Spinal cord injury and type 2 diabetes

Results from a population health survey

Jacquelyn J. Cragg, MPH
Vanessa K. Noonan, PhD
Marcel Dvorak, MD,
FRCS
Andrei Krassioukov, MD,
PhD, FRCPC
G.B. John Mancini, MD,
FRCPC, FACC
Jaimie F. Borisoff, PhD

Correspondence to
Ms. Cragg;
craggj@interchange.ubc.ca

ABSTRACT

Objective: The objective of this study was to evaluate the association between spinal cord injury (SCI) and type 2 diabetes in a large representative sample and to determine whether an association exists irrespective of known risk factors for type 2 diabetes.

Methods: Data were obtained on 60,678 respondents to the Statistics Canada 2010 Cycle of the cross-sectional Canadian Community Health Survey. Multivariable logistic regression, incorporating adjustment for confounders and probability weights to account for the Canadian Community Health Survey sampling method, was conducted to quantify this association.

Results: After adjustment for both sex and age, SCI was associated with a significant increased odds of type 2 diabetes (adjusted odds ratio = 1.66, 95% confidence interval 1.16–2.36). These heightened odds persisted after additional adjustment for smoking status, hypertension status, body mass index, daily physical activity, alcohol intake, and daily consumption of fruits and vegetables (fully adjusted odds ratio = 2.45, 95% confidence interval 1.34–4.47).

Conclusions: There is a strong association between SCI and type 2 diabetes, which is not explained by known risk factors for type 2 diabetes. *Neurology*® 2013;81:1864–1868

GLOSSARY

AOR = adjusted odds ratio; **CCHS** = Canadian Community Health Survey; **CI** = confidence interval; **OR** = odds ratio; **SCI** = spinal cord injury.

Over the last decade, researchers have noted important changes in the trends of morbidity and mortality among individuals with spinal cord injury (SCI). With advances in acute care and in the management of septicemia, renal failure, and pneumonia, chronic conditions are becoming a focus. The etiology of these comorbidities may extend beyond physical disability and may be compounded by additional autonomic and metabolic changes that occur as a result of the loss of descending control.^{1–3}

A few studies have shown or suggested an increased prevalence of type 2 diabetes among individuals with both traumatic and nontraumatic SCI.^{1,4–8} However, these studies are generally based on small, underpowered, and/or nongeneralizable convenience samples; they lack appropriate controls and proper adjustment for confounding.^{1,4–8} It thus remains uncertain whether there is excess risk of diabetes after appropriate adjustment for potential confounders in individuals with SCI. An excess risk of diabetes may contribute, at least in part, to the increased risk of stroke, heart disease, and kidney disease that occurs after SCI.^{9–12}

The current study addresses this question using the cross-sectional Canadian Community Health Survey (CCHS). The objectives of this study were to estimate the prevalence of type 2 diabetes in the SCI population, to compare this risk with a non-SCI population, and to investigate this relationship after controlling for confounders. We hypothesized that individuals with SCI have an increased odds of type 2 diabetes compared with individuals without SCI, and that this relationship is not entirely explained by known risk factors for type 2 diabetes.

From the School of Population and Public Health, Faculty of Medicine (J.J.C.), International Collaboration on Repair Discoveries (J.J.C., A.K., J.F.B.), Division of Spine, Department of Orthopaedics (M.D.), Department of Medicine, Division of Physical Medicine and Rehabilitation (A.K.), and Cardiovascular Imaging Research Core Laboratory, Division of Cardiology, Department of Medicine (G.B.J.M.), University of British Columbia, Vancouver; Rick Hansen Institute (V.K.N.), Vancouver; Acute Spine Program (M.D.), Vancouver General Hospital; GF Strong Rehabilitation Centre (A.K.), Vancouver Health Authority, Vancouver; and British Columbia Institute of Technology (J.F.B.), Burnaby, Canada.

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METHODS Data source. This study obtained population health data from the CCHS 2010 Annual Component. The CCHS is a cross-sectional survey conducted by Statistics Canada. The CCHS includes a variety of health topics, such as access to health services, health services utilization, lifestyle behaviors, demographic information, and health status. Data are obtained by trained interviewers on Canadian individuals residing in households in all the provinces and territories who are 12 years of age or older. The following individuals are excluded from the CCHS: those living in institutions, those living on reserves or Crown lands, and full-time members of the Canadian Armed Forces. To ensure representativeness of the data, Statistics Canada utilizes a multistage, stratified cluster sampling design.¹³

Standard protocol approvals, registrations, and patient consents. Ethical approval for the use of the data was obtained via the publicly available data clause from the University of British Columbia, in accordance with the Tri-Council Policy Statement.

Exposure and outcome definitions. The primary explanatory variable was self-reported SCI. SCI status was obtained with the following question: Do you have a neurologic condition caused by a spinal cord injury? The primary outcome variable was diabetes type 2 status. This was obtained with the following question: Do you have diabetes? If the respondent answered yes to this question, they were asked the following questions: How old were you when this was first diagnosed? Were you pregnant when you were first diagnosed with diabetes? Other than during pregnancy, has a health professional ever told you that you have diabetes? When you were first diagnosed with diabetes, how long was it before you were started on insulin? Do you currently take insulin for your diabetes? In the past month, did you take pills to control your blood sugar? Based on the response to these questions, using the Ng-Dasgupta-Johnson algorithm,¹⁴ Statistics Canada provides a derived variable for diabetes type: type 1 diabetes, type 2 diabetes, and gestational diabetes. Because type 2 diabetes was the outcome variable of interest, those with type 1 diabetes and gestational diabetes were excluded from the analysis. In addition, only those with valid responses for the primary explanatory variable and outcome variable were included in the analysis; non-respondents (e.g., refusals or unsure) were excluded.

Confounding. Confounding was assessed both from a theoretical (i.e., causal) perspective based on previous studies as well as a statistical perspective (i.e., in examining changes in effect sizes in the presence/absence of possible confounders). Risk factors for type 2 diabetes include age, excess body weight, high blood pressure, low activity levels, impaired glucose tolerance, dyslipidemia, and sex.¹⁵ Risk factors for traumatic SCI include age and sex.¹⁶ Risk factors for nontraumatic SCI are more difficult to examine, as nontraumatic SCI includes tumors, congenital/developmental (spina bifida), infectious (viral, bacterial, fungal, parasitic), inflammatory (multiple sclerosis), and ischemic causes, as well as several others.¹⁷ However, sex and age are well-known risk factors for the majority of nontraumatic SCIs.¹⁶ Sex and age were thus selected *a priori* as possible confounders.^{6,9,18} Sensitivity analyses were also performed to examine the effects of the following other potential confounders available within the CCHS: self-report daily energy expenditure (which takes into account both the frequency and duration of leisure activities), obesity (using body mass index derived from self-report height and weight), hypertension, smoking status, average daily alcohol consumption, and daily consumption of fruits and vegetables.

Statistical analyses. Logistic regression (bivariable and multivariable), with type 2 diabetes as the binary outcome, was used.

SCI, also binary, was the primary explanatory variable in the regression model. The multivariable logistic regression model also included the variables sex and age (treated as a continuous variable) as well as various combinations of the variables mentioned in the confounding section above. Using the results of these logistic models, unadjusted (raw) odds ratios (ORs) and adjusted odds ratios (AORs) are presented, with corresponding 95% confidence intervals (CIs). Probability weights were used to account for the CCHS sampling method (clustering and stratification). Statistics Canada provides frequency weights for each individual (the number of persons represented by that individual), which were divided by the average frequency weight for the entire analytic sample to obtain the probability weights. Thus, all reported percentages and ORs are probability weighted. SAS statistical software (version 9.3; SAS Institute, Cary, NC) was used for all statistical analyses.

RESULTS Study sample. After excluding those with invalid responses for the primary explanatory and outcome variables, and those with gestational diabetes ($n = 9$) and type 1 diabetes ($n = 145$), the final study sample included 60,678 individuals. There was a similar proportion of males and females in the total sample; the median age category for the entire sample is also shown (table 1). Among the entire sample, the prevalence of type 2 diabetes was 5.94%. The proportion of males with type 2 diabetes was higher than that of females; the median age category for individuals with type 2 diabetes was higher than those without (table 1).

SCI and type 2 diabetes. There were a total of 353 individuals with SCI; this yielded a prevalence of 0.49% for SCI in the overall sample. Among individuals with SCI, the prevalence of type 2 diabetes was 13.66% compared with 5.91% in individuals without SCI. Type 2 diabetes tended to occur at younger ages among those with SCI vs those without (figure). Table 2 provides unadjusted and adjusted ORs for type 2 diabetes. The odds of type 2 diabetes was 2.52 times greater in individuals with SCI vs individuals without SCI (95% CI 1.81–3.52). After adjusting for sex and age, the heightened odds persisted but was reduced; the age/sex AOR for type 2 diabetes was 1.66 (95% CI 1.16–2.36), suggesting confounding by sex and age.

Sensitivity analyses. We also examined the effect of additional risk factors for type 2 diabetes on the previously reported effect sizes. Table 2 provides ORs that are adjusted for age, sex, and body mass index (AOR2), as well as an OR adjusted for age, sex, smoking status, hypertension status, body mass index, daily physical activity, daily alcohol intake, and daily consumption of fruits and vegetables (AOR3). The OR adjusted for body mass index in addition to sex and age (AOR2) did not differ significantly from the OR adjusted for sex and age only (AOR1). The OR adjusted for all potential confounders (AOR3) was similar in magnitude to the unadjusted OR. In sum, regardless of the variables included in the models, all ORs indicated an approximately 2-fold increased odds.

Table 1 Characteristics of the study sample

Variable	Total, % (N = 60,678) (median age 40–44 y)	Type 2 diabetes, % (n = 4,629) (median age 60–64 y)	No type 2 diabetes, % (n = 56,049) (median age 40–44 y)
Spinal cord injury			
Yes	0.49	1.12	0.45
No	99.51	98.88	99.55
Sex			
Male	49.29	58.07	48.73
Female	50.71	41.93	51.27

Percentages are probability weighted to account for the Canadian Community Health Survey sampling method. Column percentages are shown.

Nonrespondents. A total of 2,080 individuals were excluded based on nonresponse. Because sex and age of all participants were collected regardless of their response to the SCI/diabetes questions, both sex and age of the nonresponders were examined. The sex distribution of nonresponders (50.62% male; 49.38% female) showed a similar sex distribution as in the responders (49.29% male; 50.71% female). The median age category for nonresponders was the same for responders (40–44 years).

DISCUSSION In this study, we have utilized a comprehensive national survey with more than 60,000 individuals to investigate the relationship between type 2 diabetes and SCI. We first examined the prevalence of type 2 diabetes in the SCI population: the prevalence was 13.66% among individuals with SCI compared with 5.91% in individuals without SCI. An estimate for the prevalence of diabetes in the general Canadian population has been previously reported as 11.60%; however, this estimate was calculated among individuals aged 20 to 79 years of age, and included those with type 1 diabetes.¹⁹

We next demonstrated for the first time in a large representative population that SCI is independently associated with a 2-fold increased odds of type 2 diabetes. To put this value into context, the heightened odds reported here is similar in magnitude to the estimated OR in the general population for the relationship between abdominal obesity and acute myocardial infarction.²⁰

These heightened odds of type 2 diabetes are consistent with previous evidence. Several prior studies have shown or suggested an increased prevalence of diabetes among individuals with SCI.^{1,4–8} One possible mechanism may be due to the association between sarcopenia and insulin sensitivity.²¹ It has also been

Figure Grouped bar plot of prevalence of type 2 diabetes

Weighted prevalence (%) of type 2 diabetes is shown separately for the spinal cord injury (SCI) group (green bars) and non-SCI group (orange bars) for each age category.

Table 2 ORs and corresponding 95% CIs for type 2 diabetes (probability weighted)

Variable	Unadjusted OR	AOR1	AOR2	AOR3
Spinal cord injury				
Yes	2.52 (1.81, 3.52)	1.66 (1.16, 2.36)	1.65 (1.13, 2.42)	2.45 (1.34, 4.47)
No ^a	1.00	1.00	1.00	1.00
Sex				
Male	1.46 (1.36, 1.56)	1.68 (1.57, 1.81)	1.62 (1.50, 1.75)	2.20 (1.91, 2.55)
Female ^a	1.00	1.00	1.00	1.00
Age^b				
	1.37 (1.35, 1.38)	1.37 (1.36, 1.39)	1.40 (1.39, 1.42)	1.25 (1.22, 1.29)

Abbreviations: AOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio.

AOR1 is adjusted for age and sex only; AOR2 is adjusted for age, sex, and body mass index; AOR3 is adjusted for age, sex, smoking status, hypertension status, body mass index, daily physical activity, alcohol intake, and daily consumption of fruits and vegetables.

^aReference category.

^bORs shown are the effect for one category increase (5-year groupings).

proposed that in addition to the immobility caused by SCI, individuals with SCI have unique disadvantages that may further contribute to the heightened risk relating to the loss of descending control of spinal circuits below the level of the injury. However, there has not been epidemiologic data until now to support

this hypothesis. Indeed, our multivariable analyses indicate that SCI is independently associated with type 2 diabetes.

There are some limitations of note in the current study. First, the data are derived from a cross-sectional design. It is therefore not possible to determine whether an individual's SCI preceded the onset of type 2 diabetes. However, we did perform a sensitivity analysis, restricting the study sample to a group of younger individuals, to reduce the likelihood that diabetes preceded SCI. The increased odds of diabetes persisted, but had very wide CIs because of the reduced power (results not shown).

Another limitation of this study is the lack of detailed health records; the CCHS provides no information on neurologic level of SCI, completeness of SCI, or etiology of SCI (traumatic vs nontraumatic). However, recent studies from Canada estimate that approximately 51% of prevalent SCI cases are traumatic, vs 49% nontraumatic.¹⁶ Nontraumatic SCIs are less likely to be neurologically complete, i.e., have preserved movement or sensation below the injury level²²; because completeness of injury is associated with more adverse effects on glycemic control,²³ the inclusion of individuals with nontraumatic SCI would likely dilute the observed effects seen here.

In addition, although the data here are from self-report, any misclassification of diabetes status would likely be nondifferential by SCI status (and vice versa). Furthermore, as with all observational studies, there may be residual confounding. We were not able to adjust the models for measures of dyslipidemia, for example. Moreover, body mass index does not perfectly capture adiposity, particularly in individuals with SCI. However, we were able to adjust the models for a substantial number of potential confounders that are generally not all available in clinical studies.

Comment: Increased risk for type 2 diabetes in spinal cord injury

The prevalence of diabetes is increasing globally, with an estimated 371 million individuals affected and 4.8 million people who died due to diabetes in 2012.¹ Type 2 diabetes accounts for at least 90% of all cases of diabetes, and the number of people with type 2 diabetes is increasing in every country.¹ Abnormalities of carbohydrate and lipid metabolism are more common among people in the spinal cord injury (SCI) population than in the able-bodied population.² There is increased morbidity and mortality due to type 2 diabetes in SCI.

In this issue of *Neurology*[®], Cragg et al.³ evaluate the association between SCI and type 2 diabetes in a large representative sample and determine whether there is an association irrespective of known risk factors for type 2 diabetes.

After adjustment for both sex and age, Cragg et al.³ found an increased odds of type 2 diabetes (adjusted odds ratio [OR] 1.66 [95% confidence interval (CI) 1.16–2.36]) in SCI. The heightened odds persisted after adjusting for smoking status, hypertension status, body mass index, daily physical activity, alcohol intake, and daily consumption of fruits and vegetables (fully adjusted OR 2.45 [1.34, 4.47]). The authors also performed a sensitivity analysis to test the likelihood that type 2 diabetes preceded SCI. The increased odds of type 2 diabetes persisted but had very wide CIs due to the reduced power.³

The results from this study confirm the clinical observations of increased incidence of type 2 diabetes in SCI. The findings will refocus our daily practice efforts regarding diet, glucose levels, and type 2 diabetes at SCI centers. The results will also change our priorities regarding preventive health strategies and planning long-term care for people with SCI.

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Ellen Merete Hagen, MD, PhD

From Viborg Regional Hospital, Denmark; University of Bergen, Norway; and Aarhus University, Denmark.

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Lastly, the non-SCI comparison group in this study (used for computing ORs) may include individuals with other chronic conditions that might place them at increased risk of diabetes, especially since this is a recent database. However, the effect size estimates reported here would likely be higher had the comparison group only included “healthy” individuals.

These limitations aside, the increased odds of type 2 diabetes among individuals with SCI is an impetus for future investigations. Although there is physiologic plausibility for a causal relationship between SCI and diabetes, future research is needed to better understand this. Additional case-control or ideally, cohort studies, with the use of SCI-specific registries that contain more detailed clinical information, and that have records of timing of onset of conditions, are needed to build on this evidence and to provide evidence-based guidelines. These studies will be the subject of future investigation. Going forward, it will be important for SCI-specific registries, which are gaining momentum in several countries,²⁴ to include additional physiologic data such as blood sugar and lipid profiles.

AUTHOR CONTRIBUTIONS

J.C. was responsible for the study concept/design, analysis/interpretation of the data, and drafting the manuscript. V.N., M.D., A.K., and G.B.J.M. were responsible for interpretation of the results and revising the manuscript for intellectual content. J.F.B. was responsible for the study concept/design, interpretation of the data, and revising the manuscript for intellectual content.

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DISCLOSURE

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