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Extensive Surgical Wound Lavage Reduces the Incidence and Severity of Heterotopic Ossification in Primary Total Hip Replacement: A Study of 175 Hip Replacements

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Purpose: One of the local factors contributing to the formation of heterotopic ossification includes bone debris generated during the surgery. This risk can be partially nullified by use of saline wash. Our research aim was to ascertain if extensive intraoperative lavage can reduce the incidence and severity of heterotopic ossification in primary total hip arthroplasty.

Materials and Methods: A retrospective case control radiological study of 145 patients (175 hip replacements). The control group received minimal intra-operative lavage (<1,000 mL); consisted of 90 primary hip replacements. The index group received extensive saline lavage (>3,000 mL), and included 85 primary hip replacements. Brooker classification was used to grade radiographs at one year for development of heterotopic ossification.

Results: Sixty-six patients in control group had heterotopic ossification, with six showing a significant grade (grade 3 or 4). Thirty-five patients in the index group had heterotopic ossification with no incidence of severe grade. Majority patients in the index group showed a predominantly grade 1 heterotopic ossification; 28 out of 35, as compared to 37 out of 66 in control group. There was a statistically significant difference in the incidence (P<0.05) as well as severity of heterotopic ossification between the groups (P<0.05).

Conclusion: We conclude that use of extensive lavage during total hip replacement reduces the incidence as well as severity of heterotopic ossification.

Key Words: Heterotopic, Ossification, Therapeutic irrigation, Total hip replacement, Prevention and control

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INTRODUCTION

Heterotopic ossification (HO) is ectopic bone formation out of skeletal tissue. It is usually periarticular in nature. First described in 1883 by Reidel, HO is a common complication of total hip replacement (THR)[1,2]. The incidence of HO depends on numerous factors. It has been associated with an increased prevalence after THR in male gender, hypertrophic osteoarthritis, ankylosing spondylitis, previous history of HO, and revision THR. Previous reports have documented a wide variation in the incidence of HO after THR, ranging from 8% to 90%[2,3].

THR is an effective treatment for severe pain and handicap induced by hip joint disease[4]. HO might induce a reduced range of hip motion and severe pain[3,5]. It can affect the outcome of an otherwise successful hip replacement. Therefore, decreasing the occurrence of HO for patients undergoing THR is quite important.

The etiology of HO is multifactorial and as yet only partially understood. But it is widely accepted that the ectopic bone formation is due to the deposition of bone morphogenic protein in the viable muscle tissue[6]. This is usually a direct result of muscular trauma and inadvertent but iatrogenic implantation of bone debris[7]. We postulate that this bone debris implantation can be minimized by a thorough and methodical intraoperative wound lavage.

Our aim was to identify if extensive lavage offers any protection against development of HO. Our primary hypothesis was intraoperative washout reduces the incidence of HO in primary THR. Our secondary hypothesis was that washout also reduces the severity of HO in hip replacements. The study was designed to provide evidence to a simple but effective prophylactic measure against HO.

MATERIALS AND METHODS

A retrospective case control study model was planned to identify the effect of extensive intraoperative saline lavage on formation of HO. Electronic database at our hospital was used to recruit patients in this radiological study. Patients were operated by two high-volume, fellowship trained surgeons. Both had an identical surgical technique utilizing the modified Hardinge approach with patient in lateral position. The THR implants used by both surgeons were Furlong uncemented stem for the femur and uncemented CSF socket for the acetabulum (JRI Orthopaedics, Sheffield, United Kingdom). The bearing was ceramic on polyethylene in all patients. The only difference in surgical technique was the amount of saline used during surgery. One of the surgeons, either did not use any saline wash or used less than 1,000 mL (control group), whilst the other used more than 3,000 mL of saline (index group).

Sample size calculation was done with power set at 80% and a type I error (α error) of 0.05. The sample size was estimated on the basis of the incidence of HO observed in a pilot study; 50% in the control group and 30% in the index group. The sufficient sample size was 184, i.e. 92 in each group. We identified 100 consecutive hip replacements performed by each of the 2 surgeons and assessed them for radiographic evidence of HO at one year. Patient notes, clinical data and radiographs of the 200 identified patients were studied independently by each author. We excluded patients with diagnosis of hypertrophic arthritis, post traumatic arthritis, autoimmune arthritis, heterotopic bone formation at other sites, ankylosing spondylitis and revision surgery, since these have high risk of HO. The exclusion was applied after review of patient notes, clinic letters and radiographs. If patients had any of the above diagnosis either in the past or when pre-operative radiographs were reviewed for inclusion in the study, they were excluded from the study. After exclusion the patients fell into two groups; the control group included patients where less than 1,000 mL of saline wash was used and the index group included patients who received more than 3,000 mL of intraoperative saline lavage. A battery operated pulse lavage was used in both the groups. The Stryker® InterPulse (Stryker, Kalamazoo, MI, USA) system was utilized on a high pressure setting. The approximate pressure generated was 15 psi. The lavage

Table 1. Brooker Classification[1]

Grade	Description
0	No evidence of heterotopic ossification
Grade 1	Islands of bone within soft tissue around hip
Grade 2	Bone spurs from the pelvis or femur with >1 cm between opposing end
Grade 3	Bone spurs with reduced space between the opposing bone surface of <1 cm
Grade 4	Ankylosis of hip

was done sequentially after the surgical steps of implantation of acetabular socket, implantation of femoral component, reduction of the THR and closure of the hip respectively.

Ninety THRs in control group with 78 patients (52 women, 26 men) and 85 THRs in the index group with 67 patients (46 women, 21 men) were available for review. The average age of patients in the control group was 72.05 years (range, 41-94 years). The average age of patients in the index group was 65.19 years (range, 34-94 years). Both groups were matched for age, gender, etiology, surgical approach and type of prosthesis. Being a retrospective case control study, no randomization could be done. The radiographs were assessed by both authors. Post-operative radiographs and one year radiographs were studied for HO. HO was graded according to the Brooker classification[1] (Table 1) by both authors, and had a good inter observer and intra observer reliability.

Data was checked for normality. The data was analyzed with Statistical Package for the Social Sciences (ver. 17.0; SPSS Inc., Chicago, IL, USA). Fisher exact test and chi-square test was used for categorical variables. Mann-Whitney *U* test was used for ordinal data (Brooker grading)[1]. Interrater agreement for Brooker grading was estimated by Cohen's κ statistic. A *P*-value ≤ 0.05 was considered significant. Since the number of patients needed to provide an adequate power fell short (175 instead of 184), we analyzed the *post hoc* power of our study, with a dichotomous end point in two independent study samples, and found the power to be sufficient (99%). Approval for this study was obtained from the local audit and research department of Western Sussex Hospitals Foundation NHS Trust. Formal ethical approval was not deemed necessary by the local authority as it was a retrospective radiological study.

RESULTS

One hundred forty-five patients with 175 hip replacements were available for radiological review (Table 2). In the control group, we observed 66 patients (73.3%) had signs of HO. Of these, six (6.6%) had grade 3, 37 (41.1%) had grade 1 and 23 (25.5%) had grade 2 HO. In the index group, only thirty-five (41.1%) patients had HO with no cases of grade 3 HO. Twenty eight (32.9%) showed a grade 1 and 7 (8.2%) developed grade 2. In our series, we had no incidence of grade 4 HO (bony ankylosis). There were no cases of revision surgery for any indication. There were 3 cases of superficial wound infection, 2 in the control and 1 in the index group, which settled with antibiotic

Table 2. Patient Demographics

Demographic	Control group	Index group	*P*-value
Hip replacement (n)	78 (90 hips)	67 (85 hips)	
Sex			
Males	26 (28 hips)	21 (27 hips)	>0.9
Females	52 (62 hips)	46 (58 hips)	>0.9
Age (yr)	72.05 (41-94)	65.19 (34-94)	
	Variance 87.3	Variance 181.6	
	SD 9.3	SD 13.1	
Diagnosis			
Primary osteoarthritis	75	66	>0.8
Post traumatic	8	11	>0.5
Secondary osteoarthritis*	7	8	>0.9
HO (presence)	66	35	<0.05
Grade of HO	37	28	<0.05
1			
2	23	7	<0.05
3	6	0	<0.05
4	0	0	
HO†			
In males	22 (28 hips)	18 (27 hips)	
In females	42 (62 hips)	17 (58 hips)	

SD: standard deviation, HO: Heterotopic ossification.
* Dysplastic hip, slipped capital physis perthes, † *P*=0.103 in control group and *P*<0.05 in index group for male:female proportions.

treatment. No patient had a significant functional deterioration warranting excision of HO in this study.

We identified a statistically significant difference (P<0.05) in the incidence of heterotopic ossification between the two groups. Extensive lavage did offer a significant protection against heterotopic ossification. We also conclude that the severity of heterotopic ossification is significantly reduced (P<0.05) in the lavage group.

DISCUSSION

Heterotopic ossification is not the most troublesome complication of hip arthroplasty, but it has the ability to cause some functional impairment. Higher grades are associated with worse outcomes[8]. In our patient population we identified quite an increased incidence of HO (73 and 41% respectively). We are unclear about the reasons for this increased incidence, but the reported incidence in literature is quite varied. One of the reasons for this increased incidence can be due to the muscle cutting direct lateral approach utilized in our series. But with extensive lavage the risk of developing a severe grade of HO is substantially reduced. There was improvement noted in both the incidence and severity of HO. We also observed that, in the control group, women were as likely to develop HO as men. This was an observation contrary to previous studies, where men had significantly higher risk of HO. In the control group, 42 (67.7%) women and 22 (78.5%) men developed HO whereas in the index group 17 (29.3%) women and 18 (66.6%) men developed HO.

There has been inconsistent evidence regarding correlation of the Brooker's classification with the clinical outcome. Based on a study by Brooker et al.[1], only grade IV HO was found to influence the functional outcome, whereas other studies have suggested that, other than the limitation in the range of motion, HO did not significantly influence the outcome of hip replacement[8,9]. However, a more recent study demonstrated that all grades of HO consistently correlated with limitation in the range of motion but the correlation with walking capacity, limp, use of analgesics, and most importantly satisfaction was observed only for higher-grade HO[10].

The pathophysiology is still unclear[11,12], but according to basic science literature, HO may actually start within sixteen hours of the surgical procedure. Once the osteoblastic materials are laid down, it then becomes osteoid and subsequently indistinguishable bone. The pathogenesis of HO requires three requisite components[11]. These include an inductive singling pathway, inducible osteoprogenitor cells, and a heterotopic environment that is conducive to osteogenesis[13]. This process involves an inflammatory stimulus that induces cyclooxygenase-2 (COX-2) to produce proinflammatory prostaglandins[13]. It has also been shown that hypoxia-associated oxidative stress initiates fibroblastic metaplasia to produce fibrocartilage, followed by HO[14]. Patients developing HO have elevated expression of fibroblast growth factor, transforming growth factor beta[13], the osteoclast marker C-telopeptide of type-I collagen, the osteoblast marker N-terminal propeptide of type-I procollagen, and osteocalcin[14]. The study of several genetic diseases associated with abnormal bone formation has led to the discovery of several genes that are believed to be responsible for the development of HO[12]. An ectopic skeleton is known to develop because of genetic dysregulation of bone morphogenic protein[14]. This complex interplay of inflammatory prostaglandins, growth factors, gene expression, and rich vascularity initiates the perpetual development of HO[14].

Clinically this translates into a higher risk of HO when there is presence of soft tissue trauma and necrotic tissue. Anthonissen et al.[7] were able to demonstrate the important role of muscle trauma in the development of HO after hip surgery in rat model. They concluded that prudent surgery to minimise the muscular trauma could probably minimise the severe complication of HO after hip and acetabular surgery. The amount of soft tissue trauma and necrosis seems to be an important local factor determining the development of HO. Difficult operations and surgical approaches involving division of the tendon-periosteum complex from the greater trochanter or excessive muscle retraction causing ischemia have been reported to produce a higher rate of HO[15,16]. Debridement of the necrotic gluteus minimus has been found to reduce the incidence of severe HO in acetabular surgery[17]. Rama et al.[18] showed an increased incidence of HO, including Brooker grades III and IV, in patients receiving surface replacement arthroplasty compared to those having a hip replacement. Compared to conventional hip arthroplasty, resurfacing arthroplasty needs a more extensive surgical approach to expose the femoral head and to keep it out of the way for acetabular exposure. In addition, blunt damage to the gluteal muscles by surgical instruments may also occur during the procedure. Using the posterior approach, forceful anterior translation of the femoral head during acetabular preparation can injure the gluteal muscles and rectus femoris. Such increased soft tissue trauma may be a cause of severe grade of HO[18]. Fransen et al.[19] noted the increased risk for development of HO among patients undergoing revision hip replacement, those with excessive

surgical bleeding, patients receiving a transfusion of red cells. Edwards et al.[20] observed a significantly reduced risk of HO in minimally invasive posterior approach for hip replacements. This is a further testimony to the fact that minimal soft tissue damage reduces risk of HO.

The option of effective prophylaxis does exist but is fraught with complications. Irradiation after surgery could decrease the incidence of HO[21]. However, high costs and the risk of soft tissue sarcoma inhibit the use of irradiation. Increased trials have demonstrated that nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for the prevention of HO[22-24]. Therefore, NSAIDs have been widely used for the prophylaxis of HO. However, the risk of gastrointestinal side effects caused by NSAIDs is a significant worry. Adverse reactions associated with bleeding are also common among users of these agents[22,24]. This may increase the risk of treatment discontinuation and could interfere with thromboprophylaxis after hip replacement. In a study comparing celecoxib vs. indomethacin for the prevention of HO[23], the authors reported that a significantly greater number of patients in the indomethacin group had to discontinue treatment as a result of the excessive bleeding and gastrointestinal side effects. On the other hand, COX-2 inhibitors have been related with increased cardiovascular risk[25].

A non-invasive form of prophylaxis for HO is much needed in hip surgery. A prophylactic therapy which does not have significant side effects can prove invaluable. A thorough washout of bone debris could be the answer. Our study demonstrates a safe and effective way to control HO. The group with extensive lavage showed a significant reduction in HO, providing credibility to the long accepted view of utility of washout in this consequence of hip replacement. There are some concerns about the high pressure pulse lavage causing deeper penetration of the debris. But we believe that if the lavage is done in a sequential manner, the debris are washed away as they are generated hence minimizing the risk of dissemination. There are only a handful of studies in literature which report the relation between formation of HO and use of pulsed lavage[26,27]. Sneath et al.[26] have shown no difference in incidence of HO in their patient groups, in a randomized trial, despite use of pulsed lavage. But on the contrary, another prospective case control study by Mellema et al.[27] has suggested a significant reduction in the incidence of severe grade HO with use of pulsed lavage. Unlike in our study they did not notice any improvement in the overall incidence between the groups (51% and 58%) but did notice a significant improvement in the severe grades (3% and 17%).

We do recognize that our study has limitations. First, this is a retrospective study with the potential for inherent recall bias. Second, the study involved radiological review with no clinical outcome assessment. Therefore, our conclusions are limited to radiographic analysis and we are unable to comment on the effect of our intervention on clinical outcomes. But our study was not designed to compare clinical outcomes. Third, the comparison was between two patient groups who were operated by two different surgeons hence the risk of selection bias. The study would have had better external validity if we had recruited patients from several surgeons in each group, or if single surgeon operated on both patient groups. But since both surgeons had completed the same higher fellowship training and utilized an identical surgical technique we feel the bias was minimized.

CONCLUSION

Although there is no doubt that patient factors play an important role in causation of HO, the incidence of HO can be affected by local factors. Bone debris and soft tissue trauma are local factors which can be under a surgeon's control. A thorough washout of the wound during surgery will clear out the bone debris as they accumulate. More randomized prospective studies to compare the effect of no lavage, syringe lavage and pulsed lavage will further clarify the conundrum and we sincerely feel these would prove to be invaluable research projects. Nevertheless, we are able to demonstrate that with this simple intervention, the risk of HO in THR can be significantly reduced. The washout during surgery has no harmful effects and can even help in minimizing risk of bacterial contamination. This is a technique which can be applied universally by any surgeon irrespective of the approach used. We thus recommend use of extensive saline wound lavage to be included in the surgical protocol for all hip replacements.

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CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest relevant to this article.

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