# INFLUENCE OF THE CD14 GENOTYPE POLYMORPHISM ON C-REACTIVE PROTEIN LEVELS IN PATIENTS WITH CORONARY ARTERY DISEASE

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# ABSTRACT

**Background:** Inflammation is one of the major components of atherosclerosis, which is the underlying disorder that leads to various diseases including coronary artery disease (CAD). CD14 receptor is an important mediator of inflammatory reactions and its expression is under genetic control. The allelic variant of the CD14 polymorphism located in the promoter region of the CD14 gene is associated with receptor expression and ischemic risk.

**Aim of the work:** assessment the effect of the CD14 genotype polymorphism on high sensitivity C- reactive protein (hs-CRP) levels in patients with CAD.

**Patients and methods:** We studied 70 patients, 50 pts aged (53.42±8.09; men) (cases) with angiographically proven CAD, 20 pts aged (48.25±5.66; men) (controls) with normal coronary angiography.CD14 genotypes were determined by a Polymerase Chain Reaction (PCR) Restriction Fragment Length Polymorphism Analysis (RFLP) technique. High sensitivity C- reactive protein (hs-CRP) levels measured by immunoflorocent technique using (immulite). ®

**Results.** Patients with CAD had a significantly higher frequency of the TT genotype than patients with normal coronaries 42% vs. 20% p value 0.04. TT subjects had increased (hs-CRP) levels (10.8 mg\l) compared with carriers of the C allele (CC (4.8 mg\l) - CT (5.07 mg\l)) p value 0.03. Incidence of MI is high in TT subjects. There as no significant association between genotypes, or allele frequencies, and severity of CAD p value NS.

**Conclusion. T** homozygotes of this functional polymorphism represent a genetically determined risk factor for the development of CAD.



***Keywords****: CD14 receptor; Polymorphism; Coronary artery disease; Inflammation; Atherosclerosis*

# LIST OF ABBREVIATIONS

| | |
|---|---|
| **ACB** | *Albumin cobalt binding test.* |
| **ACC** | *The American College of Cardiology.* |
| **ACE** | *Angiotensin- converting enzyme.* |
| **ACEI** | *Angiotensin- converting enzyme inhibitors.* |
| **ACS** | *Acute coronary syndrome.* |
| **ACT** | *activated clotting time.* |
| **ACUITY** | *Acute Catheterization and Urgent Intervention Triage strategy Trial.* |
| **ADP** | *Adenosine diphosphate.* |
| **AHA** | *The American Heart Association.* |
| **AP-1** | *Activating protein 1.* |
| **aPTT** | *activated partial thromboplastin time .* |
| **ARBS** | *angiotesin receptor blockers.* |
| **ARIC** | *Atherosclerosis Risk in Communities.* |
| **ASA** | *Apirine.* |
| **ASSENT-4 PCI** | *ASsessment of the Safety and Efficacy of a New Treatment Strategy with percutaneous Coronary Intervention-4 .* |
| **ATF-1** | *Activating transcription factor 1.* |
| **ATP III** | *Third Adult Treatment Panel.* |
| **B.B** | *B blockers.* |
| **bid** | *bis in die (Latin: twice-daily dosage).* |
| **BMI** | *Body mass index.* |
| **BNP** | *Brain natriuretic peptide.* |
| **BP** | *Blood pressure.* |
| **Ċ** | *Celsius degree temperature.* |
| **C** | *Cytosine nucleotide base.* |
| **C.I** | *Confidence interval.* |
| **CABG** | *Coronary artery bypass graft.* |
| **CAPRIE** | *Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events.* |
| **CC** | *Correlation coefficient.* |
| **CCB** | *calcium channel blockers.* |
| **CD** | *Cluster of differentiation .* |
| **CDC** | *Control disease center.* |
| **CHD** | *Coronary heart disease.* |
| **CHF** | *Congestive heart failure.* |
| **CKD** | *Chronic kidney disease.* |
| **CK-MB** | *Creatine kinase MB.* |

| | |
|---|---|
| **COMMIT** | *ClOpidogrel and Metoprolol in Myocardial Infarction Trial.* |
| **COMMIT/CCS-2** | *ClOpidogrel and Metoprolol in Myocardial Infarction Trial/ Chinese Cardiac Study 2.* |
| **COX-1** | *Cyclooxygenase -1.* |
| **Cp-HSP60** | *Chlamydia pneumoniae HSP60 .* |
| **CRE** | *cAMP response element.* |
| **CRP** | *C -reactive protein.* |
| **CSA** | *Chronic stable angina.* |
| **CT** | *Computed tomography.* |
| **CT** | *Computed tomographic.* |
| **cTnI** | *Cardiac Troponin I.* |
| **cTnT** | *Cardiac Troponin T.* |
| **CV** | *Cardiovascular.* |
| **CVA** | *Cerebrovascular accident.* |
| **CVD** | *Cardiovascular diseases.* |
| **D2B** | *Door-To-Balloon.* |
| **DANAMI-2** | *Danish Trial in Acute Myocardial Infarction.* |
| **dl** | *Deciliter.* |
| **DM** | *Diabetes mellitus.* |
| **DNA** | *Deoxyribonucleic acid.* |
| **DTIs** | *Direct thrombin inhibitors .* |
| **e.g.** | *example gratia (Latin = for example).* |
| **ECG** | *Electrocardiograph.* |
| **ED** | *Emergancy department .* |
| **EDTA** | *Ethylene diaminetetraacetic acid.* |
| **EIS** | *Early invasive management strategy.* |
| **ELISA** | *Enzyme-linked immunosorbent assay.* |
| **EMS** | *Emergency medical services.* |
| **ERK** | *Extracellular signal regulated kinase .* |
| **ESC** | *The European Society of Cardiology.* |
| **ExTRACT-TIMI 25** | *Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial InfarCtion Treatment, Thrombolysis In Myocardial Infarction—Study 25.* |
| **FABPs** | *Fatty acid binding proteins.* |
| **FDA** | *Food and Drug Administration.* |
| **FFA** | *Free fatty acids.* |
| **FFAu** | *Unbound free fatty acids.* |
| **FHx** | *Family history.* |
| **FINESSE** | *Facilitated INtervention with Enhanced Reperfusion Speed to Stop Events trial.* |

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|---|---|
| **G** | *Guanine nucleotide base.* |
| **GPI** | *Glycosyl phosphatidylinositol.* |
| **GPI** | *Glycoprotein IIb/IIIa inhibitor.* |
| **GRACE** | *Global Registry of Acute Coronary Events.* |
| **HDL** | *High density lipoproteins.* |
| **H-FABP** | *Heart -type fatty acid binding proteins.* |
| **HIT** | *heparin-induced thrombocytopenia .* |
| **HORIZONS-AMI** | *Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction trial.* |
| **HRT** | *Hormone replacement therapy.* |
| **HSA** | *Human serum albumin.* |
| **hs-CRP** | *High sensitivity C-reactive protein.* |
| **HTN** | *Hypertension.* |
| **hu-HSP** | *Human heat shock protein.* |
| **ICAMs** | *Intracellular adhesion molecules.* |
| **ICH** | *Intracranial hemorrhage.* |
| **ICTUS** | *Invasive Versus Conservative Treatment in Unstable Coronary Syndromes trial.* |
| **IGF-1** | *Insulin growth factor-1.* |
| **IGFBPs** | *Insulin -like growth factor binding proteins.* |
| **IHD** | *Ischemic heart disease.* |
| **IkB** | *Inhibitory kB .* |
| **IKKb** | *Activated inhibitory kB kinase b.* |
| **IL-6** | *Interleukine 6.* |
| **IM** | *Intramuscular.* |
| **IMA** | *Ischemia modified albumin.* |
| **IRAK** | *Interleukin 1 (IL-1) receptor associated kinase.* |
| **ISAR-COOL** | *the Intracoronary Stenting with Antithrombotic Regimen Cooling-off Trial.* |
| **ISAR-REACT** | *Abciximab in patients with acute coronary syndromes undergoing percutaneous coronary intervention after clopidogrel pretreatment.* |
| **JNK** | *Jun N-terminal kinase.* |
| **kg** | *Kilogram.* |
| **LBP** | *LPS binding protein.* |
| **LDL** | *Low -density lipoproteins.* |
| **LMWHs** | *Low-molecular weight heparins.* |
| **Lp-PLA** | *Lipoprotein-associated phospholipase.* |
| **LPS** | *Lipopolysaccharide.* |
| **LRRs** | *Leucine-rich repeats.* |
| **LVH** | *Left ventricular hypertrophy.* |
| **MAPK** | *Mitogen activated protein kinase .* |

| | |
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| **mCD14** | *The membrane expressed CD14.* |
| **MERLIN** | *Middlesbrough Early Revascularization to Limit Infarction.* |
| **MeSH** | *Medical Subject Heading.* |
| **MetS** | *Metabolic syndrome.* |
| **MI** | *Myocardial infarction.* |
| **MITRA** | *Maximal Individual Therapies for Acute Myocardial Infarction.* |
| **MMP** | *Matrix metalloproteinase.* |
| **MMPs** | *Metalloproteinases.* |
| **MONICA** | *Monitoring of Trends and Determinants in Cardiovascular Disease study.* |
| **MPO** | *Myeloperoxidase.* |
| **MR** | *Mitral regurgitation.* |
| **MU** | *Mega unit.* |
| **MyD88** | *Myeloid differentiation protein 88.* |
| **n** | *Number.* |
| **NA** | *not available.* |
| **NF-kB** | *Nuclear factor kB.* |
| **NHLBI** | *National Heart, Lung, and Blood Institute.* |
| **NIH** | *National Institutes of Health.* |
| **NS** | *Non significant* |
| **NSTE-ACS** | *non-ST elevation acute coronary syndrome.* |
| **NSTEMI** | *Non -ST segment elevation myocardial infarction.* |
| **NT-pro BNP** | *n-terminus pro-brain natruretic proteine.* |
| **OASIS** | *Organization to Assess Strategies for Ischaemic Syndromes Study.* |
| **P value** | *Probability value.* |
| **P1GF** | *Placenta growth factor.* |
| **PAMI** | *Primary Angioplasty in Myocardial Infarction.* |
| **PAPP-A** | *Pregnancy -associated protein A.* |
| **PCI** | *Percutaneous coronary intervention.* |
| **PLCHO** | *Plasma choline .* |
| **PLD** | *Phospholipase D.* |
| **PRAGUE** | *PTCA Units versus Emergency Thrombolysis.* |
| **PROVE IT-TIMI** | *Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction.* |
| **PURSUIT** | *Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy.* |
| **PVD** | *Peripheral vascular disease.* |
| **RCT** | *Randomized controlled trial.* |
| **REACT** | *Rescue Angioplasty versus Conservative Treatment or* |

| | |
|---|---|
| | *Repeat Thrombolysis.* |
| **REVERSAL** | *The Reversal of Atherosclerosis With Aggressive Lipid Lowering.* |
| **RITA-3** | *Third Randomized Intervention Treatment of Angina Study .* |
| **RR** | *Relative risk.* |
| **SBP** | *Systolic blood pressure.* |
| **SCAI** | *Society for Cardiovascular Angiography and Interventions.* |
| **sCD14** | *Soluble molecule CD14.* |
| **SIS** | *Selectively invasive management strategy.* |
| **SRE** | *Serum response element.* |
| **STE-ACS** | *ST elevation acute coronary syndrome.* |
| **STEMI** | *ST segment elevation myocardial infarction.* |
| **SYNERGY** | *Superior Yield of the New Strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa Inhibitors Trial.* |
| **T** | *Thymine nucleotide base.* |
| **TC** | *Total cholesterol.* |
| **TG** | *Triglycerides .* |
| **TH1** | *T-cells helper.* |
| **TIA** | *Transient ischemic attack.* |
| **TIMI** | *Thrombolysis in Myocardial Infarction.* |
| **TIMPs** | *Tissue inhibitors of metalloproteinases.* |
| **TLR4** | *Toll -like receptor 4.* |
| **TNF** | *Tumour necrosis factor .* |
| **TNF-a** | *Tissue necrosis factor-alpha.* |
| **TRAF6** | *Tumour necrosis factor receptor associated factor.* |
| **UA** | *Unstable angina.* |
| **UFH** | *Unfractionated heparin.* |
| **VCAMs** | *Vascular adhesion molecules.* |
| **VINO** | *Value of First Day Angiography/Angioplasty in Evolving Non-ST Segment Myocardial Infarction: Open Multicenter Randomized Trial.* |
| **WBCHO** | *Whole blood choline.* |
| **WHO** | *The World Health Organization.* |
| **WHS** | *Women Health Study* |

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