Are Genetic Variants of C-Reactive Protein Prognostic Markers for Further Cardiovascular Events in Patients With Coronary Heart Disease?

S Schulz 1, H Lüdike 1, A Schli 2,3, K Werdan 2, B Hofmann 4, C Gläser 5, HG Schaller 1, S Reichert 1
1 University School of Dental Medicine, Department of Operative Dentistry and Periodontology, Martin-Luther-University Halle-Wittenberg, Germany
2 Department of Medicine III, Martin-Luther University Halle-Wittenberg, Germany
3 Department of Cardiology, Paracelsus-Harz-Clinic Bad Sudekde, Germany
4 Department of Cardiothoracic Surgery, Martin-Luther University Halle-Wittenberg, Germany
5 Institute of Human Genetics and Medical Biology, Martin-Luther-University, Halle-Wittenberg, Germany

Introduction

Does periodontitis influence CAD?

C-reactive protein is involved in both diseases

CRP plays an acute phase protein in an important role in inflammation

CRP levels are increased in periodontitis and cardiovascular diseases

Periodontopathogens can enter the bloodstream and influence coronary processes

Both diseases share same inflammatory mediators

Material and Methods

Cardiovascular patients

Longitudinal cohort study (ClinicalTrials.gov Identifier: NCT01045076; n = 940)


Inclusion criteria:
in-patient stay subjects with ≥50% stenosis of the main coronary artery
German caucasian, > 18 years of age, Presence of ≥ 4 teeth

Exclusion criteria:
periodontal treatment during the last 6 months,
anaerobic therapy during the last 3 month, pregnancy

Baseline clinical examination:
Anamnesis → age, gender, smoking status, medication, existing diseases
Dental examination → plaque index, bleeding on probing, pocket depth, clinical attachment loss

Genomic investigations

DNA-isolation from EDTA-blood
Preparation of genomic DNA was carried out using the blood extraction kit (Qiagen, Hilden, Germany).

PCR reactions were carried out using Mastermix (Promega, Mannheim, Germany)

PCR-program (2min 94°C; 10 cycles: 15sec 94°C, 1min 64°C; 20 cycles: 15sec 94°C, 50sec 61°C, 30sec 72°C)

Schematic illustration of PCR fragments after restriction cleavage

CRP polymorphisms rs1800947 and rs1417938 are associated with CRP serum level in our cohort of CAD patients. Despite the CRP level as

Hypotheses of the study

Genetic variants in CRP (rs4273) and rs1417938 can influence its expression
SNPs are associated with CRP expression in CAD patients

SNPs are prognostic markers for cardiovascular events (myocardial infarction, stroke, cardiovascular death)

CRP: Circulating CRP level is a prognostic marker for cardiovascular events (myocardial infarction, stroke, cardiovascular death)

Results and discussion

CRP serum level in dependence of SNPs

Allele rs1800947
Genotype rs1800947
Allele rs1417938
Genotype rs1417938

In a complex risk model (cox regression) considering age, gender, body mass index (BMI), smoking, diabetes as potential confounders, the CRP serum level could be proven as an independent prognostic indicator for adverse cardiovascular events regarding the one-year outcome.

Conclusions

CRP polymorphisms rs1800947 and rs1417938 are associated with CRP serum level in our cohort of CAD patients. Despite the CRP level as an independent prognostic marker for adverse cardiovascular events (myocardial infarction, stroke/TIA, cardiovascular death), neither polymorphism could be proven to have prognostic value regarding the one year outcome.