Introduction and Objectives: The hemodynamic flow-induced shear stress triggering adaptive responses and atheroprotection in endothelial cells have been well recognized. However, the effects of shear stress on mitochondrial properties in endothelial cells remain unclear. We investigate the endothelial mitochondrial phenotype and functions after steady shear flow treatment.

Materials and Methods: Human umbilical vein endothelial cells (ECs) were subjected to a constant steady shear flow with shear stress of 12 dynes/cm² generated by parallel-plate flow chamber system. Confocal microscopy and Western blot were used to analyze the mitochondrial phenotype and proteins’ expression. Mitochondrial membrane potential, ATP production and oxygen consumption were assayed.

Results and Conclusions: Sheared ECs increased mitochondrial biogenesis demonstrated by the increase of PGC-1alpha, mitochondrial transcription factor A (TFAM) and mitochondrial proteins. ECs under shear showed a time-dependent increment of mitochondrial interconnected tubular formation. This phenomenon was coupled with an increased expression of fusion proteins (MFN2, OPA1) but decreased fission proteins (FIS1). Consistently, an increase of phosphorylation at S637 but decreased at S616 on Drp1 indicates that shear flow promotes mitochondrial fusion process. Shear flow increased the expression of mitochondrial antioxidant enzymes MnSOD2, TRX2, PRX3 and PRX5. Thus, a decrease of mitochondrial reactive oxygen species (ROS) revealed by MitoSox was observed in 12 hr shear-treated ECs. As a consequence, sheared ECs increase ATP production, mitochondrial membrane potential and oxygen consumption. Shear stress also increases the NAD+/NADH ratio and the expression of mitochondria-deacetylase SIRT3. Acetylated mitochondrial proteins were shown to be decreased after shear treatment. Our results suggest that steady shear flow plays an important role in promoting mitochondrial functions in ECs, further substantiates the atheroprotective role of shear stress to ECs.

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Key Words: endothelial cells, shear stress, mitochondrial functions.