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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

References


Nrf-2–HO-1–HMGB1 axis: An important therapeutic approach for protection against myocardial ischemia and reperfusion injury

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Myocardial reperfusion therapy is the optimal therapeutic strategy for acute myocardial infarction to preserve myocardial viability and function by reversing myocardial ischemia and reducing the infarct size [1]. However, the subsequent ischemia and reperfusion (I/R) injury may attenuate the therapeutic benefit [1]. Although reperfusion therapy is essential for the survival of ischemic tissue, reperfusion itself may cause additional cellular injury by causing local myocardial inflammation, accompanying with apoptosis, which could result in myocardial cell damage [2].

High mobility group box 1 protein (HMGB1), a highly conserved nuclear protein that could regulate gene transcription and maintain the nucleosome structure could be passively released from necrotic cell, apoptotic cell or actively secreted by innate immune cells (such as macrophages and monocytes) [3]. Present study shows that HMGB1 as a novel pro-inflammatory cytokine and contributes to the pathophysiological progression of myocardial I/R injury [4]. HMGB1 may promote the release of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and, which could be inhibited by HMGB1 A box peptide (a specific HMGB1 antagonist) and attenuate myocardial I/R injury [4], demonstrating that inhibiting HMGB1 expression could suppress the local myocardial inflammation in myocardial I/R injury. Hence, these suggested that HMGB1 may become a potential therapeutic target for myocardial I/R injury and anti-HMGB1 over-expression or release could attenuate myocardial I/R injury [5].

Heme oxygenase-1 (HO-1), an inducible isofrom of heme oxygenase (HO) enzymes, has been reported to be anti-inflammatory, anti-apoptotic, and anti-proliferating in several cell types, including cardiac myocytes [6]. Recently, Liu et al. [7] have further demonstrated that Hydroxysafflor Yellow A could provide a protective effect on I/R injury in H9c2 cardiomyocytes by upregulating the expression and activity of HO-1, which indicate that HO-1 may play an important protective effect on anoxia/reoxygenation or I/R injury. Additionally, Takamiya et al. [8] have further showed that the circulating levels of HMGB1 have been proven to be higher in HO-1−/− mice than HO-1+/− mice. Meanwhile, Tsoyer et al. [9] have also indicated that the release of HMGB1 in endotoxin-activated macrophages could be prevented by the HO-1 induction in vitro and septic animals in vivo. Thus, these suggested that the HO-1 induction plays an important role in anti-inflammatory effect and could prevent anoxia/reoxygenation or I/R injury by inhibiting HMGB1 release [10].

Nuclear factor-erythroid 2-related factor 2 (Nrf2), as a nuclear transcription factor, has been proven to be as a critically important mechanism for cellular protection and cell survival [11]. Of note, the cinnamon-derived dietary factor cinnamyl aldehyde has been proven to mediate Nrf-2 translocation to activate the Nrf2-dependent antioxidant response in human epithelial colon cells [12]. Importantly, the Nrf-2 translocation has been further demonstrated to regulate antioxidant response by playing an essential role in the induction of HO-1 [13]. Furthermore, Ha et al. [14] have proved that isoprotretanol could mediate HO-1 induction via Nrf-2 translocation to inhibit the HMGB1 release in LPS-activated RAW 264.7 cells and increases in survival rate of CLP-induced septic mice. In addition, Wang et al. [15] have further demonstrated that dobutamine could also mediate HO-1 induction via Nrf-2 translocation to inhibit the HMGB1 release in rat myocardial I/R injury in vivo. In conclusion, these suggested that Nrf-2 translocation could play an important role in the induction of HO-1 and Nrf-2–HO-1–HMGB1 axis regulation may exist in...
myocardial I/R injury and play a potential therapeutic approach for attenuating myocardial I/R injury. This study was partially supported by a grant from the National Natural Science Foundation of China (No. 81100146 and 81370308), grant 111023 from the Fundamental Research Funds for the Central Universities and the Specialized Research Fund for the Doctoral Program of Higher Education of China (No. 20111041120060) and the Fundamental Research Funds of Wuhan City (No. 2013070104010044).

References

Transcatheter renal sympathetic denervation despite angiographically significant proximal stenosis: Proof of concept from a case report

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Transcatheter renal sympathetic denervation, which encompasses percutaneous radiofrequency ablation of nervous fibers surrounding the renal arteries, has been recently shown effective and safe in patients with resistant hypertension, i.e. those not achieving adequate blood pressure control despite being on several anti-hypertensive agents at maximum tolerated dosage [1–3]. Pivotal trials have however excluded to date several patients, including those with significant renal artery stenosis or previous renal artery intervention. This creates a clinical dilemma for physicians taking care of patients with both resistant hypertension and renal artery stenosis, as angioplasty and stenting for renal artery stenosis have never been proved effective in improving blood pressure control or renal function [4–6]. Given our prior satisfactory experience with the mechanical properties of the ablation catheter used for transcatheter renal sympathetic denervation (Ardian Simplicity Medtronic, Minneapolis, MN, USA), such as steerability, torqueability and tip rigidity, we hypothesized that this catheter can be easily and safely employed to cross a renal stenotic lesion in order to perform more distally the ablation procedure. Accordingly, we performed such procedure in a patient with significant renal artery stenosis.

A 74-year-old man with resistant hypertension (systolic blood pressure values typically of 165–170 mmHg despite assuming four different anti-hypertensive drugs at near-maximum dosage) was admitted to our center for renal angiography and possible subsequent transcatheter renal sympathetic denervation. Right renal angiography showed normal vessel anatomy, whereas left renal angiography showed an angiographically significant stenosis at the proximal tract (Fig. 1). After careful discussion of the case with the referring physician and the attending nephrologist, we chose to perform bilateral renal ablation. Right renal ablation was performed uneventfully in a straightforward fashion. Conversely, to perform left renal ablation, we crossed the lesion with the ablation catheter exploiting roadmapping, and then performed 6 ablation runs distally to the stenotic lesion. Wall-tip contact was satisfactory in all 6 runs and no particular resistance was felt when advancing or rotating the