Endothelial Function and Carotid Intima-Media Thickness in Young Healthy Subjects Among Endothelial Nitric Oxide Synthase Polymorphisms

Umberto Paradossi, Enrica Cifoni, Simona Storti, Nicolletta Botto, Andrea Biagini, Maria Giovanna Colombo, CNR Institute of Clinical Physiology, G. Pasquarini Hospital, Massa, Italy

Background: To assess the role of the endothelial nitric oxide synthase (eNOS) gene variants as risk factors for early atherosclerosis, we sought to investigate whether two polymorphisms found in the exon 7 (Glu298→Asp) and in the promoter region (T786→C) of the eNOS gene were associated with functional changes in the endothelium, and carotid intima-media thickness (IMT).

Methods: Endothelium-dependent flow-mediated brachial artery dilation (FMD), endothelium-independent dilation response to glyceryl trinitrate (GTN), and carotid IMT were assessed by high resolution ultrasound in 98 healthy young non smoker subjects (29.8±0.5 years) genotyped for the eNOS Glu298→Asp and T786→C polymorphisms.

Results: Carotid IMT was inversely related to FMD by univariate analysis (r=-0.29, p=0.03) and after adjustment for possible confounders in all the subjects (p=0.03). In comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: These results demonstrate an atheroprotective effect of Glu298 variants of eNOS on early atherosclerosis.

Phototherapy Treats Atherosclerotic Plaque Inflammation, Induces Plaque Stabilization and Promotes Plaque Reduction

Ron Wehman, Pauline McEwan, Frank Kolodgie, Travis Moore, Steve Rychnovsky, David Hellmich, Renu Varmus, William Weintraub, David Resnick, Miravit Medical Technologies, Inc., Santa Barbara, CA

Background: Acute coronary syndromes are associated with other sites of vulnerable plaque located in areas of insignificant stenosis. Intravascular PhotopointTM photodynamic therapy (PDT) using light activation of the novel photosensitizer MV0633 is a potential treatment for these focal segments. Previous studies have shown cell depletion (Asp/Asp: 0.46±0.03 vs control 12.9±3.6% total plaque area) despite reduced plaque area. 28 days, plaque smooth muscle alpha actin content significantly increased (PDT 0.18, p=0.23; Asp/Asp: n=0.9, p=0.02). No difference in IMT was found in comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: The eNOS Glu298→Asp polymorphism may be related to early atherogene

Photodynamic Therapy Reduces Atherosclerotic Plaque Inflammation, Induces Plaque Stabilization and Promotes Plaque Reduction

Ron Wehman, Pauline McEwan, Frank Kolodgie, Travis Moore, Steve Rychnovsky, David Hellmich, Renu Varmus, William Weintraub, David Resnick, Miravit Medical Technologies, Inc., Santa Barbara, CA

Background: Acute coronary syndromes are associated with other sites of vulnerable plaque located in areas of insignificant stenosis. Intravascular PhotopointTM photodynamic therapy (PDT) using light activation of the novel photosensitizer MV0633 is a potential treatment for these focal segments. Previous studies have shown cell depletion (Asp/Asp: 0.46±0.03 vs control 12.9±3.6% total plaque area) despite reduced plaque area. 28 days, plaque smooth muscle alpha actin content significantly increased (PDT 0.18, p=0.23; Asp/Asp: n=0.9, p=0.02). No difference in IMT was found in comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: These results demonstrate an atheroprotective effect of Glu298 variants of eNOS on early atherosclerosis.

Phototherapy Treats Atherosclerotic Plaque Inflammation, Induces Plaque Stabilization and Promotes Plaque Reduction

Ron Wehman, Pauline McEwan, Frank Kolodgie, Travis Moore, Steve Rychnovsky, David Hellmich, Renu Varmus, William Weintraub, David Resnick, Miravit Medical Technologies, Inc., Santa Barbara, CA

Background: Acute coronary syndromes are associated with other sites of vulnerable plaque located in areas of insignificant stenosis. Intravascular PhotopointTM photodynamic therapy (PDT) using light activation of the novel photosensitizer MV0633 is a potential treatment for these focal segments. Previous studies have shown cell depletion (Asp/Asp: 0.46±0.03 vs control 12.9±3.6% total plaque area) despite reduced plaque area. 28 days, plaque smooth muscle alpha actin content significantly increased (PDT 0.18, p=0.23; Asp/Asp: n=0.9, p=0.02). No difference in IMT was found in comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: These results demonstrate an atheroprotective effect of Glu298 variants of eNOS on early atherosclerosis.

Photodynamic Therapy Reduces Atherosclerotic Plaque Inflammation, Induces Plaque Stabilization and Promotes Plaque Reduction

Ron Wehman, Pauline McEwan, Frank Kolodgie, Travis Moore, Steve Rychnovsky, David Hellmich, Renu Varmus, William Weintraub, David Resnick, Miravit Medical Technologies, Inc., Santa Barbara, CA

Background: Acute coronary syndromes are associated with other sites of vulnerable plaque located in areas of insignificant stenosis. Intravascular PhotopointTM photodynamic therapy (PDT) using light activation of the novel photosensitizer MV0633 is a potential treatment for these focal segments. Previous studies have shown cell depletion (Asp/Asp: 0.46±0.03 vs control 12.9±3.6% total plaque area) despite reduced plaque area. 28 days, plaque smooth muscle alpha actin content significantly increased (PDT 0.18, p=0.23; Asp/Asp: n=0.9, p=0.02). No difference in IMT was found in comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: These results demonstrate an atheroprotective effect of Glu298 variants of eNOS on early atherosclerosis.

Photodynamic Therapy Reduces Atherosclerotic Plaque Inflammation, Induces Plaque Stabilization and Promotes Plaque Reduction

Ron Wehman, Pauline McEwan, Frank Kolodgie, Travis Moore, Steve Rychnovsky, David Hellmich, Renu Varmus, William Weintraub, David Resnick, Miravit Medical Technologies, Inc., Santa Barbara, CA

Background: Acute coronary syndromes are associated with other sites of vulnerable plaque located in areas of insignificant stenosis. Intravascular PhotopointTM photodynamic therapy (PDT) using light activation of the novel photosensitizer MV0633 is a potential treatment for these focal segments. Previous studies have shown cell depletion (Asp/Asp: 0.46±0.03 vs control 12.9±3.6% total plaque area) despite reduced plaque area. 28 days, plaque smooth muscle alpha actin content significantly increased (PDT 0.18, p=0.23; Asp/Asp: n=0.9, p=0.02). No difference in IMT was found in comparison to Glu298 homozygotes, Asp/Asp carriers displayed a significantly lower FMD (Glu/Glu: 15.2±1.2% vs Asp/Asp: 9.4±1.7%, p<0.01), while FMD was unaffected by the T786→C variant (TT: 14.6±1.1%, TC: 12.2±0.8%, and CC: 12.0±0.5%, p=0.18). Neither the Glu298→Asp nor the T786→C polymorphisms influenced the GTN-mediated dilation.

Conclusion: These results demonstrate an atheroprotective effect of Glu298 variants of eNOS on early atherosclerosis.