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Original Article

Heterotopic Ossification Prophylaxis After Total Hip Arthroplasty: Randomized Trial of 400 vs 700 cGy

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ABSTRACT

Background: Heterotopic ossification (HO) is a known complication following total hip arthroplasty. Radiation is an effective prophylaxis, but an optimal protocol has yet to be determined. We performed a randomized, double-blinded clinical trial in high-risk patients to determine the efficacy of 400 vs 700 cGy doses of radiation.

Methods: One hundred forty-seven patients undergoing total hip arthroplasty and at high risk for HO at an urban medical center were randomized to receive either a single 400 or 700 cGy dose of radiation postoperatively. High risk was defined as a diagnosis of diffuse idiopathic skeletal hyperostosis, hypertrophic osteoarthritis, ankylosing spondylitis, or history of previous HO. Radiation was administered on the first or second postoperative day. A single blinded reviewer graded radiographs taken immediately postoperatively and at a minimum of 6 months postoperatively using the Brooker classification. Progression was defined as an increase in Brooker classification. Operative data including surgical approach, implant fixation, revision surgery, and postoperative range of motion data were also collected.

Results: A significantly greater portion of patients who received the 400 cGy dose demonstrated progression of HO than patients who received the 700 cGy dose. There were no wound complications. No preoperative factors were associated with a higher rate of progression. Patients who progressed had less flexion on physical examination than patients who did not progress, but this was not clinically significant.

Conclusion: Seven hundred centigray was superior to 400 cGy in preventing HO formation following total hip arthroplasty in high-risk patients and may be the more effective treatment in this population. Further studies comparing 700 cGy to dosages between 400 and 700 cGy may help to clarify if a more optimal dose can be identified.

Heterotopic ossification (HO) following total hip arthroplasty has a reported incidence of 2%-90% and can result in impingement [1,2]. Patient risk factors for HO include male gender, ankylosing spondylitis, diffuse idiopathic skeletal hyperostosis, hypertrophic osteoarthritis, as well as a history of post-traumatic arthritis with prominent osteophyte formation [2,3]. Operative risk factors have been identified as cementless implants and bilateral operations, while the lateral surgical approach remains controversial [2-5]. It is believed that surgical insult stimulates mesenchymal cells present in the soft tissue to transform into osteoblasts, peaking around 32-48 hours postoperatively [6,7]. Prophylaxis options include radiation therapy and anti-inflammatory medication. Indomethacin has been used with good results but is contraindicated for patients with gastrointestinal or renal pathology [8]. Additionally, indomethacin interferes with warfarin therapy and may inhibit bone ingrowth into porous-coated systems [9].

Radiation therapy is the only prophylaxis agent that can be administered locally rather than systematically to exclude the porous ingrowth surface and incision from the targeted treatment area. It is thought to work by preventing mesenchymal differentiation into osteoblastic cells [7]. Radiation is best given in a single dose to prevent decreasing its efficacy [10]. The ideal dose would be

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Table 1
Comparative Studies.

Authors	Number of Patients	Dose of Radiation	Radiation Protocol	Follow-Up	Outcome	Complications
Coventry and Scanlon 1981 [15]	48 patients in 42 hips	2000 rads	Ten fractions over a 12-d period	Minimum 1 y	No massive HO, defined as >3 cm in diameter, attached to the femur or pelvis, or produced severe restriction of motion	Prolonged hospital stay, nonunion of trochanteric osteotomy
Ayers et al 1986 [16]	48 hips in 42 patients	1000 rads	200 rads/d for 5-7 d via anterior and posterior portals	Average 29 mo	As effective as prior study using 2000 rads	Nonunion of trochanteric osteotomy
Hedley et al 1989 [12]	17 hips in 16 patients	600 cGy	Single dose	Minimum 6 mo	All hips Brooker 0 or 1	None reported
Pellegrini et al 1992 [17]	62 hips in 55 patients	800 cGy vs 1000 cGy	800 cGy dose given in a single dose; 1000 cGy given in 5 doses of 200 cGy	Minimum 6 mo	21% HO occurrence in both groups	Trochanteric bursitis
Fingeroth et al 1995 [18]	50 hips in 45 patients	600 cGy	Single dose	Minimum 6 mo	36% HO development compared with 88% historical control	None found
Healy et al 1995 [13]	107 hips in 94 patients	550 cGy vs 700 cGy	Both given as a single dose	Minimum 6 mo for 700 cGy group and minimum 9 mo for 550 cGy group	HO development in 63% of hips in 550 cGy group and 10% in 700 cGy ($P < .01$)	No acute or late complications noted
Padgett et al 2003 [14]	62 hips in 59 patients	500 cGy vs 1000 cGy	500 cGy given in 2 doses; 1000 cGy given in 5 doses	Minimum 6 mo	No significant difference in incidence of postoperative HO	No complications directly related to radiation treatment

high enough to prevent HO formation while being low enough to prevent future malignancy and failure of ingrowth [7,11].

While several studies have attempted to look at radiation prophylaxis for HO and progression, the ideal dose of radiation to prevent HO after total hip arthroplasty is yet unknown [10]. The current protocol at the lead authors' institution is a single dose of 700 cGy administered within 24 hours of surgery centered to the femoral neck. Prior studies show conflicting data about the minimum effective dose. Hedley et al [12] identified that a single dose of 600 cGy can be effective for HO prophylaxis. However, Healy et al found an increased rate of HO progression in a 550 cGy group compared to a 700 cGy group, while Padgett et al found no difference between a 500 cGy group and a 1000 cGy group [13,14]. A summary of these studies can be found in Table 1.

Our study aims to clarify the minimum effective dose of radiation. Padgett et al's study found that 500 cGy could be equivalent to 700 cGy; thus we wanted to study whether a dose lower than 500 could also match these results. We performed a randomized double-blinded clinical trial in patients who were at high risk for HO development after total hip arthroplasty to determine the difference in HO formation and progression between those receiving 400 vs 700 cGy prophylaxis. Our hypothesis was that there would be no difference between the 2 doses with regard to HO progression.

Materials and Methods

Patients undergoing total hip arthroplasty between July 1994 and September 1997 at an urban medical center were selected for review after institutional review board approval. High-risk patients were identified and included in the study if they met 1 or more of the following criteria: a diagnosis of diffuse idiopathic skeletal hyperostosis, hypertrophic osteoarthritis, ankylosing spondylitis, or a history of previous HO (Fig. 1). Written informed consent was obtained from all patients. Patients were assigned a preoperative risk class originally outlined by Ayers et al [16]. Class I consisted of patients diagnosed with hypertrophic osteoarthritis, ankylosing spondylitis, or diffuse idiopathic skeletal hyperostosis (Fig. 1). Class II included patients with previous contralateral HO and class III included those with ipsilateral HO. Class IV patients had prior ipsilateral HO that resulted in ankylosis. Overall demographic data were collected on all patients including age, gender, surgical side, and previous HO development.

Surgeries were performed by 1 of the 6 fellowship-trained arthroplasty surgeons at an urban medical center using a posterior or direct lateral approach (A. R., C. S., J. G., Mitchell B. Sheinkop, Josh J. Jacobs, Steven Giltilis). All acetabular components were cementless and both cemented and noncemented femoral components were used. Surgery was performed in a laminar flow suite with the use of body exhaust suits. All patients were given a first generation cephalosporin 1 hour preoperatively and for 48 hour postoperatively. Coumadin or low-molecular-weight heparin was used for deep venous thrombosis prophylaxis. Patients discontinued nonsteroidal anti-inflammatory medication 1 week preoperatively and did not restart them until 6 weeks postoperatively. Clinical Trials Number: 93090921.

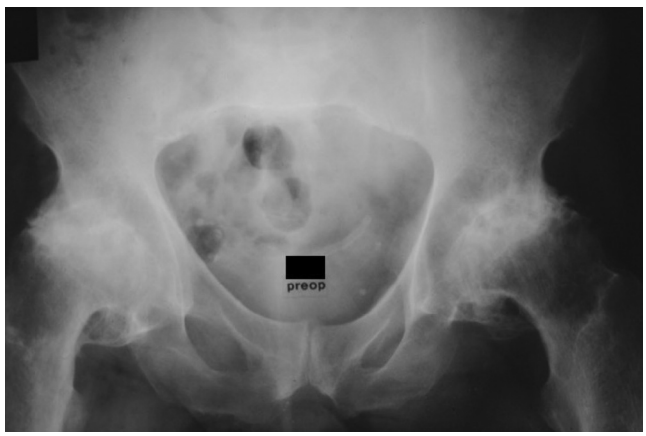

Fig. 1. Anterior-posterior pelvic radiograph demonstrating severe hypertrophic osteoarthritis in bilateral hip joints with marked joint degeneration.