Blood perfusion and bone formation before and after minimally invasive periacetabular osteotomy analysed by Positron Emission Tomography combined with Computed Tomography

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Abstract

Purpose Sufficient blood perfusion is essential for successful bone healing after periacetabular osteotomy (PAO). The purpose of this study was to quantify blood perfusion and bone formation before and after PAO analysed by positron emission tomography (PET) combined with computed tomography (CT).

Methods Twelve dysplastic patients (nine women) were included consecutively in the study and all were operated upon by the senior author (KS). Median age was 33 (23–55) years. Initially, two patients were PET scanned in a pilot study to test our models for calculation of the physiological parameters. The following ten patients had their hip joints PET/CT scanned immediately before PAO and three to four weeks after. Oxygen-15-water was used to quantify blood perfusion and Flourine-18-fluoride was used to produce quantitative images interpreted as new bone formation in the acetabular fragment.

Results The blood perfusion of the operated acetabulum before surgery was 0.07 ± 0.02 ml/min/ml, and after surgery 0.19 ± 0.03 ml/min/ml ($p=0.0003$). Blood perfusion of the

non-operated acetabulum was 0.07 ± 0.02 ml/min/ml before PAO and 0.07 ± 0.02 ml/min/ml after surgery ($p=0.47$). The fluoride-clearance per volume bone of the operated acetabulum was 0.02 ± 0.01 ml/min/ml preoperatively, and 0.06 ± 0.01 ml/min/ml postoperatively ($p=0.0005$). Fluoride-clearance of the non-operated acetabulum was 0.01 ± 0.01 ml/min/ml before PAO and 0.02 ± 0.01 ml/min/ml after PAO ($p=0.49$).

Conclusion Blood perfusion and new bone formation increased significantly in the acetabular fragment. Thus, the results of this study do not support the concern about surgically damaged vascularity after PAO.

Introduction

In periacetabular osteotomy (PAO) used for the treatment of hip dysplasia, the osteotomised acetabular fragment is reoriented and fixed with two screws to achieve better acetabular coverage. Bone healing is believed to be complete eight weeks after surgery and, from that time, the patients are allowed to fully weight-bear on the operated hip. Sufficient blood perfusion is held to be essential to successful bone healing after PAO, and from the time when Ganz et al. published their technique for performing the PAO [3], it has been a concern that PAO could potentially cause avascular necrosis of the acetabular fragment. Osteonecrosis of the acetabular fragment has been reported after PAO [2, 7, 11] and if hip osteoarthritis after PAO rapidly progresses, necrosis of the acetabular fragment should be suspected.

Beck et al. [1] performed an anatomical study of PAO through a modified Smith-Peterson approach and demonstrated that the acetabular fragment remains vascularised by

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the supra-acetabular and acetabular branches of the superior gluteal artery, the obturator artery and the inferior gluteal artery.

Blood perfusion in vivo during PAO has been studied by laser Doppler flowmetry in ten patients [5]. After complete separation of the acetabular fragment, nine out of ten patients had pulsatile signals, but the blood flow significantly decreased by 77 %. On termination of the surgical procedure, five out of eight patients showed a clear pulsatile signal in the supraacetabular area. In another study, 20 patients were examined with MRI [6], and three patients showed evidence of reduced vascularity six weeks after PAO has never been examined. The six-month scan showed some persistent vascular changes for one patient but the scan at one year showed complete resolution.

The effect on blood perfusion to the acetabular fragment and new bone formation after minimally invasive PAO has never been examined. The minimally invasive technique has been used for more than 400 cases at our institution and we have not encountered avascular necrosis of the acetabular fragment. Thus, we postulate that the minimally invasive PAO does not critically affect blood perfusion after surgery. The purpose of this study was to quantify blood perfusion and bone formation before and after PAO analysed by positron emission tomography (PET) combined with computed tomography (CT).

Patients and methods

The study was approved by The Biomedical Research Ethics Committee (Journal number: 20050005; Issue date: March 30th 2005) and registered with ClinicalTrials.gov (NCT00119444), and all patients gave signed consent for participation in the study.

Twelve dysplastic patients (nine women) scheduled for PAO were included consecutively in the study. Median age was 33 (23–55) years. The participants had the following radiographic and clinical characteristics: centre-edge angle of Wiberg [18] was 24° or less, osteoarthritis degree 0 or 1 according to the classification of Tönnis [12], closed growth zones in the pelvis, a painful hip, and minimum 110° flexion in the hip. We excluded patients with neurological illnesses, Legg-Calvé-Perthes disease, or sequelae from previous hip surgery. We also excluded patients for whom an intertrochanteric femoral osteotomy was planned.

All patients had PAO using the trans-sartorial approach [13]. The incision was made from the anterior superior iliac spine descending six centimetres distally. The fascia over the sartorius muscle was incised and the lateral femoral cutaneous nerve was exposed and was visible in the operation field throughout surgery. With this approach the tensor fasciae latae muscle and the abductor muscles are kept intact and the sartorius muscle is split in the fibre direction. The

pubic bone was osteotomised and under fluoroscopic control the ischial osteotomies and the posterior iliac osteotomy were performed. Spinal anaesthesia was administered to all patients undergoing the procedure and local infiltration analgesia was administered before the wound was closed. A solution of 50 mL ropivacaine (2 mg/mL), 1 mL ketorolac (30 mg/mL), and 0.5 mL epinephrine (1 mg/mL) was prepared and loaded into a 100 mL syringe and infiltrated in deep tissues (iliopsoas muscle, tensor fasciae latae muscle) and subcutaneous tissues. To reduce blood loss, 10 mg/kg of tranexamic acid was given at the beginning of surgery and repeated three hours postoperatively. For thromboprophylaxis, an injection of 2.5 mg fondaparinux was administered subcutaneously for two days, beginning on the day after surgery.

All patients followed the same program for PAO that included preoperative multidisciplinary information and well-defined optimised multimodal pain treatment for one week including 1 g paracetamol six-hourly starting in the post anaesthesia care unit. In cases of insufficient analgesia, when pain exceeded 30 mm on a visual analog scale up to maximum 100 mm, the patient was given supplemental oxycodone (5–10 mg orally). While in hospital (two to three days) the patients were seen daily by a physiotherapist for active hip range of motion exercises. The patients were ambulatory six hours after surgery and allowed 30 kg of weight-bearing and given instructions in maintaining the weight-bearing limit using crutches. Six to eight weeks after discharge, patients attended the outpatient clinic and radiographs were examined. If there was good callus formation and no radiographic changes in position of the acetabulum compared to postoperative recordings, progressive weight bearing was allowed up to full weight bearing. To assess the acetabular correction, the centre-edge angle and the acetabular index angle [12] were measured by one person (IM) on pre- and postoperative AP pelvic radiographs.

Initially, two patients were PET scanned with a PET scanner without CT in a pilot study to test our models for calculation of the physiological parameters. The following ten patients had their hip joints PET/CT scanned before PAO and three to four weeks after surgery. The first five patients were scanned on a Siemens Biograph 40 (USA) PET/CT scanner, and the following five on a Siemens Biograph 40 Truepoint (USA) PET/CT scanner. The PET/CT scanner combines PET and CT technology in the same gantry.

PET/CT acquisition protocol

The PET scanner was cross calibrated with the well-counter and the continuous arterial blood activity counter.

The patients had an arterial line placed in the radial artery for arterial blood sampling. A venflon was placed in an antecubital vein for tracer injection. The patients were

positioned supine on the table with the legs in neutral rotation. The legs were supported by pillows and velcro tape in order to reduce movement. A scout acquisition was performed followed by a low-dose CT-scan, a dynamic water scan, and a dynamic fluoride scan.

[O-15]-water scans

A dynamic scan was performed for 6.5 minutes after bolus injection of [O-15]-water. Simultaneous arterial blood activity was measured every 0.5 second.

[F-18]-fluoride

A dynamic scan was performed for 90 minutes after bolus injection of [F-18]-fluoride. Forty arterial blood samples were collected, with the timing: 12×5 s, 4×10s, 4×20s, 4×30s, 5×60s, 6×300 s, 5×600 s, totalling 90 minutes. The blood activity was measured in a well-counter.

Image processing

Low-dose 512×512 pixels CT images were constructed. The 128×128 pixels PET images were constructed and corrected for random events, detector sensitivity, dead-time, attenuation, and scatter.

Image analysis

The CT images were transferred to a Syngo Multimodality Workplace (VE36A SL10P25, Siemens). In the software (MI application, molecular imaging), transverse images were chosen and the number of images showing the relevant part of the lower acetabulum were noted. The multiframe polygon function was chosen and the regions of interest (ROI) were manually drawn on the approximately five axial CT images (4-mm slice thickness) covering the relevant part of the acetabulum. At first, the ROIs were drawn on the postoperative CT images in order to define the area below the osteotomy line (Fig. 1). The ROIs were drawn on the first CT image and then copied to the following images below and adjusted to fit the bony edges of the acetabulum. After that, the ROI defined on the postoperative CT images for both operated and non-operated acetabulum were copied to the preoperative CT images.

The regions of interest were then projected onto the dynamic [O-15]-water and the [f-18]-fluoride scans and mean time-activity curves were generated.

Compartment analysis

Perfusion was determined from the [O-15]-water scans. A one-compartment model was used. The time-activity

Fig. 1 Three-dimensional reconstruction based on CT images of hip illustrating region of interest (*red area*) defined for the right acetabular fragment (*green*) after surgical correction at periacetabular osteotomy

curves were fitted for K_1 , k_2 , and the delay, where K_1 is the perfusion [ml blood/min/ml bone]. The fluoride-clearance per volume bone (K_i) [ml blood/min/ml bone] was determined by applying Patlak graphical analysis to the time-activity curves of the fluoride scans, fitting the data from 45 to 90 minutes.

Statistics

Distribution of the data for blood perfusion and bone formation were assessed with scatter-plots and histograms, and normally distributed data were presented as mean $\pm$ one standard deviation (SD). In the normally distributed data the paired *t*-test was used to evaluate differences pre- and post-operative. Intercooled Stata software version 11.0 (StataCorp, College Station, TX) was used for statistical computations

Results

Acceptable correction of the acetabulum at PAO was demonstrated by the radiographic data (Table 1). Patlak analysis showed that the Patlak curves were reasonably flat from 45 to 90 minutes. They curved for times less than 45 minutes. Also non-linear regression with fitting for K_1 , k_2 and k_3 was not stable if only the first 45 minutes were used. It turned out, that 90 minutes were required in order to calculate the fluoride uptake (K_i). Some patients had pain and could not stay in the scanner for the entire 90 minutes of the fluoride scan, which, therefore, could not be analysed. The water scans were as expected very noisy. Some of the water time-activity curves were too noisy to be analysed with the compartment model. Therefore data of sufficiently high quality was available for five out of ten patients for the water scans and for six out of ten patients for the fluoride scans (Table 2).

Table 1 Demographic data and results of clinical and radiographic examinations of the ten patients operated on by the periacetabular osteotomy

Case no.	Gender	Age at surgery (years)	Osteoarthritis degree at surgery	AI-angle preop./postop.	CE-angle preop./postop.
1-dx	F	23	0	14/0	20/30
2-dx	M	43	0	18/5	14/30
3-sin	F	33	0	16/13	20/32
4-dx	F	55	0	17/5	20/34
5-dx	F	29	1	27/12	0/26
6-sin	M	31	0	17/8	20/35
7-dx	F	24	0	10/−4	19/35
8-sin	M	36	0	19/−3	15/30
9-dx	F	44	0	11/−3	22/35
10-sin	F	34	1	28/1	0/27

F female, M male, dx dexter, sin sinister

The mean blood perfusion on the operated acetabulum before surgery was 0.07 ± 0.02 ml/min/ml, and after surgery 0.19 ± 0.03 ml/min/ml ($p=0.0003$). Blood perfusion on the non-operated acetabulum was 0.07 ± 0.02 ml/min/ml before PAO and 0.07 ± 0.02 ml/min/ml after surgery ($p=0.47$). The mean fluoride-clearance per volume bone on the operated acetabulum was 0.02 ± 0.01 ml/min/ml preoperatively, and 0.06 ± 0.01 ml/min/ml postoperatively ($p=0.0005$). Fluoride-clearance on the non-operated acetabulum was 0.01 ± 0.01 ml/min/ml before PAO and 0.02 ± 0.01 ml/min/ml after PAO ($p=0.49$). All analysed fluoride-scans had the duration of 90 minutes, fitted from 45 to 90 minutes. Shorter analysis periods were tried, but the results varied up to a factor of two.

Discussion

The blood flow to the acetabular fragment has been of some concern in PAO used for the treatment of hip dysplasia. This

study shows that blood perfusion increased significantly in the acetabular fragment, demonstrating that blood perfusion to the acetabular fragment is not compromised three to four weeks after minimally invasive PAO. New bone formation in the acetabular fragment on the operated side increased significantly, also indicating sufficient blood perfusion. Thus it seems that the biological response to PAO is that bone blood flow increases and the mineralisation next to the osteotomy site accelerates. During minimally invasive PAO care is taken to position the osteotomy lines as far from the joint as possible in order to leave a large bony fragment with potential for sufficient blood supply, and these results convince us that this procedure is appropriate.

This is the first paper applying PET/CT to quantify blood perfusion and bone formation before and after PAO in vivo. We were inspired by a study [10] quantifying blood perfusion and new bone in the allograft around revisions of total hip arthroplasty. The group has performed several PET

Table 2 Blood perfusion and fluoride-clearance measured by PET/CT on the operated acetabulum and the non-operated acetabulum before and after periacetabular osteotomy for ten patients with hip dysplasia

Case no.	Preop. blood perfusion operated side ml/min/ml	Postop. blood perfusion operated side ml/min/ml	Preop. blood perfusion contralateral side ml/min/ml	Postop. blood perfusion contralateral side ml/min/ml	Preop. fluoride-clearance operated side ml/min/ml	Postop. fluoride-clearance operated side ml/min/ml	Preop. fluoride-clearance contralateral side ml/min/ml	Postop. fluoride-clearance contralateral side ml/min/ml
1-dx	0.05	Missing	0.05	Missing	0.002	0.06	0.002	0.02
2-dx	0.05	Missing	0.05	Missing	0.03	0.06	0.02	0.03
3-sin	0.06	0.20	0.06	0.06	0.03	0.07	0.02	0.02
4-dx	0.06	0.15	0.06	0.06	0.02	0.05	0.02	0.01
5-dx	0.10	Missing	0.09	Missing	0.01	0.04	0.01	0.01
6-sin	0.08	Missing	0.07	Missing	0.02	Missing	0.01	Missing
7-dx	0.07	0.20	0.07	0.07	Missing	Missing	Missing	Missing
8-sin	0.06	0.18	0.07	0.06	0.02	0.06	0.02	0.01
9-dx	Missing	0.20	Missing	0.14	0.02	Missing	0.02	Missing
10-sin	0.10	0.23	0.10	0.10	Missing	Missing	Missing	Missing

dx dexter, sin sinister

studies [14, 15, 17] on orthopaedic patients and report the method to be sensitive to visualise osteonecrosis that cannot be seen on plain radiographs [16]. That study did not report technical problems as we had in this study, namely, failed PET scannings due to patient movement during scanning or technical problems affecting the data sampling. Because of the long acquisition time of the PET scan, it was difficult for the patients to lie unmoving for 90 minutes. Furthermore, these patients have hip pain both before surgery and three to four weeks after, and thus they were informed prior to the PET/CT scanning that they could have oral analgesia if they thought it would be a problem to lie motionless. Most patients asked for oral analgesia before the PET scannings.

From these two PET/CT scannings, the dose of radiation to each patient was equivalent to three times the normal background radiation; thus, we could not justify asking more patients than the included ten patients to undergo PET/CT scanning, although we would have liked to have had data on more patients.

PET/CT image artefacts are due primarily to metallic implants, respiratory motion, use of contrast media and image truncation [9]. The presence of metallic implants is seen as areas of high density, which cause artefacts on the CT images [4]. The two titanium screws that fix the acetabular fragment after the periacetabular osteotomies caused only minor artefacts that did not interfere with the ROIs on the CT images. To minimise the presence of artefacts due to metallic implants, the physician asked the patient to remove all metallic objects prior to scanning.

The PAO is a technically demanding procedure and can be prone to creation of secondary mechanical abnormalities of the hip joint if the acetabular correction is excessive or insufficient and these two conditions can lead to further labral and cartilage degeneration. The patients in this study were operated upon via minimally invasive PAO and satisfactory correction of the acetabular morphology was obtained after PAO. The mean duration of the minimally invasive PAO is 70 (50–85) minutes [8] and average intraoperative blood loss is 250 (200–350) mL [13]. It is likely that blood flow may be more seriously affected with longer surgery time and greater blood loss.

In conclusion, blood perfusion of the acetabular fragment is not critically compromised after minimally invasive PAO and the formation of new bone in the fragment increases within the first postoperative month. Thus, the results of this study do not support the concern about surgically damaged vascularity after PAO. We found PET/CT to be a useful method for evaluation of blood perfusion and bone formation but problems

with patient motion should be considered before initiating a similar study.

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Contribution of authors All co-authors took part in the planning of this study and in the writing of this article. Flemming Hermansen and Theis Thillemann were responsible for PET scanning of the patients. Kjeld Søballe diagnosed and operated upon all patients. As the first author Inger Mechlenburg was responsible for coordination of the different elements in this study and responsible for the inclusion of the patients and overall responsible for the decisions made in this study. All authors declare that they have no financial or personal relationships with other people or organisations that could inappropriately influence their work.

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