

KIDNEY DAMAGE IN RHEUMATOID ARTHRITIS: A MODERN VIEW OF THE PROBLEM

<https://doi.org/10.5281/zenodo.12541991>

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Abstract: *The scientific review is devoted to one of the modern views on the problems of medicine – kidney damage in rheumatoid arthritis. The analysis of literary data on the prevalence of rheumatoid arthritis is carried out. According to the research data of recent years, chronic kidney disease (CKD) in patients with RA is observed significantly more often. The issues of prevalence and risk factors of chronic kidney disease in rheumatoid arthritis are considered. The results of clinical and review studies of Russian and foreign authors on the problem of kidney damage in rheumatoid arthritis are summarized.*

Key words: *rheumatoid arthritis, kidney damage, chronic kidney disease, amyloidosis, cardiovascular damage.*

ПОРАЖЕНИЯ ПОЧЕК ПРИ РЕВМАТОИДНЫЙ АРТРИТ : СОВРЕМЕННЫЙ ВЗГЛЯД НА ПРОБЛЕМУ

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Резюме: *Научный обзор посвящен одной из современным взглядам проблем медицины – поражению почек при ревматоидном артрите. Проведен анализ литературных данных по распространенности ревматоидного артрита. Согласно данным исследований последних лет, хроническая болезнь почек (ХБП) у пациентов с РА отмечается достоверно чаще. Рассматриваются вопросы распространенности и факторов риска хронической болезни почек при ревматоидном артрите. Обобщены результаты клинических и обзорных исследований российских и зару-бежных авторов по проблеме поражения почек при ревматоидном артрите.*

Ключевые слова: *ревматоидный артрит, поражение почек, хроническая болезнь почек, амилоидоз, сердечно-сосудистое поражение.*

Rheumatoid arthritis is currently considered an autoimmune systemic disease of unknown etiology, characterized by chronic erosive arthritis (synovitis) and systemic inflammatory lesions of internal organs (Nasonov E.L., 2008; Chichasova N.V., 2009; Goodson N.J., Wiles N.J., Lunt M. et al., 2002). The high medical and social significance of RA is due not only to its high prevalence, but also to early disability: 10-15 years after the

onset of the disease, approximately 90% of patients lose their ability to work, and a third become completely disabled (Roccatello D., Ferro M., Cesano G. et al., 2000; Shen P., He L., Huang D., 2008; Scott D.L., 2002).

Rheumatoid arthritis is a disease that occurs with a frequency of about 1% in the general population, with women suffering 2.5 times more often than men (Serov V.V., Varshavsky V.A., Ivanov A.A., 2000; Chichasova N.V., Nasonov E.L. et al., 2002; Gabriel S.E., 2001).

Most often, RA begins between the ages of 40 and 70, and the incidence increases with age (McQueen F.M., Stewart N., Crabbe J. et al., 1998; Weyand C.M., 2000). PA may be accompanied by extra-articular systemic manifestations (Harris E.D., 1993; Turesson C., O.Tallon W.M., Crowson C.S. et al., 2003).

The prevalence of chronic kidney disease (CKD) in patients with RA significantly exceeds the similar indicator in the general population and ranges from 15 to 50% (Voloshinova E.V., Tyapkina M.A., Rebrov A.P., 2011; Karstila K., Korpela M., Sihvonen S., Mustonen J., 2007). K. Karstila et al. (2007), I. Avalos et al. (2008) and A.M. Van Sijl et al. (2011) emphasize that the most common cause of death in patients with RA, especially against the background of CKD, are cardiovascular diseases (mortality is recorded for coronary heart disease and stroke, which occurred against the background of CKD and CRF), as in the general population, but at an earlier age (on average, 10 years earlier).

Kidney damage is one of the most severe visceral manifestations of RA. Symptoms of kidney damage in such patients are observed in approximately 10-25% of cases (Icardi A., Araghi P., Ciabattoni M. et al., 2003; Korpela M., 1993; Maiideli B.F., Hoffman G.S., 2001). Progressive renal failure (PN) and uremia are among the leading causes of death in patients with PA (Doran M.F., Pond G.R., Crowson C.S. et al., 2002; Sihvonen S., Korpela M., Laippala P. et al., 2004).

In terms of the frequency of kidney damage, RA is in third place, second only to such diseases as systemic lupus erythematosus and systemic vasculitis (Boers M., Croonen A.M., Dijkmans B.A.C. et al. 1987). There is still no consensus on the nature of kidney pathology in RA, and the literature data contradict each other (Icardi A., Araghi P., Ciabattoni M. et al., 2003; Koivuniemi R., Paimela L., Suomalainen R. et al., 2008).

The growing population of people with rheumatic diseases creates considerable difficulties for practical health care. Due to its multifactorial origin, complex and not fully understood pathogenesis, rheumatoid arthritis (RA) remains the focus of researchers' attention [12, 14, 16, 53, 62]. RA is based on chronic progressive damage to the connective tissue of predominantly peripheral (synovial) joints by the type of erosive-destructive polyarthritis.

Kidney diseases in this category of patients can be associated with the development of secondary amyloidosis, as well as various morphological forms of glomerulonephritis, as well as acute and chronic drug-induced interstitial nephritis (Icardi A., Araghi P., Ciabattoni M. et al., 2003). There are significant differences in the prevalence of secondary

amyloidosis in RA in the literature: the incidence of the latter ranges from 15 to 60% (Edmonds J.P., Winyard S.E., Guo P.G. et al., 1997; Karstila K., Korpela M., Sihvonon S. et al., 2007). G. Chevrel et al. (2001) noted that AA amyloidosis in rheumatic diseases accounts for about 34% of cases, and in RA it can reach 83%. A. Icardi et al. (2003) showed that glomerulonephritis in PA occurred in 60-65%, amyloidosis in 20-30% of cases, and less frequently, chronic and acute interstitial nephritis.

According to the literature, the main causes of kidney damage in patients with RA are rightly considered to be the disease itself and the drugs used to treat it (Sarkisova I.A., 2006; Firenstein G.S., 2003). With RA, various morphological variants of glomerulonephritis (GN), interstitial nephritis, pyelonephritis, very rare - granulomatous changes and vasculitis of the kidneys are possible (Sokka T., Abelson B., Pincus T., 2008; Riise T., Jacobsen B.K., Gran J.T. et al., 2001, Kanevskaya M.Z. et al., 2003). In 11 - 60% of cases, RA is complicated by the development of amyloidosis (Buxbaum J., 1998; Karstila K., Korpela M. et al., 2007). There are indications in the literature of a combination of AA amyloidosis of the kidneys with glomerulonephritis (Koivuniemi R., Paimela L., Suomalainen R. et al., 2008; Koseki Y., Teraï C, Moriguchi M. et al., 2001). Mesangioproliferative glomerulonephritis (MezPGN) is the most common form of kidney damage in PA (Icardi A., Araghi P., Ciabattoni M. et al., 2003; Nagy J., Wittmann I., 2005) and can be a significant cause of the development of PN.

Thus, according to E.M. Shilov (2002) and co-authors, the ten-year renal survival rate in MezPGN is 64%. Even more rapid development of PN is caused by rare forms of glomerulopathies: mesangiocapillary glomerulonephritis (MCGN), focal segmental glomerulosclerosis (FSGS), rapidly progressive glomerulonephritis (RPGN), which many authors consider to be a manifestation of rheumatoid vasculitis (Icardi A., Araghi P., Ciabattoni M. et al., 2003; Weyand CM., 2000). The most serious kidney damage in RA is secondary amyloidosis (Sarkisova I.A., 2006). R. Myllykangas-Luosujarvi et al. (1999) showed that the life expectancy of patients with RA and amyloidosis is reduced by 7.7 years. The results of dialysis in patients with renal amyloidosis against the background of RA are worse than in patients with other chronic kidney diseases (Bergesio F., Ciciani A. M., Santostefano M. et al, 2007; Gabriel S., 2001).

Bohle et al. (1993) already emphasized that when the kidneys are involved, there is no complete parallelism between the clinical manifestations and the massiveness of amyloid deposition in the glomeruli. As indicated by O.S. Mueller (2007), E.T. Stoopler et al. (2003), accurate diagnosis of amyloidosis (100%) is possible only with the help of nephrobiopsy (NB).

There are isolated reports on the negative impact of moderate proteinuria (Shilov E.M., Tareeva I.E., Ivanov A.A. et al., 2002). The impact of hematuria on the course of glomerulonephritis is contradictory. According to E.M. Shilov et al. (2002), V.L. Duman et al. (2005), in IgA nephropathy, hematuria in the OAM of more than 50 erythrocytes in the field of vision worsens the prognosis, and macrohematuria worsens it even more. Many authors include age, male gender, RF, ESR, CRP and the use of corticosteroids (CS) among

other independent negative factors affecting the prognosis in patients with RA with kidney damage (Gabriel S., 2001; Frederick W. et al, 1994).

According to T. Sokka, T. Pincus (2008), the improvement of the clinical condition may be due to the fact that the tactics of RA treatment have changed, becoming more aggressive due to the use of methotrexate (MT) and other DMARDs. RA therapy, including gold salts, MT and biological agents, reduces mortality in patients with PA (Sokka T., Abelson B., Pincus T., 2008). HJ. Lachmann et al. (2007) believe that early and aggressive treatment of RA is the main one in the prevention of AA amyloidosis, which at low values of circulating SAA can even lead to regression of amyloid deposits, as well as affect survival.

The unfavorable prognostic significance of kidney damage in rheumatoid arthritis (RA) has actively attracted the attention of researchers in recent years [1]. One or another clinical variant of kidney involvement in the pathological process in rheumatoid arthritis is observed in most patients [2]. Various variants of kidney damage in rheumatoid arthritis have been described, in particular, glomerulonephritis, amyloidosis, vasculitis, as well as iatrogenic forms (analgesic tubulopathy, membranous nephropathy, etc.) [5]. It is noteworthy that in real clinical conditions, morphological verification of renal pathology in such patients may not be performed for a long time due to a number of objective reasons. Early manifestations of functional renal disorders, especially when moderate, do not always attract the attention of clinicians, while the progression of chronic kidney disease (CKD) in RA can be rapid, especially in old age, as well as in association with cardiovascular pathology [1,6].

According to some researchers, the development of CKD in RA may be associated with cardiovascular damage to a greater extent than with the activity of RA itself [6]. It is noteworthy that the volume of data on factors contributing to the development of cardiovascular pathology, as well as various types of nephropathy and chronic kidney disease in RA is insufficient, and the available information is scattered and somewhat contradictory [7, 10]. It is noteworthy that recently leading world experts have proposed to distinguish RA in elderly people - with an onset over 60 years old (the so-called elderly-onset rheumatoid arthritis) [11], and a tendency towards an increase in the incidence of this form has been noted [12].

This variant of the disease has some differences from RA with onset at a younger age (lower arthritis activity, more frequent seronegativity, usually a more favorable course), at the same time it should be noted that the features of the formation of cardiovascular and renal pathology both in early and late onset of RA continue to be studied.

Epidemiology of rheumatoid arthritis. RA is common in all countries of the world and in all climatic and geographical zones with a frequency of 0.5–1.3% (0.3–1.2%). As shown by foreign researchers, RA affects from 0.24 to 1% of the population [46]. According to WHO (World Health Organization) reports, over 20 million people worldwide suffer from RA [65]. A number of studies have found that the prevalence of RA is higher in cities than

in rural areas, which indicates the influence of differences in the environment [44]. The annual incidence of RA in the USA and Northern European countries is approximately 40 cases per 100 thousand population [25–57]. According to literary data, the annual incidence of RA is approximately 0.02% of the population [10. Kalyuzhina MI, Bukharova EO, Shatuta AYU, et al. Functional and morphological state of the kidneys in patients with rheumatoid arthritis // Bulletin of Siberian Medicine. 2009; 8 (4 (2)): 51-54. doi: 10.20538/1682-0363-2009-4 (2) -51-54 10]. Studies conducted in Russia show that the absolute number of adult patients with RA reaches 671 thousand people, and the relative prevalence of RA is 247 - 610 per 100 thousand of the population [37]. Approximately the same relative prevalence of RA is presented in another work [38]. According to the reports of the Republican Medical Information Center, in Kyrgyzstan in 2018, a total of 17,722 patients with RA were registered, and the prevalence was 415 per 100 thousand population [9]. As shown in Fig. 1, in recent years, the number of patients with musculoskeletal diseases has been growing in Kyrgyzstan, as in other CIS countries. Earlier, in the works of V.A. Nasonova, it was noted that RA is generally more common in women than in men (4:1). Moreover, in women, the incidence of RA increases with age [20]. In addition, a higher incidence of RA has been established among first-degree relatives of patients than in the general population. These data are fully confirmed at present [46]. Obviously, the prevalence of RA is twice as high in women as in men. The risk of developing RA is 3.6% in women and 1.7% in men. It is reported that one in 12 women and one in 20 men may develop an inflammatory autoimmune rheumatic disease during their lifetime [45]. A large study by A. Nakajima, R. Sakai, E. Inoue and Harigai M in Japan showed that the prevalence of RA is 0.65% [59]. As stated, in recent years, the number of patients with musculoskeletal diseases has been growing in Kyrgyzstan. If in 2014 the number of patients with musculoskeletal diseases was 859.5 per 100 thousand population, then in 2018 this figure increased to 1155.7 per 100 thousand population [9]. It is well known that RA is the leading cause of musculoskeletal diseases. In Kyrgyzstan, A.T. Mamasaidov made a great contribution to the development of clinical rheumatology. Thus, under the leadership of A.T. Mamasaidova studied lesions of the central nervous system, liver and some aspects of immunopathology in patients with RA [6, 11, 13, 15, 17, 18, 41, 42].

In recent years, the cost of medical care has increased significantly worldwide. All researchers recognize that diseases of the musculoskeletal system make the greatest contribution to the reduction and/or loss of working capacity. The above-mentioned study noted that with late diagnosis of RA, about 90% of patients lose their ability to work, a third of them become disabled [5]. The studies show that among 1,500 people with RA, 68% of patients had limitations in working capacity, and 2/3 of them were completely disabled. In 83.4% of cases, the causes of loss of working capacity were the recurrent course of RA and insufficient effectiveness of treatment [2, 37].

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