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Computerized tomography-based radiotherapy improves heterotopic ossification outcomes ☆

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ABSTRACT

Purpose: To report the impact of computerized tomography (CT) based radiotherapy (RT) on heterotopic ossification (HO) outcomes.
Methods: This is a single institution, retrospective study of 532 patients who were treated for traumatic acetabular fractures (TAF). All patients underwent open-reduction internal-fixation (ORIF) of the TAF followed by RT for HO prophylaxis. Postoperative RT was delivered within 72 h, in a single fraction of 7 Gy. The patients were divided into 2 groups based on RT planning: CT (A) vs. clinical setup (B).
Results: At a median follow up of 8 years the incidence of HO was 21.6%. Multivariate regression analysis revealed that group (A) vs. (B) had HO incidence of 6.6% vs. 24.6% ($p < 0.001$), respectively. Furthermore, HO Brooker grade ≥ 3 was observed in 2.2% vs. 10.8% ($p = 0.007$) in group (A) vs. (B), respectively. Thus, the odds of developing HO and Brooker grades ≥ 3 were 4.7 and 4.5 times higher, respectively, in patients who underwent clinical setup.
Conclusion: Our data suggest that using CT based RT allowed more accurate delineation of the tissues and better clinical outcomes. Although CT-based RT is associated with additional cost the efficacy of CT-based RT reduces the risk of HO, thereby decreasing the need for additional surgical interventions.

Introduction

Heterotopic ossification (HO) is the pathological process of bone formation in non-osseous tissues following trauma and/or surgical intervention. Many clinicians recommend prophylactic radiotherapy (RT) and/or non-steroidal anti-inflammatory medications (NSAIDs) to prevent HO formation. Several factors appear critical to HO formation; traumatic injury, cellular signals from the site of injury, adequate supply of mesenchymal cells, and the appropriate tissue microenvironment are all thought to contribute to the development of HO in injured tissues [1]. Prophylactic RT has been commonly used to reduce the risk of HO after traumatic acetabular fractures (TAF) because there appears to be a 50% or higher risk of HO in these patients after surgery using a posterior approach [2]. Radiation therapy presumably decreases the risk of HO, at least partly, by inhibiting the proliferation of pluripotent mesenchymal cells that could potentially differentiate into osteoblastic stem cells. It is usually delivered postoperatively and within 72 h of surgery [3–5]. However, preoperative RT delivered at 1, 2, 4, 16, and 18 h before surgery has also been used [6–8]. The most common procedure likely to generate HO is an open reduction and internal fixation (ORIF) of a TAF, closely followed by total hip arthroplasty (THA). In a recent meta-analysis that reported the incidence of HO after TAF status post ORIF, it was observed that the incidence of HO formation after RT prophylaxis alone was 27%, 37% after indomethacin prophylaxis alone, and 12% after both RT combined with indomethacin. Patients who received no prophylaxis had a 58% incidence of HO [9].

The impact of CT-based simulation and treatment planning on HO outcomes in patients who underwent RT prophylaxis, to the best of our knowledge, has never been studied before. We hypothesized that an association may exist between the method of simulation and treatment planning used and the risk of HO. We thus, retrospectively reviewed the incidence and the severity of HO among patients who

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underwent HO prophylaxis using external beam RT after computerized tomography (CT) based simulation and treatment planning compared to clinical simulation on the linear accelerator (LINAC) followed by treatment. Portal images were reviewed prior to treatment delivery in all cases.

Methods and materials

Study objective

We tested the hypothesis that a positive association exists between simulation techniques and the risk of HO following operative management of TAF. Identifying patients who are at increased risk of developing HO would allow us to tailor a more effective post-operative prophylactic treatment regimen that is individualized for the patient. Eventually, we anticipate that such patient-specific plans would decrease patient morbidity/mortality and decrease medical costs.

Study schema and patient population

This study represents a single-institution; retrospective investigation performed at a Level I trauma center, and was fully approved by our Institutional Review Board. For all patients the following data were tabulated: age, race, and gender; types and causes of fracture and surgical approach used; date of accident, date of ORIF, body mass index (BMI), RT modality, and indomethacin use. For this study, the patients were stratified into two groups according to the type of simulation they underwent and time interval (in days) from the date of their accident to the date of prophylactic RT:

- Group A: CT-based simulation and 3-D RT planning and treatment after review of portal images.
- Group B: clinical (LINAC)-based simulation and treatment after review of portal images.

Patient eligibility, follow up, and design

Between January 2004 and January 2010, 532 patients were identified who has had operative management of TAF in the Department of Orthopedic Surgery followed by prophylaxis of HO in the Department of Radiation Oncology. All patients had required ORIF and received prophylactic RT with or without indomethacin. All underwent adequate follow-up evaluations.

Surgical treatment

All surgical procedures were performed by two trauma fellowship trained, orthopedic surgeons (G.R. and M.G.). All patients underwent ORIF via the posterior approach (Kocher–Langenbeck) with the patient positioned in the lateral or prone position. Early patient mobilization with toe-touch weight bearing as tolerated was implemented for all patients.

Radiation treatment

RT was delivered prophylactically to all the patients and given within 72 h after the ORIF. Seven hundred cGy was delivered in a single fraction to the midplane, using 6- to 18- mV photons. Treatment fields included the soft tissues around the proximal femur and acetabulum without any bone shielding (Figs. 1 and 2) [10].

Medical treatment

Forty percent (213/532) of the entire cohort received RT with indomethacin; specifically, 33% (30/90) and 41% (183/442) of the patients in groups A and B, respectively. Indomethacin was prescribed at the discretion of the surgeon at a dose of 25 mg three times daily, after meals, beginning on postoperative day 1 and continued thereafter for 6 weeks.

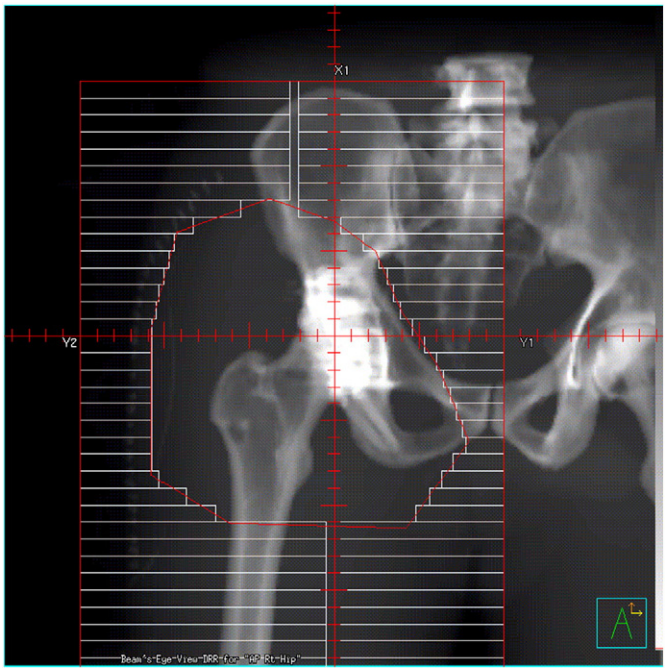

Fig. 1. Shows the anterior–posterior RT portal for right TAF status post ORIF followed by a single fraction of 700 cGy, prescribed to midplane.

Follow-up

Patients had routine follow-up appointments at 2 weeks, 1 month, 3 months, 6 months, and 1 year from the day of hospital discharge. Standard X-rays (AP, PA, and oblique) of the affected joint were obtained for evaluation of HO, avascular necrosis of the femoral head and loosening, malunion, or non-union of the fracture. Computed tomography of the pelvis was obtained when considered clinically appropriate. All patient medical records and X-rays were reviewed to determine the efficacy of the RT in preventing HO. Heterotopic ossification was evaluated by three independent reviewers: a radiologist (MK), an orthopedic surgeon (GR and/or MG), and a radiation oncologist (W.M) [11–13].

Hypothesis and study endpoints

We evaluated the impact of CT based simulation and three dimensional-RT (3D-RT) treatment planning on the rate and severity of HO using the Brooker staging system [14]. Our primary goal was to determine whether the CT based simulation and RT based planning decreased the risk of HO. Our secondary goal was to use the methodology of simulation as a predictor for HO after ORIF for TAF and prophylactic RT.

Statistical methods

Chi-square test, univariate analysis, and multiple logistic regression analysis were used to compare the rates of HO formation in the different groups, after adjusting all other factors that could potentially affect HO formation (e.g., age, gender, race, cause and type of fracture, surgical exposure, BMI, and the use of indomethacin).