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Prevalence and incidence of ischemic heart disease in multiple sclerosis: A population-based validation study

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Abstract

Background: Studies suggest an altered risk of ischemic heart disease (IHD) in multiple sclerosis (MS), but data are limited. We aimed to validate and apply administrative case definitions to estimate the incidence and prevalence of IHD in MS.

Methods: Using administrative data we identified persons with incident MS (MSPOP) and a matched general population (GPOP) cohort. We developed case definitions for IHD using ICD-9/10 codes and prescription claims, compared them to medical records, then applied them to evaluate the incidence and prevalence of IHD.

Results: Agreement between medical records and the administrative definition using ≥1 hospital or ≥2 physician claims over 5 years was moderate (kappa=0.66; 95% CI: 0.42–0.90). In 2005, the age-standardized prevalence of IHD was 6.77% (95% CI: 5.48–8.07%) in the MSPOP and 6.11% (95% CI: 5.56–6.66%) in the GPOP. The prevalence of IHD was higher in the MSPOP than the GPOP among persons aged 20–44 years (prevalence ratio 1.87; 95% CI: 1.65–2.12) and aged 45–59 years (prevalence ratio 1.21; 95% CI: 1.08–1.35). The incidence of IHD was also higher in the MSPOP (incidence rate ratio 1.24; 95% CI: 0.97–1.59).

Conclusions: More than 5% of the MSPOP has IHD. The incidence of IHD was higher than expected in persons aged <60 years. Further evaluation of this issue is warranted.

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1. Introduction

In immune-mediated conditions such as rheumatoid arthritis and psoriasis, the risk of ischemic heart disease (IHD) is increased (Crowson et al., 2005; Gelfand et al., 2006). Several

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studies suggest that diabetes, hypertension and hyperlipidemia are common in multiple sclerosis (MS) (Marrie et al., 2008, 2012a,b). While these conditions are associated with an increased risk of IHD, findings regarding the risk of IHD in MS are conflicting (Fleming and Blake, 1994; Redelings et al., 2006; Allen et al., 2008); (Koch-Henriksen et al., 1998). The issue of comorbid IHD is an important one in MS because it increases the risk of premature death, and is associated with increased risks of cerebrovascular and peripheral vascular disease (Alberts et al., 2009; Mehlsen et al., 2010). Further, IHD is associated with increased disability progression in MS (Marrie et al., 2010). Finally, new disease-modifying medications are emerging where the presence of comorbid cardiac disease may influence the safety of using those therapies (Cohen, 2009; European Medicines Agency, 2012). Thus it is important that the risk of IHD in MS be better characterized; and this can only be done if methods for the ascertainment of IHD amongst individuals with MS are developed and validated.

We aimed to develop and validate a case definition for ischemic heart disease using administrative data; and to apply this definition to estimate the incidence and prevalence of IHD in persons with MS and a matched cohort from the general population. Unlike prior studies we did not limit our study to hospitalized persons, to comprehensively assess the incidence and prevalence of IHD.

2. Materials and methods

2.1. Study setting

This was a population-based analysis of administrative (health claims) data for the period 1984–2005, conducted in Manitoba, a Canadian province with a population of approximately 1.2 million (Health Information Management Branch, 2008).

2.2. Administrative data

Manitoba Health, a provincial government department, provides health care services to 98% of the population (Health Information Management Branch, 2008). Since 1984 all hospital, physician and prescription claims submitted to Manitoba Health include a personal health identification number (PHIN) which uniquely identifies the person receiving the service. Each hospitalization record includes admission and discharge dates, and up to 16 discharge diagnoses listed using International Classification of Disease (ICD)-10-CA codes. Before 2004, discharge diagnoses were recorded using five-digit ICD-9-CM codes. Physician claims include the date of service, and three-digit ICD-9-CM code for one physician-assigned diagnosis for all physicians irrespective of physician type (e.g. primary care provider versus specialist). Since 1996 the Drug Programs Information Network captures the date, drug name and identification number for all outpatient prescription drugs which are dispensed to Manitoba residents.

2.3. Study populations

Previously, we validated an administrative case definition for MS (Marrie et al., 2010) which we applied to identify all persons with MS in Manitoba. We used the date of the first claim for demyelinating disease (e.g. transverse myelitis) as the date of MS diagnosis. To ensure that we were using incident cases of MS we required a five-year lookback period with no demyelinating disease claims. Since our data were available from 1984 onward this meant that the first MS case could be identified in 1989. After excluding persons with any diagnostic codes for demyelinating disease, we identified a cohort from the general population, matched on sex, year of birth and region of residence (postal code) to the MS cohort, with up to 5 "controls" for each case. Controls were assigned the same index date as their matched controls. A population registry is maintained by Manitoba Health, and it is updated when an individual moves into or out of Manitoba, changes marital status, or dies. Thus persons with MS or their matched controls were included in the analysis from the index date until the end of the study (2005), death or emigration from Manitoba, whichever came first.

2.4. Validation cohort

As detailed elsewhere, our validation cohort included 430 persons with definite MS (Marrie et al., 2010) drawn from two studies (Horton et al., 2010; Marrie et al., 2010). In both studies, participants consented to review of their medical records, and to linkage of their administrative and clinical data. A blinded, trained, abstractor used a standardized data collection form to capture comorbidities from the medical records of all participants (Marrie et al., 2010). Participants also completed a questionnaire regarding their comorbidities, including heart disease (Horton et al., 2010).

2.5. Case definitions for IHD

After a literature review, we selected ICD-9/10 codes for IHD (410–414, I20–I25) (Austin et al., 2002; Rector et al., 2004; Lix et al., 2008; Varas-Lorenzo et al., 2008). We generated lists of prescription medications available for treatment of IHD in Canada using the Anatomic Therapeutic Chemical system, including C01 (cardiac therapy), C07 (beta-blockers), C08 (calcium channel blockers), and C09 (agents acting on renin-angiotensin system) (Lix et al., 2008). Finally, we developed candidate case definitions, varying the number of physician, hospital and prescription claims required and the number of years used to classify a person as having IHD.

Using the validation cohort, we compared the classification of IHD cases using administrative definitions with cases defined by medical records review, using sensitivity, specificity, positive predictive value and negative predictive value. Youden's J, an index that equally weights sensitivity and specificity, was calculated as: (sensitivity+specificity) −1 (Youden, 1950). We also report a kappa (κ) statistic for the agreement between administrative and medical records data, interpreting κ as follows: slight (0–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect agreement (0.81–1.0) (Landis and Koch, 1977).

2.6. Prevalence and incidence

We applied selected case definitions to both study populations. Once a person met the case definition for IHD, he or she was defined as affected in all subsequent years while alive and

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