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- 1 Risk of cardiovascular disease in Chinese patients with rheumatoid arthritis: a cross-
- 2 sectional study based on hospital medical records in 10 years
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Abstract

- 2 Objective Though the risk of cardiovascular disease (CVD) inrheumatoid arthritis (RA) has been
- 3 establishedin Western population, little is known aboutthe risk in Chinese people with RA. Our
- 4 objective was to estimate the risk of CVD in Chinese people with RA using hospital medical records
- 5 data.

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Methods

- 7 The inpatients medical record database 2005-2015 of Sichuan provincial people's hospital was
- 8 examined. All individuals with a primary diagnosis of RA were included as cases, and those of
- 9 osteoarthritis (OA) were included as controls, which consisted of the unmatched dataset. Then, RA
- 10 cases and OA controls were matched by sex and age at 1:1 ratio, forming the matched dataset. The
- morbidity of CVD (including ischemia heart disease (IHD), congestive heart failure (CHF), et al), stroke
- 12 and arthrosclerosis were extracted from the database, so as the demographic data and comorbidities
- related to CVD. Multiple logistic regression analysis was used to estimate the risk of CVD in RA adjusted
- 14 for demographics and comorbidities using the unmatched dataset. Sensitivity analysis was conducted
- 1) considering interaction terms between RA and comorbidities, and 2) using multivariable conditional
- 16 logistic regression for the matched dataset.
- 17 ResultsThe unmatched datasetcomprised of 1824RA cases and 1995 OA controls and the matched
- 18 dataset comprised of 1022 pairs of sex and age matched RA and OA patients. RA exhibited increased
- odds of prevalent CVD compared with OA, and the adjusted ORs (95%CIs) for CVD, stroke, IHD, CHF,
- 20 and atherosclerosis were1.86(1.42-2.43), 1.11(0.71-1.74), 1.47(0.97-2.24), 2.09(1.03-4.22), and 2.49
- 21 (1.97-3.13), respectively, and was 2.26 (1.29-3.96) for IHD further adjusted for interaction term. The
- 22 matched dataset analysisfound similar results.

- 1 **Conclusions**Chinese people with RA were approximated 2 times more likely to have CVD, IHD, CHF and
- 2 atherosclerosis compared with those with OA. The findings justified the need of further longitudinal
- 3 study to establish the causal-relationship between RA and CVD and to estimate the precise risk in this
- 4 population.
- 5 **Key words:** rheumatoid arthritis, cardiovascular disease, risk, osteoarthritis, Chinesepopulation

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic,inflammatory disease associated with persistentinflammatory synovitis, progressive joint destruction,and an excess mortality when compared tothe non-RA individuals.[1-5]RA affectsestimated 0.42% of the Chinese population, approximately 5,745,600 people.[6] It is evident that RAincreases the riskof cardiovascular diseases (CVD) in addition to traditional CVD risk factors.[2]Systemic inflammation and the 'accelerated atherosclerosis'in RA areconsideredas the main mechanism linking RA and CVD.[7]Osteoarthritis (OA) — a leading causeof pain and disability, isgenerally considered as a chronic wear and tearjoint condition without systemic inflammation, thus was employed as non-systemic inflammatory comparator in previous studies.[8, 9][4]However, the risk of CVD in Chinese people with RA is unclear and evidence from epidemiological study is lacking.Acknowledge of the relative risk is relevant for optimal management andcare of people with RA and prevention of CVD.[10]The objective of this study was to estimate the risk of CVD in Chinese peoplewith RA comparing with those with osteoarthritis (OA) as controls.

Methods

Data source and patient definition

The study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (SPPH) on using anonymous medical records data for scientific research purpose (No. 2016-27). This cross-sectional study used the inpatients medical record database (MRD) of SPPH, which records demographics, diagnoses (using ICD-10 codes), procedures (using ICD-CM-9 codes) and expenditure of all inpatients from 2005-2015. All patients with a principal discharge diagnosis of RA (ICD-10 codes: M05.0-M06.9) from 2005-2015 were included, and all patients with a principal discharge diagnosis of

- 1 OA (ICD-10 codes: M15.0-M19.9) were selected as controls. We focused on the principal diagnosis of
- 2 discharge to maximize the validity of the case and control definition. Patients with discharge diagnosis
- 3 of both RA and OA were excluded to avoid the overlapping effect.
- 4 Two datasets were generated. The first is an unmatched dataset containing all included RA or OA
- 5 patients. The second was the matched dataset in which patients with RA and OA were matched at 1:1
- 6 ratio by sex and age (per 5 years), which was used for the sensitivity analysis.

Cardiovascular diseases

- 8 The primary outcomes in this study were CVD and stroke. Secondary outcomes were specific
- 9 cardiovascular conditions: ischaemic heart diseases (IHD), congestive heart failure (CHF) and
- 10 atherosclerosis (AS). All outcomes were defined by diagnoses recorded in the MRD using ICD-10 codes
- 11 (S1 Table).[11]

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Covariatesor confounders

- 13 Confounders considered were age, gender, and comorbidities related to CVD including hypertension,
- 14 hyperlipidemia, diabetes mellitus or hyperglycaemia (referred as the diabetes mellitus in the rest of
- the text) and chronic obstructive pulmonary disease (COPD).[9, 12-15]Gender and age were extracted
- 16 from the MRD. Comorbiditieswere defined by secondary diagnoses of discharge which were recorded
- in the database using ICD-10 codes (S1 Table).[11]

Statistical analysis

- 19 Characteristics of participants were described before the association analyses. Continuous and
- 20 categorical variables were described using mean and standard deviation (SD) and frequency and
- 21 percentage, respectively. For univariate analysis, ANOVA was conducted for the former, and Chi square
- 22 test for the latter.

1 Logistic regression was used to estimate the associations between RA and CVD outcomes using the

unmatched dataset, in which unadjusted and adjusted odds ratios (ORs) with its 95% confidence

intervals (CIs) were estimated, considering all covariates describe above. Sensitivity analysis was

conducted 1) considering significant interaction terms of RA and comorbidities using the unmatched

dataset, and 2) using multivariable conditional logistic regression analysis for the matched dataset.

Model fit was tested using Bayesian information criterion (BIC).[16]All statistical analyses were

conducted using STATA 13.0. The significance level was 0.05.

Results

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Participants and characteristics

10 There were 2,235 OA patients and 3914 RA patients identified from the databasebetween2005 and

2015. After removing patients with discharge diagnoses of both OA and RA, 2184 patients with OA and

2390 with RA remained. Then, readmissions were removed and the last record of a patient

hospitalization was selected, leaving 1995 patients with OA and 1824 patients with RA, which consisted

of the unmatched dataset of 3819 participants. Finally, RA and OA patients were matched by sex and

age (per 5 years), forming the matched dataset of 2044 patients with either OA or RA (1022 each) (Fig

16 1).

Fig 1 Flow chart of selection of participants

20 The characteristics of participants with RA (cases) and OA (controls) are presented and compared in

Table 1.In the unmatched dataset, patients with OA were significantly older (63.0 vs. 52.4 years), with

more women (74.6% vs. 69.6%), hypertension (22.1% vs. 10.6%), hyperlipidemia (11.6% vs. 5.0%) and

less COPD (2.0% vs. 4.3%) compared with patients with RA.There was no significant difference

- ofdiabetes mellitusbetween the two groups. In the matched dataset, age, sex, and the proportion of
- 2 patients with hypertention, hyperlipdemia, IHD or stroke was similar between the two groups. However,
- 3 there were significantly more diabetes mellitus (p=0.01) and COPD (p=0.00)in RA cases than OA
- 4 controls.

5 Table 1 Characteristics of rheumatoid arthritis (RA) cases and osteoarthritis controls (OA)

	Unmatched	dataset		Matched	dataset	
	OA (%)	RA (%)	р	OA (%)	RA (%)	р
No. of participants	1,995	1,824		1,022	1,022	
Mean age (SD), year	63.0(0.3)	52.4(0.4)	0.00	58.5(0.4)	57.8(0.4)	0.25
Age group, year			0.00			1.00
<45	146(7.3)	553(30.3)		142(13.9)	142(13.9)	
45-49	111(5.6)	191(10.5)		105(10.3)	105(10.3)	
50-54	174(8.7)	202(11.1)		103(10.1)	103(10.1)	
55-59	265(13.3)	243(13.3)		152(14.9)	152(14.9)	
60-64	334(16.7)	229(12.6)		183(17.9)	183(17.9)	
65-69	327(16.4)	178(9.8)		151(14.8)	151(14.8)	
70-74	303(15.2)	114(6.3)		99(9.7)	99(9.7)	
75-79	221(11.1)	66(3.6)		58(5.7)	58(5.7)	
80-84	83(4.2)	37(2.0)		22(2.2)	22(2.2)	
85+	31(1.6)	11(0.6)		7(0.7)	7(0.7)	
Women	1,488(74.6)	1,270(69.6)	0.00	702(68.7)	702(68.7)	1.00
Comorbidity						
Hypertension	441(22.1)	194(10.6)	0.00	148(14.5)	167(16.3)	0.24
Hyperlipdemia	231(11.6)	92(5.0)	0.00	75(7.3)	69(6.8)	0.60
Diabetes mellitus	251(12.6)	198(10.9)	0.10	103(10.1)	144(14.1)	0.01
COPD	39(2.0)	78(4.3)	0.00	12(1.2)	64(6.3)	0.00
Outcomes						
CVD	166(8.3)	139(7.6)	0.43	53(5.2)	105(10.3)	0.00
IHD	76(3.8)	44(2.4)	0.01	23(2.3)	34(3.3)	0.14
Myocardial infarction	3 (0.15)	2 (0.11)				
CHF	17(0.9)	21(1.2)	0.35	5(0.5)	18(1.8)	0.01
Stroke	74(3.7)	34(1.9)	0.00	29(2.8)	27(2.6)	0.79
Arthrosclerosis	216(10.8)	234(12.8)	0.06	65(6.4)	203(19.9)	0.00

⁶ Numbers are frequencies (percentages) unless otherwise specified, CVD: cardiovascular disease, IHD:

Association analysis

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For the unmatched dataset, significant more patients with RA had CVD (adjusted OR: 1.86, 95%CI 1.42-

⁷ ischaemic heart disease, CHF: congestive heart disease, COPD: chronic obstructive pulmonary disease

- 2.43), CHF (adjusted OR: 2.09, 1.03-4.22) and atherosclerosis (adjusted OR: 2.49, 1.97-3.13) than OA
- 2 patients adjusted for age, sex, hypertension, hyperlipidemia, diabetes mellitus and COPD. However, no
- difference was found for stroke (adjusted OR: 1.11, 0.71-1.74) and IHD (adjusted OR: 1.47, 0.97-2.24)
- 4 between the two groups adjusted for other variables. (Table 2)

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- 5 In the sensitivity analysis using matched dataset, the findings were similar to that of unmatched
- dataset analysis. Significant more patients with RA had CVD (adjusted OR: 2.19, 1.49-3.21), CHF
- 7 (adjusted OR: 6.95, 1.50-32.21) and atherosclerosis (adjusted OR:4.95, 3.36-7.28) than OA controls.
- 8 Still, no difference of patients with stroke (adjusted OR: 1.13, 0.57-2.25) and IHD (adjusted OR:1.83,
- 9 0.94-3.56) was found between the two groups adjusted for other variables.(Table 2)

Table 2 Risk of cardiovascular diseases in rheumatoid arthritis (RA) compared with osteoarthritis (OA)

	Unmatched datas	Unmatched dataset OR (95%CI)		Matched dataset OR (95%CI)	
	Unadjusted	Adjusted	Unadjusted	Adjusted	
Cardiovascular disease					
RA vs. OA	0.91(0.72-1.15)	<u>1.86(1.42-2.43)</u> *	2.09(1.49-2.95)*	2.19 (1.49-3.21)*	
Age, per 5 years	1.42(1.34-1.50)*	1.38(1.30-1.47)*	1.42(1.31-1.54)*	/	
Women	0.90(0.69-1.16)	0.94(0.71-1.24)	0.70(0.50-0.98)*	/	
Hypertension	4.64(3.63-5.93)*	2.72(2.07-3.57)*	3.79(2.68-5.38)*	1.98(1.07-3.65)*	
Hyperlipidemia	2.33(1.68-3.23)*	1.81(1.26-2.58)*	1.67(0.98-2.85)	1.66(0.64-4.32)	
Diabetes mellitus	2.74(2.07-3.63)*	1.51(1.11-2.04)*	2.34(1.57-3.49)*	1.57(0.76-3.25)	
COPD	2.63(1.62-4.29)*	1.21(0.71-2.05)	3.43(1.93-6.11)*	1.94(0.63-6.01)	
Stroke					
RA vs. OA	0.49(0.33-0.74)*	1.11(0.71-1.74)	0.93(0.55-1.58)	1.13(0.57-2.25)	
Age, per 5 years	1.58(1.43-1.74)*	1.47(1.32-1.64)*	1.54(1.35-1.76)*	/	
Women	0.83(0.55-1.26)	0.78(0.50-1.21)	0.75(0.44-1.31)	/	
Hypertension	7.38(4.99-10.92)*	3.84(2.50-5.90)*	7.44(4.33-12.79)*	4.80(1.65-13.93)*	
Hyperlipidemia	2.72(1.67-4.45)*	1.84(1.08-3.12)*	1.93(0.86-4.34)	1.21(0.26-5.62)	
Diabetes mellitus	2.60 (1.66-4.06)*	1.22(0.76-1.96)	2.51(1.35-4.67)*	1.33(0.41-4.25)	
COPD	1.91 (0.82- 4.44)	0.83(0.34-2.04)	2.05(0.72-5.81)	0.38(0.07-1.93)	
Ischaemic heart disease					
RA vs. OA	0.62(0.43-0.91)*	1.47(0.97-2.24)	1.49(0.87-2.56)	1.83(0.94-3.56)	
Age, per 5 years	1.66(1.51-1.82)*	1.59(1.43-1.76)*	1.74(1.51-2.01)*	/	
Women	1.01(0.68-1.52)	1.08(0.70-1.67)	0.78(0.45-1.34)	/	

Hypertension	6.49(4.48-9.39)*	3.37(2.25-5.05)*	4.57(2.67-7.83)*	4.40(1.28-15.05)*
Hyperlipidemia	1.83(1.08-3.10)*	1.24(0.70-2.18)	1.58(0.66-3.74)	0.62(0.11-3.64)
Diabetes mellitus	2.61(1.71-3.99)*	1.30(0.83-2.05)	1.99(1.04-3.81)*	1.09(0.35-3.32)*
COPD	2.35(1.12-4.94)*	0.98(0.44-2.17)	2.59(1.01-6.69)*	1.38(0.28-6.87)
Congestive heart disease	!			
RA vs. OA	1.36(0.71-2.58)	2.09(1.03-4.22)*	3.65(1.35-9.86)*	6.95(1.50-32.21)*
Age, per 5 years	1.36(1.18-1.57)*	1.27(1.08-1.49)*	1.29(1.07-1.57)*	/
Women	0.47(0.25-0.90)*	0.57(0.29-1.10)	0.41(0.18-0.94)*	/
Hypertension	4.62(2.43-8.78)*	3.59(1.77-7.29)*	5.18(2.26-11.84)*	13.69(1.13-166.48)*
Hyperlipidemia	0.29(0.04-2.12)	0.22(0.03-1.64)	Exactly the same	(omitted)
Diabetes mellitus	2.72(1.31-5.64)*	1.57(0.73-3.36)	2.04(0.75-5.55)	1.27(0.18-9.18)
COPD	4.96(1.90-12.95)*	2.05(0.72-5.80)	4.00(1.16-13.77)*	3.95(0.19-82.30)
Atherosclerosis				
RA vs. OA	1.21 (1.00- 1.48)	<u>2.49(1.97-3.13)</u> *	3.65(2.72-4.90)*	4.95(3.36-7.28)*
Age, per 5 years	1.31(1.26-1.37)*	1.31(1.25-1.38)*	1.30(1.22-1.38)*	/
Women	0.92(0.74-1.14)	0.96(0.76-1.21)	0.92(0.70-1.21)	/
Hypertension	3.88(3.14-4.81)*	2.47(1.94-3.15)*	3.34(2.49-4.46)*	1.83(0.98-3.42)
Hyperlipidemia	3.75(2.89-4.88)*	3.51(2.63-4.69)*	3.55(2.43-5.17)*	5.62(2.23-4.14)*
Diabetes mellitus	2.20(1.71-2.84)*	1.21(0.92-1.60)	1.73(1.22-2.44)*	0.91(0.43- 1.92)
COPD	3.24(2.14-4.89)*	1.61(1.02-2.54)*	3.05(1.84-5.07)*	1.31(0.35-4.87)

- 1 CI: confidence interval, COPD: chronic obstructive pulmonary disease. The number of observations for
- 2 multivariate conditional logistic regression analysis for cardiovascular disease, ischaemic heart disease,
 - congestive heart disease,, stroke and atherosclerosis was 292, 106, 46, 108 and 404
- 4 respectively.*p<0.05

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- 6 Moreover, findings were similar for CVD, stroke, CHF and atherosclerosis in the sensitivity analysis
- 7 considering interaction terms of RA and comorbidities using the unmatched dataset. However,
- 8 patients with RA were significantly more likely to have IHD (adjusted OR: 2.26, 1.29-3.96) than patients
- 9 with OA adjusted for other variables and the interaction term of RA and hypertension. (S2 Table)

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Discussion

- 12 This study included3819Chinese patients with RA orOAconsecutively admittedto a medical centre
- 13 between 2005 and 2015. Important covariables such as age, sex, and comorbidities related to CVD were
- 14 adjusted in the estimate of association between RA and CVD. RA and OA, CVD, and comorbidities

related to CVD were defined by physician's diagnoses recorded as ICD-10 codes in MRD, which reduced information bias and enhanced the accuracy of variable definition. We found 1) the prevalence of CVD in Chinese patients with RAadmitted to hospital was 7.6%-10.3%;2) RA patients were approximately twice morelikely to have CVD, IHD, CHF and atherosclerosis than peoplewith OA; and 3) the risk ofstrokewere not significantly different between the two groups, whilean incremental (from nonsignificant to significant)risk of IHD was found when more covariables or their interaction were adjusted. The approximately 2 foldedrisk of total CVD, IHD and CHF in Chinese people with RA found in this study is comparable to previous studies inother populations (mainly Caucasians).[2, 17, 18] For Chinese population, Chung and colleaguesfound a 38% increase of risk of acute myocardial infarction in patients with RAcomparing with non-RA population in a cohort studyin Taiwan;unfortunatelythe risk of total CVD andother specific CVD were not estimated.[19]The association between RA and CVD is further supported by our finding thatthe risk of atherosclerosis increasedin RA, for it is considered as the main mechanism underlying RA and CVD morbidity linked by systemic inflammation.[7, 20]However, we found a positive but non-significant risk of stroke, and anincrementalrisk(from non-significant to significant) of IHDin people with RA when more covariables or interaction were adjusted. The increased riskof stroke and IHDin RA has been shown in large sample sizedlongitudinal studies and meta-analysis in other population.[2, 18]Thenon-significant finding of stroke and IHD may be due to the small number of events and lack of power in this study. Furthermore, the risk of CVD in RA compared with OA may not be able tobe directly interpretedas the risk compared with non-RA general population. Because evidence has emerged recently that OA may also increase the risk of CVD compared with the

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- 1 general population, though it is still controversial.[21, 22] Therefore, the CVD risk inChinesepeoplewith
- 2 RAcomparing withthe general population might be higher than the estimatein our study.
- 3 This study has several limitations. Firstly, the participants in this study wereall inpatients consecutively
- 4 admitted to a medical centre. Therefore, selection bias may be introduced, for inpatients are generally
- 5 more severe in disease status than outpatients or community patients, but this situation may be
- 6 evenbetween RA cases and OA controls. Secondly, some covariables or confounders of CVD were not
- 7 included in the analysis for they were absence in the database such as obesity, smoking and anti-
- 8 rheumatic drugs. There is evidence that obesity is more prevalent in patients with OA than in RA.[17,
- 9 21] Thus, the risk of CVD in RA compared with OA may be higher if obesity was controlled for.
- 10 Furthermore, diabetes and COPD were adjusted in the analysis, which are positively associated with
- obesity and smoking, thus their effect on CVDmay be indirectly and partially adjusted. Thirdly, detailed
- 12 analysis on sub-category of CVDs such as myocardial infarction was not possible due to thesmall
- 13 number of events. Finally, the natural of the cross-sectional study design prevented us to yieldacausal-
- 14 relationshipbetween RA and CVD.

- 15 In conclusion, Chinese people with RA were approximated 2 times more likely to have CVD, IHD, CHF
- and atherosclerosiscompared with people with OA. Further longitudinal study is needed to establish
- therisk of total and specific CVDin Chinese peoplewith RA.
- 19 **Contribution of authors**: KZ, WZ conceptualized the study, KZ, CFG, WZ contributed to the study design,
- 20 FKX acquiredthedata, KZ conducted the analysis and wrote the first draft, all authors contributed to
- critically appraisal and intellectual interpretation of the findings and revision of the final report.
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Supporting information

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- S1Table. ICD-10 codes of outcomes and covariates
- 13
- 14 S2Table. Sensitivity analysis using unmatched dataset adjusted for covariables and interaction terms
- with rheumatoid arthritis (RA). RA: rheumatoid arthritis; OA: osteoarthritis, COPD: chronic obstructive
- pulmonary disease; & Diabetes mellitus or hyperglycemia; \$ No significant interaction term was
- detected; *Bayesian information criterion in favor of the model; *p<0.05

Supporting information

S1 Table. ICD-10 codes of outcomes and covariates

Variable	ICD-10 code
Outcomes	_
Cardiovascular disease	
Rheumatic heart disease	105.0-109.9
Ischemic heart disease	120.0-125.9
Myocardial infarction	121.x, 122.x, 125.2
Pericarditis	130.0-132.9
Endocarditis	133.0-133.9
Valve disorders	134.0-137.9
Myocarditis	140.0-141.9
Cardiomyopathy	142.0-143.9
Conduction disorders	144.0-145.9
Arrhythmias	146.0-149.9
Congestive heart failure	150.0-150.9
Other heart disease	151.0-151.9
Atherosclerosis	170.0-170.9
Stroke	160.0-164.9
	H34.1
	G45.0-G45.9
Covariable	
Hypertension	110.0-115.9
Hyperlipidemia	E78.0-E78.5
Diabetes mellitus	E10.0-E14.9
Hyperglycaemia	R73.0-R73.9
Chronic obstructive pulmonary diseases	J40.0-J44.9
	J47.0-J47.9

Supporting information

S2 Table. Sensitivity analysis using unmatched dataset adjusted for covariables and interaction terms with rheumatoid arthritis (RA)

	(,
	Adjus	ted OR (95%CI)
Cardiovascular disease⁺		
RA vs. OA	2.12	<u>(1.60-2.83)</u> *
Age (per 5 years)	0.93	(0.70-1.23)
Women	1.38	(1.30-1.47)*
Hypertension	2.76	(2.10-3.63)*
Hyperlipidemia	2.47	(1.64-3.71)*
Diabetes mellitus ^{&}	1.49	(1.10-2.02)*
COPD	1.17	(0.69-2.00)
RA # Hyperlipidemia	0.29	(0.11-0.71)*
Stroke ^{\$}		
RA vs. OA	1.11	(0.71-1.74)
Age (per 5 years)	0.78	(0.50-1.21)
Women	1.47	(1.32-1.64)*
Hypertension	3.84	(2.50-5.90)*
Hyperlipidemia	1.84	(1.08-3.12)*
Diabetes mellitus ^{&}	1.22	(0.76-1.96)
COPD	0.83	(0.34-2.04)
Ischemic heart disease		
RA vs. OA	2.26	(1.29-3.96)*
Age (per 5 years)	1.08	(0.70-1.67)
Women	1.59	(1.43-1.76)*
Hypertension	4.84	(2.87-8.18)*
Hyperlipidemia	1.23	(0.70-2.17)
Diabetes mellitus ^{&}	1.25	(0.79-1.96)
COPD	1.01	(0.46-2.23)
RA # Hypertension	0.37	(0.16-0.88)*
Congestive heart failure		
RA vs. OA	2.69	(1.28-5.65)*
Age (per 5 years)	0.54	(0.28-1.04)
Women	1.28	(1.09-1.51)*
Hypertension	3.65	(1.80-7.42)*
Hyperlipidemia	0.20	(0.03-1.54)
Diabetes mellitus ^{&}	1.54	(0.71-3.30)
COPD	6.93	(1.82-26.31)*
RA # COPD	0.12	(0.02-0.93)*
Atherosclerosis		
RA vs. OA	2.60	(2.05-3.31)*

Age (per 5 years)	0.95	(0.75-1.20)
Women	1.32	(1.25-1.39)*
Hypertension	2.47	(1.94-3.15)*
Hyperlipidemia	3.50	(2.62-4.68)*
Diabetes mellitus ^{&}	1.21	(0.92-1.60)
COPD	2.73	(1.32-5.63)*
RA # COPD	0.44	(0.17-1.09)

RA: rheumatoid arthritis; OA: osteoarthritis, COPD: chronic obstructive pulmonary disease; & Diabetes mellitus or hyperglycemia; \$ No significant interaction term was detected; *Bayesian information criterion in favor of the model; *p<0.05