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ORIGINAL PAPER

Size of ischial fibro-ostosis is associated with heterotopic ossification after total hip arthroplasty

Jakob Bollmann[1] · Christian Bergdolt[1] · Peter R. Aldinger[2] · Michael W. Maier[1] · Tobias Gotterbarm[1] · Christian Merle[1]

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Abstract

Purpose The hypothesis of the present study was that degenerative fibro-ostosis (FO) of the ischial hamstring tendon insertion is a risk factor for heterotopic ossification (HO) following THA.

Methods We followed 103 consecutive patients (43 males, 60 females, mean age 61 years) who underwent unilateral cementless THA for primary hip osteoarthritis and investigated the incidence of HO within the first 12 months after surgery. On pre-operative radiographs, a standardized evaluation for FO of the ischial hamstring tendon insertion concerning horizontal, vertical, and square dimensions was performed. HO was classified according to Brooker on radiographs at 12 months post-operatively.

Results At follow-up, 56 patients (54%) had no radiographic evidence of HO, 23 (22%) were classified as Brooker I, 17 (17%) as II, 6 (6%) as III, and 1 (1%) as IV, respectively. Patients with post-operative HO had significantly greater vertical (3.0 mm vs. 2.3 mm, $p = 0.001$) and horizontal (47.9 mm vs. 39.1 mm, $p = 0.025$) dimensions of FO than patients without HO. Patients with FO and a vertical dimension of ≥ 2.5 mm were more likely to develop HO (55.6%) than patients with a vertical FO dimension of less than 2.5 mm (34.7%, OR = 2.35 $p = 0.047$). A weak correlation between the vertical and horizontal size of FO and the severity of HO was observed.

Conclusion Radiographic evidence of asymptomatic FO is a potential risk factor for the development of HO following THA and may be used as a simple diagnostic tool to pre-operatively identify patients at risk for post-operative HO. This association has not been previously described and further research to confirm the present findings and to justify additional prophylactic treatment in these patients is warranted.

Keywords Heterotopic ossification · Total hip arthroplasty · Ischial fibroostosis · Risk factor

Introduction

Heterotopic ossifications (HO) are benign bone formations of the soft tissue associated with craniocerebral trauma, spinal cord injury, skin burns, genetic disorders, or musculoskeletal surgical interventions and trauma [1–3]. The pathophysiology is still unclear, but it has been postulated that osteoblastic cells associated with HO originate from inappropriate differentiation of pluripotent mesenchymal stem cells as a result of a complex interaction between several local and systemic factors [4].

The occurrence of HO after total joint replacement is well described, particularly following total hip arthroplasty (THA) [5]. Since THA is one of the most common operations [6], the prevention and therapy of HO remain a clinical challenge. In the literature, the incidence of HO after THA varies significantly between 5 and 90% [7]. This variation of incidence may be partly explained by the fact that in most cases, post-operative HO is of limited extent and radiographic evidence of HO remains asymptomatic in 80–90% of patients [8]. However, extensive post-operative HO is a relevant cause for patient dissatisfaction with the procedure as it may severely compromise the functional outcome leading to pain, swelling, and restriction of movement, impairing the daily life of patients with problems in climbing stairs or getting up from chairs [9]. Therapeutic options for extensive and symptomatic HO following THA are limited to surgical removal and

✉ Christian Merle
christian.merle@med.uni-heidelberg.de

[1] Department of Orthopedic and Trauma Surgery, University of Heidelberg, Schlierbacher Landstraße 200a, 69118 Heidelberg, Germany

[2] Diakonie Clinic Paulinenhilfe, Rosenbergstrasse 38, 70176 Stuttgart, Germany

radiotherapy with varying clinical results [10]. Prophylactic therapy with NSAIDs (non-steroidal anti-inflammatory drugs) is generally recommended and the decision for additional (neo-) adjuvant radiation is based on individual risk factors, such as HO of the contralateral side, male gender, hypertrophic osteoarthritis, post-operative haematoma, surgical exposure, or risk diseases such as diffuse idiopathic skeletal hyperostosis (DISH) or ankylosing spondylitis [11–13].

Fibroostosis (FO) describes a calcified enthesitis associated with traumatic damage or chronic overuse on the bone insertions of tendons, ligaments, or capsules [14]. It can also appear after a bursitis, tendinitis, or associated with an underlying rheumatic, metabolic, or endocrine disease [15]. In most cases, FO alterations are small and remain asymptomatic but can be painful if there is a reactive inflammatory response in the surrounding soft tissue or bone [16]. The most common FO is the calcaneal spur, a bony outgrowth from the calcaneal tuberosity [17]. FO of the hamstring origin at the os ischium is frequently detected in pelvis radiographs and its association with the occurrence of HO following THA has not been investigated.

Therefore, the present study aims to investigate whether the radiographic presence and the extent of FO of the ischial hamstring tendon insertion is a potential risk factor for the appearance of HO following primary THA in patients with end-stage hip osteoarthritis. The hypothesis of the present study was that degenerative fibro-ostosis (FO) of the ischial hamstring tendon insertion is a risk factor for HO following THA.

Material and methods

Study cohort

In the present retrospective cohort study, we included a consecutive series of patients with unilateral end-stage hip osteoarthritis with a minimum age of 18 years. Between 2006 and 2007, 460 patients were identified from our institutional database who received a unilateral cementless total hip replacement. In all patients, the same stem (CLS, Zimmer, Warsaw IN, USA), press-fit cup (Allofit, Zimmer, Warsaw IN, USA), bearing type (Biolox ceramic heads, Plochingen, Germany; Durasul Polyethylene Inlays, Zimmer, Warsaw IN, USA), and the same surgical modified transgluteal Bauer approach was used [18]. All patients received a post-operative prophylaxis with a NSAID for 14 days. We excluded patients with previous revision surgery, pre-operative heterotopic ossifications, pre-operative or post-operative infection, secondary hip osteoarthritis following trauma, hip dysplasia, slipped capital femoral epiphysis (SCFE), and metabolic or rheumatic diseases. Further exclusion criteria were missing or inadequate radiographs, patients lost to follow-up, and patients with different implants or surgical approaches. In detail, 138 had to be excluded because of post-traumatic osteoarthritis or previous ipsilateral hip surgery, 112 by reason of incomplete, missing, or inadequate radiographs, 68 because of dysplastic hip osteoarthritis, and 39 because of medical comorbidities related to bone metabolism. One hundred three patients matched the inclusion criteria and were included in the study.

All study procedures involving human participants were in accordance with the ethical standards of the institutional research committee of the University of Heidelberg and with the 1964 Helsinki declaration and its later amendments or comparable ethical standard.

Radiographic protocols and measurements

Pre-operatively and at 12-month follow-up, all patients received a standardized low-centered anterior-posterior x-ray of the pelvis. All images were taken with the central beam focused at the symphysis pubis. To minimize errors of pelvic tilt [19] and rotation in the radiographic projection, all radiographs were assessed by two independent reviewers (CB and CM) for the following criteria before inclusion of the patient: symmetry of the obturator foramina with central position of the os coccygis in the relation to the symphysis, distance of the coccygis to the symphysis pubis 20–50 mm without overlap [20]. Patients were included only when both reviewers judged the pre and post-operative radiograph as adequate for further evaluation. All pre and post-op images were calibrated using the known diameter of the femoral head on the x-ray at 12-month follow-up and the corresponding distance between the teardrops on the pre-operative radiograph.

The pre-operative appearance of fibroostosis of the ischial hamstring tendon insertion was evaluated using Roman V1.70 software (Rontgen Monogrammetric Analysis, Institute of Orthopaedics, Oswestry, UK) [21]. Following calibration, the extent of the ischial fibroostosis in maximum vertical length measured as perpendicular length to a tangent on the os ischium [mm], the maximum horizontal length [mm], and the ratio between the affected horizontal extent and the total horizontal ischial length [%] as well as the fibroostotic area [mm^2] (Fig. 1) were measured. On the post-operative radiograph, the appearance of HO was assessed according to the Brooker classification [22] (Table 1).

Statistical analysis

For the statistical analysis, we used SPSS V24.0 (IBM Corporation, NY, USA). For metric variables, the minimum, mean, maximum, and standard deviation were assessed in exploratory data analysis. Measurements were performed by two independent observers and intra-class correlation (ICC) was assessed using a two-way model for absolute agreement for all measurements in 20 randomly selected patients. To detect the differences in the mean vertical,

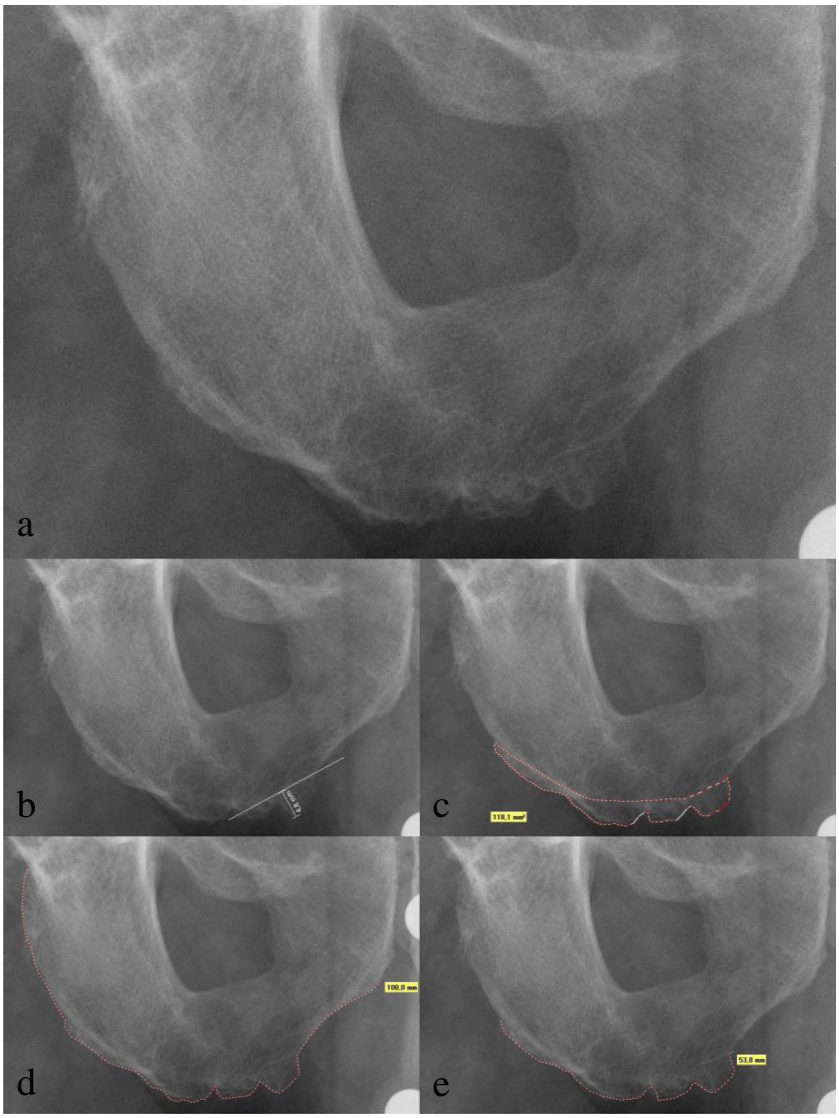

Fig. 1 **a** Plain x-ray cutout showing ischial fibro-ostosis. **b** Maximum vertical length of FO (4.8 mm). **c** Area of FO on the ischial bone (118.1 mm^2). **d** Total horizontal ischial length (100.0 mm). **e** Maximum horizontal length of ischial FO (53.8 mm)

horizontal, and plain area of FO as well as a difference in surgery duration and age at surgery between patients with and without HO, a two-sided *t* test was used. To detect a gender preference as well as a difference of more than 2.5 mm or less than 2.5 mm of maximum vertical FO between patients with and without HO, a Fisher's exact test was used. Spearman rank correlation was performed to assess the correlation between FO dimensions (mm) and Brooker Grade. A *p* value of $p < 0.05$ was defined as statistically significant.

Results

The study cohort comprised of 43 male (42%) and 60 (58%) female patients. The mean age at surgery was 61 years (18–79). At 12-month follow-up, 56 (54%) patients showed no radiographic evidence of HO whereas 47 (46%) patients presented with various degrees of HO: 23 (22%) patients were classified as Brooker Grade I, 17 (17%) as Brooker Grade II, 6 (6%) as Brooker Grade III, and 1 (1%) as Brooker Grade IV (Fig. 2).

Table 1 Brooker classification I–IV

Grade I	Islands of bone lie within the soft tissues about the hip
Grade II	Bony spurs protrude from either the femur or the pelvis, with a gap of more than 1 cm between opposing bony ends
Grade III	The gaps between the spurs are less than 1 cm
Grade IV	Apparent ankylosis of the hip due to the heterotopic ossification

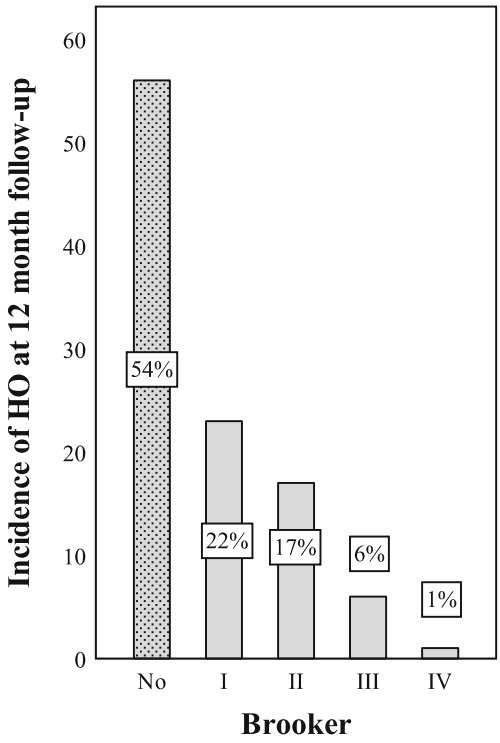

Fig. 2 Bar chart of the post-operative appearance of HO. 46% of our patients showed heterotopic ossifications after THA. The majority was classified as Brooker 1 (22%) and Brooker 2 (17%)

Fibro-ostotic alterations at the ischial hamstring tendon insertion could be detected in all 103 patients on magnified radiographs. The mean vertical length was 2.6 mm (0.3–6.6 mm), the mean horizontal length was 43.1 mm (15.8–108.9 mm), the mean horizontal ratio was 32.6% (12.6–79.4%), and the mean FO area was 74.2 mm^2 (10.5–278.3 mm^2). Details and the distribution of FO in the study cohort are presented in Table 2. The mean vertical length of FO in patients with HO was 3.0 mm (1.0–6.6 mm, SD = 1.15) and the mean vertical length in patients without HO was 2.3 mm (0.3–5.3 mm, SD = 0.97). This difference was statistically significant ($p = 0.001$). Similarly, the mean horizontal length of FO in patients with HO was 47.9 mm (15.8–108.9 mm, SD = 21.86) and in patients without HO 39.1 mm (16.8–94.2 mm, SD = 17.52). This difference was statistically significant ($p = 0.025$). The mean horizontal ratio in patients with HO (36.0%, 12.6–79.4%, SD = 15.38) was significantly higher than in patients without HO (29.8%, 13.4–55.6%, SD = 11.90, $p = 0.024$). The FO area between patients with HO (mean = 82.9 mm^2, 14.0–205.1 mm^2, SD = 50.31) and without HO (mean = 67.0 mm^2, 10.5–278.30 mm^2, SD = 52.38) showed no significant difference ($p = 0.121$).

Mean values, minimum, maximum, and standard deviation of FO parameters in relation to Brooker grade are presented in Table 3.

A weak correlation between the vertical dimension ($r = 0.260$, $p = 0.008$), horizontal dimension ($r = 0.205$, $p = 0.037$), and horizontal ratio ($r = 0.195$, $p = 0.048$) of FO and the severity of HO could be detected. No significant correlation between the area of FO and Brooker Grade was observed ($r = 0.187$, $p = 0.058$) (Fig. 3).

In the performed subanalysis, 49 patients demonstrated a vertical length of FO < 2.5 mm. In this group, 17 patients developed a HO and 32 did not. Fifty-four patients had a vertical length of fibro-ostosis ≥ 2.5 mm. In this group, 30 patients developed an HO and 24 did not. There was a statistically significant difference between these two groups (OR = 2.35, $p = 0.047$). We could not detect any association of post-operative HO and gender ($p = 0.108$), the surgical duration ($p = 0.182$), or the patient age ($p = 0.482$). Measurement reliability analysis demonstrated a good to excellent agreement for both inter- and intra-observer measurements (ICCs range 0.64–0.99).

Discussion

Heterotopic ossification is a common radiographic finding after THA [5] and remains asymptomatic in the majority of patients. However, excessive HO is associated with compromised functional outcome and may lead to worse post-operative pain [9, 23]. Several risk factors for HO following THA have been previously described. These factors can be subdivided into two main groups. The modifiable risk factors include the surgical approach, the amount of exposure, soft

Table 2 Distribution of FO in the study cohort

Radiographic parameter	Mean (range)	Minor	Intermediate	Major
Vertical length	2.6 mm (0.3–6.6 mm)	< 2.5 mm $n = 49$	2.5–5 mm $n = 52$	> 5 mm $n = 2$
Horizontal length	43.1 mm (15.8–108.9 mm)	< 30 mm $n = 32$	30–60 mm $n = 53$	> 60 mm $n = 18$
Horizontal ratio	32.6% (12.6–79.4%)	< 30% $n = 53$	30–50% $n = 35$	> 50% $n = 15$
FO area	74.2 mm^2 (10.5–278.3 mm^2)	< 50 mm^2 $n = 43$	50–150 mm^2 $n = 48$	> 150 mm^2 $n = 12$

Table 3 Distribution of FO [mean(min–max;SD)] in relation to Brooker Grades

Radiographic parameter	No HO $n = 56$	Brooker I $n = 23$	Brooker II $n = 17$	Brooker III $n = 6$	Brooker IV $n = 1$
Vertical length [mm]	2.3 (0.3–5.3;0.97)	3.0 (1.0–4.9;1.12)	3.1 (1.7–4.5;0.92)	2.8 (1.5–6.6;1.93)	2.3
Horizontal length [mm]	39.1 (16.8–94.2;17.52)	48.3 (16.4–85.5;21.03)	46.4 (15.8–108.9;24.27)	43.5 (28.7–54.9;12.29)	91.6
Horizontal ratio [%]	29.8 (13.4–55.6;11.90)	35.2 (12.6–61.2;13.63)	35.9 (13.6–79.5;17.83)	33.6 (22.3–43.0;8.96)	71.5
FO area [mm^2]	66.98 (10.5–278.3;52.38)	87.7 (28.5–205.1;54.10)	74.1 (14.0–185.0;44.52)	75.6 (30.3–138.2;47.98)	164.3

tissue damage and bony preparation, cemented fixation, and remaining bone particles [13]. The nonmodifiable risk factors are the development of HO after contralateral THA, previous ipsilateral hip surgery, hypertrophic osteoarthritis, male gender, diffuse idiopathic skeletal hyperostosis, ankylosing spondylitis, and African American ethnicity [11, 12, 24].

The present study identified fibroostotic (FO) alterations of the os ischium as a novel risk factor for the occurrence of HO following THA that has previously not been described. The presented data demonstrate that both the vertical and horizontal extent of FO of the ischial hamstring tendon origin is associated with HO development. The incidence for developing HO after THA in patients with a vertical length of FO ≥ 2.5 mm (55.6%) was significantly higher ($p = 0.047$) than in patients with FO < 2.5 mm (34.7%). There was a weak but statistically significant correlation between both vertical and horizontal dimensions of FO and the severity of HO.

Potential limitations of the present study have to be addressed. Because of the strict inclusion criteria, our findings are limited to patients with primary OA and cannot be applied to all indications for THA. The retrospective study design and potential measurement errors as a result of pelvic tilt and rotation have to be considered. Furthermore, measurements were taken on plain radiographs and no three-dimensional reconstructions were available. However, the present study aimed to strictly exclude all local and systemic patient-related confounding factors by the described exclusion criteria. Furthermore, strict quality criteria for radiographs were applied to reduce positioning-related measurement inaccuracies.

All patients received prophylactic NSAIDs and there was a limited number of patients with severe HO (Brooker III and IV) in the study cohort which may have led to an underpowered correlation analysis. As a result of the rather weak

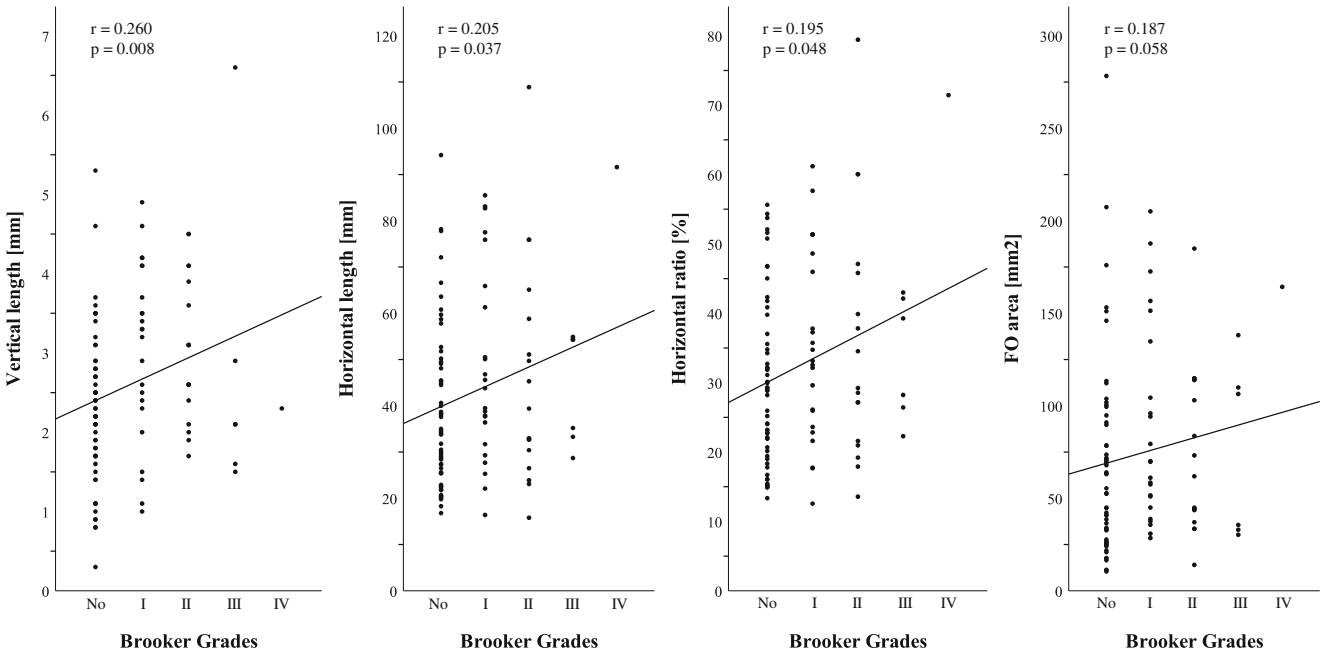

Fig. 3 Scatterplots showing the FO dimensions (vertical, horizontal, horizontal ratio and area) in relation to Brooker Grades. A weak correlation between the vertical dimension ($r = 0.260$, $p = 0.008$), horizontal dimension ($r = 0.205$, $p = 0.037$), and horizontal ratio ($r = 0.195$, $p = 0.048$) of FO and the severity of HO could be detected

correlation between the vertical and horizontal dimensions of FO and the severity of HO, additional prophylactic treatment (i.e., preoperative radiation) cannot be routinely recommended based on the present findings. Similarly, the present cohort is rather small to allow for a comparison of clinical follow-up data and radiographic findings so that further studies are necessary to confirm the hypothesis of this investigation.

There is no uniform strategy for the clinical prophylaxis of HO following THA. Evidence-based guidelines do not exist [25]. To reduce the incidence of HO after THA, prophylactic therapies based on personalized risk factors were established in the last decades [7]. The post-operative administration of NSAIDs (non-steroidal anti-inflammatory drugs) is generally accepted. NSAIDs reduce the production of prostaglandin, especially prostaglandin-E2, which seems to be a relevant systemic factor to enhance the formation of HO [13]. The most reported NSAID is indometacin, followed by ibuprofen, diclofenac, or meloxicam [26, 27]. The post-operative administration of NSAIDs is routinely recommended for all patients without contraindications by the majority of surgeons [25].

A recent meta-analysis has confirmed various previous studies and shown that NSAIDs significantly reduce the incidence of HO following THA [28]. Whereas, selective NSAIDs decrease gastrointestinal side effects compared to non-selective NSAIDs, no significant difference was detected with respect to the prevention of post-operative HO. Interestingly, a high rate of discontinuation due to gastrointestinal and non-gastrointestinal side effects has been reported which may compromise the desired prevention [28].

On the other hand, in the presence of additional risk factors or contraindications for NSAIDs, pre-operative or post-operative radiation has been reported as a viable option for prevention of HO [29]. The treatment is usually done with a single dose of 7–8 Gy 4–24 h before the THA or in the first 72 h after the operation [30]. Performing the radiation pre-operatively or post-operatively did not seem to make a difference and depends on the clinical infrastructure and preference of the surgeon and radiotherapists [10].

The findings of the present study suggest that fibro-ostotic alterations of the os ischium should be identified preoperatively at the time of indication for THA. FO seems to be an additional risk factor which may be speculatively be explained in the context of activated bone metabolism as described for known risk factors such as hypertrophic osteoarthritis, diffuse idiopathic skeletal hyperostosis (DISH), or ankylosing spondylitis [11, 12]. In conclusion, the radiographic occurrence of asymptomatic FO at the ischial hamstring tendon insertion is a potential risk factor for the development of HO after THA and may be used as a simple diagnostic tool to pre-operatively identify patients at risk for post-operative HO. This association has not been previously described and further research to confirm these findings and to justify additional prophylactic treatment in these patients is warranted.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

All study procedures involving human participants were in accordance with the ethical standards of the institutional research committee of the University of Heidelberg and with the 1964 Helsinki declaration and its later amendments or comparable ethical standard.

Informed consent Informed consent was obtained from all individual participants included in the study.

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