

ECTOPIC OSSIFICATION FOLLOWING TOTAL HIP ARTHROPLASTY: IS DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS A RISK FACTOR?

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SUMMARY

Total hip arthroplasty may be followed by ectopic bone formation. An increased frequency has been suspected in patients with diffuse idiopathic skeletal hyperostosis (DISH). In 204 patients we found that, of the 38 subjects with pre-existing DISH, 29% developed postoperative ossification compared with only 10% in those without DISH ($p < 0.01$). DISH is therefore a risk factor for postoperative ectopic bone formation. In a separate study of 1325 patients (not analysed for spinal DISH), we looked for correlations between the severity of postoperative ectopic bone and clinical measurements. Even for the more severe ossification grades ($n = 112$), only 10% reported serious pain and only 26% had reduced hip flexion ($<70^\circ$). Thus, periprosthetic ectopic bone is not sufficiently important to justify the routine use of preventative drugs such as bisphosphonates in patients with DISH undergoing total hip replacement.

KEY WORDS: Ectopic bone, Hip arthroplasty, Diffuse idiopathic skeletal hyperostosis.

THE formation of periprosthetic ectopic calcification and ossification in the first months following total hip replacement arthroplasty is well known. (In this paper we will use only the term 'ossification'. Persistent calcification usually becomes trabecular with time.) Reports of its frequency vary. A notable degree of periarticular postoperative ossification was seen in 5% of Charnley's patients [1]. Others have reported frequencies of 8-90% [2-6].

No consensus is found in the literature about the clinical significance of this abnormality in terms of pain or reduced motion (ROM). However, symptoms seem to occur in 1-5%, especially loss of movement [7].

Predisposing factors which have been examined include operative technique, haemorrhage and infection [1, 8, 9]. DeLee *et al.* [3] stated that the degree of preoperative reduced ROM influenced the amount of postoperative ossification. Male sex, osteoarthritis, hyperglycaemia and obesity are other factors which have been incriminated [2, 10-12]. Several authors have suggested that DISH (formerly called Forestier's disease) might be a risk factor (Fig. 1) [2, 13-16], others have denied any influence of DISH [17].

The objective of this retrospective radiologi-

cal and clinical study was to elucidate two questions. First, do patients with pre-existing spinal hyperostosis develop ectopic bone more frequently around their hip arthroplasty than controls without DISH? Second, are such bone formations associated with serious pain or restricted hip function?

PATIENTS AND METHODS

There were two groups of patients:

Group 1 consisted of 204 consecutive patients with an original M.E. Müller straight-stem prosthesis, operated on in the years 1977/1978 (subgroup Ia, $n = 91$) and 1979/1980 (subgroup Ib, $n = 113$), respectively. They all underwent sur-

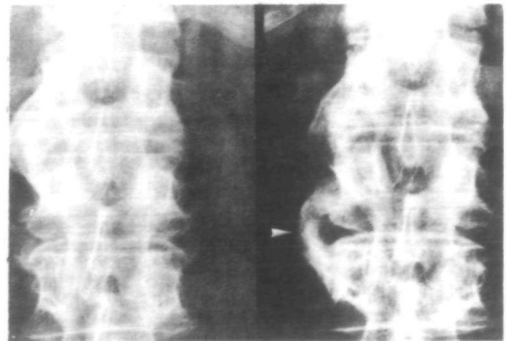


FIG. 1.—Typical flowing ossification in a 67-year-old male with DISH on the spine. Within 2 years (left to right), a new lateral bridge developed between L2 and L3.

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TABLE I
CLASSIFICATION FOR ECTOPIC PERIPROSTHETIC BONE
FORMATION*

Class I:	Islands of bone within the soft tissues about the hip.
Class II:	Bone spurs from the pelvis or proximal end of the femur, leaving at least 1 cm between opposing surfaces.
Class III:	Bone spurs from the pelvis or proximal end of the femur, reducing the space between opposing bone surfaces to less than 1 cm.
Class IV:	Apparent bone ankylosis of the hip.

* After Brooker *et al.* [4].

gery in the University Clinic for Orthopaedic Surgery in Bern. These patients were followed up after 5 years in 1983 and 1985, respectively. Of the 204 patients 117 were men with a mean age of 67 ± 8 (range 43–84) years at follow-up, and 87 were women, mean age 70 ± 10 (range 35–89).

Group II consisted of 1325 patients with a Müller prosthesis, operated on in different Swiss clinics for orthopaedic surgery and examined again after 1 year (mean age: men 64 ± 9 ; women 66 ± 11).

Radiological investigation

At the 5-year follow-up, all the patients of *group I* had an anteroposterior radiograph of the pelvis. In addition, patients in subgroup Ia ($n = 91$) had anteroposterior (AP) and lateral radiographs of the thoracic and/or lumbar spine. Those of subgroup Ib ($n = 113$) had AP and lateral radiographs of the chest and 49 had additional spinal views.

A rheumatologist (H.F.) and two orthopaedic surgeons (P.B. and P.E.) first examined all radiographs of the spine and chest of group I independently, looking for DISH. The criteria used were those of Resnick [18], and required flowing calcification and ossification along the anterolateral aspect of at least four contiguous vertebral bodies and absence of extensive 'degenerative' disc disease. Radiographs which did not completely fulfil these criteria were classified as 'probable DISH'. The individual assessments were compared and where discordant, the films were regraded by both observers together. The pelvic radiographs of group I were evaluated similarly for any ectopic bone formation about the prosthesis. Radiographs of spine and pelvis were not seen simultaneously, thus making the grading 'blind'.

The degree of ossification was defined according to the scale of Brooker (Table I) [4, 7]. This

refers to ossification situated between the greater trochanter and the upper border of the acetabulum, and was adequate since changes develop laterally in 94% [3] (Fig. 2).

All *group II*-patients had an AP radiograph of the pelvis 1 year after operation but views of the spine were not routinely obtained.

Clinical investigation

In group II, we graded patients' hip pain as none, slight, moderate or severe 1 year post-operatively and measured their maximal hip flexion as $>90^\circ$, $70-90^\circ$, $30-70^\circ$ or $<30^\circ$.

RESULTS

The radiological prevalence of DISH was 38/204 (19%) (Table II). In subgroup Ia the prevalence of DISH was 25%, higher than in the subgroup Ib (13%). In more than half of the patients in subgroup Ib the diagnosis of DISH had to be made from a chest radiograph. DISH was more frequent in men than in women.

Table III shows the frequency of the different degrees of postoperative ossification (0–IV). The main findings are illustrated in Fig. 3 and 74% of 38 DISH probands formed postoperative grade I–IV ossification, compared with only 58% of the 151 non-DISH probands. The difference was not significant ($\chi^2 = 2.65$, $p = 0.1$). When only the more severe grades III and IV were compared, there were 29% in the DISH-probands and 10% in non-DISH-probands ($\chi^2 = 7.72$, $p < 0.01$).

The correlations between postoperative ossification, pain and reduced ROM are shown for group II in Fig. 4. Of patients with no or

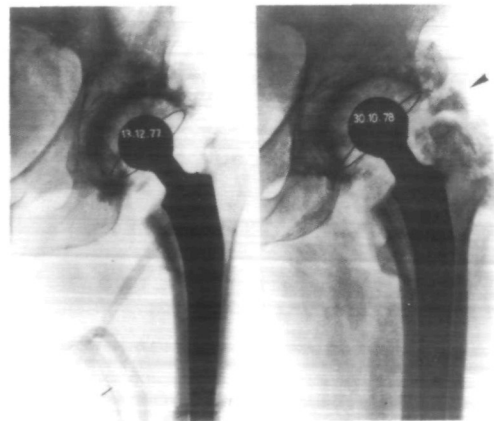


Fig. 2.—Formation of ectopic ossification (grade III–IV, after Brooker) following total hip arthroplasty.

TABLE II
PREVALENCE OF DISH (SUBGROUPS IA, IB, TOTAL GROUP I) IN 204 PATIENTS UNDERGOING TOTAL HIP ARTHROPLASTY

No. (%)	Group Ia	Group Ib	Total
Total	91 (100)	113 (100)	204 (100)
Men	51 (56)	70 (62)	121 (59)
DISH	23 (25)	15 (13)	38 (19)
Men	18 (78)	11 (73)	29 (76)
Non-DISH	61 (67)	90 (80)	151 (74)
DISH probable	7 (8)	8 (7)	15 (7)

TABLE III
FREQUENCY OF ECTOPIC BONE FORMATION FOLLOWING HIP ARTHROPLASTY IN PATIENTS WITH DISH AND WITHOUT DISH (CLASSIFICATION I-IV AFTER BRÖCKER)

Class	DISH no. (%)	Non-DISH no. (%)	DISH prob. no. (%)	Total no. (%)
0	10 (26)	64 (42)	3 (20)	77 (38)
I	13 (34)	52 (35)	7 (47)	72 (35)
II	4 (11)	20 (13)	0	24 (12)
III	6 (16)	11 (7)	5 (33)	22 (11)
IV	5 (13)	4 (3)	0	9 (4)
Total	38 (100)	151 (100)	15 (100)	204 (100)

slight ossifications (classes 0-II), 4% experienced moderate or severe pain. In patients with marked ossification (classes III-IV) the frequency was 10%. Postoperative flexion of less than 70° was found in 6% of grades 0-II and in 26% of grades III-IV. Both findings were statistically significant ($\chi^2 = 9.8$, $p < 0.01$; $\chi^2 = 54.19$, $p < 0.001$, respectively).

DISCUSSION

The prevalence of spinal DISH in 19% of our population agrees with previous published studies of similar ages [7, 11, 12], as does the greater prevalence of ossification in men [2, 3, 10, 11].

Severe postoperative ectopic bone formation around the hip arthroplasty was three times more frequent in those with spinal DISH. Irrespective of DISH, other authors have noted postoperative ossification in 10% of patients [3, 8].

This threefold increased frequency in DISH-probands supports the hypothesis that DISH predisposes to ectopic bone formation as part of a generalized 'ossifying diathesis'. Blasingame *et al.* [7] suggested a correlation between vertebral hyperostosis and ectopic bone formation based on a small series of patients. Jacqueline [16]

found ossification in 57 of 67 subjects with DISH, but in only 10 of 33 controls. The severity of these ossifications and the criteria used for the diagnosis of DISH were not given. Pilet *et al.* [11] in a similar study, used less rigorous criteria for DISH and found 22.4% postoperative ossification in subjects with DISH and 9.6% in controls (grades III-IV), and this is in accord with our results.

Our second question concerned the clinical significance of ectopic ossification. Others have suggested a relationship with pain or impaired hip function [6-8, 10, 19, 20] and Pilet *et al.* [11] found a favourable postoperative ROM in 66% of males with DISH compared with 83% in those without. They concluded that DISH does not contra-indicate total hip replacement.

Our results indicate that ectopic bone formation about the hip is associated less with pain than with functional impairment. We noted moderate and severe pain in our group II of 1325 arthroplasties and this was significantly more frequent in marked ossification (10% versus 4% in controls). However, this is not a striking prevalence. Restricted flexion of less than 70° was found in 26% of 'ossifying' patients versus 6% in 'non-ossifying'.

We may conclude that approximately 30% of patients with DISH develop serious ectopic bone formation following hip replacement and

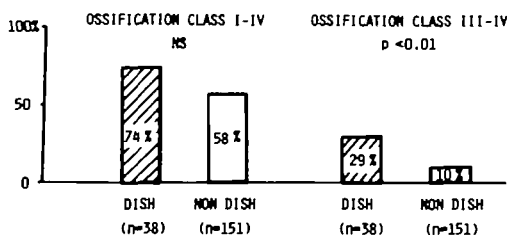


FIG. 3.—Frequency (percentage) of postoperative ectopic bone formation in DISH and non-DISH probands.

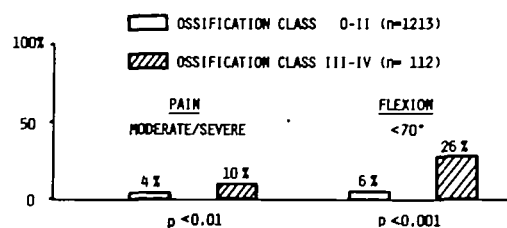


FIG. 4.—Correlation of degree of ossification with pain and reduced ROM 1 year after hip arthroplasty (group II, $n = 1325$).

70% will remain free. Only 25% of those with ectopic bone show important loss of ROM and only 6% develop serious pain. This means that only 7.5% of all patients with DISH suffer from restricted ROM and 1.8% from pain. This low risk does not justify the use of drugs in an attempt to prevent ossification. Bisphosphonates have proved relatively effective in this situation, but the recommended 4 months of treatment is both expensive and may cause side-effects [21-23]. Prevention should be confined to patients with a history of severe ossification of the other hip or other articulations.

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REFERENCES

- Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. *J Bone Joint Surg [Br]* 1972;**54**:61-76.
- Lazansky M. Complications revisited: the debit side of total hip replacement. *Clin Orthop* 1973;**95**:96-103.
- DeLee J, Ferrari A, Charnley J. Ectopic bone formation following low friction arthroplasty of the hip. *Clin Orthop* 1976;**121**:53-9.
- Brooker AF, Bowerman JW, Robinson RA, Riley Jr LH. Ectopic ossification following total hip replacement. *J Bone Joint Surg [Am]* 1973;**55**:1626-32.
- Nollen AJG, Sloof TJ. Para-articular ossification after total hip replacement. *Acta Orthop Scand* 1973;**44**:230-41.
- Rosendahl S, Krogh Christoffersen J, Nørgaard M. Para-articular ossification following hip replacement. *Acta Orthop Scand* 1977;**48**:400-4.
- Blasingame JP, Resnick D, Coutts RD, Danzig LA. Extensive spinal osteophytosis as a risk factor for heterotopic bone formation after total hip arthroplasty. *Clin Orthop Rel Res* 1981;**161**:191-7.
- Holz U, Kraner F, Weller S. Periartikuläre Verknochnerungen nach Hüfttotalendoprothesen. *Z Orthop* 1977;**115**:146-58.
- Rigler HF, Harries CM. Heterotopic bone formation after total hip arthroplasty. *Clin Orthop* 1976;**117**:209-16.
- Ritter MA, Vaughan RB. Ectopic ossification following total hip replacement. *J Bone Joint Surg [Am]* 1977;**59**:345-51.
- Pilet F, Waldburger M, Livio JJ. Periarticular ossification following total hip prosthesis in cases of diffuse idiopathic skeletal hyperostosis. *Rev Chir Orthop* 1983;**69**:455-63.
- Julkunen H, Heinonen OP, Pyörälä K. Hyperostosis of the spine in an adult population, its relationship to hyperglycemia and obesity. *Ann Rheum Dis* 1971;**30**:605-12.
- Forestier J, Rotes-Querol J. Senile ankylosing hyperostosis of the spine. *Ann Rheum Dis* 1950;**9**:321-30.
- Forestier J, Lagier R. Ankylosing hyperostosis of the spine. *Clin Orthop Rel Res* 1971;**74**:65-83.
- Resnick D, Limovita RJ, Feingold ML. Post-operative heterotopic ossification in patients with ankylosing hyperostosis of the spine (Forestier's disease). *J Rheumatol* 1976;**3**:313-20.
- Jacqueline F. Ankylose osseuse de coxopathies hyperostotiques (4 observations). *Rhumatologie* 1983;**35**:231-5.
- Bundrick TJ, Cook DE, Resnik CS. Heterotopic bone formation in patients with DISH following total hip replacement. *Radiology* 1985;**155**:595-7.
- Resnick D, Niwayama G. Diffuse idiopathic skeletal hyperostosis (DISH): ankylosing hyperostosis of Forestier and Rotes-Querol. In: Resnick D, Niwayama G, eds. *Diagnosis of bone and joint disorders*. Philadelphia: WB Saunders, 1981;**2**:1416-52.
- Kromann-Andersen C, Scherff Sørensen T, Hougaard K, Zdravkovic D, Frigaard E. Ectopic bone formation following Charnley hip arthroplasty. *Acta Orthop Scand* 1980;**51**:633-8.
- Slätis P, Kiviluoto O, Santavirta S. Ectopic ossification after hip arthroplasty. *Ann Chir Gynaecol* 1978;**67**:89-93.
- Finerman GAM, Stover SL. Heterotopic ossification following hip replacement or spinal cord injury: two clinical studies with EHDP. *Metab Bone Dis Relat Res* 1981;**4/5**:337-42.
- Sloof TJH, Feith R, Bijvoet OLM, Nollen AJG. The use of a disphosphonate in para-articular ossifications after total hip replacement. *Acta Orthop Belg* 1974;**40**:820-8.
- Thomas BJ, Amstutz HC. Results of the administration of diphosphonate for the prevention of heterotopic ossification after total hip arthroplasty. *J Bone Joint Surg [Am]* 1985;**67**:400-3.

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