

ORAL PRESENTATION

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Hemorrhage promotes inflammation and myocardial damage following acute myocardial infarction

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Background

Myocardial hemorrhage, in association with microvascular obstruction (MVO), has recently been speculated to be a new independent predictor of adverse outcomes following acute myocardial infarction (AMI) [1,2]. However, whether hemorrhage is simply a marker of severity or is a cause of myocardial damage and adverse remodeling post-AMI is still under question. Our previous study suggested that hemorrhage may contribute to MVO following reperfusion [3]. The purpose of this study was to mechanistically determine whether hemorrhage, per se, worsens infarct and MVO size and tissue inflammation following an ischemic insult.

Methods

Myocardial hemorrhage was artificially induced in a porcine model via intracoronary injection of collagenase as previously described [3]. The study involved three groups of animals (N = 9) subjected to ischemia-reperfusion injury in the left anterior descending artery (LAD): Group 1 (N = 3): 8 min ischemia with collagenase; Group 2 (N = 3): 45 min occlusion with saline; and Group 3 (N = 3): 45 min occlusion with collagenase. Imaging was performed on a 3T MRI scanner (MR 750, GE Healthcare) at 24 hrs post-reperfusion. Edema/Inflammation was evaluated by T2 quantification using a T2-prepared spiral sequence and hemorrhage was identified by T2* determined using a multi-echo gradient-echo acquisition. Infarct and MVO size was computed using early and late enhancement imaging (EGE, LGE). Explanted hearts were sectioned and assessed by gross pathology.

Results

Group 1 demonstrated minimal infarction (only in 1 animal, 1.3 g) with significant hemorrhage as indicated by T2* (Figure 1) where as Group 2 was non-hemorrhagic with a small infarction (1.3 ± 0.8 g). In contrast, animals in Group 3 demonstrated greater hemorrhage (Figure 1), an infarct size significantly larger than the other two groups (10.7 ± 3.2 g, p = 0.03) and a higher incidence of MVO (2.5 ± 3.7 g). In Group 1, edema (measured by T2) near hemorrhagic sites was mild but detectable (43.8 ± 0.4 vs 36 ± 0.9 ms remote, p = 0.01) suggesting that hemorrhage itself is associated with an inflammatory response. In Group 2, edema in the infarcted tissue, was also mild (44.2 ± 1.1 vs 37.5 ± 0.7 ms remote, p < 0.01) where as it was extensive in Group 3 (51.8 ± 3.1 vs 37.9 ± 0.6 ms remote, p = 0.02). Edema severity in Group 3 was significantly greater than the other two groups (p < 0.05). TTC staining confirmed the CMR observations (Figure 2).

Conclusions

Our novel findings demonstrate that hemorrhage is an important component of ischemia-reperfusion injury and may not simply be a bystander but an active contributor to cell damage and inflammation beyond the initial ischemic insult. A mechanistic understanding of the pathophysiology of reperfusion hemorrhage in vivo in the setting of AMI by CMR will potentially aid better management of the high-risk patients who are prone to adverse long-term outcomes.

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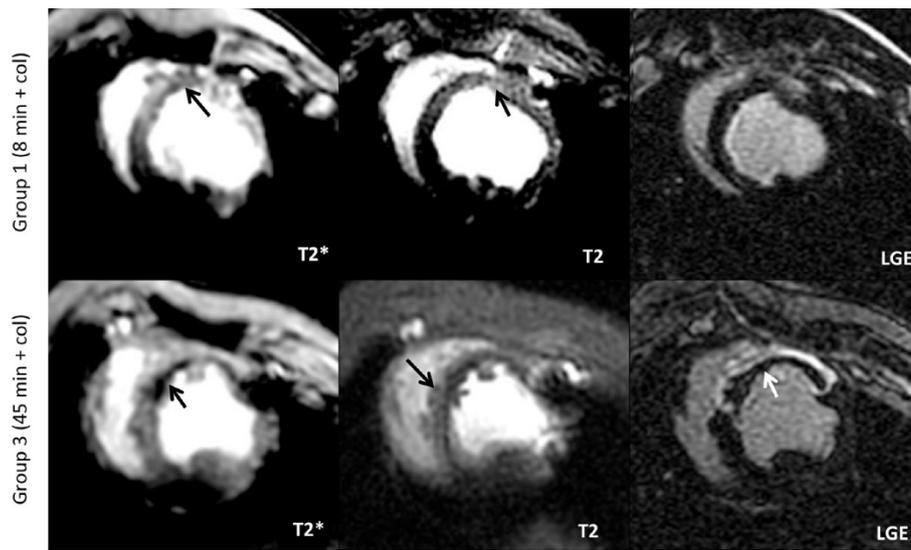


Figure 1 Representative CMR images from animals in Groups 1 and 3. T2*-weighted images (TE = 16 ms) demonstrate hemorrhage in both groups (arrows) but greater in Group 3. T2-weighted images (TE = 88 ms) identify elevated signal or edema (arrows) in the periphery of the hemorrhage or infarct core. Note that hemorrhage with greater ischemic insult in Group 3 is associated with a larger infarct size and the presence of MVO (arrow). Infarction was minimal in Group 1.

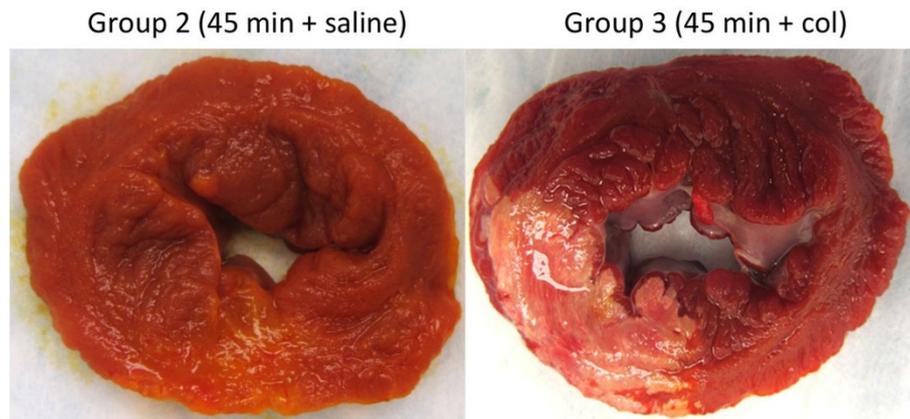


Figure 2 Gross pathological sections of porcine hearts subjected to 45 min occlusion treated with either saline or collagenase (col). TTC staining indicates region on necrosis appearing white. Note that collagenase induced haemorrhage appears red on TTC stain and is associated with extended necrosis.

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