

A SOCIEDADE PORTUGUESA DE ATEROSCLEROSE contou com a colaboração da SANOFI para o desenvolvimento deste projecto

# SERVIÇO DE INFORMAÇÃO CIENTÍFICA



A informação ao serviço da saúde

## Dos Factores de Risco à Reabilitação das Doenças Vasculares

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**Heavy Alcohol Consumption is Associated with Impaired Endothelial Function.**

Tanaka A, Cui R, Kitamura A, Liu K, Imano H, Yamagishi K, Kiyama M, Okada T, Iso H; CIRCS Investigators.

**AIM:** Previous studies have reported that moderate alcohol consumption is protective against cardiovascular disease, but heavy alcohol consumption increases its risk. Endothelial dysfunction is hypothesized to contribute to the development of atherosclerosis and cardiovascular disease. However, few population-based studies have examined a potential effect of alcohol consumption on endothelial function.

**METHODS:** This study included 404 men aged 30-79 years who were recruited from residents in 2 communities under the Circulatory Risk in Communities Study in 2013 and 2014. We asked the individuals about the frequency and volume of alcohol beverages and converted the data into grams of ethanol per day. Endothelial function was assessed by brachial artery flow-mediated dilation (FMD) measurements during reactive hyperemia. We performed cross-sectional analysis of alcohol consumption and %FMD by logistic regression analysis, adjusting for age, baseline brachial artery diameter, body mass index, systolic blood pressure, low-density lipoprotein cholesterol, HbA1c, smoking, antihypertensive medication use, and community.

**RESULTS:** Individuals who drank  $\geq 46$  g/day ethanol had a lower age-adjusted mean %FMD than non-drinkers ( $p < 0.01$ ). Compared with non-drinkers, the age-adjusted odds ratios (ORs) (95% confidence interval) of low %FMD ( $< 5.3\%$ ) for former, light ( $< 23.0$  g/day ethanol), moderate (23.0-45.9 g/day ethanol), and heavy ( $\geq 46.0$  g/day ethanol) drinkers were 1.61 (0.67-3.89), 0.84 (0.43-1.66), 1.09 (0.52-2.25), and 2.99 (1.56-5.70), respectively. The corresponding multivariable-adjusted ORs were 1.76 (0.69-4.50), 0.86 (0.42-1.76), 0.98 (0.45-2.12), and 2.39 (1.15-4.95), respectively.

**CONCLUSIONS:** Heavy alcohol consumption may be an independent risk factor of endothelial dysfunction in Japanese men.

PMID: 27025680 [PubMed - as supplied by publisher]

**Comparative Effectiveness of Personalized Lifestyle Management Strategies for Cardiovascular Disease Risk Reduction.**

Chu P(1), Pandya A(2), Salomon JA(3), Goldie SJ(2), Hunink MG(4).

**BACKGROUND:** Evidence shows that healthy diet, exercise, smoking interventions, and stress reduction reduce cardiovascular disease risk. We aimed to compare the effectiveness of these lifestyle interventions for individual risk profiles and determine their rank order in reducing 10-year cardiovascular disease risk.

**METHODS AND RESULTS:** We computed risks using the American College of Cardiology/American Heart Association Pooled Cohort Equations for a variety of individual profiles. Using published literature on risk factor reductions through diverse lifestyle interventions—group therapy for stopping smoking, Mediterranean diet, aerobic exercise (walking), and yoga—we calculated the risk reduction through each of these interventions to determine the strategy associated with the maximum benefit for each profile. Sensitivity analyses were conducted to test the robustness of the results. In the base-case analysis, yoga was associated with the largest 10-year cardiovascular disease risk reductions (maximum absolute reduction 16.7% for the highest-risk individuals). Walking generally ranked second (max 11.4%), followed by Mediterranean diet (max 9.2%), and group therapy for smoking (max 1.6%). If the individual was a current smoker and successfully quit smoking (ie, achieved complete smoking cessation), then stopping smoking yielded the largest reduction. Probabilistic and 1-way sensitivity analysis confirmed the demonstrated trend.

**CONCLUSIONS:** This study reports the comparative effectiveness of several forms of lifestyle modifications and found smoking cessation and yoga to be the most effective forms of cardiovascular disease prevention. Future research should focus on patient adherence to personalized therapies, cost-effectiveness of these strategies, and the potential for enhanced benefit when interventions are performed simultaneously rather than as single measures.

PMID: 27025969 [PubMed - in process]

Conn Med. 2016 Feb;80(2):85-90.

### Hyperuricemia and Cardiovascular Disease in Patients with Hypertension.

Acevedo A, Benavides J, Chowdhury M, Lopez M, Pena L, Montenegro A, Lievano M, Lombo B.

**BACKGROUND:** Little is known about the role of serum uric acid in cardiovascular events. We studied the prevalence of hyperuricemia and the association between uric acid level and various cardiovascular risk factors.

**METHODS:** This cross-sectional study was based on a population of patients with hypertension who attended a hypertension clinic in a university hospital in Bogotá, Colombia. Bivariate analysis and multivariate logistic regression models were utilized to investigate the relationship between hyperuricemia and cardiovascular risk factors.

**RESULTS:** The study population included 444 patients. The overall prevalence of hyperuricemia was 28.8%. Male gender (OR 2.3), age (OR 1.03), BMI (OR 1.09), triglyceride level (OR 1.005) and low HDL (OR 0.96) were significantly associated with hyperuricemia.

**CONCLUSIONS:** Prevalence of hyperuricemia is high in patients with hypertension. Serum uric acid is significantly associated with parameters of the metabolic syndrome. Hyperuricemia should be acknowledged and monitored as a risk factor for cardiovascular disease.

PMID: 27024979 [PubMed - indexed for MEDLINE]

**Relation between periodontal disease and arterial stiffness.**

Nicolosi LN, Lewin PG, Rudzinski JJ, Pompeo M, Guanca F, Rodríguez P, Gelpi RJ, Rubio MC.

**BACKGROUND AND OBJECTIVE:** Periodontal disease has been described as playing a role in the atherosclerosis process, and its relation with intimal thickness and vascular endothelial function (EF) has been investigated. The present study sought to determine whether there are differences in parameters of arterial stiffness and EF between patients with and without severe periodontal disease (SPD).

**MATERIAL AND METHODS:** Patients referred to the School of Dentistry University of Buenos Aires, were assessed. Demographic characteristics, atherogenic risk factors and concomitant pathologies were recorded. Patients with known cardiovascular pathology were excluded. Using carotid Doppler ultrasound an operator assessed arterial stiffness parameters: compliance, elastic modulus (EM),  $\beta$  stiffness index ( $\beta$ SI) and vascular EF by brachial artery flow-mediated dilatation. The patients were divided into two groups: with and without SPD.

**RESULTS:** Forty patients were included; 60% were women; 15 were in the SPD group and 25 in the group without SPD. Respective results of the studied variables were: age  $56.53 \pm 17.58$  vs.  $51.12 \pm 12.97$  years (NS); probing depth  $2.53 \pm 1.30$  (95% CI 1.81-3.25) vs.  $1.25 \pm 0.51$  (95% CI 1.31-1.73)  $p = 0.02$ ; clinical attachment level  $4.80 \pm 2.00$  (95% CI 3.69-5.91) vs.  $1.72 \pm 0.93$  (95% CI 1.33-2.11)  $p = 0.001$ ; intimal thickness  $0.10 \pm 0.17$  (95% CI 0.095-0.11) vs.  $0.82 \pm 0.18$  (95% CI 0.074-0.98) (NS); EM  $48.33 \pm 12.53$  vs.  $38.86 \pm 7.69$  ( $p = 0.005$ );  $\beta$ SI  $4.21 \pm 1.03$  vs.  $3.64 \pm 1.02$  ( $p = 0.004$ ); EF  $16.13 \pm 5.02$  vs.  $22.76 \pm 4.50$  ( $p = 0.0003$ ). Correlation between: EM and clinical attachment level  $r = 0.58$  ( $p < 0.001$ ),  $\beta$ SI and clinical attachment level  $r = 0.66$  ( $p < 0.001$ ), EF and clinical attachment level  $0.59$  ( $p < 0.001$ ).

**CONCLUSIONS:** Parameters of arterial stiffness and EF were worse in patients with SPD and correlated moderately with clinical attachment level.

PMID: 27018040 [PubMed - as supplied by publisher]



**Total cholesterol as a risk factor for coronary heart disease and stroke in women compared with men:  
A systematic review and meta-analysis.**

Peters SA, Singhatheh Y, Mackay D, Huxley RR, Woodward M.

**BACKGROUND:** Raised total cholesterol is a strong risk factor for cardiovascular disease (CVD). It remains unknown whether sex differences exist in the relationship between total cholesterol and CVD outcomes.

**METHODS:** PubMed was searched in December 2014 for cohort studies reporting on the relationship between total cholesterol and coronary heart disease (CHD) and total stroke, separately in men and women. Random effects meta-analyses with inverse variance weighting were used to obtain adjusted pooled sex-specific relative risks (RR) and women-to-men ratio of RRs (RRRs).

**RESULTS:** Data from 97 cohorts, 1,022,276 individuals, and 20,176 CHD and 13,067 stroke cases were included. The pooled RR (95% confidence interval) for CHD associated with a 1-mmol/L increase in total cholesterol was 1.20 (1.16; 1.24) in women and 1.24 (1.20; 1.28) in men, resulting in a RRR of 0.96 (0.93; 0.99). Corresponding RRs for the risk of total stroke were 1.01 (0.98; 1.05) in women, and 1.03 (1.00; 1.05) in men, with a pooled RRR of 0.99 (0.93; 1.04). Pooled RRRs (95% CI) comparing individuals in the highest TC category to those in the lowest, such as the highest versus lowest third, were 0.87 (0.79; 0.96) for CHD and 0.86 (0.76; 0.97) for total stroke.

**CONCLUSION:** Raised total cholesterol is a strong risk factor for CHD, with evidence of a small, but significantly stronger, effect in men compared to women. Raised total cholesterol had little effect on the risk of total stroke in both sexes.

PMID: 27016614 [PubMed - in process]

**Global Cardiovascular Risk Assessment: Strengths and Limitations.**

Redon J(1,)(2).

Global cardiovascular (CV) risk assessment tries to answer the questions: who factors. The most used score chart is the Framingham Cardio Vascular Risk Score, The will benefit from intervention? And when should non-pharmacologic and pharmacologic treatment be started? Used for the assessment of CV risk in the presence of one main CV risk factor, the presence of previous CV disease, diabetes, chronic kidney disease, coronary heart disease and severely elevated single risk factors, are situations with a high or very high risk. For the majority of subjects without any of the above, a calculation of risk can help to decide the best management. The methodology of assessing global CV risk has both strength and limitations. Several computational methods have been developed to assess global CV risk but no risk estimation can consider all the potential risk although in Europe the Systematic Coronary risk evaluation is widespread. strengths of the global CV risk scores depend on the methodology applied at the time of construction: (a) appropriate statistical methods (representative sample, sufficient power, clear definition of the outcomes); (b) inclusion of appropriate risk factors (age, sex, conventional risk factors, and inclusion of others that can be relevant). Once developed, the function requires internal and external validity as well as calibration. There are several limitations, which have been solved with different approaches. In the case of hypertension, one element is introduced in the score charts, the presence of hypertension-induced organ damage offering a refinement of the approach to the global CV risk.

PMID: 26993498 [PubMed - as supplied by publisher]

**Primary care based screening for cardiovascular risk factors in patients with psoriasis.**

Rutter MK, Kane K, Lunt M, Cordingley L, Littlewood A, Young HS, Chew-Graham CA, Hilton R, Symmons DP, Griffiths CE.

**BACKGROUND:** Studies assessing cardiovascular disease (CVD) risk factors in patients with psoriasis have been limited by selection bias, inappropriate controls or a reliance on data collected for clinical reasons.

**PURPOSE:** To investigate whether CVD risk factor screening of patients with psoriasis in primary care augments the known prevalence of CVD risk factors in a cross-sectional study **METHODS:** Patients listed as having psoriasis in Primary Care were recruited, screened and risk assessed by QRISK2.

**RESULTS:** Two hundred and eighty-seven patients attended (mean age 53 years; 57% female; 94% white British; 22% severe disease; 33% self-reported psoriatic arthritis. The proportion with known and screen-detected (previously unknown) risk factors was: hypertension: 35% known, 13% screen-detected; hypercholesterolaemia: 32% and 37%; diabetes: 6.6% and 3.1%; and chronic kidney disease 1.1% and 4.5%. At least one screen-detected risk factor was found in 48% and two or more risk factors in 21% of patients. One in three patients (37%) not known to be high risk were found to have a high (>10%) 10-year CVD risk. Amongst the participants receiving treatment for known CVD risk factors, nearly half had suboptimal levels for blood pressure (46%) and cholesterol (46%).

**CONCLUSIONS:** Cardiovascular risk factor screening of primary care-based adults with psoriasis identified a high proportion of patients: a) at high CVD risk; b) with screen-detected risk factors and c) with sub-optimally managed known risk factors. limited responses of clinicians to identified risk factors before universal CVD screening can be recommended.

PMID: 26990294 [PubMed - as supplied by publisher]

**Obesity and Cardiovascular Disease: a Risk Factor or a Risk Marker?**

Mandviwala T, Khalid U, Deswal A.

In the USA, 69 % of adults are either overweight or obese and 35 % are obese. Obesity is associated with an increased incidence of various cardiovascular disorders. Obesity is a risk marker for cardiovascular disease, in that it is associated with a much higher prevalence of comorbidities such as diabetes, hypertension, and metabolic syndrome, which then increase the risk for cardiovascular disease. However, in addition, obesity may also be an independent risk factor for the development of cardiovascular disease. Furthermore, although obesity has been shown to be an independent risk factor for several cardiovascular diseases, it is often associated with improved survival once the diagnosis of the cardiovascular disease has been made, leading to the term "obesity paradox." Several pathways linking obesity and cardiovascular disease have been described. In this review, we attempt to summarize the complex relationship between obesity and cardiovascular disorders, in particular coronary atherosclerosis, heart failure, and atrial fibrillation.

PMID: 26973130 [PubMed - in process]

J Occup Environ Med. 2016 Mar;58(3):221-6.

**Dose-Response Relation Between Work Hours and Cardiovascular Disease Risk: Findings From the Panel Study of Income Dynamics.**

Conway SH, Pompeii LA, Roberts RE, Follis JL, Gimeno D.

**OBJECTIVES:** The aim of this study was to examine the presence of a dose-response

**METHODS:** A retrospective cohort study of 1926 individuals from the Panel Study of Income Dynamics (1986 to 2011) employed for at least 10 years. Restricted cubic spline regression was used to estimate the dose-response relationship of work hours with CVD.

**RESULTS:** A dose-response relationship was observed in which an average workweek of 46hours or more for at least 10 years was associated with an increased risk of CVD. Compared with working 45hours per week, working an additional 10hours per week or more for at least 10 years increased CVD risk by at least 16%.

**CONCLUSION:** Working more than 45 work hours per week for at least 10 years may be an independent risk factor for CVD.

PMCID: PMC4782603 [Available on 2017-03-01]

PMID: 26949870 [PubMed - in process]

**The gender gap in risk factor control: Effects of age and education on the control of cardiovascular risk factors in male and female coronary patients. The EUROASPIRE IV study by the European Society of Cardiology.**

De Smedt D, De Bacquer D, De Sutter J, Dallongeville J, Gevaert S, De Backer G, Bruthans J, Kotseva K, Reiner Ž, Tokgözoğlu L, Clays E.

**OBJECTIVE:** The aim of this study was to investigate gender related differences in the management and risk factor control of patients with coronary heart disease (CHD), taking into account their age and educational level.

**METHODS:** Analyses are based on the EUROASPIRE IV (EUROpean Action on Secondary and Primary Prevention through Intervention to Reduce Events) survey. Males and females between 18 and 80years of age, hospitalized for a first or recurrent coronary event were included in the study.

**RESULTS:** Data were available for 7998 patients of which 75.6% were males. Overall, females had a worse risk factor profile compared to males and were more likely to have 3 or more risk factors (29.5% vs. 34.9%;  $p < 0.001$ ) across all age groups. A significant gender by education interaction ( $p < 0.05$ ) and gender by age interaction effect ( $p < 0.05$ ) was found. Furthermore, males were more likely to have a LDL-cholesterol on target (OR=1.50[1.28-1.76]), a HbA1c on target (OR=1.33[1.07-1.64]), to be non-obese (OR=1.45[1.30-1.62]) and perform adequate physical activity (OR=1.71[1.46-2.00]). In contrast males were less likely to be non-smokers (OR=0.71[0.60-0.83]). Furthermore, males were less likely to have made a dietary change (OR=0.78[0.64-0.95]) or a smoking cessation attempt (OR=0.70[0.50-0.96]) and more likely to have received smoking cessation advice if they were smokers (OR=1.52[1.10-2.09]).

**CONCLUSION:** Whereas gender differences in CHD treatment are limited, substantial differences were found regarding target achievement. declined with decreasing age and higher education.

PMID: 26913370 [PubMed - in process]

11. Can J Cardiol. 2016 Apr;32(4):505-13.

**Physical Activity, Sedentary Behaviours, and Cardiovascular Health: When Will Cardiorespiratory Fitness Become a Vital Sign?**

Després JP.

Although it is generally agreed upon that a physically active lifestyle and regular exercise are good for heart health, it is much less appreciated by the public that the prolonged hours of sedentary time resulting from sitting at work or screen time are also risk factors for cardiovascular outcomes and other cardiometabolic diseases. In this short narrative review, evidence is discussed and prudent recommendations are made in the context of the sedentary, affluent lifestyle that characterizes a large proportion of our population. It has become overwhelmingly clear that a sedentary lifestyle is a powerful risk factor for cardiovascular and other chronic diseases. In addition, vigorous physical activity and exercise is also associated with metabolic and cardiovascular adaptations that are compatible with cardiovascular health. In that regard, cardiorespiratory fitness, a reliable metric to assess the ability of the cardiovascular system to sustain prolonged physical work, has been shown to be the most powerful predictor of mortality and morbidity, way beyond classical cardiovascular disease (CVD) risk factors such as smoking, cholesterol, hypertension, and diabetes. On the basis of the evidence available, it is proposed that both dimensions of overall physical activity level (reducing sedentary time and performing regular physical activity or endurance type exercise) should be targeted to reduce CVD risk. Finally, because of the robust evidence that poor cardiorespiratory fitness is an independent risk factor for CVD and related mortality, it is proposed that this simple physiological metric should be incorporated as a vital sign in CVD risk factor evaluation and management.

PMID: 26907579 [PubMed - in process]

**Air particulate matter and cardiovascular disease: the epidemiological, biomedical and clinical vidence.**

Du Y, Xu X, Chu M, Guo Y, Wang J.

Air pollution is now becoming an independent risk factor for cardiovascular morbidity and mortality. Numerous epidemiological, biomedical and clinical studies indicate that ambient particulate matter (PM) in air pollution is strongly associated with increased cardiovascular disease such as myocardial infarction (MI), cardiac arrhythmias, ischemic stroke, vascular dysfunction, hypertension and atherosclerosis. The molecular mechanisms for PM-caused cardiovascular disease include directly toxicity to cardiovascular system or indirectly injury by inducing systemic inflammation and oxidative stress in peripheral circulation. Here, we review the linking between PM exposure and the occurrence of cardiovascular disease and discussed the possible underlying mechanisms for the observed PM induced increases in cardiovascular morbidity and mortality.

PMCID: PMC4740122

PMID: 26904258 [PubMed]



**Risk factor assessment and counselling for 12 months reduces metabolic and cardiovascular risk in overweight or obese patients with schizophrenia spectrum disorders: The CRESSOB study.**

Gutiérrez-Rojas L, Pulido S, Azanza JR, Bernardo M, Rojo L, Mesa FJ, Martínez-Ortega JM.

**BACKGROUND:** Metabolic syndrome (MS) and cardiovascular risk factors (CRF) have been associated with patients with schizophrenia. The main objective is to assess the evolution of CRF and prevalence of MS for 12 months in a cohort of overweight patients diagnosed with schizophrenia schizophreniform disorder or schizoaffective disorder in which the recommendations for the assessment and control of metabolic and cardiovascular risk were applied.

**METHODS:** The Control of Metabolic and Cardiovascular Risk in Patients with Schizophrenia and Overweight (CRESSOB) study is a 12-month, observational, prospective, open-label, multicentre, naturalistic study including 109 community mental health clinics of Spain. The study included a total of 403 patients, of whom we could collect all variables related to CRF and MS in 366 patients. Of these 366 patients, 286 completed the follow-up, (baseline, months 3, 6 and 12) where they underwent a complete physical examination and a blood test (glucose, cholesterol and triglycerides), they were asked about their health-related habits (smoking, diet and exercise) and they were given a series of recommendations to prevent cardiovascular risk and MS.

**RESULTS:** A total of 403 patients were included, 63% men, mean age (mean; (SD)) 40.5 (10.5) years. After 12 months, the study showed statistically significant decrease in weight ( $p<0.0001$ ), waist circumference ( $p<0.0001$ ), BMI ( $p<0.0001$ ), blood glucose ( $p=0.0034$ ), total cholesterol ( $p<0.0001$ ), HDL cholesterol ( $p=0.02$ ), LDL cholesterol ( $p=0.0023$ ) and triglycerides ( $p=0.0005$ ). There was a significant reduction in the percentage of smokers ( $p=0.0057$ ) and in the risk of heart disease at 10 years ( $p=0.0353$ ).

**CONCLUSION:** Overweight patients with schizophrenia who receive appropriate medical care, including CRF monitoring and control of health-related habits experience improvements with regard to most CRFs.

PMID: 26905887 [PubMed - in process]

Diabetes. 2016 Feb 19. pii: db151517. [Epub ahead of print]

**Risk factors for Cardiovascular Disease in Type 1 Diabetes.**

Diabetes Control and Complications Trial (DCCT)-Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group, Nathan DM, Bebu I, Braffett BH, Orchard TJ, Cowie CC, Lopes-Virella M, Schutta M, Lachin JM.

Risk factors for CVD are well-established in type 2 but not type 1 diabetes (T1DM). We assessed risk factors in the long-term (mean 27 years) follow-up of the Diabetes Control and Complications Trial (DCCT) T1DM cohort. Cox proportional hazards multivariate models assessed the association of traditional and novel risk factors, including HbA1c, with major atherosclerotic cardiovascular events (MACE: fatal or non-fatal myocardial infarction or stroke) and any-CVD (MACE plus confirmed angina, silent MI, revascularization or congestive heart failure). Age and mean HbA1c were strongly associated with any-CVD and with MACE. For each percentage point increase in mean HbA1c, the risk for any-CVD and for MACE increased by 31% and 42%, respectively. CVD and MACE were associated with seven other conventional factors such as blood pressure, lipids and lack of ACE-inhibitor use, but not with gender. The areas under the receiver operating characteristics curves for the association of age and HbA1c taken together with any-CVD and for MACE were 0.70 and 0.77, respectively, and for the final models, including all significant risk factors, were 0.75 and 0.82. Although many conventional CVD risk factors apply in T1DM, hyperglycemia is an important risk factor second only to age.

PMCID: PMC4839209 [Available on 2017-05-01]

PMID: 26895792 [PubMed - as supplied by publisher]

Heart. 2016 May 15;102(10):790-5.

**Atherosclerotic cardiovascular disease in patients with chronic inflammatory joint disorders.**

Agca R, Heslinga SC, van Halm VP, Nurmohamed MT.

Inflammatory joint disorders (IJD), including rheumatoid arthritis (RA), ankylosing spondylitis (ASp) and psoriatic arthritis (PsA), are prevalent conditions worldwide with a considerable burden on healthcare systems. IJD are associated with increased cardiovascular (CV) disease-related morbidity and mortality. In this review, we present an overview of the literature. Standardised mortality ratios are increased in IJD compared with the general population, that is, RA 1.3-2.3, ASp 1.6-1.9 and PsA 0.8-1.6. This premature mortality is mainly caused by atherosclerotic events. In RA, this CV risk is comparable to that in type 2 diabetes. Traditional CV risk factors are more often present and partially a consequence of changes in physical function related to the underlying IJD. Also, chronic systemic inflammation itself is an independent CV risk factor. Optimal control of disease activity with conventional synthetic, targeted synthetic and biological disease-modifying anti rheumatic drugs decreases this excess risk. High-grade inflammation as well as anti-inflammatory treatment alter traditional CV risk factors, such as lipids. In view of the above-mentioned CV burden in patients with IJD, CV risk management is necessary. Presently, this CV risk management is still lacking in usual care. Patients, general practitioners, cardiologists, internists and rheumatologists need to be aware of the substantially increased CV risk in IJD and should make a combined effort to timely initiate CV risk management in accordance with prevailing guidelines together with optimal control of rheumatic disease activity. CV screening and treatment strategies need to be implemented in usual care.

PMID: 26888573 [PubMed - in process]

**Hypertension and obstructive sleep apnea.**

Cai A, Wang L, Zhou Y.

Obstructive sleep apnea (OSA) is a major modifiable risk factor of hypertension and hypertensive patients with OSA are at increased risk for cardiovascular diseases. A substantial number of studies have revealed that OSA and hypertension have synergistic effects on the cardiovascular system and, therefore, it is clinically important and relevant to increase our understanding of the pathophysiological interactions between OSA and hypertension. In our present review, after briefly reviewing the characteristics and pathophysiological effects of OSA, we focus on the current understanding of OSA-associated hypertension, the potential approaches for treatment of OSA and the effect of OSA treatment on hypertension management. We hope our present review will shed light for future studies that investigate effective therapeutic strategies to simultaneously improve the management of OSA and hypertension. Hypertension Research advance online publication, 18 February 2016; doi:10.1038/hr.2016.11.

PMID: 26888120 [PubMed - as supplied by publisher]

World J Diabetes. 2016 Feb 10;7(3):45-9.

**Role of diabetes in heart rhythm disorders.**

Koektuerk B, Aksoy M, Horlitz M, Bozdog-Turan I, Turan RG.

The incidence of diabetes mellitus (DM) is increasing rapidly. DM is the leading cause of cardiovascular diseases, which can lead to varied cardiovascular complications by aggravated atherosclerosis in large arteries and coronary atherosclerosis, thereby grows the risk for macro and microangiopathy such as myocardial infarction, stroke, limb loss and retinopathy. Moreover diabetes is one of the strongest and independent risk factor for cardiovascular morbidity and mortality, which is associated frequently with rhythm disorders such as atrial fibrillation (AF) and ventricular arrhythmias (VA). The present article provides a concise overview of the association between DM and rhythm disorders such as AF and VA with underlying pathophysiological mechanisms.

PMCID: PMC4733448

PMID: 26862372 [PubMed]

**Diabetes Mellitus, ArterialWall, and Cardiovascular Risk Assessment.**

Kozakova M, Palombo C.

Diabetes mellitus is an independent risk factor for atherothrombotic cardiovascular disease. Adults with diabetes are two to four times more likely to develop heart disease or stroke than adults without diabetes. The two major features of diabetes, i.e., hyperglycemia and insulin-resistance, trigger arterial stiffening and increase the susceptibility of the arterial wall to atherosclerosis at any given age. These pathological changes in the arterial wall may provide a functional and structural background for cardiovascular events. The present paper provides a critical overview of the clinical evidence linking diabetes-related metabolic abnormalities to cardiovascular risk, debates the pathophysiologic mechanisms through which insulin resistance and hyperglycemia may affect the arterial wall, and discusses the associations between vascular biomarkers, metabolic abnormalities and cardiovascular events.

PMCID: PMC4772221

PMID: 26861377 [PubMed - in process]

**Circadian misalignment increases cardiovascular disease risk factors in humans.**

Morris CJ, Purvis TE, Hu K, Scheer FA.

Shift work is a risk factor for hypertension, inflammation, and cardiovascular disease. This increased risk cannot be fully explained by classic risk factors. One of the key features of shift workers is that their behavioral and environmental cycles are typically misaligned relative to their endogenous circadian system. However, there is little information on the impact of acute circadian misalignment on cardiovascular disease risk in humans. Here we show-by using two 8-d laboratory protocols-that short-term circadian misalignment (12-h inverted behavioral and environmental cycles for three days) adversely affects cardiovascular risk factors in healthy adults. Circadian misalignment increased 24-h systolic blood pressure (SBP) and diastolic blood pressure (DBP) by 3.0 mmHg and 1.5 mmHg, respectively. These results were primarily explained by an increase in blood pressure during sleep opportunities (SBP, +5.6 mmHg; DBP, +1.9 mmHg) and, to a lesser extent, by raised blood pressure during wake periods (SBP, +1.6 mmHg; DBP, +1.4 mmHg). Circadian misalignment decreased wake cardiac vagal modulation by 8-15%, as determined by heart rate variability analysis, and decreased 24-h urinary epinephrine excretion rate by 7%, without a significant effect on 24-h urinary norepinephrine excretion rate. Circadian misalignment increased 24-h serum interleukin-6, C-reactive protein, resistin, and tumor necrosis factor- $\alpha$  levels by 3-29%. We demonstrate that circadian misalignment per se increases blood pressure and inflammatory markers. Our findings may help explain why shift work increases hypertension, inflammation, and cardiovascular disease risk.

PMCID: PMC4790999 [Available on 2016-09-08]

PMID: 26858430 [PubMed - in process]

**Epicardial fat: a new cardiovascular therapeutic target.**

Iacobellis G.

Epicardial fat is the visceral fat depot of the heart. Given its rapid metabolism, organ fat specificity and simple objective measurability, epicardial fat can serve as target for pharmaceutical agents targeting the adipose tissue. Epicardial fat has shown to significantly respond to thiazolidinediones, glucagon like peptide 1 receptor agonists, dipeptidyl peptidase-4 inhibitors and statins. Epicardial fat may represent a measurable risk factor and modifiable therapeutic target. Targeted pharmaceutical interventions may allow the epicardial fat to resume its physiological role. A drug-induced browning effect on epicardial fat suggests the development of pharmacological strategies to increase energy consumption. The potential of modulating the epicardial fat transcriptome with targeted pharmacological agents can open new avenues in the pharmacotherapy of cardio-metabolic diseases.

PMID: 26848943 [PubMed - in process]



**Hypoglycemia: Adverse Cardiovascular Outcomes in Non-Critically Ill People with Type 2 Diabetes.**

Akhavan P, Aghili R, Malek M, Ebrahim Valojerdi A, Khamseh ME.

**BACKGROUND:** Hypoglycemia is associated with adverse health outcomes and can result in vascular events in diabetic patients. The impact of hypoglycemia on cardiovascular outcomes in non-critically ill people with diabetes is not well-determined. So, we examined short-term cardiovascular outcomes of hypoglycemic events in people with type 2 diabetes treated with insulin during routine clinical care.

**METHODS:** This study was conducted in Tehran, Iran from January 2012 to January 2013. One hundred and twenty non-critically ill people with type 2 diabetes on oral glucose lowering drugs were enrolled. Insulin therapy was initiated for uncontrolled diabetes. The patients were educated to perform self-monitoring of blood glucose on a daily basis. Furthermore, they were asked to record the results if they experienced any symptom indicative of hypoglycemia during the 24 weeks of the study. The occurrence of any major cardiovascular event including unstable angina, fatal or non-fatal myocardial infarction, fatal and non-fatal stroke, or death from cardiovascular cause was also evaluated based on the patients' hospital records.

**RESULTS:** There were 210 hypoglycemic episodes and 31 major cardiovascular events. Forty four percent of patients with documented hypoglycemic episodes developed cardiovascular events compared to 15.6% of those who did not experience any hypoglycemia ( $P = 0.001$ ). The odds ratio for occurrence of major cardiovascular events related to hypoglycemia was 7.41 (CI = 2.15-25.47) with a risk ratio of 2.66.

**CONCLUSION:** Hypoglycemia is a major risk factor for occurrence of the first major cardiovascular event in non-critically ill people with type 2 diabetes initiating insulin therapy.

PMID: 26838076 [PubMed - in process]

**Early cardiovascular events in women with a history of gestational diabetes mellitus.**

Goueslard K, Cottenet J, Mariet AS, Giroud M, Cottin Y, Petit JM, Quantin C.

**BACKGROUND:** The effect of gestational diabetes mellitus (GDM) on cardiovascular diseases (CVD) is not assessed within the first 10 years postpartum, regardless of subsequent diabetes. The aim of this study was to determine the risk of CVD events related to GDM within 7 years of postpartum.

**METHODS:** This nationwide population-based study of deliveries in 2007 and 2008 with a follow-up of 7 years was based on data from the French medico-administrative database. Two groups were formed: women with a history of GDM and women without GDM or previous diabetes. CVD included angina pectoris, myocardial infarction, stroke, heart bypass surgery, coronary angioplasty, carotid endarterectomy and fibrinolysis. Hypertensive disease was assessed separately. Determinants studied included age, obesity, subsequent diabetes mellitus and hypertensive diseases during pregnancy. Adjusted odds ratios for outcomes were calculated using multiple logistic regressions.

**RESULTS:** The hospital database recorded 1,518,990 deliveries in 2007 and 2008. Among these, 62,958 women had a history of GDM. After adjusting for age, DM, obesity and hypertensive disorders in pregnancy, GDM was significantly associated with a higher risk of CVD (adjusted Odds Ratio aOR = 1.25 [1.09-1.43]). Considering each variable in a separate model, GDM was associated with angina pectoris (aOR = 1.68 [1.29-2.20]), myocardial infarction (aOR = 1.92 [1.36-2.71]) and hypertension (aOR = 2.72 [2.58-2.88]) but not with stroke.

**CONCLUSIONS:** A history of GDM was identified as a risk factor of CVD, especially coronary vascular diseases, within the 7 years postpartum. A lifestyle changes from postpartum onwards can be recommended and supported.

PMCID: PMC4728938

PMID: 26817691 [PubMed - in process]

**Wrist circumference as a novel negative risk factor for cardiovascular disease among adult men: a median follow-up of 9 years.**

Derakhshan A, Eslami A, Bozorgmanesh M, Sheikholeslami F, Azizi F, Hadaegh F.

**PURPOSE:** Wrist circumference is an easy to measure anthropometric index of body frame and bone size. The aim of this study was to examine the association of wrist circumference with incidence of cardiovascular disease (CVD) among adult men.

**METHODS:** For this study 2531 male participants aged  $\geq 30$  years, without any history of CVD were selected and followed from 1999 to 2011. Cox proportional hazard models and logistic regression were used to examine the relation of wrist circumference with incident CVD.

**RESULTS:** A total of 339 cases of CVD were reported throughout a median follow-up of 9.4 years. In the multi-variable Cox model, 1 unit increase of wrist circumference was inversely associated with incident CVD with a HR (95 % CI) of 0.84 (0.72-0.98, P value = 0.02). The receiver operating characteristics curve in a logistic regression model for wrist circumference in prediction of CVD showed a cutoff of 17.75 cm, beyond which was associated with a lower risk for CVD.

**CONCLUSION:** In a population with a high prevalence of CVD risk factors, it was shown that a higher wrist circumference was associated with lower risk for incident CVD. Further studies are needed to explore the underlying mechanisms of this inverse relation.

PMID: 26809978 [PubMed - as supplied by publisher]

**Universal screening for cardiovascular disease risk factors in adolescents to identify high-risk families: a population-based cross-sectional study.**

Khoury M, Manlhiot C, Gibson D, Chahal N, Stearne K, Dobbin S, McCrindle BW.

**BACKGROUND:** Universal screening of children for dyslipidemia and other cardiovascular risk factors has been recommended. Given the clustering of cardiovascular risk factors within families, one benefit of screening adolescents may be to identify "at-risk" families in which adult members might also be at elevated risk and potentially benefit from medical evaluation.

**METHODS:** Cross-sectional study of grade 9 students evaluating adiposity, lipids and blood pressure. Data collected by Heart Niagara Inc. through the Healthy Heart Schools' Program. Parents completed questionnaires, evaluating family history of dyslipidemia, hypertension, diabetes and early cardiovascular disease events in parents and siblings (first-degree relatives), and grandparents (second-degree relatives). Associations between positive risk factor findings in adolescents and presence of a positive family history were assessed in logistic regression models.

**RESULTS:** N=4014 adolescents ages 14-15 years were screened; 3467 (86 %) provided family medical history. Amongst adolescents, 4.7 % had dyslipidemia, 9.5 % had obesity, and 3.5 % had elevated blood pressure. Central adiposity (waist-to-height ratio  $\geq 0.5$ ) in the adolescent was associated with increased odds of diabetes in first- (OR:2.0 (1.6-2.6),  $p < 0.001$ ) and second-degree relatives (OR:1.3 (1.1-1.6),  $p = 0.002$ ). Dyslipidemia was associated with increased odds of diabetes (OR:1.6 (1.1-2.3),  $p < 0.001$ ), hypertension (OR:2.2 (1.5-3.2),  $p < 0.001$ ) and dyslipidemia (OR:2.2 (1.5-3.2),  $p < 0.001$ ) in first degree relatives. Elevated blood pressure did not identify increased odds of a positive family history.

**CONCLUSIONS:** Presence of obesity and/or dyslipidemia in adolescents identified through a universal school-based screening program is associated with risk factor clustering within families. Universal pediatric cardiometabolic screening may be an effective entry into reverse cascade screening.

PMCID: PMC4721118

PMID: 26795037 [PubMed - in process]

**Lipid metabolism and the risk factors of cardiovascular disease: implication of dietary omega-3 polyunsaturated fatty acids.**

Balogun KA(1,)(2).

Cardiovascular disease (CVD) is a complicated and multifarious disease, and is the number one cause of mortality worldwide. The pathogenesis of CVD is attributed to the interaction between genetics and environment. There are numerous data that support the cardioprotective properties of omega (n)-3 polyunsaturated fatty acids (PUFA); however, there are also controversial reports. Considering the reported sex and age differences in the pathophysiology of CVD and the metabolism of n-3 PUFA, it is imperative to consider these factors in the cardioprotective effects of n-3 PUFA. The current thesis investigated the effects of n-3 PUFA on the risk factors of CVD, such as dyslipidemia and obesity, with a particular focus on how sex, age, and dose of n-3 PUFA affect lipid and lipoprotein metabolism. The plasma concentrations of lipids and lipoproteins of C57BL/6 mice offspring at weaning and 16 weeks post weaning were chosen as study outcomes to assess the sex, age, and dose-specific effects of n-3 PUFA on markers of dyslipidemia, a well-known risk factor of CVD. A longer exposure to a postnatal diet high in n-3 PUFA increased plasma concentration of low-density lipoprotein (LDL) cholesterol in the offspring in a sex-specific manner; however, the profile of this increase was less atherogenic, as the high n-3 PUFA group had a lower plasma concentration of very small LDL particles in both males and females. There was no effect of high n-3 PUFA diet observed on plasma concentration of high-density lipoprotein cholesterol; however, the high n-3 PUFA group had a higher cholesterol efflux in the male offspring but not in female offspring. Lipidomic analyses revealed that high n-3 PUFA diet led to higher hepatic and plasma concentrations of n-3 PUFA-containing bioactive lipids, such as phosphatidylcholine, lysophosphatidylcholine and free fatty acids, which could positively influence pathways involved in cardioprotection. The effects of dietary n-3 PUFA on obesity at the cellular level was also investigated, using adipocyte hypertrophy as the outcome measure of adipose tissue enlargement. Diet high in n-3 PUFA prevented adipocyte hypertrophy in males, with no effect in females. High n-3 PUFA diet also led to the down regulation of the messenger RNA expression of acyl-CoA: diacylglycerol acyltransferase 2, fatty acid binding protein-4, peroxisome proliferator-activated receptor protein  $\gamma$ , and leptin in males, which are key proteins involved in adipocyte hypertrophy; however, no effect was observed in females. The last study assessed the effects of dose and duration of exposure to dietary n-3 PUFA on docosahexaenoic acid accretion in the brain, and the expression of neurotrophins known to have neuroprotective and cardioprotective benefits. Dietary n-3 PUFA led to an age-dependent increase in the expression of brain-derived neurotrophic factor, tropomyosin receptor kinase, and phosphorylated cyclic AMP response element binding protein. In conclusion, the results from the current thesis

demonstrate a sex-, dose-, and age-specific effect of n-3 PUFA on risk factors of CVD, and on novel regulatory pathways by which n-3 PUFA could reduce dyslipidemia and obesity. The results also suggest that n-3 PUFA could be neuroprotective and cardioprotective through a common neurotrophin signalling pathway.

PMID: 26778139 [PubMed - in process]

**Chronic hepatitis C virus infection, a new cardiovascular risk factor?**

Domont F, Cacoub P.

Among the large scope of extra hepatic manifestations related to hepatitis C virus (HCV) infection, many studies recently evaluated the frequency and characteristics of cardiovascular involvement. To assess the current published data on HCV infection and cardiovascular diseases. Published studies on cardiovascular disease, i.e. cerebrovascular accident and ischaemic heart disease in subjects with HCV infection were analysed from literature databases. Subjects with HCV chronic infection have an increased prevalence of carotid atherosclerosis and increased intima-media thickness compared to healthy controls or those with hepatitis B or non-alcoholic steatohepatitis. Active chronic HCV infection appears as an independent risk factor for ischaemic cerebrovascular accidents. Active chronic HCV infection is associated with increased risk of ischaemic heart disease. In some studies, successful interferon-based therapy showed a beneficial impact on the cardiovascular risk. The risk of major cardiovascular events is higher in patients with HCV infection compared to controls, independent of the severity of the liver disease or the common cardiovascular risk factors. The beneficial impact of interferon-based therapy needs to be confirmed with new direct antiviral interferon-free agents in prospective studies with extended follow-up.

PMID: 26763484 [PubMed - in process]

**Frequency and Risk Factors for Cerebral Arterial Disease in a HIV/AIDS Neuroimaging Cohort.**

Edwards NJ, Grill MF, Choi HA, Ko NU.

**BACKGROUND:** Infection with HIV predisposes patients to a myriad of neurologic disorders, including cerebrovascular disease. The pathophysiology is likely multifactorial, with proposed mechanisms including infectious vasculitis, HIV-induced endothelial dysfunction and adverse effects of combination antiretroviral therapy (cART). Epidemiologic data on clinically evident cerebral vasculopathy in HIV-infected adults is scarce, even though stroke hospitalizations are rising in this patient population.

**METHODS:** A total of 6,298 HIV-infected adults (San Francisco General Hospital, 2000-2013) were screened to generate a cohort of patients with dedicated neuroimaging of the intra- and extracranial cerebral vasculature. We extracted information regarding the extent of HIV disease (including serial viral load and CD4 counts), cardiovascular disease risk factors and exposure to cART (cross-referenced with pharmacy records) and performed multivariate logistic regression analysis to identify predictors of vasculopathy.

**RESULTS:** Of 144 patients, 55 patients (38.2%) had radiographic evidence of cerebral vasculopathy. Twenty (13.9%) had a vasculopathy characterized by vessel dolichoectasia and intracranial aneurysm formation. Thirty-five patients (24.3%) had intra- and or extracranial stenosis/occlusion. cART use (OR 2.27, 95% CI 1.03-5) and tobacco abuse (OR 2.35, 95% CI 1.04-5.25) were independently associated with the development of any vasculopathy, whereas cART use was also an independent risk factor for the stenosis/occlusion subtype specifically (OR 2.87, 95% CI 1.11-7.45).

**CONCLUSIONS:** There was a high frequency of cerebral arterial disease in this neuroimaging cohort of HIV/AIDS patients. A history of cART use and a history of tobacco abuse were independent risk factors for vasculopathy, though these findings should be confirmed with large-scale prospective studies.

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PMID: 26751784 [PubMed - in process]



**Postprandial hyperlipidemia as a potential residual risk factor.**

Nakamura K, Miyoshi T, Yunoki K, Ito H.

Statin therapy targeting reduction of low-density lipoprotein cholesterol (LDL-C) decreases the risk of coronary heart disease (CHD) and all-cause mortality. However, a substantial number of cases of CHD are not prevented and residual risk factors remain unsettled. A high triglyceride (TG) level is considered to be an important and residual risk factor. Postprandial hyperlipidemia is a condition in which TG-rich chylomicron remnants are increased during the postprandial period and hypertriglyceridemia is protracted. Postprandial hyperlipidemia evokes atherogenesis during the postprandial period. Several prospective studies have revealed that non fasting serum TG levels predict the incidence of CHD. Values of TG, remnant lipoprotein cholesterol, and remnant lipoprotein TG after fat loading were significantly higher in diabetes patients with insulin resistance than in diabetes patients without insulin resistance. Endothelial dysfunction is an initial process of atherogenesis and it contributes to the pathogenesis of CHD. Postprandial hyperlipidemia (postprandial hypertriglyceridemia) is involved in the production of proinflammatory cytokines, recruitment of neutrophils, and generation of oxidative stress, resulting in endothelial dysfunction in healthy subjects, hypertriglyceridemic patients, or type 2 diabetic patients. Effective treatment has not been established till date. Ezetimibe or omega-3 fatty acids significantly decrease postprandial TG elevation and postprandial endothelial dysfunction. Ezetimibe or omega-3 fatty acids added to statin therapy reduce serum TG levels and result in good outcomes in patients with CHD. In conclusion, postprandial hyperlipidemia is an important and residual risk factor especially in patients with insulin resistance syndrome (metabolic syndrome) and diabetes mellitus. Further studies are needed to establish effective treatment.

PMID: 26744235 [PubMed - in process]

**Association of Sleep Duration with Stroke in Diabetic Patients: Analysis of the National Health Interview Survey.**

Akinseye OA, Ojike NI, Akinseye LI, Dhandapany PS, Pandi-Perumal SR.

**BACKGROUND:** Habitual sleep duration is increasingly being recognized as an important risk factor for stroke. We sought to describe the association between sleep duration and stroke in a cohort of individuals with diabetes.

**METHODS:** Data from the National Health Interview Survey for the years 2004-2013 were used. Only those answering "yes" to the question "Have you EVER been told by a doctor or other health professional that you have diabetes or sugar diabetes?" were included in the analysis. Sleep duration was categorized as short ( $\leq 6$  hours), normal (7-8 hours), or long ( $\geq 9$  hours). Self-reported diagnosis of stroke was the main outcome of interest.

**FINDINGS:** A total number of 26,364 self-reported diabetic individuals provided data for analysis. Stroke was reported in 9.1% of short sleepers, 16.1% of long sleepers, and 8.3% of normative sleepers ( $P < .05$ ). In the unadjusted model, short and long sleepers had an increased odds of stroke compared to normal sleepers (odds ratio [OR]=1.12, 95% confidence interval [CI]: 1.02-1.23,  $P = .01$ ; and OR=2.18, 95% CI: 1.96-2.42,  $P = .01$ ; respectively), but the association between short sleep and stroke became nonsignificant after multivariate adjustment (OR=1.15, 95% CI: .95-1.40,  $P = .16$ ) except in white participants. The association between long sleep duration and stroke persisted (OR=1.46, 95% CI: 1.16-1.84,  $P = .01$ ), especially in males (OR=1.62, 95% CI: 1.14-2.28) and in white participants (OR=1.97, 95% CI: 1.47-2.65).

**CONCLUSION:** In diabetic patients, abnormal sleep duration was associated with increased risk of stroke, and this association varied among different sex and ethnic groups.

PMID: 26738814 [PubMed - in process]

Rheumatology (Oxford). 2016 May;55(5):809-16.

**Cardiovascular risk factor management in patients with RA compared to matched non-RA patients.**

Alemao E, Cawston H, Bourhis F, Al M, Rutten-van Mölken MP, Liao KP, Solomon DH.

**OBJECTIVE:** RA is associated with a 50-60% increase in risk of cardiovascular (CV) death. This study aimed to compare management of CV risk factors in RA and matched non-RA patients.

**METHODS:** A retrospective cohort study was conducted using UK clinical practice data. Patients presenting with an incident RA diagnosis were matched 1:4 to non-RA patients based on a propensity score for RA, entry year, CV risk category and treatment received at index date (date of RA diagnosis). Patients tested and treated for CV risk factors as well as those attaining CV risk factor management goals were evaluated in both groups.

**RESULTS:** Between 1987 and 2010, 24 859 RA patients were identified and matched to 87 304 non-RA patients. At index date, groups had similar baseline characteristics. Annual blood pressure, lipids and diabetes-related testing were similar in both groups, although CRP and ESR were higher in RA patients at diagnosis and decreased over time. RA patients prescribed antihypertensives increased from 38.2% at diagnosis to 45.7% at 5 years, from 14.0 to 20.6% for lipid-lowering treatments and from 5.1 to 6.4% for antidiabetics. Similar treatment percentages were observed in non-RA patients, although slightly lower for antihypertensives. Modest (2%) but significantly lower attainment of lipid and diabetes goals at 1 year was observed in RA patients.

**CONCLUSION:** There were no differences between groups in the frequency of testing and treatment of CV risk factors. Higher CV risk in RA patients seems unlikely to be driven by differences in traditional CV risk factor management.

PMCID: PMC4830910

PMID: 26705329 [PubMed - in process]

**Relationship Between Sedentary Behavior and Cardiovascular Risk.**

Same RV, Feldman DI, Shah N, Martin SS, Al Rifai M, Blaha MJ, Graham G, Ahmed HM.

The majority of adults do not meet current guideline recommendations for moderate to vigorous physical activity. Recent research has linked a high amount of sedentary behavior with an increased risk of obesity, diabetes, the metabolic syndrome, cardiovascular disease, and death. This correlation with sedentary behavior even extends to individuals who meet recommended physical activity goals during the remainder of their day, which implies that sedentary behavior may represent a distinct cardiovascular risk factor that is independent of the overall amount of physical activity. During the past several years, there has been significant interest in identifying and understanding the mechanisms through which sedentary behavior affects cardiovascular health. In this review, we critically evaluate the literature pertaining to sedentary behavior and cardiovascular risk with an emphasis on studies published over the past year, and we suggest possible interventions that may help reduce sedentary behavior time.

PMID: 26699633 [PubMed - in process]

**Do Stroke Patients Know Their Risk Factors?**

Soomann M, Vibo R, Kõrv J.

**BACKGROUND:** Risk factor management is the key to stroke prevention. Although several studies have assessed the awareness of different risk factors in the general public, there are limited data available on how well acute stroke patients know their own risk factors. The aim of this study was to assess stroke patients' informedness of their own stroke risk factors.

**METHODS:** All consecutive eligible acute stroke and transient ischemic attack patients hospitalized at the Tartu University Hospital, Department of Neurology, during 9 months in 2010 were interviewed about different stroke risk factors within 72 hours from hospitalization. The respective information was also retrieved from medical records.

**RESULTS:** Of the 341 patients admitted during the study period, 195 were eligible for the interview. Diabetes was the best known risk factor (89%) followed by hypertension (80%), atrial fibrillation (78%), previous stroke (77%), and heart failure and/or ischemic heart disease (66%).

**CONCLUSIONS:** We found that acute stroke patients are best informed of their diabetes and worst informed of their ischemic heart disease and/or heart failure. There is, however, room for amelioration in the awareness of all of the studied risk factors. More attention should be addressed to explaining the risks and treatment options to patients at risk of stroke and the general population.

PMID: 26654663 [PubMed - in process]

**Anxiety as a risk factor in cardiovascular disease.**

Allgulander C.

**PURPOSE OF REVIEW:** The narrative review covers recent studies of anxiety as a companion in cardiovascular disease.

**RECENT FINDINGS:** Prospective population-based studies and studies of cases with known cardiovascular disease have been conducted, as well as studies of intervention with coronary bypass grafting, heart transplants, and implantable cardioverter-defibrillators, and subsequent rehabilitation programs. Mental stress-induced myocardial ischemia (MSIMI) stands for this emerging research arena.

**SUMMARY:** Anxiety has emerged as perhaps the most important risk factor for cardiovascular disease, determining other known risk factors, such as depression, substance use, overweight, and a sedentary lifestyle. Anxiety also increases the risk of major cardiac events in coronary heart disease. There is a need for elucidating the influence of anxiety in takotsubo and in white-coat hypertension. Managing anxiety is of vital importance in patients who have received heart transplants, to ascertain adherence to immunosuppressants.

PMID: 26575295 [PubMed - in process]

**Insulin resistance: an additional risk factor in the pathogenesis of cardiovascular disease in type 2 diabetes.**

Patel TP, Rawal K, Bagchi AK, Akolkar G, Bernardes N, Dias Dda S, Gupta S, Singal PK.

Sedentary life style and high calorie dietary habits are prominent leading cause of metabolic syndrome in modern world. Obesity plays a central role in occurrence of various diseases like hyperinsulinemia, hyperglycemia and hyperlipidemia, which lead to insulin resistance and metabolic derangements like cardiovascular diseases (CVDs) mediated by oxidative stress. The mortality rate due to CVDs is on the rise in developing countries. Insulin resistance (IR) leads to micro or macro angiopathy, peripheral arterial dysfunction, hampered blood flow, hypertension, as well as the cardiomyocyte and the endothelial cell dysfunctions, thus increasing risk factors for coronary artery blockage, stroke and heart failure suggesting that there is a strong association between IR and CVDs. The plausible linkages between these two pathophysiological conditions are altered levels of insulin signaling proteins such as IR- $\beta$ , IRS-1, PI3K, Akt, Glut4 and PGC-1 $\alpha$  that hamper insulin-mediated glucose uptake as well as other functions of insulin in the cardiomyocytes and the endothelial cells of the heart. Reduced AMPK, PFK-2 and elevated levels of NADP(H)-dependent oxidases produced by activated M1 macrophages of the adipose tissue and elevated levels of circulating angiotensin are also cause of CVD in diabetes mellitus condition. Insulin sensitizers, angiotensin blockers, superoxide scavengers are used as therapeutics in the amelioration of CVD. It evidently becomes important to unravel the mechanisms of the association between IR and CVDs in order to formulate novel efficient drugs to treat patients suffering from insulin resistance-mediated cardiovascular diseases. The possible associations between insulin resistance and cardiovascular diseases are reviewed here.

PMID: 26542377 [PubMed - in process]

**Nocturnal indicators of increased cardiovascular risk in depressed adolescent girls.**

Waloszek JM, Woods MJ, Byrne ML, Nicholas CL, Bei B, Murray G, Raniti M, Allen NB, Trinder J.

Depression is an independent risk factor for cardiovascular disease in adults, and recent literature suggests preclinical signs of cardiovascular risk are also present in depressed adolescents. No study has examined the effect of clinical depression on cardiovascular factors during sleep. This study examined the relationship between clinical depression and nocturnal indicators of cardiovascular risk in depressed adolescent girls from the general community (13-18 years old; 11 clinically depressed, eight healthy control). Continuous beat-to-beat finger arterial blood pressure and heart rate were monitored via Portapres and electrocardiogram, respectively. Cardiovascular data were averaged over each hour for the first 6 h of sleep, as well as in 2-min epochs of stable sleep that were then averaged within sleep stages. Data were also averaged across 2-min epochs of pre-sleep wakefulness and the first 5 min of continuous non-rapid eye movement sleep to investigate the blood pressure dipping response over the sleep-onset period. Compared with controls, depressed adolescents displayed a similar but significantly elevated blood pressure profile across sleep. Depressed adolescents had significantly higher systolic and diastolic blood pressure and mean arterial pressures across the entire night ( $P < 0.01$ ), as well as during all sleep stages ( $P < 0.001$ ). Depressed adolescents also had higher blood pressure across the sleep-onset period, but the groups did not differ in the rate of decline across the period. Higher blood pressure during sleep in depressed adolescent females suggests that depression has a significant association with cardiovascular functioning during sleep in adolescent females, which may increase risk for future cardiovascular pathology.

PMID: 26543013 [PubMed - in process]



**Sleep characteristics and cardiovascular risk in children and adolescents: an enumerative review.**

Matthews KA, Pantesco EJ.

Cardiovascular risk factors develop in childhood and adolescence. This enumerative review addresses whether sleep characteristics, including sleep duration, continuity, quality, and daytime sleepiness, are associated with cardiovascular risk factors in young people. Thirty-nine studies were identified, which examined the following risk factors: metabolic syndrome, glucose and insulin, lipids, blood pressure, and cardiovascular responses to psychological stressors. Due to the availability of other reviews, 16 longitudinal studies of obesity published in 2011 and later were also included in this report. Excluded from the review were studies of participants with suspected or diagnosed sleep disorders and reports from sleep deprivation experiments. Combining studies, evidence was strongest for obesity, followed by glucose, insulin, blood pressure (especially ambulatory blood pressure), and parasympathetic responses to psychological stressors. There was little evidence for metabolic syndrome cluster, lipids, and blood pressure responses to psychological stressors. The more positive associations were obtained for studies that incorporated objective measures of sleep and that included adolescents. The foundational evidence is almost entirely cross-sectional, except for work on obesity. In summary, available evidence suggests that the associations between sleep characteristics and cardiovascular risk vary by risk factor. It is time to conduct studies to determine antecedent and consequent relationships, and to expand risk factors to include markers of inflammation.

PMCID: PMC4689674 [Available on 2017-02-01]

PMID: 26459685 [PubMed - in process]

Lupus. 2016 Feb;25(2):177-84.

**Metabolic syndrome is not only a risk factor for cardiovascular diseases in systemic lupus erythematosus but is also associated with cumulative organ damage: a cross-sectional analysis of 311 patients.**

Demir S, Artim-Esen B, Şahinkaya Y, Pehlivan Ö, Alpay-Kanitez N, Omma A, Erer B, Kamalı S, Gül A, Aral O, Öcal L, İnanç M.

**BACKGROUND/PURPOSE:** Patients with systemic lupus erythematosus (SLE) have increased rates of cardiovascular disease (CVD) that are one of the major causes of mortality. The aim of this study was to determine the frequencies of metabolic syndrome (MetS) and CVD in SLE patients and investigate the link between these and clinical features of SLE.

**METHODS:** A total of 311 SLE patients were consecutively assessed for cumulative organ damage (SDI/SLICC scores), history of CVD and MetS as defined by the National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III). Clinical data of SLE patients were collected from the records.

**RESULTS:** The mean age of the patients was  $40.2 \pm 13.4$  years and 89% were female. The frequencies of CVD and MetS were 15.2% and 19%, respectively. In this SLE cohort increased age, cumulative damage, disease duration and CVD were associated with MetS. CVD was associated with disease duration, cumulative damage, pericarditis, hematologic involvement, lymphopenia, thrombocytopenia, neurological involvement and antiphospholipid antibody (aPL) positivity. Hydroxychloroquine (HCQ) use was found as a protective factor for CVD.

**CONCLUSION:** In SLE patients, MetS was associated with CVD and both increased with disease duration. Patients who developed MetS and/or CVD had increased cumulative organ damage. Certain clinical features of SLE and the presence of aPL were also associated with CVD. There was a significant protective effect of HCQ from CVD. The prevention of MetS and long-term use of HCQ may be beneficial in improving the prognosis of SLE.

PMID: 26354963 [PubMed - in process]

**Arterial stiffness and sedentary lifestyle: Role of oxidative stress.**

Lessiani G, Santilli F, Boccatonda A, Iodice P, Liani R, Tripaldi R, Saggini R, Davì G.

Sedentary lifestyle is a risk factor for the development of cardiovascular disease, and leads to a quantifiable impairment in vascular function and arterial wall stiffening. We tested the hypothesis of oxidative stress as a determinant of arterial stiffness (AS) in physically inactive subjects, and challenged the reversibility of these processes after the completion of an eight-week, high-intensity exercise training (ET). AS was assessed before and after ET, measuring carotid to femoral pulse wave velocity (PWV) with a Vicorder device. At baseline and after ET, participants performed urine collection and underwent fasting blood sampling. Urinary 8-iso-PGF2 $\alpha$ , an in vivo marker of lipid peroxidation, total, HDL and LDL cholesterol, and triglyceride concentrations were measured. ET was associated with significantly reduced urinary 8-iso-PGF2 $\alpha$  ( $p < 0.0001$ ) levels. PWV was significantly reduced after ET completion ( $p < 0.0001$ ), and was directly related to urinary 8-iso-PGF2 $\alpha$  ( $Rho = 0.383$ ,  $p = 0.021$ ). After ET, cardiovascular fitness improved [peak oxygen consumption ( $p < 0.0001$ ), peak heart rate ( $p < 0.0001$ )]. However, no improvement in lipid profile was observed, apart from a significant reduction of triglycerides ( $p = 0.022$ ). PWV and triglycerides were significantly related ( $Rho = 0.466$ ,  $p = 0.005$ ) throughout the study period. PWV levels were also related to urinary 8-iso-PGF2 $\alpha$  in our previously sedentary subjects. We conclude that regular physical exercise may be a natural antioxidant strategy, lowering oxidant stress and thereby the AS degree.

PMID: 26044182 [PubMed - in process]

**Vascular age to determine cardiovascular disease risk: A systematic review of its concepts, definitions, and clinical applications.**

Groenewegen KA, den Ruijter HM, Pasterkamp G, Polak JF, Bots ML, Peters SA.

**BACKGROUND:** Vascular age is an alternate means of representing an individual's cardiovascular risk. Little consensus exists on what vascular age represents and its clinical utility has not been determined. We systematically reviewed the literature to provide a comprehensive overview of different methods that have been used to define vascular age, and to examine its potential clinical value in patient communication and risk prediction.

**DESIGN:** This was a systematic review with data sources of PubMed and Embase.

**RESULTS:** We identified 39 articles on vascular age, 20 proposed to use vascular age as a communication tool and 19 proposed to use vascular age as a means to improve cardiovascular risk prediction. Eight papers were methodological and 31 papers reported on vascular age in study populations. Of these 31 papers, vascular age was a direct translation of the absolute risk estimated by existing cardiovascular risk prediction models in 15 papers, 12 derived vascular age from the reference values of an additional test, and in three papers vascular age was defined as the age at which the estimated cardiovascular risk equals the risk from non-invasive imaging observed degree of atherosclerosis. One trial found a small effect on risk factor levels when vascular age was communicated instead of cardiovascular risk.

**CONCLUSION:** Despite sharing a common name, various studies have proposed distinct ways to define and measure vascular age. Studies into the effects of vascular age as a tool to improve cardiovascular risk prediction or patient communication are scarce but will be required before its clinical use can be justified.

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**Fast Food Pattern and Cardiometabolic Disorders: A Review of Current Studies.**

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**BACKGROUND:** There are growing concern globally regarding the alarming trend of fast food consumption and its related cardiometabolic outcomes including overweight and obesity. This study aimed to review the current evidences available in relation to adverse effects of fast food pattern on cardiometabolic risk factors.

**METHODS:** Relevant articles including epidemiological and clinical studies with appropriate design and good quality were obtained through searches of the Medline, PubMed, Scopus databases and Google scholar with related key words including "fast foods", "processed foods", "obesity", "overweight", "insulin resistance", "diabetes", "cardiovascular disease", "metabolic syndrome", "dyslipidemia" and "hypertension".

**RESULTS:** Fast food consumption and out-of-home eating behavior is a main risk factor for lower diet quality, higher calorie and fat intake and lower micronutrients density of diet. Frequent consumption of fast foods was accompanied with overweight and abdominal fat gain, impaired insulin and glucose homeostasis, lipid and lipoprotein disorders, induction of systemic inflammation and oxidative stress. Higher fast food consumption also increases the risk of developmental diabetes, metabolic syndrome and cardiovascular disease.

**CONCLUSION:** This review provides further evidence warning us against the irreparable effects of fast food consumption on public health especially the increasing global burden of obesity and cardiovascular diseases.

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**Cardiovascular disease risk in women with premature ovarian insufficiency: A systematic review and meta-analysis.**

Roeters van Lennep JE, Heida KY, Bots ML, Hoek A; collaborators of the Dutch Multidisciplinary Guideline Development Group on Cardiovascular Risk Management after Reproductive Disorders.

**AIMS:** The purpose of this review was to assess the relationship between premature ovarian insufficiency (POI), defined as natural menopause <40 years, and risk of ischaemic heart disease (IHD), stroke and overall cardiovascular disease (CVD). **METHODS AND RESULTS:** We performed a systematic search in PubMed (1966-2012), EMBASE (1980-2012). Studies were included if they were prospective, follow-up >3 years, assessment of age menopause <40 years, and incident cases of fatal or nonfatal IHD, stroke, or overall CVD. Relative risks (RRs) and 95% confidence interval (CI) were pooled using a random-effect model. Overall, 10 observational studies were identified, comprising 190,588 women (follow-up 4-37 years) with 9440 events (2026 events for IHD (seven studies) and 6438 events for stroke (seven studies) and 976 for total CVD (two studies). POI was assessed by questionnaire and incident cases through certification and event registers. POI was related to an increased risk of developing or dying from IHD (hazard ratio (HR) 1.69, 95% CI 1.29-2.21, p=0.0001) and total CVD (HR 1.61, 95% CI 1.22-2.12, p=0.0007). No relation was found for stroke (HR 1.03, 0.88-1.19, p=0.74). We found no evidence for heterogeneity.

**CONCLUSION:** POI is an independent though modest risk factor of IHD and overall CVD but not of stroke. Because of the limited impact of POI on CVD risk compared to classical cardiovascular risk factors, it is unlikely that POI will be implemented as modifier of cardiovascular risk classification.

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**Obesity and cardiovascular outcomes: a review.**

Ghoorah K, Campbell P, Kent A, Maznyczka A, Kunadian V.

The prevalence of obesity is increasing at an epidemic rate globally with more than 1 billion adults overweight and at least 300 million of them clinically obese. This is expected to rise further in the next 20 to 30 years. Obesity is known to be an independent risk factor for serious health conditions, including hypertension, type 2 diabetes, and cardiovascular diseases. Given the association of obesity with cardiovascular disease, it could be speculated that obese individuals would have adverse outcomes after a cardiovascular event compared to those with normal body mass index (BMI). However, various studies have reported a paradoxical U-shaped relationship between obesity and mortality from various diseases, including myocardial infarction and heart failure, suggesting that patients with higher BMI have similar or lower short- and long-term mortality rates. This phenomenon has been termed the 'obesity paradox' or 'reverse epidemiology'. The goal of this review is to evaluate the potential mechanisms behind the obesity paradox and its implications.

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