Impact of late surgical intervention on heterotopic ossification of the hip after traumatic neurological injury

F. Genet,
J.-L. Marmorat,
C. Lautridou,
A. Schnitzler,
L. Mailhan,
P. Denormandie

From L'Hôpital Raymond Poincaré, Garches, France

Heterotopic ossification (HO) of the hip after injury to the central nervous system can lead to joint ankylosis. Surgery is usually delayed to avoid recurrence, even if the functional status is affected. We report a consecutive series of patients with HO of the hip after injury to the central nervous system who required surgery in a single, specialised tertiary referral unit. As was usual practice, they all underwent CT to determine the location of the HO and to evaluate the density of the femoral head and articular surface. The outcome of surgery was correlated with the pre-, peri- and post-operative findings.

In all, 183 hips (143 patients) were included of which 70 were ankylosed. A total of 25 peri-operative fractures of the femoral neck occurred, all of which arose in patients with ankylosed hips and were associated with intra-articular lesions in 18 and severe osteopenia of the femoral head in seven. All the intra-articular lesions were predicted by CT and strongly associated with post-operative complications.

The loss of the range of movement before ankylosis is a more important factor than the maturity of the HO in deciding the timing of surgery. Early surgical intervention minimises the development of intra-articular pathology, osteoporosis and the resultant complications without increasing the risk of recurrence of HO.

F. Genet, MD, Physical Medicine and Rehabilitation
A. Schnitzler, MD, Physical Medicine and Rehabilitation
Service de Médecine Physioque et de Réadaptation
J.-L. Marmorat, MD, Orthopaedic Surgeon
C. Lautridou, MD, Orthopaedic Surgeon
P. Denormandie, MD, Orthopaedic Surgeon
Service de Chirurgie Orthopédique et Traumatologique
Hospitalier R. Poincaré, 104 Boulevard R. Poincaré, 92380 Garches, France.

L. Mailhan, MD, PhD, Physical Medicine and Rehabilitation
Service de Médecine Physique et de Réadaption
Centre Saint Marie, 167 rue Raymond Losserand 75014, Paris, France.

Correspondence should be sent to Dr F. Genet; e-mail: francois.genet@rpc.aphp.fr

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Heterotopic ossification (HO) occurs in 10% to 20% of patients who have sustained a traumatic brain injury[1,2] and in 16% to 53% of those with an injury to the spinal cord.[3,4] The hip is the most frequently affected site and the extra-articular bone growth can limit the range of movement. Total joint ankylosis occurs in 5% to 16% of affected hips.[5,6]

A limited range of movement or fixed deformity caused by the ectopic bone formation compromises the rehabilitation in these patients, who frequently have widespread neurological sequelae. The negative effect on functional ability may be major with, in many cases, loss of independence.[7,8]

Medical management of HO has a limited effect.[4,9] The onset of HO occurs within four to 12 weeks of the injury and therefore prevention should begin in the intensive-care unit.[10] Indometacin has been shown to have a preventative effect if administered during the peri-operative period for total hip replacement (THR).[9,11,12] It has also been shown to have a preventative effect in patients with an injury to the spinal cord.[13] The absolute effectiveness of bisphosphonates has not been proven and if they are used, treatment should be maintained for about six months.[7,9,14,15] Radiotherapy is effective in preventing ossification after THR,[11,16] but ineffective once HO has formed. Prophylaxis by radiation therapy is not advised in patients who are unconscious because the formation and the location of HO cannot be predicted. However, this technique is as effective as other methods of prevention, provided that it is administered in the first 72 hours post-operatively, at a minimum single dose of approximately 600 cGy.[17] Several studies have suggested that there is no statistically significant difference between the use of pre-operative (< 4 hours pre-operatively) or post-operative (< 72 hours post-operatively) radiotherapy.[11] Physiotherapy helps to conserve the range of movement but it must not be forced or induce pain and it often only slows down the process of joint ankylosis[7,8,18] with the aim of securing the limb in a functional range while awaiting surgery.[8] This approach to treatment was suggested by Cullen et al[7] because of its non-invasive nature and its potential to maintain or to improve function. According to the authors, early post-operative mobilisation is essential, either manually or using mechanised continuous passive mobilisation.[9] Some adjuncts such as the use of shock-waves are currently being evaluated.[19]

The only effective treatment for established HO is surgical excision.[6,8,13] Surgical indications have recently changed.[6] The time from the accident does not seem to be a decisive factor[6,13,17] since the level of maturity of the HO does not seem to affect recurrence.[6,20] The indications for surgery are linked to considerations of function, hygiene such as access to the perineum in the event of limited abduction for bathing and bladder care, pain and vascular and nerve compression, and may be carried out even in patients with extensive neurological lesions as soon as comorbidities are under control.[7,20-22]

An extensive delay before surgery leads to ankylosis which is prognostically poor for functional recovery.[2] Our aim therefore was to assess the repercussions of pre-operative ankylosis of the hip on post-operative complications and difficulties during surgery for HO of the hip after injury to the central nervous system (CNS).

Table I. Classification of articular lesions as shown by CT

No articular lesion
Focal articular lesion
Global articular lesion
Intra-articular fusion

Table II. CT grading system for evaluating the bone density of the femoral head compared with that of the iliac wing according to Carlier et al[23]

Grade	Compared with the iliac wing
1	Normal
2	Moderate bone loss
3	Severe bone loss
4	Bone density similar to that of fat

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Patients and Methods

We carried out a prospective study on a consecutive series of patients who developed HO of the hip after injury to the CNS between 1997 and 2007 and who required surgical intervention to improve their range of movement. This study was undertaken in a single centre with retrospective data analysis which in accordance with French law did not require ethical approval. All the patients or their legal representative in those who were mentally impaired, consented to the surgery.

The indication for surgery was symptomatic HO for which medical care had been ineffective. Troublesome symptoms included pain and compression or functional restriction of nerves or vessels. Functional discomfort was variable and depended on the neurological status, and the abilities of the patient and not simply on the range of movement. Patients who had previous removal of HO and presented with a recurrence or had follow-up of < ten months were excluded. Before referral to us, all the patients had been hospitalised in an intensive-care unit or specific rehabilitation unit of an institution for severe post-traumatic CNS injuries.

A total of 143 patients (183 hips) were included in the study. A further seven with recurrent HO and 13 with a follow-up of less than ten months were excluded. The mean follow-up was 37 months (10 to 180) and no patient was lost to follow-up.

There were 114 males and 29 females with a mean age at the time of surgery of 34.5 years (15 to 65.8). Of the 183 hips, 118 (64.5%) had developed HO after traumatic brain injury and 65 (35.5%) after injury to the spinal cord. In 70 hips (53 patients, 37%) there was ankylosis. The remaining 113 hips with HO (90 patients) had only a reduced range of movement in the flexion-extension plane. CT revealed 18 articular lesions in the ankylosed group, and none in the non-ankylosed group.

Before surgery, patients received routine clinical and radiological assessment. The following factors were recorded: age, gender, aetiology, other sites of HO and the ability or otherwise to walk. Anteroposterior (AP) and lateral radiographs were taken to establish the relationship of the HO to the joint (anterior, posterior, circumferential or lateral) and CT was used to reveal articular lesions as detailed in Table I. CT included reconstruction and arteriovenous opacification. Localisation and extent of the ectopic bone were recorded according to the Garland classification.[15] Bone density of the femoral head and neck was assessed according to a CT classification system developed by Carlier et al,[23] by comparing the density with that of the iliac wing (Table II). The pre-operative evaluation did not include measurement of levels of serum alkaline phosphatase, Tc99 bone scanning or identification of the HLA B27 status. None of the patients had received prophylactic treatment for HO such as administration of non-steroidal anti-inflammatory agents or radiotherapy. No patient had a fracture of the pelvis or hip.

All the surgery was performed by the same surgeon (PD). The surgical goal was resection of the necessary amount of bone to allow restoration of movement in the flexion-extension plane, internal and external rotation and abduction. During the operation, special care was given to haemostatic control and the protection of the neurovascular structures. Ectopic bone was removed in small wedges, and the bleeding bone surfaces were temporarily controlled with bone wax. Attempts were made to preserve the joint in all cases. A capsulotomy was performed only if a fracture of the femoral neck occurred during the intervention or if pre-operative CT had identified an intra-articular lesion. In patients who had previously sustained an impacted femoral neck or sub-capital fracture without chondral lesions, the femoral head was preserved and stabilised by internal fixation. An excision arthroplasty of the hip was carried out if patients were unable to stand up or walk because of the severity of

Table III. Clinical and radiological assessment of the two groups

	Group	
	Ankylosis	**No ankylosis**
Number of patients	53	90
Number of hips*		
TBI	48	70
SCI	22	43
Total	70	113
Number of patients with HO† at other locations	7 (3 knees, 5 elbows, 2 shoulders)	6 (4 knees, 4 elbows)
Ability to walk before surgery	0	5
Mean (range, SD) hip ROM‡ (°)	0	38 (5 to 57; 10.4)
Location of the HO		
Anterior	32	57
Posterior	20	26
Circumferential	18	11
Lateral	0	19
Articular lesion (CT)	18	0

* TBI, traumatic brain injury; SCI, spinal-cord injury
† HO, heterotopic ossification
‡ ROM, range of movement

their neurological deficits. A THR was performed in patients who were able to stand or walk pre-operatively for displaced fractures or severe chondral lesions of the femoral head.

All the patients received intravenous peri-operative antibiotic prophylaxis and prophylactic anticoagulation (cefazoline 2 g before induction and 1 g every four hours during surgery, and enoxaparine 0.4 subcutaneous injection once per day). Post-operatively, gentle mobilisation was started on the second day, and progressed as tolerated. A non-steroidal anti-inflammatory agent (ketoprofene 150 mgm prolonged release, one capsule twice daily), was given for ten days after surgery. Neither radiotherapy not indometacin was used. The patients were then followed up in the rehabilitation unit in the same institution, with regular clinical and radiological examinations.

Statistical analysis. This was carried out using Systat 9 Dela software (Systat Software, Point Richmond, California) for Windows. Descriptive analysis included the mean, SD, extremes and percentages.

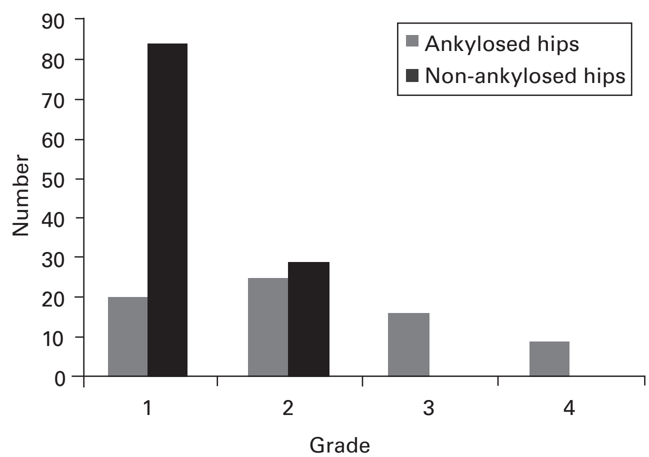

Fig. 1

Bar chart showing the distribution of mineralisation of the femoral head according to the classification of Carlier et al.[23]

Results

The main results are presented in Table III. Femoral-head density is shown in Figure 1 and the mean delay from diagnosis of HO to surgical intervention for each group is shown in Table IV.

Operative findings. Every hip with HO had surgery. The femoral head was preserved in 158 hips (86.3%). In 25 (13.7%), an intraoperative iatrogenic sub-capital fracture of the femoral neck occurred when the joint was mobilised after resection of the HO. All these fractures occurred in the ankylosed group and were associated with articular lesions or fusion and severe osteopenia of the femoral neck in 18 hips, and with severe osteopenia alone in seven. After identification of an intra-operative fracture, 12 patients underwent THR, eight required an excision arthroplasty and five with impacted sub-capital fractures, were treated conservatively. Histological examination of the femoral heads showed no pathological HO within the articulation.

Table V gives details of the post-operative range of movement and that at the last clinical visit. There were no post-operative complications in the non-ankylosed hips. In the ankylosed group, ten of the 70 hips, had post-operative complications. Of the five hips with an impacted subcapital

Table IV. The mean delay (months; range) from diagnosis of heterotopic ossification to surgery

	Number of hips	Delay
Ankylosed group		
With articular lesion	18	85.5 (46.8 to 339.6)
Without articular lesion	52	14.7 (0.9 to 46.8)
Total	70	34.9 (0.9 to 339.6)
Non-ankylosis	113	40.8 (4.5 to 337.4)
Total	183	36.8 (0.90 to 339.6)

Table V. The mean (range) range of movement of the operated hips in degrees in both groups

	Group	
	Ankylosis	No ankylosis
Before surgery	0 (60 to 110)	38 (5 to 57)
After surgery	90 (0 to 100)	95 (80 to 125)
Last follow-up	63 (0 to 100)	83 (5 to 120)

fracture which was treated conservatively, four developed a symptomatic nonunion. Of the eight hips for which an excision arthroplasty had been chosen, there were three cases of stiffness caused by spasticity. Complications such as deep infection occurred in three of the hips in which a THR had been carried out. At the last follow-up at a mean of 42 months (5 to 60), the mean range of movement of these hips was 55° (20° to 90°).

Discussion

Our study was designed to investigate the impact of late surgical intervention on patients with HO of the hip. The development of HO after traumatic brain injury or injury to the spinal cord is still poorly understood.[4,24-26] Peri-articular ossification of the hip frequently limits the range of movement of a joint and may cause ankylosis.[25,27] Osteoporosis underlying the ankylosis can comprise the outcome of surgery and interfere with rehabilitation. We believe that as disuse osteoporosis develops in ankylosed, immobile patients like ours, the risk of intra-operative fracture increases. Stover et al[5] showed that the risk of fracture secondary to disuse osteopenia increased significantly with the delay in operative treatment. Therefore in patients with ankylosis of the hip, management of HO can be complicated and careful pre-operative assessment is required.

Pre-operative assessment and risk of fracture. As is current practice, radiography and CT were performed in our patients to determine the mineral density of the femoral neck.[23] Radiological evaluation alone in these cases is insufficient.[23] Since ectopic bone overlies the femoral neck, it can obscure underlying osteoporosis, leading to an underestimation of the risk of fracture.[28] As such, CT is essential for the determination of the bone mineral density and intra-articular lesions.[23] Only patients with severe loss of bone density (grades 3 and 4) developed fractures. In addition, CT can be used to evaluate the proximity of the HO to neurovascular structures which helps in selecting the appropriate surgical approach. In our study, ankylosed hips had a significantly lower bone density as determined by CT (Fig. 1). These patients had an increased risk of fracture which may be caused by minimal manipulation of the hip and probably cannot be avoided either at the time of surgery or in the immediate post-operative period.

Ankylosis and intra-articular lesions. In addition to severe osteoporosis, ankylosis is complicated by the presence of intra-articular lesions, which we observed in 18 of 70 hips. Guillaumat[29] described pathological changes in the joint line associated with HO, but did not give an explanation while Gacon et al[26] considered it to be neurotrophic arthropathy. Stover et al[5] found that the joint surfaces were sometimes atrophied with a very narrow joint space. HO is a peri-articular disorder and ankylosis is based on the formation of extra-articular ectopic bone.[27] Our study did not identify HO within the articular space, and we speculate that it is only ankylosis which induces articular degradation. The effects of immobilisation on joints are well documented.[30] Prolonged immobilisation causes obliteration of the joint space by fibro-fatty proliferation and fibrous ankylosis.[31,32] Baker, Thomas and Kirkaldy-Willis[33] observed a similar sequence of changes in spinal fusion. These human studies show striking parallels to animal studies.[31,34] The protean effects of stress deprivation appear to be common to all studies on synovial joints. Salter and Field[35] observed pressure necrosis at points of cartilage-to-cartilage contact when compression was applied. In our study, none of the non-ankylosed hips had an articular lesion. It would therefore appear that even the slightest movement seems to preserve the integrity of the joint. Several authors have speculated that the results after surgery for HO of the hip depend essentially on the pre-operative range of movement.[1,2,36-38] Moreover, when ankylosis occurred, the outcome depended essentially on the degree of neuromuscular involvement.[2,15,36-38] Our study confirms that the presence of an intra-articular lesion is an additional factor which determines outcome. In the series of patients studied by Sarafis et al,[2] surgery was undertaken on 22 ankylosed hips with HO between 18 and 57 months after the diagnosis was made. No intra-articular lesions were recorded. However, the three patients who underwent surgery after 36 months had poor results with a post-operative range of movement of between 10° and 15°. By comparison, the four patients operated on before two years had good or excellent results with a range of movement of between 70° and 90°. In our study, none of the ankylosed hips, which were operated on within two years of diagnosis, had articular lesions and this further supports our belief in earlier surgical intervention.

Intraoperative risk of fracture of the femoral neck. Surgery in patients with HO has the additional risk of intraoperative fracture of the femoral neck.[5,36-38] In our series, this complication occurred secondarily to severe osteoporosis, possibly due to factors such as non-weight-bearing and neurological disease.[28,39] In the ankylosed group, 35% of hips had grade-3 or grade-4 osteoporosis according to our CT grading system and, by contrast, the non-ankylosed hips were in grade 1 or grade 2. Fractures occurred only in the ankylosed group (25 of 70 hips, 35.7%). We believe that as disuse osteoporosis develops in ankylosed, immobile patients, the risk of intraoperative fractures increases. Three surgical options were pursued in the case of intraoperative fractures. For patients who were able to walk before surgery, a conservative approach was followed in the absence of articular lesions (impacted subcapital fracture treated by internal fixation; five patients) and a THR was used for those with articular lesions (12 patients). In patients with injury to the spinal cord who were unable to walk and had risk factors for sepsis such as self-catheterisation with bacteriuria and for hip subluxation due to hypertonia with flexion spasms, an excision arthroplasty was carried out (eight patients). For patients at risk of fracture, the different strategies for dealing with a fracture should be discussed before surgery.

Surgery and recurrences. Surgical complications are common and the risk of recurrent HO is considerable.[27,40,41] It has long been believed that resection of HO should not be carried out until it is mature.[27,39,40] However, no adequate prospective, controlled studies are available to confirm this concept and early resection of immature HO may not be predictive of a higher rate of recurrence.[6,14,18,20,42] We believe that ankylosis is a more important factor than maturity of the HO in deciding the time of surgery. Early resection of HO may prevent intra-articular complications such as an intraoperative fracture of the femoral neck. However, in these cases the patient's family should be informed of all potential complications before surgery.

In conclusion, estimation of bone mineral density in the femoral neck for patients with HO of the hip after injury to the CNS is essential to assess the risk of intra-operative fracture and the functional outcome. Waiting for ankylosis to form as a result of HO for patients with injuries to the CNS maximises the development of intra-articular pathology and osteoporosis and increases the risk of complications during and after surgery. Based on the presence of risk factors such as osteoporosis and/or articular lesions determined before surgery, as well as the neurological and functional status, potential strategies may be discussed with patients pre-operatively in case a fracture should occur during the operation.

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