Original Article

Can three-phase skeletal scintigraphy predict the outcome and determine the timing of removal of bone distracters in avascular necrosis of femur using a novel corticostomy technique?

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ABSTRACT

Introduction: ^{99m}Tc-Methylene diphosphonate (^{99m}Tc-MDP) three phase bone scintigraphy (TPS) is beneficial to evaluate the success of femoral head revascularization using novel distraction osteogenesis techniques with bone muscle pedicle grafts. This pilot study was undertaken to evaluate the feasibility and utility of ^{99m}Tc-MDP three phase bone scintigraphy in predicting outcome in patients with femoral avascular necrosis (Ficat staging 2 or 3) using a new surgical technique and external fixator device as part of the distraction osteogenesis technique. We also wanted to find out if bone scan can determine the timing of removal of bone distracters and thus improve the clinical outcome.

Methods: 39 newly diagnosed patients with femoral AVN underwent a new modified Iliazaro technique in a nearby specialised Orthopaedic centre. 40 hips with Ficat and Arlet stage II and III in the age group of 18 to 33 years were included (Male: Female = 38: 01). Necessary clearance from institutional review board was obtained. Patients were assessed both subjective and objectively for the presence of pain (Harris Hip score), range of movements, radiological and TPS findings of the affected hip joints. TPS of hip joints was performed pre and postoperatively using 15 mCi of ^{99m}Tc-MDP intravenously. Patients who did not show improvement in bone scan at 6th week had follow up scans at 10th and 14th week respectively. Radiographic correlation was also obtained.

Results: Clinical and TPS imaging data were analysed. Clinical scoring **(**Harris hip score, HHS) was done pre and postoperatively in all patients. TPS demonstrated good improvement in cortical blood flow to the femoral head after revascularization at 6 weeks in 30 out of 40 hips (i.e. 75%) using this new surgical technique and fixator device. 7 patients showed improvement at 10th week and remaining 2 patients showed no improvement even at 14th week post-surgery. Quantitation was also performed to substantiate the visual findings using perfusion index (PI), initial uptake ratio (IUR) in soft tissue phase image and delayed uptake ratio (DUR) in skeletal phase image in all patients. Patients demonstrated significant improvement in Postop DUR when compared to preop. DUR values. HHS improved from 57 to 83 in 75% patients postoperatively indicating a good success of this surgical technique. All the data was analysed using SPSS software version. Statistical significance was accepted when $p<0.05$.

Conclusion: TPS is a simple, reliable and cost effective investigation in the non-invasive assessment of distraction osteogenesis in AVN patients using this novel technique of corticostomy and gluteus medius pedicle graft at greater trochanter. It is a good tool to assess new bone formation. Intensity of MDP uptake at affected femoral head is a marker of restored metabolism and can be effectively used in timing the removal of bone distracters which is usually 6 weeks in majority of cases.

Key words: Three phase bone scan; ^{99m}Tc-MDP; Avascular necrosis femur; Distraction osteogenesis; Gluteus medius pedicle graft; Corticostomy

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INTRODUCTION

Avascular necrosis (AVN) also known as osteonecrosis is a devastating disease with relentless course in young patients. In spite of years of research and refinement in the treatment of osteonecrosis, there are several unsolved issues in surgical management like the variations in revascularization technique, poor success rate due to instability of the revascularised bony fragments etc. Anatomical imaging modalities are used in the identification of AVN. Patients are usually classified by Ficat and Arlet system of classification which includes both radiological and presenting symptoms. Stages 0 to 2 were described as early stages and Stages 3 and 4 were classified as late stages. Those in pre collapse stage identified by radiograph or MRI with less symptoms can be addressed by initiating bone remodeling surgery popularly known as distraction osteogenesis. This procedure is based on the principle in which new bone develops in an area subjected to gradual tension [1]. This technique was further developed and popularized by Professor Gavril Ilizarov during the 1950s for limb lengthening and reconstruction. He used infinitely-adaptable circular fixator with fine-wire bone fragment fixation [2].

Over the first half of the 20th century, the lengthening devices ranged from the traction Thomas splint device of Codivilla, to various bed mounted and semi-portable external fixation devices. The early limb lengtheners employed distraction osteogenesis to fill the distraction gap produced by their fixators. It was not however until the 1950's and 60's that the biology of distraction osteogenesis became understood. This was largely due to Ilizarov and his group in Kurgan, USSR [2].

Of the surgical procedures that are available, many are aimed at delaying the progress of the disease and not to arrest it. Femoral head collapse in advanced stages of AVN can lead to limb shortening. Distraction osteogenesis (DO) is widely accepted as a technique to augment the affected skeleton, with protocols recommending the timing to start distraction after an osteotomy or to remove distractors. The principle of DO is based on the fact that if the two ends of a fracture are drawn apart by fractions of a millimeter each day after an initial period of close apposition, a fracture can be stretched to initiate new bone formation and results in limb lengthening. The same principle is extended to redirect vascular supply to the diseased femoral head in AVN.

Post revascularisation, challenge lies in identifying the bony fragment that are truly revascularised as it calls for better stabilisation of the ischemic bony component to enhance healing. This information is important early during the postoperative period for AVN which can be provided by a simple ^{99m}Tc-Methylene diphosphonate (^{99m}Tc-MDP) three phase bone scintigraphy.

Because bone scintigraphy is well known as a gold standard for quantitative measurement of bone formation, we conducted this pilot study to evaluate its feasibility and utility for assessing new bone formation by using a variation of ilizarov's technique with a newly devised external fixator and corticostomy technique for distraction osteogenesis. Secondly we also wanted to study if MDP three phase bone scintigraphy (TPS) can determine the timing of removal of bone distractors.

METHODS

39 patients (Male: Female = 38: 01) between 18 to 33 years of age with newly diagnosed femoral AVN were considered. A careful history, clinical and biochemical examination was part of the study. Inclusion criteria : 1) Patients with hip pain of less than 3 weeks duration 2) Recent X-ray or MRI correlation showing obvious signs of femoral head involvement i.e Ficat stage II or III, 3) Patients with no documented co morbidities 4) Patients who are candidates for distraction osteogenesis and can expect a favourable outcome (restoration of femoral head vascularity) were included. Exclusion criteria: 1) Children, pregnant and lactating women 2) suspected osteomyelitis or history suggestive of arthritis 2) patients suffering from chronic illness /poor general condition who can have delayed healing 3) Patients on medications like steroids or bisphosphonates that can alter MDP uptake pattern, were not included in the study. Prior to bone scan, patients were thoroughly assessed both subjective and objectively for the presence of pain using Harris Hip score. The range of movement at hip joints was also tabulated.

The Harris hip score (HHS) is frequently used to measure the clinical outcome after total hip arthroplasty [3]. Harris (1969) developed this score with a rating scale of 100 points and with domains of pain, function, activity, deformity, and motion. HHS survey form has four subscales incorporated in the scoring system. The first involves measuring pain severity (44 points); function, which is made up of daily activities and gait (47 points); the absence of deformity, which is a subscale that measures hip flexion, adduction, internal rotation, leg length discrepancy and range of motion measures (4 points), and range of motion (5 points). The survey included 10 question items and higher scores represent less dysfunction and better outcomes. All patients underwent radiological examination.

Fical et al. staging [4] of AVN that was used in our patients is described below;

Stage 0: is preclinical and preradiographic stage, ie, a "silent hip with no changes are visible on radiograph

Stage 1: is preradiographic but the patient presents with ischemic pain in the groin with or without radiation down the front of the thigh.

Stage 2: Patient displays radiographic signs of increased density, diffusely increased porosity and/or cystic changes. The radiographs would show flattening of the contour of the head of the femur, the "out-of-round sign" and the classic crescent sign in the head of the femur as the patient's disorder progresses from the early to late stages.

Stage 3*:* is characterized by disruption of the normal round contour of the head and accumulation of sequestrum that might increase or maintain the normal joint space.

Stage 4*:* presents with complete collapse of the femoral head into a flattened contour and decreased joint space (i.e. osteoarthritis with joint space narrowing).

Preoperative three phase regional ^{99m}Tc-MDP bone scan was performed 7 to 10 days prior to surgery. All patients underwent a new modified corticotomy procedure of greater trochanter and a specially designed external fixator was used. This was undertaken at a specialised orthopaedics centre as part of treatment for AVN. An immediate postoperative radiogram was obtained to check the position of device. Subsequent X-rays were performed at 2nd , 6th and 12th weeks to look for callus formation. TPS was done in Nuclear medicine department of Amrita Institute of medical sciences, Cochin, India. Patients who did not show improvement in bone scan at 6th week postoperatively underwent follow up bone scans at 10th and 14th week, respectively.

Surgical procedure

The technique of distraction was divided into four sequential periods.

(1) Osteotomy and device fixation: The patient was placed on fracture table and a lateral approach was used to expose the trochanteric area. An external fixator with specially designed half pins, side plate and nuts were used for this procedure. A rectangular area measuring 5 x 3 cm was marked at the cortico-cancellous junction at greater trochanter. Multiple drilling and curettage of necrotic bone at femoral head was undertaken. A unicortical bone fragment was then cut with intact Gluteus medius insertion (modified corticotomy) as a vascular pedicle graft to help restore femoral head vascularity.

(2) *Latency period*: This was of five to seven days and represented the time required for reparative fibrous callus formation.

(3) Distraction period: The distraction period was the time when a traction force was applied to the bone segments and a new bone regenerate was formed. The external fixator was applied as shown in the Figure 1 with the distracting pin in the corticotomy fragment. Wound was closed in layers. Post operatively controlled fractional distraction at the rate of 0 .5 mm per day was initiated 10 days after surgery and continued for 21 days.

(4) Consolidation period: Stabilization period was of six weeks duration. The device was removed based on findings of TPS imaging (improvement in vascularity). Majority showed improvement at 6th week. Weight bearing was permitted 4 months after surgery. This period allows mineralization of the newly formed bone tissue prior to removal of the distraction device.

Three phase bone scintigraphy

^{99m}Tc-MDP three phase bone scan was performed in the midphase of the distraction period. Immediately after the bolus injection of 740 MBq into the right medial antecubital vein followed by flushing with 20 mL saline, perfusion phase images were obtained, with 128 x 128 matrix, in the anterior view every 2 sec for 2 min.

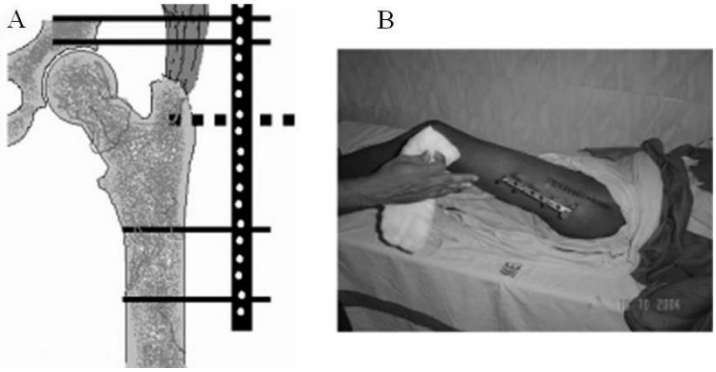

Fig 1. A) Schematic representation illustrating the sites and position of external fixator into different sites of femur B) Stable fixation of the osteotomized bone segments with the fixator in a patient with Left hip AVN.

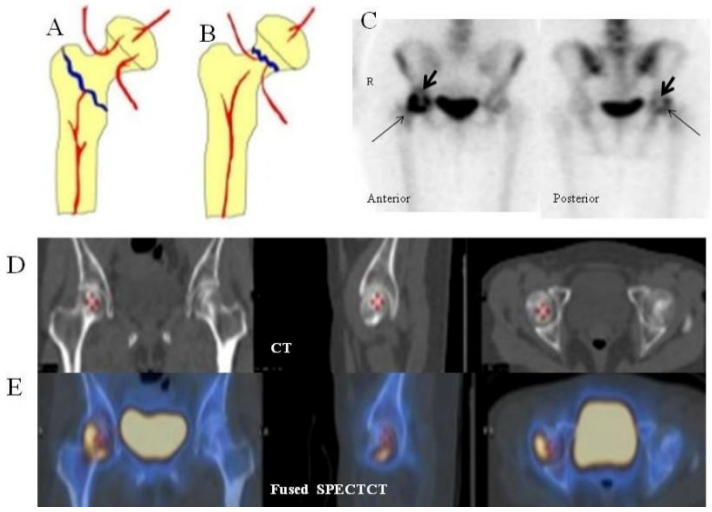

Fig 2. A) Diagram showing the arterial supply to femoral head by 3-4 branches of retinacular blood vessels and by obturator artery through ligamentum teres. This vascular supply to femoral head is preserved in trochanteric fracture, while in Subcapital fracture (B), there is disruption of retinacular arteries leading to avascular necrosis (C) Planar bone scan (anterior, posterior views) shows focal cold defect (Thick arrow) in head of right femur with increased uptake corresponding to subcapital fracture site (Thin arrow). (D) CT image in transaxial, sagittal and coronals planes & (E) Fused SPECT CT image in transaxial, sagittal and coronals planes (crosshair shows the cold defect – AVN site).

The blood pool phase image was obtained at 5th min post injection for 500 kilo counts (kcts), with 256 x 256 matrix. A delayed anterior, posterior static image of hip joints was obtained 3 hours later with 256 x 256 matrix for 500 kcts. Energy discrimination was centered on 140 keV with a 20% window. All data were obtained using a large-field-of-view gamma camera (Optima NM/CT 640 from GE Healthcare) equipped with a low-energy, high-resolution, parallel hole collimator. SPECTCT of hips was also performed.

Periodic clinical, radiological and TPS assessments were done. Success in this study was defined as postoperative increase in Harris hip score (HHS) by 20 points, with radiological improvement and no additional femoral collapse. All cases also showed an increase in MDP uptake at affected site in postop bone scan by a factor of at least 2.

RESULTS

TPS was interpreted both visually and semi-quantitatively by a senior nuclear physician.

SPECTCT of pelvis was also performed in patients with AVN due to fracture to clearly discern the femoral head (Figures 2 and 3).TPS demonstrated good improvement in cortical blood flow to the femoral head after revascularization at 6 weeks in 30 out of 40 hips (i.e. 75%) using this new surgical technique (Figure 4). Distractors were removed from those hips displaying good MDP uptake at affected femoral heads at 6 weeks and weight bearing was permitted at 4th month. 7 hips showed improvement at 10th week and remaining 2 patients showed no improvement even at 14th week, postoperatively.

Perfusion index (PI) derived from the immediate vascular phase images, Initial uptake ratio (IUR) from soft tissue phase image and Delayed uptake ratio (DUR) from skeletal phase image was obtained in all patients from TPS images. For semi-quantitative analysis of IUR and DUR, on the blood-pool image and delayed skeletal image, we set manually the region of interest (ROI) on the distraction segment and set a symmetric ROI on the contralateral normal area as a control. Radiographs were used as reference. The uptake ratio of the blood-pool image (IUR) and the uptake ratio of the delayed image (DUR) were calculated by dividing the count density of the distraction segment by that of the contralateral normal area in each image. For PI calculation, we set symmetric ROIs on the distraction segment and on the contralateral normal area. The time activity curve of each ROI was generated, and the PI was determined by dividing the peak count of the arterial phase of the distraction segment by that of the contralateral normal area. When a peak count was not obtained, the time activity curve always showed a shoulder point, which was the turning point between the rapid count increase due to the arterial phase and the steady-state or gradual count increase due to ^{99m}Tc-MDP accumulation to the distraction segment and the contralateral normal area. In such cases, the count of the turning point of the time activity curve was used to calculate the PI.

Apart from TPS analysis, all hips were clinically assessed by the Harris hip score (HHS) a quantitative measurement of pain, functional impairment and physical examination. A maximum score of 100 is assigned to each asymptomatic hip.

There is significant improvement in PI and IUR in pre and post op bone scans in 30 hips.

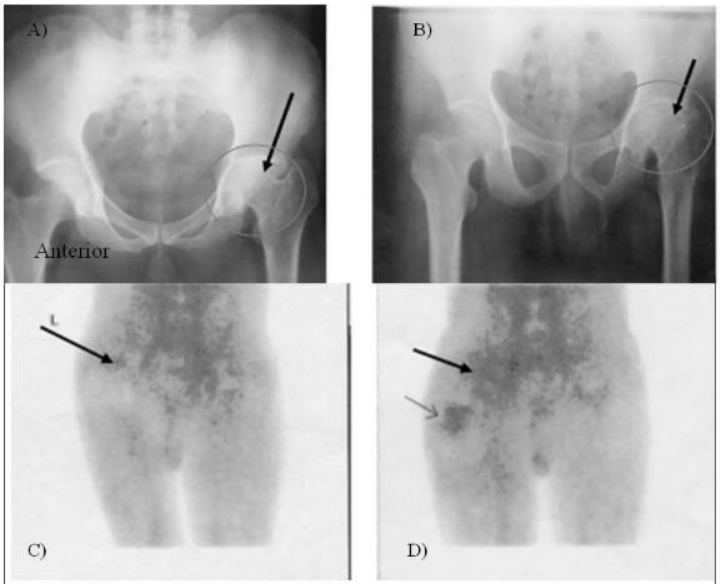

Fig 3. Pelvic X Ray – pre and postop (A, B), C & D are MDP soft tissue phase static images. Thick arrow in image D depicts focal increased soft tissue MDP uptake in right femoral head signifying restoration of femoral head blood flow. Thin arrow indicates soft tissue uptake in torchanteric region due to implant insertion.

Mean Preop. PI values were 0.7 ± 0.2 and IUR values was 1.1± 0.3 while postop PI value 1.55± 0.2 and IUR 1.78 ± 0.2 respectively. Similarly there was a significant improvement in Postop DUR when preop. DUR values were compared; mean Preop. DUR and Postop DUR were 1.9 ± 0.2 and 3.2 ± 0.4 respectively. (Figures 2 and 3)

All the hips which were stable or showed improvement on imaging postoperatively were also clinically stable and improved at 6 months follow up. In our patients, most common indicator of improvement was resolution of pain of the affected hip. HHS improved from 57 to 83 in 75% patients with focal increased MDP uptake in affected site by at least 50%.

Bone distractor was removed from 30 hips that showed restored revascularisation at 6th week. There was delayed response in 7 hips (MDP uptake was less than 50% at 6th week), that may be attributed to delayed bone remodelling due to postoperative or other unknown causes. Subsequent TPS imaging showed higher PI and IUR values in 7 hips which although resulted in delayed removal of distractor but indirectly ensures better clinical outcome. Thus TPS serves to be robust marker to determine the time of removal of bone distractor. Two patients who had persistent pain and displayed no significant improvement in MDP uptake on TPS were counselled for hip replacement surgery. Radiological improvement was judged by reduction in the density of the necrotic portion of the femoral head; return to normal density of the pre-operative rarefied areas; restoration of the normal trabecular pattern; disappearance of the crescent sign; healing of cystic areas and of the fracture line within the necrotic area or between it and the healthy bone; improvement in the shape of the femoral head.

DISCUSSION

There is scarcity of literature on usage of bone scan in assessing therapy response in AVN in our Indian population. The present study is intended to analyse the surgical response and clinical outcome of AVN patients (Ficat stages III/ IV) using TPS. To our knowledge, this is the first study in Indian patients evaluating the role of TPS in femoral AVN using a new corticostomy technique with muscle pedicle grafting. A large number of surgical techniques have been devised in order to reverse the process and regain a painless mobile hip. However, treatment outcomes are highly unpredictable, particularly in the latter Ficat stages of the disease.

Historically the technique used by Ilizarov, a Russian surgeon, in 1951 has distinct advantages over other methods of fixation. The bone fixator used in Ilizarov femoral configuration is stiff in torsion and anteroposterior bending, while flexible during axial loading. He was able to achieve a full control over the manipulation of bone segments, regardless of their size shape or anatomic location. Ilizarov divided 2/3 rd of bony cortex with a narrow osteotome and completed the corticostomy by rotational osteoclasis, thereby causing minimal trauma to the periosteum and bone marrow.

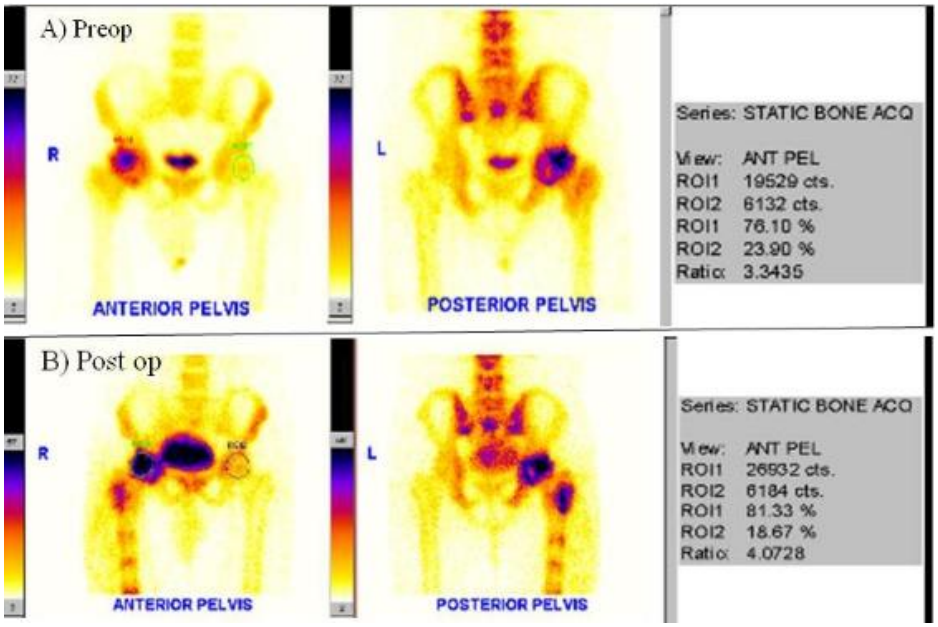

Fig 4. Three phase regional bone scan (A, Pre and B, postop) - Delayed skeletal phase static image (Anterior, posterior pelvis) in a patient with right femoral AVN. Postop images (B) at 6th week show focal intense MDP uptake in femoral head region indicating successful restoration of bone metabolism.

His lengthening protocol utilized a 5-7 day latency period followed by a distraction of 1 mm per day performed in four increments of 0.25 mm.

Usually the osteotomy technique is suitable for small stage 3 AVN lesions. But it deforms the femur and thereby makes the subsequent Total hip replacement (THR) difficult. Thus it is not a method of choice in young patients and can be associated with significant morbidity. Variations in technique like the rotational acetabular osteotomy described by Keiji Matsuda in 2005 redistributes weight bearing courses and maintains limb length. However success of this technique has not be documented as long term follow ups has not been described. A few others have used free vascularised fibular graft in an attempt to revascularise the site of AVN but that has been shown produce significant donor morbidity and there is lack of long term follow ups while using various muscle pedicle bone grafts.

The trap door procedure popularized by Ko et al. [6] uses cancellous bone graft harvested from the iliac crest, to fill the defect in the femoral head after complete evacuation of the necrotic bone. These bone graft can be introduced through a cortical window in the femoral neck or via a ‘trapdoor’ through the articular cartilage of the femoral head. Mont et al. [7] had reported their observations with this procedure in 24 Ficat stage III and 6 stage IV hips. With an average follow up of 56 months, 73% their patients had well to excellent results. In advanced stages of the disease resurfacing of femoral head can be a successful interim procedure. The mean survival of the prosthesis was 10.5 years.

Apart from the surgical modifications, the device used for DO is also important and plays a major role in femoral head revascularization and limb lengthening. Factors that can affect Distraction include; Rate of distraction, Frequency of distraction, Latency period, Rigidity of fixation, Adequate consolidation period, and the length of regenerate. The distracter design also influences various factors: difficulty or ease of placing or withdrawing the device after the consolidation, adequacy of the distracter anchorage to achieve stability of the bone blocks, and interference or not with the functions of the involved bone or adjacent soft tissues due to its size. The most important factor is the direction of the distraction applied. Thus, the distraction axis can be parallel to the anatomic axis of the femur but not to the biomechanical axis of the loading of the bone, which can produce different deformities in the knee when the elongation is completed.

Stable fixation of the osteotomized bone segments is a critical factor in successful distraction. Studies have demonstrated that stable fixation is associated with excellent regenerate bone formation without a cartilaginous intermediate and with complete remodeling after approximately 10 weeks of rigid external fixation.

In this background revascularization of the femoral head appears the most rational approach. Corticotomy and distraction albeit older techniques aim at

revascularising the femoral head and is based on the following sound scientific principles – distraction angiogenesis, joint distraction, modification of the bio-mechanics of hip joint and decompression of the bone. Ilizarov has proved that controlled gradual distraction of corticotomy fragment can produce increased vascularity in the limb. According to Paley et al. joint distraction can prevent collapse of the femoral head [8] and Pauwels et al. [9] has demonstrated that lateralization of the Gluteus medius insertion increases the lever arm resulting in better muscle function. Bone decompression reduces the intra osseous hyper tension which is a known etiological factor for osteonecrosis. The new surgical approach incorporates all these principles. Another recent study [10] was undertaken in paediatric population (19 patients) with proximal femoral ischemic deformities. A new C-shaped pertrochanteric osteotomy along with neck lengthening utilizing distraction osteogenesis principles was used. This procedure was designed to restore the femoral anatomical ratios between neck, shaft, and the head, and redress the biomechanics of the proximal femur with resultant sufficient containment of the femoral head within the acetabulum. This study showed good results favoring the implementation of this procedure in children with femoral head ischemia.

Our study with three phase bone scintigraphy revealed that MDP uptake in femoral head especially in delayed image is a good predictor to objectively document osteogenesis and bone metabolism. Corticostomy with muscle pedicle grafting at greater trochanter restores the blood supply to femoral head to a large extent as seen in this study. Thus it serves as a good option while using rigid external fixator in young patients with AVN. TPS is the only and most effective modality to predict surgical outcome after distraction osteogenesis in AVN. It also serves as a robust marker to determine the time of removal of bone distractor based of MDP uptake percentage on sequential imaging. Vascular and soft tissue phase images reflect the restoration of regional blood flow and hyperaemic status of femoral head if any. While the three hour delayed image reflects the activity of bone metabolism by demonstrating focal increased MDP concentration corresponding to site of osteogenesis. The quantitative indices also substantiate reliability and accuracy of TPS in the follow up evaluation of distraction osteogenesis with gluteus medius pedicle grafting.

CONCLUSION

We conclude that TPS is a simple, reliable and cost effective investigation in the non-invasive assessment of distraction osteogenesis in AVN patients using this novel technique of corticostomy and gluteus medius pedicle graft. It also guides in timing the removal of distractor. Recognizing persisting femoral head photopenia by bone scan can guide the orthopaedician to delay removal of bone distracters and avoid further progression of disease.

Delayed images of TPS are found to be the most important set of images that reflect the bone metabolism. Intensity of MDP uptake at affected femoral head is a marker of restored metabolism and can be used in timing the removal of bone distracters at 6 weeks in majority of cases.

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