Dynamic gadolinium-enhanced MRI evaluation of porcine femoral head ischemia and reperfusion

Abstract Objective: To examine the potential of gadolinium (Gd)-enhanced dynamic MRI in the detection of early femoral head ischemia. Furthermore, to apply a three-compartment model to achieve a clinically applicable MR index for femoral head perfusion during the steady state and arterial hip joint tamponade. Design and materials: In a porcine model femoral head perfusion was measured by radioactive tracer microspheres and by using a dynamic Gd-enhanced MRI protocol. Femoral head perfusion measurements and MRI tests were performed unilaterally before, during and after the experimentally induced ischemia of one of the hip joints. Ischemia was induced by increasing intra-articular pressure to 250 mmHg. Results: All pigs showed ischemia of the femoral head epiphysis under hip joint tamponade followed by reperfusion to the same level as before joint tamponade. In two cases perfusion after removal of tamponade continued to be low. In dynamic MRI measurements increases in signal intensity were seen after intravenous infusion of Gd-DTPA, followed by a slow decrease in signal intensity. The signal-intensity curve during femoral head ischemia had a minor increase. Also the coefficient determined was a helpful indicator of femoral head ischemia. Conclusions: Femoral head blood flow as measured by microspheres fell significantly under joint tamponade. Early detection of this disturbed regional blood flow was possible using a dynamic MRI procedure. A biomathematical model resulted from the evaluation of the intervals of signal intensity over time which allows detection of bone blood flow changes at a very early stage. Using this new method earlier detection of femoral head necrosis may be possible.

Keywords Femoral head · Dynamic gadolinium-enhanced MRI · Ischemia

Introduction

The pathogenesis of avascular necrosis of the femoral head has been extensively investigated both experimentally and clinically [1, 2, 3]. Ischemia is assumed to be the central factor in the pathogenesis of osteonecrosis. Publications on venous congestion and intraosseous thromboembolic events have, however, added new aspects to the understanding of the ischemic nature of bone necrosis [4, 5, 6, 7].
To minimize the progression of disease early joint-preserving therapies such as core decompression, electrical stimulation and oxygen therapy have been advocated. Magnetic resonance imaging (MRI) has been used in the last 15 years for the specific diagnosis of this condition [1, 8, 9]. However, due to the lack of symptoms drawing attention to femoral head necrosis it has not always been possible to diagnose the disease early enough to obtain optimal benefit from joint-preserving therapies.

The purpose of this study was to examine the potential of gadolinium-enhanced dynamic MRI in the detection of early femoral head ischemia. Furthermore, we applied a three-compartment model to achieve a clinically applicable MR index for femoral head perfusion during the steady state and arterial hip joint tamponade.

Materials and methods

Experimental design

Blood flow measurement of the femoral head and dynamic MRI was performed in 3- to 4-month-old skeletally immature domestic pigs weighing 46–50 kg. Thirty animals were randomized into four groups. Group 1 (n=11) was randomized to unilateral hip joint tamponade, group 2 additionally received steroid treatment prior to hip joint tamponade (n=11), group 3 underwent a unilateral sham operation of the hip (n=4) while group 4 received steroid treatment prior to the sham operation (n=4). The rationale of steroid treatment was to examine the effect of steroids on femoral head blood flow, which is discussed elsewhere [10].

The study was divided into three phases: femoral head blood flow measurement, followed by dynamic MRI, was performed (1) in the steady state, (2) at the end of 6 h of hip joint tamponade, and (3) 4 h after releasing hip joint tamponade. The experiment complied with the Danish Law on Animal Experiments and was approved by the Danish Ministry of Justice.

Anesthetic technique

The animals were premedicated with 25 mg midazolam (Dormicum; Hoffman-La Roche, Basel, Switzerland) and 200 mg azaperon (Stresnil; Janssen Pharmaceutica, Beerse, Belgium) intramuscularly. Intravenous anesthesia was induced by 20 mg etomidate (Hypnomidate; Janssen Pharmaceutica, Beerse, Belgium) and, after orotracheal intubation, maintained by a combination of 30 ml ketamine (Ketaminol Vet; Veterinaria, Switzerland) 50 mg/ml, 4 ml pethidine hydrochloride (Petidin Amino; Amino, Switzerland) intramuscularly, and (3) 4 h after releasing hip joint tamponade. The experiment complied with the Danish Law on Animal Experiments and was approved by the Danish Ministry of Justice.

Femoral head blood flow measurement

Radioactive tracer microspheres (New England Nuclear, Boston, Mass.) with a diameter of 15 µm and labelled with isotopes of tin (113Sn, phase 1), ruthenium (103Ru, phase 2) and cerium (141Ce, phase 3) were used to measure femoral head blood flow. For administration of the microspheres, a pigtail catheter (6.0 Fr, Cook, Denmark) inserted in the right carotid artery was advanced into the left ventricle under fluoroscopic control. Another pigtail catheter (6.0 Fr) was advanced into the thoracic aorta via the left carotid artery. Microspheres (5.0×10⁹) were suspended in 5 ml 10% dextrose solution and, after injection, the batch was agitated for 5 min on a Whirlimixer (Fisons, Loughborough, UK). The spheres were injected through the pigtail catheter into the left ventricle over a period of 30 s followed by flushing with 5 ml 37 °C heparin-saline. Reference blood sampling from the aorta was started 30 s before the injection, continued until 4 min after the injection [11].

The spheres are assumed to embolize the microcirculation in proportion to regional blood flow [12]. After the last blood flow and MR measurement, the pig was killed with an intracardiac injection of 40 ml potassium chloride solution. The femoral heads from both the operated and the contralateral hip were removed from the cadaver. The total femoral head effusion was carefully separated from the epiphyseal plate, cut, and distributed into preweighed counting vials. The reference blood samples and total femoral head effusion were counted by multichannel spectrometry (Packard Cobra, Packard Instrument Company, Meriden, Conn.) with the channels set for the three principal emission energies for the isotopes used. The counts in each channel were corrected for background, spill-over, and decay during counting. According to Hales [12] we determined the absolute femoral head (FH) regional blood flow (RBFFH, ml min⁻¹ 100 g⁻¹) as:

\[ \text{RBF}_{\text{FH}} = \frac{(C_{\text{FH}} \times SR \times 100)}{W_{\text{FH}} \times C_{\text{REF}}} \]

where \( C_{\text{FH}} \) denotes the count rate of a predefined region (cpm), \( C_{\text{REF}} \) denotes the count rate of the reference blood sample from the thoracic aorta (cpm), SR denotes the sampling rate of the reference blood sample (ml min⁻¹) and \( W_{\text{FH}} \) denotes the weight of the total FH sample.

Dynamic gadolinium-enhanced MRI

Dynamic MRI of both femoral heads was performed after microsphere injection in phases 1, 2 and 3 on a 1.5 T unit (Gyrosan; Philips Medical Systems, Best, The Netherlands). T₁-enhanced fast field echo (FFE) sequences (TR=36.6 ms, TE=17.9 ms, flip