# Carotid intima-media thickness as a marker for cardiovascular risk in northern Alberta patients with rheumatoid arthritis on biologics

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## Abstract

Carotid intima media thickness (cIMT) measurement is a validated surrogate measure of cardiovascular (CV) risk. Our aim was to evaluate baseline cIMTs in a cross-sectional study of northern Alberta inflammatory arthritis (IA) patients on biologics to determine if cIMT correlates with traditional CV factors, arthritis activity measures or risk scores.

CIMT's were performed on 51 IA patients at the Mazankowski Heart Institute as part of their evaluation in the "Cardiovascular Risk Reduction Clinic for Inflammatory Rheumatic Diseases". Baseline CV risk assessment included traditional cardiovascular risk factors, IA disease activity indices and fasting lipids and glucose. Univariable followed by multivariable logistic regression analyses were performed to identify associations between CV and IA risk factors and the composite outcomes of a) cIMT > 0.9 mm or b) presence of plaque or both a) and b).

CIMTs were performed on 51 IA patients, mean age 59.5 (SD 11.8) years, female:male = 39:12. Baseline mean arthritis activity measures included: disease duration 18 (SD 13) years, ESR 18 (SD 20) mm/hr, CRP 6.3 (SD 8.7) mg/L, 34 RF +/ 33 anti-CCP + patients, DAS28 2.44 (SD 1.34). All patients had been on at least one biologic, 34 with past exposure to prednisone, 16 with past exposure to COX2's/NSAIDs. Traditional CV risk factors included: 8 current smokers (15.7 (SD 30.8) pack-year history), 4 diabetics (2 on oral hypoglycemic, 1 on insulin/ oral hypoglycemic, 2 on diet), 20 patients with systolic hypertension, 14 patients with dyslipidemia (mean values (mmol/L): total cholesterol 4.9 (SD 0.91), LDL 2.8 (SD 0.72), HDL 1.46 (SD 0.45), total cholesterol/HDL 3.52 (SD 0.84), triglycerides 1.42 (SD 0.68) mmol/L. Eighteen patients had family history of premature CVD, 9 patients with personal history of CVD, mean Framingham 11.9% (SD 8.1), Framingham with EULAR multiplicative factor 1.5 = 20.3 % (SD 12.2). Mean cIMT was 0.709 mm(SD 0.190) and 25 patients had plaques on at least one of the 6 sites measured. Extra-articular manifestations (OR 11.8 (95% CI 1.9-72.1) were associated with worse cIMTs and plaque while prednisone appeared protective against poor cIMT measures (OR 0.13 (95% CI 0.02-0.81).

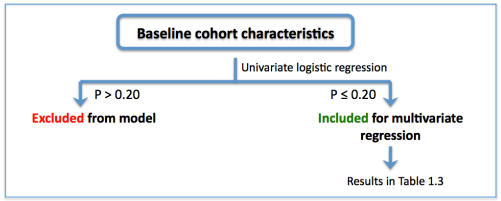
CIMT may serve as an inexpensive screening tool for cardiovascular risk stratification in IA patients. Attention should be paid to extra-articular manifestations in IA patients as a surrogate marker of increased cardiovascular risk, as recommended by EULAR. The protection afforded by any past use of prednisone requires further evaluation, given the small sample size of this cohort.

## Methods

•51 Inflammatory arthritis patients attended a CV risk reduction clinic in Edmonton, AB. Baseline cohort characteristics (Table 1) included patient demographics, inflammatory arthritis disease history and bloodwork, traditional CV risk assessment and medication history.

•CV risk was determined using the Framingham and Reynold' s risk score and patients were offered individualized risk reduction strategies as indicated (lipid lowering agents, smoking cessation, anti-hypertensive medication and dietetic counseling.

•cIMT measurements were preformed at a subsequent visit for all consenting patients. Univariate and multivariate regression were performed to determine which baseline cohort characteristics corrolate with worse cIMT measurements (>0.9mm or plaque present).




## Table 1. Baseline cohort characteristics

| Baseline Characteristics | | | | Mean ± SD |
|---|---|---|---|---|
| Demographics | | Age | (yrs) | 59.5 ± 11.8 |
| | | Female | (%) | 76.5 (39F, 12M) |
| Disease information | Disease history | Age at diagnosis | (yrs) | 42.6 ± 14.1 |
| | | Disease duration | (yrs) | 18.0 ± 12.8 |
| | | Morning stiffness | (min) | 131 ± 377 |
| | | Extra-articular manifestations | (%) | 36 (18/50) |
| | Blood markers | ESR | (mm/hr) | 17.6 ± 19.7 |
| | | ESR > 20 mm/hr | (%) | 32 (15/47) |
| | | CRP | (mg/L) | 6.3 ± 8.7 |
| | | CRP > 8 mg/L | (%) | 24 (12/50) |
| | | RF seropositive | (%) | 68 (34/50) |
| | | CCP seropositive | (%) | 66 (34/50) |
| | Disease indices | CDAI | | 11.6 ± 9.3 |
| | | SDAI | | 77.9 ± 96.0 |
| | | Physician VAS | | 3.4 ± 2.1 |
| CV risk factors | Smoker status | Never smoked | (%) | 41 (21/51) |
| | | Former smoker | (%) | 43 (22/51) |
| | | Current smoker | (%) | 16 (8/51) |
| | Diabetic status | Diabetes | (%) | 8 (4/51) |
| | | HbA1C | (%) | 5.8 ± 0.6 |
| | | Fasting blood glucose | (mM) | 5.3 ± 0.8 |
| | Lipid profile | Dyslipidemia | (%) | 28 (13/47) |
| | | Total cholesterol | (mM) | 4.9 ± 0.9 |
| | | LDL | (mM) | 2.8 ± 0.7 |
| | | HDL | (mM) | 1.5 ± 0.4 |
| | | Triacylglycerols | (mM) | 1.4 ± 0.7 |
| | | ApoB | (g/L) | 0.8 ± 0.2 |
| | | Lipoprotein A | (g/L) | 0.3 ± 0.4 |
| | Blood pressure | Hypertensive | (%) | 43 (20/47) |
| | | Systolic BP | (mmHg) | 129 ± 20 |
| | | Diastolic BP | (mmHg) | 75 ± 13 |
| | History of CVD | Personal history | (%) | 35 (18/51) |
| | | Family history | (%) | 18 (9/50) |
| | CV Risk indeces | Framingham risk | | 11.8 ± 8.1 |
| | | Reynold's risk | | 2.7 ± 3.3 |
| | | EULAR multiplier | (%) | 88 (45/51) |
| Medications | Prior use of: | NSAIDS | (%) | 70 (35/50) |
| | | COX-2 inhibitos | (%) | 44 (22/50) |
| | | Anti-malarials | (%) | 76 (38/50) |
| | | Methotrexate | (%) | 96 (48/50) |
| | | Sulfasalazine | (%) | 30 (15/50) |
| | | Leflunomide (Arava) | (%) | 62 (31/50) |
| | | Azathioprine (Imuran) | (%) | 2 (1/50) |
| | | Gold | (%) | 28 (14/50) |
| | | Prednisone | (%) | 68 (34/50) |
| | | Biologics (any) | (%) | 96 (48/50) |
| | | Cholesterol lowering agent | (%) | 21 (10/48) |
| | | Low dose ASA | (%) | 24 (12/50) |

## Table 2. Carotid Intima-Media Thickness Measurements

| Artery Measured | | Mean Intima-Media Thickness ± SD | Number of arteries |
|---|---|---|---|
| All arteries | (mm) | 0.73 ± 0.39 | 272 |
| Arteries > 0.9 mm | (mm) | 1.26 ± 0.70 | 44 |
| Arteries with plaques | (mm) | 1.11 ± 0.42 | 41 |
| Arteries > 0.9 mm or plaques | (mm) | 1.19 ± 0.69 | 68 |
| Location | | | |
| Right CCA | (mm) | 0.714 +/ - 0.029 | 50 |
| Right carotid bulb | (mm) | 0.803 +/- 0.033 | 48 |
| Right ICA | (mm) | 0.560 +/- 0.017 | 40 |
| Left CCA | (mm) | 0.731 +/- 0.025 | 51 |
| Left carotid bulb | (mm) | 0.859 +/- 0.044 | 44 |
| Left ICA | (mm) | 0.559 +/- 0.025 | 39 |

CCA; Common Carotid Artery, ICA; Internal Carotid Artery.

## Table 3. Multivariate Regression Results

| Cohort Characteristic | Adjusted OR (95% CI) | p-value |
|---|---|---|
| Age > 55 yrs | 0.77 (0.12, 5.06) | 0.790 |
| Extra articular manifestations | 11.77 (1.92, 72.09) | 0.008 |
| Prior prednisone use | 0.13 (0.02, 0.81) | 0.029 |
| Elevated ESR ( ≥ 20 mm/hr) | 3.08 (0.60, 15.83) | 0.176 |

## Conclusions

• The presence of extra articular manifestations of inflammatory arthritis correlated with worse cIMT measurements (adjusted OR = 11.8) whereas prior use of prednisone was protective from poor cIMT values (adjusted OR = 0.13).

• Limitations include small cohort size (51 patients) and short follow up (2 years). Existing patients are currently being followed annually with repeat CIMTs to evaluate progression.

• The use of cIMT as a screening tool of CV risk in at-risk inflammatory arthritis patients has potential and warrants further research.

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