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Low Rates of Heterotopic Ossification After Resurfacing Hip Arthroplasty With Use of Prophylactic Radiotherapy in Select Patients

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Abstract

Recent reports have noted higher rates of heterotopic ossification (HO) with surface replacement arthroplasty (SRA) than with traditional total hip arthroplasty in the absence of postoperative HO prophylaxis. This study reports rates and grades of HO in 44 SRA patients with at least 1 year of follow-up. Heterotopic ossification prophylaxis was used in 32 (73%) of 44 cases. Heterotopic ossification prophylaxis consisted of radiotherapy (22/32), nonsteroidal anti-inflammatory drugs (8/32), or both (2/32). One case of clinically significant HO was documented in the no-prophylaxis group. This strategy of selective HO prophylaxis in patients felt by orthopedic surgeons to be at high risk of HO resulted in low rates of clinically relevant HO after SRA (1/44, 2.3%). Further study is needed to establish optimal selection criteria for HO prophylaxis after SRA.

Keywords

surface replacement arthroplasty; heterotopic ossification; prophylactic radiation

Total hip arthroplasty (THA) is the standard treatment of symptomatic, severe hip osteoarthritis. As experience with metal-on-metal articulation has grown, evidence has emerged supporting the use of surface replacement arthroplasty (SRA) in selected patients. Compared with THA, SRA offers the advantage of conservation of more femoral bone stock. This approach has shown promising early results in young active male patients. Several studies comparing clinical outcomes after SRA and THA have shown advantages to SRA with respect to higher levels of activity [1], range of motion [2], and return to intense sports activities [3], whereas other studies have shown similar clinical outcomes between SRA and THA [4,5]. These findings have led to the increased use of SRA, particularly in younger patients.

Heterotopic ossification (HO), or abnormal bone formation in soft tissues, is sometimes seen around the hip following THA [6]. Known risk factors include revision surgery, hypertrophic osteoarthritis, ankylosing spondylitis, and male gender. In addition, surgical

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technique and the amount of local tissue trauma can impact the likelihood of HO [7,8]. Symptomatic HO can result in decreased range of motion at the affected joint, as well as local pain and edema. Heterotopic ossification is classified radiographically via the Brooker classification [9]. Classes III and IV are considered clinically significant HO. Nonsteroidal anti-inflammatory drugs (NSAIDs), typically indomethacin, and radiotherapy (RT) are commonly used as prophylactic measures against HO formation [6].

The exposure for SRA involves more manipulation of the soft tissues than is necessary for a primary THA, and concern has arisen that SRA may result in higher rates of clinically significant HO. A prospective evaluation of HO rates in a cohort of patients undergoing SRA, without postoperative HO prophylaxis, demonstrated Brooker class III HO in 8.2%, with 58.6% of patients demonstrating some degree of HO [10]. Within the context of a randomized trial examining THA vs SRA, Rama et al [11] demonstrated a significantly higher rate of class III and IV HO in SRA patients (12.6%) as compared with THA patients (2.1%) ($P = .02$); all patients in both arms received postoperative oral celecoxib while hospitalized (3–5 days). However, the use of prophylactic RT following SRA has not been rigorously studied. Therefore, we examined patients undergoing SRA at our institution to assess baseline rates of HO following SRA and quantify the impact of postoperative prophylaxis.

Material and Methods

An institutional review board–approved database of all patients undergoing hip arthroplasty at our institution was reviewed. Forty-four patients who underwent SRA and had postoperative imaging and clinical follow-up for at least 11 months (to include all 1-year postoperative appointments) were identified.

Surgical Methods

All SRA procedures were performed via a posterior approach with release of the anterior capsule. Surgeries were performed by 3 fellowship-trained attending arthroplasty surgeons (MWS, n = 9; JPH, n = 3; and RLI, n = 32). A cementless acetabular component with a mean outer diameter of 54 mm (range, 42–64 mm) was used for the metal-metal surface arthroplasties, and cemented femoral components were used in all cases. Components were manufactured by Biomet Orthopedics, LLC (Warsaw, IN): M2a Magnum acetabular component and a cemented Recap femoral component (n = 39), Smith & Nephew Inc (London, UK): Birmingham Hip Resurfacing (n = 3), Wright Medical Technology, Inc (Arlington, TN) (n = 1), and Zimmer, Inc (Warsaw, IN): Durom acetabular and femoral components (n = 1).

Prophylaxis

Radiation prophylaxis consisted of 7.5 Gy prescribed to midplane (routine shielding of the acetabular bone in-growth surface), delivered postoperatively in all patients within 72 hours of surgery (median, postoperative day 1). Energy was 6 MV in 12 patients (50%) and 10 MV in 12 patients (50%). Median field size was 5 cm (4.9–6.7) by 12 cm (9.1–14.3). Pharmacologic prophylaxis (NSAIDS) consisted of 4 weeks of either celecoxib 100 mg bid (n = 6) or indomethacin 50 mg bid (n = 4).

Data Analysis

Both anteroposterior and lateral radiographs obtained at the 1-year postoperative visit (range, 11–14.5 months) were reviewed for evidence of HO. Two physicians (DMC and CSP) were blinded to all clinical information pertaining to the patient (ie, RT use), reviewed the radiographs, and assigned a Brooker class per the original report [9]. Diagnostic

radiology reads were available to guide interpretation, and comparisons were made to the immediate postoperative radiographs. Disagreements occurred in 9 (20.5%) of 44 patients and were never more than 1 class. These radiographs were resolved by a third reviewing physician (TJK) to generate a consensus HO grade. Fisher exact test was used to determine the statistical significance of relationships between dichotomous variables and both HO rates and radiation use. Student test was used to determine the statistical significance of relationships between continuous variables and both HO rates and radiation use.

Results

Patient and operative characteristics for all patients are shown in Table 1. Two patients had a prior history of hip surgery including a recent ipsilateral hip arthroscopy and a remote ipsilateral incision and drainage for a staphylococcal infection. No serious surgical complications were noted. Six patients (14%) received transfusions during their postoperative hospital stay. There were no femoral neck fractures or deep wound infections. No migration of the femoral or acetabular components was observed, but 2 patients (4.5%) underwent revision THA at 14 and 36 months for recurrent/persistent pain in the operated hip. These rates of early failure after SRA are consistent with previously reported studies [12]. Median orthopedic follow-up was 3.0 years (0.9–4).

Prophylactic radiation was delivered in 24 (55%) of 44 patients, whereas NSAID prophylaxis was used in 10 (23%) patients. Two patients received both radiation and NSAID prophylaxis, and 12 (27%) patients received no prophylaxis. Use of prophylaxis and choice of prophylaxis were based on surgeon preferences. Heterotopic ossification was documented in 13 (29.5%) of 44 patients (Table 2).

Heterotopic ossification was Brooker class I in 6 patients (13.6%), class II in 6 patients (13.6%), and class III in 1 patient that did not receive any prophylaxis (2.3%). No class IV Brooker HO was observed. Rates of class II to IV HO were not significantly affected by radiation or NSAID prophylaxis. Similarly, gender, body mass index, diagnosis, estimated blood loss, and operative time did not appear to impact the rate of HO (Table 3). In contrast, patients who developed Brooker grades 2 to 4 HO tended to be younger (mean age 45 years, ± 4 years) than those who developed no or low-grade HO (mean age 52 years, ± 1 year) (P = .03). Incidences of HO occurring following radiation prophylaxis, NSAID prophylaxis, or no prophylaxis are presented in Table 4.

As prophylaxis use was not predefined, we assessed impact of pretreatment variables on delivery of RT (Table 5). No factor appeared to predict the use of radiation prophylaxis except for age; patients who received prophylactic radiation (mean age 49 years, ± 2 years) were significantly younger than those who did not receive prophylactic radiation (mean age 54 years, ± 2 years) (P = .03).

Discussion

Surface replacement arthroplasty is becoming a more common procedure for severe hip osteoarthritis, particularly in younger, more active patients. However, randomized evidence demonstrates that rates of significant HO are higher after SRA than following THA [11] in patients without specific postoperative HO prophylaxis. In this report, we demonstrate low rates of clinically significant HO in a young, predominantly male cohort when HO prophylaxis (RT and/or NSAID therapy) was used at the orthopedic surgeon's discretion.

Identified risk factors for HO (following THA) include extensive periarticular osteophytosis, osteoarthrosis, HO in the contralateral hip following surgery, trochanteric osteotomy, subtrochanteric femoral osteotomy, lateral or anterolateral approach, and previous hip

surgery [7,8]. These data suggest that the degree of local tissue trauma plays a role in HO formation. Furthermore, these reports and others [10,11] consistently identify male gender as a risk factor for HO development. As patients undergoing SRA tend to be younger men, and this approach involves more local soft tissue trauma than with primary THA, HO may be a more problematic entity in the SRA patient population than in primary THA patients. Therefore, careful consideration of prophylactic therapy is warranted.

Nonsteroidal anti-inflammatory drugs, typically indomethacin, and RT are commonly used as prophylaxis against HO. Indomethacin has been suggested to reduce HO [13,14], but is accompanied by gastrointestinal adverse effects and has been shown to increase rates of bone nonunion [15] when compared with no prophylaxis or RT prophylaxis. Numerous studies have demonstrated the efficacy of RT prophylaxis [16–18], with appealing adverse effect profiles. A meta-analysis of randomized trials between NSAIDs and RT demonstrated superiority of postoperative RT for HO prophylaxis as compared with NSAIDs, with the efficacy of RT dependent on dose [19].

Use of prophylactic therapy in our patient cohort was heterogeneous and not prespecified. Nonetheless, 32 (73%) of 44 patients received prophylaxis, with RT used in 24 (55%) of 44 patients. Neither RT nor any prophylaxis was significantly associated with freedom from class II to IV HO. However, the use of prophylactic therapies only in patients deemed at high risk for HO development by the surgeon, based on patient-related factors and intraoperative factors, would likely result in low HO rates in observed, low-risk patients and, likewise, low HO rates in higher-risk patients who received effective prophylactic therapies, obscuring the impact of prophylaxis. Furthermore, SRA is a new technique; and the limited size of the presented patient cohort may also contribute to a lack of statistical impact of these therapies. Nonetheless, our rates of HO are lower than the rates of HO published in prospective cohorts without prophylaxis; and none of the 32 patients receiving prophylaxis developed clinically significant (class III–IV) HO. Back et al [10] demonstrated an any-class HO rate of 58.6% following SRA in 220 patients, with class III HO noted in 8.2% of patients. In 103 patients randomized to SRA, Rama et al [11] identified any-class HO in 45% of patients and class III to IV HO in 13% of patients. Our corresponding rates of any-class HO (29.5%) and class III to IV HO (2.3%) appear favorable to these rates (Table 6), suggesting that prophylactic measures may be of benefit in patients undergoing SRA.

Our data suggest a trend toward lower HO development in older patients despite lower rates of prophylactic RT utilization in these patients. Whether age is a relevant factor in HO development is unclear from previous studies. Few studies have identified age as a predisposing factor to HO formation. These studies have suggested that advanced age may predispose to HO formation, but this relationship appears to be stronger in older women and may be tied to an underlying relationship between osteoporosis and HO [20,21]. Numerous other large studies have failed to identify a relationship between HO formation and age [8,10]. Whether this questionable association between advanced age and HO formation following THA is relevant to populations undergoing SRA is unclear and may not be in conflict with our findings that younger patients (predominantly male) tended to have higher rates of HO following SRA despite receiving more prophylactic therapies.

Limitations of our study include the retrospective nature and the lack of uniform protocol regarding incorporation of prophylactic measures following SRA. The use of NSAID therapy and/or RT prophylaxis was at the discretion of the surgeon, without predefined risk factors guiding the incorporation of these therapies. Although the use of RT and/or NSAID prophylaxis was not correlated with lower rates of grade 2 to 4 HO in this study, prophylactic therapies were used only in patients deemed at higher risk for HO formation by the surgeon based on patient-related factors and intraoperative factors that cannot be

adequately accounted for in a retrospective series. However, the low rates of grade 2 to 4 HO in patients without prophylaxis (8%) suggest that orthopedic surgeons can identify patients that are at low risk for HO, and that uniform utilization of prophylaxis may not be necessary following SRA. Although the presented rates of clinically significant HO in this report are lower than those reported in other series, the results of this analysis should be considered hypothesis generating and deserve study in prospective studies.

In summary, we demonstrate low rates of clinically relevant HO in a young, predominantly male patient cohort undergoing SRA for severe hip osteoarthritis. No patients receiving prophylaxis demonstrated clinically relevant HO, and no toxicity was demonstrated attributable to prophylactic measures. Additional studies are required to determine the efficacy, and merits, of radiation and NSAID HO prophylaxis in this clinical setting.

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Table 1

Patient and Operative Characteristics

Characteristic	n (% or Range)
Gender	
Male	30 (68%)
Female	14 (32%)
Age	
Median	52 (29–63)
BMI	
Median	27.3 (21.1–34.6)
Diagnosis	
Osteoarthritis	36 (82%)
Developmental dysplasia	5 (11%)
Postinfectious	1 (2%)
Avascular necrosis	1 (2%)
Juvenile rheumatoid arthritis	1 (2%)
Laterality	
Right	28 (64%)
Left	16 (36%)
Estimated blood loss	
Median	500 mL (200–1000 mL)
Operative time	
Median	152 min (115–236 min)
Orthopedic follow-up	
Median	3 y (0.9–4 y)

Please see “Materials and Methods” for specific surgical approach. No patient had a prior history of HO. Two patients had a prior history of hip surgery including a recent ipsilateral hip arthroscopy and a remote ipsilateral incision and drainage for a staphylococcal infection. BMI indicates body mass index.

Table 2

Heterotopic Ossification Rates Following SRA

Grade	n	%
0	31	70
1	6	14
2	6	14
3	1	2
4	0	0

Table 3

Effect of Patient, Operative, and Treatment Characteristics on HO

	Brooker Grade, n		
Characteristic	**0–1**	**2–4**	***P***
Gender			
Male (n = 30)	26 (87%)	4 (13%)	.66
Female (n = 14)	11 (79%)	3 (21%)	
Age			
<Median (n = 21)	16 (76%)	5 (24%)	.23
≥Median (n = 23)	21 (91%)	2 (9%)	
BMI			
<Median (n = 22)	18 (82%)	4 (18%)	1.0
≥Median (n = 22)	19 (86%)	3 (14%)	
Diagnosis			
Osteoarthritis (n = 36)	29 (81%)	7 (19%)	.32
Other (n = 8)	8 (100%)	0 (0%)	
Estimated blood loss *			
<Median (n = 18)	14 (78%)	4 (22%)	.68
≥Median (n = 24)	21 (88%)	3 (12%)	
Operative time †			
<Median (n = 20)	17 (85%)	3 (15%)	1.0
≥Median (n = 20)	17 (85%)	3 (15%)	
Radiation prophylaxis			
Yes (n = 24)	19 (79%)	5 (21%)	.43
No (n = 20)	18 (90%)	2 (10%)	
NSAID prophylaxis			
Yes (n = 10)	9 (90%)	1 (10%)	.67
No (n = 34)	28 (82%)	6 (28%)	
Any prophylaxis			
Yes (n = 32)	26 (81%)	6 (19%)	.65
No (n = 12)	11 (92%)	1 (8%)	

* In 2 cases, estimated blood loss was not reported.

† In 4 cases, operative time was not reported.

Table 4

Incidence of HO by Use of Prophylaxis

Brooker Grade	Radiation * (n = 24)	NSAIDs[ref] (n = 8)	No Prophylaxis (n = 12)
0	16 (66.7%)	7 (87.5%)	8 (66.7%)
1	3 (12.5%)	–	3 (25%)
2	5 (20.8%)	1 (12.5%)	–
3	–	–	1 (8.3%)

* Radiation group included 2 patients also receiving NSAIDs.

Table 5

Effect of Patient, Operative, and Treatment Characteristics on Radiation Use

Characteristic	Radiation (n =24)	No Radiation (n =20)	*P*
Gender			
Male (n = 30)	17 (57%)	13 (43%)	.43
Female (n = 14)	7 (50%)	7 (50%)	
Age			
<Median (n = 21)	14 (67%)	7 (33%)	.14
>Median (n = 23)	10 (43%)	13 (57%)	
BMI			
<Median (n = 22)	11 (50%)	11 (50%)	.76
>Median (n = 22)	13 (59%)	9 (41%)	
Diagnosis			
Osteoarthritis (n = 36)	18 (50%)	18 (50%)	.26
Other (n = 8)	6 (75%)	2 (25%)	
Estimated blood loss *			
<Median (n = 18)	11 (61%)	7 (39%)	.54
>Median (n = 24)	12 (50%)	12 (50%)	
Operative time †			
<Median (n = 20)	8 (40%)	12 (60%)	.20
>Median (n = 20)	13 (65%)	7 (35%)	
NSAID prophylaxis			
Yes (n = 10)	2 (20%)	8 (80%)	.027
No (n = 34)	22 (65%)	12 (35%)	

* In 2 cases, estimated blood loss was not reported.

† In 4 cases, operative time was not reported.

Table 6

Reported Rates of HO Following SRA

Brooker Grade	Rama et al [11] (n = 103)	Back et al [10] (n = 220)	Current Series (n = 44)
0	55%	41%	70%
1	12%	37%	14%
2	19%	13%	14%
3	8%	8%	2%
4	5%	0%	0%