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Contrast agents in acute myocardial infarction

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Abstract

The experimental design in examination of acute myocardial infarctions should be valid in terms of flow, perfusion and re-flow after intervention. The contrast agents concentration in experimental studies can be measured by microdialysis.

We have assessed the usefulness of different extracellular and blood pool contrast agents for visualization of the area at risk in coronary artery occlusions. The double contrast technique, where Dy-DTPA-BMA was combined with Gd-DTPA-BMA yielded a superior infarct visualization. Blood pool agents for example NC100/150 injection is also promising in first path myocardial perfusion imaging. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Myocardium; Blood supply; Magnetic resonance; Contrast enhancement

The treatment of acute myocardial infarction aims at limitation of infarct size. This can be achieved by early restitution of myocardial perfusion either by the use of thrombolytic agents or by the performance of an immediate angioplasty. Reperfusion therapy has lowered mortality in patients suffering from acute myocardial infarction. When restitution of flow is not feasible, myocardium may be salvaged by pharmacological means, such as -blockade.

In order to assess the effect of therapeutic measures on acute myocardial infarction dynamics, a non-invasive imaging technique that permits detection of reperfusion and determination of myocardial viability would be useful [4,9,10]. Ideally, hypoperfused myocardium in patients with suspected angina pectoris should be detected by non-invasive techniques in order to select appropriate patients for transcatheter therapeutic interventions or coronary by-pass [5,6].

There is a lack of definition of acute myocardial infarction in the literature. Time from 15 min to several weeks from onset of symptoms to examination are encountered. From practical, clinical and scientific points we think therapy should be started within 4–6 h after onset of symptoms. After that time period, it is probably of no benefit to start an intervention or operation concerning the state of the area at risk.

The experimental design is important in evaluation of contrast agents in acute myocardial infarctions. In the experimental studies, the flow should be checked. There are too many contradictory studies on perfusion and reflow after intervention in the present literature. The contrast agent concentration should also be measured in normal and infarcted regions to get a better knowledge about the effect of different contrast agents in different types of tissue. This can also be made dynamically by microdialysis at least for extracellular contrast agents.

We have assessed the usefulness of Dy-DTPA-BMA-induced signal reduction, as an indicator of myocardial viability [8]. Myocardial infarction was induced in 17 domestic pigs by ligating a diagonal branch of the left anterior descending coronary artery (LAD). In six pigs, Dy-DTPA-BMA (1 mmol/kg b.w.) was administered 4 h after induction of ischaemia. In five additional pigs, Gd-DTPA-BMA (0.3 mmol/kg b.w.) and Dy-DTPA-BMA (1 mmol/kg b.w.) were simultaneously injected after 4 h of ischaemia to ascertain whether Dy-DTPA-BMA counteracted the signal enhancement effect of Gd-DTPA-BMA. A further six pigs with infarctions, not administered contrast medium, served as controls. All pigs were sacrificed after 6 h of ischaemia, and the

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extirpated hearts were investigated with MR (ex vivo). The concentrations of Dy and Gd were determined in tissue samples from infarcted and non-ischaemic myocardium. The extracellular concentrations of both contrast media were monitored over time during 2 h in the double-contrast group (in vivo), using a microdialysis technique and analysed by inductively coupled plasma atomic emission spectrometry (ICP-AES).

The infarctions demonstrated a high SI in the proton density- and T2-weighted sequences, in both the Dy-DTPA-BMA and control groups, although the former group demonstrated a 3-fold greater concentration of Dy in infarcted compared with non-ischaemic myocardium. Dy-DTPA-BMA thus did not counteract the Gd-DTPA-BMA-induced enhancement of the infarcted tissue despite a 3-fold higher concentration. This lack of detectable susceptibility effects of Dy may be caused by a loss of cell membrane integrity in the infarcts, resulting in a homogeneous intra- and extracellular distribution of the contrast agent. This hypothesis of an expanded volume of distribution in infarcted tissue was further supported by the microdialysis data, demonstrating a similar extracellular concentration of contrast agents in infarcted and non-ischaemic myocardium, despite a proven 3-fold greater concentration in infarcted tissue samples.

To investigate whether Gd-DTPA-BMA-enhanced MR imaging (ex vivo) permits differentiation between reperfused and non-reperfused myocardial infarction, and whether Dy-DPTA-BMA-enhanced MR imaging enables a differentiation between reversible and irreversible myocardial injury following reperfusion, myocardial infarction was induced in 24 domestic pigs (divided into four groups) by placing a patched ligature around a diagonal branch of the LAD [7]. Four additional hearts were reperfused after 2 min of brief occlusion, not long enough to cause irreversible injury. Myocardial infarction was also induced in 12 pigs to ascertain whether a double-contrast method, combining a positive and a negative MR contrast agent, could improve the visualization of reperfused myocardial infarctions, compared with a single-contrast technique using Gd-DTPA-BMA alone. Radiolabeled microspheres were used to confirm ischaemia and to verify reperfusion in infarcted myocardium. The concentrations of Dy and Gd in tissue samples from infarcted, reversibly injured and non-ischaemic myocardium were determined by ICP-AES.

The reperfused infarctions were strongly enhanced in the T1-weighted images, corresponding to a 5-fold higher Gd concentration compared with non-ischaemic myocardium. Hearts subjected to occlusion without reperfusion demonstrated only a peripheral rim enhancement of the infarctions, while the central parts demonstrated a SI and Gd content similar to that of non-ischaemic myocardium.

In the proton density- and T2-weighted sequences, reperfused, infarcted myocardium demonstrated a high SI despite a 5-fold higher Dy-concentration compared with both non-reperfused infarcted and non-ischaemic myocardium. Reversibly injured myocardium could not be distinguished from adjacent non-ischaemic myocardium, probably due to a preserved cell membrane integrity, preventing Dy-DTPA-BMA from entering the cells. Dy-DTPA-BMA-induced signal reduction may thus serve as an indicator of myocardial viability.

The double-contrast technique, whereby Dy-DTPA-BMA was injected in addition to Gd-DTPA-BMA, yielded a superior infarct visualization in the T2-weighted sequences, compared with the single-contrast technique using Gd-DTPA-BMA alone. This improvement of infarct visualization could be attributed to Dy-induced loss of SI, due to susceptibility effect in non-ischaemic myocardium. The double-contrast technique thus resulted in an excellent infarct visualization in both T1- and T2-weighted sequences.

The blood pool agent NC100150 injection has also been used in first pass myocardial perfusion imaging [1–3]. The results are promising but up till now the best contrast to noise of infarcted myocardium against normal myocardium has been achieved with the combination of Dysprosium and extracellular Gadolinium labeled agents.

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