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Hypothyroidism risk associated with rheumatoid arthritis

A population-based retrospective cohort study

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Abstract

Studies on the thyroid disease risk in patients with rheumatoid arthritis (RA) associated with comorbidities are limited. This population-based retrospective cohort study investigated the hypothyroidism risk in patients with RA and the role of comorbidities.

We used Taiwan National Health Insurance Research Database to identify 16,714 RA patients newly diagnosed in 2000 to 2008 and 66,856 control persons without RA, frequency matched by sex, age, and index year. Incidence and the RA group to controls hazard ratio of hypothyroidism were estimated.

The hypothyroidism incidence was 1.74-fold higher in the RA group than in controls (16.6 vs 9.52 per 10,000 person–years), with the Cox method estimated adjusted hazard ratio of 1.67 (95% confidence interval = 1.39–2.00) after controlling for covariates. Near 75% of the study population were women, with the incidence 3.6-time higher than men in both groups. The hypothyroidism incidence increased with age, from 12.1 per 1000 person–years in 20 to 39 years to 20.0 per 1000 person–years in 60+ years in RA patients, higher than that in controls (7.17 vs 10.0 per 1000 person–years, respectively by age). Each comorbidity was related to an increased incidence and higher in the RA group than in controls. Among all comorbidities, stroke exerted the greatest impact in the RA group with an adjusted hazard ratio of 3.85 (95% confidence interval = 1.24–12.0).

RA patients have an increased risk of developing hypothyroidism; this risk was pronounced in women and the elderly. RA patients should be closely monitored to prevent the development of hypothyroidism.

Abbreviations: aHR = adjusted hazard ratio, CI = confidence interval, CKD = chronic kidney disease, CRP = C-reactive protein, CVD = cardiovascular disease, DM = diabetes mellitus, HR = hazard ratio, ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification, IHD = ischemic heart disease, LHID = Longitudinal Health Insurance Database, RA = rheumatoid arthritis, RCIPD = Registry of Catastrophic Illness Patient Database, SLE = systemic lupus erythematosus, TNHI = Taiwan National Health Insurance.

Keywords: hypothyroidism, insurance, retrospective study, rheumatoid arthritis

1. Introduction

Rheumatoid arthritis (RA) is the most common inflammatory arthritis, which affects approximately 0.75% of the population.[1] It is a severe chronic disease that can cause deformities and disability due to irreversible damage in the tendons, joints, and bones.[2,3] In addition, RA patients also feature extra-articular manifestations involving other organs, including the thyroid gland.[4]

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Thyroid autoimmunity is common in immune-mediated diseases, and is most commonly presenting as Hashimoto thyroiditis and Graves disease.[5–7] Graves disease is a disorder mainly associated with thyroid-stimulating autoantibodies.[6] Whereas, Hashimoto thyroiditis is characterized by gradual thyroid failure and existence of a goiter combined with T cell infiltration found in histological analysis.[7] The prevalence of overt hypothyroidism found in community surveys ranges from 0.1% to 2%.[8–13] Subclinical hypothyroidism is prevalent in adults higher, ranging from 4% to 10%, and older women are at higher risk.[9,10,12,14]

Earlier studies, even in the 1960s, have reported that patients with RA are at increased risk of thyroid dysfunctions.[15–20] An earlier controlled prospective study found that thyroid dysfunction is almost 3 times greater in patients with RA than in controls without RA.[17] However, RA patients with thyroid disorder developed may further develop other autoimmune disorders. Comprehensive literature reviews conducted by the Ferrari et al[21] and Fallahi et al[22] group demonstrated a significant increase of the prevalence of RA (2.4%) in autoimmune thyroiditis patients compared with nontoxic multinodular goiter (0.4%) patients and controls (0.6%). A study in The Netherlands also found women with RA are 3 times more likely than general women to develop clinical hypothyroidism, and women with both RA and hypothyroidism are at an elevated risk of developing a cardiovascular disease (CVD).[18] However, hypothyroidism risk in RA patients has thus far been rarely examined in a systematic manner. A cross-sectional study in Israel comparing 11,782 RA patients and 57,973 controls found that hypothyroidism is more prevalent in RA patients than in controls (16.0% vs 11.7%, $P < .001$).[20] However, the role of comorbidities was not evaluated in studies. We, therefore, conducted a retrospective cohort study to investigate hypothyroidism risk in RA patients using claims data from the Taiwan National Health Insurance (TNHI) program and to assess the role of comorbidities.

2. Methods and materials

2.1. Source of data

We identified our study population from 2 sub-databases in the TNHI, the Registry of Catastrophic Illness Patient Database (RCIPD) and the Longitudinal Health Insurance Database (LHID). TNHI is a compulsory program for 23 million residents in Taiwan.[23] LHID includes the health claims data of 1 million residents randomly selected from TNHI. RCIPD enrolled patients with severe disorders for 30 categories requiring long-term care and a higher cost, such as cancers, chronic mental illnesses, and autoimmune diseases, etc. Patients with definite RA according to the 1987 revised American College of Rheumatology criteria[24] and those diagnosed by rheumatologists were included in the RA cohort. The application for catastrophic illness status was scrutinized by peer review. Both databases contain information on basic demographic variables (sex, birthdate, income, insured unit, urbanization level of resident area), and inpatient and outpatient medical cares and costs. Diseases in medical records are coded with the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).

The present study was approved by the China Medical University and Hospital Research Ethic Committee (CMUH104-REC2-115). Identifications of insured people in LHID and RCIPD had been changed into surrogate numbers for privacy protection. No consents are required for this study.

2.2. Study population

This study consisted of 2 study cohorts, a RA cohort and a non-RA cohort. The RA cohort consisted of RA patients (ICD-9-CM 714.0) newly registered in RCIPD from 2000 to 2008, excluding patients under 20 years old. Individuals without any RA diagnosis in LHID were selected as control frequency matched by sex, age, and index date with the sample size being 4 times that of the RA cohort for a better power of test. Individuals with missing information on sex, birthdate, insured unit, and/or urbanization level of residence area were excluded (N = 6970). The index date for patients with RA was defined as the first diagnosed date of RA, and the index date for non-RA individuals was defined as the same date for matching cases. Both cohorts excluded individuals with the history of hypothyroidism (ICD-9-CM 244). Follow-up observation was terminated on the date of hypothyroidism diagnosis, the date on which the subject withdrew from health insurance, or on December 31, 2011.

Baseline comorbidities of hypertension (ICD-9-CM 401.xx-405.xx), ischemic heart disease (IHD; ICD-9-CM 410.xx-414.xx), stroke (ICD-9-CM 430.xx-438.xx), diabetes mellitus (DM, ICD-9-CM 250.xx), hyperlipidemia (ICD-9-CM 272.xx), and chronic kidney disease (CKD; ICD-9-CM 580.xx-589.xx) were identified from the medical records and considered in data analysis.

2.3. Statistical analysis

Distributions of baseline variables were presented with number and percentage, including sex, age, insured unit, urbanization, and comorbidities, and examined with Chi-square test between RA and non-RA cohorts. Mean ages and standard deviations were also calculated and compared between the 2 cohorts using t test. We used the Kaplan–Meier method to estimate the cumulative incidence of hypothyroidism and incident curves were evaluated using the log rank test. Incidence density of hypothyroidism by the end of follow-up was estimated for 10,000 person–years. The Cox proportional hazards regression model was used to estimate the RA cohort to non-RA cohort hazard ratio (HR) and 95% confidence intervals (CI) of hypothyroidism. We first pooled the data of 2 cohorts to assess the incidence rates and HRs of hypothyroidism associated with demographic status. Adjusted HR (aHR) was estimated with multivariable model controlling for sex, age, insured unit, urbanization, and comorbidities (hypertension, IHD, stroke, DM, hyperlipidemia, and CKD). We also calculated aHR with the multivariable model by excluding comorbidities. We then used the multivariable model to calculate the RA cohort to non-RA cohort HR of hypothyroidism by sex, age, and comorbidity. In the model, variables of sex, age, insured unit, urbanization, and comorbidities were included in the multivariable model for measuring aHRs. SAS software for Windows (Version 9.4, SAS Institute, Cary, NC) was used for data analysis and R software (R Foundation for Statistical Computing, Vienna, Austria) was used to plot the cumulative incidence. All significance levels were set at two-sided for $P < .05$.

3. Results

Our study population included 16,714 patients in the RA cohort and 66,856 controls without the disease. With a mean age of near

Table 1

Distribution of demographic status and comorbidity compared between cohorts with and without rheumatoid arthritis.

	RA cohort N = 16,714		Non-RA cohort N = 66,856		
Variable	**n**	**%**	**n**	**%**	***P*-value**
Sex					.99
Female	12,494	74.7	49,976	74.7	
Male	4220	25.3	16,880	25.3	
Age, yr					.99
20–39	3379	20.2	13,516	20.2	
40–59	8770	52.5	35,080	52.5	
≥60	4565	27.3	18,260	27.3	
Means (SD)	51.7	(14.1)	51.4	(14.4)	
Insured unit					<.001
Government, school employees	943	5.64	6852	10.3	
Private enterprise employees	3745	22.4	26,560	39.7	
Industrial employees	4112	24.6	13,411	20.1	
Farmers, fishermen	4542	27.2	11,237	16.8	
Low-income, veterans, retired	3372	20.2	8796	13.2	
Urbanization					<.001
Level 1 (highest)	4115	24.6	20,386	30.5	
Level 2	4908	29.4	19,468	29.1	
Level 3	2637	15.8	11,701	17.5	
Level 4 (lowest)	5054	30.2	15,301	22.9	
Comorbidity					
Hypertension	4833	28.9	18,764	28.1	.03
IHD	2446	14.6	8964	13.4	<.001
Stroke	414	2.48	1848	2.76	.04
DM	1736	10.4	6815	10.2	.47
Hyperlipidemia	2966	17.8	12,068	18.1	.36
CKD	1725	10.3	4072	6.09	<.001

CKD = chronic kidney disease, DM = diabetes mellitus, IHD = ischemic heart disease, RA = rheumatoid arthritis, SD = standard deviation.

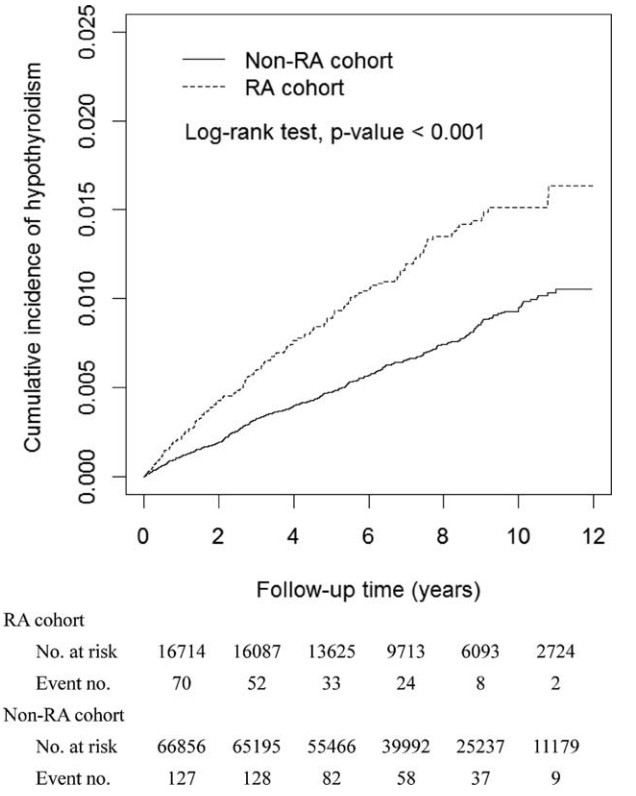

Figure 1. Cumulative incidence of hypothyroidism in the non-RA and RA cohorts. RA = rheumatoid arthritis.

51.5 years, approximately 75% of study population were women (Table 1). The RA population had more blue-collar workers and rural residents than the non-RA cohort. The RA cohort had slightly higher baseline prevalence rates of hypertension, IHD, and CKD, and a lower stroke prevalence than the non-RA cohort, but the differences were significant.

The Kaplan-Meier method plotted figure shows that the cumulative incidence of hypothyroidism was 0.65% greater in the RA cohort than in the non-RA cohort ($P < .001$) (Fig. 1). Hypothyroidism cases occurred somewhat earlier in the RA cohort than in the non-RA cohort. The incidence density of hypothyroidism was near 1.7 times higher in the RA cohort than in the non-RA cohort (16.6 vs 9.52 per 10,000 person–years), with an aHR of 1.67 (95% CI = 1.39–2.00) after controlling for all covariates (Table 2). The aHR changed slightly to 1.71 without controlling for comorbidities in the analysis model. This pooled data showed a 3.6-time higher incidence in women than in men. The incidence increased with age, was higher in government and school employees and in the low income/veteran/retired populations. Residents living in highly urbanized areas and most rural areas also had a higher incidence of hypothyroidism.

Incidence rates of hypothyroidism and the RA cohort to the non-RA cohort HRs by strata of sex, age, and comorbidity are shown in Table 3. The gap of incident hypothyroidism between the 2 cohorts was much greater in women than in men (8.6 compared to 2.3 per 10,000 person–years). Incidence increased with age in both cohorts and the increment was greater in the RA cohort than in the non-RA cohort. Each assessed comorbidity was related with increased incident hypothyroidism, which was also greater in the RA cohort than in the non-RA cohort. RA patients with a history of stroke showed the highest incidence, which was 3 times greater than that of the non-RA cohort (30.6 compared to 10.2 per 10,000 person–years), with an aHR of 3.85 (95% CI = 1.24–12.0) for the RA cohort. We have further analyzed the prevalence rates of comorbidities in the excluded group. All prevalence rates of comorbidities were higher in the excluded group than in the RA cohort (Table 4). However, the hazards of developing hypothyroidism were not significantly different between the 2 groups (Table 5).

4. Discussion

The major finding in this study was that RA patients had a substantially higher risk of developing hypothyroidism than subjects from the general population without RA, with an aHR of 1.67. Our finding is consistent with an Israeli cross-sectional study, which found the prevalence of hypothyroidism to be 1.4 times greater in patients with RA than in the controls.[20] Our study also found that the risk of hypothyroidism increased with age and was higher in women than in men in both cohorts. In each sex and age stratum, the incidence was consistently higher in the RA cohort than in the non-RA cohort. Our study showed that the hypothyroidism incidence gap between patients ≥60 years and 20 to 39 years was much greater for RA patients than for controls (7.9 compared to 2.8 per 1000 person–years). The Israeli study also showed a higher prevalence of hypothyroidism in older

Table 2

Incidence and Cox model measured hazard ratios of hypothyroidism by rheumatoid arthritis status and demographic status.

Variables	Event no.	Person–years	IR	HR (95% CI)		
				Univariate	Multivariate*	Multivariate†
RA						
No	441	463,063	9.52	Ref	Ref	Ref
Yes	189	113,823	16.6	1.74 (1.47–2.07)	1.67 (1.39–2.00)	1.71 (1.43, 2.04)
Sex						
Female	579	438,464	13.2	3.61 (2.71–4.80)	3.78 (2.83–5.05)	3.80 (2.85, 5.08)
Male	51	138,422	3.68	Ref	Ref	Ref
Age, yr						
20–39	100	122,315	8.18	Ref	Ref	Ref
40–59	354	306,745	11.5	1.41 (1.13–1.76)	1.27 (1.01–1.60)	1.42 (1.14, 1.78)
≥60	176	147,826	11.9	1.44 (1.13–1.85)	1.14 (0.85–1.53)	1.62 (1.25, 2.10)
Insured unit						
Government, school employees	75	54,109	13.9	1.56 (1.21–2.06)	1.44 (1.10–1.90)	1.46 (1.11, 1.92)
Private enterprise employees	184	209,223	8.79	Ref	Ref	Ref
Industrial employees	143	123,017	11.6	1.32 (1.06–1.65)	1.08 (0.86–1.36)	1.12 (0.89, 1.41)
Farmers, fishermen	115	108,692	10.6	1.21 (0.95–1.52)	0.99 (0.74–1.35)	1.04 (0.77, 1.41)
Low-income, veterans, retired	113	81,844	13.8	1.57 (1.24–1.98)	1.37 (1.04–1.80)	1.40 (1.06, 1.84)
Urbanization						
Level 1 (highest)	206	169,589	12.2	Ref	Ref	Ref
Level 2	187	169,000	11.1	0.91 (0.75–1.11)	0.88 (0.72–1.07)	0.89 (0.73,1 .09)
Level 3	83	98,665	8.41	0.69 (0.54–0.89)	0.73 (0.56–0.95)	0.73 (0.56, 0.95)
Level 4 (lowest)	154	139,632	11.0	0.91 (0.74–1.12)	0.89 (0.70–1.15)	0.90 (0.71, 1.16)

CI = confidence interval, CKD = chronic kidney disease, DM = diabetes mellitus, HR = hazard ratio, IHD = ischemic heart disease, IR = incidence rates, per 10,000 person–years, RA = rheumatoid arthritis.
* Multivariate Cox proportional hazards regression model including RA, sex, age, insured unit, insured amount, urbanization, hypertension, IHD, stroke, DM, hyperlipidemia, and CKD.
† Multivariate Cox proportional hazards regression model by controlling for sex, age, insured unit and urbanization.

Table 3

Incidence and RA cohort to non-RA cohort hazard ratio of hypothyroidism by stratum of sex, age, and comorbidity.

Variables	RA cohort			Non-RA cohort			RA cohort to non-RA cohort	
							HR (95% CI)	
	Event no.	Person–years	IR	Event no.	Person–years	IR	Crude	Adjusted*
Sex								
Women	174	86,709	20.1	405	351,756	11.5	1.74 (1.46–2.08)	1.66 (1.38–2.00)
Men	15	27,114	5.53	36	111,308	3.23	1.71 (0.94–3.12)	2.01 (1.05–3.84)
Age, yr								
20–39	30	24,706	12.1	70	97,608	7.17	1.70 (1.11–2.61)	1.63 (1.04–2.56)
40–59	103	61,124	16.9	251	245,622	10.2	1.65 (1.31–2.08)	1.50 (1.18–1.92)
≥60	56	27,993	20.0	120	119,833	10.0	2.00 (1.45–2.74)	2.05 (1.44–2.92)
Comorbidity								
Hypertension								
No	125	83,411	15.0	293	339,879	8.62	1.74 (1.41–2.51)	1.59 (1.28–1.99)
Yes	64	30,412	21.0	148	123,184	12.0	1.75 (1.31–2.35)	1.71 (1.25–2.35)
IHD								
No	149	98,788	15.1	345	404,506	8.53	1.77 (1.46–2.15)	1.71 (1.39–2.09)
Yes	40	15,034	26.6	96	58,557	16.4	1.62 (1.12–2.35)	1.46 (0.98–2.18)
Stroke								
No	182	111,536	16.3	431	453,289	9.51	1.72 (1.44–2.04)	1.63 (1.36–1.96)
Yes	7	2286	30.6	10	9774	10.2	3.01 (1.15–7.91)	3.85 (1.24–12.0)
DM								
No	162	103,313	15.7	391	419,994	9.31	1.69 (1.40–2.02)	1.62 (1.33–1.96)
Yes	27	10,509	25.7	50	43,070	11.6	2.21 (1.38–3.52)	1.90 (1.14–3.15)
Hyperlipidemia								
No	141	94,970	14.9	324	383,004	8.46	1.76 (1.44–2.14)	1.66 (1.34–2.04)
Yes	48	18,853	25.5	117	80,059	14.6	1.74 (1.24–2.43)	1.61 (1.12–2.30)
CKD								
No	162	102,560	15.8	388	437,505	8.87	1.78 (1.48–2.14)	1.76 (1.45–2.14)
Yes	27	11,263	24.0	53	25,558	20.7	1.14 (0.72–1.82)	1.08 (0.65–1.78)

CI = confidence interval, CKD = chronic kidney disease, DM = diabetes mellitus, HR = hazard ratio, IHD = ischemic heart disease, IR = incidence rates, per 1000 person-years, RA = rheumatoid arthritis.
* Model mutually adjusted for sex, age, insured unit, insured amount, urbanization, hypertension, IHD, stroke, DM, hyperlipidemia, and CKD.

Table 4

Distribution of comorbidities compared between RA cohorts and excluded population due to missing data.

	RA cohort N = 16,714		Excluded group N = 6970		
Variable	**n**	**%**	**n**	**%**	***P*-value**
Comorbidity					
Hypertension	4833	28.9	3078	44.2	<.001
IHD	2446	14.6	1525	21.9	<.001
Stroke	414	2.48	263	3.77	<.001
DM	1736	10.4	1070	15.4	<.001
Hyperlipidemia	2966	17.8	1772	25.4	<.001
CKD	1725	10.3	852	12.2	<.001

CKD = chronic kidney disease, DM = diabetes mellitus, IHD = ischemic heart disease, RA = rheumatoid arthritis.

RA patients than in younger ones.[20] This is compatible with the finding in a case-control study on hypothyroidism in systemic lupus erythematosus (SLE) patients, which also shows a higher hypothyroidism risk in older patients than in younger patients.[25] These data reflect that the risk of developing hypothyroidism associated with aging is stronger for those with RA or SLE, and both are autoimmune disorders.

RA is a disorder well-known to be more prevalent in women than in men. Women were affected 3 times as often as men in our study, and the risk of developing hypothyroidism in women was near 4 times as often as men. Previous studies have also shown a remarkable imbalance in the occurrence of autoimmune diseases between men and women, and that women are at higher risk for RA and/or hypothyroidism.[20,26–28] In the Israeli study, the odds ratio of having hypothyroidism is 3.5 (95% CI = 3.24–3.79, $P < .001$) for women compared to men. Furthermore, a case-control study on hypothyroidism risk in SLE patients also demonstrated that the prevalence of hypothyroidism is significantly greater in females, with an odds ratio of 4.54 (95% CI 3.74–5.51, $P < .001$).[25] The reason for a high prevalence of RA risk in women is not clearly known. Genetic (X-linked) factors and unfavorable hormonal factors are likely involved.[3]

In this study, nearly 75% of RA patients were women, who had the incidence of hypothyroidism 3.6 times greater than men had. Therefore, the mechanism associating with hormonal abnormality for both RA and the development of hypothyroidism may be valid. The development of RA has been associated with inflammation and proinflammatory cytokines.[29] For example, pro-inflammatory cytokines, such as tumor necrosis factor-αand interleukin-6, are involved in pathogenesis of both RA and atherosclerosis.[30] There are growing evidences showing that RA patients have a higher prevalence of related comorbid chronic diseases, such as CVD, diabetes, hypertension, and dyslipidemia.[31,32] In our study, most baseline comorbidities were more prevalent in the RA cohort than in the controls, with the exception of DM and hyperlipidemia. Factors associated with RA and associated comorbid diseases may underlie the association between RA and hypothyroidism.

Patients with RA and hypothyroidism have an increased risk of CVD,[18,33–35] which may be due to the inflammatory-based endothelial dysfunction secondary to the nitric oxide reduction.[36,37] Inflammation leads to deteriorated lipid profiles and low HDL levels.[38,39] Hypothyroidism can lead to dyslipidemia characterized by elevated levels of low-density lipoprotein cholesterol and total cholesterol through a decreased uptake of low-density lipoprotein cholesterol by liver cells.[40] The Rotterdam study in The Netherlands showed that elderly women with RA and subclinical hypothyroidism had a higher risk for atherosclerosis and myocardial infarction associated with an insulin resistance related dyslipidemia.[41,42] Patients who have both RA and hypothyroidism are at higher risk for atheroma formation than patients with RA alone.[43] Inflammation has an important role in atherogenesis, which is associated with elevated C-reactive protein (CRP) and CVD.[44–46] It is well known that statin therapy can reduce serum cholesterol and CRP levels and can further reduce CVD events.[47,48] Although some studies have found higher inflammation markers (erythrocyte sedimentation rate or CRP) in patients with hypothyroidism, others have failed to confirm these findings.[49,50] Studies have assessed whether inflammation and endothelial damage are amplified and whether cardiovascular risk is further increased in RA patients comorbid with hypothyroidism.[18,34,37,49,50] Findings are not consistent among these studies. McCoy et al[34] found that patients with RA and hypothyroidism have twice the risk of CVD. However, Hueston et al[50] did not find that individuals with subclinical hypothyroidism are at an elevated risk of cardiac inflammation. Our study also showed that the hypothyroidism risk increased further in patients with comorbidity of hypertension, IHD, stroke, and hyperlipidemia, and was higher in the RA cohort than in the non-RA cohort. Among these baseline comorbidities, stroke was least prevalent but was associated with the highest incidence in patients with RA. We have further analyzed the

Table 5

Incidence of hypothyroidism and RA cohort to excluded group hazard ratio.

	RA cohort			Excluded group			RA cohort to excluded group	
							HR (95% CI)	
Variable	**Event no.**	**Person–years**	**IR**	**Event no.**	**Person–years**	**IR**	**Crude**	**Adjusted**
Hypothyroidism	189	113,823	16.6	84	47,457	17.7	1.07 (0.83, 1.38)	0.91 (0.69, 1.18)

CI = confidence interval, HR = hazard ratio, IR = incidence rates, per 1000 person–years, RA = rheumatoid arthritis.

prevalence rates of comorbidities in the excluded group. All prevalence rates of comorbidities were higher in the excluded group than in the RA cohort (Table 4). However, the hazards of developing hypothyroidism were not significantly different between the 2 groups (Table 5).

This study demonstrated that individuals with RA in the Asian population have a higher risk of developing hypothyroidism, based on the data from a large sample size. Our findings can be generalized to the general population with a minimal tendency of selection bias. However, several limitations in the interpretation of our findings ought to be considered. Information in laboratory test results for hypothyroidism was not available in the insurance database. The present study design lacks validation in the diagnosis of hypothyroidism. Data on severity scales for RA, such as disease activity, functional impairment, and physical damage, were also unavailable. Moreover, whether the treatment for RA have an impact on the risk of developing hypothyroidism was not assessed in this study. Further study may consider the treatment of using biological antirheumatic agents, comparing with nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drug.[51,52]

In conclusion, our study provides further support to the association between autoimmune disease and development of hypothyroidism. RA was significantly associated with a higher risk of hypothyroidism, and the hypothyroidism risk may be increased in patients with comorbid cardiovascular disorders. Our findings also suggest the need to closely monitor RA patients so that hypothyroidism can be detected early. Prognosis of hypothyroidism in RA patients may be improved with timely medical intervention.

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