Arch Orthop Trauma Surg (1986) 105:263–267

Archives of Orthopaedic and Traumatic Surgery

Development of Heterotopic Ossification Around the Hip

A Long-term Follow-up of Patients Who Underwent Surgery with Two Different Types of Endoprostheses

T. S. Lindholm, T. Viljakka, E. Vankka, L. Popov, and T. C. Lindholm

Orthopaedic Hospital of the Invalid Foundation, Tenholantie 10, SF-00280 Helsinki, Finland

Summary. Heterotopic ossification has been reported in many pathological situations, most important clinically as a sequel to hip arthroplasty and spinal trauma. The etiology of heterotopic ossification is yet not clear, but the disease is supposed to be connected with trauma. Heterotopic bone was found in 53% (1.2% with the severe form) of 623 patients operated on at the Orthopaedic Hospital of the Invalid Foundation, Helsinki, Finland; the operations included 849 arthroplasties. The rate of heterotopic ossification was higher after revision arthroplasty, following operation of the contralateral side, in men, and in primary coxarthrosis, and the incidence was higher with the Brunswik (metal-on-plastic) endoprosthesis than in the McKee-Farrar type (metal-on-metal). Heterotopic bone formation generally seemed to increase and to be more manifest during long-term observation.

Heterotopic ossification can be found in many pathological situations, such as soft tissue trauma [17, 21, 33], neurological diseases and paraplegia [8, 9, 12–14, 22, 26, 30, 35], burns, and complications to orthopedic surgery [3, 10, 20, 23]. Because of the increased practice of endoprosthetic surgery, heterotopic ossification around the hip has become more common and leads to clinical symptoms such as pain and sometimes to a limitation of movement.

The pathogenesis of ectopic ossification is still unknown. According to one theory presented long ago, it is a primitive tissue metaplasia that, in certain situations, causes any mesenchymal cell to start bone production [13]. Other theories cite the surgical trauma as causing these changes [34]. Migration of preosteoblasts in the bone marrow, or perivascular connective-tissue cell growth from the surrounding area invading the traumatic sphere are supposed by others to be starting factors [18]. Finally, there is no definitive explanation of ectopic ossification, but according to most hypotheses, the pathogenesis of the trauma plays an important role in the change of mesenchymal cells to bone forming cells [32]. A predisposing factor for heterotopic ossification in total hip replacement may be the earlier noted ectopic bone formation, resulting in the fact that on the contralateral side, in 90% of the patients, and, in 60%, the severity is the same as at the other side. Hypertrophic and bilateral arthrosis of the hip, male sex, severe preoperative limitation of movement, earlier treatment of the same hip, infection, diffuse hyperostosis, and ankylopoietic spondyloarthrosis are also predisposing factors [1, 2, 16]. Even overweight, advanced age, the type of endoprosthesis, physical activity, duration of surgery, and surgical bleeding are factors that may influence the formation of heterotopic bone [4, 6, 7, 11, 16].

The incidence of ectopic bone formation varies from 5% to 90%, probably due both to the different methods used and to the grading techniques [3–6, 10, 16, 20, 24, 25, 27]. In a severe form it appears in 2%–3% of cases.

Very soon after total hip replacement, increased local pain around the operated hip is noted clinically; usually, a general or local rise in temperature and swelling can also be seen around the site of the operation. A limitation of movement and stiffness may

Offprint requests to: T. Sam Lindholm (address above)

develop, and, in severe cases, a full ankylosis can be seen.

Histologically, the ectopic bone consists primarily of an amorphous mass; thereafter, the first changes are noted in the inter- and perimuscular connective tissues. Bone trabeculae can be seen in the tissue, characterized peripherally by strong osteogenic activity and hypervascularization. Even degeneration and necrosis are noted in the surrounding muscle.

In some places the bone is mature, forms trabeculae, and shows high osteoblastic activity. For 12–18 months the bone continuously matures and forms trabeculae in the manner of normal bone [28].

Regarding laboratory findings, serum alkaline phosphatase is raised during the active stage of the disease, usually following the 3rd postoperative week. Other serum enzymes prove to be normal; however, the erythrocyte sedimentation rate (ESR) may be somewhat raised [13, 19].

Dense roentgenological areas can be noted around the operated hip about 3 weeks postoperatively. As a rule, ectopic bone formation is noticeable on roentgenograms 6 weeks after surgery, and in 95% of the patients, this "disease" developed 3 months postoperatively [27].

In the study reported here we compared the effects of the two different kinds of endoprostheses – one of them metal-on-metal, the other plastic-on-metal, both of them anchored using acrylic cement – which were connected with ectopic bone formation. We also used a long follow-up period to find whether conditions change in the long term.

Patients and Methods

Our series consisted of 623 patients, 198 of them men, 425 of them women, with a mean age of 61.6 years; they were operated upon using total hip replacement (THR) during the years 1970–1978 at the Orthopaedic Hospital of the Invalid Foundation in Helsinki, Finland.

The patients were examined 3, 6 and 12 months postoperatively, with subsequent controls every year. Radiological examinations were routinely performed in connection with the clinical examination. In this follow-up investigation, all X-ray pictures were systematically checked retrospectively. The grading of ectopic ossification around the hip operated upon was estimated using the method suggested by Rosendahl et al. [31].

The follow-up period varied between 6 months and 11 years, with a mean of 4.2 years. The McKee-Farrar endoprosthesis was used in the earlier investigation period (392 operations); Brunswik endoprostheses were used in the latter part of the investigation (396 operations). Other prostheses were used in 61 cases, which gives a total number of 849 operations. There were 749 primary operations and 100 reoperations.

Results

Ectopic ossification occurred in 52.4% of all patients, grade I appearing in 34.5%, grade II in 16.7%, and grade III in 1.2% of the patients. Ectopic bone formation was more common in reoperations, comprising 67% of the patients, 5% being severe cases (Fig. 1). The incidence was higher in operations of the contralateral hip than in primary operations (Table 1). Among Brunswik arthroplasties, ectopic bone formation was found in 59.9% of the patients,

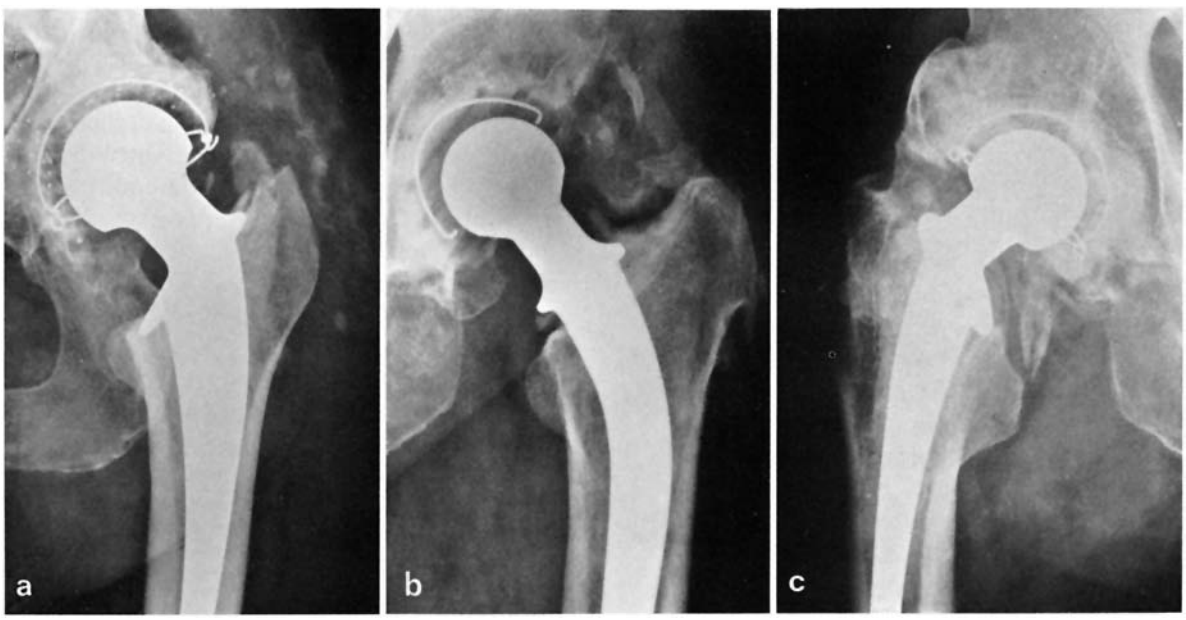

Fig. 1a–c. Amount of heterotopic bone around the hip in grade I (**a**), grade II (**b**), and grade III (**c**), according to the classification introduced by Rosendahl et al. [31]

Table 1. Occurrence of heterotopic bone formation in primary and revision arthroplasty in 849 operated hips

Grade	Primary operations	Contralateral primary operations	Reoperations
	No. (%)	No. (%)	No. (%)
0	307 (50.9)	64 (43.8)	38 (33)
I	198 (32.8)	54 (37)	41 (41)
II	93 (15.4)	26 (17.8)	21 (21)
III	5 (0.8)	2 (1.4)	5 (5)
Total no.	603	146	100

Table 2. Occurrence of heterotopic bone formation in primary arthroplasty related to two different endoprosthetic designs

Grade	McKee-Farrar		Brunswik	
	No.	(%)	No.	(%)
0	187	(60)	110	(40.1)
I	81	(26)	114	(41.6)
II	44	(14.1)	45	(16.4)
III	—	—	5	(1.8)
Total no.	312		274	

Table 3. Occurrence of heterotopic bone formation in primary total hip replacement: correlation between men and women

Grade	Women		Men	
	No.	(%)	No.	(%)
0	266	(51.7)	105	(44.7)
I	171	(33.3)	81	(34.5)
II	74	(14.4)	45	(19.1)
III	3	(0.6)	4	(1.7)
Total no.	514		235	

Table 4. Occurrence of heterotopic bone formation in primary hip replacement related to indications

Indication	No. of operations	Ectopy (%)	Ectopy in %, grades II–III
Primary osteoarthritis	578	50.2	19.1
Secondary osteoarthritis after fracture	38	31.1	2.9
Other secondary osteoarthritis	108	45.2	15.0
Rheumatoid arthritis	51	41.0	10.0
Osteoarthritis previously operated with osteotomy	53	56.3	24.6

Table 5. Heterotopic bone formation in total hip replacement during a long-term follow-up period

1. Follow-up 3–5 years	No. of patients (n = 197)	
Grade	2 months	At last follow-up
0	138	96
I	45	63
II	14	38
III	—	—
2. Follow-up 6–9 years	No. of patients (n = 247)	
Grade	2 months	At last follow-up
0	179	127
I	61	79
II	7	38
III	—	3
3. Follow-up 10 years or more	No. of patients (n = 60)	
Grade	2 months	At last follow-up
0	44	30
I	11	21
II	5	9
III	—	—

while among McKee-Farrar arthroplasties the figure was 40%. Grade-III cases were more common in Brunswik patients (1.8% versus 0%) (Table 2).

In connection with primary operations, ectopic ossification was somewhat more common in women than in men (Table 3). Ectopic bone formation was more common in primary osteoarthritis than in patient groups operated upon because of other indications. Previously performed operations also proved to give a higher incidence (Table 4). After a follow-up varying from 2 to 6 months, ectopic bone formation was found in 28% of the patients. The corresponding values were 51% after 2–5 years' follow-up, 47.7% after 6–9 years' follow-up, and 50% after 10 years' follow-up. The condition seemed to increase and become more manifest during long-term observation periods as compared with the situation 2 months postoperatively. In three patients ectopic bone tissue decreased during the follow-up period. As a rule, the condition was constant 6 months–1 year postoperatively (Table 5).

In four cases the ectopic bone was extirpated surgically. All these patients were men aged 64–76 years (mean age 68.7 years) at the time of operation. The endoprostheses used were the Brunswik type (3) and the Lubinus type (1) for the primary operation. In all cases the indication for surgery was primary coxarthrosis; in 75% of the cases there was "hypertrophic" osteoarthritis in addition.

Table 6. Heterotopic ossification in total hip replacement before and after surgical extirpation in four patients

Primary grade	Grade after reoperation	Final grade, time sequence (months)
2	3	3
3	2[a]	8
3	3	6
3	3	2

[a] The only cases in which the patients improved subjectively as well as objectively

The reoperations consisted of two removals of the ectopia and two removals of the ectopia with change of the endoprosthesis shaft to a Brunswik and Lubinus femoral stem because of aseptic loosening. The time of reoperation following primary operation was 6 months in two cases, 5.5 months, and 3 months. Ectopia showed again after surgical extirpation 2, 2, 6, and 8 months later respectively (grade III, mean 4.5 months). In one case the operation gave a positive result. No other measures, such as administration of prophylactic drugs, were taken (Table 6).

Discussion

The amount of ectopic ossification around the hip was about 53% in the cases presented, while the corresponding amount for grade-III ectopic bone was 1.2%. In cases of reoperations these figures were 70% and 3.2% resepctively. In contralateral operated hips ectopic bone appeared in 58% of the cases. These figures are in accordance with those in other reports [20, 24, 25, 29].

The Brunswik type endoprosthesis (plastic-on-metal) showed 61.5%, the McKee-Farrar type (metal-on-metal) 48% ectopic bone formation.

The choice of endoprosthetic aid has not been noted to influence the degree of ectopia. In some other experiments, however, an endoprosthesis without cement was shown to produce less ectopia. Weight exceeding 60 kg, age of more than 60 years, and extended operation time all correlate positively to ectopic bone formation [21].

Ectopic bone was more common in men (57%) than in women (48.5%). The figures were 37% for patients younger than 50 years, 56% for patients with primary coxarthrosis, 41% for patients suffering from rheumatoid arthritis, 32.5% for patients with collum fractures, and 43% for patients with secondary coxarthrosis. As a rule, the amount of ectopic bone became more manifest after its establishment during the first 2–6 months.

Treatment with diphosphonates (EHDP) or nonsteroid anti-inflammatory drugs will probably lead to good results in some cases by preventing the development of ectopic bone. EHDP have been reported to prevent heterotopic bone formation [34] or to delay its occurrence [4, 17], while McCollister Evarts et al. [24] observed a reduced incidence of heterotopic ossification following postoperative radiation therapy. Indomethacin has been found to prevent postoperative heterotopic ossification after total hip replacement [2], and similar results have been gained from treatment with ibuprofen [15].

Extirpation of ectopic bone around the hip, alone or combined with revision surgery, did not considerably influence the development of new ossification in this series. Surgical removal of ectopic bone involves a high degree of recurrence [16, 27, 30]. Accordingly, the removal of ectopic bone has to be combined with administration of EHDP, indomethacin, or radiation therapy, or with autogenous fat transplants [29].

In conclusion, the formation of ectopic bone around the hip joint in connection with total hip replacement is still an unsolved problem, which must be reckoned with. Prophylactic treatment with nonsteroid anti-inflammatory drugs like indomethacin or ibuprofen seems so far to be a simple method, worthy of special notice, and one that is to be recommended.

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Received January 14, 1986