

MITOCHONDRIAL DNA COPY NUMBER CORRELATES WITH OXIDATIVE STRESS AND PREDICTS MORTALITY IN HEMODIALYSIS PATIENTS

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Background:

Oxidative stress is highly prevalent in hemodialysis patients and may contribute to atherosclerosis and mortality. Copy number of mitochondrial DNA (mtDNA) is affected by oxidative stress in blood circulation. However, the roles of mtDNA copy number and oxidative stress in hemodialysis patients are incompletely defined. The aim of the present study is to test whether mtDNA copy number correlates with oxidative stress and predicts all-cause mortality in hemodialysis patients.

Methods:

Ninety-five non-diabetic hemodialysis patients and 95 age and gender-matched healthy subjects were enrolled. Plasma thiobarbituric acid-reactive substances (TBARS) and plasma free thiol were estimated as indicators of oxidative damage to plasma lipids and antioxidant defense, respectively. Mitochondrial copy number in the peripheral blood leukocyte was measured by determining relative amounts of nuclear DNA and mtDNA by quantitative PCR. Hemodialysis patients were categorized into two groups according to mtDNA copy number above or below median. All-cause mortality of hemodialysis patient was registered during a follow-up of 3 years.

Results:

Hemodialysis patients showed higher TBARS levels, lower free thiols levels and higher mtDNA copy numbers compared with normal control subjects. Plasma TBARS level was a significant factor contributing positively to the mtDNA copy number ($p=0.024$). Patients with mtDNA copy number greater than the median had greater all-cause mortality than patients with low mtDNA copy number (17.0 % versus 4.2 %; log rank test: $p=0.038$). A one-log increase in mtDNA copy number was independently related to an increase hazard for mortality (hazard ratio 251.89; 95% confidence interval 4.30 to 14740.76).

Conclusion:

Hemodialysis patients had higher oxidative stress and mtDNA copy number than healthy subjects. MtDNA copy number correlates with oxidative stress and predicts mortality in hemodialysis patients.

Key Words:

Mitochondrial DNA copy number, oxidative stress, hemodialysis.