

Update in Cardiovascular Disease in Patients With Rheumatic Diseases

Patompong Ungprasert^{1,2}

¹Division of Rheumatology, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA. ²Department of medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Over the past few decades, an increased incidence of cardiovascular diseases among patients with rheumatic illnesses has been increasingly recognized. Chronic inflammation is believed to be the pathogenetic link. This review aims to summarize the up-to-date evidence of role of inflammation in the pathogenesis of premature atherosclerosis and recent epidemiological studies in this area. *Journal of Nature and Science*, 1(3):e59, 2015.

Rheumatic disease | Cardiovascular disease | Premature atherosclerosis | Epidemiology

Introduction

Increased incidence of cardiovascular disease (CVD) in patient with rheumatic diseases has been observed for over a decade. Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are the first two rheumatic disorders known to increase risk of coronary artery disease (CAD) and other CVD [1, 2]. Several subsequent epidemiological studies have demonstrated this increased risk among patients with other rheumatic diseases as well. The deleterious effect of chronic inflammation on endothelial cells has been shown to be the cornerstone of the mechanistic link [3]. This review aims to provide an up-to-date review of the pathogenesis of premature atherosclerosis in patients with selected autoimmune diseases as well as up-to-date summary of recent epidemiological studies.

Pathogenesis

The role of inflammation, the near-universal underlying process for autoimmune disorders, in the initiation and progression of atherosclerosis, the cornerstone of the pathogenesis of CVD, is well-recognized. It has been shown that endothelial dysfunction and direct endovascular injury from inflammatory cytokine, activated inflammatory cells and oxidative stress may accelerate the progression of atherosclerosis [4-8]. Furthermore, chronic inflammation has been demonstrated to promote the coagulation cascade, resulting in a hypercoagulable state [9, 10], another predisposing factor for the development of coronary artery disease and other CVD.

Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroid are two most commonly used drugs in patients with rheumatic diseases. Both medications are, however, notorious for their adverse effects [11-13], including on the cardiovascular system, which might be another contributory factor to the increased risk of CVD in these patients.

NSAIDs, particularly specific COX-2 inhibitor, have been shown to increase risk of myocardial infarction and ischemic stroke, resulting in a withdrawal of one COX-2 inhibitor (rofecoxib) from the market [14]. A recent meta-analysis also suggested that subjects who used NSAIDs had a higher risk of developing venous thromboembolism [15, 16].

The effect of corticosteroids might be relatively less clear as epidemiological studies assessing their cardiovascular effect in patients with chronic inflammatory diseases yielded inconsistent results [17-19]. Use of corticosteroids is associated with an increased prevalence of atherosclerotic risk factors, including diabetes mellitus, hypertension, and dyslipidemia [20]. However, their anti-inflammatory property might provide a cardiovascular protective effect in patients with chronic inflammatory disorders, particularly on endothelial function [21].

Rheumatoid arthritis

RA is one of the first rheumatic diseases found to have an increased cardiovascular burden [1]. A recent meta-analysis of 24 observational studies had demonstrated a 59% and 52% excess mortality from coronary artery disease (CAD) and cerebrovascular disease, respectively [22]. Another meta-analysis found that patients with RA had a higher risk of venous thromboembolism (VTE) compared with general population with the risk ratio (RR) of 1.96 [23, 24].

Psoriatic arthritis

Psoriasis is well-known for co-morbidity [25, 26]. Since the association between CVD and RA has been recognized, attention has turned to the seronegative arthritis, particularly psoriatic arthritis (PsA) as well. A recent large population-based has demonstrated a 24% excess incidence of CVD in patients with PsA [27].

Idiopathic inflammatory myositis

Idiopathic inflammatory myositis (IIM) is a group of autoimmune disorder characterized by inflammation of skeletal muscle [28]. Dermatomyositis and polymyositis are the major subtype of IIM [29, 30]. Increased risk of CAD, stroke and VTE has been shown in recent meta-analyses with RR of 2.24, 1.61 and 2.85, respectively [31-33].

Systemic sclerosis

Increased incidence of CAD was demonstrated in a meta-analysis with RR of 1.82 [34] while increased incidence of ischemic stroke was demonstrated in a large population-based study (RR of 1.43) [35].

Giant cell arteritis

Giant cell arteritis (GCA) is the most common form of vasculitis in Western countries and is characterized by medium and large-vessel granulomatous arteritis. GCA typically affects adults older than 50 years of age with a peak incidence among those aged 75-85 years [36]. Interestingly, a recent meta-analysis of six studies comprised of 10,868 patients did not find statistically significant elevated risk of CAD among patient with GCA [37]. One possible explanation for this negative result is related to a lower baseline CVD risk as several studies have found a lower prevalence of diabetes mellitus (DM) and dyslipidemia among patients with GCA compared with non-GCA controls [38-40].

Mixed connective tissue disease

Cardiac involvement is common in patients with mixed connective tissue disease (MCTD) [41]. However, with the rarity of the disease, there is not population-based study to assess CVD risk among patients with MCTD compared with general population.

Conflict of interest: No conflicts declared.

Corresponding Author: Patompong Ungprasert, MD.

200 1st street SW, Rochester, MN, USA. Tel 507-284-2511.

E-mail: Ungprasert.Patompong@mayo.edu;

P.Ungprasert@gmail.com.

© 2015 by the Journal of Nature and Science (JNSCI).

Summary

Cardiovascular complications are common in patients with rheumatic diseases. Physicians should be aware of this association,

and an appropriate management for conventional cardiovascular risk factor modification should be incorporated to the routine care for these patients.

- del Rincón ID, 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.
- Farhey Y, Hess EV. Accelerated atherosclerosis and coronary disease in SLE. *Lupus* 1997;6:572-7.
- Mason JC, Libby P. Cardiovascular disease in patients with chronic inflammation: mechanisms underlying premature cardiovascular events in rheumatologic conditions. *Eur Heart J* 2014 Nov 27. pii: ehu403. [Epub ahead of print]
- Ait-Oufella H, Sage AP, Mallat Z, et al. Adaptive (T and B cells) immunity and control by dendritic cells in atherosclerosis. *Circ Res* 2014;114:1640-60.
- Montecucco F, Mach F. Common inflammatory mediators orchestrate pathophysiological processes in rheumatoid arthritis and atherosclerosis. *Rheumatology (Oxford)* 2009;48:11-22.
- Rho YH, Chung CP, Oeser A, et al. Interaction between oxidative stress and high-density lipoprotein cholesterol is associated with severity of coronary artery calcification in rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2010;62:1473-80.
- Niessner A, Sato K, Chaikof EL, et al. Pathogen-sensing plasmacytoid dendritic cells stimulate cytotoxic T-cell function in atherosclerotic plaque through interferon-alpha. *Circulation* 2006;114:2482-9.
- Hansen S, Lassig G, Pistrosch E, et al. Endothelial dysfunction in young patients with long-term rheumatoid arthritis and low disease activity. *Atherosclerosis* 2003;170:177-80.
- Xu J, Lupu F, Esmen CT. Inflammation, innate immunity and blood coagulation. *Hamostaseologie* 2010;30:5-6, 8-9.
- Esmen CT. The interactions between inflammation and coagulation. *Br J Haematol* 2005;131:417-30.
- Ungprasert P, Kittanamongkolchai W, Price C, et al. What is the Safest non-steroidal anti-inflammatory drugs? *Am Med J* 2012;3:115-23.
- Ungprasert P, Permpalung N, Summachiwakij S, et al. A case of recurrent acute pancreatitis due to intra-articular corticosteroid injection. *JOP* 2014;15:208-9.
- Ungprasert P. Acute pancreatitis in an elderly patient following intra-articular administration: case report. *Reactions* 2014;1497:15-9.
- Bresalier RS, Sandler RS, Quan H, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Engl J Med* 2005;352:1092-102.
- Ungprasert P, Srivali N, Wijarnprecha K, et al. Non-steroidal anti-inflammatory drugs and risk of venous thromboembolism: a systematic review and meta-analysis. *Rheumatology (Oxford)* 2014 Sep 24. pii: keu408. [Epub ahead of print]
- Ungprasert P. NSAIDs increase the risk of VTE. *Reactions* 2014;1552:13.
- Wei L, MacDonald TM, Walker BR. Taking glucocorticoid by prescription is associated with subsequent cardiovascular disease. *Ann Intern Med* 2004;141: 764-70.
- Maradit-Kremers H, Reinalda MS, Crowson CS, et al. Glucocorticoids and cardiovascular and cerebrovascular events in polymyalgia rheumatic. *Arthritis Rheum* 2007;57:279-86.
- Toms TE, Panoulas VF, Douglas KM, et al. Lack of association between glucocorticoid use and presence of the metabolic syndrome in patients with rheumatoid arthritis: a cross-sectional study. *Arthritis Res Ther* 2008;10:R145.
- Sholter DE, Armstrong PW. Adverse effects of corticosteroids on cardiovascular system. *Can J Cardiol* 2000;16:505-11.
- Voisard R, Seitzer U, Baur R, et al. Corticosteroid agents inhibit proliferation of smooth muscle cells from human atherosclerotic arteries in vitro. *Int J Cardiol* 1994;43:257-67.
- Aviña-Zubieta JA, Choi HK, Sadatsafavi M, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Arthritis Rheum* 2008 ;59:1690-7.
- Ungprasert P, Srivali N, Spanuchart I, et al. Risk of venous thromboembolism in patients with rheumatoid arthritis: a systematic review and meta-analysis. *Clin Rheumatol* 2014;33:297-304.
- Ungprasert P, Srivali N, Spanuchart I, et al. Reply to the letter "Need for supplementary data in a recent meta-analysis about risk of venous thromboembolism in patients with rheumatoid arthritis". *Clin Rheumatol* 2014;33:1021-3.
- Ungprasert P, Sanguankeo A, Upala S, et al. Psoriasis and risk of venous thromboembolism: a systematic review and meta-analysis. *QJM* 2014;107:793-7.
- Wohlrab J, Fiedler G, Gerdes S, et al. Recommendations for detection of individual risk for comorbidities in patients with psoriasis. *Arch Dermatol Res* 2013;305:91-8.
- Ogdie A, Yu Y, Haynes K, et al. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study. *Ann Rheum Dis* 2015;74:326-32.
- Ungprasert P, Leeaphorn N, Hosiriluck N, et al. Clinical features of inflammatory myopathies and their association with malignancy: a systematic review in asian population. *ISRN Rheumatol* 2013;2013:509354.
- Ungprasert P, Leeaphorn N, Kue-A-Pai P, et al. Cryoglobulinemic glomerulonephritis in a patient with polymyositis. *Am J Med* 2014;127:e7-8.
- Ungprasert P, Bethina NK, Jones CH. Malignancy and idiopathic inflammatory myopathies. *N Am J Med Sci* 2013;5:569-72.
- Ungprasert P, Suksaranjit P, Spanuchart I, et al. Risk of coronary artery disease in patients with idiopathic inflammatory myopathies: a systematic review and meta-analysis of observational studies. *Semin Arthritis Rheum* 2014;44:63-7.
- Ungprasert P, Cheungpasitporn W, Wijarnprecha K, et al. Risk of ischemic stroke in patients with polymyositis and dermatomyositis: a systematic review and meta-analysis. *Rheumatol Int* 2014 Oct 30. [Epub ahead of print]
- Ungprasert P, Sanguankeo A. Risk of venous thromboembolism in patients with idiopathic inflammatory myositis: a systematic review and meta-analysis. *Rheumatol Int* 2014;34(10):1455-8.
- Ungprasert P, Charoenpong P, Ratanasrimetha P, et al. Risk of coronary artery disease in patients with systemic sclerosis: a systematic review and meta-analysis. *Clin Rheumatol* 2014;33:1099-104.
- Chiang CH, Liu CJ, Huang CC, et al. Systemic sclerosis and risk of ischaemic stroke: a nationwide cohort study. *Rheumatology (Oxford)* 2013;52:161-5.
- Ungprasert P, Sanguankeo A, Upala S, et al. Risk of malignancy in patients with giant cell arteritis and polymyalgia rheumatica: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2014;44:366-70.
- Ungprasert P, Koster MJ, Warrington KJ. Coronary artery disease in giant cell arteritis: A systematic review and meta-analysis. *Semin Arthritis Rheum* 2014 Oct 29. pii: S0049-0172(14)00251-0 [Epub ahead of print]
- Schmidt J, Kermani TA, Muratore F, et al. Statin use in giant cell arteritis: a retrospective study. *J Rheumatol* 2013;40:910-5.
- Gonzalez-Gay MA, Pineiro A, Gomez-Gigirey A, et al. Influence of traditional risk factors of atherosclerosis in the development of severe ischemic complications in giant cell arteritis. *Medicine* 2004;83:342-7.
- Gonzalez-Juanatey C, Lopez-Diaz MJ, Martin J, et al. Atherosclerosis in patients with biopsy-proven giant cell arteritis. *Arthritis Rheum* 2007;57:1481-6.
- Ungprasert P, Wannarong T, Panichsillapakit T, et al. Cardiac involvement in mixed connective tissue disease: a systematic review. *Int J Cardiol* 2014;171:326-30.