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Review

Coexistence of ischemic heart disease and rheumatoid arthritis patients—A case control study☆

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ABSTRACT

Background: Over the last few decades, several studies have demonstrated the connection between Rheumatoid Arthritis (RA) and Ischemic Heart Disease (IHD). The additional risk for RA patients to also suffer from IHD varies based on the definition of the diseases in question, the populations evaluated, and the variables included in the studies.

Objectives: To quantify the association between RA and IHD according to certain demographics as well as traditional cardiovascular risk factors in order to determine their roles in the development of coronary artery disease among patients with RA.

Methods: Using data from the largest HMO in Israel, the Clalit Health Services, we selected for patients with RA. These patients were compared with age and sex matched controls with regards to the prevalence of IHD in a case–control study.

Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis.

Results: The study included 11,782 patients with RA and 57,973 age and sex matched controls. The prevalence of IHD in patients with RA was increased compared with the prevalence in controls (16.6% and 12.8% respectively, $P < 0.001$). In a multivariate analysis, RA was associated with higher proportions of IHD (OR 1.346, 95% confidence interval 1.255–1.431).

Contents

1. Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory disease that leads to progressive joint deformity, significant disability, and premature death. Most studies investigating mortality in patients with RA have found increased mortality rates compared to the general population; largely due to cardiovascular diseases, specifically Ischemic Heart Disease (IHD) [1–4].

It is generally accepted that patients with RA have a greater risk of developing IHD. This association has been demonstrated in several

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studies over the past few decades and several explanations have been proposed as to the mechanism of this relationship. The prevailing concept asserts that there is acceleration of atherosclerosis by the chronic continuous inflammation of RA. Another theory suggests that traditional cardiovascular risk factors are simply more common among RA patients [5,6].

The goal of our study was to demonstrate the linkage between RA and IHD as well as enhance its validity by using the large medical database of the Clalit Health Services (CHS), the largest Health Maintenance Organization (HMO) in Israel. Using this database allowed for very large sample sizes of high quality, data not seen in other studies. Furthermore, the data used allowed for stratification of the association between RA and IHD according to several demographic characteristics as well as traditional cardiovascular risk factors in order to quantify how crucial their contribution is in developing coronary artery disease among patients with RA.

2. Methods

The study was designed as a retrospective case–control study utilizing the Clalit Health Services (CHS) database. The CHS is the largest managed care organization in Israel, serving a population of approximately 3,800,000 enrolees. The CHS have a comprehensive database with continuous real-time input from pharmacies, medical care facilities, and administrative systems.

Patients were defined as having RA when there was at least one documented diagnosis of RA in the medical records registered by a physician in the community or when RA was listed in the diagnoses of discharge letters from a hospital. Five control patients were randomly selected for each case patient and all were matched by age and sex. The control group was randomly selected from the list of CHS members frequency-matched to cases regarding sex and age, excluding patients with RA. Data available from the CHS database included age, sex, socioeconomic status (SES), body mass index (BMI), smoking status, medications purchased, and diagnoses of chronic diseases, including hyperlipidemia, ischemic heart disease (IHD), hypertension (HTN) and diabetes mellitus (DM). These diagnoses were extracted from the CHS chronic diseases registry which is based on data from hospital and primary care physicians' reports, and validated by primary physicians. The validity of diagnoses in this registry was previously found to be of high value [7–11].

The distribution of sociodemographic and clinical factors was compared between patients with and without RA using Chi-square test for sex, socioeconomic status, chronic diseases, and a t-test for age. The prevalence of IHD was compared between the study groups as well as in age, sex, socioeconomic status, hyperlipidemia, smoking, HTN and DM subgroups. Odd's ratios (OR) across strata were tested using Breslow–Day and Tarone's tests. A logistic regression model was used to estimate the association between RA and IHD in a multivariate analysis. Statistical analysis was performed using SPSS software, version 18 (SPSS, Chicago, IL, USA).

3. Results

The study included 11,782 patients with RA and 57,973 age and sex-frequency matched controls. Characteristics of the study population are presented in Table 1. The proportion of IHD in patients with RA was increased compared with the controls (16.6% and 12.8% respectively, $P < 0.001$). There was also a significant increase in smoking, DM, HTN, and hyperlipidemia in patients with RA. In Table 2 we described odds ratios and confidence intervals for prevalence of IHD in patients with RA and controls stratified by age, sex, smoking, hyperlipidemia, BMI, HTN, DM and socioeconomic status (SES). The prevalence of IHD was much higher among males (Table 2). The association was also significant among medium SES group, smoking, HTN, DM, and hyperlipidemia (Table 2). The association was also noted among individuals with a higher BMI (Table 2).

In a multivariate analysis RA was associated with IHD (OR 1.346, 95% CI 1.255–1.431). Age, male sex, smoking, DM, BMI, and especially HTN and hyperlipidemia were all independently associated with IHD (Table 3).

Table 1
Descriptive characteristics of the study population ($n = 69{,}755$) SD-standard deviation.

	No RA (n = 57,973)	RA (n = 11,782)	OR	p value
Age mean (SD)	60.8 (17.0)	61.1 (17.0)	1.00 [1.00;1.00]	0.174
Gender:				
Male	13,384 (23.1%)	2679 (22.7%)	0.98 [0.94;1.03]	0.413
Female	44,589 (76.9%)	9103 (77.3%)	Ref.	Ref.
BMI mean (SD)	28.0 (6.58)	28.2 (6.21)	1.00 [1.00;1.01]	<0.01
SES:				
Low	22,657 (39.2%)	4505 (38.3%)	Ref.	Ref.
Medium	22,831 (39.5%)	4816 (41.0%)	1.06 [1.01;1.11]	<0.001
High	12,334 (21.3%)	2438 (20.7%)	0.99 [0.94;1.05]	0.831
Smoking:				
No	41,302 (71.2%)	7917 (67.2%)	Ref.	Ref.
Yes	16,671 (28.8%)	3865 (32.8%)	1.21 [1.16;1.26]	<0.001
Hypertension:				
No	33,578 (57.9%)	6244 (53.0%)	Ref.	Ref.
Yes	24,395 (42.1%)	5538 (47.0%)	1.22 [1.17;1.27]	<0.001
Diabetes:				
No	44,741 (77.2%)	8789 (74.6%)	Ref.	Ref.
Yes	13,232 (22.8%)	2993 (25.4%)	1.15 [1.10;1.21]	<0.001
IHD:				
No	50,532 (87.2%)	9831 (83.4%)	Ref.	Ref.
Yes	7441 (12.8%)	1951 (16.6%)	1.35 [1.28;1.42]	<0.001
Hyperlipidemia:				
No	23,207 (40.0%)	4369 (37.1%)	Ref.	Ref.
Yes	34,766 (60.0%)	7413 (62.9%)	1.13 [1.09;1.18]	<0.001

Table 2
Association with IHD by risk factors including RA.

	No IHD (n = 60,363)	IHD (n = 9392)	OR	p value
Age mean (SD)	58.9 (16.9)	73.6 (10.6)	1.08 [1.07;1.08]	<0.001
Gender:				
Male	12,513 (20.7%)	3550 (37.8%)	2.32 [2.22;2.43]	<0.001
Female	47,850 (79.3%)	5842 (62.2%)	Ref.	Ref.
BMI mean (SD)	27.9 (6.62)	29.1 (5.73)	1.03 [1.03;1.03]	<0.001
SES:				
Low	23,743 (39.4%)	3419 (36.5%)	Ref.	Ref.
Medium	23,658 (39.3%)	3989 (42.6%)	1.17 [1.11;1.23]	<0.001
High	12,823 (21.3%)	1949 (20.8%)	1.06 [0.99;1.12]	0.076
RA:				
No	50,532 (83.7%)	7441 (79.2%)	Ref.	Ref.
Yes	9831 (16.3%)	1951 (20.8%)	1.35 [1.28;1.42]	<0.001
Smoking:				
No	43,531 (72.1%)	5688 (60.6%)	Ref.	Ref.
Yes	16,832 (27.9%)	3704 (39.4%)	1.68 [1.61;1.76]	<0.001
Hypertension:				
No	38,207 (63.3%)	1615 (17.2%)	Ref.	Ref.
Yes	22,156 (36.7%)	7777 (82.8%)	8.30 [7.85;8.79]	<0.001
Diabetes:				
No	48,569 (80.5%)	4961 (52.8%)	Ref.	Ref.
Yes	11,794 (19.5%)	4431 (47.2%)	3.68 [3.52;3.85]	<0.001
Hyperlipidemia:				
No	26,975 (44.7%)	601 (6.40%)	Ref.	Ref.
Yes	33,388 (55.3%)	8791 (93.6%)	11.8 [10.9;12.9]	<0.001