# Cardiovascular Disease Risk Factors May Negatively Impact Rheumatoid Arthritis Disease Outcomes:

## Findings from the Ontario Best Practices Research Initiative (OBRI)

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## BACKGROUND

- Cardiovascular disease (CVD) is recognized as an important comorbidity for patients with rheumatoid arthritis (RA)[1].
- RA disease activity is influenced by cardiovascular comorbidities.
- Higher comorbidity burden adversely affect RA treatment response[2-3].
- The Ontario Best Practices Research Initiative (OBRI) includes a clinical registry of RA patients (OBRI-RA registry) followed in routine care in Ontario, Canada (www.obri.ca).

## OBJECTIVE

- To explore the effects of CVD and CVD risk factors (RF) on RA treatment outcomes.

## METHODS

- **Study Design:** Retrospective cohort study
- **Study Population:**
  - All patients enrolled with the OBRI-RA registry
  - English speaking adult patients with active RA
  - Has complete baseline data and at least 1 year of follow-up
- **Data Collection:**
  - Data collection: January 2008 to January 2017.
  - Participating rheumatologists collect clinical data at baseline and every 6 months or at any visit.
  - Patients telephone interviews at baseline, every 3 months for the first 2 years, and then every 6 months.
- **Exposure:** Patients were classified into mutually exclusive groups:

  (1) **CVD**: myocardial infarction (MI), coronary artery disease (CAD), transient ischemic attacks (TIA), stroke, and peripheral arterial disease (PAD);

  (2) **CVD RFs**: hypertension (HTN), dyslipidemia (DLD), diabetes mellitus (DM), or Current smoking;

  (3) **No CVD/no CVD RFs**.
- **Outcomes:** Disease Activity Score-28 (DAS28), Clinical Disease Activity Index (CDAI), Swollen Joint Count 28 (SJC28) and Heath Assessment Questionnaire – Disability Index (HAQ-DI)
- **Statistical Analysis:**
  - Multivariable linear regression analysis
  - Adjusting for clinical and demographic confounders
  - Multiple imputation n=20

## RESULTS

- The baseline characteristics are summarized in **Table 1**.
- 110 (5.4%) patients had CVD, 917 (45.1 %) had CVD RF.

## RESULTS

**Table 1**. Baseline characteristics of the cohort.

| Characteristics | No CVD/RF (N=917) | CVD (N=110) | CVD RF (N=1006) | P-value |
|---|---|---|---|---|
| **Socio-demographics** | | | | |
| Age (yrs.), mean (SD) | 53.0 (12.7) | 66.6 (9.4) | 60.8 (10.9) | **<0.0001** |
| Sex, n (%) | | | | |
| Female | 770 (84.0%) | 55 (60.0%) | 763 (75.8%) | **<0.0001** |
| Male | 147 (16.0%) | 44 (40.0%) | 243 (24.2%) | |
| Education, n (%) | | | | |
| High school or less | 335 (36.5%) | 66 (60.0%) | 512 (50.9%) | **<0.0001** |
| Post-secondary | 581 (63.4%) | 44 (40.0%) | 492 (48.9%) | |
| OHIP plus (private or ODB program), n (%)≠ | 684 (74.6%) | 60 (54.5%) | 666 (66.2%) | **<0.0001** |
| Urban residence, n (%) | 756 (82.4%) | 89 (80.9%) | 818 (81.3%) | 0.76 |
| **Clinical Characteristics** | | | | |
| RA duration (yrs.), mean (SD) | 7.6 (8.8) | 10.0 (11.5) | 8.4 (9.8) | 0.45 |
| CRP (mg/l), mean (SD)€ | 12.6 (21.4) | 14.2 (20.5) | 13.4 (21.5) | 0.24 |
| SJC-28 (range: 0-28), mean (SD) | 5.4 (4.9) | 5.9 (5.3) | 5.7 (5.0) | 0.40 |
| DAS28, mean (SD) | 4.2 (1.6) | 4.6 (1.6) | 4.4 (1.5) | **0.0004** |
| CDAI score, mean (SD) | 19.9 (13.5) | 22.0 (14.5) | 21.4 (13.8) | **0.04** |
| HAQ score, mean (SD) | 1.0 (0.8) | 1.2 (0.8) | 1.2 (0.7) | **<0.0001** |
| **Treatments** | | | | |
| Prior use of biologics, n (%) | 222 (24.2%) | 28 (25.5%) | 272 (27.0%) | 0.37 |
| On Biologics, n (%) | 136 (14.8%) | 16 (14.5%) | 129 (12.8%) | 0.43 |
| On conventional DMARDs, n (%) | 563 (61.4%) | 68 (61.8%) | 630 (62.6%) | 0.86 |
| On NSAIDs, n (%) | 31 (3.4%) | 3 (2.7%) | 30 (3.0%) | 0.85 |
| On steroid, n (%) | 178 (19.4%) | 22 (20.0%) | 200 (19.9%) | 0.96 |
| **Comorbidities** | | | | |
| Depression, n (%) | 230 (25.1%) | 40 (36.4%) | 313 (31.1%) | **0.003** |
| Lung disease, n (%) | 141 (15.4%) | 33 (30.0%) | 216 (21.5%) | **<0.0001** |
| GI and liver disease, n (%) | 173 (18.9%) | 35 (31.8%) | 265 (26.3%) | **<0.0001** |
| Cancer, n (%) | 103 (11.2%) | 29 (26.4%) | 152 (15.1%) | **<0.0001** |
| Osteo- or degenerative arthritis, n (%) | 339 (37.0%) | 52 (47.3%) | 468 (46.5%) | **<0.0001** |

- CVD was associated with higher disease activity measured in DAS28 and worse functional status at baseline but not at 1-year (**Table 2-3).**
- CVD RF was associated with significantly higher DAS28 baseline and 1-year follow up.
- CVD RF became significantly associated with higher CDAI at 1 year.

## RESULTS

**Table 2**. Impact of CVD and RF on clinical outcomes at cohort entry.

| | β - coefficient (95% CI); p-value | | | |
|---|---|---|---|---|
| CVD status | DAS28-ESR± N=2033 | CDAI± N=2033 | SJC-28± N=2033 | HAQ-DI± N=2033 |
| No CVD / RFs | Ref | Ref | Ref | Ref |
| CVD | **0.29 (0.01,0.56), 0.04** | 1.22 (-1.26,3.70), 0.34 | 0.09 (-0.86,1.04), 0.85 | **0.15 (0.01,0.29), 0.04** |
| CVD RFs / No CVD | **0.13 (0.002,0.26), 0.04** | 0.77 (-0.38,1.93), 0.19 | -0.01 (-0.45,0.43), 0.96 | **0.16 (0.10,0.23), <0.0001** |

± adjusted for age, gender, education level, health insurance type, comorbidities, HAQ-pain score, concurrent treatments and CRP

**Table 3**. Impact of CVD and RF on clinical outcomes at 1-year follow up.

| | β - coefficient (95% CI); p-value | | | |
|---|---|---|---|---|
| CVD status | DAS28-ESR± N=1965 | CDAI± N=1965 | SJC-28± N=1965 | HAQ-DI± N=1965 |
| No CVD / RFs | Ref | Ref | Ref | **Ref** |
| CVD | 0.12 (-0.14,0.38), 0.37 | 0.50 (-1.45,2.46), 0.61 | 0.44 (-0.21,1.10), 0.19 | 0.09 (-0.02,0.19), 0.10 |
| CVD RFs / No CVD | **0.17 (0.05,0.30), 0.01** | **0.96 (0.05,1.87), 0.04** | 0.29 (-0.01,0.60), 0.06 | 0.03 (-0.02,0.08), 0.17 |

± adjusted for age, gender, education level, health insurance type, comorbidities, HAQ-pain score, concurrent treatments CRP, and baseline disease activity

## CONCLUSIONS

- CVD and traditional CVD RF independently predicted certain RA disease outcome at baseline and 1-year follow up
- Lack of significance in CVD may be secondary to limited sample size
- CVD and RFs may be perceived as a systemic marker for advanced RA.
- Patients with CVD RF maybe treatment-resistant
- Self-perceived impact of comorbidity may also be driving this relationship
- Investigation into the magnitude of effect for the individual CVD RFs, and whether differences in RA treatment patterns by CVD status may mediate this relationship is warranted.

## REFERENCES

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