

Severe burn-induced mitochondria recruitment of calpain causes aberrant of mitochondrial dynamics and heart dysfunction

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Abstract

Mitochondria damage is an important cause of heart dysfunction after severe burn. However, the pathophysiological process remains unclear. This study aims to examine the mitochondrial dynamics in the heart after severe burn, and the role of μ -calpain, a cysteine protease, in this scenario. Rats were subjected to thermal injury treatment, and calpain inhibitor MDL28170 was given intravenously 1 h before burn injury. Compared with the sham group, the rats in the burn group displayed weakened heart performance and decreased mean arterial pressure, which was accompanied by a diminishment of mitochondria function. Furthermore, severe burn increased the level of calpain in mitochondria, reflected by immunofluorescence staining and activity test. In contrast, treatment with MDL28170 diminished these responses to a severe burn. Severe burn induced morphological defects of mitochondria, and decreased the abundance of mitochondria. Of note, severe burn increased the percentage of the mitochondria with bigger size, but decreased the smaller ones. Analysis of dynamic proteins revealed that severe burn caused an increase of fission protein DRP1 in the mitochondria and a decrease of inner membrane fusion protein OPA1. Similarly, these alterations were also blocked by MDL28170. Last but not the least, inhibition of calpain yielded the emergence of more elongated mitochondria along with membrane invagination in the middle of the longitude, an indicator of the fission process. Overall, these results for the first time provide evidence that mitochondria recruitment of calpain confers heart dysfunction after severe burn, which involves mitochondrial dynamics damage.

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