

Investigation of asymmetric dimethylarginine in patients with coronary artery disease

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Introduction: The concentrations of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase are increased in patients with coronary artery disease (CAD). An elevated concentration of ADMA in the plasma and pericardial fluid (PF) is an independent predictor of worse cardiovascular events in patients undergoing coronary revascularization. We aimed to investigate the changes of pericardial and plasma ADMA levels in patients with CAD, who underwent percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery.

Patients and Methods: 64 patients who underwent PCI or CABG surgery were enrolled in this study (65.5 ± 8.2 years). 52 patients who underwent the valve replacement (VR) served as control subjects (59 ± 6.9 years). Exercise stress test was performed on a treadmill according to the Bruce protocol. ADMA levels were determined by using liquid chromatography — tandem mass spectrometry. Furthermore L-arginine and ADMA concentrations were determined in plasma and PF of patients undergoing coronary artery bypass graft (CABG, n=28) or valve replacement (VR, n=25).

Results: Patients in the CAD group had significantly elevated plasma concentrations of ADMA at rest, compared to the control group ($0.59 \pm 0.02 \mu\text{M/l}$ vs. $0.46 \pm 0.03 \mu\text{M/l}$; $p<0.01$). ADMA decreased immediately after stent implantation in the PCI group. There was no discernible increase in ADMA in the off-pump CABG group. In contrast, the levels of ADMA were significantly elevated in the group of patients who underwent cardiopulmonary bypass (CPB) ($F=0.416$, $p<0.685$ and $F=14.751$, $p<0.001$ for the off-pump and CPB groups, respectively). Similarly, a significant increase in ADMA was observed in the peripheral blood ($F=30.738$, $p<0.001$) during CPB, while during the off-pump CABG surgery, ADMA remained largely unchanged. The L-arginine/ADMA ratio of both plasma (125.4 ± 10.7 vs. 76.7 ± 8.7) and PF (110.4 ± 7.2 vs. 80.8 ± 6.04) were significantly higher in the CABG group compared to the VR group. Furthermore, there was a significant positive correlation between plasma and pericardial L-arginine levels in the CABG group. The PF ADMA was higher in the VR than CABG group.

Conclusion: This clinical study highlights the importance of the investigation of both plasma and pericardial ADMA levels in patients with CAD. Changes of ADMA, and L-arginine/ADMA ratio are reliable, as well as the feasible markers of ischemia-reperfusion injury occurring in patients who underwent coronary revascularization.

KEYWORDS: asymmetric dimethylarginine, coronary revascularization, coronary artery disease.

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