

Bibliografía

1. Ranganath VK, Maranian P, Elashoff DA, Woodworth T, Khanna D, Hahn T, *et al.* Comorbidities are associated with poorer outcomes in community patients with rheumatoid arthritis. *Rheumatology (Oxford)*. 2013;52:1809-17.
2. Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, *et al.* Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis*. 2014;73:62-8.
3. Peters MJ, Symmons DP, McCarey D, Dijkmans BA, Nicola P, Kvien TK, *et al.* EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. *Ann Rheum Dis*. 2010;69:325-31.
4. Turesson C, Jarenros A, Jacobsson L. Increased incidence of cardiovascular disease in patients with rheumatoid arthritis: results from a community based study. *Ann Rheum Dis*. 2004;63:952-5.
5. Turesson C, Matteson EL. Malignancy as a comorbidity in rheumatic diseases. *Rheumatology (Oxford)*. 2013;52:5-14.
6. Askling J, Forede CM, Brandt L, Baecklund E, Bertilsson L, Feltelius N, *et al.* Risks of solid cancers in patients with rheumatoid arthritis and after treatment with tumour necrosis factor antagonists. *Ann Rheum Dis*. 2005;64:1421-6.
7. Singh JA, Cameron C, Noorbaloochi S, Cullis T, Tucker M, Christensen R, *et al.* Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis. *Lancet*. 2015; 386:258-65.
8. Listing J, Strangfeld A, Kary S, Rau R, von Hinueber U, Stoyanova-Scholz M, *et al.* Infections in patients with rheumatoid arthritis treated with biologic agents. *Arthritis Rheumatol*. 2005;52:3403-12.
9. Gough AK, Lilley J, Eyre S, Holder RL, Emery P. Generalised bone loss in patients with early rheumatoid arthritis. *Lancet*. 1994;344:23-7.
10. Matcham F, Norton S, Scott DL, Steer S, Hotopf M. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. *Rheumatology (Oxford)*. 2016;55:268-78.
11. Norton S, Koduri G, Nikiphorou E, Dixey J, Williams P, Young A. A study of baseline prevalence and cumulative incidence of comorbidity and extra-articular manifestations in RA and their impact on outcome. *Rheumatology (Oxford)*. 2013;52:99-110.
12. Radner H, Smolen JS, Aletaha D. Impact of comorbidity on physical function in patients with rheumatoid arthritis. *Ann Rheum Dis*. 2010;69:536-41.
13. Geryk LL, Carpenter DM, Blalock SJ, DeVellis RF, Jordan JM. The impact of co-morbidity on health-related quality of life in rheumatoid arthritis and osteoarthritis patients. *Clin Exp Rheumatol*. 2015;33:366-74.
14. Gabriel SE, Crowson CS, O'Fallon WM. Comorbidity in arthritis. *J Rheumatol*. 1999;26:2475-9.
15. Baillet A, Gossec L, Carmona L, Wit M, van Eijk-Hustings Y, Bertheussen H, *et al.* Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. *Ann Rheum Dis*. 2016;75:965-73.
16. Choy E, Ganeshalingam K, Semb AG, Szekanecz Z, Nurmohamed M. Cardiovascular risk in rheumatoid arthritis: recent advances in the understanding of the pivotal role of inflammation, risk predictors and the impact of treatment. *Rheumatology (Oxford)*. 2014;53:2143-54.
17. Yeh ET. CRP as a mediator of disease. *Circulation*. 2004;109:II- 11-4.
18. Ridker PM, Cook N. Clinical usefulness of very high and very low levels of C-reactive protein across the full range of Framingham Risk Scores. *Circulation*. 2004;109:1955-9.
19. Ridker PM, Rifai N, Stampfer MJ, Hennekens CH. Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation*. 2000;101:1767-72.
20. Biasucci LM, Liuzzo G, Fantuzzi G, Caligiuri G, Rebuffi AG, Ginnetti F, *et al.* Increasing levels of interleukin (IL)-1Ra and IL-6 during the first 2 days of hospitalization in unstable angina are associated with increased risk of in-hospital coronary events. *Circulation*. 1999;99:2079-84.
21. Gabay C, Msihid J, Paccard C, Zilberstein M, Graham NM, Boyapati A. Sarilumab significantly suppress circulating biomarkers of bone resorption and cardiovascular risk compared with adalimumab: biomarker analysis from the phase 3 MONARCH study. *Ann Rheum Dis*. 2017;76:570.
22. Giles GT, Sttar N, Gabriel S, Ridker PM, Gay S, Warne C, *et al.* Cardiovascular Safety of Tocilizumab Versus Etanercept in Rheumatoid Arthritis: A Randomized Controlled Trial. *Arthritis Rheumatol*. 2019;72:31-40.
23. Dixon WG, Watson KD, Lunt M, Hyrich KL, British Society for Rheumatology Biologics Register Control Centre Consortium,
24. Silman AJ, *et al.* Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor α therapy: Results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum*. 2007;56:2905-12.
25. Levitsky A, Brismar K, Hafström I, Hambardzumyan K, Lourduoss C, van Vollenhoven RF, *et al.* Obesity is a strong predictor of worse clinical outcomes and treatment responses in early rheumatoid arthritis: results from the SWEFOT trial. *RMD Open*. 2017;3:e000458.

26. Nikiphorou E, Norton S, Young A, Dixey J, Walsh D, Helliwell H, *et al.* The association of obesity with disease activity, functional ability and quality of life in early rheumatoid arthritis: data from the Early Rheumatoid Arthritis Study/Early Rheumatoid Arthritis Network UK prospective cohorts. *Rheumatology (Oxford)*. 2018;57:1194-02.
27. Schulman E, Bartlett SJ, Schieir O, Andersen KM, Boire G, Pope JE, *et al.* Overweight, Obesity, and the Likelihood of Achieving Sustained Remission in Early Rheumatoid Arthritis: Results From a Multicenter Prospective Cohort Study. *Arthritis Care Res (Hoboken)*. 2018;70:1185-91.
28. Liu Y, Hazlewood GS, Kaplan GG, Eksteen B, Barnabe C. Impact of Obesity on Remission and Disease Activity in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. *Arthritis Care Res (Hoboken)*. 2017;69:157-65.
29. Balsa A, Lojo-Oliveira L, Alperi M, García M, Ordoñez C, Pérez L, *et al.* Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring in clinical practice: the Spanish cohort of the COMORA study. *Reumatol Clin*. 2017;15:102-8.
30. Abella V, Scotece M, Conde J, Pino J, Gonzalez-Gay MA, Gómez-Reino JJ, *et al.* Leptin in the interplay of inflammation, metabolism and immune system disorders. *Nat Rev Rheumatol*. 2017;13:100-9.
31. George MD, Østergaard M, Conaghan PG, Emery P, Baker DG, Baker JF. Obesity and rates of clinical remission and low MRI inflammation in rheumatoid arthritis. *Ann Rheum Dis*. 2017;76:1743-6.
32. Kearsley-Fleet L, Davies R, De Cock D, Watson KD, Lunt M, Buch MH, *et al.* Biologic refractory disease in rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. *Ann Rheum Dis*. 2018;77:1405- 12.
33. Singh S, Facciorusso A, Singh AG, Vande Casteele N, Zarrinpar A, Prokop LJ, *et al.* Obesity and response to anti-tumor necrosis factor- α agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. *PLoS One*. 2018;13:e0195123.
34. Arad Uand, Elkayam O. Association of Serum Tocilizumab Trough Concentrations with Clinical Disease Activity Index Scores in Adult Patients with Rheumatoid Arthritis. *J Rheumatol*. 2019;46:1577-81.
35. Genovese MC, Fleischmann R, Mangan E, van Adelsberg J, Iglesias-Rodriguez M, Dukovic D, *et al.* Efficacy and Safety of Sarilumab in Subgroups of Patients with Rheumatoid Arthritis from 2 Phase 3 Studies. [Abstract 1632]. *Arthritis Rheumatol*. 2016;68:2032.
36. De Benedetti F, Rucci N, Del FA, Peruzzi B, Paro R, Longo M, *et al.* Impaired skeletal development in interleukin-6-transgenic mice: a model for the impact of chronic inflammation on the growing skeletal system. *Arthritis Rheum*. 2006;54:3551-63.
37. Abdel Meguid MH, Hamad YH, Swilam RS, Barakat MS. Relation of interleukin-6 in rheumatoid arthritis patients to systemic bone loss and structural bone damage. *Rheumatol Int*. 2013;33:697-703.
38. Zerbini CAF, Clark P, Mendez-Sanchez L, Pereira RMR, Messina OD, Uña CR, Adachi JD, *et al.* Biologic therapies and bone loss in rheumatoid arthritis. *Osteoporosis Int*. 2017;28:429-46.
39. Aurrecochea E, Llorca Díaz J, Diez Lizuain ML, McGwin G Jr, Calvo-Alen J. Gender-associated comorbidities in rheumatoid arthritis and their impact on outcome: data from GENIRA. *Rheumatol Int*. 2017;37:479-85.
40. Hodes GH, Menard C, Russo SJ. Integrating Interleukin-6 into depression diagnosis and treatment. *Neurobiol Stress*. 2016;4:15- 22.
41. Dowlati,Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, *et al.* A meta-analysis of cytokines in major depression. *Biol Psychiatry*. 2010;67:446-57.
42. Haapakoski R, Mathieu J, Ebmeier KP, Alenius H, Kivimäki M. Cumulative meta-analysis of interleukins 6 and 1 β , tumour necrosis factor alpha and C-reactive protein in patients with major depressive disorder. *Brain Behav Immun*. 2015;49:206-15.
43. Smolen JS, Weinblatt ME, Sheng S, Zhuang Y, Hsu B. Sirukumab, a human anti-interleukin-6 monoclonal antibody: a randomised, 2-part (proof-of concept and dose finding), phase II study in patients with active rheumatoid arthritis despite methotrexate therapy. *Ann Rheum Dis*. 2014;73:1616-25.
44. Corominas H, Alegre C, Narváez J, Fernández-Cid CM, Torrente- Segarra V, Gómez MR, *et al.* Correlation of fatigue with other disease related and psychosocial factors in patients with rheumatoid arthritis treated with tocilizumab: ACT-AXIS study. *Medicine (Baltimore)*. 2019;98:e15947.
45. Strand V, Hagino O, Guillonneau S, Boklage S, Reaney M, Sadeh J, *et al.* Depressive symptoms in patients with rheumatoid arthritis in sarilumab target and mobility trials and impact of treatment. *Ann Rheum Dis*. 2018;77:964.
46. Strand V, Hagino O, Guillonneau S, Boklage S, Reaney M, Sadeh J, *et al.* Impact of treatment in patients with rheumatoid arthritis and depressive symptoms in the MONARCH phase 3 trial of sarilumab. *Ann Rheum Dis*. 2018;77:332.
47. Kim SC, Pawar A, Desai RJ, Solomon DH, Gale S, Bao M, *et al.* Risk of malignancy associated with use of tocilizumab versus other biologics in patients with rheumatoid arthritis: A multi-database cohort study. *Semin Arthritis Rheum*. 2019;49:222-8.
48. Mori S, Yoshitama T, Hidaka T, Sakai F, Hasegawa M, Hashiba Y, *et al.* Comparative risk of hospitalized infection between biological agents in rheumatoid arthritis patients: A multicenter retrospective cohort study in Japan. *PLoS One*. 2017;12:e0179179.
49. Grøn KL, Arkema EV, Glinthorg B, Mehnert F, Østergaard M, Dreyer L, *et al.* Risk of serious infections in patients with rheumatoid arthritis treated in routine care with abatacept, rituximab and tocilizumab in Denmark and Sweden. *Ann Rheum Dis*. 2019;78:320-7.

50. Pawar A, Desai RJ, Solomon DH, Santiago Ortiz AJ, Gale S, Bao M, *et al.* Risk of serious infections in tocilizumab versus other biologic drugs in patients with rheumatoid arthritis: a multidatabase cohort study. *Ann Rheum Dis.* 2019;78:456-64.
51. Lillegraven S, Greenberg JD, Reed GW, Saunders K, Curtis JR, Harrold L, *et al.* Immunosuppressive treatment and the risk of diabetes in rheumatoid arthritis. *PLoS One.* 2019;14:e0210459.
52. Castañeda S, Remuzgo-Martínez S, López-Mejías R, Genre F, Calvo-Alén J, Llorente I, *et al.* Rapid beneficial effect of the IL-6 receptor blockade on insulin resistance and insulin sensitivity in non-diabetic patients with rheumatoid arthritis. *Clin Exp Rheumatol.* 2019;37:465-73.
53. Genovese MC, Fleischmann R, Hagino O, Hu CC, Pena-Rossi C, Sadeh J, *et al.* The Effect of Sarilumab in Combination with Dmards on Fasting Glucose and Glycosylated Hemoglobin in Patients with Rheumatoid Arthritis with and without Diabetes. [Abstract 1822]. *Arthritis Rheumatol.* 2017;69:2651.
54. Nemeth E, Rivera S, Gabayan V, Keller C, Taudorf S, Pedersen BK, *et al.* IL-6 mediates hypoferrremia of inflammation by inducing the synthesis of the iron regulatory hormone hepcidin. *J Clin Invest.* 2004;113:1271-6.
55. Burmester GR, Hagino O, Dong Q, Stanislav M, Gomez-Centeno A, Selmi C, *et al.* Unique Changes in Hemoglobin with Sarilumab Versus Adalimumab Are Independent of Better Disease Control in Patients with Rheumatoid Arthritis (RA). [Abstract 1528]. *Arthritis Rheumatol.* 2018;70:1688.