Multimorbidity Phenotypes and their Relationship with Patient Outcomes and Health Care Utilization in US Veterans with Rheumatoid Arthritis

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OBJECTIVE & SPECIFIC AIMS

Objective: Derive unique multimorbidity phenotypes in US Veterans with rheumatoid arthritis (RA) and test their predictive ability for health care outcomes and utilization.

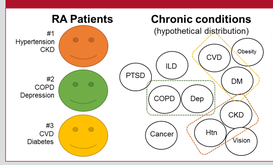
Specific Aim 1: Determine the burden of, and factors associated with, multimorbidity and the unique interactions of chronic conditions in RA.

Specific Aim 2: Derive novel multimorbidity phenotypes using "big-data" approaches and demonstrate their predictive ability for hospitalizations, mortality, and health care utilization in RA.

BACKGROUND

- Multimorbidity is one of the leading problems facing the US health care system, particularly in areas where access to care and health disparities exist[1]
- Rheumatoid arthritis, an autoimmune condition that predisposes to the development of additional chronic diseases and poor long-term health outcomes, serves as a valuable model to study multimorbidity[2]
- An optimal method to assess multimorbidity in both clinical and research settings is lacking, resulting in knowledge gaps for assessing and managing high-risk patients
- Novel informatics approaches have the potential to harmonize the multimorbidity assessments between clinical and research settings – allowing for future efforts to study health outcomes as well as design and test multimorbidity interventions

Figure 1. Comparison of multimorbidity assessments



Multimorbidity assessments		
Assessment	Application	Strengths/Limitations
Single condition (e.g. CVD)	Pt 1. None Pt 2. None Pt 3. CVD	Strengths: Simple, biological basis Limitations: Ignores other comorbidities, not generalizable to most clinical settings
Comorbidity index (e.g. Charlson)	Pt 1. Score = 2 Pt 2. Score = 1 Pt 3. Score = 3	Strengths: Includes multiple conditions, quantifies burden Limitations: Complex, no clinical use, lose information on individual comorbidities, no biological basis
Multimorbidity patterns (novel)	Pt 1. Renovascular Pt 2. Severe respiratory Pt 3. Cardiometabolic	Strengths: Condenses large amount of data into useful patterns, biological basis, can be quantified for outcomes research Limitations: Requires expertise to derive

APPROACH

- Historical cohort study within the Veterans Health Administration database (Corporate Data Warehouse [CDW]) from 2000-2014 to study multimorbidity burden, chronic condition interactions, and identify multimorbidity phenotypes in RA vs. matched controls.
- Identification of RA patients through administrative data algorithms (RA diagnostic codes, medications, antibody testing) and matched controls (matched on year of birth, year of VA enrollment, and gender)
- Assessment of chronic conditions (condition selection informed by systematic literature review and clinical experience) within CDW by diagnostic codes during the required 12 month period before index date
- Patient factors (e.g. age, sex, race, urban/rural residence, socioeconomic status, tobacco use, benefits) selected from CDW
- Aim 1 (Cross-sectional): Comparison of multimorbidity burden and specific chronic conditions (dyads/triads) between RA and matched controls. Identification of patient factors associated with multimorbidity
- Aim 2 (Longitudinal): Factor and cluster analysis performed on baseline chronic conditions to identify multimorbidity phenotypes. Resulting phenotypes will be used to predict future hospitalization, mortality, and health care utilization (identified within CDW or the National Death Index) and compared with other established comorbidity indices (e.g. Charlson and Rheumatic Disease Comorbidity Index)

Table 1. Summary of design, methods, and statistical approaches

Specific Aim	Data source	Outcome(s)	Statistical approach
Aim 1. Multimorbidity burden and chronic disease interactions	National VA (RA and controls)	a. Multimorbidity burden and associated patient factors b. Chronic disease dyads/triads	a. McNemar's, GEE b. O/E ratios
Aim 2. Multimorbidity phenotypes, patient outcomes, and health care utilization	National VA (RA)	a. Multimorbidity phenotypes b. Hospitalization, mortality, & health care utilization	a. Factor & cluster analysis b. Cox & negative binomial regression

NEXT STEPS/DELIVERABLES

- Selection of matched non-RA controls
- Complete queries of chronic conditions within CDW
- Analysis: Compare chronic conditions between RA and non-RA patients and identify patient factors associated with multimorbidity
- Perform factor and cluster analysis to identify novel multimorbidity phenotypes in RA
- Complete queries for hospitalizations, mortality, and health care utilization
- Analysis: assess predictive potential of multimorbidity phenotypes for patient outcomes and health care utilization
- Analysis: contrast predictive potential of multimorbidity phenotypes with other comorbidity indices
- Career Development/Research Training:
  - Complete PhD in Clinical & Translational research through Mentored Scholars Program
  - Complete VA Health Informatics 10x10 program
  - Conduct and interpretation of data mining approaches

CONCLUSIONS

Novel informatics approaches to characterize multimorbidity in RA may help align clinical care and outcomes research for this high-risk population.

RESULTS

Table 2. Frequency of patients in the VA fulfilling RA algorithms from 1/1/2000 – 4/1/2018

Algorithm	Components	Broad ICD		Restricted ICD***	
		Number of Patients	VARA identified (%) n = 2610	Number of Patients	VARA identified (%) n = 2610
1	RA diagnostic codes	119470	2602 (99.7)	116945	2602 (99.7)
2	RA diagnostic codes + rheumatologist diagnosis	81964	2601 (99.7)	79088	2601 (99.7)
3	RA diagnostic codes + rheumatologist diagnosis + DMARD	70079	2588 (99.2)	67869	2588 (99.2)
4	RA diagnostic codes + rheumatologist diagnosis + DMARD*	79176	2600(99.6)	76390	2600(99.6)
5	RA diagnostic codes + rheumatologist diagnosis + (DMARD* or Positive autoantibody**)	72819	2594 (99.4)	70511	2594 (99.4)
6	RA diagnostic codes + rheumatologist diagnosis + (DMARD* or Positive autoantibody**) + exclusion of Ank Spond and PsA	67235	2551 (97.7)	65156	2551 (97.7)

Diagnostic codes were at least 2 ICD-9/ICD-10 for RA, 30 days apart

* DMARD not required if at least 2 diagnoses were made by rheumatologist, ** Rheumatoid factor or anti-CCP antibody above reference value, *** Restricted ICD9 includes 714.0, 714.1, 714.2, 714.81 & ICD10 includes M05.x, M06.x (excludes M06.4 & M06.1)

Abbreviations: VARA, Veterans Affairs Rheumatoid Arthritis Registry; RA, rheumatoid arthritis; DMARD, disease-modifying anti-rheumatic drug; Ank spond, ankylosing spondylitis; PsA, psoriatic arthritis

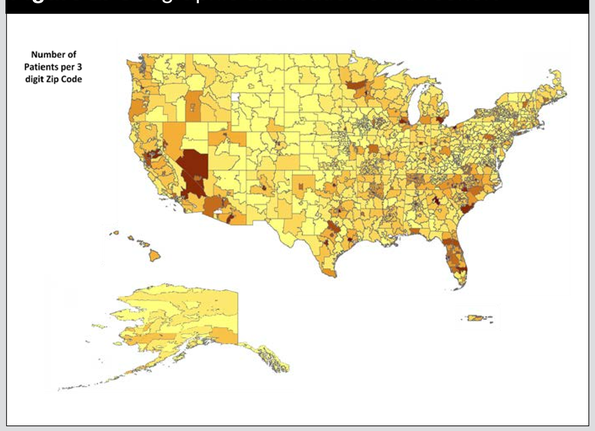
Table 3. Characterization of National VA RA cohort by medication ever use and autoantibody status, compared to participants within the VARA registry

	National VA					VARA				
Algorithm	% Any DMARD	% bDMARD	% MTX	% RF positive	% aCCP positive	% Any DMARD	% bDMARD	% MTX	% RF positive	% aCCP positive
1	75.4	27.2	51.9	56.5	56.4	99.5	56.9	83.3	84.0	83.8
2	85.0	34.6	59.4	58.7	56.9	99.5	56.9	83.3	84.0	83.8
3*	100.0	40.5	69.5	61.5	60.1	100.0	57.2	83.7	84.1	84.0
4	88.5	35.8	61.5	59.2	57.4	99.5	56.9	83.3	84.0	83.8
5	96.2	38.9	66.9	64.2	63.0	99.5	57.0	83.5	84.2	83.8
6	96.0	36.7	66.6	65.7	62.2	99.8	56.8	83.5	84.4	84.3
Restricted RA Codes: 714.0, 714.1, 714.2, 714.81										
6	96.0	37.4	67.2	67.3	63.9	99.8	56.8	83.5	84.4	84.3
Restricted to 2010-2018										
6	96.3	36.0	65.0	60.4	59.1	99.6	49.7	82.2	81.8	87.2

*Algorithm required DMARD prescription

DMARD and methotrexate % are those who had a prescription at any time during follow-up; RF and aCCP positive based on the number of patients, could be categorized into positive or negative CCP status; bDMARD includes: abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab, tocilizumab, tofacitinib

Figure 2. Geographic distribution of RA cohort



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