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ORIGINAL STUDY

Total hip arthroplasty in heart transplant patients

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Avascular necrosis of the femoral head (AVNFH) is a known complication after heart transplantation. In order to assess the efficacy and complications of cementless total hip arthroplasty (THA) in this population, the authors analysed 24 cementless THAs in 18 patients with advanced AVNFH (stage II affecting more than 15% of the articular surface, stage III and IV according to the Ficat-Arlet classification) after a heart transplant procedure. Average duration of follow-up was 35.4 months (range : 16 to 66). Pain and function scores (Harris Hip Score and WOMAC arthritis index) showed significant improvement from the preoperative levels. There was no evidence of component loosening, heart-related complications or infection following the THA. Cementless THA is a reasonable treatment option for advanced avascular necrosis of the femoral head following heart transplant procedures.

Keywords : total hip arthroplasty ; avascular necrosis ; heart transplant.

INTRODUCTION

Avascular necrosis of the femoral head (AVNFH) is a known complication of solid organ transplantation. Osteonecrosis after renal transplantation was reported by Jones *et al* in 1965. Danzing *et al* (*8*) reported avascular necrosis after cardiac transplantation in 1976. Some authors believe that prolonged treatment with corticosteroids and other immunosuppresive agents is responsible for the occurrence of osteonecrosis (*15,16,21*). These agents display direct cellular toxicity and cause vascular injury and intramedullary haemorrhage, cellular hypertrophy with bone marrow infiltration and intravascular fat embolism. In these patients, the prevalence of bilateral disease has ranged from 59% to 80%, although the onset of symptoms is usually asymmetric (*16*).

The number of heart transplantation procedures has increased over the last few years. There were ten transplants performed in Spain in 1984, while in 2001 this figure increased to 340. Survival rates have increased in cardiac transplantation due to advances in surgical techniques, better patient selection and improvements in the inmunosuppresive agents used. As a result, the prevalence of osteonecrosis after heart transplantation has increased in recent years.

Management of avascular necrosis of the femoral head after heart transplant procedures is based on the stage of the disease. Treatment

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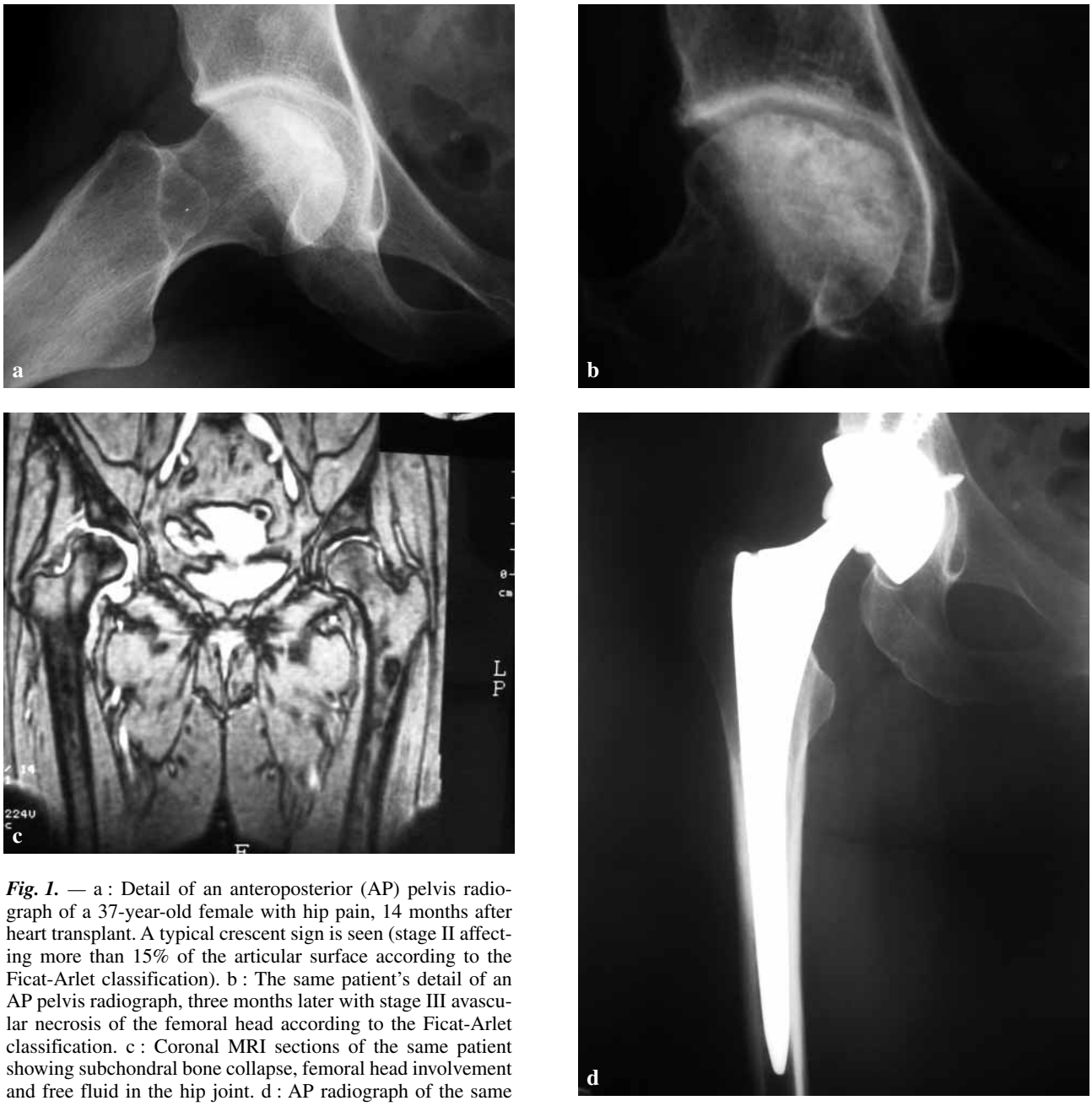


Fig. 1. — a : Detail of an anteroposterior (AP) pelvis radiograph of a 37-year-old female with hip pain, 14 months after heart transplant. A typical crescent sign is seen (stage II affecting more than 15% of the articular surface according to the Ficat-Arlet classification). b : The same patient's detail of an AP pelvis radiograph, three months later with stage III avascular necrosis of the femoral head according to the Ficat-Arlet classification. c : Coronal MRI sections of the same patient showing subchondral bone collapse, femoral head involvement and free fluid in the hip joint. d : AP radiograph of the same patient after right total hip replacement.

regimens for AVNFH have included nonsurgical management, arthrodesis, bone grafting and musculo-osseous pedicled transfer, intertrochanteric osteotomy, cup arthroplasty and total hip arthroplasty (THA). In later stages, when collapse and significant deformation of the head are present – stage II affecting more than 15% of the articular surface and stage III-IV according to the Ficat-Arlet classification –, a reconstructive procedure is the treatment of choice *(21)*. However, these patients have traditionally been approached with great hesitancy because of their compromised immune status and poor bone stock secondary to the use of steroids.

The purpose of this study was to assess the functional and radiographic results as well as complications of total hip arthroplasty in heart transplant patients.

MATERIALS AND METHODS

Three hundred eleven heart transplant procedures were performed at the authors' institution, between 1994 and 2006. Sixty-two patients who died within the first 7 months after heart transplant were excluded. Among the remaining 249 patients, 18 developed symptomatic AVNFH. Six cases were bilateral. Therefore, the incidence of AVNFH in these 249 heart transplant patients was 7.2% (18/249).

Patients with AVNFH in advanced stages of the disease were treated with total hip arthroplasty. Six patients who had bilateral disease were treated with bilateral arthroplasty (25%) (fig 2). A total number of 24 THA procedures were carried out on these patients (table I).

Exclusion criteria were a pre-existing osteonecrosis of the hip, a history of inflammatory arthritis, previous hip surgery, and previous systemic corticosteroid treatment. No patients were excluded from the study based on these criteria. The patients were studied retrospectively. The average duration of follow-up was 35.4 months (range : 15 to 66 months) (table I).

All patients who were noted by the transplant team to have musculoskeletal symptoms were referred to an orthopaedic surgeon. In addition to radiographs, bone scans and MRI studies were used to confirm the diagnosis of avascular necrosis. The time interval from the heart transplantation to the presentation of avascular necrosis ranged between seven and fifteen months (average 11.3 months) (table I), and the time interval between the first symptoms of AVNFH and THA was 14.4 months (range, 5 to 24 months) (table I). In our series joint arthroplasty was done on average 27 months after transplantation (range : 12 to 39 months). Two patients had more than one site of avascular necrosis (8.4%) ; one had bilateral involvement of the humeral head and second lumbar vertebra and the other developed lateral femoral condyle necrosis.

Two patients of the 249 survivors group had a rejection episode in the first postoperative month ; they were both treated successfully with short courses of methylprednisolone. These patients developed bilateral AVNFH 7 and 9 months respectively after the rejection episode ; in one of them, AVNFH occurred simultaneously in both hips and in the other the onset was consecutive with a one-month interval between both hips.

The grading of AVN stages was done according to the Ficat and Arlet scale. Eight hips were in an advanced transition stage (33.3%), 14 hips were stage III (58.3%) and three were stage IV (8.4%).

There were fifteen men and three women (4.6/1). The average age at the time of arthroplasty was 50 years (range : 24 to 66 years) (table I). Six patients developed bilateral AVNFH (25%). All patients were admitted to the hospital three days prior to the surgery and were followed up by both the orthopaedic and transplant surgical services. General anaesthesia was used in ten patients and regional anaesthesia in eight. Perioperative inmunosupressors (corticosteroid, azathioprine and ciclosporine) were given. Prophylactic cephalosporin antibiotic was administered : one dose preoperatively and three doses of one gram during the first day after operation. Thromboembolism prophylaxis was with low-molecular-weight heparin. All arthroplasties were performed using a lateral surgical approach without a trochanteric osteotomy.

A cementless hydroxyapatite-coated acetabular cup with multiple screw holes (Reflection, Smith&Nephew, Memphis, TN, U.S.A), and a cementless femoral stem with metaphyseal hydroxyapatite coating (Synergy, Smith&Nephew, Memphis, TN, U.S.A) were used in all hips. Alumina bearing surfaces were used in 19 replacements and an Oxinium - cross-linked polyethylene pairing in five. The components were inserted with a press-fit technique and adjunctive fixation as determined by the preoperative use of templates (figs 1, 2, 3).

The length of hospital stay after surgery ranged from four to seven days. Two days after operation, all patients were instructed to walk with two crutches, and to continue using crutches for eight to twelve weeks.

The average blood replacement was 1.2 unit of red blood cell concentrate (range : 0 to 3).

Clinical and radiographic follow-up was performed immediately after the operation, at six weeks, three months, six months and twelve months after operation and annually thereafter. Clinical results were assessed using the Harris hip score and the WOMAC scores *(2,12)*. Radiographic evaluation was performed according to the guidelines described by Johnston *et al (18)*. The acetabular components were assessed for radiolucencies at the bone-implant interface, position and changes in position of the acetabular cup and migration or breakage of the screws. To facilitate the assessment of the radiolucent lines, Hodgkinson *et al's (13,14)* criteria were used in this series. The demarcation, regardless of the thickness of the radiolucent line, was categorised as type 0 when there was no demarcation, as type 1 when the line was in

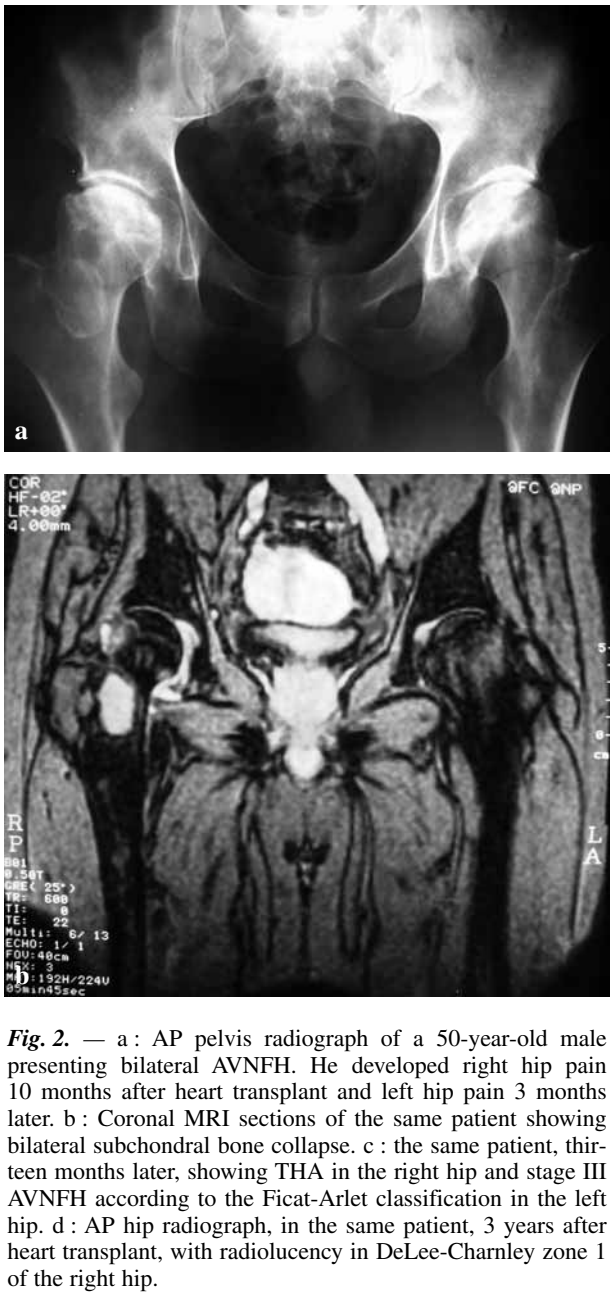


Fig. 2. — a : AP pelvis radiograph of a 50-year-old male presenting bilateral AVNFH. He developed right hip pain 10 months after heart transplant and left hip pain 3 months later. b : Coronal MRI sections of the same patient showing bilateral subchondral bone collapse. c : the same patient, thirteen months later, showing THA in the right hip and stage III AVNFH according to the Ficat-Arlet classification in the left hip. d : AP hip radiograph, in the same patient, 3 years after heart transplant, with radiolucency in DeLee-Charnley zone 1 of the right hip.

zone 1 of De Lee and Charnley, as type 2 when it was in zones 1 and 2, as type 3 when in all 3 zones, and as type 4 when the acetabular cup had migrated. Radiographic cup loosening was based on Schmalzried and Harris' criteria (*25*).

Heterotopic ossification (HO) was assessed using the Brooker classification (*6*). Loosening of the femoral component was evaluated using Engh's criteria defining stable bone fixation, stable fibrous fixation and unstable fibrous implant fixation (*11*). Bone stress-shielding evaluation was performed using Engh's classification (*11*).

Complications were classified into those pertaining to the THA and those related to the heart transplant.

Table I. — Register of the heart transplant patients. TX : heart transplant ; THR : total hip replacement

	AGE	HARRIS PRE	HARRIS POST	TX-SYMPTOMS	SYMPTOMS-THA	FOLLOW-UP TIME
CASE 1	37	42	94	14 MONTHS	24 MONTHS	20 MONTHS
CASE 2	50	30	83	10 MONTHS	13 MONTHS	25 MONTHS
CASE 3	50	32	86	13 MONTHS	16 MONTHS	20 MONTHS
CASE 4	62	34	85	12 MONTHS	15 MONTHS	26 MONTHS
CASE 5	62	32	86	13 MONTHS	18 MONTHS	25 MONTHS
CASE 6	34	33	84	11 MONTHS	18 MONTHS	60 MONTHS
CASE 7	34	35	85	13 MONTHS	19 MONTHS	57 MONTHS
CASE 8	42	34	81	10 MONTHS	5 MONTHS	35 MONTHS
CASE 9	49	37	85	14 MONTHS	18 MONTHS	47 MONTHS
CASE 10	56	34	89	11 MONTHS	14 MONTHS	15 MONTHS
CASE 11	58	33	82	15 MONTHS	15 MONTHS	38 MONTHS
CASE 12	53	31	81	12 MONTHS	17 MONTHS	42 MONTHS
CASE 13	49	28	85	9 MONTHS	16 MONTHS	34 MONTHS
CASE 14	49	33	86	9 MONTHS	20 MONTHS	30 MONTHS
CASE 15	63	31	83	11 MONTHS	12 MONTHS	66 MONTHS
CASE 16	66	34	75	9 MONTHS	13 MONTHS	41 MONTHS
CASE 17	66	36	77	10 MONTHS	15 MONTHS	38 MONTHS
CASE 18	57	34	80	7 MONTHS	14 MONTHS	40 MONTHS
CASE 19	52	32	85	11 MONTHS	13 MONTHS	36 MONTHS
CASE 20	39	37	85	9 MONTHS	8 MONTHS	26 MONTHS
CASE 21	39	39	86	12 MONTHS	12 MONTHS	22 MONTHS
CASE 22	51	34	80	10 MONTHS	9 MONTHS	30 MONTHS
CASE 23	46	30	82	11 MONTHS	11 MONTHS	40 MONTHS
CASE 24	52	31	88	14 MONTHS	10 MONTHS	36 MONTHS

RESULTS

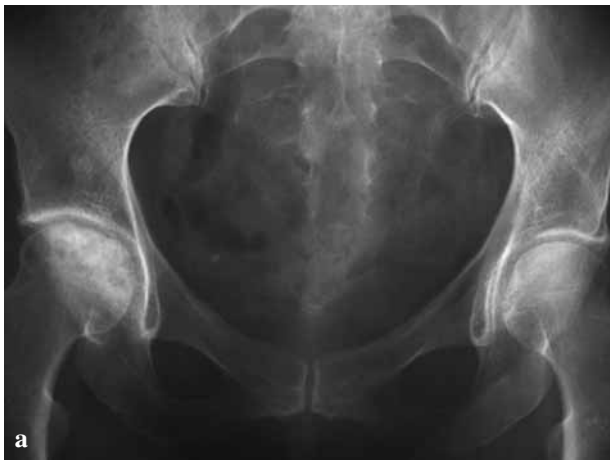
The average Harris hip score in the 18 patients with 24 THAs rose from a preoperative value of 33.5 points (range : 28 to 42) to 83.8 points (range : 75 to 94) after operation (table I). With regard to pain, the preoperative score was 17.7 (range : 0 to 20) versus 41.8 (range : 30 to 44) at follow-up. The score for walking distance improved from 3.8 to 7. All patients were unlimited in their ability to walk, except for a patient with contralateral knee pain that prevented him from walking. The need for support during walking also improved from a score of 2.6 (range : 0 to 3) to 7.2 (range : 5 to 11) after THA.

There was an obvious improvement in hip mobility. Hip flexion improved by 13° (range : from 91.5° to 104.5°), extension did not change, internal and external rotations improved by 7° and 8° respectively, abduction changed from 25.7° to 35.8° and adduction changed from 22.9° to 30.5° ; there were no flexion contractures of the hip or knee.

The functional outcome evaluated using the WOMAC scale also showed marked improvement. More specifically the pain score rose from 3.4 preoperatively to 9.3. Before surgery, nine patients suffered from incapacitating pain, four had moderate pain and one had slight pain. Postoperatively, three patients had slight pain and eleven had no pain.

Function improved from a 4.2 pre-operative average difficulty to a 9.8 post-operative average difficulty to accomplish the actions described in this scale (walking, going up and down stairs, dressing, and performing domestic tasks). Before THA ten patients had major difficulty (0-3) and four patients had a moderate difficulty level (3-6). At latest follow-up, one patient had moderate difficulty, eight had slight difficulty and five had no difficulties.

Radiological evaluation of the acetabular component following the Johnston parameters showed



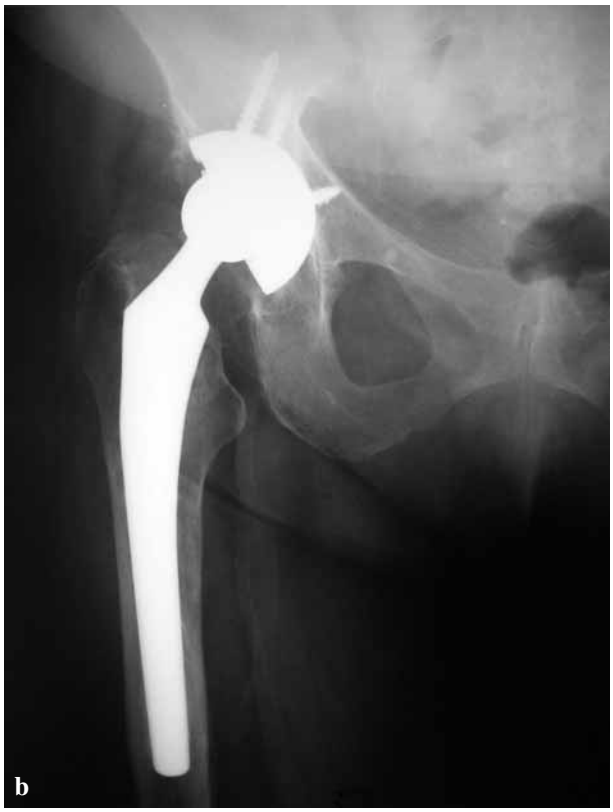


Fig. 3. — a : AP radiograph of a 53-year-old male with stage III AVNFH according to the Ficat-Arlet classification. b : the same patient 18 months after THA, presenting Brooker type 2 heterotopic ossification.

that one patient developed osteolysis in De Lee-Charnley zone 1 three years after THA, but he was asymptomatic (fig 2). No acetabular component migration, protrusion or loosening, based on Hodgkinson's criteria, were noted.

Two patients (14.2%) developed Brooker grade I heterotopic ossifications and one presented a grade II.

With regard to the femoral component, using the nomenclature described by Johnston, all patients presented a good varus-valgus alignment and none presented femoral stem subsidence with reference to the greater and lesser trochanter. One patient presented radiolucent lines in zones 4 and 7 but he remained asymptomatic 4 years and 2 months after THA. When analysing bone stress shielding, four hips in three patients (21.4%) presented resorption areas on the proximal medial femoral edge, grade 1 according to Engh's classification. No patient presented bone stress-shielding grade 2, 3 or 4. According to Engh's criteria, all femoral components presented stable bone fixation.

There were no heart-related complications after the arthroplasty. One patient presented a superficial infection two days after surgery ; it was cleared with a 10-day oral antibiotic treatment. One patient developed deep venous thrombosis confirmed by echo-doppler and received a high dose of low molecular weight heparin for two weeks. No dislocations or periprosthesic fractures occurred. No patient had revision THA surgery during the follow-up period of this study.

DISCUSSION

Although THA performed for AVNFH in heart transplant recipients has not been extensively reported, the small numbers of reported cases has shown encouraging results. In 1977 Burton *et al* (*7*) reported bilateral THA in two patients followed for 14 and 6 months respectively. In 1986 Isono and Woolson (*17*) performed THA in 10 cardiac transplant patients, of which nine had bilateral AVNFH ; these patients were highly satisfied with the results of their arthroplasty at last follow-up examination (average of 34 months). Although the follow-up period was short in both studies they concluded that the complication rate for THA in heart transplant recipients was similar to that in patients who

did not have heart transplant, and their patients had no pain or limp, and had a normal range of motion.

In 1957 Pietrogrande and Mastromarino (*23*) reported the first case of steroid-associated osteonecrosis. Since then the literature is replete with articles discussing the cause, pathogenesis, diagnosis, staging and treatment of osteonecrosis (*15,21*). However the cause of osteonecrosis following organ transplantation remains debated.

This series analyses the clinical and radiographic findings following cementless THA in patients who developed AVNFH following cardiac transplantation. Several interesting correlations have been noted. The incidence of AVNFH in this series is 7.2%, very similar to that reported by other authors such as Isono *et al* (*17*) and Bradbury *et al* (*3*). Marston *et al* (*22*) reported a prevalence of AVNFH after transplant between 3% and 40%.

The average time interval of 11.3 months between heart transplantation and the subsequent development of hip symptoms is similar to that reported by Danzing *et al* (*8*), Briggs *et al* (*5*). Bradbury *et al* (*3*) reported an average of 5 months (range : 2 to 11).

In our series, patients tolerated their symptoms for five months to two years from the first symptoms until THA was performed ; the average time interval was 15.6 months. THA was done on average 27 months after transplantation (range : 12 to 39).

The average age at the time of arthroplasty was 52 years (range : 34 to 66). There has been a certain reluctance to advise THA for patients with AVNFH after heart transplant (*7*). This is because these patients are much younger than patients with degenerative joint disease at the time arthroplasty is required, and it is generally accepted that the survivorship for THA in young patients is less than in older patients (*10,24*). In addition in heart transplant patients with high doses of corticoids, surgeons have traditionally approached these patients with great hesitancy because the patient who is immunosupressed seems to have a higher rate of complications such as infections and an earlier incidence of failure than patients of a similar age but with other disorders of the hip.

Functional and radiographic outcomes in the present series, analysed at an average of 35.4 months (range : 15 to 66), have been highly satisfactory according to the Harris scale and WOMAC parameters, especially with regard to pain. No implant loosenings or migrations were found, no dislocations or periprosthetic fractures occurred, no patient had revision THA during the follow-up period. The most common complication was heterotopic ossification (HO), seen in 15.8% of THAs. This did not significantly interfere with hip function in these patients because none of them fit into Brooker's class III or IV. Isono *et al* (*17*) and Kenzora *et al* (*20*) reported this complication as the most frequent in their series.

These excellent clinical and radiological outcomes are partly explained by a short follow-up period (36.5 months) and because these patients were probably less active than other patients of similar age without cardiac allografts. These two factors may explain why there were no early failures in this young population in contradiction to previous studies by Dorr *et al* (*10*).

General complications following THA occurred in one patient (5.3%) who presented a deep venous thrombosis without pulmonary embolism. One patient presented a superficial infection that was cleared in ten days, no hip developed purulent drainage, or evidence of deep infection. The majority of patients had prolonged serous drainage from their hip incision (4-7 days) after operation, which was thought to be due to slow wound healing secondary to the maintenance steroid immunosuppression. There were no failures of the transplanted organs. The complication rate in this group is similar to that reported in the literature (*7,17*). Bradford *et al* (*4*)) reported general complications following THA in 20% of the patients.

In our study general anaesthesia was administered in 9 patients and regional anaesthesia in 5 patients. These patients are certainly at increased risk for anaesthesia, but with proper management and careful monitoring using the standard patient anaesthesia protocol, the risk of anaesthesia can be reduced to reasonable levels, as outlined by Kanter and Samuels (*19*).

Our goal in these patients must be therefore to institute some type of definitive treatment as early as possible. We consider that, in incipient stages I

and in transition stages (II) affecting < 15% of the articular surface, decompression of the femoral head may postpone the progress of the necrosis. However, in transition stage affecting > 15%, or in stage III and IV, bone has no capacity for remodelling, and joint replacement surgery must be done (*21*). When the patient shows significant collapse of the femoral head, he is treated symptomatically until pain and disability necessitate some type of arthroplasty. In this series the patients with AVNFH after heart transplant were treated with THA because the majority (63.1%) were stage III or IV at the time of diagnosis, and those patients that presented initially with stage II progressed to stage III within two or three months fig 1).

The majority of authors (*4,7,16,17*) reported the use of a cemented THA in their series, because they considered that a noncemented femoral prosthesis in an osteopenic proximal femur would, in all likehood, migrate. Isono *et al* (*17*) recommended using cemented rather than cementless implants because of the concern about successful bony fixation in patients who have impaired osteogenesis secondary to relatively high maintenance doses of steroids. In our series, the implants used were cementless with ceramic bearing surfaces, because in our opinion, this offers the younger patient the safest and most durable bearing surface currently available in THA (*9*). All the implants presented stable bony fixation according to Engh's classification (*11*), at the last available follow-up evaluation and no implant required revision to date. The systemic administration of high corticosteroid doses does not appear to compromise implant integration into the bone, in spite of the osteogenesis inhibition produced by the steroids (*7*).

Another treatment, such as hemi-surface replacement, which may be useful in patients with AVNFH when bone quality is adequate and when acetabular cartilage is relatively normal (*1*)) was not used in this series because we considered that these patients did not fulfil these criteria. Isono *et al* (*17*) established that the results from cup arthroplasty and surface arthroplasty did not compare with those of total hip arthroplasty, and both procedures had high failure rates, regardless of the diagnosis, and were therefore not recommended.

In conclusion, based on the functional and radiographic results in this study, it appears that heart-transplant patients should be considered suitable candidates for cementless THA, despite their compromised immune status, their age or the supposed negative effect of the steroids on osseointegration of the implant, as satisfactory results can be achieved without any need for specific intraoperative or postoperative measures (*7*).

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