ORIGINAL ARTICLE

Prevalence and Associated Factors of Chronic Kidney Disease in Rheumatoid Arthritis Patients at Ratchaburi Hospital, Thailand

Chonachan Petcharat, MD[1]

[1] Department of Medicine, Ratchaburi Hospital, Ratchaburi, Thailand

Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease, common in Thailand. The prevalence of chronic kidney disease (CKD) in Thai RA patients is uncertain.

Objective: To study the prevalence and associated factors of CKD in RA patients.

Materials and Methods: A retrospective study based on medical records was conducted. Participants were RA patients who visited Ratchaburi Hospital between May 2022 and October 2022. CKD was defined according to an eGFR below 60 mL/minute/1.73 m^2 by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The prevalence of CKD and associated factors was determined. Logistic regression was used to analyze the data.

Results: The present study included three hundred and two patients with a mean (SD) age of 53.7 (±12.1) years. Median (IQR) RA disease duration was 60.0 (97.7) months. The prevalence of CKD was 19.2%, consisting of 13.2% at stage 3a, 4.0% at stage 3b, 2.0% at stage 4, and 0% at stage 5. The factors associated with CKD were age of 60 years or older, hypertension, dyslipidemia, age of RA onset of 60 years or older, more than three months of joint pain before disease-modifying antirheumatic drugs (DMARDs) treatment, higher erythrocyte sedimentation rate (ESR) and RA treatment without methotrexate ($p<0.05$). The findings from the multivariate analysis of factors associated with CKD revealed that hypertension (adjusted OR 2.84, 95% CI 1.36 to 5.90), more than three months of joint pain before DMARDs treatment (adjusted OR 56.70, 95% CI 12.64 to 254.41), higher ESR (adjusted OR 1.01, 95% CI 1.01 to 1.03), and RA treatment without methotrexate (adjusted OR 5.45, 95% CI 1.87 to 15.89) were associated with CKD after adjusting for age.

Conclusion: The prevalence of CKD in RA patients was higher than in normal population. Factors associated with CKD were hypertension, more than three months of joint pain before DMARDs use, and higher ESR and RA treatment without methotrexate. Results from the present study should be applied to the management plans for patients with RA.

Keywords: Prevalence; Rheumatoid arthritis; Chronic kidney disease

Received 19 January 2024 | Revised 9 April 2024 | Accepted 11 April 2024

J Med Assoc Thai 2024;107(5):356-62

Website: http://www.jmatonline.com

Rheumatoid arthritis (RA) is a chronic inflammatory disease, characterized by symmetrical polyarthritis, progressive destruction of joints, and extra-articular organs involvement that also increases mortality[1,2]. A previous systematic review showed that the risk of incident chronic kidney disease (CKD) was significantly increased among patients with RA with the pooled risk ratio of 1.52 (95% CI 1.28 to 1.80)[3]. Furthermore, in one study, RA patients with renal disease had significantly increased mortality compared to those with normal renal function, with a hazard ratio (HR) of 1.78 (95% CI 1.34 to 2.31)[4]. Previous studies reported that the prevalence of CKD in patients with RA ranges from 5% to 50% based on studies of different designs[5,6]. Kidney diseases in RA patients have various potential causes, including drug-related renal disease, such as non-steroidal anti-inflammatory drugs (NSAIDs) and some types of disease-modifying antirheumatic drugs (DMARDs) as gold compounds, D-penicillamine, and cyclosporin, secondary renal amyloidosis and various types of glomerulonephritis[7]. A previous study showed that the traditional risk factors of CKD, such as hypertension, diabetes mellitus, and renal stones, are associated with CKD in the Thai

Correspondence to:

Petcharat C.

Department of Medicine, Ratchaburi Hospital, Amphoe Muang Ratchaburi, Ratchaburi 70000, Thailand.

Phone: +66-85-3516945

Email: chonjeep@gmail.com

How to cite this article:

Petcharat C. Prevalence and Associated Factors of Chronic Kidney Disease in Rheumatoid Arthritis Patients at Ratchaburi Hospital, Thailand. J Med Assoc Thai 2024;107:356-62.

DOI: 10.35755/jmedassocthai.2024.5.13991

population[8]. Focused reports in RA population show that elevated inflammatory markers and cardiovascular disease (CVD) at baseline are associated with future CKD[9,10]. However, few studies have specifically investigated CKD in patients with RA. Although a previously reported prevalence of CKD in Thailand stands at 17.5%[8], which is quite high, the research focusing on Thai patients with RA is currently lacking. Addressing this gap in knowledge could significantly contribute to a better understanding and managing of RA in the Thai population. Therefore, the present study was conducted to assess the prevalence and identify the associated factors of CKD in patients with RA at Ratchaburi Hospital, Thailand.

Materials and Methods

A retrospective study based on medical records was undertaken after approval from the Human Research Ethics Committee of Ratchaburi Hospital (approval No. 038/2023). The present study included RA patients continuously followed up at the Ratchaburi Hospital outpatient unit between May 2022 and October 2022. Exclusion criteria were patients under 18 years old, missing two serum creatinine measurements or more than 90 days apart, and having overlapping syndrome or other autoimmune diseases.

Data collection and outcome assessment

Variables collected from medical records included age, gender, duration of RA, age at diagnosis of RA, positivity or negativity of rheumatoid factor (RF), using of NSAIDs, DMARDs, biological drugs, corticosteroid, two laboratory creatinine measurements 90 days apart, RA disease activity, number of joint involvement at the onset of RA and at the time of data collection, comorbidities including hypertension, dyslipidemia, diabetes mellitus, stroke, and ischemic heart disease.

The diagnosis of RA was made according to the criteria of the American College of Rheumatology (ACR) 1987 or ACR/European League Against Rheumatism collaborative initiative (EULAR) RA 2010[11,12]. CKD was defined by two consecutive declines in estimated glomerular filtration rates (eGFR) to less than 60 mL/minute/1.73 m^2 at least 90 days apart using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation[13,14]. The first serum creatinine level was used for data analysis in the present study.

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics, version 21.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as number with percentage and continuous variables as mean with standard deviation (SD) or median with range as appropriate. Chi-square test or Fisher's exact test for categorical variables and student t-test or Mann-Whitney U test was used for continuous variables and statistically significant at p-value less than 0.05. Logistic regression analysis was used to explore the associations among factors influencing CKD. For the univariate analysis, the possible associated factors were included. When there was statistical significance, it was also analyzed by multiple logistic regression to identify potential associated factors. Associated factors of CKD were revealed after adjusting confounding factors at the confidence level of 95% and statistically significant at p-value less than 0.05.

Results

Study population characteristics and prevalence of CKD

Three hundred two patients were included in the present study, of whom 242 were female (80.1%). The mean (SD) age was 59.7 (±12.1) years with RF positivity 62.3%. The median duration of RA disease was 60 (range 0 to 252) months. The main DMARDs treatments were methotrexate at 87.4% and antimalarial drug at 88.4%. Almost all patients had used NSAIDs, thus 98.7%, to control RA pain. Only four patients had a history of NSAIDs or salicylic drug allergy.

The overall prevalence of CKD was 19.2% (58/302 patients). Clinical characteristics of overall RA patients and RA patients with or without CKD are summarized in Table 1. Figure 1 shows the eGFR of all RA patients stratified by eGFR level.

Associated factors of CKD in RA patients

Regarding clinical characteristics comparing RA patients with and without CKD, the univariate analysis of possible associated factors for CKD was performed. The results of the present study found that elderly patients aged over 60 years were significantly associated with CKD (OR 3.78, 95% CI 1.91 to 7.47). In addition, the elderly onset RA with age at diagnosis 60 years or older was also an important associated factor. Comorbidities that are traditional risk factors of CKD include hypertension or dyslipidemia, which were found to be the significant related factors of

Table 1. Characteristics of RA patients comparing with CKD and without CKD

Characteristics	All participants (n=302)	CKD (n=58)	Non-CKD (n=244)	p-value*
Age (years); mean±SD	59.7±12.1	67.2±9.3	57.9±11.9	<0.005†
Age ≥60 years; n (%)	169 (56.0)	46 (79.3)	12 (20.7)	<0.005
Female sex; n (%)	242 (80.1)	46 (79.3)	196 (80.3)	0.861
Associated conditions; n (%)				
Hypertension	108 (35.8)	34 (58.6)	74 (30.3)	<0.005
Diabetes	29 (9.6)	8 (13.8)	21 (8.6)	0.228
Dyslipidemia	89 (9.5)	24 (41.4)	65 (26.6)	0.027
Ischemic heart disease or stroke	11 (3.6)	3 (5.2)	8 (3.3)	0.489
BMI (kg/m^2); mean±SD	23.2±4.4	24.5±3.2	23.7±4.7	0.411†
Obesity; n (%)	105 (34.8)	23 (39.7)	82 (33.6)	0.385
Disease duration (months); median (min-max)	60.0 (0 to 252)	63.0 (0 to 252)	59.5 (0 to 246)	0.223††
Age at onset of RA (years); mean±SD	53.2±12.6	60.33±9.9	51.5±12.6	<0.005†
Age at onset of RA ≥60 years; n (%)	99 (32.8)	34 (58.6)	65 (26.6)	<0.005
>3 months of joint pain before DMARDs; n (%)	135 (44.7)	56 (96.6)	79 (32.4)	<0.005
Arthritis at RA diagnosis >10 joints; n (%)	22 (7.3)	3 (5.2)	19 (7.8)	0.588**
Arthritis ≥1 joint at collect data date; n (%)	80 (26.5)	16 (27.6)	64 (26.2)	0.833
ESR (mm/hour); median (IQR)	42 (3 to 170)	56 (6 to 131)	40 (3 to 170)	0.001††
Rheumatoid factor; n (%)	188 (62.3)	31 (53.4)	157 (64.3)	0.124
NSAIDs exposed; n (%)	298 (98.7)	58 (100)	240 (98.4)	0.592**
Sulfasalazine current used; n (%)	71 (23.5)	8 (13.8)	63 (25.8)	0.052
Methotrexate current used; n (%)	264 (87.4)	43 (74.1)	221 (90.6)	0.001
CQ or HCQ current used; n (%)	267 (88.4)	48 (82.8)	219 (89.8)	0.135
Leflunomide current used; n (%)	140 (46.4)	22 (37.9)	118 (48.4)	0.152
Cyclosporin current used; n (%)	5 (1.7)	2 (3.4)	3 (1.2)	0.234
Prednisolone current used; n (%)	171 (56.6)	28 (48.3)	143 (58.6)	0.154
Biologic agent used; n (%)	6 (2.0)	2 (3.4)	4 (1.6)	0.375

BMI=body mass index; RA=rheumatoid arthritis; DMARDs=disease modifying antirheumatic drugs; ESR=erythrocyte sedimentation rate; NSAIDs=non-steroidal anti-inflammatory drugs; CQ or HCQ=chloroquine or hydroxychloroquine; SD=standard deviation; IQR=interquartile range

* p-value was observed difference between characteristics of patients with CKD and without CKD by chi-square test, ** Fisher exact test, † Student's t-test, †† Mann-Whitney U test

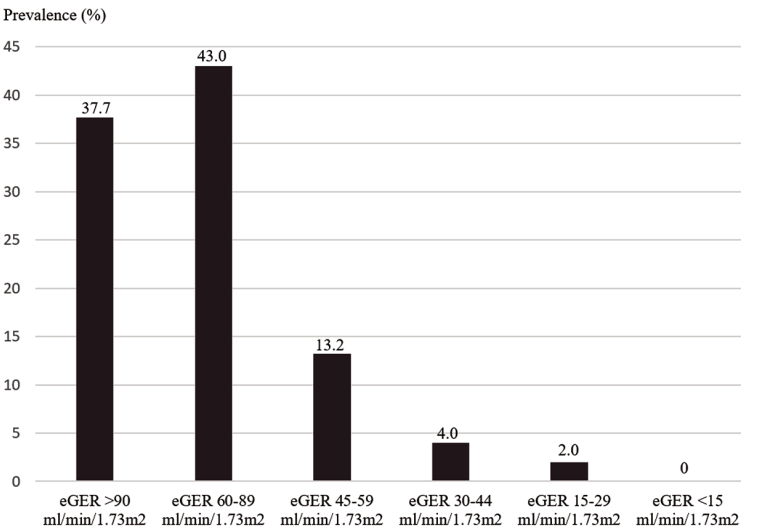

Figure 1. The estimated glomerular filtration rate (eGFR) of all RA patients stratified by eGFR level.

The eGFRs were calculated by the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation[13]

Table 2. Univariate and multivariate logistic regression analysis of associated factors for chronic kidney disease in rheumatoid arthritis patients

Variable	Univariate analysis*			Multivariate analysis**		
	OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Age ≥60 years	3.78	1.91 to 7.47	<0.001	1.45	0.61 to 3.44	0.405
Hypertension	3.26	1.81 to 5.87	<0.001	2.84	1.36 to 5.90	<0.001
Dyslipidemia	1.94	1.07 to 3.52	0.028	-	-	-
Onset of RA ≥60 years	3.90	2.15 to 7.07	<0.001	-	-	-
Joint pain over 3 months before DMARDs used	58.48	13.92 to 245.78	<0.001	56.70	12.64 to 254.41	<0.001
RA treatment without MTX	3.35	1.62 to 6.94	0.001	5.45	1.87 to 15.89	0.002
ESR	1.02	1.01 to 1.03	0.001	1.01	1.01 to 1.03	0.036

RA=rheumatoid arthritis; DMARDs=disease modifying antirheumatic drugs; MTX=methotrexate; ESR=erythrocyte sedimentation rate; OR=odds ratio; CI=confidence interval

* Univariate analysis was analyzed by binary logistic regression, ** Independent variables with p<0.05 from univariate analysis were analyzed in multivariate analysis including age ≥60 years, hypertension, joint pain over 3 months before DMARDs used, RA treatment without methotrexate and ESR with Nagelkerke R2=0.51 and predicted overall correct=83.80%

CKD with OR 3.26 (95% CI 1.81 to 5.87) and OR 1.94 (95% CI 1.07 to 3.52), respectively. Furthermore, ESR, an active RA inflammatory marker, was a relevant factor of CKD with OR 1.02 (95% CI 1.01 to 1.03). RA treatment regimen without methotrexate was another significant factor with OR 3.35 (95% CI 1.62 to 6.94). Finally, the data showed that patients with a history of joint pain longer than three months before starting DMARDs were associated with CKD with OR 58.48 (95% CI 13.92 to 245.78) compared with those who received DMARDs at early onset of RA as shown in Table 2.

In the present study, due to the number of patients with CKD, only five factors significantly associated with CKD were further analyzed in a multivariate analysis. The multivariate analysis revealed that hypertension (adjusted OR 2.84, 95% CI 1.36 to 5.90), a history of joint pain for over three months before DMARDs initiation (adjusted OR 56.70, 95% CI 12.64 to 254.41), RA treatment without methotrexate (MTX) (adjusted OR 5.45, 95% CI 1.87 to 15.89), and ESR (adjusted OR 1.01, 95% CI 1.01 to 1.03) were significantly associated with CKD, after adjusting for age of 60 years or older, as shown in Table 2.

Discussion

The present study showed the prevalence of CKD in Thai RA patients was 19.52%, which is higher than the previously reported prevalence of CKD in the Thai population, which was 17.5%[8]. Previous reports have noted that the prevalence of CKD in RA patients varied from 5% to 50% depending on the patient population, RA treatment, and the equation used to calculate eGFR[5,6]. Hickson et al.[10] evaluated 813 RA patients in the U.S. and showed that the incidence of CKD was higher in patients with RA than in those without RA, at 25.0% versus 20.0% (p=0.03). They used the eGFR-EPI equation to determine CKD, similar to the present study. However, the differences lie in the patient population, with a higher prevalence of CKD in the general population in the U.S. than in the general population in Thailand, and the ethnic differences. Cross-sectional population-based cohort study of 102 patients in Finland with RA and without nephropathy demonstrated that 28% developed CKD within 15 years, which is higher than the prevalence reported in the present study[15]. This difference could be attributed to the difference in the patient population, definition of CKD, and patient characteristics. Regarding Asian RA patient study, Hanaoka et al.[16] reported that RA patients treated with biologic DMARDs for RA progressed to CKD within five years at a rate of 8.0%, which is lower than the prevalence reported in the present study. The reason for this difference may be due to the rapid control of RA disease activity with biologic DMARDs as the patients in the author's study were treated with biologic DMARDs only 2% of the time.

In the present analysis, various RA characteristics and treatment were associated with CKD in patients with RA, including elderly patients, hypertension, dyslipidemia, elderly onset RA, MTX use, and history of joint pain over three months before DMARDs was used. Daoussis et al.[9] found that advanced age and increased cholesterol levels were independently associated with decreased kidney function in a single-center cross-sectional study of 400 patients with RA, similar to the present study. On the other hand, Hickson et al.[10] reported that the presence of CVD at baseline (HR 1.77, 95% CI 1.14 to 2.73, p=0.01) was associated with increased risk of CKD.

This might be possible that a lower proportion of the author's patients had CVD, at 3.6%, than they did, at 11.0%, which prevents the author from making any statement about this.

The present study showed the association between the higher level of ESR and CKD. This was consistent with the previous study that suggested that chronic inflammation in patients with RA leads to prevalent kidney disease[10,17]. This was primarily due to a number of causes including AA amyloidosis[16]. Specifically, among the patients included in the present study, 28.9% had been living with RA for more than 10 years. It is well known that patients with longstanding inflammation may develop secondary amyloidosis in RA[18,19]. On the other hand, chronic inflammation may directly promote kidney injury by inducing inflammation in the glomerulus and tubulointerstitium. Inflammation has been reported to contribute to glomerular injury through the infiltration of inflammatory cells such as monocytes and macrophages, which stimulate the proliferation of mesangial cells, leading to renal scarring[20]. Furthermore, the present study demonstrated that treatment without MTX was associated with CKD in RA patients. In the present study, 38 patients did not receive MTX treatment due to intolerance of its side effects or the development of interstitial lung diseases. Among these patients, 42.1% of those who did not receive MTX had arthritis at the data collection date, which was higher than the 24.2% observed in patients who were treated with MTX. This finding suggests that MTX, which is a cornerstone of RA treatment, may effectively control arthritis and imply control inflammation associated with RA, potentially leading to a decreased incidence of CKD in RA patients.

Interestingly, the present study showed that joint pain over three months before DMARDs treatment was associated with CKD in RA patients. This may result in those patients potentially having longer period of uncontrolled inflammation in RA and more time exposed to other nephrotoxic drugs like NSAIDs. Previous studies had shown an association between NSAIDs and reduced kidney function impairment in patients with RA[16,21,22]. Unfortunately, the present study was unable to determine differences between patients with and without NSAIDs use, as nearly all patients in this study, or 98.7%, were exposed to NSAIDs.

The primary strength of the present study is that it was the first study in Thailand to assess the prevalence of CKD in RA patients and its associations. Furthermore, the author was able to perform a comprehensive review of outpatient medical records from Ratchaburi Hospital, a tertiary care hospital in Thailand, which allowed for accurate assessment of patient characteristics and kidney function. The next point is that the author used the CKD-EPI creatinine equation, which is a well-known equation for estimating kidney function. However, this equation has not yet been validated in patients with RA[23]. Acknowledging this issue, the author employed the CKD-EPI equation, which has been found in a recent meta-analysis to estimate GFR more accurately than the other equation in the comparison of risk for mortality and end-stage renal disease prediction[24]. The present study has limitations. As the present study is a retrospective medical chart review, data related to potential risk factors were missing such as composite disease activity of RA, frequency of NSAIDS use, use of herbal medicine and over-the-counter drugs, or hidden previous renal disease. Hence, further study is warranted to investigate other factors that may affect eGFR. Furthermore, some patients diagnosed with diabetes, hypertension, or dyslipidemia, which were the traditional risk factors of CKD according to the prevalence and risk factors of CKD in the Thai adult population, according to the Thai SEEK study, did not mentioned about the duration or severity of those conditions in the study. The author also did not use urine protein excretion rates or report the prevalence of hematuria to classify CKD. Therefore, an understanding of the true prevalence and risk of CKD or reduced kidney function in patients with RA may not have been fully explored. Given the retrospective nature of the present study, the author was limited to deriving associations only from the findings. Further prospective studies are needed to gain more conclusive insight into RA and reduced kidney function. Finally, although the sample size was sufficient to explore the prevalence of CKD in RA, it was too small to identify the associated factors of CKD. Only five factors that were in the univariate analysis were included in the multivariate analysis. Ideally, a prospective study and a large number of patients are needed to determine associated factors or risk factors of CKD in RA patients.

Conclusion

From the present study, the prevalence of CKD in RA patients was 19.2% at Ratchaburi Hospital, Thailand. Factors significantly associated with CKD included hypertension, duration of joint pain before DMARDs use, higher ESR, and RA treatment without MTX. The findings of the current study will help

increase awareness and be helpful in managing RA.

What is already known on this topic?

Previous studies reported that the prevalence of CKD in patients with RA ranged from 5% to 50% based on studies of different designs. To the best of the author's knowledge, the prevalence in Thailand is still unknown. In previous studies, factors associated with CKD have been found in RA patients such as age, previous CVD, and inflammatory markers. However, there is limited information about CKD and its related factors in Thai RA.

What does this study add?

This study shows that the prevalence of CKD in Thai RA patients is 19.2%. Hypertension, duration of joint pain before DMARDs use, higher ESR and RA treatment without MTX are important factors associated with CKD.

Conflicts of interest

The author declared no conflict of interest.

References

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016;388:2023-38.
2. Scott DL, Symmons DP, Coulton BL, Popert AJ. Long-term outcome of treating rheumatoid arthritis: results after 20 years. Lancet 1987;1:1108-11.
3. Raksasuk S, Ungprasert P. Patients with rheumatoid arthritis have an increased risk of incident chronic kidney disease: a systematic review and meta-analysis of cohort studies. Int Urol Nephrol 2020;52:147-54.
4. Sihvonen S, Korpela M, Mustonen J, Laippala P, Pasternack A. Renal disease as a predictor of increased mortality among patients with rheumatoid arthritis. Nephron Clin Pract 2004;96:c107-14.
5. Helin HJ, Korpela MM, Mustonen JT, Pasternack AI. Renal biopsy findings and clinicopathologic correlations in rheumatoid arthritis. Arthritis Rheum 1995;38:242-7.
6. Karie S, Gandjbakhch F, Janus N, Launay-Vacher V, Rozenberg S, Mai Ba CU, et al. Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study. Rheumatology (Oxford) 2008;47:350-4.
7. Braun A, Zeier M. Rheumatoid arthritis and the kidney: uneasy companions. Nephron Clin Pract 2004;96:c105-6.
8. Cha'on U, Tippayawat P, Sae-Ung N, Pinlaor P, Sirithanaphol W, Theeranut A, et al. High prevalence of chronic kidney disease and its related risk factors in rural areas of Northeast Thailand. Sci Rep 2022;12:18188.
9. Daoussis D, Panoulas VF, Antonopoulos I, John H, Toms TE, Wong P, et al. Cardiovascular risk factors and not disease activity, severity or therapy associate with renal dysfunction in patients with rheumatoid arthritis. Ann Rheum Dis 2010;69:517-21.
10. Hickson LJ, Crowson CS, Gabriel SE, McCarthy JT, Matteson EL. Development of reduced kidney function in rheumatoid arthritis. Am J Kidney Dis 2014;63:206-13.
11. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.
12. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62:2569-81.
13. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005;67:2089-100.
14. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
15. Karstila K, Korpela M, Sihvonen S, Mustonen J. Prognosis of clinical renal disease and incidence of new renal findings in patients with rheumatoid arthritis: follow-up of a population-based study. Clin Rheumatol 2007;26:2089-95.
16. Hanaoka H, Kikuchi J, Hiramoto K, Saito S, Kondo Y, Kaneko Y. Decreased chronic kidney disease in rheumatoid arthritis in the era of biologic disease-modifying anti-rheumatic drugs. Clin Kidney J 2022;15:1373-8.
17. Kochi M, Kohagura K, Shiohira Y, Iseki K, Ohya Y. Inflammation as a risk of developing chronic kidney disease in rheumatoid arthritis. PLoS One 2016;11:e0160225.
18. Cunnane G, Whitehead AS. Amyloid precursors and amyloidosis in rheumatoid arthritis. Baillieres Best Pract Res Clin Rheumatol 1999;13:615-28.
19. Lachmann HJ, Goodman HJ, Gilbertson JA, Gallimore JR, Sabin CA, Gillmore JD, et al. Natural history and outcome in systemic AA amyloidosis. N Engl J Med 2007;356:2361-71.
20. Bertani T, Abbate M, Zoja C, Corna D, Perico N, Ghezzi P, et al. Tumor necrosis factor induces glomerular damage in the rabbit. Am J Pathol 1989;134:419-30.
21. Chiu HY, Huang HL, Li CH, Chen HA, Yeh CL, Chiu SH, et al. Increased risk of chronic kidney disease in rheumatoid arthritis associated with cardiovascular complications - a national population-based cohort study. PLoS One 2015;10:e0136508.

22. Möller B, Pruijm M, Adler S, Scherer A, Villiger PM, Finckh A. Chronic NSAID use and long-term decline of renal function in a prospective rheumatoid arthritis cohort study. Ann Rheum Dis 2015;74:718-23.
23. Anders HJ, Rihl M, Loch O, Schattenkirchner M. Prediction of creatinine clearance from serum creatinine in patients with rheumatoid arthritis: comparison of six formulae and one nomogram. Clin Rheumatol 2000;19:26-9.
24. Matsushita K, Mahmoodi BK, Woodward M, Emberson JR, Jafar TH, Jee SH, et al. Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate. JAMA 2012;307:1941-51.