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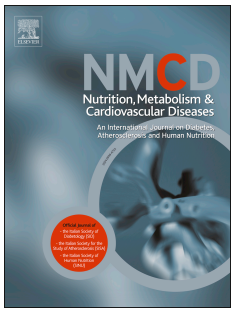

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Association between habitual coffee consumption and metabolic syndrome in type 1 diabetes

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Abbreviations: eGDR, estimated glomerular disposal rate; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein; MS, metabolic syndrome; T1D, type 1 diabetes

Abstract

Background and aims: In the general population, habitual coffee consumption is inversely associated with the metabolic syndrome, a syndrome that is rather common also in patients with type 1 diabetes. However, whether coffee intake is beneficially related to the metabolic syndrome also in type 1 diabetes, is not known. We, therefore, studied the potential association between coffee consumption and the metabolic syndrome in a large population of individuals with type 1 diabetes. Furthermore, we investigated whether coffee consumption is associated with insulin resistance (estimated glucose disposal rate, eGDR), kidney function (estimated glomerular filtration rate, eGFR), and low-grade chronic inflammation (high-sensitivity C-reactive protein, CRP).

Methods and results: Data from 1040 participants in the Finnish Diabetic Nephropathy Study were included in these cross-sectional analyses. Metabolic syndrome was assumed if at least 3 of the following cardiovascular risk factors were present: central obesity, high blood pressure, low HDL-cholesterol concentration, high triglyceride concentration, and hyperglycaemia. Subjects were categorized based on self-reported daily coffee intake: non-consumers (<1 cup/d), low (≥1 cups/d <3), moderate (≥3 cups/d <5), and high coffee consumption (≥5 cups/d). In multivariable logistic regression analysis, moderate and high coffee consumption was associated with increased odds of the metabolic syndrome. Moreover, any level of coffee consumption was associated with increased risk of the blood pressure-component. An increasing trend was observed in the eGFR with increasing coffee consumption.

Conclusions: In type 1 diabetes, high coffee intake is associated with the metabolic syndrome, and especially its blood pressure-component.

Introduction

The metabolic syndrome (MS) represents a cluster of risk factors for cardiovascular disease [1]. Although habitually associated with type 2 diabetes, the MS is also highly prevalent in patients with type 1 diabetes (T1D) [2]. Importantly, in this patient group the MS is an independent predictor of cardiovascular events, and premature mortality [3]. Therefore, identifying risk factors related to the MS is of major importance.

In two meta-analyses, coffee consumption has been inversely related to the MS [4, 5]. Particularly, a negative association between coffee consumption and the MS has been most evident in high habitual intakes, those exceeding 3 cups of coffee per day [6]. Moreover, long-term coffee consumption has been associated with decreased risk of cardiovascular disease [7] and type 2 diabetes [8]. The beneficial effects of coffee have been attributed to its bioactive components, caffeine, diterpenes, phenolic acids, and melanoidins [9]. However, the acute effects seem to differ from the observed long-term effects [10] as, in a meta-analysis of observational studies, coffee consumption showed no substantial effects on the risk of hypertension, but in a meta-analysis of randomized controlled trials, an acute rise in blood pressure was reported [5]. Moreover, acute reducing effects of coffee on insulin sensitivity have been observed [8, 11].

To our knowledge, reports on the relationship between habitual coffee consumption and the MS in T1D have not been published. Our aim was, therefore, to fill in this gap in knowledge. Furthermore, we investigated the association between coffee consumption and insulin sensitivity, assessed by the estimated glucose disposal rate (eGDR), and low-grade chronic inflammation, examined by high-sensitivity C-reactive protein (hsCRP). As subclinical inflammation is related to the progression of diabetic nephropathy [12], the association between coffee intake and the estimated glomerular filtration rate (eGFR) was also investigated.

Methods

Subjects were participants of the Finnish Diabetic Nephropathy (FinnDiane) Study, which aims to identify risk factors for long-term complications of T1D. Included in these cross-sectional analyses

were all individuals with known MS status and a completed diet questionnaire (n=1040, age 46.7 ± 0.4 years, 45% men). Individuals with end-stage renal disease (dialysis or renal transplant) or eGFR <30 mmol/l were excluded. T1D was defined as onset of diabetes before the age of 35 years and permanent insulin therapy started within one year of the diagnosis. All participants signed an informed consent prior to study participation. The protocol was approved by the Ethics Committee of the Helsinki and Uusimaa Hospital District.

At the study visit, blood pressure was measured twice in the sitting position following a 10-minute rest. A mean of the two measurements was calculated. Weight and height were measured in light clothing without wearing shoes, and body mass index (kg/m^2) was calculated. Waist circumference was measured at the midway between the lowest rib and iliac crest. The attending physician recorded data on medication use and diabetic complications using a standardized questionnaire. Proliferative diabetic retinopathy was defined as history of retinal laser treatment. Data on smoking, defined as smoking at least one cigarette per day, were self-reported.

Patients were asked to abstain from drinking tea, coffee and caffeinated beverages for 12 hours prior to the drawing of blood. Fasting was not required, but light, low-fat breakfast was allowed to treat or prevent potential hypoglycaemia. HbA_{1c} was measured locally at each study centre using standardized assays. Serum triglyceride and total cholesterol concentrations (Konelab 60i; Thermo Fischer scientific Inc., Waltham, MA, USA), and HDL-cholesterol concentration (HTS 7000 Plus Bio; Perkin Elmer, Wellesley, MA, USA) were measured enzymatically. Serum creatinine concentrations were determined as previously described [2]. Until April 2008, serum hsCRP concentrations were measured with a photometric, immunochemical method (Orion Diagnostica, Espoo, Finland), and thereafter by immunoassay (Modular analyzer, Roche Diagnostics, Basel, Switzerland). Individuals with hsCRP levels >10.0 mg/l were excluded from the hsCRP analyses, as high values are suggestive of acute infection. Insulin sensitivity was assessed using an equation for estimated glucose disposal rate modified for HbA_{1c} instead of HbA_1 [13].

Renal status was assessed based on the urinary albumin excretion rate (AER). Participants were categorized having normal AER (<20 µg/min, or <30 mg/24h), microalbuminuria (20 µg/min ≤ AER <200 µg/min, or 30 mg/24h ≤ AER <300 mg/24h), or macroalbuminuria (AER ≥200 µg/min, or AER ≥300 mg/24h) in at least two out of three consecutive urine collections. Diabetic nephropathy was

defined as macroalbuminuria. Based on a single measurement of serum creatinine, estimated glomerular filtration rate was calculated [14].

Physical activity was assessed by a self-administered questionnaire on leisure-time physical activity [15]. The duration of the activities was multiplied by the activity- and intensity-specific metabolic equivalent of task (MET) to calculate the total amount of weekly leisure-time physical activity. Based on the sum of weekly MET hours, patients were categorized as sedentary (<10 MET h/week), moderately active (10-40 MET h/week), and active (>40 MET h/week).

MS was defined according to the criteria by Alberti et al [16]. Accordingly, MS was assumed when at least three of the following criteria coexist: waist circumference ≥94 cm in men and ≥80 cm in women, triglyceride concentration ≥1.7 mmol/l or lipid lowering medication, HDL-cholesterol concentration <1.0 mmol/l in men and <1.3 mmol/l in women or medication to increase HDL-cholesterol concentration, blood pressure ≥130/85 mmHg or use of antihypertensive medication, and fasting blood glucose concentration ≥110 mg/dl. In the current study, all subjects had T1D and, by definition, met the criterion for hyperglycaemia. A metabolic syndrome score, ranging between 1 and 5, was calculated for each participant, to reflect the number of fulfilled components of the metabolic syndrome. This score was used as a continuous variable in the generalized linear regression analysis.

The methods to study dietary intake in the FinnDiane Study have been previously described [17]. In short, during the study visit, the participants completed a validated [18] diet questionnaire. This questionnaire intends to capture data on the participants' habitual food intake. Of importance to the current study, coffee consumption was assessed using two separate questions. First, subjects were asked to report the number of cups of coffee consumed daily. Four categories were formed: non-consumers (<1 cup/d), and those with low (≥1 cups/d <3), moderate (≥3 cups/d <5), and high coffee consumption (≥5 cups/d). Non-consumers served as a reference group in the analyses. Second, the participants reported the type of coffee (filtered, boiled, instant, or other types of coffee) habitually consumed.

After returning the diet questionnaire, participants were asked to complete a three-day exercise and food record. The allocated days were consecutive and included two weekdays and one

weekend day. In this record, participants reported all foods and beverages consumed, home blood glucose measurements, administered insulin dosages, and physical activities. With a ten-week interval, the record keeping was repeated to collect data from a total of six days per participant. The Diet 32 software (version 1.4.6.2, AIVO, Turku, Finland), and from August 2014 onwards the AivoDiet software (version 2.0.2.3, AIVO, Turku, Finland), based on the Finnish National Food Composition Database, were used to calculate energy and nutrient intakes. In the current paper, data were included from all participants who had completed the food record for at least three days. From the food record entries, the average daily energy, macronutrient, and fibre intakes were calculated. High alcohol intake was defined as ≥20 g/d alcohol in men and ≥10 g/d in women [19].

Descriptive data were reported as percentages (categorical variables), mean ± standard deviation (parametric data), and median (interquartile range) (non-parametric data). The respective statistical comparisons were conducted with Chi-squared test, one-way ANOVA, and Kruskal-Wallis test. Logistic regression analysis was used to assess associations between coffee consumption categories and the MS and its components. Generalized linear regression was used to study the association between continuous variables and coffee consumption groups. All *P*-values were based on two-tailed tests. A *P*-value <0.05 was considered statistically significant. The statistical analyses were performed using IBM SPSS Statistics 22.0 for Windows (IBM Corp, Armonk, NY, USA).

Results

Data from a total of 1040 participants were available for the analyses (Table 1). Of the participants, 13% were non-consumers, while 22%, 36% and 29% reported low, moderate, and high coffee intakes, respectively. The frequencies of men and smokers were the highest among individuals in the highest coffee category. Age and frequency of the MS increased towards the higher coffee consumption categories. Regarding the components of the MS, the non-consumers and the high intake group were the ones with the lowest and the highest frequencies of the triglyceride- and the HDL-components, respectively. Moreover, the frequencies of individuals fulfilling the blood pressure-component was observed to increase with increasing coffee consumption. Dietary intakes in the four groups of coffee consumption are shown in

Supplementary table 1, which shows differences in energy and alcohol (as percentages of total energy) intakes amongst the groups.

In the logistic regression analysis, adjusted for age, sex, energy intake, alcohol intake, physical activity, and smoking, the odds of the MS was higher in the moderate and high coffee consumption groups, with non-consumers as reference (Table 2). Of the components of the MS, any level of coffee consumption was associated with increased odds of fulfilling the blood pressure-component. This association was evident also in those with no antihypertensive medication. Of the continuous variables, only the metabolic syndrome score was associated with coffee consumption (Supplementary table 2). Here, the lowest scores were observed in the non-consumers (median, interquartile range 2.92, 2.64–3.20), and the highest scores in the high coffee consumption group (3.33, 3.15–3.52).

The observed and the adjusted means of eGDR, eGFR and hsCRP in the four groups are shown in Table 3. In the final model, the mean eGFR increased towards the higher coffee consumption categories. In contrast, no differences were observed amongst the four groups in eGDR and hsCRP.

Of the coffee consumers, 825 (91%) drank filtered coffee. Due to the small number of individuals reporting habitual consumption of other coffee types, they were pooled for the subsequent analyses. The basic characteristics of those habitually consuming filtered coffee and other types of coffee, were no different (data not shown). Adjusted for age, sex, smoking, energy intake, alcohol intake, and physical activity, consuming filtered coffee was associated with increased risk of the MS. However, coffee type was not associated with the odds of the individual components of the MS. Finally, in the fully adjusted generalized linear model, no differences were observed in eGDR, eGFR, and hsCRP levels between the two groups.

Discussion

In general population, coffee consumption has been associated with beneficial health effects, including reduced risk of MS [4, 5] and type 2 diabetes [8]. As MS is frequently observed also in T1D [2], and since it is an independent risk factor for cardiovascular complications [3], we wanted to elucidate whether there is an association between coffee consumption and MS also in this high-

risk population. In contrast to the previous observations in other populations, coffee consumption was associated with higher odds of MS in the current study. Particularly, compared to non-consumers, those with moderate (≥3 cups/d <5) and high (≥5 cups/d) coffee intakes had increased risk of MS. Any level of coffee consumption was additionally associated with increased odds of fulfilling the blood pressure-component. Finally, of interest to individuals with T1D, increasing coffee consumption was associated with higher eGFR.

The reason behind the disparity between the observations made in general population and in the current study is not known. Different characteristics of the study populations may offer a potential explanation. First, all participants in the current study had T1D and, by definition, fulfilled the blood glucose criterion. Moreover, compared to the healthy population, patients with T1D may more frequently use lipid lowering and antihypertensive medication and therefore, more often fulfil the lipid and the blood pressure criterion. Thus, compared to the general population, individuals with T1D may be more readily categorized with MS.

In the current study, the association between coffee consumption and the MS seems to be mainly driven by the blood pressure component. Indeed, none of the other components had any association with habitual coffee consumption. In a previous meta-analysis, an inverse association between coffee consumption and hypertension was reported [20]**.** Analyses of potential confounders, in that paper, revealed smoking as a potential effect modifier in the association between coffee consumption and the risk of hypertension. In the current study, however, coffee consumption was associated with the blood pressure component of the MS independent of smoking. Moreover coffee, as well as insulin, has the potential to activate the sympathetic nervous system. Therefore, it could be speculated, that the increase seen in blood pressure with coffee consumption, could rather be related to an interaction between coffee and insulin dosing. Adding insulin in the model did, however, not change the current results, suggesting that coffee has an independent effect on the blood pressure.

In a meta-analysis of six prospective studies, including over 170,000 individuals, an inverse J-shaped curve was observed with the risk of hypertension increasing up to three daily cups of coffee, and thereafter decreasing with higher intakes [21]. The authors speculated that the pressor effect of caffeine could explain the increase in the blood pressure in the low-consumption group.

However, with increasing habitual consumption, tolerance to the caffeine-induced pressor effect may develop [9], thereby dissolving the blood pressure-raising effects [11]. We are unfortunately not aware of the coffee consumption history of the participants but the reported habitual coffee consumption at any level was associated with an increased risk of fulfilling the blood pressure-component of the MS. As almost half of our population had antihypertensive medication, and thus fulfilled the blood pressure criterion, the results may not be directly comparable with the results obtained from other populations. Therefore, we repeated the analysis in a sub-population excluding those with antihypertensive medication. Also in this population all levels of coffee consumption were associated with increased odds of fulfilling the blood pressure-component.

Coffee consumption was not associated with the triglyceride- or the HDL-cholesterol-components, in the current study. Previous results regarding coffee consumption and the serum lipid concentrations are somewhat inconsistent. In a large cross-sectional population-based survey, high coffee consumption was associated with reduced triglyceride levels [22], while in another study moderate coffee consumption was associated with increased triglyceride concentrations in men [23]. In an intervention study, however, coffee consumption did not affect the lipid profile [24]. The inconsistencies observed may partly be related to the differences in the types of coffee consumed. Indeed, boiled, unfiltered coffee contains higher amounts of coffee oils than filtered coffee, and has been associated with increased lipid concentrations [9]. Instead, filtered coffee may not affect the serum lipid levels at all [25]. In the current study, the majority of participants reported habitually consuming filtered coffee. Potentially due to a low number of individuals drinking non-filtered coffee, filtered coffee was, as seen in the whole population, associated with increased risk of MS. However, we were unable to detect any differences in the lipid-components of the MS based on the type of coffee consumed. Moreover, the current observations may not be directly comparable to those obtained in other populations, as individuals with T1D tend to have a more favourable lipid profile compared to the healthy population [26].

The literature regarding the association between coffee consumption and the waist circumference is also inconsistent. While reports connecting coffee intake to reduced risk of obesity [9] and lower waist circumference have been published [22], a number of studies have reported no such associations [19, 26]. Our observations are in concordance with the latter studies. Proposed mechanisms that connect coffee intake to a reduced risk of obesity include improved β-cell

function [27] and increased energy expenditure [28]. However, based on the results from a Mendelian randomization study, the potential association is most likely explained by confounding or reverse causation, rather than by a direct biological effect [29].

We calculated eGDR, as a measure of insulin sensitivity, but there was no association between coffee consumption and this marker. To our knowledge, no other studies have assessed the insulin sensitivity and coffee consumption in T1D. Interestingly, in healthy subjects, a meta-analysis of randomized controlled trials showed that acute caffeine ingestion reduces insulin sensitivity [30]. Again, the acute effects seem to differ from the long-term effects, as habitual consumption has been associated with reduced risk of type 2 diabetes in the general population [8].

Chlorogenic acids found in coffee are suggested to reduce subclinical inflammation via their antioxidative capacities [8]. As low-grade inflammation is associated with both insulin resistance and renal disease in T1D [31], we investigated whether habitual coffee consumption is associated with hsCRP and eGFR. While no clear association was observed between coffee consumption and hsCRP, there was an increasing trend in the eGFR with increasing coffee consumption. The mechanism explaining such an observation is not known. However, in concordance with our results, coffee consumption was also associated with higher eGFR in general population [32]. In that study, coffee consumption was investigated longitudinally, and as changes in eGFR or risk of rapid eGFR decline were not associated with coffee consumption, the authors concluded that the observed positive association between coffee consumption and eGFR was unlikely a result of glomerular hyperfiltration.

One of the limitations of the study is the cross-sectional design, as such a design cannot reveal causalities. This study will, however, serve as a baseline for our future investigations, where the association between coffee consumption and health outcomes will be longitudinally assessed. Another limitation is the use of a self-reported questionnaire to study the coffee consumption. While self-reported data may be subject to recall bias, the questionnaire has been validated against a six-day food record and was observed to show reasonable relative validity [18]. In general, individuals taking part in health-related studies may be more health-conscious. This may limit the generalizability of our results to other individuals with T1D, at large. However, if such selection bias has taken place, it has most likely diluted our observations. If needed to prevent or

treat hypoglycaemia, a light, low-fat breakfast was accepted prior to the study visit. Of the components of the MS, consuming a light breakfast would most likely affect the triglyceride concentrations. However, as fulfilling this component of the MS also includes the use of lipid lowering medication, the net effect of the potential low-fat breakfast is likely moderate. While it is unlikely that habitual coffee consumption habits were associated with the need to eat breakfast prior to the study visit, the current observations need to be interpreted in the light of this limitation. Finally, we cannot exclude the effect of other confounding factors, which were not measured or controlled for in the analyses. With these limitations in mind, it should be noted that this is the first study to assess the association between coffee intake and MS and its components in individuals with T1D.

In conclusion, moderate and high coffee consumption is associated with an increased risk of MS, while any level of coffee consumption is associated with higher odds of fulfilling the blood pressure-component of the MS. Moreover, increasing coffee intake is associated with higher eGFR. Whether habitual coffee consumption will have any negative or beneficial effects on health outcomes, in this population of patients with type 1 diabetes, will be assessed in future studies.

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Table 1 Characteristics of the study population divided by coffee consumption groups (n = 1040)

	Non-consumers (<1 cup/d) n = 134 (12.9%)	Low consumption (≥1 cups/d <3) n = 230 (22.1%)	Moderate consumption (≥3 cups/d <5) n = 371 (35.7%)	High consumption (≥5 cups/d) n = 305 (29.3%)	*P*
Basic characteristics					
Men, %	34.3	32.2	45.0	59.7	<0.001
Age, years	40 ± 13	46 ± 15	48 ± 14	49 ± 12	<0.001
Diabetes duration, years	21 (15 – 34)	30 (17 – 41)	27 (20 – 39)	29 (20 – 38)	<0.001
HbA1c, mmol/mol	63 (56 – 72)	65 (56 – 76)	63 (56 – 71)	65 (59 – 74)	0.103
BMI, kg/m^2	25.8 (23.2 – 28.3)	25.7 (23.1 – 28.4)	25.3 (23.4 – 28.4)	25.7 (23.4 – 28.3)	0.927
Retinopathy, %	23	38	28	32	0.021
Diabetic nephropathy, %	6	9	11	12	0.232
eGFR, ml/min	120 (110 – 129)	115 (99 – 127)	111 (96 – 123)	107 (96 – 118)	<0.001
eGDR, mg/kg/min	7.1 (4.5 – 8.8)	5.2 (4.0 – 8.3)	5.4 (4.1 – 7.9)	4.9 (3.6 – 7.5)	<0.001
hsCRP, mg/l	1.19 (0.56 – 2.91)	1.31 (0.60 – 2.50)	0.97 (0.48 – 2.29)	0.91 (0.45 – 2.10)	0.033
Physical activity					0.442
Sedentary, %	26	33	31	28	
Moderately active, %	52	51	55	52	
Active, %	22	16	14	20	
Current smoking, %	3	10	12	22	<0.001
Antihypertensive medication, %	31	53	48	53	<0.001
Lipid-lowering medication, %	23	35	33	43	0.001
Components of the metabolic syndrome					
Metabolic syndrome, %	51	64	65	70	0.002
Waist component, %	56	55	55	57	0.966
Waist circumference, cm					
Men	89 (84 – 97)	93 (86 – 101)	93 (86 – 100)	94 (87 – 103)	0.084
Women	84 (77 – 96)	83 (75 – 93)	83 (76 – 92)	82 (77 – 89)	0.544
Triglyceride component, %	34	43	40	50	0.011
Triglyceride, mmol/l	0.92 (0.72 – 1.19)	0.99 (0.75 – 1.39)	0.89 (0.70 – 1.26)	1.01 (0.77 – 1.36)	0.012
HDL component, %	32	43	41	51	0.002

HDL, mmol/l					
Men	1.39 (1.17 – 1.61)	1.50 (1.17 – 1.80)	1.53 (1.28 – 1.77)	1.41 (1.16 – 1.68)	0.022
Women	1.70 (1.32 – 1.94)	1.72 (1.42 – 2.09)	1.76 (1.42 – 2.04)	1.62 (1.40 – 2.06)	0.572
BP component, %	57	78	79	83	<0.001
Systolic BP, mmHg	128 (119 – 141)	135 (122 – 151)	137 (127 – 150)	137 (127 – 148)	<0.001
Diastolic BP, mmHg	76 ± 9	77 ± 10	77 ± 9	78 ± 9	0.509

Data are presented as percentages for categorical variables, mean ± standard deviation for continuous normally distributed variables, and median (interquartile range) for continuous non-normally distributed variables. Respective statistical comparisons amongst the four groups were conducted with Chi-squared test, ANOVA, and Kruskal-Wallis test. BMI, body mass index; eGFR, estimated glomerular filtration rate; eGDR, estimated glucose disposal rate; hsCRP, high-sensitivity C-reactive protein; physical activity level, sedentary (weekly MET h <10), moderately active (≥10 and ≤40), active (weekly MET h >40); HDL, high-density lipoprotein cholesterol; BP, blood pressure.

Table 2 Associations between coffee consumption categories and the metabolic syndrome and its components

Outcome variable	Model	Non-consumers (<1 cup/d)	Low consumption (≥1 cups/d <3)	Moderate consumption (≥3 cups/d <5)	High consumption (≥5 cups/d)
Metabolic syndrome	M1	1	1.61 (0.96 – 2.70)	1.40 (0.87 – 2.56)	2.07 (1.24 – 3.45)**
	M2	1	1.56 (0.86 – 2.83)	1.76 (1.02 – 3.06)*	2.13 (1.17 – 3.87)*
Waist circumference component	M1	1	0.89 (0.54 – 1.47)	0.96 (0.60 – 1.52)	1.12 (0.69 – 1.83)
	M2	1	0.91 (0.51 – 1.63)	1.19 (0.70 – 2.05)	1.17 (0.66 – 2.08)
Triglyceride component	M1	1	1.35 (0.79 – 2.33)	0.92 (0.55 – 1.53)	1.46 (0.86 – 2.46)
	M2	1	1.44 (0.76 – 2.73)	1.01 (0.55 – 1.83)	1.65 (0.88 – 3.07)
Triglyceride component[1]	M1	1	1.04 (0.42 – 2.54)	0.58 (0.24 – 1.42)	0.79 (0.31 – 2.03)
	M2	1	1.10 (0.38 – 3.21)	0.56 (0.19 – 1.65)	0.69 (0.21 – 2.24)
HDL-cholesterol component	M1	1	1.39 (0.81 – 2.39)	1.13 (0.68 – 1.87)	1.86 (1.10 – 3.14)*
	M2	1	1.34 (0.71 – 2.53)	1.19 (0.66 – 2.15)	1.84 (0.99 – 3.42)
HDL-cholesterol component[1]	M1	1	0.93 (0.36 – 2.38)	1.17 (0.50 – 2.75)	1.62 (0.65 – 4.04)
	M2	1	0.76 (0.24 – 2.35)	1.18 (0.43 – 3.22)	0.92 (0.28 – 3.04)
Blood pressure component	M1	1	2.67 (1.47 – 4.89)**	2.01 (1.18 – 3.44)*	2.05 (1.14 – 3.69)*
	M2	1	2.80 (1.40 – 5.62)**	2.40 (1.29 – 4.48)**	2.19 (1.08 – 4.44)*
Blood pressure component[2]	M1	1	2.66 (1.31 – 5.39)**	2.31 (1.22 – 4.36)*	2.51 (1.27 – 4.94)**
	M2	1	2.48 (1.09 – 5.67)*	2.43 (1.17 – 5.05)*	2.31 (1.03 – 5.18)*

Data are presented as odds ratio (95% confidence interval). Logistic regression analysis. Model 1, adjusted for age, sex, and energy intake; Model 2, additionally adjusted for alcohol intake, physical activity, and smoking status. * $p<0.05$, ** $p<0.01$, [1] Participants without lipid-lowering medication, [2] Participants without antihypertensive medication.

Table 3 Associations between coffee consumption categories and eGDR, eGFR, and hsCRP

Outcome variable	Model	Non-consumers (<1 cup/d)	Low consumption (≥1 cups/d <3)	Moderate consumption (≥3 cups/d <5)	High consumption (≥5 cups/d)	*P*
eGDR	M1	7.1 (6.6 – 7.5)	5.9 (5.6 – 6.3)	6.0 (5.7 – 6.2)	5.5 (5.2 – 5.8)	<0.001
	M2	6.4 (6.0 – 6.8)	5.7 (5.4 – 6.0)	6.0 (5.8 – 6.3)	5.8 (5.6 – 6.1)	0.189
	M3	6.4 (6.0 – 6.8)	5.8 (5.5 – 6.1)	6.0 (5.8 – 6.3)	5.8 (5.6 – 6.1)	0.180
eGFR	M1	116.8 (112.4 – 121.3)	110.0 (106.5 – 113.4)	107.4 (104.8 – 110.1)	104.2 (101.3 – 107.2)	<0.001
	M2	106.4 (103.2 – 109.6)	106.8 (104.4 – 109.2)	108.6 (106.7 – 110.4)	109.8 (107.7 – 111.9)	0.036
	M3	105.8 (103.1 – 108.4)	107.2 (105.1 – 109.2)	108.4 (106.9 – 110.0)	109.9 (108.2 – 111.7)	0.006
hsCRP	M1	2.04 (1.67 – 2.41)	1.96 (1.68 – 2.34)	1.61 (1.40 – 1.82)	1.58 (1.35 – 1.82)	0.009
	M2	1.91 (1.54 – 2.28)	1.91 (1.63 – 2.19)	1.61 (1.41 – 1.82)	1.67 (1.43 – 1.90)	0.124
	M3	1.93 (1.56 – 2.30)	1.88 (1.61 – 2.16)	1.62 (1.41 – 1.82)	1.68 (1.44 – 1.91)	0.135

Data are presented as mean (95% Wald Confidence Interval). Generalized linear model. eGDR, estimated glucose disposal rate; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein. Model 1, unadjusted; Model 2, adjusted for age and sex; Model 3, adjusted for age, sex, nephropathy status, and energy intake.

Association between habitual coffee consumption and metabolic syndrome in type 1 diabetes

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Highlights

- Coffee intake has been associated with health benefits in the general population
- Whether coffee exerts health benefits also in type 1 diabetes is not known
- High coffee consumption was associated with higher odds of metabolic syndrome
- All coffee intake levels were associated with increased risk of blood pressure component
- An increasing trend between eGFR and coffee consumption was observed