

ROMATOİD ARTRİT HASTALARINDA İNSÜLİN DİRENCİ VE METABOLİK SENDROM SIKLIĞI

Yazar:

Nilüfer AYGÜN BİLECİK



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2. Bacon PA, Moots RJ. Extra-articular rheumatoid arthritis. In: Kopman WJ (Ed). *Arthritis and Allied Conditions*. 13th Ed, Pennsylvania: Williams and Wilkins 1997; 71: 1088.
3. Dedhia HV, DiBartolomeo A. Rheumatoid arthritis. Review. *Crit Care Clin* 2002; 18: 841-54.
4. Sattar N, McCarey WD, Capell H. Explaining how “high-grade” systemic inflammation accelerates vascular risk in rheumatoid arthritis. *Circulation* 2003; 108: 2957 – 63.
5. Mutru O, Laakso M, Isomaki H, Koota K. Cardiovascular mortality in patients with rheumatoid arthritis. *Cardiology* 1989; 76: 71-7.
6. Masharani U, Karam JH, Germen MS. Pancreatic hormones and diabetes mellitus. In: Greenspan FS, Gardner DG, editors. *Basic and Clinical Endocrinology*. 7th ed. New York: The McGraw-Hill Companies 2004; 646-58.
7. Henry RR. Insulin Resistance: From predisposing factor to therapeutic target in type 2 diabetes. *Clin Ther* 2003; 25(suppl): 47-63.
8. Nilsson S. Research contributions of Eskil Kylin *Sven Med Tidskr* 2001; 5(1): 15-28.
9. Enzi G, Busetto L, Inelmen EM, Coin A, Sergi G. Historical perspective: visceral obesity and related comorbidity in Joannes Baptista Morgagni's ‘De Sedibus et Causis Morborum per Anatomen Indagata’ *Int Journ of Obesity* 2003; 27: 534–5.

10. Chung CP, Avalos I, Oeser A, Gebretsadik T, Shintani A, Raggi P, et al. High prevalence of the metabolic syndrome in patients with systemic lupus erythematosus: association with disease characteristics and cardiovascular risk factors. *Ann Rheum Dis* 2007; 66: 208–14.
11. Rho YH, Choi SJ, Lee YH, Ji JD, Choi KM, Baik SH, et al. The prevalence of metabolic syndrome in patients with gout: a multicenter study. *J Korean Med Sci* 2005; 20: 1029–33.
12. Boyer GS, Lanier AP, Templin DW. Prevalence rates of spondyloarthropathies, rheumatoid arthritis, and other rheumatic disorders in an Alaskan Inupiat Eskimo population. *J Rheumatol* 1988; 15(4): 678-83.
13. Hochberg MC. Adult and juvenile rheumatoid arthritis: Current epidemiologic concepts. *Epidemiol Rev* 1981; 3: 27-44.
14. Spector TD. Rheumatoid arthritis. *Rheum Dis Clin North Am* 1990; 16(3): 513-37.
15. Beasley RP, Bennett PH, Lin CC. Low prevalence of rheumatoid arthritis in Chinese. Prevalence survey in a rural community. *J Rheumatol* 1983; (10 Suppl): 11-5.
16. Minaur N, Sawyers S, Parker J, Darmawan J. Rheumatic disease in an Australian 7-6 – Aboriginal community in North Queensland, Australia. A WHO-ILAR COPCORD study. *J Rheumatol* 2004; 31(5): 965-72.
17. MacGregor AJ, Snieder H, Rigby AS. Characterizing the quantitative genetic contribution to rheumatoid arthritis using data from twins. *Arthritis Rheum* 2000; 43(1): 30-7.
18. Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. *JAMA* 1949; 140: 659-62.
19. Bergstrom G, Bjelle A, Sorensen LB, Sundh V, Svanborg A. Prevalence of rheumatoid arthritis, osteoarthritis, chondrocalcinosis and gouty arthritis at age 79. *J Rheumatol* 1986; 13(3): 527-34.
20. Hochberg MC. Changes in the incidence and prevalence of rheumatoid arthritis in England and Wales, 1970-1982. *Semin Arthritis Rheum* 1990; 19(5): 294-302.
21. Criswell LA, Merlino LA, Cerhan JR, et al. Cigarette smoking and the risk of rheumatoid arthritis among postmenopausal women: results from the Iowa Women's Health Study. *Am J Medicine* 2002; 112: 465-71.
22. Huizinga TW. Genetics in rheumatoid arthritis. *Best Pract Res Clin Rheumatol* 2003; 17(5): 703-16.
23. Stastny P. Association of the B-cell alloantigen DRw4 with rheumatoid arthritis. *N Engl J Med* 1978; 298(16): 869-71.
24. Siman AJ, Pearson JE. Epidemiology and genetics in rheumatoid arthritis. *Arthritis Res* 2002; 4(suppl 3): 265-72.
25. Weyand CM. New insights into the pathogenesis of rheumatoid arthritis. *Rheumatology* 2000; 39(suppl 1): 3-8.
26. Goronzy JJ, Zettl A, Weyand CM. T cell receptor repertoire in rheumatoid arthritis. *Int Rev Immunol* 1998; 17: 339-63.

27. Inman RD. Infectious etiology of rheumatoid arthritis. *Rheum Dis Clin North Am* 1991; 17(4): 859-70.
28. Van Der Heijde IM, Wilbrink B, Tchetverikov I. Presence of bacterial and bacterial proteoglycans in the joints of patients with rheumatoid arthritis and other arthritides. *Arthritis Rheum* 1998; 41: 162.
29. Hoffman RW, O'Sullivan FX, Schafermeyer KR. Mycoplasma infection and rheumatoid arthritis: Analysis of their relationship using immunoblotting and ultrasensitive PCR detection method. *Arthritis Rheum* 1997; 40: 1219.
30. Depper JM, Zvaifler NJ. Epstein-Barr virus: Is relationship to the pathogenesis of rheumatoid arthritis. *Arthritis Rheum* 1981; 24(6): 755-61.
31. Balandraud N, Meynard JB, Auger I, Sovran H. Epstein-Barr virus load in the peripheral polymerase chain reaction. *Arthritis Rheum* 2003; 48(5): 1223-8.
32. Cohen BJ, Buckley MM, Clewley JP, Jones VE. Human parvovirus infection in early rheumatoid and inflammatory arthritis. *Ann Rheum Dis* 1986; 45(10): 832-8.
33. Nikkari S, Luukkainen R, Mottonen T, Meurman O. Does parvovirus B19 have a role in rheumatoid arthritis? *Ann Rheum Dis* 1994; 53(2): 106-11.
34. Lechner F, Vogt HR, Seow HF. Expression of cytokine mRNA in lentovirus-induced arthritis. *Am J Pathol* 1997; 151: 1053.
35. Olsen NJ, Kovacs WJ. Hormones, pregnancy, and rheumatoid arthritis. *J Gend Specif Med* 2002; 5(4): 28-37.
36. Spector TD, Roman E, Silman AJ. The pill, parity, and rheumatoid arthritis. *Arthritis Rheum* 1990; 33(6): 782-9.
37. Silman A, Kay A, Brennan P. Timing of pregnancy in relation to the onset of rheumatoid arthritis. *Arthritis Rheum* 1992; 35(2): 152-5.
38. Persellin RH. The effect of pregnancy on rheumatoid arthritis. *Bull Rheum Dis* 1976 – 77; 27(9): 922-7.
39. Brennan P, Silman A. Breast-feeding and the onset of rheumatoid arthritis. *Arthritis Rheum* 1994; 37(6): 808-13.
40. Merlino LA, Cerhan JR, Criswell LA, Mikuls TR, Saag KG. Estrogen and other female reproductive risk factors are not strongly associated with the development of rheumatoid arthritis in elderly women. *Semin Arthritis Rheum* 2003; 33(2): 72-82.
41. Drossaers-Bakker KW, Zwinderman AH, van Zebe D, Breedveld FC, Hazes JM. Pregnancy and oral contraceptive use do not significantly influence outcome in long term rheumatoid arthritis. *Ann Rheum Dis* 2002; 61(5): 405-8.
42. Bresnihan B. Preventing joint damage as the best measure of biologic drug therapy. *J Rheumatol* 2002; 29(65) :39-43.
43. Hale LP, Haynes BF. Pathology of rheumatoid arthritis and associated disorders. In Koopman WJ (ed). *Arthritis and allied conditions*. Lippincott Williams and Wilkins, Philadelphia 2001; 1103-27.

44. Strand V, Kavanaugh AF. The role of interleukin-1 in bone resorption in rheumatoid arthritis. *Rheumatology (Oxford)* 2004; 43(Suppl-3): III10-III16.
45. Dayer JM. The process of identifying and understanding cytokines: from basic studies to treating rheumatic diseases. *Best Pract Res Clin Rheum* 2004; 18(1): 31-45.
46. Martel W, Hayes JT, Duff IF. The pattern of bone erosion in the hand and wrist in rheumatoid arthritis. *Radiology* 1965; 84: 204-14.
47. Goldring SR. Bone and joint destruction in rheumatoid arthritis: what is really happening? *J Rheumatol* 2002; 29 Suppl 65: 44-8.
48. Oelzner P, Franke S, Muller A, Hein G, Stein G. Relationship between soluble markers of immune activation and bone turnover in post-menopausal women with rheumatoid arthritis. *Rheumatology (Oxford)* 1999; 38(9): 841-7.
49. Lohmander LS, Hoerrner LA, Lark MW. Metalloproteinases, tissue inhibitors and proteoglycan fragments in knee synovial fluid in human osteoarthritis. *Arthritis Rheum* 1993; 36: 181-9.
50. Jofe I, Epstein S. Osteoporosis associated with rheumatoid arthritis: pathogenesis and management. *Semin Arthritis Rheum* 1991; 20: 256-72.
51. Deodhar AA, Woolf AD. Bone mass measurement and bone metabolism in rheumatoid arthritis: A review. *Br J Rheumatol* 1996; 35: 309-22.
52. Woolf AD. Osteoporosis in rheumatoid arthritis-the critical view point. *Br J Rheumatol* 1991; 30: 82-4.
53. Brown FE, Brown ML. Long-term results after tenosynovectomy to treat the rheumatoid hand. *J Hand Surg* 1988; 13 – A(5): 704-8.
54. Abhilash J, Fionula B, Jagdeep N. Treatment of rheumatoid tenosynovitis with cytokine inhibitors. *Lancet* 2002; 360: 1565-6.
55. Hagen FW, Hofmann GO, Mittlmeier T, Wasmer G, Bergmann M. The cruciate ligaments in knee replacement. *Int Orthop* 1989; 13(1): 13-6.
56. Neurath MF. Detection of Luse bodies, spiralled collagen, dysplastic collagen, and intracellular collagen in rheumatoid connective tissues: an electron microscopic study. *Ann Rheum Dis* 1993; 52(4): 278-84.
57. Wada M, Imura S, Baba H, Shimada S. Knee laxity in patients with osteoarthritis and rheumatoid arthritis. *Br J Rheumatol* 1996; 35: 560-3.
58. Recklies AD, Poole AR, Banerjee S. Pathophysiologic aspects of inflammation in diarthrodial joints. In Buckwalter JA, Einhorn TA, Simon SR (eds). *Orthopaedic Basic Science, American Academy of Orthopaedic Surgeons, Park Ridge, IL* 2000; 489-530.
59. Abramson SB, Amin A. Blocking the effects of IL-1 in rheumatoid arthritis protects bone and cartilage. *Rheumatology* 2002; 41: 972-80.
60. Johnson LL, Dyer R, Hupe DJ. Matrix metalloproteinases. *Curr Opin Chem Biol* 1998; 37: 466-71.

61. Nietfeld JJ, Wilbrink B, Helle M. Interleukin-1-induced interleukin-6 is required for the inhibition of proteoglycan synthesis by interleukin-1 in human articular cartilage. *Arthritis Rheum* 1990; 33(11): 1695-701.
62. Hauselmann HJ, Flechtenmacher J, Michal L. The superficial layer of human articular cartilage is more susceptible to interleukin-1-induced damage than the deeper layers. *Arthritis Rheum* 1996; 39: 478-88.
63. Firestein GS. Invasive fibroblast-like synovocytes in rheumatoid arthritis. Passive responders or transformed aggressors. *Arthritis Rheum* 1996; 39: 1781-90.
64. Bresnihan B. Pathogenesis of joint disease in RA. *J Rheumatol* 1999; 26(3): 717-9.
65. Burmester GR, Stuhlmüller B, Keyszer G, Kinne RW. Mononuclear phagocytes and rheumatoid arthritis. Mastermind or workhorse in arthritis? *Arthritis Rheum* 1997; 40: 5 – 18.
66. Hochberg MC, Chane RW, Dwosh I. The ACR 1991 revised criteria for the classification of the global functional status in rheumatoid arthritis. *Arthritis Rheum* 1992; 25: 498-502.
67. Arnett FC, Edworth SM, Bloch DA. The ARA 1987 revised criteria for classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31: 315-24.
68. Van der Heijde DMFM. Radiographic imaging: the “gold standard” for assessment of disease progression in rheumatoid arthritis. *Rheumatology* 2000; 39(suppl 1): 9-16.
69. Graudal N. The natural history and prognosis of rheumatoid arthritis: association of radiographic outcome with process variables, joint motion and immune proteins. *Scand J Rheumatol* 2004; 118: 1-38.
70. Kaarela K, Kautiainen H. Continuous progression of radiological destruction in seropositive rheumatoid arthritis. *J Rheumatol* 1997; 24(7): 1285-7.
71. De Carvalho A, Graudal H, Jorgensen B. Radiologic evaluation of the progression of rheumatoid arthritis. *Acta Radiol Diagn* 1980; 21(1): 115-21.
72. Sculco TP. The knee joint in rheumatoid arthritis. *Rheum Dis Clin North Am* 1998; 24(1): 143-56.
73. Magyar E, Talerma A, Feher M, Wouters HW. The pathogenesis of the subchondral pseudocyst in rheumatoid arthritis. *Clin Orthop* 1974; 100: 341-8.
74. Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. *JAMA* 1949; 140: 59-62.
75. Conaghan PG, McGonagle D, Wakefield R, Emery P. New approaches in imaging of early rheumatoid arthritis. *Clin Exp Rheumatol* 1999; 17(6 suppl 18): 37-42.
76. Chen TS, Cruess JV 3rd, Ali M, Troum OM. Magnetic resonance imaging is more sensitive than radiographs in detecting change in size of erosions in rheumatoid arthritis. *J Rheumatol* 2006; 33(10): 1957-67.

77. Gonzalez-Juanatey C, Testa A, Garcia-Castelo A, Garcia-Porrua C, Llorca J, Gonzalez – Gay MA. Active but transient improvement of endothelial function in rheumatoid arthritis patients undergoing long-term treatment with anti-tumor necrosis factor alpha antibody. *Arthritis Rheum* 2004; 51: 447-50.
78. Gonzalez-Juanatey C, Gonzalez-Gay MA. Long-term rheumatoid arthritis and endothelial dysfunction. *Atherosclerosis* 2004; 176: 197-8.
79. Hurlimann D, Forster A, Noll G, Enseleit F, Chenevard R, Distler O, et al. Anti-tumor necrosis factor-alpha treatment improves endothelial function in patients with rheumatoid arthritis. *Circulation* 2002; 106: 2184-7.
80. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. *Arterioscler Thromb* 1991; 11:1245-9. Sattar N, McCarey DW, Capell H, McInnes IB inflammation accelerates vascular risk in rheumatoid arthritis. *Circulation* 2003; 108: 2957 – 63.
81. ACR 2008 Recommendations, *Arthritis& Rheum* 2008.
82. Grundy, SM, Cleeman, JJ, Daniels, SR. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005; 112:2735. (2001 kriterlerinin UPDATE'i)
83. Alberti KG, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group The metabolic syndrome-a new worldwide definition. *Lancet* 2005; 366(9491): 1059-62.
84. The pathogenesis of atherosclerosis. In Braunwald E, Fauci A, Kasper D, Hauser S, Longo Dan L, Jameson Larry J (Eds.). *Harrison's principles of internal medicine* 15th ed. New York: Mc Graw Hill Co 2001; 1377-86.
85. Martel W, Hayes JT, Duff IF. The pattern of bone erosion in the hand and wrist in rheumatoid arthritis. *Radiology* 1965; 84: 204-14.
86. Graudal N. The natural history and prognosis of rheumatoid arthritis: association of radiographic outcome with process variables, joint motion and immune proteins. *Scand J Rheumatol* 2004; 118: 1-38.
87. Kaarela K, Kautiainen H. Continuous progression of radiological destruction in seropositive rheumatoid arthritis. *J Rheumatol* 1997; 24(7): 1285-7.
88. De Carvalho A, Graudal H, Jorgensen B. Radiologic evaluation of the progression of rheumatoid arthritis. *Acta Radiol Diagn* 1980; 21(1): 115-21.
89. Rajavashisth TB, Liao JK, Galis ZS, Tripathi S, Laufs U, Tripathi J, et al. Inflammatory cytokines and oxidized low density lipoproteins increase endothelial cell expression metalloproteinase. *J Biol Chem* 274: 11924–11929,1999. Ram M, Sherer Y, Shoenfeld Y. Matrix metalloproteinase-9 and autoimmune 89 77. *Ann Intern Med* 144:249.
90. Grundy, SM, Cleeman, JJ, Daniels, SR. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005; 112:2735. (2001 kriterlerinin UPDATE'i)

91. Alberti KG, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group The metabolic syndrome--a new worldwide definition. *Lancet* 2005; 366(9491): 1059-62.
92. The pathogenesis of atherosclerosis. In Braunwald E, Fauci A, Kasper D, Hauser S, Longo Dan L, Jameson Larry J (Eds.). *Harrison's principles of internal medicine* 15th ed. New York: Mc Graw Hill Co 2001; 1377-86.
93. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications; Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva: WHO Department of Noncommunicable Disease Surveillance; 1999. http://www.diabetes.com.au/pdf/who_report.pdf
94. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European group for the study of Insulin Resistance (EGIR) *Diabet Med* 1999; 16(5): 442-3.
95. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications; Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva: WHO Department of Noncommunicable Disease Surveillance; 1999.
96. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European group for the study of Insulin Resistance (EGIR) *Diabet Med* 1999; 16(5): 442-3.
97. Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486-7.
98. Strazzullo P, Barbato A, Siani A. Diagnostic criteria for metabolic syndrome: a comparative analysis in an unselected sample of adult male population *Metabolism Clinana Experimental* 2008; 57: 355-61.
99. Einhorn D, Reaven GM, Cobin RH, Ford E, Ganda OP, Handelsman Y et al. American College of Endocrinology position statement on the insulin resistance syndrome. *Endocr Pract* 2003; 9(3): 237-52.
100. International Diabetes Federation. Worldwide definition of the metabolic syndrome http://www.idf.org/webdata/docs/MetS_def_update2006.pdf
101. Onat A, Senocak M. Obesity in Turkish adults: prevalence, validity as a coronary risk factor and interrelation with other risk factors. *Int J Ang* 1995; 4: 94-8.
102. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/ National Heart, Lung and Blood Insitute Scientific Statement. *Circulation* 2005; 112: 2735-52.
103. Sanisoglu SY, Oktenli C, Hasimi A. Prevalence of metabolic syndrome-related disorders in large adult population in Turkey. *BMC Public Health* 2006; 6: 92-3.

104. Turkoglu Ç. [Editorial] Metabolik sendrom ve Koroner Kalp Hastalığı Anadolu Kardiyol Derg 2004; 4: 17-8.
105. Iwai N, Tago N, Yasui N, Kokubo Y, Inamoto N, Tomoike H, Shioji K Genetic analysis of 22 candidate genes for hypertension in the Japanese population Journal of Hypertension 2004; 22(6): 1119-26.
106. Isıldak M, Sain Güven G, Gürlek A. Metabolik sendrom ve insulin direnci Hacettepe Tıp Dergisi 2004; 35: 96-9.
107. Haslam DW, James WP. Obesity. Lancet 2005; 366: 1197-209.
108. Waki H, Tontonoz P, Endocrine Functions of Adipose Tissue Annu Rev Pathol Mech Dis 2007; 2: 315-6.
109. Undurti N. Das, Metabolic Syndrome X: An Inflammatory Condition? Current Hypertension Reports 2004; 6: 66-73.
110. Allison DB, Heshka S. Toward an empirically derived typology of obese persons. Int J Obes 1991; 15: 741-54.
111. You T, Nicklas BJ. Effects of Exercise on Adipokines and the Metabolic Syndrome Current Diabetes Reports 2008; 8: 7-11.
112. Hamid YH, Rose CS, Urhammer SA, Glümer C, Kristiansen OP, et al Variations of the interleukin-6 promoter are associated with features of the metabolic syndrome in Caucasian Danes Diabetologia 2005; 48: 251-60.
113. Pearson T, Mensah AG, Alexander WR. Markers of inflammation and cardiovascular disease. Circulation 2003; 107: 499-511.
114. Ridker M, Hennekens CH, Buring JE. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women N Engl J Med 2000; 342: 836-43.
115. Timpson NJ. C-reactive-protein and it's role in metabolic syndrome mendelian randomisation study Lancet 2005; 366: 1954-9.
116. Florez H. C-reactive protein is elevated in obese patients with the metabolic syndrome Diabetes Research and Clinical Practise 2006; 71: 92-100.
117. Anand SS, Razak F, Yi Q. C-reactive protein as a screening test for cardiovascular risk in a multi ethnic population. Arterioscler Thromb Vasc Biol 2004; 24: 1509-15.
118. Pearson T, Mensah AG, Alexander WR. Markers of inflammation and cardiovascular disease. Circulation 2003; 107: 499-511.
119. Hergenç G, Onat A. Toplumumuzda Ürik Asid Düzeyleri: Metabolik Sendromun bir belirleyicisi ve koroner hastalığın özellikle kadınlarda bir göstergesi. Türk Kardiyol Dern Ars 2004; 32: 71-81.
120. Taniguchi Y, Hayashi T, Tsumura K, Endo G, Fuji S, Okada K. Serum uric acid and the risk for hypertension and type 2 diabetes in Japanese men: the Osaka Health Survey. J Hypertens 2001; 19: 1209-15. Fang J, Alderman MH Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. JAMA 2000; 283: 2404-10.

121. Franse LV, Pahor M, Di Bari M. Serum uric acid, diuretic treatment and risk of cardiovascular events in the Systolic Hypertension in the Elderly Program (SHEP). *J Hypertens* 2000; 18: 1149-54.
122. Culleton BF, Larson MG, Kannel WB, Levy D. Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. *Ann Intern Med* 1999; 131: 7-13.
123. Coban E, Sari R, Ozdogan M, Akcıt F. Levels of plasma fibrinogen and d-dimer in patients with impaired fasting glucose. *Exp Clin Endocrinol Diabetes* 2005; 113(1): 35 – 7.
124. Rantapaae-Dahlqvist S, Solveig DJ. Lipoprotein(a), lipids and lipoproteins in patients with rheumatoid arthritis. *Ann Rheum Dis* 1991; 50: 366-8.
125. Bacon AP, Moots JR. Extra-articular rheumatoid arthritis. In: Koopman JW (ed). *Arthritis and Allied Conditions. A Textbook of Rheumatology*. Baltimore: Williams and Wilkins 1997; 1071-88.
126. Lorber M, Aviram M, Linn S, Scharf Y, Brook JG. Hypocholesterolaemia and abnormal high density lipoprotein in rheumatoid arthritis. *Br J Rheum* 1985; 24: 250-5.
127. Lakatos J, Harsagyi A. Serum total, HDL, LDL-cholesterol and triglyceride levels in patients with rheumatoid arthritis. *Clin Biochem* 1988; 21: 93-6.
128. Chung CP, Oeser A, Solus* Cardiology An ASIR, single-chamber, rate-modulated pulse generator. See Pacemaker. JF, Avalos I, Gebretsadik T, Shintani A, et al. Prevalence of the metabolic syndrome is increased in rheumatoid arthritis and is associated with coronary atherosclerosis. *Atherosclerosis* 2007; 29.
129. Karimi M, Mazloomzadeh S, Kafan S, Amirmoqhadami H *Int J Rheum Dis*. 2011 Aug;14(3):248-54. doi: 10.1111/j.1756-185X.2011.01595.x. Epub 2011 Mar 14.
130. Sidiropoulos PI, Karvounaris SA, Boumpas DT. *Arthritis Res Ther*. 2008;10(3):207. Epub 2008 May 8.
131. Svenson KL, Lundqvist G, Wide L, Hallgren K. Impaired Glucose Handling in Active Rheumatoid Arthritis: Relationship to The Secretion of Insulin and Counter Regulatory Hormones *Metabolism* 1987; 36: 940-3.
132. Paoliss G, Valentini G, Giugliano D, Marazzo G, Tirri R, Gallo M, et al: Evidence for Peripheral Impaired Hadnling in patients with Coonective Tissue Diseases *Metabolism* 1991; 40: 902-7.
133. Hanh-Hung Dao1,2, Quan-Trung Do3, Junichi Sakamoto1Dao. *Arthritis Research & Therapy* 2010, 12:R218.
134. Lim S. C-reactive protein level as an independent risk factor of metabolic syndrome in the Korean population & CRP as risk factor of metabolic syndrome. *Diabetes Research and Clinical Practice* 2005; 70: 126–33.
135. Anand SS, Razak F, Yi Q. C-reactive protein as a screening test for cardiovascular risk in a multi ethnic population. *Arterioscler Thromb Vasc Biol* 2004; 24: 1509–15.

136. Gonzalez-Gay MA, Gonzalez-Juanatey C, Martin J. Rheumatoid arthritis: a disease associated with accelerated atherogenesis. *Semin Arthritis Rheum* 2005; 35: 8-17.
137. Laaksonen DE, Niskanen L, Nyyssönen K, Punnonen K, Tuomainen TP, Valkonen VP, Salonen R, Salonen JT. C-reactive protein and the development of the metabolic syndrome and diabetes in middle-aged men. *Diabetologia* 2004;47(8): 1403-10. Epub 2004 Jul 28.
138. Akbal A, Selçuk B, Gürcan A, Kurtaran A, Ersöz M, Akyüz M. 2009, Cilt 24, Sayı 4, Sayfa(lar) 202-205.
139. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. *Circ J* 2005; 69(8): 928-33.
140. Rathmann W, Funkhouser E, Dyer AR, Roseman JM. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. *Coronary Artery Risk Development in Young Adults. Ann Epidemiol* 1998; 8(4): 250-61.
141. Imperatore G, Riccardi G, Iovine C, Rivellese AA, Vaccaro O. Plasma fibrinogen: a new factor of the metabolic syndrome. *Diabetes Care* 1998; 21: 649-54.
142. Ford ES. The metabolic syndrome and C-reactive protein, fibrinogen, and leucocyte count: findings from the Third National Health and Nutrition Examination Survey. *Atherosclerosis* 2003; 168: 351-8.
143. Rumley A, Emberson JR, Wannamethee SG, Lennon L, Whincup PH, Lowe GD. Effects of older age on fibrin D-dimer, C-reactive protein, and other hemostatic and inflammatory variables in men aged 60-79 years. *J Thromb Haemost* 2006; 4: 982-7.
144. Metabolic syndrome in rheumatoid arthritis patients over the age of 60 – more than just an anti-inflammatory effect? A cross sectional study. Tracey E Toms 1,2, Vasileios F Panoulas1, Holly John1, Karen MJ Douglas1 and George D Kitas1,2 Received: 1 Apr 2009 Revisions requested: 11 May 2009 Revisions received: 22 Jun 2009 Accepted: 16 Jul 2009 Published: 16 Jul 2009 *Arthritis Research & Therapy* 2009, 11:R110 (doi:10.1186/ar2765)
145. Hurlimann D, Forster A, Noll G, Enseleit F, Chenevard R, Distler O, et al. Anti-tumor necrosis factor-alpha treatment improves endothelial function in patients with rheumatoid arthritis. *Circulation* 2002; 106: 2184-7.
146. Wek RC, Anthony TG. Obesity: stressing about unfolded proteins. *Nat Med* 2010; 16(4): 374-6. No abstract available. Erratum in: *Nat Med*. 2010 May;16(5):607.
147. Hurt-Camejo E, Paredes S, Masana L, Camejo G, Sartipy P, Rosengren B, et al. Elevated levels of small, low-density lipoprotein, any organic compound that is composed of both protein and the various fatty substances classed as lipids, including fatty acids and steroids such as cholesterol. with high affinity for arterial matrix components in patients with rheumatoid arthritis:

possible contribution of phospholipase A2 to this atherogenic atherogenic adj initiating, increasing, or accelerating atherogenesis. atherogenic adjective Referring to the ability to initiate or accelerate atherogenesis—the depositi- on of atheromas, lipids, and profile. *Arthritis Rheum* 2001; 44: 2761-7.

148. Munro R, Morrison E, McDonald AG, Hunter JA, Madhok R, Capell HA. Effect of disease modifying agents on the lipid profiles of patients with rheumatoid arthritis. *Ann Rheum Dis* 1997; 56: 374-7.