort study based on the Copenhagen City Heart Study (1991–1993). The degree of VE was measured among 9075 participants without type 1 or 2 diabetes at baseline. To detect type 2 diabetes in the follow-up period, two different approaches were used: In the first substudy, type 2 diabetes was defined based on blood samples and questionnaires from a follow-up study in 2001–2003 (N = 4708). The second substudy was register-based, and the study population was linked to the Danish Hospital Discharge Register to detect registrations with type 2 diabetes until 2014.

Results: A high degree of VE was associated with an increased risk of developing type 2 diabetes in both substudies.

In the first substudy, the OR for developing type 2 diabetes was 2.56 (95% CI, 1.53; 4,29, P < 0,001) among the quartile of participants reporting the highest degree of VE.

In the second substudy, the OR was 1.31 (95% CI, 0.99; 1.72, P = 0.053) for this group.

Conclusion: The results indicate that VE may be a useful measure in clinical practice in order to discover individuals at risk of type 2 diabetes.

1. Introduction

Type 2 diabetes is a major public health issue and poses a big economic challenge worldwide [1]. As diabetes is considered a global epidemic, it is of great relevance and importance to uncover risk factors that effectively identifies empirically supported preventive interventions.

The term Vital Exhaustion (VE) describes a state of physical and mental exhaustion characterized by excessive fatigue, feelings of demoralization and increased irritability [2]. Overwork or the inability to solve a long-standing problem was identified as possible instigators for VE [3]. VE is widely studied in relation to cardiovascular diseases, e.g. proving to be predictive of stroke [4], isolated angina pectoris, myocardial infarctions and fatal coronary heart disease [3] and has previously been associated with a higher risk of all-cause mortality [5]. Furthermore, Schnor et al. have recently suggested that VE is one of the most important risk factors for coronary heart disease [6]. Thus, VE has been shown to predict heart disease and stroke, which are both common causes of death in people with diabetes [7]. Furthermore, there is convincing evidence that heart disease and diabetes share several psychological risk factors such as socioeconomic position, stress, and depression [8–12], suggesting that VE, in addition to being predictive of heart disease and mortality, may be a risk factor for diabetes.

This is the first study to prospectively investigate the association between VE and the risk of type 2 diabetes. Some studies have indicated a correlation between the two: A cross sectional study found an association between a high VE score and self-reported diabetes [5] and a study of mediating psychosocial factors of the close relationship between socio-economic status and metabolic syndrome, found a significant graded association between VE and the risk of a high metabolic syndrome score [13]. As the metabolic syndrome is a group of risk

* Corresponding author.
E-mail addresses: sasia.volden@gmail.com (S. Volden), calw@sund.ku.dk (C.L. Wimmelmann), tfma@sund.ku.dk (T. Flensborg-Madsen).

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factors associated with development of type 2 diabetes [14], this study also supports the hypothesis of an association between VE and type 2 diabetes. Congruently, a study exploring several psychological risk factors in men found VE to be most consistently linked to metabolic changes leading to type 2 diabetes [15]. Thus, there are some indications that a high degree of VE would elevate the risk of developing type 2 diabetes. However, no studies have specifically investigated this association, and the aim of the current study is to prospectively investigate the association of VE and later risk of type 2 diabetes in a large Danish population.

2. Materials and methods

2.1. Study population

Baseline data were obtained from the Copenhagen City Heart Study (CCHS), which is a large prospective study, comprising a random sample of Danish women and men aged 20 and older living in the Copenhagen area. At the first examination in 1976–1978, 14,233 participants (response rate 74%) were examined and filled in a self-administered questionnaire. Four following examinations were conducted in 1981–1983 (CCHS2), 1991–1993 (CCHS3), 2001–2003 (CCHS4) and 2012–2015 (CCHS5) examining the original participants and a small supplementary subsample of 20–24 year olds. Using the unique personal identification number (CPR number), this population can be followed by linkage to several Danish registers, allowing diverse prospective studies with minimal loss during follow-ups. The CCHS is described in details elsewhere [16].

Information on VE was available in CCHS3 wherefore data in the present study were based on participants in this sample with an attendance number and response rate of N = 10,135 (61%). Exclusion criteria applying to 1060 participants included: unanswered questions concerning self-reported diabetes or VE, and pre-existing diabetes. These exclusion criteria were selected to prevent participants with diabetes at baseline and thereby minimizing the risk of reverse causation. Retained in the study were 9075 individuals (5166 women and 3909 men) in the age range of 21 to 98, with a mean age of 57.7 years.

2.2. Assessment of vital exhaustion and diabetes

2.2.1. Vital exhaustion

VE was originally part of the Maastricht Questionnaire [17]. In this study VE was assessed with the shortened, 17-item questionnaire used in CCHS3, which has been used in several other studies [5,6,18]. Answers of “yes” or “no” yielded 1 or 0 points depending on the question (illustrated in Fig. 1) and the answer “not sure” was scored 0.5 points. This resulted in total scores from 0 to 17 with higher scores reflecting a greater degree of VE. In line with a previous study using the CCHS data [18], sample quartiles were used to group the VE score into four categories (see Tables 2 and 3) resulting in a cutoff for “high VE” of 6.5 and 6 for substudy 1 and substudy 2, respectively.

2.2.2. Diabetes mellitus, type 2

All participants with diabetes 1 or 2 at baseline were excluded from the study. Diabetes at baseline (n = 749) was assessed using questionnaires (self-reported diabetes), blood samples (cases with plasma glucose above 11.1 were excluded) and registrations in the Danish Hospital Discharge Register (LPR).

In the first substudy, classification of type 2 diabetes during follow-up was based on the questionnaires (self-reported diabetes) and blood samples from CCHS4. The attendance number and response rate in this sample was N = 6038 (50%) of which 4708 participants attended both CCHS3 and CCHS4 and were therefore included in the first substudy. The follow-up time in this study was the 10 years between the two examinations.

In the second substudy, classification of type 2 diabetes was solely based on information obtained from registers. By virtue of the CPR number in the Danish National Central Personal Register, the study population was linked to The Danish Hospital Discharge Register (LPR) and The Register of Causes of Death [19]. LPR contains records of all admissions to and diagnoses by Danish hospitals since 1976 [20]. The participants were followed from their examination date at CCHS3 until first registration of type 2 diabetes, emigration or death, and if not obtained, the participants were followed until November 2014. In this study, type 2 diabetes was defined according to WHO's International Classification of Diseases (ICD) by ICD-8 code 250: Non-insulin dependent diabetes mellitus (NIDDM) and ICD-10 codes E11: non-insulin dependent diabetes mellitus (NIDDM), E13: Other specified diabetes mellitus and E14: Unspecified diabetes mellitus. ICD-8 codes were used for diagnoses given in the period from 1977 to 1993. From 1994 and onwards, the ICD-10 classification system was used [21].

2.3. Statistical analyses

The two main analyses of substudies 1 and 2 were completed with logistic regression, estimating odds ratios (ORs) and 95% confidence intervals (95% CIs). A preliminary analysis found no significant interaction between VE and sex why all analyses are shown for women and men collectively.

Confounders were chosen based on theoretical considerations and were all measured at baseline: Sex, age, yearly income, educational level, alcohol intake, smoking, BMI, level of physical activity, cohabitant status, and satisfaction with social contact. The logistic regression models were adjusted for these confounders, for which descriptive information is presented in Table 1. All were included as categorical variables in the logistic regression models. A test for trend analyses was conducted by including VE as a continuous variable in the logistic regression analyses (Tables 2 and 3).

The outcome of type 2 diabetes was sometimes accompanied with a diagnosis of type 1 diabetes. As the focus of the present study is type 2 diabetes, the analyses are based on the incidents with type 2 diabetes as the only diagnosis and individuals with both diagnoses were deleted from the analyses. A supplementary analysis comprising both groups was made and showed similar results as the main analysis; however deletion was still favoured in order to avoid a misclassification bias.

Analyses of the 17 questions' individual association with type 2 diabetes were conducted by logistic regression (data not shown).

Finally, to investigate the role of reverse causation, sensitivity analyses were conducted in substudy 2, in which all individuals with a diagnosis of type 2 diabetes within the first year after VE assessment were omitted from the analyses.

All statistical analyses were performed in IBM SPSS statistics, version 22.

3. Results

3.1. Characteristics of the study population

Table 1 presents characteristics of women and men separately comprising each group of VE score.

A total of 73.4% of the participants reported a VE score of one or more. The scores ranged across the scale from 0 to 17 points with women generally reporting a higher degree of VE than men with the average VE score among women being 4.2 compared with 3.0 for men (data not shown). Congruently, a high degree of VE (VE score of 6 or more) was reported by 28.8% of the women and 17.8% of men (Table 1). Individuals in the group with a VE score of 6 or higher were most likely to be women, 35–65 years old, have an annual income lower than 300,000 before taxes, have a shorter education, smoke, have a low physical activity level and be moderately or very satisfied with their social relationships. The majority of men and women in the highest VE group reported an alcohol consumption of > 14 units per