Validation of Myocardial Edema in Acute Myocardial Infarction using Quantitative CT
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Introduction  Acute myocardial infarction (AMI) leads to accumulation of fluid in the interstitium as a result of enhanced cellular and vascular leakiness. Hence, myocardial edema is a hallmark of acute ischemic injury and can be used to delineate the extent of myocardium at risk, from which clinical decision on revascularization can be informed. Edema is not usually assessed by cardiac CT due to the similar enhancement (x-ray attenuation) between myocardium and water. We developed a functional CT technique for imaging myocardial edema. This method relies on tracer kinetic modeling of the retention of x-ray contrast in myocardium following a small bolus injection (BI). We validated this method in a pig model of reperfused AMI against a model-independent constant infusion (CI) method and cardiac magnetic resonance (CMR) T2-weighted imaging.

Methods  Animal model: AMI was induced in five Landrace pigs (40-60 kg) using a catheter-based approach, where a balloon catheter was advanced to the distal left anterior descending artery (LAD) and inflated to obstruct the downstream blood flow for one hour followed by reperfusion. Data acquisition: CT and CMR studies were performed on day 12±3 post ischemic insult. In each CT study, dynamic contrast-enhanced (DCE) heart images were acquired with a 64-row GE CT750 HD scanner after bolus injection of contrast (0.7 mL·kg

-1 at 3 mL·s

-1) using a 3-phase prospective ECG gating protocol: 1st phase: 22 axial scans at every 1-2 s, 2nd phase: 6 axial scans at every 14 s, 3rd phase: 4 axial scans at every 30 s. Next, the same dose of contrast was constantly infused intravenously for one hour. The heart was scanned five times both before and after contrast infusion. CMR T2W images of the heart were acquired on the same day with a Siemens Biograph PET/MR scanner using a routine clinical protocol. Data analysis: DCE CT heart images were analyzed using a modified Johnson-Wilson-Lee model that accounted for contrast exchanges among vascular, interstitial and cellular spaces in injured myocardium to estimate extravascular contrast distribution volume (ECDV, in units of ml/g) as a surrogate measure of edema. The five pre- and post- infusion CT heart images were averaged and registered to each other using a 3D non-rigid algorithm. The difference image, generated by subtracting the average pre-infusion image from the average post-infusion image, was normalized to the arterial blood enhancement to derive partition coefficient (PC) as a surrogate measure of distribution volume in myocardium. Myocardial signal intensities in the CMR T2W images were recorded using Osirix (Pixmeo). Mean ECDV and PC values and T2W signal intensities in the apical-septal (LAD territory) and mid-lateral (non-LAD territory) wall of left ventricle were compared using one-way ANOVA.

Results  ECDV in the infarcted apical-septal wall was 0.46±0.18 ml/g, which was higher than that in the normal mid-lateral wall (0.22±0.10 ml/g, p<0.05). Similarly, PC in the apical-septal wall was statistically higher than that in the mid-lateral wall (0.59±0.15 vs. 0.29±0.05, p<0.05). CMR T2W images confirmed the same apical segment with higher ECDV and PC than normal was edematous. The corresponding signal intensities in infarcted and normal myocardium were 65.6±55.7 and 34.0±39.0 (p<0.05 from infarcted) arbitrary units.

Conclusion  Intercellular and interstitial edema coupled with enhanced leakiness in cardiomyocytes provide additional spaces for CT contrast to distribute. Thus, ECDV is a useful marker of edema in acutely injured myocardium. ECDV measured with the proposed model-based BI technique agreed with the reference CI method and CMR T2W imaging. CT has high accessibility, throughput and low operating cost, and could be an emerging modality to assess edema and at-risk myocardium in the acute infarction setting. The proposed technique does not require prolonged contrast infusion which will facilitate the clinical workflow.