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Heterotopic ossification after total hip arthroplasty: a narrative review of modifiable risk factors

Pietro Spolettini[1,2], Jacopo Ambrosini[1,2], Nicholas Elena[1,2], Carlo Ambrosini[1], Stefano Giaretta[1]

[1] *Orthopaedics and Traumatology Unit, San Bortolo Hospital, Vicenza, Italy;*
[2] *Department of Orthopaedics and Trauma Surgery, University of Verona, Verona, Italy*

Summary

Total hip arthroplasty is a popular procedure for treatment of fractures and degenerative diseases of the hip. It is a highly successful procedure with high satisfaction of patients, although the success rate can be limited by the development of heterotopic ossification around the hip. This narrative review aims to analyse the peri-operative modifiable risk factors for heterotopic ossification formation to help especially young surgeons choose the correct way to prevent this problematic complication. The search was conducted on PubMed and the final set includes 32 articles. Results are grouped in five paragraphs: non-steroidal anti-inflammatory drugs and radiation therapy, surgical approach, surgical time and use of drainage and type of implant. In light of this narrative review, we suggest the systematic use of NSAIDs as preventive therapy, adoption of minimally invasive surgical approaches aiming to reduce both surgical time and soft tissue damage and discourage the use of drainage and short stems in total hip arthroplasty.

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Correspondence
Pietro Spolettini
Orthopaedics and Traumatology Unit, San Bortolo Hospital, viale Ferdinando Rodolfi 37, 36100 Vicenza, Italy. E-mail: pietro.spolettini@aulss8veneto.it

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Introduction

Total hip arthroplasty (THA) is one of the most successful procedures in orthopaedic surgery and has been described as the operation of the century [1]. However, heterotopic ossification (HO), or the formation of lamellar bone within extra skeletal soft tissues, is still a relatively common complication related to the procedure that may compromise its success and usually appears from 3 to 12 weeks after the procedure [2]. The incidence of HO after THA varies from 8 to 90% in literature [3], but a recent meta-analysis [4] reported an average incidence of 30% and that age at the time of surgery is not a significant risk factor for HO development.

The underlying mechanism of HO formation remains uncertain, although the role of cytokines in traumatised tissues is well known [5] and therefore the use of non-steroidal anti-inflammatory drugs (NSAIDs) is the logical consequence of this evidence. Various risk factors have been studied and a recent meta-analysis identified male gender, cemented implant, bilateral operations, ankylosing spondylitis and ankylosed hip as significant risk factors, while rheumatoid arthritis was protective for HO [4].

The most accepted and used classification for HO around the hip is the Brooker classification [6], which divides HO in four stages, from the presence of isolated bone fragments within periarticular soft tissue (grade I) to ossification with apparent ankylosis of the hip (grade IV). However, given the fact that this classi-

fication is based on plain antero-posterior radiographs of the pelvis, it may underestimate or over-estimate the actual extension of HO, thus some authors suggest the use of different X-ray projections or CT scan to reduce ambiguities [7]. In 2017 DeBaun et al. [8] developed an anatomical classification of HO based on CT scans with a 3D reconstruction to accurately localize HO and plan the surgical approach for excision. They divide HO in three types: anteriorly-based (type I), best excised through anterior approach, posteriorly-based (type II), best excised through posterior approach, medially-based (type III), best excised through medial approach. The development of HO has a relevant impact on patient satisfaction after THA. In particular, the development of Brooker grade I and II HO does not affect the clinical outcome after THA, while reduction of the range of motion (ROM) does not improve in the post-operative period when Brooker grade III and IV HO are found [9]. Given the invalidating symptoms related to this finding, especially local pain and joint immobility, it is important to appropriately treat patients in order to reduce the incidence of this complication.

Materials and methods

This narrative review is intended to discuss the relevant literature that has studied the risk factors related to HO formation after total hip arthroplasty. The search for publications was carried out on PubMed and narrowed to articles between 2006 and 2023. The search terms were "total hip arthroplasty heterotopic ossification", "heterotopic ossification NSAIDs", "heterotopic ossification radiation therapy", "heterotopic ossification surgical drainage", and "heterotopic ossification surgical approach". A total of 1780 publications were retrieved. After applying inclusion criteria, which were the full text availability, article written in English, topic on total hip replacement, and after reading the abstract, 32 articles were included in the review.

Results

Nonsteroidal anti-inflammatory drugs and radiation therapy

In order to prevent the development of HO various nonsteroidal anti-inflammatory drugs (NSAIDs) have been studied, especially indomethacin and COX-2 inhibitors such as etoricoxib and celecoxib. Indomethacin has been for a long time the gold standard preventive therapy for HO, but its side effects and the length of treatment led to the study of new treatment protocols. At the beginning, the treatment protocol with indomethacin lasted 6 weeks, but more recent evidence suggests that a treatment protocol with 75 mg divided in three doses daily for at least 7 days starting in the immediate post-operative period does not provide any additional risk to the patient [10]. However, given the side effects related to indomethacin, especially those involving the gastrointestinal system, selective COX-2 inhibitors have been studied as well. When compared to indomethacin, there is no significant difference in selective COX-2 inhibitors efficacy to prevent HO formation [11,12], but some authors found a difference in the rate of discontinuation due to side effects of indomethacin [13]. Recent data suggest the use of selective COX-2 inhibitors for prevention of HO after THA [14]. Moreover, recent studies took into consideration the use of aspirin, which might be an effective therapy in preventing both HO and venous thromboembolism in low-risk patients [15,16].

Radiation therapy has been studied for about 40 years to prevent HO formation. Given the lack of literature after 2006, we enlarged the search period to 1997 just for this topic of the review. Studies in the late 90's showed efficacy of both pre-operative and post-operative radiation therapy [17] but, given the logistic difficulties associated with early pre-operative radiation therapy within 4 hours prior to surgery, a protocol of radiation therapy performed the evening before surgery was studied in the early 2000's with demonstrated efficacy in preventing HO [18,19]. However, in the past years there has been concern regarding possible implant loosening and carcinogenesis linked to radiotherapy. A recent study with 10 years of follow-up suggests that radiation therapy is relatively safe in terms of carcinogenesis [20], even though some tumours may develop after a longer time and the lack of cases in patients who underwent radiation therapy for HO prophylaxis might be attributable to the relatively older age of patients [21]. Thus, more studies with younger patients are mandatory in order to assess the absolute safety of this treatment. Even though there is evidence of equal effectiveness between radiation therapy and NSAID treatment in preventing HO formation, there is a significant difference in cost effectiveness. In fact, radiation therapy is approximatively 45 times more expensive than NSAID therapy [22] and this is a variable that must be considered, especially in healthcare systems that rely on public resources.

According to our experience, our routine protocol consists in administration of indomethacin 75 mg twice a day for 15 days. However, for patients with a history of gastrointestinal disease, we consider the use of COX-2 inhibitors. In the future, the use of aspirin might be taken into consideration as it seems to be effective in preventing HO formation, VTE and reduces the risk of prosthetic joint infection [23].

Surgical approach

The influence of the surgical approach on HO development has been widely studied over the years. The most commonly performed surgical approach worldwide is the postero-lateral approach (PA). Compared with the direct lateral approach (DLA), THA performed with PA leads to less HO formation [24]. Moreover, the posterior approach performed with mini-incision has shown efficacy in reducing HO formation even more, and incisions wider than 10 cm were associated with higher risk

of HO formation [25]. The difference in HO formation between direct anterior approach (DAA) and PA is still unclear, since some authors found differences between the two approaches [26] with others finding no difference [27,28].

In 2017, Hurlimann et al. [29] compared four different surgical approaches for THA (Watson-Jones, Bauer, minimally invasive direct anterior approach and minimally invasive antero-lateral approach). The Watson-Jones approach was associated with a higher rate of HO formation, while lower complication rates were seen after minimally invasive surgery (MIS). The direct anterior approach, avoiding detachment of hip abductors and short rotators of the hip, is supposed to be the less invasive surgical approach, and literature shows its superiority compared to DLA [30,31]. However, some authors found no significant difference in HO formation between DAA and DLA[32].

Hartford and Bellino [33] suggested that the complication rate, including HO formation, decreases with the surgeon's experience and with pulsatile irrigation after the preparation of the acetabulum and the femur with 3 L of normal saline irrigation for each site. This finding is consistent with another study of Kantak et al. [34] that found a significant difference in the incidence and severity of HO between the control group that received < 1000 ml intra-operative lavage and the index group that received > 3000 ml intra-operative lavage. We strongly believe that the surgical approach plays the most important role as an intra-operative risk factor for HO formation. Therefore, we choose the direct anterior approach as the routine approach for hip arthroplasty and hemiarthroplasty along with the use of a soft tissue protector to minimize soft tissue trauma and bone debris spreading during surgery. If for any reason the direct anterior approach cannot be performed, such as in obese patients, we recommend the choice of minimally invasive approaches whenever possible. Despite the surgical approach, we recommend pulsatile irrigation with more than 3000 ml of saline solution after preparation of the femur and acetabulum to remove as much bone debris as possible.

Surgical time

Another risk factor that has been considered in recent years is surgical time, since long-lasting surgery might be linked with more complex surgery and wider surgical approach resulting in greater soft tissue trauma. To the best of our knowledge, we found only two studies focused on surgical time: Aprato et al. [35] analysed 1225 THA and found that surgery lasting more than 90 minutes is linked with higher risk of developing HO, while Edwards et al. [25] found a significant correlation between surgery lasting more than 60 minutes and higher grades of HO. These findings suggest the need to create teams of surgeons and operating theatre nurses who regularly perform total hip arthroplasties together to standardise the procedure as much as possible to reduce surgical time.

Use of drainage

The use of intra-articular drainage varies from surgeon to surgeon, and there's very little literature regarding its relationship with HO. Despite the shortage of studies, there is consensus in considering the use of intra-articular drainage as an intra-operative risk factor for development of HO after total hip arthroplasty [36,37]. We do not recommend the use of drainage in total hip arthroplasty performed with a direct anterior approach since it is a minimally-invasive approach. Instead, we suggest taking extra care in performing thorough haemostasis and to pay attention in not damaging the tensor fasciae latae during acetabular and femoral preparation to reduce blood loss as much as possible and the formation of haematomas in deep soft tissues originating from the muscles.

Type of implant

The choice of the implant varies among surgeons depending both on their experience and bone quality of the patient. The difference between cemented and uncemented implants has been studied. Pavlou et al. [38] suggested that the reaming of the femoral canal to introduce cemented implants might spread bone debris in the surgical field that could act as a source of osteoprogenitor cells and increase the risk of HO, while impaction broaching used in uncemented implants minimises this event. Another study published in 2011 [39] found that uncemented implants are not related to higher risk of HO, while a meta-analysis published in 2015 found cemented implants to be a risk factor for HO formation as well [4].

In 2017, Kutzner et al. [40] studied the relationship between short stems and HO and suggested that the use of short stems might reduce the risk of HO formation thanks to the different surgical technique required to implant those stems. Thanks to the round-the-corner technique, the use of short stems is particularly suitable for minimall- invasive surgery (in reducing both soft tissue trauma and the spread of bone debris in the surgical field. However, given that the use of short stems is relatively recent, studies with long-term follow up are not available and the use of these stems seems to be related to a higher risk of periprosthetic fractures [41], we do not recommend the use of short stems as a routine choice. Moreover, the risk of HO formation should not influence the surgeon's choice regarding the type of implant to use.

The main limitation of this study is represented by the fact that this was a narrative review and therefore it was not a rigorous systematic review; however, the literature reported was carefully evaluated by expert hip surgeons and we believe that this summary might represent a useful tool for young surgeons in daily practice to achieve the best treatment for their patients. We believe that by applying the precautions reported herein we might be able to significantly reduce the incidence of HO in patients who undergo hip surgery.

Conclusions

Given the available literature and our experience, we suggest the use of minimally-invasive surgical approaches whenever possible and to use the same surgical approach in most cases to accelerate the learning curve leading to shorter surgical times and less blood loss. We discourage the routine use of surgical drainage since the risk of blood loss is very low in minimally-invasive surgery and the use of drainage increases the risk of HO formation. Moreover, we encourage the prevention of HO using NSAIDs in the post-operative period rather than radiation therapy as it is easier to carry out and more cost effective.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

PS, SG: conceptualisation and methodology; PS, NE, JA, CA: investigation and data curation; PS, JA: writing - original draft preparation; SG, NE, CA: writing - review and editing; SG: supervision. All authors have read and agreed to the published version of the manuscript.

Ethical consideration

Not applicable.

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