

CARDIO ROUNDS NEWSLETTER

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IN THIS ISSUE

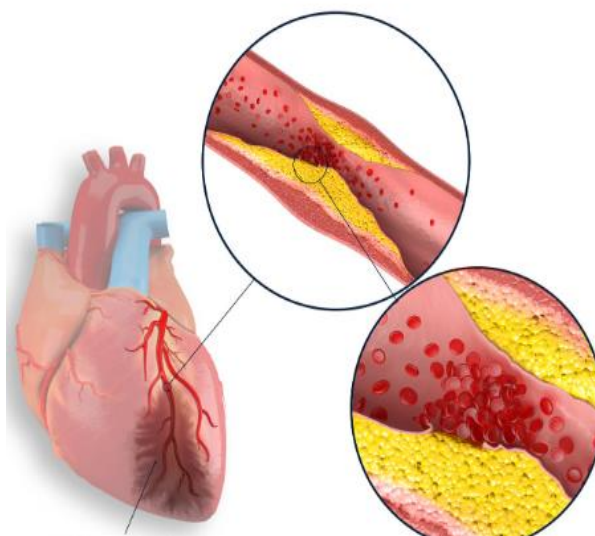
Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you “Cardio rounds” which contains latest and interesting news in the field of Cardiology

- **To Assess the Dual elevated remnant cholesterol and C-reactive protein in myocardial infarction, atherosclerotic cardiovascular disease, and mortality**
- **Evaluate The Association Between Retirement and Cardiovascular Disease: A Longitudinal Study.**
- **Assess the predictors of long-term absence of coronary artery calcium (CAC) in individuals with high Blood Pressure**
- **Mitochondrial Myopathy Presenting with Bilateral Lower Extremity Weakness and Swelling.**

To Assess the Dual elevated remnant cholesterol and C-reactive protein in myocardial infarction, atherosclerotic cardiovascular disease, and mortality

Introduction: Elevated remnant cholesterol and low-grade inflammation each by themselves are observationally and causally related with increased risk of myocardial infarction and atherosclerotic cardiovascular diseases and both are observationally connected with increased all-cause mortality¹. Remnant cholesterol is termed as the cholesterol content of a subset of the triglyceride-rich lipoproteins (TRLs) called remnants, which have increased in prevalence due to the global obesity and metabolic syndrome epidemic². Evidence from epidemiology and genetic studies indicated that remnant cholesterol was causally associated with cardiovascular disease (CVD) and all-cause mortality³. The aim of this study is to evaluate that dual 5 elevated remnant cholesterol and low-grade inflammation marked by elevated C-reactive protein is associated with the highest risk of myocardial infarction, ASCVD, and all-cause mortality.



Method: The Copenhagen General Population Study is a cohort study recruited at random 4 white Danish individuals aged 20-100 in 2003-2015 from the general population of the 5 greater Copenhagen area, using the national Danish Civil Registration System with a 43 % 6 participation rate. Information on lifestyle and medication was obtained through a 7 questionnaire. Plasma total cholesterol, HDL cholesterol, triglycerides, and high-sensitivity C-reactive 19 proteins were measured at baseline drawn at the same study visit using standard hospital 20 assays. Low-density lipoprotein (LDL) cholesterol was calculated by the Martin-Hopkins 21 method Atherosclerotic cardiovascular disease included cardiovascular mortality, non-fatal 17 myocardial infarctions, non-fatal stroke, and coronary revascularization.

Results: A median follow-up of 9.5 years in 103,221 individuals, 2,454 experienced myocardial infarctions, 5,437 experienced atherosclerotic cardiovascular diseases, and 10,521 died. Higher remnant cholesterol levels were associated with higher C-reactive protein levels, 13 unrelated to age, sex, and LDL cholesterol levels. Multivariable adjusted hazard ratios for myocardial infarction, atherosclerotic cardiovascular diseases, and all-cause mortality increased with both higher remnant cholesterol and higher C-reactive protein.

Compared to individuals in the lowest tertile of both remnant cholesterol and C2 reactive protein, the multivariable adjusted hazard ratios for myocardial infarction and all-cause mortality increased with both higher remnant cholesterol and higher C-reactive protein, free of each other. For the same reference group, in individuals with the highest tertile of both remnant cholesterol and C-reactive protein, the multivariable adjusted hazard ratios were 2.2 for

myocardial infarction and 1.4 for all-cause mortality. Corresponding values for only the highest tertile of remnant cholesterol were 1.6 and 1.1 and for only the highest tertile of C-reactive protein 1.7 and 1.3. Compared to individuals in the lowest tertile of both remnant cholesterol and C reactive protein, the multivariable adjusted hazard ratios for myocardial infarction and all-cause mortality improved with both higher remnant cholesterol and higher C-reactive protein as shown in figure 1.

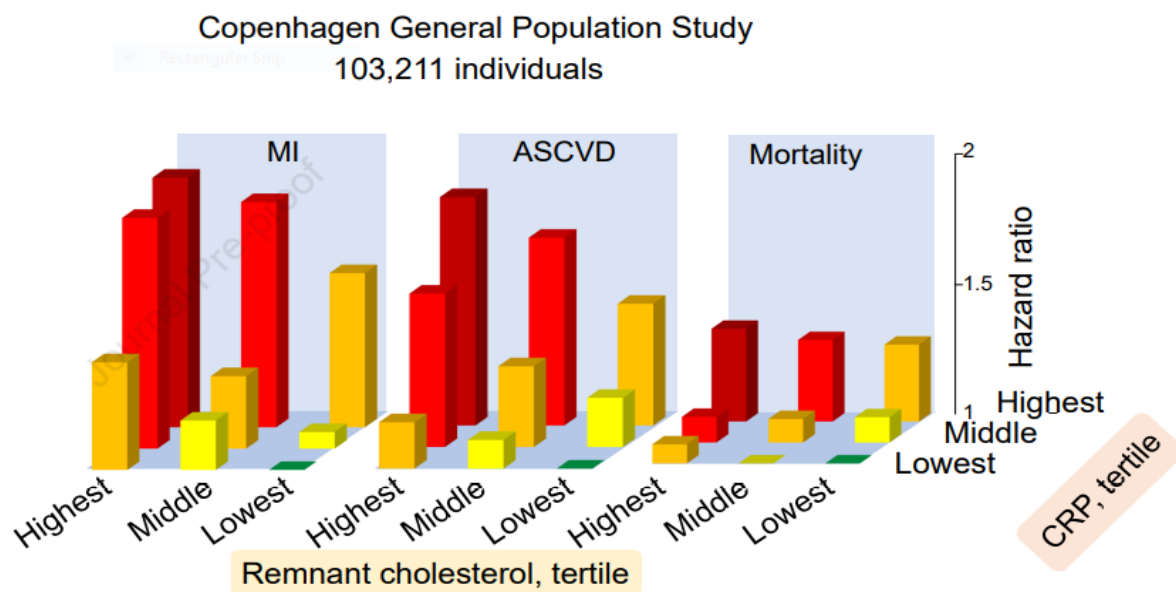


Figure 1 Elevated remnant cholesterol and C-reactive protein in morbidity and mortality.

Discussion:

Study found that Low-grade inflammation marked by elevated C-reactive protein adds predictive value to remnant cholesterol in determining risk of atherosclerotic cardiovascular disease and ultimately mortality. low-grade inflammation also plays an important role in arterial plaque formation, progression, and rupture that initiates myocardial infarction and Journal Pre-proof atherosclerotic cardiovascular disease⁴

Conclusion: Study concludes that dual elevated remnant cholesterol and C-reactive protein deliberate the highest risk of myocardial infarction, atherosclerotic cardiovascular disease, and all-cause mortalities, that is, compared to either of these two factors individually.

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Study concludes that dual elevated remnant cholesterol and C-reactive protein deliberate the highest risk of myocardial infarction, atherosclerotic cardiovascular disease, and all-cause mortalities, that is, compared to either of these two factors individually.

Evaluate The Association Between Retirement and Cardiovascular Disease: A Longitudinal Study

Introduction:

Worldwide, population aging has led to reduction ratios of workers to pensioners and people are now spending longer in retirement. Cardiovascular disease (CVD) ranks as the leading cause of mortality worldwide, killing 16.5 million people aged 55, some literatures have explored the association between retirement and CVD but these findings are not consistent¹. The potential health effects of retirement are largely neglected and studies found that retirees had a higher risk of being diagnosed with CVD than working people. Retirement may influence the development of CVD through behavioural pathways, such as changes in smoking, alcohol consumption, physical activity, and diet. The aim of this study is to investigate the association of retirement with CVD and various risk factors.

Method: Data comprised 396 904 observations from 106 927 unique individuals aged 50–70 years, with a mean follow-up period of 6.7 years. Fixed-effects instrumental variable regressions were performed using the State Pension Age (SPA) as an instrument. The outcomes comprised the occurrence of heart disease and stroke. A total of six CVD risk factors, namely hypertension, diabetes, obesity, physical inactivity, smoking and binge drinking were evaluated. Retirement status was analysed based on the harmonized variable of self-reported labour force status

Results:

A total of 106,927 individuals were followed up for a mean period of 6.7 year and the descriptive statistics by labour force status for 396 904 observations from 106 927 individuals, which consisted of 217 166 (54.7%) with working status and 179 738 (45.3%) with retired status. As shown in figure 2, subgroup analyses, some heterogeneous associations of retirement

with CVD and risk factors was established. People who retired over 5 years ago exhibited larger reductions in heart disease risks and physical inactivity, whereas those who retired within 5 years presented a clearer reduction in stroke, compared with their equivalent.

Study found 2.2%-point decrease in the risk of heart disease and a 3.0%-point decrease in physical inactivity among retirees, compared with workers. In both sexes, retirement was associated with a decreased heart disease risk. People with high educational levels showed relations between retirement and decreased risks of stroke, obesity and physical inactivity. People who retired from non-physical labour exhibited reduced risks of heart disease, obesity and physical inactivity, whereas those who retired from physical labour indicated an increased risk of obesity

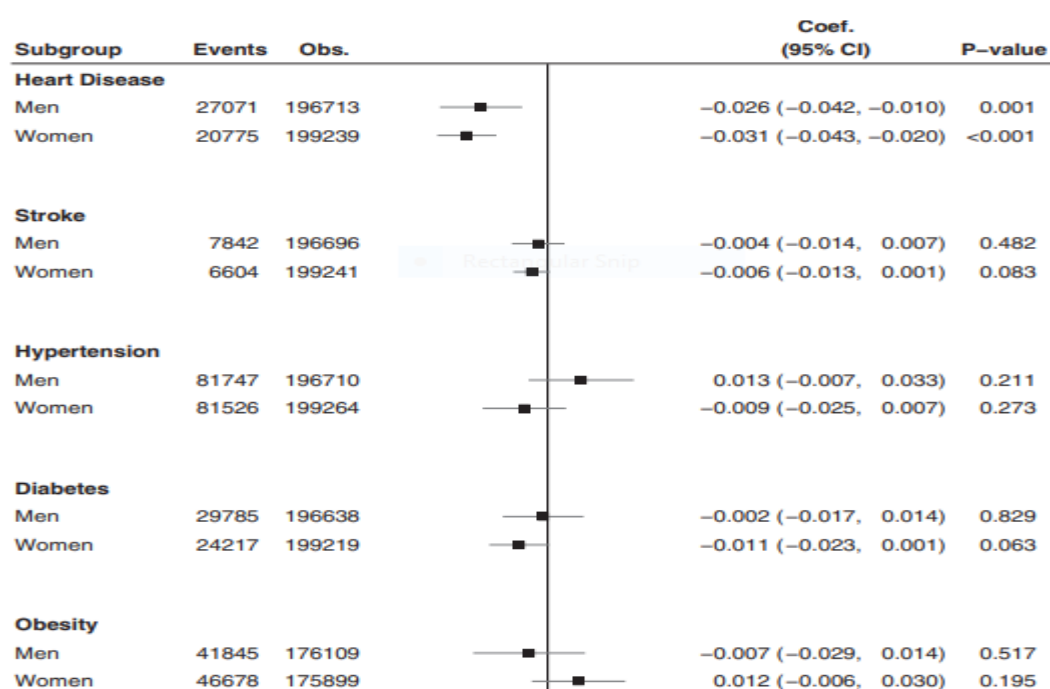


Figure 2 Analysis by sex for the association of retirement with cardiovascular diseases and risk factors

Discussion: Updated results and highlights the importance of reassessing the possible beneficial retirement effects on cardiovascular health. In this study FEIV models also presented decreased physical inactivity after retirement, consistent with previous findings³.

Conclusion:

The study concludes that retirement was associated with a decreased heart disease risk. Policy makers need to consider the benefits of raising SPA and allowing older people to continue working versus the costs.

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Assess the predictors of long-term absence of coronary artery calcium (CAC) in individuals with high Blood Pressure

Introduction:

Worldwide, High blood pressure (BP) is a major risk factor for atherosclerotic cardiovascular disease (ASCVD) accounting for an estimated 8.5 million deaths from stroke, coronary artery disease, other vascular diseases, and chronic kidney disease. Assessment of coronary artery calcium (CAC) is a highly specific feature of coronary atherosclerosis and a powerful tool for ASCVD risk stratification, with a consistent prognostic value for cardiovascular morbidity and mortality¹. In particular, about 40% of individuals with Metabolic syndrome and/or T2D do not have coronary artery calcium. The absence of CAC, is associated with a very low risk for incident ASCVD. It is important recognize the predictors of healthy arterial aging among individuals with Metabolic syndrome and/or T2D to develop a more precise approach for the primary prevention of ASCVD. The aim of this study is to predictors of long-term absence of coronary artery calcium (CAC) in individuals with high BP, which is an indicator of healthy arterial aging

Method:

Study enrolled 6,814 multi-ethnic participants aged 45–84years who did not have ASCVD at baseline. MESA used either a multi-detector computed tomography or a cardiac-gated electron-beam computed tomography to assess CAC. ASCVD events were categorized as incident coronary artery disease, stroke, or other incident ASCVD according to the protocol. Study analysed data from participants with high BP in the Multi-Ethnic Study of Atherosclerosis who had baseline CAC = 0 and underwent a second CAC scanning after 10 years. Multivariable

logistic regression was used to evaluate the association between various risk factors for atherosclerotic cardiovascular disease (ASCVD) and long-term CAC.

Results:

The baseline characteristics of 830 participants with high BP and no detectable CAC were included in the study. During a follow-up of 9.4 ± 0.5 years, 46.5% of participants maintained persistent CAC = 0. Concomitant to those with incident CAC, participants with long-term CAC = 0 were younger and had fewer ASCVD risk factors, such as lower levels of systolic BP and fasting glucose, more favourable lipid profiles, and lower 10-year ASCVD risk scores. Similar incident CAC, there was a tendency for the incidence of ASCVD to increase with a graded elevation of systolic BP rather than diastolic BP. As shown in figure 3 tendency towards an association between long-term CAC = 0 and incident ASCVD events in this high-BP sample. A lower incidence of ASCVD events was observed in high-BP participants with long-term CAC = 0 compared to those with incident CAC.

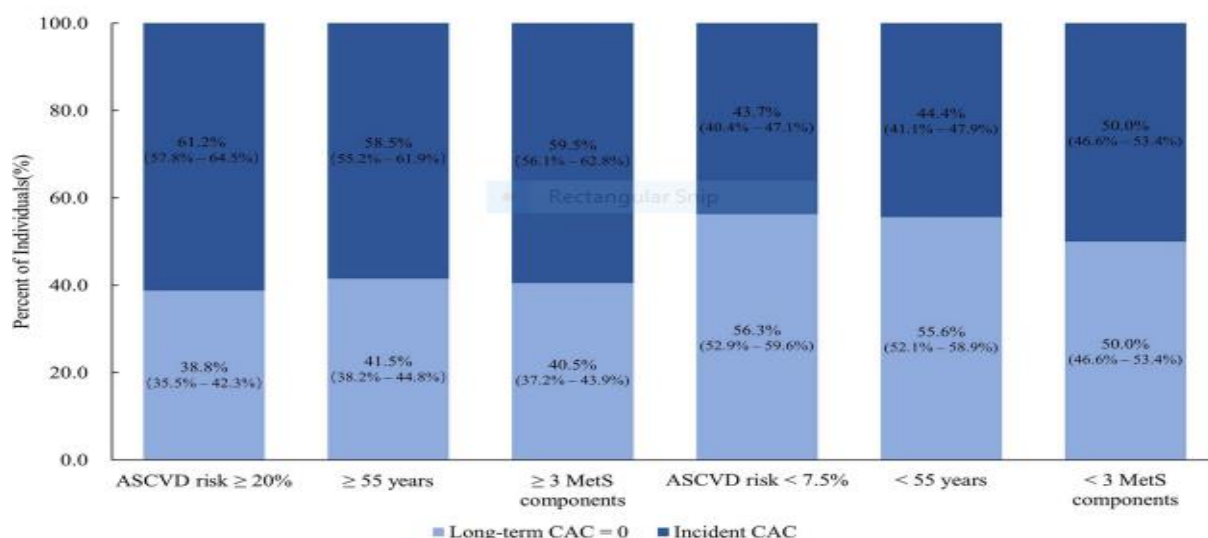


Figure: 3 Percentage of participants with and without long-term coronary artery calcium (CAC)

Discussion:

Study found that about 30% MESA participants with high BP have a baseline CAC = 0, among whom 46.5% maintain long-term CAC = 0 afterward a follow-up of 10 years and analysis of ambulatory BP has established that higher asleep systolic BP and higher awake and asleep diastolic BP were associated with higher CAC scores³.

Conclusion:

Study found that over 40% of individuals with high BP and no detectable CAC at baseline remained CAC = 0 over a decade of follow-up and analysis of cardiometabolic profile in the hypertensive population helps to prevent or delay the development of CAC and subsequent ASCVD events

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Mitochondrial Myopathy Presenting with Bilateral Lower Extremity Weakness and Swelling

Introduction:

Patients with bilateral lower limb weakness are usually assessed for several disorders, including, but not limited to, stroke, peripheral neuropathy, Guillain-Barre syndrome, multiple sclerosis, disk herniation. Mitochondrial diseases can be easily missed and underdiagnosed, particularly in adults, as these diseases do not have delicate and specific biomarkers and often require invasive testing to establish a diagnosis¹. The identification of cardiac dysfunction is particularly significant because of its impact on quality of life, morbidity, mortality, and especially because it is agreeable to treatment. Some mitochondrial syndromes, such as Kearns-Sayre syndrome (KSS) include cardiac dysfunction as an essential feature². The clinical manifestations of mitochondrial disease can be broadly classified into 3 categories: chronic progressive external ophthalmoplegia, skeletal muscle-central nervous system syndromes, or pure myopathy. The aim of this study is to report a case of Mitochondrial Myopathy Presenting with Bilateral Lower Extremity Weakness and swelling.

Case Report

A 21-year-old male patient was referred to our emergency centre for suspected deep vein thrombosis, chief complaints include 3-week history of weakness, pain, and swelling in both legs which began after he arrived in the United States from India. He revealed “flu-like” symptoms 4 months prior to presentation, which he had expected was due to a coronavirus (COVID) infection. He had received the Covaxin vaccine in India approximately 2 months

prior to presentation. On examination, he had bilateral ptosis limited extraocular movements, tachycardia, jugular venous distension, bilateral 2+ pitting edema up to his knees, bilateral 4/5 Medical Research Council grade weakness of his lower extremities, mild tenderness of his upper and lower extremity proximal and distal muscle groups, and absent deep tendon reflexes with bilateral foot drop.

The neurologic consultant determined that the proximal muscle weakness with greater than distal muscle weakness. Chest X-ray and computed tomography (CT) angiography of the chest/abdomen/pelvis showed findings suggestive of volume overload with cardiomegaly, small bilateral pleural effusions, distended inferior vena cava and iliac veins, and body wall edema as shown in figure 4. Her overall clinical picture was deemed more consistent with TCM, and anticoagulation therapy was subsequently discontinued. Following supportive care, she was discharged in a stable condition and had complete resolution of her apical dyskinesia at four weeks follow up. Mitochondrial myopathy was in the differential diagnosis, and a surgical biopsy of the patient's rectus femoris revealed scattered ragged-blue fibers, scattered ragged fibers, and cytochrome-c oxidase negative fibers with increased perimysial and endomysial connective tissue, consistent with active and chronic primary mitochondrial myopathy. The patient was treated successfully with furosemide, metoprolol, and methylprednisolone. On follow up appointments, he reported improved symptoms and was near his baseline. He will require serial electrocardiograms and close follow-up with the cardiology outpatient clinic for the possibility of developing an atrioventricular block and may need a permanent pacemaker in the future

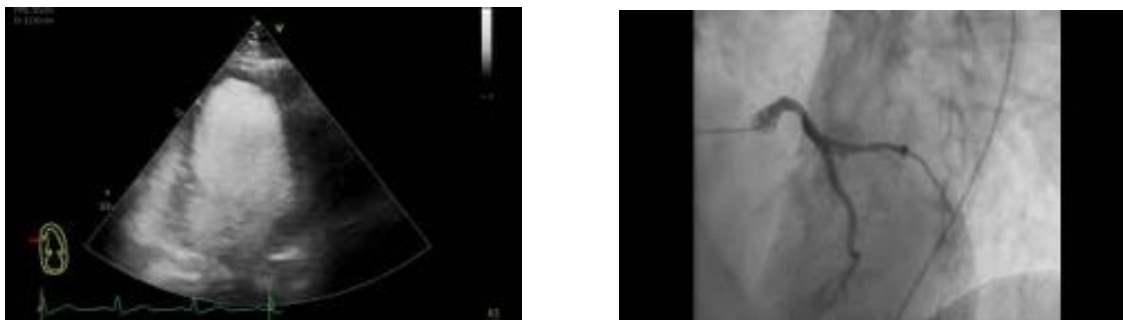


Figure 3 Left heart catheterization & Transthoracic echocardiogram

Discussion:

The key findings in this case were vital to reach the correct diagnosis were his history of childhood ptosis, muscle tenderness on examination, and elevated lactate and creatinine kinase

on presentation. Elevated lactate levels are reported to have a sensitivity ranging from 34% to 62% and a specificity of 83% to 100% for mitochondrial disease³.

Conclusion: Case study found that genetic testing is the gold standard for diagnosing mitochondrial disease, an open vastus lateralis biopsy can also be used for confirmation. Recommended treatment trials should include CoQ10, alpha-lipoic acid, and riboflavin supplementation.

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