Validation of Self-Reported Cardiovascular Disease and Associated Co-Morbidities in a Large Canadian Cohort of Early Inflammatory Arthritis

Lillian Barra1*, Kyle Arsenault-Mehta1, Janet E. Pope1, Carol Hitchon2, Gilles Boire3, Orit Schieir4, Carter Thorne5, Diane Tin6, Edward C. Keystone7, Boulos Harauqui8, Shahin Jamal9, Susan Bartlett10 and Vivian P. Bykerk10

1Department of Medicine, Division of Rheumatology, Western University, London, Canada
2Department of Medicine, Division of Rheumatology University of Manitoba, Winnipeg, Canada
3Department of Medicine, Division of Rheumatology, Université de Sherbrooke, Sherbrooke, Canada
4Department of Medicine, Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, Canada
5Southlake Health Center, Newmarket, Canada
6Institut de Rhumatologie de Montréal and University of Montreal, Montreal, Canada
7Vancouver Coastal Health, Vancouver, Canada
8Royal Victoria Hospital, Montreal, Canada
9Hospital for Special Surgery, New York, United States

*Corresponding author: Lillian Barra, Department of Medicine, Division of Rheumatology, Western University, London, Canada. Tel: 5197091133; E-mail: lillian.barra@sshc.london.on.ca

Received date: February 06, 2017; Accepted date: February 16, 2017; Published date: February 23, 2017

Copyright: ©2017 Barra L, et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: Cardiovascular disease (CVD) and risk factors for CVD (smoking, hypertension, dyslipidemia and diabetes) are commonly associated with Rheumatoid Arthritis (RA). We aimed to determine the validity of self-reported CVD events and risk factors in the Canadian Early Arthritis Cohort (CATCH).

Methods: CATCH is a multicenter inception cohort of patients with early RA. Various co-morbidities and pharmacologic therapies are self-reported at baseline and at each follow-up visit. Using a randomly selected subgroup of subjects enrolled in CATCH from one representative site, we performed a detailed review of their complete medical record to identify diagnoses of CVD events, risk factors and drug therapies. The validity of self-reported variables was determined using the Cohen’s kappa statistic.

Results: The validation subgroup (N=141) was similar to the entire CATCH population (N=2626) with respect to baseline demographics and RA disease characteristics. There was very good agreement between self-report and the medical record for cardiovascular or cerebrovascular events (kappa=0.66), as well as for hypertension and diabetes (kappa=0.70 and 0.81, respectively). Subjects tended to under-report dyslipidemia and the reporting of lipid-lowering and antiplatelet/anticoagulant agents was inaccurate compared to the medical record.

Conclusion: Self-reported cardiovascular disease, hypertension and diabetes was representative of the medical record suggesting that these self-reported variables are valuable for future studies of this early RA population.

Keywords: Cardiovascular; Rheumatoid arthritis; Cohort

Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory disease affecting predominately the joints, but also with multiple systemic manifestations and complications. Cardiovascular disease (CVD), including coronary heart disease and cerebral vascular disease is common in RA patients and is a major cause of death [1,2]. In addition, RA patients have higher rates of risk factors for CVD, including cigarette smoking, hypertension, diabetes mellitus, obesity and dyslipidemia [3,4]. The treatment of RA involves exposure to medications known to increase CVD risk: corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) [5]. Therefore, studying cardiovascular associated co-morbidities and treatment is critical for determining ways to improve outcomes in RA. Given that complete medical record review to ascertain co-morbidities is often costly and impractical, particularly for large cohorts with long-term follow-up, most studies reporting on CVD in RA rely on self-report [1]. Herein we present a study validating self-reported CVD risk factors, events and treatment using a subgroup of patients from a large prospective ongoing cohort, the Canadian Early Arthritis Cohort (CATCH).

Methods

Study subjects are enrolled in a Canadian multicenter inception cohort of patients with early inflammatory arthritis with ongoing recruitment (CATCH), described in detail elsewhere [6]. In brief, subjects were enrolled from July 2003 to May 2015 and were included if: age >16 years, persistent synovitis for 6 weeks to 12 months and ≥ 2 swollen joints or 1 swollen metacarpophalangeal or proximal interphalangeal joint with ≥ 1 of: positive rheumatoid factor (RF), positive anti-cyclic citrullinated peptide 2 (anti-CCP2), morning stiffness >45 min, response to nonsteroidal anti-inflammatory drugs,
or painful metatarsophalangeal squeeze test. Subjects were excluded if diagnosed by the treating physician with another rheumatologic condition other than RA. Over the course of the study >90% of subjects met either the 1987 American College of Rheumatology (ACR) or the 2010 ACR/European League Against Rheumatism (EULAR) classification criteria for RA [7]. Subjects are followed every 3 months for the first year, then at 18 months and yearly. The study was approved by the research ethics boards of all the centers involved, and consent was obtained according to the Declaration of Helsinki.

In CATCH, CVD risk factors and events were self-reported by a self-administered questionnaire. Study staff could assist subjects with the completion of the questionnaire. For the baseline visit, the questionnaire specifically asked if the subjects had ever received a diagnosis by a physician for the following: diabetes, hypertension, hyperlipidemia, angina, heart attack, stroke or mini-stroke. For follow-up visits, the questionnaire asked that the subject list all medication and specify any new diagnoses, hospitalizations and reasons for hospitalizations, as well as the dates associated with these events. In order to validate these self-reported variables, the medical record of a subgroup consisting of randomly selected CATCH study subjects from one recruitment site (St. Joseph’s Health Care, London, Canada) was reviewed.

The selected site is a high recruitment site for CATCH; it is a tertiary care academic center and the enrolled subjects from this site are representative of the entire cohort. The medical records reviewed consisted of electronic and paper records from all inpatient and outpatient hospital visits from January 1995 to May 2015) from St. Joseph’s Health Care and London Health Sciences Centre).

CVD events were defined as acute coronary syndrome (diagnosed by a physician and confirmed by EKG, imaging and/or biomarkers) or cerebrovascular event (diagnosed by a neurologist with a documented history and physical exam consistent with stroke or transient ischemic attack and/or imaging). Hypertension was defined as a blood pressure of >140/90 documented in 3 separate visits with no documentation of “white coat syndrome” or a physician documented that the subject was prescribed an antihypertensive drug for the treatment of hypertension.

A diagnosis of diabetes was defined as per the 2013 Canadian Diabetes Association clinical practice guidelines [8] or a physician documented that the patient was taking insulin or other hypoglycemic agents. Hyperlipidemia was defined as per the 2012 Canadian Cardiovascular Society guidelines [9]. The validity of self-reported variables was determined using the Cohen’s kappa statistic and % agreement between self-reported variables and those determined by chart review (sum of observations that agreed divided by total observations).

Results

At the time of the validation study, 2626 subjects were enrolled in CATCH with a mean follow-up of 3.4 (SD 2.1) years. The demographics and clinical characteristics of the included subjects are shown in Table 1 and did not differ significantly between CATCH and the validation subgroup (N=141) where the mean age was 54 (SD 14) years and RA symptom duration prior to enrollment was 7 (SD 3) months.

The majority (80%) were females, seropositive (75%) and prior or current smokers (54%). Subjects had moderate disease severity with DAS28 score of 4.31 (SD 1.52) and HAQ-DI of 0.81 (0.66).

Table 1: Baseline demographics and clinical features of study subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>CATCH (%)</th>
<th>Validation Subgroup (%)</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Event</td>
<td>22 (16)</td>
<td>119 (84)</td>
<td>15 (11)  126 (89)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>17 (12)</td>
<td>124 (88)</td>
<td>19 (13)  122 (87)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41 (29)</td>
<td>100 (71)</td>
<td>52 (37)  89 (63)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>19 (13)</td>
<td>122 (87)</td>
<td>46 (33)  95 (67)</td>
</tr>
<tr>
<td>Aspirin/ Anti-platelet agent</td>
<td>9 (6)</td>
<td>132 (94)</td>
<td>22 (16)  119 (86)</td>
</tr>
<tr>
<td>Lipid-lowering Agent</td>
<td>0</td>
<td>141 (100)</td>
<td>22 (16)  119 (86)</td>
</tr>
</tbody>
</table>

Table 2: Validity of self-reported variables in CATCH.

At each CATCH follow-up visit, patients are asked to list all current medications (including over-the-counter drugs and herbal remedies). We found that the reliability of reporting aspirin/anti-platelet and...
lipid-lowering agents was fair at best (refer to Table 2: kappa for aspirin reporting =0.33; none of the patients who had been prescribed lipid-lowering agents based on the medical record reported it on the CATCH questionnaire). All patients diagnosed with dyslipidemia had been prescribed a lipid-lowering agent as per the medical record, which did not comment on adherence or termination of therapy due to adverse events in these patients. Only 7 of the 15 (47%) patients diagnosed with a cardiovascular event had an antplatelet or anticoagulant agent listed as part of their medical record at any time after the event.

Discussion

Cardiovascular outcomes and risk factors are important factors to consider in the management of RA. In this study we performed a thorough review of the medical record of a random subgroup of subjects enrolled in a large multicenter RA cohort (CATCH) with ongoing follow-up in order to validate self-reported co-morbidities. We used standard definitions for the diagnosis of cardiovascular events and risk factors and ensured that the diagnoses were confirmed by appropriate laboratory and imaging investigations.

It is common practice for prospective studies to use questionnaire-based self-reported variables; however, the accuracy of self-report has been shown to vary widely in validation studies [10]. Several factors can explain the variability, including study design, disease complexity and study subject characteristics [10]. RA is a complex systemic autoimmune disease usually requiring life-long therapy with multiple agents and it is associated with many complications and co-morbidities, which can be overwhelming for patients and may lead to difficulties understanding all their medical conditions and treatments [11]. In the CATCH questionnaire potential co-morbidities are listed for patients to select in order to assist with recollection. However, patients may not be aware that they should report diagnoses even if they are asymptomatic or treated and under good control, which may explain the under-reporting of dyslipidemia and hypertension [12].

Although there was very good agreement between self-report and the medical record for CVD events, heart conditions and stroke tended to be over-reported by study subjects. It is possible that some of the diagnoses reported by the subjects were made at another hospital and were not captured by the treating physicians at the study centre. Alternatively, there are many non-cardiac causes of chest pain, dyspnea and leg edema and the study subjects may have over-reported these as angina, heart attack or heart failure.

Self-report of lipid lowering and antiplatelet/anticoagulant agents were inaccurate in our study. Patients may not have been aware that these non-rheumatic drugs are relevant to their rheumatologic condition and therefore may not have reported them. In addition, aspirin, which is over-the-counter may not have been reported by patients or captured in the medical record. It may be necessary to specifically ask patients in the questionnaire whether they take aspirin in order to improve accuracy. Linking components of the electronic medical record to the CATCH database may also improve the accuracy.

In conclusion, CATCH is one of the largest prospective cohorts of early RA and contains a wealth of information regarding various aspects of RA, including complications and co-morbidities that account for the majority of RA mortality and significantly affect morbidity. In this validation study we found very good agreement between the medical record and self-reported cardiovascular and cerebrovascular events, hypertension and diabetes, supporting the use of these self-reported variables to address important clinical and epidemiologic questions within the CATCH cohort.

Disclosures

The Canadian Early Inflammatory Arthritis Cohort (CATCH) study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada-Founding sponsor since January 2007; Hoffmann-LaRoche, UCB Canada, Bristol-Myers Squibb Canada, AbbVie Corporation and Janssen Biotech since 2011; Medexus Inc. since 2013; Eli Lilly Canada and Sanofi Canada since 2016. The authors do not have any additional disclosures for this manuscript. The study was approved by the research ethics boards of all the centers involved, and written informed consent was obtained according to the Declaration of Helsinki (approval #12982E).

References