Systematic Review and Meta-Analysis

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Diabetes mellitus and arthritis: is it a risk factor or comorbidity?

A systematic review and meta-analysis

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Abstract

Background: Investigators have explored the association between diabetes mellitus and arthritis for a long time; however, there are uncertainties and inconsistencies among various studies. In this study, we tried to explore the relationship between diabetes mellitus and the overall risk of arthritis, as well as the potential modifiers for this relationship.

Methods: We conducted a comprehensive literature search through PubMed and identified 36 eligible studies. The overall analyses, subgroup analyses, as well as sensitivity analyses, were conducted to illustrate the association between diabetes mellitus and arthritis. Study quality was evaluated using the Newcastle-Ottawa Quality Assessment Scale. All statistical analyses were conducted using STATA SE version 13.0.

Results: In our study, 36 eligible studies were identified and involved in the meta-analysis. The overall association between diabetes mellitus and arthritis is 1.61 (95% confidence interval [CI]: 1.14–2.28, $P = .007$). The association exists only in nongouty arthritis, where we observed the estimated odds ratio (OR) 1.33 (95% CI: 1.05–1.67, $P < .001$). The opposite point estimates from different types of diabetes may indicate possible different associations for type I (OR: 0.98, 95% CI: 0.18–5.39, $P = .985$) or type II diabetes (OR: 1.28, 95% CI: 0.88–1.84, $P = .194$).

Conclusion: Diabetes mellitus performs more likely as a comorbidity of arthritis rather than a risk factor; however, more studies will be helpful to increase the confidence of identifying the association between diabetes and arthritis.

Abbreviation: NOS = Newcastle-Ottawa Quality Assessment Scale.

Keywords: arthritis, comorbidity, diabetes mellitus, risk factor, meta-analysis

1. Introduction

Arthritis is a highly prevalent disease with the number of patients around 355 million globally, with more than 100 million in China and more than 50 million in the United States.[1] In the Asian area, there is 1 case of arthritis in every 6 people, which is considered as the leading cause of disability. What makes it worse were multiple comorbidities of arthritis, such as diabetes mellitus, heart disease, chronic respiratory conditions, and so on.[2] On the other hand, some studies examined diabetes as a risk factor for different types of arthritis.[3–5] However, most studies that explored diabetes as a risk factor do not consider any potential confounders or biases. There may be existing confounders that lead to the conclusion that diabetes increases the future risk of arthritis.

Several studies focus on the diabetes as a risk factor and the risk of different types of arthritis.[5,6] Although they came out with a positive conclusion, the sample sizes of included studies were too limited to be reliable. Besides, no previous study has examined the association between diabetes and the overall arthritis risk. Although there was a study that indicates differential associations of type I and type II diabetes and the risk of gout, no study has revealed any differences in the association for the risk of other kinds of arthritis.[6] The study also demonstrates the differences between treated and untreated type II diabetes.[6] Therefore, we reasonably assumed the associations may differ through blood glucose levels. Besides, the risk of diabetes was firmly established to be associated with the gender.[7] It could be a potential modifier in the association between diabetes and arthritis.

Therefore, we conducted a systematic review and meta-analysis to explore the relationship between diabetes and the overall risk of arthritis. Subgroup analyses were performed to assess the potential effect measure modification of different populations, genders, types of diabetes, and types of arthritis. We also proposed to distinguish studies according to their reports with either crude odds ratios (ORs) or adjusted ORs, thus,

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including them as another potential modifier for the association of diabetes and the risk of arthritis. For studies with different study types and study qualities, sensitivity analyses were conducted.

2. Material and methods

2.1. Literature search

We conducted a comprehensive literature search through PubMed using the keywords and medical subject headings related to diabetes mellitus and arthritis (Fig. 1). Besides, a complemented search by screening the reference lists of previous meta-analyses was conducted. The search results were restricted to English-language studies with human subjects. We included all arthritic studies that reported the prevalence of diabetes at baseline, even if diabetes is not the exposure of interest. Since the pathology of adolescents and children is always distinct from adults, we also excluded studies with arthritic patients less than 18 years old. Multiple reports on the same trail were considered as duplicates. The most recent reports or the reports with longest follow-up time and all necessary information were included in the meta-analysis.

2.2. Data extraction

Information was extracted as follows: first author, year of publication, title, study region, mean age, gender distribution, disease status, number of participants, type of arthritic endpoints, total number of cases/controls, events of cases/controls. In order to improve the reliability of the study results, included studies were evaluated quantitatively by the star rating system of Newcastle-Ottawa Quality Assessment Scale (NOS).[8]

2.3. Statistical analysis

Considering the substantial heterogeneity, a variation on the inverse-variance method was necessary to synthesize results from multiple studies. The DerSimonian and Laird random-effects model was used to estimate the OR to compare the odds of having diabetes between arthritic patients and controls. In order to better explore the heterogeneity, subgroup analyses and sensitivity analyses were performed. Subgroup effects were evaluated for each type of the predetermined potential modifiers, including populations, genders, types of diabetes, types of arthritis, and adjustments of models. Besides, sensitivity analyses were conducted according to study types and study qualities. Potential publication bias was evaluated using the Funnel plots and the Egger test. Two-sided $P \leq .05$ was considered as significant. Statistical analyses were performed using STATA SE version 13.0 (STATA Corp., College Station, TX).

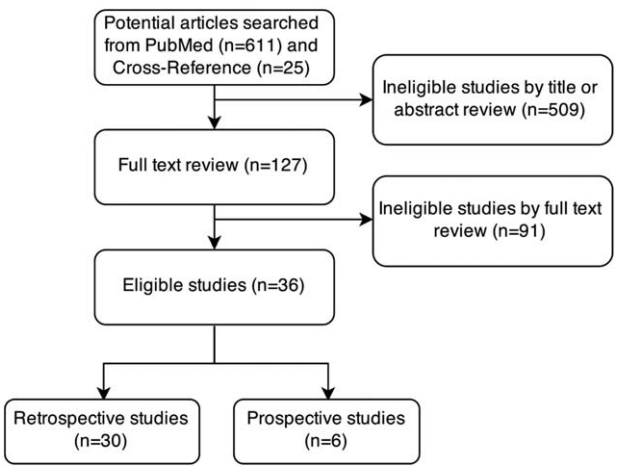

Figure 1. Flow diagram of collection and identification for eligible studies.

3. Results

3.1. Description and study quality

A total of 30 case–control studies and 6 cohort studies were eligible, and the main characteristics of these studies are shown in Table 1. In total, these studies involved 147,034 cases and 1372,948 controls. The average age of the selected population is 48.2 years old, the average body mass index is 26.1 kg/m^2, and the percentage of men is 56.3%. Among them, there are 5 studies from Asia and 11 studies from Europe, 19 from North America, and 1 from South America. For each study, the basis population characteristics are summarized in Table 1.

We evaluated the quality of included studies using NOS. Results for both cohort studies and case–control studies are presented in Supplemental table S1, http://links.lww.com/MD/B683. Three major categories of items were examined for cohort studies, including selection (4 questions relating to the representative of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, and demonstration that outcome of interest was not present at start of study), comparability (comparability of cohorts on the basis of the design or analysis), and outcome/exposure (cohort studies: assessment of outcome, long enough follow-up, and adequate follow-up of cohorts; case–control studies: ascertainment of exposure, same method for cases and controls, nonresponse rate). A study would be awarded 1 star for the achievement of each item in each category. Larger number of stars indicates a higher quality. Among 6 cohort studies, 2 achieved the maximum of 4 stars for selection, 5 achieved the maximum of 2 stars for comparability, and 4 achieved the maximum of 3 stars for outcome. In the assessment of case–control studies, 18 had 4 stars for selection, 29 achieved 2 stars for comparability, and 9 achieved 3 stars for exposure. There is a superiority of prospective studies over retrospective studies, while the overall study quality is relatively good.

3.2. The risk of arthritis and publication bias

The results of all included studies are shown in Fig. 2. We found an association between diabetes and arthritis with the point estimate 1.61 and confidence interval of 1.14 to 2.28 from the random effects model. With a conservational P-value of .007, this result is reliable. However, the extremely high heterogeneity was found by the indicator I^2 statistic of 99.4%. Figure 3 shows the Egger Funnel plot of included studies, for which a high variance was observed even in large sample size studies. However, this result conflicts with the Egger test ($P = .504$, no publication bias indicated); thus, the substantial heterogeneity could be the possible explanation.

3.3. Subgroup analyses

The results for subgroup analyses are summarized in Table 2.

3.3.1. Population. Studies were stratified according to different populations: North American population, European population

Table 1

Characteristics of literatures included in the meta-analysis.

Reference	Outcome	Percentage of men (%)	Age	BMI	Area
Alkaabi et al[9]	RA	50.00	56.0	27.0	UK
Buettner et al[10]	Arthritis	46.50	56.8	28.6	USA
Cemeroglu et al[11]	OA	0.00	65.5	–	Turkey
Chen et al[12]	Gout	0.00	42.3	23.3	Taiwan
Chung et al[13]	RA	58.60	58.6	–	USA
Chung et al[14]	RA	23.01	52.0	–	Taiwan
Cohen et al[15]	Gout	47.55	65.4	27.0	USA
Del Rincón et al[16]	RA	11.44	59.6	28.6	USA
Del Rincón et al[17]	RA	42.23	43.9	27.5	USA
Doran et al[18]	RA	26.90	58.1		USA
Gerli et al[19]	RA	27.84	62.1	25.1	Italy
Giles et al[20]	RA	48.00	59.0	–	USA
González-Senac et al[21]	Gout	95.00	58.7	29.4	Spain
Goulenok et al[22]	RA	20.00	54.0		France
Husted et al[23]	PsA	57.96	48.7	28.6	Canada
Janssens et al[24]	Gout	49.28	–	–	The Netherlands
Kremers et al[25]	RA	26.26	57.1	–	USA
Krishnan et al[26]	Gout	100.00	46.0	27.6	USA
Krishnan et al[27]	Gout	100.00	68.8	–	USA
Krishnan[3]	Gout	100.00	46.3	27.7	USA
Kuo et al[28]	Gout	51.16	42.5	–	Taiwan
Lee et al[29]	Gout	49.58	–	–	Taiwan
Liao et al[30]	RA	29.00	–	–	Sweden
Maradit-Kremers et al[31]	RA	26.90	58.0	–	USA
McEntegart et al[32]	RA	0.00	57.0	–	UK
Monk et al[33]	RA	66.17	58.8	–	UK
Nieves-Plaza et al[34]	OA	64.36	53.5	–	USA
Peters et al[35]	RA	54.73	62.0	–	The Netherlands
Roddy et al[36]	Gout	76.51	62.5	–	UK
Rodríguez et al[6]	Gout	73.43	–	–	USA
Roman et al[37]	RA	2.00	47.5	25.2	USA
Rudominer et al[38]	RA	1.10	46.2	25.1	USA
Salinas et al[39]	RA	17.00	56.6	–	Argentina
Tam et al[4]	PsA	44.57	48.4	25.1	Hong Kong
Velez et al[40]	PsA	47.00	50.0	30.4	USA
Zhu et al[41]	Gout	48.20	47.0	–	USA

BMI = body mass index, OA = osteoarthritis, PsA = psoriatic arthritis, RA = rheumatoid arthritis.

and Asian population, and results are shown in Supplemental Fig. S1, http://links.lww.com/MD/B683. Similar associations were found in North American (OR: 1.54, 95% confidence interval [CI]: 1.18–2.05, $P=.002$) and European population (OR: 1.51, 95% CI: 1.03–2.21, $P=.034$). However, the missing association in Asian ($P=.096$) could be results of either population difference or insufficient number of included studies.

3.3.2. Gender. We also explored the gender-difference of the association between diabetes and arthritis (Supplemental Fig. S2, http://links.lww.com/MD/B683). However, no difference was found by categorizing studies according to gender.

3.3.3. Type of diabetes. Supplemental Fig. S3, http://links.lww.com/MD/B683 gave results of different diabetes types. Although we observed insignificant estimates ($P=.985$ for type I diabetes and $P=.194$ for type II diabetes), the point estimates from different types of diabetes are opposite. Insignificance could be explained by the insufficient sample sizes.

3.3.4. Type of arthritis. In Supplemental Fig. S4, http://links.lww.com/MD/B683, we showed results from subgroup analysis based on the types of arthritis (i.e., gout or not). The association between diabetes and gout was1.56 (95% CI: 0.84–2.88, $P=.159$), while the association between diabetes with other arthritis was 1.45 (95% CI: 1.18–1. 78, $P<.001$).

3.4. Sensitivity analyses

The results for sensitivity analyses are summarized in Table 3.

3.4.1. Study type. We first conducted sensitivity analysis by different study types (i.e., prospective study and retrospective study). Results showed a significant association in the subgroups of retrospective studies (OR: 1.60, 95% CI: 1.06–2.41), while this association was missing among prospective studies (OR: 1.48, 95% CI: 0.97–2.27) (Supplemental Fig. S5, http://links.lww.com/MD/B683). Since the average follow-up time of prospective studies was more than 7 years, it did not seem that a short follow-up time is the explanation for the missing association. On the other hand, the substantial heterogeneities were not solved by separating studies by their type.

3.4.2. Study quality. In order to examine any impact of study quality on results, sensitivity analysis was conducted when restricting to studies with full 9 stars according to NOS. It showed a significant and even stronger results, which indicated that study

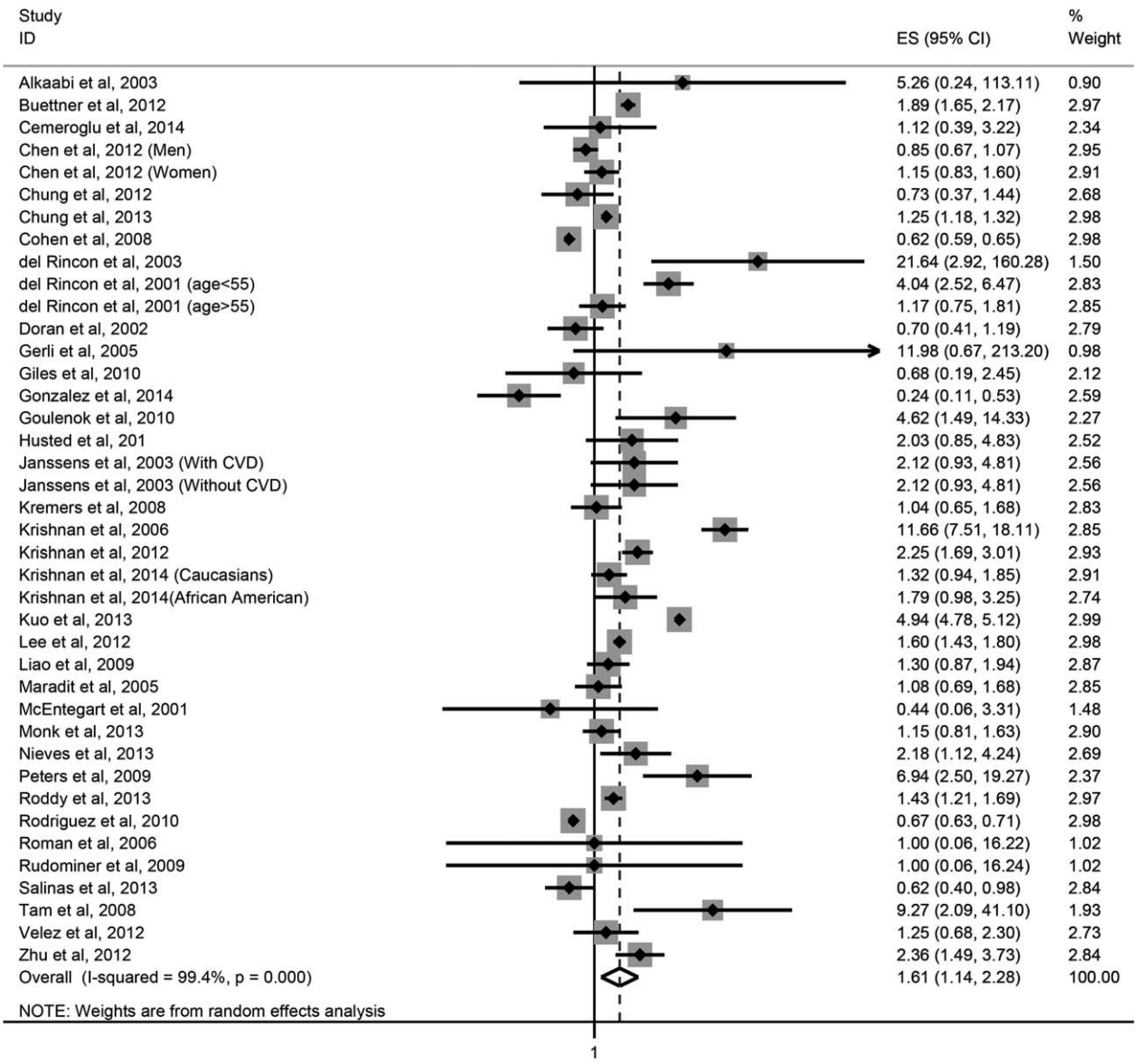

Figure 2. Forest plot from analysis for the association between diabetes mellitus and arthritis.

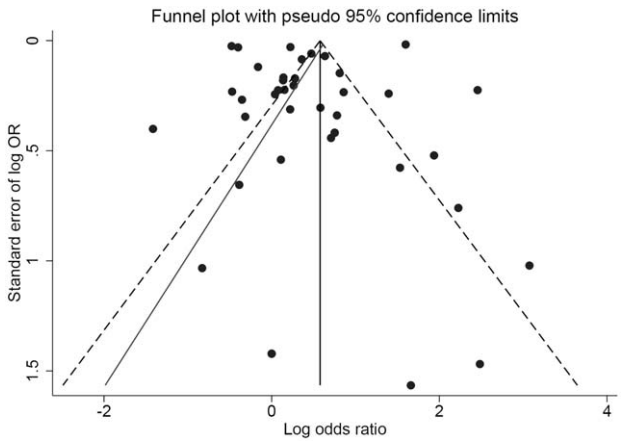

Figure 3. The Egger funnel plots of the overall effect.

Table 2

Odds ratio estimates from subgroup analyses (overall effect, population, gender, type of diabetes, and type of arthritis).

Factors		Study number	OR (95% CI)	*P*
Overall		36	1.61 (1.14, 2.28)	.007
Population	North America	21	1.54 (1.18, 2.05)	.002
	Europe	12	1.51 (1.03, 2.21)	.034
	Asia	6	1.91 (0.89, 4.10)	.096
Gender	Men	6	1.72 (0.88, 3.35)	.112
	Women	5	1.77 (0.94, 3.32)	.077
Type of diabetes	Type I diabetes	3	0.98 (0.18, 5.39)	.985
	Type II diabetes	10	1.28 (0.88, 1.84)	.194
Type of arthritis	Nongouty	24	1.45 (1.18, 1.78)	<.001
	Gout	12	1.56 (0.84, 2.88)	.159

CI = confidence interval, OR = odds ratio.

Table 3

Odds ratio estimates from sensitivity analyses (study type, study quality).

Restriction		Study number	OR (95% CI)	*P*
Study type	Prospective study	6	1.48 (0.97, 2.27)	.070
	Retrospective study	30	1.60 (1.06, 2.41)	.027
Study quality	Full stars (9 stars)	10	1.99 (1.29, 3.08)	.002

CI = confidence interval, OR = odds ratio.

quality may slightly weaken the association but not able to change the conclusion (Supplemental Fig. S6, http://links.lww.com/MD/B683).

4. Discussion

In this study, we presented a meta-analysis to investigate the associations between diabetes and arthritis. There were 36 studies that included 147,034 cases and 1372,948 controls. This systematic review and meta-analysis of association study revealed the association between diabetes and the risk of arthritis is 1.61 (95% CI: 1.14–2.28), which indicates that arthritic patients have 61% higher odds of having diabetes compared to the population without arthritis.

In order to explore the robustness of study results and the substantial heterogeneity, we conducted sensitivity analyses and subgroup analyses. We found different study types resulted in different conclusions, and significant association was found only in retrospective studies but not in prospective studies. The possible explanations for the differences in sensitivity analyses can be the number of prospective studies might be insufficient to get a significant result; or the recall bias could be partly responsible for the different conclusions between prospective and retrospective studies. However, the significant association was still observable (OR: 1.99, 95% CI: 1.29–3.08) when we restricted studies to those with 9 stars in study quality. This result was consistent with the overall effect and indicated that study quality would not affect the overall study conclusion.

In the subgroup analyses, the potential effect measure modification was examined. Although both gender groups and diabetes types were considered as important roles in the examining the association between diabetes and the risk of arthritis, neither of them was verified to perform as an effect modifier in the present meta-analysis. On the other hand, we observed differences when we categorized studies as gouty or nongouty arthritis. Gout is also known as metabolic arthritis, which is more likely believed to be related to metabolic symptoms than other kinds of arthritis.[42] However, our study failed to come out with a similar conclusion as expected. Except for the insufficient number of eligible studies, other explanations are necessary to explore the reasons for the unexpected outcome.

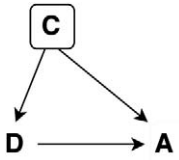

Figure 4. Directed acyclic graph that included diabetes mellitus as a comorbidity of arthritis.

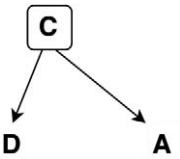

Figure 5. Directed acyclic graph that included diabetes as a risk factor of arthritis.

Adjustment of OR seems to perform as another modifier in the relationship between diabetes as a risk factor and the development of arthritis. The relation between diabetes and arthritis can be described as either directed acyclic graph shown in Fig. 4 or Fig. 5.[43] In Fig. 4, diabetes (D) performs as a risk factor in the development of arthritis (A). If there are certain confounders (C), the association might be strengthened/balanced. However, the association would definitely exist after controlling for the confounders. In Fig. 5, diabetes (D) works as a comorbidity of arthritis (A). There is neither direct nor intermediate relation between them, but a link through certain confounders (C) can be observed. Therefore, we do not expect any associations after the adjustment. In this study, we found the significant association among crude ORs, but not in adjusted estimates. We suspect that confounders or bias may exist in the association between diabetes and the risk of arthritis. Besides, it is also possible that diabetes only associates with nongouty arthritis. Our study rejects results from a previous meta-analysis, which only included unadjusted models and outcomes of rheumatoid arthritis. In conclusion, more studies are necessary to confirm whether diabetes performs as a comorbidity of arthritis or a risk factor of it.

4.1. Availability of data and materials section

The authors declare that the data in the paper is available in database online, and the materials used in the paper are widely approved.

Acknowledgments

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References

[1] Barbour KE, Helmick CG, Theis KA, et al. Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States. Morb Mortal Wkly Rep 2013;62:869–73.
[2] Gabriel SE, Crowson CS, O'Fallon WM, et al. Comorbidity in arthritis. J Rheumatol 1999;26:2475–9.
[3] Krishnan E. Gout in African Americans. Am J Med 2014;127:858–64.
[4] Tam LS, Tomlinson B, Chu TT-W, et al. Cardiovascular risk profile of patients with psoriatic arthritis compared to controls—the role of inflammation. Rheumatology 2008;47:718–23.
[5] Boyer JF, Gourraud PA, Cantagrel A, et al. Traditional cardiovascular risk factors in rheumatoid arthritis: a meta-analysis. Joint Bone Spine 2011;78:179–83.
[6] Rodríguez LA, Soriano FC, Choi HK, et al. Impact of diabetes against the future risk of developing gout. Ann Rheum Dis 2010;69:2090–4.
[7] La Greca AM, Swales T, Klemp S, et al. Adolescents with diabetes: gender differences in psychosocial functioning and glycemic control. Child Health Care 1995;24:61–78.
[8] Wells GA, Shea B, O'connell D, et al. The newcastle-ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Appl Eng Agric 2000;18:727–34.
[9] Alkaabi JK, Ho M, Levison R, et al. Rheumatoid arthritis and macrovascular disease. Rheumatology 2003;42:292–7.

[10] Buettner C, Rippberger MJ, Smith JK, et al. Statin use and musculoskeletal pain among adults with and without arthritis. Am J Med 2012;125:176–82.
[11] Cemeroglu O, Aydin HI, Yasar ZS, et al. Hand and heart, hand in hand: is radiological hand osteoarthritis associated with atherosclerosis? Int J Rheum Dis 2014;17:299–303.
[12] Chen JH, Yeh WT, Chunang SY, et al. Gender-specific risk factors for incident gout: a prospective cohort study. Clin Rheumatol 2012; 31:239–45.
[13] Chung CP, Giles JT, Petri M, et al. Prevalence of traditional modifiable cardiovascular risk factors in patients with rheumatoid arthritis: comparison with control subjects from the multi-ethnic study of atherosclerosis. Semin Arthritis Rheum 2012;41:535–44.
[14] Chung WS, Lin CL, Peng CL, et al. Rheumatoid arthritis and risk of acute myocardial infarction—a nationwide retrospective cohort study. Int J Cardiol 2013;168:4750–4.
[15] Cohen SD, Kimmel PL, Neff R, et al. Association of incident gout and mortality in dialysis patients. J Am Soc Nephrol 2008;19:2204–10.
[16] Del Rincón I, Williams K, Stern MP, et al. Association between carotid atherosclerosis and markers of inflammation in rheumatoid arthritis patients and healthy subjects. Arthritis Rheum 2003;48:1833–40.
[17] Del Rincón I, Williams K, Stern MP, et al. High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. Arthritis Rheum 2001;44:2737–45.
[18] Doran MF, Crowson CS, Pond GR, et al. Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. Arthritis Rheum 2002;46:2287–93.
[19] Gerli R, Sherer Y, Vaudo G, et al. Early atherosclerosis in rheumatoid arthritis: effects of smoking on thickness of the carotid artery intima media. Ann N Y Acad Sci 2005;1051:281–90.
[20] Giles JT, Malayeri AA, Fernandes V, et al. Left ventricular structure and function in patients with rheumatoid arthritis, as assessed by cardiac magnetic resonance imaging. Arthritis Rheum 2010;62:940–51.
[21] González-Senac NM, Bailén R, Torres R, et al. Metabolic syndrome in primary gout. Nucleosides Nucleotides Nucleic Acids 2014;33:185–91.
[22] Goulenok TM, Meune C, Gossec L, et al. Usefulness of routine electrocardiography for heart disease screening in patients with spondyloarthropathy or rheumatoid arthritis. Joint Bone Spine 2010; 77:146–50.
[23] Husted JA, Thavaneswaran A, Chandran V, et al. Cardiovascular and other comorbidities in patients with psoriatic arthritis: a comparison with patients with psoriasis. Arthritis Care Res 2011;63:1729–35.
[24] Janssens HJEM, Van de Lisdonk EH, Bor H, et al. Gout, just a nasty event or a cardiovascular signal? A study from primary care. Fam Pract 2003;20:413–6.
[25] Kremers HM, Crowson CS, Therneau TM, et al. High ten-year risk of cardiovascular disease in newly diagnosed rheumatoid arthritis patients: a population-based cohort study. Arthritis Rheum 2008;58:2268–74.
[26] Krishnan E, Baker JF, Furst DE, et al. Gout and the risk of acute myocardial infarction. Arthritis Rheum 2006;54:2688–96.
[27] Krishnan E, Bharathi L, Vivek B. Low-level lead exposure and the prevalence of gout: an observational study. Ann Intern Med 2012; 157:233–41.
[28] Kuo CF, Yu KH, See LC, et al. Risk of myocardial infarction among patients with gout: a nationwide population-based study. Rheumatology 2013;52:111–7.
[29] Lee MY, Lin KD, Hsiao PJ, et al. The association of diabetes mellitus with liver, colon, lung, and prostate cancer is independent of hypertension, hyperlipidemia, and gout in Taiwanese patients. Metabolism 2012; 61:242–9.
[30] Liao KP, Gunnarsson M, Källberg H, et al. Specific association of type 1 diabetes mellitus with anti-cyclic citrullinated peptide-positive rheumatoid arthritis. Arthritis Rheum 2009;60:653–60.
[31] Maradit-Kremers H, Crowson CS, Nicola PJ, et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum 2005;52:402–11.
[32] McEntegart A, Capell HA, Creran D, et al. Cardiovascular risk factors, including thrombotic variables, in a population with rheumatoid arthritis. Rheumatology 2001;40:640–4.
[33] Monk HL, Muller S, Mallen CD, et al. Cardiovascular screening in rheumatoid arthritis: a cross-sectional primary care database study. BMC Fam Pract 2013;14:150.
[34] Nieves-Plaza M, Castro-Santana L, Ront YM, et al. Association of hand or knee osteoarthritis with diabetes mellitus in a population of Hispanics from Puerto Rico. J Clin Rheumatol 2013;19:1–6.
[35] Peters MJL, Van Halm VP, Voskuyl AE, et al. Does rheumatoid arthritis equal diabetes mellitus as an independent risk factor for cardiovascular disease? A prospective study. Arthritis Care Res 2009;61: 1571–9.
[36] Roddy E, Muller S, Hayward R, et al. The association of gout with sleep disorders: a cross-sectional study in primary care. BMC Musculoskelet Disord 2013; 14:119.
[37] Roman MJ, Moeller E, Davis A, et al. Preclinical carotid atherosclerosis in patients with rheumatoid arthritis. Ann Intern Med 2006;144w: 249–56.
[38] Rudominer RL, Roman MJ, Devereux RB, et al. Independent association of rheumatoid arthritis with increased left ventricular mass but not with reduced ejection fraction. Arthritis Rheum 2009;60:22–9.
[39] Salinas MJH, Bertoli AM, Lema L, et al. Prevalence and correlates of metabolic syndrome in patients with rheumatoid arthritis in argentina. J Clin Rheumatol 2013;19:439–43.
[40] Velez NF, Wei-Passanese EX, Husni ME, et al. Management of psoriasis and psoriatic arthritis in a combined dermatology and rheumatology clinic. Arch Dermatol Res 2012;304:7–13.
[41] Zhu YY, Pandya BJ, Choi HK. Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007–2008. Am J Med 2012;125:679–87.
[42] Schlesinger N. Management of acute and chronic gouty arthritis: present state-of-the-art. Drugs 2004;64:2399–416.
[43] Wang L. Directed acyclic graph. Encyclopedia Syst Biol 2013;574–1574.