ASSOCIATIONS OF CIRCULATING TNFALPHA AND IL-18 WITH MYOCARDIAL INFARCTION AND CARDIOVASCULAR RISK MARKERS: THE GLASGOW MYOCARDIAL INFARCTION STUDY

(ARTIGO ORIGINAL)

Welsh P, Woodward M, Rumley A, Lowe G.

Background: There are a lack of data on the associations of circulating levels of TNFalpha and IL-18 with myocardial infarction (MI), and on the extent of confounding by classical and inflammatory risk markers. **Methods:** We measured TNFalpha and IL-18 in plasma from 446 MI cases and 477 age- and sex-matched controls from North Glasgow. **Results:** TNFalpha and IL-18 were elevated in cases compared to controls (TNFalpha medians 0.99 pg/ml [interquartile range 0.65-1.64 pg/ml] versus 0.77 pg/ml [0.52-1.22 pg/ml], p<0.0001; IL-18 medians 287 pg/ml [212-404 pg/ml] versus 271 pg/ml [200-373 pg/ml], p=0.01). IL-18 was moderately associated with HDL cholesterol r=-0.22, triglycerides r=0.16, and BMI r=0.14 (p for all < or =0.003) in the control population, but not among cases. TNFalpha had few associations with classical risk factors among cases or controls. TNFalpha had a significant association with MI: odds ratio (OR) 1.66 (95% confidence interval; 1.10-2.50), comparing extreme thirds after adjusting for classical risk factors, which was reduced on further adjustment for other inflammatory markers (OR 1.47; 0.91-2.37). IL-18 showed no association by thirds after adjustment for classical risk factors (OR 1.07; 0.70-1.62). **Conclusions:** Circulating levels of IL-18 and TNFalpha were elevated in those with previous MI, but only TNFalpha retained an association after adjustment for classical risk factors. Independently elevated TNFalpha among those with previous MI may reflect cardiac expression of TNFalpha in ongoing myocardial remodeling. [**Cytokine 2009; 47(2): 143-147]**

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MICROCIRCULATORY EFFECTS OF CHANGING BLOOD HEMOGLOBIN OXYGEN AFFINITY DURING HEMORRHAGIC SHOCK RESUSCITATION IN AN EXPERIMENTAL MODEL

(ARTIGO ORIGINAL)

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Microvascular responses to blood volume restitution using red blood cells (RBCs) with modified hemoglobin (Hb) oxygen affinity were studied in the hamster window chamber model during resuscitation from hemorrhagic shock. Allosteric effectors inositol hexaphosphate and 5-hydroxymethyl-2-furfural were introduced into the RBCs by electroporation to decrease and increase Hb-oxygen affinity. In vitro P50s (partial pressure of oxygen at 50% Hb saturation) were modified to 10 and 50 mmHg (normal P50, 32 mmHg). Awake hamsters were subjected to hemorrhage of 50% of blood volume, followed by a shock period of 1 h, and then resuscitated with 25% blood volume with high or low P50 RBCs (hematocrit, 50%). After resuscitation, base excess was significantly lower than baseline in the high-P50 RBC group (HP50; 0.3 +/- 2 vs. 5.0 +/- 1.7 mM) and MAP was lower than baseline in the low-P50 RBC group (LP50; 93 +/- 6 vs. 109 +/- 6 mM). Arteriolar diameter and flow were significantly lower in the HP50. Functional capillary density in the HP50 was significantly lower than LP50 at 60 and 90 min after resuscitation. There was no significantly difference in arteriolar PO2. Tissue PO2, venular PO2, and oxygen delivery were higher in LP50 than in HP50. There was no significant difference in oxygen extraction. Oxygen extraction ratio (oxygen extraction/oxygen delivery) x 100 was significantly higher in HP50 than in LP50. These results suggest that lowering blood P50 in resuscitation provides improved microvascular function in comparison with higher P50. **[Shock 2009; 31(6):645-652]**

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META-ANALYSIS: RETINAL VESSEL CALIBER AND RISK FOR CORONARY HEART DISEASE

(ARTIGO ORIGINAL)

McGeechan K, Liew G, Macaskill P, Irwig L, Klein R, Klein BE, Wang JJ, Mitchell P, Vingerling JR, Dejong PT, Witteman JC, Breteler MM, Shaw J, Zimmet P, Wong TY.

Background: Retinal vessel caliber may be a novel marker of coronary heart disease (CHD) risk. However, the sex-specific effect, magnitude of association, and effect independent of traditional CHD disease risk factors remain unclear. PURPOSE: To determine the association between retinal vessel caliber and risk for CHD. **Data sources:** Relevant studies in any language identified through MEDLINE (1950 to June 2009) and EMBASE (1950 to June 2009) databases. **Study selection:** Studies were included if they examined a general population, measured retinal vessel caliber from retinal photographs, and documented CHD risk factors and incident CHD events. **Data extraction:** 6 population-based prospective cohort studies provided data for individual participant meta-analysis. **Data synthesis:** Proportional hazards models, adjusted for traditional CHD risk factors, were constructed for retinal vessel caliber and incident CHD in women and men. Among 22,159 participants who were free of CHD and followed for 5 to 14 years, 2219 (10.0%) incident CHD events occurred. Retinal vessel caliber changes (wider venules and narrower arterioles) were each associated with an increased risk for CHD in women (pooled multivariable-adjusted hazard ratios, 1.16 [95% CI, 1.06 to 1.26] per 20-microm increase in venular caliber and 1.17 [CI, 1.07 to 1.28] per 20-microm decrease in arteriolar caliber) but not in men (1.02 [CI, 0.94 to 1.10] per 20-microm increase in venular caliber and 1.02 [CI, 0.95 to 1.10] per 20-microm decrease in arteriolar caliber). Women without hypertension or diabetes had higher hazard ratios. **Limitation:** Error in the measurement of retinal vessel caliber and Framingham variables was not taken into account. **Conclusion:** Retinal vessel caliber changes were independently associated with an increased risk for CHD events in women. **[Ann Intern Med 2009; 151(6):404-413].**

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WALL-TO-LUMEN RATIO OF RETINAL ARTERIOLES AS A TOOL TO ASSESS VASCULAR CHANGES

(ARTIGO DE REVISÃO)

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The retina offers a beautiful and unique opportunity tovisualize and examine the body's microvasculature safely, repeatedly, quickly, and noninvasively in vivo. Retinal arterioles appear to undergo similar changes as cerebral and peripheral arterioles in hypertension, indicating that retinal arteriolar abnormalities mirror structural and functional microvascular changes elsewhere in end-organ tissues.1 Since the pioneering work by Keith et al5 in 1939, several studies have confirmed the prognostic significance of retinal vascular abnormalities on mortality attributed to a cardiovascular cause. However, although there is solid evidence for the prognostic significance of advanced retinopathy, the evidence of a prognostic impact of early retinal vascular abnormalities on cardiovascular risk stratification is less well established. It was suggested that methodological issues might be the cause for the lack of a solid evidence that early retinal vascular abnormalities are closely linked to cardiovascular risk. Therefore, much research effort over the last decade has focused on the development of new methodological approaches to enable more precise and reliable detection and evaluation of early retinal vascular abnormalities in hypertensive patients. A new approach focuses on retinal arteriolar structural parameters by using scanning laser Doppler flowmetry (SLDF) with automatic full-field perfusion imaging analyses (AFFPIAs).This approach allows the assessment of both the outer diameter (OD) and inner diameter (ID) of retinal arterioles in vivo and, thus, analyzes vascular remodeling of retinal arterioles by calculating wall:lumen ratio, wall thickness, and wall cross-sectional area (volume of wall per unit of length) of retinal arterioles. These methods do not need to determine diameter of retinal venules, which are also subject to changes in cardiovascular disease. This review introduces and describes this new methodology, explains the improved power of measuring retinal vascular changes, and discusses our recent findings using this tool. **[Hypertension 2009; 54(2):384-387]**

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