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Metabolic syndrome and its risk factors in Rheumatoid arthritis

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Abstract
Metabolic syndrome is clusters of dyslipidemia, obesity, hypertension, and diabetes mellitus. Its prevalence increases in autoimmune diseases as RA. Metabolic syndrome increases risk for cardiovascular diseases as ischemic heart disease, subclinical atherosclerosis, and hypertension, it is preferred to detect metabolic syndrome and risk factors for it in RA patients, to decreases risk for cardiovascular diseases and for better controlling of activity.

Keywords: Rheumatoid arthritis, metabolic syndrome, dyslipidemia, hypertension

Introduction
A systemic, chronic, inflaming, and autoimmune condition is rheumatoid arthritis (RA). It primarily impacts the synovial joints, causing bone erosion and cartilage degeneration that subsequently results in disability and impairment of function. However, every synovial joint might be impacted, RA primarily impacts the tiny joints of both feet and hands, often equally and symmetrical bilaterally. Since it affects the entire body, includes the lungs, heart, and eyes, it is a systemic illness. The intimal lining layer of the affected RA joints exhibits hyperplasia and the synovial lining exhibits enhanced cellularity [1]. Activated T cells, macrophages, monocytes, and neutrophils are the main cell types implicated in synovial inflammatory response. Increasing expression of adhesion molecules implicated in pro-inflammatory mediators like chemokines and cytokines occurs concurrently with increasing cellularity [2].
The metabolic syndrome (MetS) is a collection of medical conditions of metabolic basis that raises the chance of developing diabetes type 2 and cardiovascular illness. Resistance to insulin and Dyslipidemia, hypertension, increased waist circumference, and sedentary lifestyles are the major hazards of MetS [3].

Mechanism of MetS in RA
MetS incidence is currently demonstrated to rise with age, the existence of positive serology, or extra-articular symptoms. Numerous reasons, such as generalized inflammatory response, higher levels of pro-inflammatory cytokines, drugs utilized for treating RA, and other factors have been proposed for the occurrence of MetS in individuals with RA. A reduction in HDL has been linked to vitamin D insufficiency, much as corticosteroids cause dyslipidemia and decreased glucose metabolism, and TNF- and IL-6 antagonists may also cause dyslipidemia. Furthermore, being overweight is a consequence of immobility brought on by joint inflammation and abnormalities. Leptin, adiponetin, resistin, TNF-, IL-1, and IL6 are examples of the adipocytokines that the AT is known to release. Patients with RA have higher amounts of adipokines, which may play a role in the pathophysiology of the illness [4].

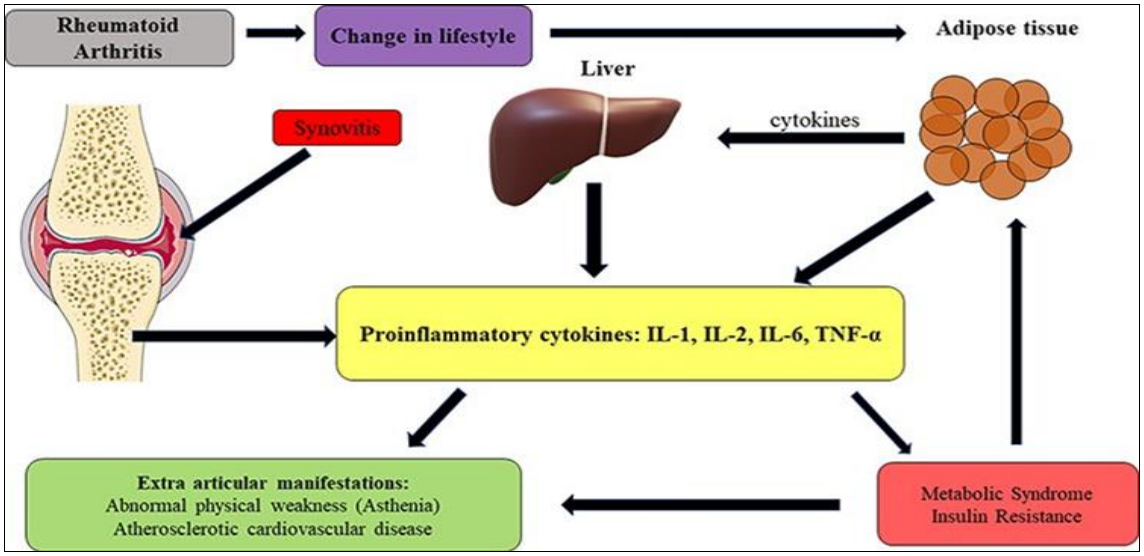

Fig 1: Mechanism of MetS in RA [5].

Risk factors for metabolic syndrome

1. Dyslipidemia

There are various mechanisms in which insulin resistance causes an atherogenic dyslipidemia. A defective insulin signaling causes lipolysis to rise, which raises FFA levels since insulin typically inhibits lipolysis in adipocytes. FFAs act as an ingredient for the production of TGs in the liver. The formation of apoB, the primary lipoprotein of very low-density lipoprotein (VLDL) particles, is stabilized by FFAs, increasing the amount of VLDL produced. Since apoB is generally destroyed by insulin via PI3K-dependent pathways, increased insulin resistance directly boosts the synthesis of VLDL [6].

2. Hypertension

Intolerance to glucose, obesity, and dyslipidemia are the three most prevalent metabolic disorders, which are all linked to hypertension. Studies indicate that both hyperglycemia and high insulin levels increase the production of angiotensinogen, which together may help people with resistance to insulin suffer hypertension by activating the renin-angiotensin-aldosterone system (RAAS). There is proof that hyperinsulinemia and resistance to insulin cause the sympathetic nervous system to become activated, which in turn causes the kidneys to absorb more salt, the heart to pump more blood, and the arteries to constrict, causing hypertension [7]. Adipocytes have recently been shown to also make aldosterone in reaction to adipose tissue. The adipocyte might be seen in this context as a tiny RAAS [8].

3. Diabetes mellitus

Diabetes of type 2 is regarded as a side effect of MetS. The probability for acquiring diabetes mellitus in those with poor glucose tolerance increases by twofold in an existence of MetS. Prediabetes and MetS most likely refer to the same illness since they use various biological markers to define it. When MetS is present, cardiovascular problems are more common than they are in people with diabetes mellitus who do not have MetS [9].

A varied mix of insulin resistance (mostly in the liver and muscles) and a reduction in insulin production by pancreatic beta cells make up the pathophysiology of diabetes mellitus. Both genetic and environmental variables may have an impact on both. The dysregulation of the production of hormones in the entero-insular and entero-hypothalamic axis, which emphasizes the various characteristics of the illness, is another modification that might be linked to the pathophysiology of diabetes mellitus [10].

4. Chronic stress and glucocorticoid actions (GCs)

Patients with a familial tendency to be subjected to a permissive environment may experience inadequate growth hormone release, chronic hypercortisolism, and hypogonadism, which may result in the accumulation of visceral fat. To encourage the differentiation of preadipocytes into adipocytes, which could raise body fat mass, GCs enhance the functions of enzymes that facilitate fatty acid production and encourage the secretion of lipoproteins which trigger the hepatic gluconeogenic pathway. They also inhibit adipocytes' uptake of insulin-stimulated amino acids and improve lipolysis or lipid oxidation, resulting in peripheral resistance to insulin. The frequency of MetS characteristics among these individuals, total urine GC metabolites, and plasma levels of cortisol all showed a strong association. The fasting glucose, systolic blood pressure, and insulin levels were all favorably linked with the secretion rate and peripheral clearance of cortisol in these individuals. As a consequence of these hormonal changes, hypertension, dyslipidemia, and DM are possible outcomes. They may also cause an increase in visceral obesity and sarcopenia, as well as a reactive insulin hypersecretion [11, 12].

5. Obesity

Central obesity is a significant aspect of the MetS, acting as both a symptom and a contributor to it due to the rising adiposity's correlation with high WC and reduced insulin sensitivity [13].

6. Smoking

Smoking has a substantial dose-dependent association with atherosclerotic and cardiovascular disorders. Endothelial and lipoprotein metabolism are disturbed in smokers. It is manifested by a slowed atherogenesis process, lower arterial compliance, and impaired endothelium-dependent vasodilation. (14) The endothelium is unable to function as it

should in terms of its normal physiological and defensive processes due to a number of causes, including oxidative stress, advanced glycation products, hyperglycemia, FFAs, and inflammatory cytokines or adipokines. Additionally, endothelial dysfunction and a proatherogenic vascular bed are caused by a decrease in nitric oxide, a crucial regulator of endothelial homeostasis, and a rise in reactive oxygen species [15].

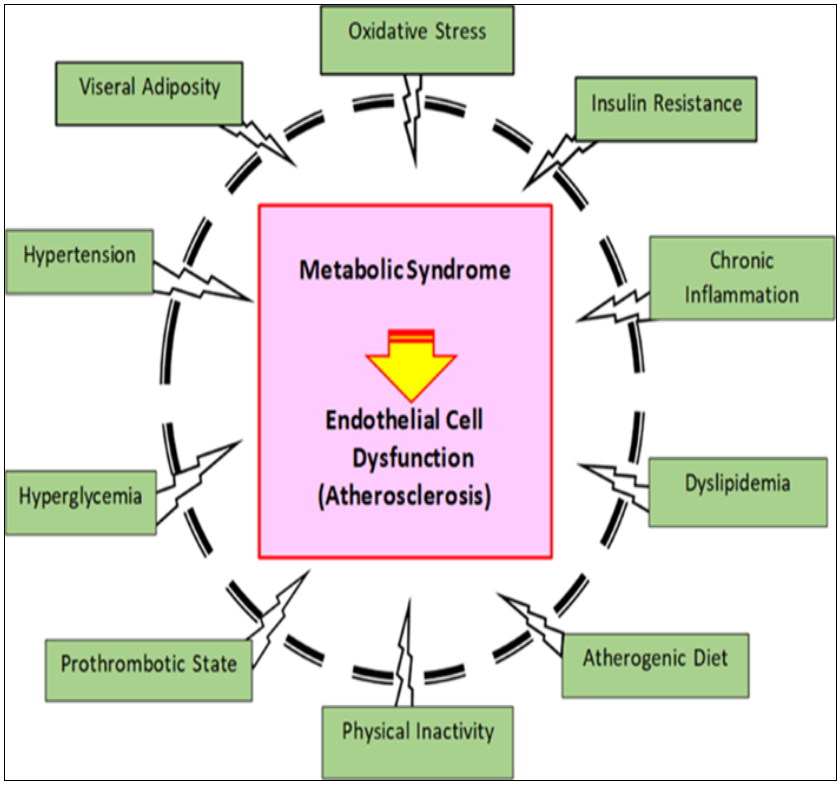

Fig 2: Risk factors for metabolic syndrome [16].

Metabolic syndrome and cardiac affection

The evaluation of carotid intimal medium thickness (IMT) may identify early subclinical atherosclerosis and raise the possibility of cardiovascular illnesses in individuals with RA. A higher risk for lesions of atherosclerosis and cardiovascular events was associated with rising levels in IMT, as measured in several vascular subjects. IMT is elevated in RA individuals and corresponds not only with conventional CV risk factors but additionally with the severity of the disease and its duration, GC usage, CRP or ESR levels, and von Willebrand factor values. Diastolic blood pressure, IR, and GC usage were the only independent indicators of an elevated IMT in individuals with RA. A higher IMT is an essential indicator of atherosclerotic plaques, according to almost all research that looked at their existence [17]. In individuals with early atherosclerosis, the examination of CIMT identifies thickening of the medial layer of the arterial wall and is a reliable predictor of cardiac events. Additionally, a few traditional CVD risk variables including age, hypertension, and dyslipidemia have been linked to increased CIMT. Changes in CIMT are the result of a series of actions that start with changes in NO bioavailability and endothelin-1 levels, that as time passes result in a rise in the generation of free radicals, inflammatory cytokines, adhesion molecules, and thrombotic factors that cause the proliferation of smooth muscle [18].

Carotid Artery Assessment by Ultrasound

The measurement of CIMT and evaluation of carotid artery plaque are two independent methodologies that have been utilized to determine CVD risk using carotid ultrasonography. CIMT values <0.8 mm is correlated with normal healthy people (Figure 3). While any intravascular abnormality measuring 1.5 mm or more or taking up more than 50% of the artery wall was carotid plaque. Individuals with plaque scores of 0, 1, 2, and 3 were categorized as having none, mild, moderate, or severe carotid atherosclerosis, correspondingly [19-20].

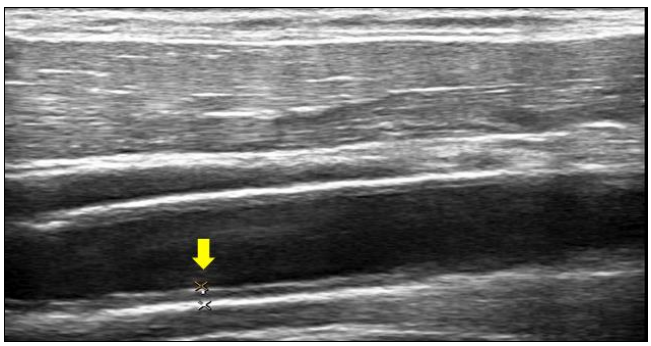

Fig 4: MSUS longitudinal scan of carotid artery showing increased thickness of intima-media in RA patient.

Carotid intima-media thickness represents morphologic process that while subintimal process, carotid plaque, might be more indicative of atherosclerosis than cardiovascular risk markers like hypertension [21, 22].

Conclusion

The CIMT is a fundamental tool to detect early subclinical atherosclerosis, especially in individuals with old age,

hypertension, high BMI especially increased WC, high disease activity and with longer duration of the disease.

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Conflict of Interest: Nil

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