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Relationship Between Adiponectin and apoB in Individuals With Diabetes in the Atlantic PATH Cohort

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Context: The increasing prevalence of obesity and diabetes greatly influences the risk for cardiovascular (CV) comorbidities and affects the quality of life of many people. However, the relationship among diabetes, obesity, and cardiovascular risk is complex and requires further investigation to understand the biological milieu connecting these conditions.

Objective: The aim of the current study was to explore the relationship between biological markers of adipose tissue function (adiponectin) and CV risk (apolipoprotein B) in body mass index (BMI)–matched participants with and without diabetes.

Design: Nested case-control study.

Setting: The Atlantic Partnership for Tomorrow's Health (PATH) cohort represents four Atlantic Canadian provinces: Newfoundland and Labrador, New Brunswick; Nova Scotia; and Prince Edward Island.

Participants: The study population (n = 480) was aged 35 to 69 years, 240 with diabetes and 240 without diabetes.

Main Outcome Measures: Groups with and without diabetes were matched for sex and BMI. Both measured and self-reported data were used to examine disease status, adiposity, and lifestyle factors. Immunoassays were used to measure plasma markers.

Results: In these participants, plasma adiponectin levels were lower among those with diabetes than those without diabetes; these results were sex-specific, with a strong relationship seen in women. In contrast, in participants matched for sex and adiposity, plasma apoB levels were similar between participants with and those without diabetes.

Conclusion: Measures of adiposity were higher in participants with diabetes. However, when matched for adiposity, the adipokine adiponectin exhibited a strong inverse association with diabetes.

Freeform/Key Words: adiponectin, apolipoprotein B, obesity, diabetes

Abbreviations: apoB, apolipoprotein B; BMI, body mass index; CV, cardiovascular; HEI, healthy eating index; PATH, Partnership for Tomorrow's Health.

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The global prevalence of diabetes continues to rise, and according to the World Health Organization, 422 million people worldwide had diabetes mellitus in 2014 [1]. The burden of diabetes is of great concern because 1.5 million deaths are directly caused by diabetes [1]. Diabetes places a huge economic burden on the health care system and greatly affects an individual's quality of life [2, 3]. In Canada, diabetes affects approximately 7% of the population and is more prevalent in men than women older than age 45 years [4]. The Atlantic Canada provinces have the highest proportion of residents living with diabetes in Canada [4]. Obesity is a risk factor for type 2 diabetes [5] and cardiovascular (CV) events, such as myocardial infarction and stroke [6]. The common biological milieu and interconnectivity among obesity, diabetes, and CV disease are not clear and require additional investigation.

Adipose tissue has functions that go beyond simply storing fat; it plays a fundamental role as an endocrine organ, contributing to glucose homeostasis, energy balance, and inflammation [7]. When energy substrates are consumed in excess of energy needs, the adipose tissue undergoes hyperplasia and hypertrophy to accommodate the excess lipid. The pathological consequence of adipose tissue expansion is inflammation in the fat tissue and increased inflammatory cytokine secretion, which in turn is associated with multiple cardiometabolic alterations [8]. Thus, the metabolic function and altered adipokine secretion from adipose tissue may be a crucial factor contributing to CV risk in people with diabetes.

The adipokine adiponectin is produced and secreted by adipocytes and is found in circulation at relatively high levels (~2 to 30 μg/mL) in healthy individuals [9, 10]. Recent work has shown that adiponectin levels can be used to predict the progression of patients from normoglycemia to prediabetes [11]. In addition, research over the past decade has demonstrated a negative association between circulating adiponectin levels and obesity, diabetes, and CV events [9, 12–15].

Guidelines to lower the risk for adverse CV events have emphasized the importance of lowering low-density lipoprotein cholesterol levels. However, apolipoprotein B (apoB), the main protein in triglyceride-rich very-low-density lipoprotein and low-density lipoprotein particles, has been suggested as a superior measure of CV disease risk [16, 17]. Interestingly, an inverse association has been reported between apoB and adiponectin concentrations in men [18], and more recently apoB has been associated with increased glucose levels [19]. However, the relationship between adiponectin and apoB in women and those with diabetes remains to be determined. Therefore, the aim of the current study was to explore the relationship between serum markers of adipose tissue function (adiponectin) and CV risk (apoB) in both obese and nonobese populations with and without diabetes.

1. Participants and Methods

A. Study Population and Data Collection

Details on recruitment and data collection have been previously described [20]. Participants for a nested case-control study were derived from the Atlantic Partnership for Tomorrow's Health (PATH) cohort. All participants provided written informed consent before completing any study-related procedures. Original data and sample collection procedures were approved by the appropriate research ethics boards in each Atlantic Canada province (Nova Scotia, New Brunswick, Newfoundland and Labrador, and Prince Edward Island). The Dalhousie University Research Ethics Board approved the secondary analysis of biological samples. Questionnaire data were collected from 31,174 participants aged 35 to 69 years who were residents of the four Atlantic provinces between 2009 and 2015. Of these participants, 30,830 responded (yes or no) to ever being diagnosed with diabetes and 24,773 participants had data on both diabetes and height and weight measures needed to calculate body mass index (BMI) (Fig. 1).

To examine plasma markers of adiponectin and apoB in a subset of participants, we conducted a case-control study nested within the Atlantic PATH cohort with matching to increase study efficiency. Because participants with diabetes had higher measures of

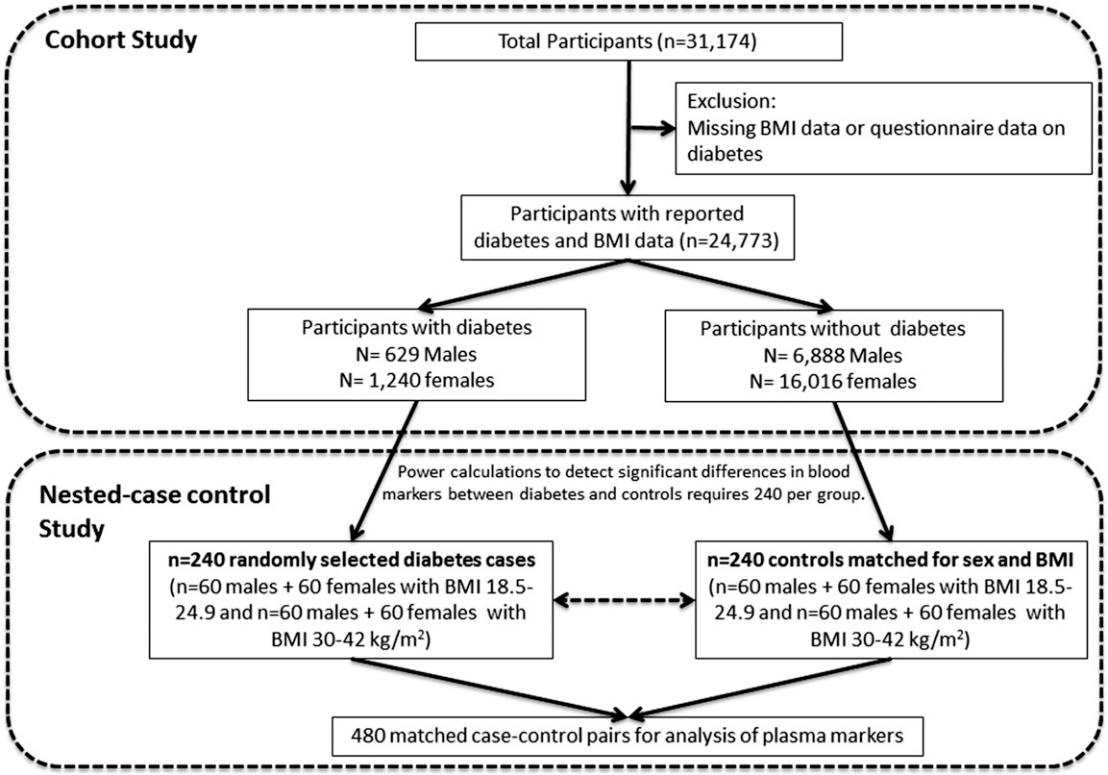

Figure 1. Flow diagram showing sample selection for nested case-control study.

adiposity (Table 1) and adiposity is also a cofounder for adiponectin levels, a subset of participants with diabetes was randomly selected and a control group without diabetes was matched for BMI. In addition, because sex is known to influence plasma levels of adiponectin [21] and apoB [22], the subgroups with or without diabetes also contained the same number of men and women. Sample size calculations were based on the number of participants needed to observe significant differences in plasma adiponectin and apoB. On the basis of means and standard deviations from previous studies [19, 23], an α value of 0.05 (two-sided), and power of 80%, the sample size for each group would be 165 to 237 participants to detect differences in plasma apoB and adiponectin levels between those with and without diabetes. Thus, each group was rounded up to 240 participants (ever diagnosed with diabetes, n = 240; never diagnosed with diabetes, n = 240) and was matched for sex and BMI (60 men and 60 women with BMI of 18.5 to 24.9 kg/m^{2}and 60 men and 60 women with BMI of 30 to 42 kg/m^2 in each group) (Fig. 1).

B. Assessment of Disease and Lifestyle Risk Factors

The estimate of the diagnosed prevalence of diabetes and CV disease (higher blood pressure, myocardial infarction, and stroke) was derived from self-reported information. Additional questions related to lifestyle and behavior, including diet, smoking, alcohol consumption, and education were assessed. The education level achieved was categorized as high school or lower, college level (trade/community college), and university level or higher (university certificate, bachelor's and graduate degree). For smoking behavior, participants were categorized as current smoker, former smoker, and never smoker. For alcohol consumption, participants were classified as an abstainer, occasional drinker (<3 times/month), regular drinker (1 to 3 times/week), and habitual drinker (4 to 7 times/week). A set of food-frequency questions were used to assess fruit and vegetable intake as well as calculate a healthy eating index (HEI) score for each participant as previously described [20]. In brief, the HEI is a

Table 1. Characteristics of Matched Diabetic and Nondiabetic Participants

Characteristic	Total	Nondiabetic	Diabetic	*P* Value
Men (n)	240	120	120	1.000
Women (n)	240	120	120	
Province, n (%)				0.275
Nova Scotia	270 (56.25)	145 (60.42)	125 (52.08)	
New Brunswick	127 (26.46)	55 (22.92)	72 (30.00)	
Newfoundland and Labrador	73 (15.21)	35 (14.58)	38 (15.83)	
Prince Edward Island	10 (2.08)	5 (2.08)	5 (2.08)	
Education, n (%)				0.619
High School or less	97 (20.34)	47 (19.75)	50 (20.92)	
College level	194 (40.67)	93 (39.08)	101 (42.26)	
University level	186 (38.99)	98 (41.18)	88 (36.82)	
Waist-to-hip ratio, n (%)[a]	246 (54.73)	120 (52.86)	129 (56.58)	0.426
Abdominal obesity, n (%)[b]	197 (42.64)	94 (41.05)	103 (44.21)	0.492
BMI > 30 kg/m^2, n (%)	237 (53.99)	118 (53.88)	119 (54.10)	0.640
CV variables, n (%)				
High blood pressure	250 (52.1)	120 (50.00)	130 (54.17)	0.361
MI	23 (4.86)	8 (3.33)	15 (6.44)	0.117
Stroke	7 (1.48)	3 (1.25)	4 (1.71)	0.678
Statin use	173 (36.04)	186 (22.50)	121 (49.48)	<0.001
Smoking status				0.306
Never	228 (47.50)	121 (50.42)	107 (44.58)	
Former	204 (42.50)	99 (41.25)	105 (43.75)	
Current	48 (10.00)	20 (8.33)	28 (11.67)	
Alcohol drinking				<0.001
Abstainer	71 (14.79)	24 (10.00)	47 (19.58)	
Occasional drinker	220 (45.83)	104 (43.33)	116 (48.33)	
Regular drinking	109 (22.71)	58 (24.17)	51 (21.25)	
Habitual drinker	80 (16.67)	54 (22.50)	26 (10.83)	
Fruits and vegetables (five a day)	207 (43.13)	105 (43.75)	102 (42.50)	0.782
Age (y)	55.37 ± 8.38	54.28 ± 8.68	56.45 ± 7.94[c]	0.004
Height (cm)	165.46 ± 8.44	165.92 ± 8.51	165 ± 8.36	0.232
Weight (km)	78.89 ± 20.88	79.12 ± 20.72	78.66 ± 21.09	0.810
Waist (cm)	92.29 ± 15.48	92.13 ± 15.33	92.44 ± 15.65	0.826
Hips (cm)	104.97 ± 12.57	105.00 ± 12.89	104.95 ± 12.27	0.967
BMI (kg/m^2)	28.70 ± 6.78	28.64 ± 6.80	28.75 ± 6.77	0.857
Waist-to-hip ratio	0.89 ± 0.09	0.88 ± 0.08	0.88 ± 0.09	0.747
Percentage fat mass	33.97 ± 9.62	34.14 ± 9.35	33.80 ± 9.91	0.697
Fat mass index (kg/m^2)	10.17 ± 4.99	10.14 ± 5.01	10.20 ± 6.13	0.912
BMI at age 18 y (kg/m^2)	23.86 ± 6.00	23.36 ± 5.85	24.35 ± 6.13	0.210
Change in BMI from age 18 y (kg/m^2)	2.29 ± 7.29	3.18 ± 7.32	1.43 ± 7.18	0.068
Vegetable intake (servings/d)	2.30 ± 1.41	2.35 ± 1.40	2.26 ± 1.41	0.507
Fruit intake (servings/d)	2.03 ± 1.31	2.08 ± 1.38	1.98 ± 1.24	0.409
Healthy eating index	39.13 ± 8.60	39.59 ± 8.42	38.67 ± 8.78	0.388
Adiponectin (μg/mL)	7.33 ± 5.57	7.88 ± 6.19	6.78 ± 4.81[c]	0.030
apoB (mg/dL)	62.67 ± 22.64	62.67 ± 22.95	62.66 ± 22.37	0.996

Values expressed with a plus/minus sign are the mean ± standard deviation.
Abbreviation: MI, myocardial infarction.
[a]Waist-to-hip ratio >0.9 for men and >0.85 for women.
[b]Waist circumference ≥102 cm for men and ≥88 cm for women.
[c]$P < 0.01$.

continuous variable with a minimum score of 0 (indicating poorest dietary habits) and a maximum score of 60 (indicating optimal dietary habits).

C. Assessment of Obesity and Body Composition

In the Atlantic PATH cohort, anthropometric indices, including height, weight, and waist and hip circumference, were self-reported by participants; for some participants they were

measured in an assessment center by research nurses. In the nested case-control study, all participants had measured BMI data and 88% had measured waist circumference and waist-to-hip ratio data. Only when measured anthropometric indexes were unavailable were self-reported anthropometric data used to calculate abdominal obesity and waist-to-hip ratio above guidelines. Participants with a BMI of $<$18.5, 18.5 to 24.9, 25.0 to 29.9 and $>$30.0 kg/m^2 were considered underweight, normal weight, overweight, and obese, respectively. The waist-to-hip ratio was set at $>$0.90 for men and $>$0.85 for women [24]. Abdominal obesity was defined as having a waist circumference $\geq$102 cm for men and $\geq$88 cm for women [20, 24]. Tanita Segmental Body Composition Analyzer was used to assess body composition by bioelectrical impedance for participants who visited an assessment center. The fat mass and fat-free mass indices were calculated by dividing fat mass and fat-free mass by height in meters squared, respectively [25].

D. Biological Samples and Analysis of Plasma Proteins

Blood samples were collected by a phlebotomist on a subgroup of 21,160 participants who visited an assessment center. Samples were shipped, divided into aliquots, and stored in CryoTubes (Sarstedt) in −80°C freezers at the processing laboratories within 24 to 48 hours of being collected. Blood samples for plasma preparation were collected in tubes containing EDTA and were separated by centrifugation at 1500*g* for 10 minutes. Plasma levels of adiponectin were measured with a magnetic bead-based immunoassay (Bio-Plex Pro, Bio-Rad Laboratories, #171A7003M). Data were captured on the Bio-Plex 200 system and analyzed in duplicate using the Bio-Plex Manger 6.0 software (BioRad). Plasma levels of apoB were analyzed by an enzyme-linked immunosorbent assay (R&D Systems, #DAPBOO) and microplate reader, following manufacturer's instructions.

E. Statistical Analysis

Data analyses were performed with IBM SPSS Statistics (version 22) software. Continuous variables were presented as mean ± standard deviation. Categorical variables were presented as counts (percentages). Significant associations between participants with or without diabetes and demographic, behavioral, and adiposity measures and CV events were determined by χ^2 analysis. Differences in anthropometric measures and plasma markers between participants with and without diabetes were analyzed by using an unpaired *t* test. To address the impact of statin medication on plasma markers, a sensitivity analysis was performed by removing all participants taking statins from the analysis. For continuous variables, the comparison of four groups (men, women, diabetes, no diabetes) was performed by using a two-way analysis of variance. The relationship between adiponectin and apoB concentrations with anthropometric measures was analyzed by using Pearson correlation coefficients. Logistic regression models were used to assess adiponectin or apoB as predictors of the prevalence of diabetes. Variables in the predictive models that had a *P* value $<$0.05 (age and alcohol use) were retained in the final model. The association between diabetes and each plasma marker is presented by odds ratios with 95% confidence intervals.

2. Results

Overall, 7.6% of the participants (7.14% of women and 8.67% of men) in the Atlantic PATH cohort indicated that they had been diagnosed with diabetes (Supplemental Table 1). Because participants with diabetes in the Atlantic PATH cohort had higher reported measures of adiposity (Supplemental Table 1), a subset of participants was matched for BMI (Table 1) to examine plasma markers of adiponectin and apoB in participants with and without diabetes. In the nested case-control study participants (n = 480), the prevalence of CV disease and lifestyle factors, such as smoking status and diet quality, were similar between participants with and without diabetes (Table 1). The overall prevalence of high blood pressure,

myocardial infarction, and stroke was 52.1%, 4.7%, and 1.5%, respectively. The prevalence of abdominal obesity and a waist-to-hip ratio above guidelines was similar between those with and those without diabetes (Table 1). Overall, 36% of participants reported taking statins, and this percentage was higher in patients with diabetes than in those without diabetes (Table 1).

Levels of apoB were similar between participants with and without diabetes; however, adiponectin levels were higher in participants without diabetes than in those with diabetes (Table 1). When participants currently taking statins were removed from the analysis, apoB concentrations did not differ between those with diabetes and those without (64.5 mg/dL vs 62.4 mg/dL, respectively). To explore variation in plasma markers between sexes, levels of apoB and adiponectin in participants with and without diabetes were analyzed separately in both men and women. Levels of apoB were similar between men with and without diabetes as well as in women [Fig. 2(A)]. In contrast, plasma adiponectin levels were 1.44 μg/mL higher in women compared with men [Fig. 2(B)]. Plasma adiponectin levels were similar between men with and without diabetes, whereas levels in women with diabetes were 1.88 μg/mL lower than in women without diabetes [Fig. 2(B)].

The relationship between plasma adiponectin or apoB concentrations and anthropometric variables was analyzed by using Pearson correlation coefficients. A weak-positive association was found between adiponectin levels and plasma apoB levels (Table 2). A weak-positive association was also found between plasma apoB levels and HEI and plasma adiponectin levels (Table 2). Because plasma adiponectin levels were clearly different between participants with and without diabetes (Table 1 and Table 2), we used logistic regression models to explore the relationship between adiponectin levels and diabetes. Plasma adiponectin levels were inversely associated with diabetes (Table 3). This relationship remained after adjustment for age, education, smoking, alcohol use, and intake of five fruits and/or vegetables per day (Table 3). In the sex-specific analysis, the association was apparent only in women in both unadjusted and adjusted models (Table 3). We also divided participants into tertiles according to plasma adiponectin levels and used logistic regression to estimate the relationship between lower levels of adiponectin (the lowest adiponectin tertile, adiponectin <3.85 μg/mL) and the risk for diabetes. Overall there was a trend toward an association. However, stratified analysis showed that the inverse association between the lowest adiponectin tertile and diabetes prevalence was pronounced only for women (Supplemental Table 2). By contrast, there was no association between plasma apoB levels and diabetes (Table 3; Supplemental Table 2).

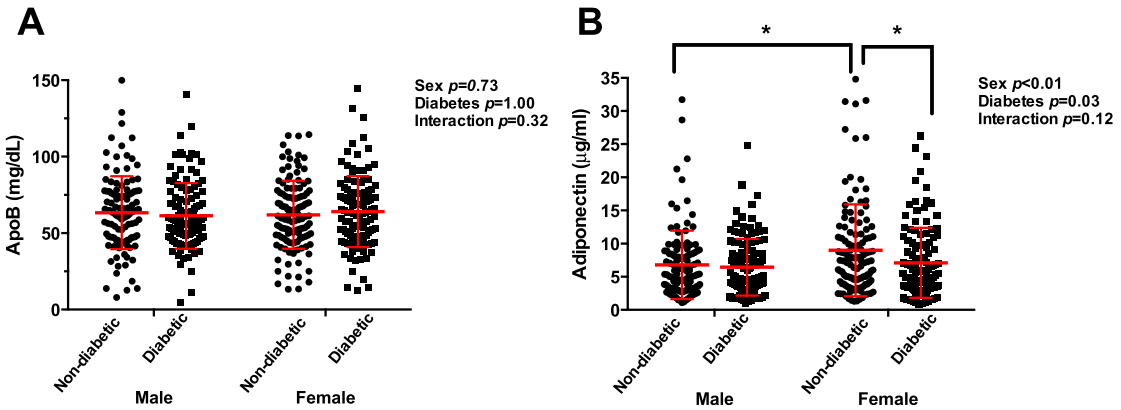

Figure 2. Scatterplot showing plasma apoB (A) and adiponectin (B) levels in diabetic or nondiabetic men and women. Data are presented as mean ± standard deviation (n = 120 per group). Data were analyzed by using a two-way analysis of variance with the main effects of sex and diabetes and, if justified, by Tukey multiple comparisons test. *$P < 0.05$. Black symbols represent individual data points and red bars represent means ± standard deviation.

Table 2. Associations of Adiponectin and apoB with Age and Anthropometric Variables

	Adiponectin		apoB	
Variable	**R**	***P* Value**	**R**	***P* Value**
Age	−0.051	0.143	0.042	0.189
Waist in cm	−0.02	0.335	−0.031	0.256
Waist-to-hip ratio	0.031	0.258	−0.009	0.425
BMI in kg/m^2	0.032	0.248	−0.002	0.486
Percentage fat mass	0.006	0.453	0.044	0.174
Fat mass index in kg/m^2	0.018	0.355	0.024	0.308
Healthy eating index	0.026	0.343	**0.107**	**0.045**
Plasma apoB and adiponectin	**0.078**	**0.050**	**0.078**	**0.050**

Unless otherwise noted, results are expressed as Pearson correlation coefficients. Boldface indicates statistical significance ($P \leq 0.05$).

3. Discussion

As the prevalence of obesity and diabetes continue to rise, there is a need for a greater understanding of the interconnectivity among these conditions and CV disease risk. This study characterizes members of the Atlantic PATH cohort with or without diabetes and explores the relationship between the serum markers adiponectin and apoB in a subsample of these two groups. There were clear differences in adiposity measures and CV events between participants with and without diabetes in the overall Atlantic PATH cohort. In a subset of 480 participants matched for sex and adiposity, plasma apoB levels were similar between participants with and without diabetes; however, plasma adiponectin levels were lower in participants with diabetes than in those without diabetes. Further investigation indicated that an inverse association between plasma adiponectin levels and the prevalence of diabetes was sex-specific, with a strong relationship apparent only in women.

BMI is an estimate of overall adiposity but does not assess body fat distribution or composition. In the current study, we included measures of waist circumference, waist-to-hip ratio, and fat mass to estimate body fat distribution and composition. In agreement with previous research [26] in a similarly aged population that used magnetic resonance imaging to assess body composition and adipose mass distribution, we observed increased adipose

Table 3. Logistic Regression Models of Adiponectin and apoB with Diabetes

	Adiponectin		apoB	
Variable	**Odds Ratio (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
Total				
Unadjusted	0.964 (0.933–0.997)	0.032	1.000 (0.992–1.008)	0.996
Model 1	0.966 (0.934–0.999)	0.043	1.000 (0.992–1.008)	0.916
Model 2	0.959 (0.925–0.993)	0.018	0.999 (0.991–1.007)	0.828
Men				
Unadjusted	0.986 (0.934–1.040)	0.596	0.996 (0.985–1.007)	0.478
Model 1	0.989 (0.937–1.045)	0.704	0.995 (0.984–1.007)	0.436
Model 2	0.971 (0.916–1.029)	0.317	0.993 (0.981–1.005)	0.257
Women				
Unadjusted	0.950 (0.909–0.993)	0.022	1.004 (0.993–1.015)	0.483
Model 1	0.950 (0.909–0.993)	0.023	1.004 (0.992–1.015)	0.524
Model 2	0.951 (0.909–0.995)	0.028	1.004 (0.993–1.016)	0.476

Model 1: adjusted for age; model 2: adjusted for age and alcohol use.
Abbreviation: CI, confidence interval.

mass (measured by bioelectrical impedance) and higher abdominal adipose in participants with diabetes compared with those without diabetes. Likewise, we observed greater abdominal adipose tissue mass in women (data not shown).

There is some controversy in the literature regarding abdominal obesity or percentage body fat as better predictors than BMI for quantifying CV risk [27–31]. On the other hand, BMI may be more strongly associated with adipokine status than measures of waist circumference, waist-to-hip ratio, and percentage body fat [32]. Altered levels of adipokines are closely related to obesity-related metabolic complications [33]. Adipose tissue serves as an active endocrine organ, secreting a variety of adipokines that regulate energy intake, energy expenditure, and endocrine function [34]. The adipokine adiponectin is of particular interest with respect to obesity, diabetes, and CV risk [9, 12–15]. With the development of obesity, adipose tissue mass increases by first enlarging in size, then by storing more lipids as triacylglycerols; adipocyte numbers then increase to accommodate excess lipids. Data in preclinical models and cultured adipocytes demonstrate that adiponectin levels may be altered long before the amount of lipid in the adipocytes changes [35, 36].

Plasma adiponectin levels and insulin resistance are both independent predictors of very-low-density lipoprotein apoB concentrations in men, although likely through different mechanisms [18]. In addition, men with higher apoB levels (>87 mg/dL) have a higher risk for diabetes [19]. In contrast, we did not observe any difference in apoB concentrations between participants with and those without diabetes in the current study. However, this may be because only 13% of participants in the current study had plasma apoB values >87 mg/dL. In addition, we must acknowledge differences in the populations, ethnicity, sex, and methods for examining apoB levels between the current study and previous reports. Future studies with more detailed information on participant health status (such as progression and duration of disease) may be useful in exploring the relationship between changes in plasma apoB levels and diabetes progression.

Even obese individuals who are considered to have a “metabolically healthy” phenotype (absence of metabolic abnormalities such as dyslipidemia, insulin resistance, and hypertension) are at an increased risk for CV events [37]. Furthermore, metabolically healthy individuals often progress to an unhealthy state or develop disease [38, 39]. Thus, it may be useful to consider measuring other circulating markers, such as adiponectin, to indicate early tissue dysfunction and risk for disease development. The changes in markers of CV risk such as apoB levels may not occur until a later time point, once the ability of adipose tissue has become overwhelmed and the liver starts to deal with the excess lipids in the body. Future research should examine baseline plasma values and incidence of disease over time (follow-up study). Participants in the Atlantic PATH cohort will be followed for 30 years, which will provide an excellent opportunity to explore some of these relationships over time.

The use of objectively measured anthropometric variables on most participants and a large sample size are major strengths of the Atlantic PATH cohort. A limitation of the current study is that the current use of medications was not considered before the case-control sample nested within the cohort was examined. Although statin use was considered in the sensitivity analysis and even after removal of those currently taking statins, no difference was found in those with diabetes compared with those without. Perhaps not that surprising given that previous research has shown that not all individuals respond to statin therapy with respect to achieving optimal apoB levels [40]. Nonetheless, future studies should explore the use of not only statins but other medications that may influence plasma adiponectin and apoB levels in these populations. Future research should also focus on age and changes in adipose depot distribution (*e.g.*, intra-abdominal fat). Interestingly, adiponectin levels appear to increase with age, and with increasing age body composition changes: Lean mass declines whereas fat mass increases, resulting in an overall reduction in metabolically active tissues and altered fat distribution [32, 41, 42]. Finally, more research is needed to understand the influence of disease progression relative to circulating plasma markers and measures of adiposity.

4. Conclusions

In summary, we examined an important relationship between two plasma markers of metabolic risk in a subsample of participants with and without diabetes in the Atlantic PATH cohort. This study demonstrates that participants in the Atlantic PATH cohort with diabetes have a higher prevalence of obesity (BMI > 30 kg/m^2), abdominal obesity, and percentage fat mass as well as a higher prevalence of CV events. In the case-control study nested within the cohort, participants with similar levels of obesity and prevalence of CV events, plasma adiponectin was lower in participants with diabetes than those without diabetes. In conclusion, adiponectin appears to be a unique marker of adipocyte function that exhibits a strong inverse association with diabetes. Further research is needed to explore other markers and mechanisms that may further improve our understanding of diabetes.

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