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Expression of high-mobility group box protein 1 in diabetic foot atherogenesis

C.F. Tsao[1], W.T. Huang[2], T.T. Liu[2], P.W. Wang[1], C.W. Liou[3], T.K. Lin[3], C.J. Hsieh[1] and S.W. Weng[1]

[1]Mitochondrial Research Unit, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan
[2]Department of Pathology, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan
[3]Mitochondrial Research Unit, Department of Neurology, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan

Corresponding author: S.W. Weng
E-mail: wenwen@adm.cgmh.org.tw

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ABSTRACT. The role of high mobility group box 1 (HMGB1) has been demonstrated in stroke and coronary artery disease but not in peripheral arterial occlusive disease (PAOD). The pathogenesis of HMGB1 in acute and chronic vascular injury is also not well understood. We hypothesized that HMGB1 induces inflammatory markers in diabetic PAOD patients. We studied 36 diabetic patients, including 29 patients with PAOD, who had undergone amputation for diabetic foot and 7 nondiabetic patients who had undergone amputation after traumatic injury. Expression of HMGB1 and inflammatory markers were quantified using immunohistochemical staining. Mitochondrial DNA copy number was quantified using real-time polymerase chain reaction. Compared with that in the traumatic amputation group, HMGB1 expression in vessels was significantly higher in the diabetes and diabetic

PAOD groups. In all subjects, arterial stenosis grade was positively correlated with the expression levels of HMGB1, 8-hydroxyguanosine, malondialdehyde, vascular cell adhesion molecule 1, and inflammatory markers CD3, and CD68 in both the intima and the media of vessels. Furthermore, HMGB1 expression level was positively correlated with 8-hydroxyguanosine, vascular cell adhesion molecule 1, nuclear factor-κB, CD3, and CD68 expression. Within the PAOD subgroup, subjects with HMGB1 expression had higher expression of the autophagy marker LC3A/B and higher mitochondrial DNA copy number. HMGB1 may be an inflammatory mediator with roles in oxidative damage and proinflammatory and inflammatory processes in diabetic atherogenesis. Moreover, it may have dual effects by compensating for increased mitochondrial DNA copy number and increased autophagy marker expression.

Key words: Atherosclerosis; Diabetes mellitus; Diabetic foot; High mobility group box 1; Peripheral arterial occlusive disease

